PEDIATRIC TYPE 1 DIABETES IN THE KINGDOM OF BAHRAIN: CHARACTERIZING THE POPULATION & DEVELOPING A TAILORED LOCAL APPROACH TO OPTIMAL MANAGEMENT

BY

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DECLARATION OF ORIGINALITY

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ABSTRACT

**Background:** The prevalence of diabetes in the Middle East is amongst the highest worldwide, Bahrain ranks amongst the top 10 countries. In particular, increasing number of children are being diagnosed with type 1 diabetes mellitus (T1DM) posing a significant public health concern.

**Objective:** The aim of this thesis was to characterize the population by exploring lifestyle, dietary and health risk factors associated with pediatric T1DM and to undertake a local needs assessment to inform the development of management strategies.

**Methodology:** An observational case-control study of children with T1DM and healthy controls (n=59 and 53; mean age 9.66±1.72 and 9.02±1.88 years respectively) was conducted to ascertain baseline characteristics of children with T1DM as compared to healthy children with a subsequent more detailed prospective investigation (n=20) of the T1DM population, which included a focus on vitamin D intake and status. A systematic review of the effectiveness of interventions that seek to improve the management of children and adolescents with T1DM and a qualitative study using focus groups with service-users and healthcare workers were undertaken to inform the development of a specific educational package targeting the needs of Bahraini children with diabetes and their families. The findings of all phases were amalgamated to inform the design of an education package and associated feasibility study.

**Results:** Children with T1DM appeared to be more likely to have suffered from an illness before diagnosis of T1DM than their healthy counterparts. Dietary inadequacies were common in Bahraini children irrespective of diabetes diagnosis, particularly excessive sodium intakes, whilst children with T1DM consumed significantly more calories than controls and more protein.
relative to their RDA. Serum vitamin D as measured by CLIA assay method (standard practice) and by UPLC/MSMS (gold standard) classified 72% and 50% respectively of the children as having suboptimal vitamin D levels. It appears that dietary intake, sunlight exposure and physical activity may to some extent impact the vitamin D status of children with T1DM. The systematic review identified facilitators of successful interventions aimed at children and adolescents with T1DM such as theoretical based interventions. It also highlighted barriers to the real-life integration of such interventions. These factors and the themes identified by the focus groups such as a need to focus on adolescents prior to transitioning were incorporated into the educational package.

**Conclusion:** Children with diabetes do appear to differ from age matched controls with respect to health factors and socio-demographic characteristics. Larger confirmatory studies are urgently needed. The feasibility and acceptability testing of the proposed educational package is currently ongoing with a planned pilot test of the program within the coming year.
ACKNOWLEDGEMENTS

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To my three children, I hope that someday when you are older you will be proud of me and I hope above all, that you forgive me for all the time I had to spend away from you.

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STATEMENT OF CONTRIBUTIONS

Fatima Al-Haddad conducted all mentioned studies and wrote the present Thesis including the manuscripts.

Dr. Kathryn Hart provided permanent scientific supervision for all aspects of the study

Dr. Abdulrahman Musaiger provided permanent scientific supervision especially for the nutritional aspects.

Dr. Mahmood Al-Qallaf supervised the manuscripts.

Laboratory work was performed at the Salmaniya Medical Complex laboratory by professionally trained staff, Al-Salmaniya, Bahrain

Laboratory work used to analyze serum vitamin D using UPLC/MSMS was performed at Princess Al-Jawhara Center for Molecular Medicine and Inherited Disorders by a professional Metabolic Specialist, Al Salmaniya, and Bahrain
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ABBREVIATIONS

7-DHC  7-dehydroxycholesterol
AMDR  Acceptable Macronutrient Distribution Range
ADA  American Diabetes Association
BMI  Body Mass Index
BSA  Bovine serum albumin
CBT  Cognitive behavioral therapy
CLIA  Chemiluminescence immunoassays
CPAQ  Child Physical Activity Questionnaire
CRD  Centers for Reviews & Dissemination
CONSORT  Consolidated Standards of Reporting Trials
DAWN  Diabetes Attitudes, Wishes, and Needs Study
DC  Dendric cells
DCCT  Diabetes Control and Complications Trial
DEPICTED  Development and Evaluation Of A Psycho-social Intervention in Children and Teenagers Experiencing Diabetes
DNA  Deoxyribose nucleic acid
DRF  Diabetes Registry Form
DRI  Dietary Reference Intakes
DQOLY  Diabetes Quality of Life Youth Questionnaire
EAR  Estimated Average Requirement
EER  Estimated energy requirement
EPIC  Evidence into Practice Information Counts
FFQ  Food frequency questionnaire
FR  Food recalls
G6PD  Glucose-6-phosphate deficiency
GFR  Glomerular filtration rates
GDM  Gestational diabetes mellitus
HbA1c  Hemoglobin A1c
HCP  health care provider
HLA  Human leukocyte antigen
HNF1α  Hepatic nuclear factor 1 alpha
HNF1β  Hepatocyte nuclear factor-1β
HPLC  High pressure liquid chromatography
HPLC/MS  High pressure liquid chromatography /Mass Spectrometry methods
HTA  Health Technology Assessment
IL  Interleukin
IL-1ra  Interleukin-1 receptor antagonist
IL-1α  Interleukin-1 alpha IL-1α
IL-1β  Interleukin -1β
INF-γ  Interferon gamma
IPF1  Insulin protein factor 1
ISPAD  International Society for Pediatric and Adolescent Diabetes
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>IT</td>
<td>Intensive therapy</td>
</tr>
<tr>
<td>LHC</td>
<td>Local health centers</td>
</tr>
<tr>
<td>MET</td>
<td>Metabolic Equivalent</td>
</tr>
<tr>
<td>MDI</td>
<td>Multiple Daily Injections</td>
</tr>
<tr>
<td>MHC</td>
<td>Major histocompatibility complex</td>
</tr>
<tr>
<td>MI</td>
<td>Motivational interviewing</td>
</tr>
<tr>
<td>MODY</td>
<td>Maturity-onset diabetes of the young</td>
</tr>
<tr>
<td>NPDA</td>
<td>National Pediatric Diabetes Audit</td>
</tr>
<tr>
<td>NHS HTA</td>
<td>National Health Service Technology Assessment</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Healthcare and Excellence</td>
</tr>
<tr>
<td>NKc</td>
<td>Natural killer cells</td>
</tr>
<tr>
<td>PAID</td>
<td>Problem Areas in Diabetes Questionnaire</td>
</tr>
<tr>
<td>PEU</td>
<td>Pediatric Diabetes Unit</td>
</tr>
<tr>
<td>PTH</td>
<td>Parathyroid hormone</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>QualPDS</td>
<td>Qualitative Pediatric Diabetes study</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized control trial</td>
</tr>
<tr>
<td>RDA</td>
<td>Recommended dietary allowance</td>
</tr>
<tr>
<td>RIA</td>
<td>Radioimmunoassay</td>
</tr>
<tr>
<td>ROS</td>
<td>Reactive oxygen species</td>
</tr>
<tr>
<td>SCD/T</td>
<td>Sickle cell disease/trait</td>
</tr>
<tr>
<td>SCT</td>
<td>Social cognitive theory</td>
</tr>
<tr>
<td>SFBT</td>
<td>Solution focused brief therapy</td>
</tr>
<tr>
<td>SLP</td>
<td>Social learning principal</td>
</tr>
<tr>
<td>SMC</td>
<td>Salmaniya Medical Complex</td>
</tr>
<tr>
<td>T1DM</td>
<td>Type 1 diabetes mellitus</td>
</tr>
<tr>
<td>T2DM</td>
<td>Type 2 diabetes mellitus</td>
</tr>
<tr>
<td>TEE</td>
<td>Total energy expenditure</td>
</tr>
<tr>
<td>TGF-b1</td>
<td>Transforming growth factor beta 1</td>
</tr>
<tr>
<td>TH1</td>
<td>T helper 1</td>
</tr>
<tr>
<td>TH2</td>
<td>T helper 2</td>
</tr>
<tr>
<td>TNF</td>
<td>Tumor necrosis factor</td>
</tr>
<tr>
<td>TRIGR</td>
<td>Trial to reduce IDDM in the genetically at risk</td>
</tr>
<tr>
<td>UKPDS</td>
<td>United Kingdom Prospective Diabetes Study</td>
</tr>
<tr>
<td>UPLC/MS</td>
<td>Ultra-Pressure Liquid Chromatography/ Mass Spectrometry</td>
</tr>
<tr>
<td>UVb</td>
<td>Ultraviolet B light</td>
</tr>
<tr>
<td>VDR</td>
<td>Vitamin D receptor</td>
</tr>
</tbody>
</table>
1.0 INTRODUCTION

1.1 BACKGROUND AND SIGNIFICANCE

The Kingdom of Bahrain is a small island at the heart of the Arabian Gulf and like many of its’ neighboring countries it has not escaped the epidemic of diabetes. Of particular concern is the growing number of children being diagnosed with type 1 diabetes mellitus (T1DM) in the Kingdom, which has more than doubled in the past ten years alone (1). In Bahrain’s largest serving hospital, the Salmaniya Medical Complex, health statistics have revealed that the incidence rate of T1DM in children has increased from 8 per 100,000 in 1995 to 20 per 100,000 in 2010 (1).

The prevalence of adults with diabetes (type I and II) in the Middle East and the North African region is considered among one of the highest worldwide (2). Bahrain, in fact, ranks amongst the top 10 countries for prevalence of diabetes worldwide (3) and is already strained by the economic and health-care burden imposed by this disease in the adult population. This increase is of major concern as it not only confers significant costs and morbidity, but is also taxing healthcare facilities and resources. The World Health Organization (WHO) estimates that approximately one in four adult deaths is attributed to diabetes in the Eastern Mediterranean region (4), with diabetes-related deaths in Bahrain increasing from 9% in 2002 to 12% in 2010 (5).

Nordic countries such as Finland, Sweden and Norway have reported some of the highest incidence rate of T1DM in children under 15 years of age according to a published study by
Patterson et al (6). This was followed by Saudi Arabia and the United Kingdom with Kuwait ranking 10th as shown in Table 1.

Table 1 Countries with the highest reported incidence rate of pediatric T1DM according to published data in 2013

<table>
<thead>
<tr>
<th>Rank</th>
<th>Country</th>
<th>Incidence rate (per 100,000 population aged under 15 years)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Finland</td>
<td>57.6</td>
</tr>
<tr>
<td>2</td>
<td>Sweden</td>
<td>43.1</td>
</tr>
<tr>
<td>3</td>
<td>Norway</td>
<td>32.8</td>
</tr>
<tr>
<td>4</td>
<td>Saudi Arabia</td>
<td>31.4</td>
</tr>
<tr>
<td>5</td>
<td>United Kingdom</td>
<td>28.2</td>
</tr>
<tr>
<td>6</td>
<td>Canada</td>
<td>25.9</td>
</tr>
<tr>
<td>7</td>
<td>Denmark</td>
<td>25.1</td>
</tr>
<tr>
<td>8</td>
<td>United States of America</td>
<td>23.7</td>
</tr>
<tr>
<td>9</td>
<td>Australia</td>
<td>22.5</td>
</tr>
<tr>
<td>10</td>
<td>Kuwait</td>
<td>22.3</td>
</tr>
</tbody>
</table>

Source: Patterson, 2014

In Bahrain, little or no data is currently available on the lifestyle, dietary, or medical factors, including the role of infection or childhood illnesses, on the risk of T1DM. After diagnosis it is well recognized that a healthy diet that meets the recommendations for children living with diabetes and a healthy lifestyle are important in maintaining good blood glucose control and in preventing long-term complications (7). No studies, to the best of the author’s knowledge, have looked into the diet or lifestyle factors of children with diabetes in the Kingdom of Bahrain. There is an urgent need for more research on this under-researched yet clinically significant population.
1.2. Current Dietary Habits of Bahraini Children

Musaiger and Gregory (8, 9) were the first to describe the dietary habits of school children in the Kingdom. The children were found to skip breakfast more than any other meal of the day and compensated with a heavy mid-morning snack. The authors also noted a decrease in the consumption of bread as age increased whilst consumption of carbonated beverages increased. In a more recent study, Gharib et al (10) further describes the dietary pattern among Bahraini school children; snacking was a common occurrence with consequently high daily sugar consumption. Sweets and soda drinks were often consumed but milk, fruit and vegetables were not consumed regularly (10). The authors found the average energy intake of children to be similar to the Estimated Average Requirement (EAR) but dietary fiber fell short of the requirements whilst fat intake, particularly saturated fats, exceeded the recommendation.

1.3. Factors Affecting Dietary Intake in Bahrain

1.3.1. Geographical Location

The Kingdom Of Bahrain is an archipelago of 33 islands, Bahrain being the largest. It lies only 24 kilometers from the east coast of Saudi Arabia and approximately 28 kilometers from Qatar. In literal translation Bahrain means “between two seas.”
The Arabian Gulf waters are known to host a variety of fish, a typical food staple. Bahrain was given the pseudo name of the “island of a million palm trees” due to its abundance of palm trees and dates. However after the discovery of oil, followed by a rapid economic growth spurt and the ongoing land reclamation projects that have since paved the way for luxury hotel resorts, there has been a decline in fishing and consequently price inflation. Musaiger et al (11) identified these changes in food consumption and described a decrease in the intake of fresh fish and dates but an increase in processed foods. The authors described these effects as pertaining to increasing income and literacy, food price fluctuations, food subsidy policy, and the influence of immigrant food habits (11).

1.3.2. Socioeconomic and Demographic Factors

Along with the increase in wealth, education and standard of living, there has been a rapid expansion of infrastructure in Bahrain. In 1952 the Public Health Department was established and was responsible for implementing a solid healthcare infrastructure, providing
free health care for all citizens and residents (12). As a result, over the past three decades, Bahrain has seen a rapid change in morbidity, with a decline in communicable disease, but an increase in chronic diseases such as diabetes (13-16).

Due to the sweeping effects of globalization and the “fast food nation” trend, new dietary habits are quickly replacing older healthier habits in the Kingdom. The impact of media and advertisement on dietary choices was also described as a factor contributing to changes in Bahraini diet (11). Lifestyle factors such as a skew towards a more sedentary lifestyle, an increase in obesity, are all having an impact on the nutritional intake of Bahraini youth (17).

1.3.3. RELIGION, CULTURE AND TRADITIONAL FACTORS

Bahrain is a liberal Muslim country and religion has an impact on diet. Foods consumed in Bahrain are Halal (food prepared according to Islamic dietary law) and although alcohol is served it is considered Haram (forbidden). Familial relationship ties are often centered on food.

1.4. COMMON NUTRITIONAL RELATED DEFICIENCIES

1.4.1 VITAMIN D DEFICIENCY

Although it is perhaps difficult to comprehend how sun-rich countries so close to the equator can suffer from vitamin D deficiency, it has, nevertheless, been a major public health concern in the Middle East for the past decade (18). In a recent study looking at the vitamin D levels of 403 mothers in labor and their newborns in Bahrain, 358 (88.8%) of the mothers and 364 (90.3%) of the newborns were found to be deficient as defined by a 25(OH)D level below 50 nmol/l (19). Furthermore, according to the same cut offs, vitamin D levels were found to be deficient in 233 (64%) men used as controls in the study (20). A high income, smoking, lack of
sun exposure and high body mass index were significantly associated with vitamin D deficiency in men (20) whereas for females, living in flats, lower educational attainment, the use of veil, gravida $\geq 4$, and not using multivitamins, vitamin D or calcium supplements, were found to be significantly associated with vitamin D deficiency (19). Moreover, a study looking into the dietary intake of vitamin D of these couples found a low mean intake of vitamin D (21) and a significant association between dietary intake and 25(OH)D levels in both men and women (21).

1.4.2 RICKETS

An inadequate intake of calcium, vitamin D or both can result in rickets. Considering the prevalence of vitamin D deficiency in the Middle East, the high incidence rate of rickets in the region (22, 23) is not surprising. Limited sun exposure and religious/cultural practices which include wearing the veil (22, 23) are believed to contribute to vitamin D deficiency.

1.4.3 IRON DEFICIENCY ANEMIA

Iron deficiency anemia is a common problem in the Middle Eastern region, being described as one of the major public health concerns in Bahrain (24). In a review conducted by Musaiger et al in 2002, looking at iron deficiency anemia in children and pregnant women in the Arab Gulf countries, the author found the prevalence rate amongst preschool children and school-aged children to range from 20% to 67% and 12.6% to 50% respectively; whilst the number of pregnant women suffering from iron deficiency anemia ranged from 22.7% to 54%.(24). Musaiger identified risk factors associated with iron deficiency anemia in children in these Middle Eastern countries which include poor infant feeding habits and in particular inappropriate weaning practices using foods with a low iron bioavailability in children. Parasitic infection and geographical location with a higher prevalence in rural rather than urban areas was
also identified as risk factors for both children and pregnant women. Parity and early age at marriage were identified as factors associated with iron deficiency anemia in pregnant women. (24)

1.5 Defining Diabetes

Diabetes is a metabolic disorder characterized by either a complete or relative lack of the function of insulin producing beta cells in the pancreatic islets resulting in a hyperglycemic state (25). Chronic hyperglycemia can lead to long term damage to the kidneys, heart, eyes, nerves and blood vessel (25). Hyperglycemia can result from the autoimmune destruction of the beta cells in the pancreas resulting in the impairment of insulin secretion or, a defect of insulin action which leads to disturbances in carbohydrate, fat, and protein metabolism resulting in insulin resistance (26). Though classically two major forms exist (type 1 and type 2 diabetes), they are not completely distinctive and may overlap in clinical manifestation.

Type 1 diabetes mellitus (T1DM), previously known as juvenile diabetes or insulin-dependent diabetes, results from an autoimmune destruction of the beta cells which consequently leads to an increase in blood and urine sugar levels resulting in impaired glucose tolerance as described earlier (27). The classical symptoms of T1DM are frequent urination (polyuria), excessive thirst (polydipsia), excessive hunger (polyphagia) and weight loss (26).

The treatment of T1DM involves the lifetime use of exogenous insulin to help maintain normal blood sugar levels. Insulin is often injected subcutaneously although some prefer using an insulin pump to deliver insulin. Success rates of pancreas transplants have improved (28)
although they are not without risk and complications. Pancreatic islet cell transplantations are currently in the experimental phase but show promising results (29).

Type 2 diabetes (T2DM), previously known as non-insulin dependent diabetes mellitus, has been increasing in the pediatric population and has become a major public health concern (30). With T2DM the islet cells are able to produce and secrete insulin however there appears to be reduced function or potency due to insulin resistance. Both genetic and environmental factors play a role in the development of insulin resistance (31) with contributions from age, lifestyle habits, physical activity, dietary intake and obesity. Obesity is one of the markers of T2DM in children with approximately 85% of those diagnosed being overweight or obese (32).

Treatment of T2DM involves making lifestyle changes such as a shift from a sedentary lifestyle to a more active one, eating healthier low fat foods with a focus on whole grains, fruits and vegetables, and weight loss if overweight to help control and maintain blood sugar levels. When dietary and lifestyle factors fail to normalize blood sugar then medications are often used. Oral hypoglycemic agents may be given alone or in conjunction with insulin injections.

Maturity-onset diabetes of the young also known as MODY, was previously believed to be a form of type 2 diabetes (33). However with advances in molecular studies, MODY is now referred to as a monogenic diabetes, caused by mutations in an autosomal dominant gene (34). It typically presents before 25 years of age (34) and frequently in childhood or early adolescence (35). It is not uncommon that people with MODY be mistakenly diagnosed with T1DM or T2DM (34). The six gene mutations known to cause MODY are glucokinase (MODY2), hepatic nuclear factor 1 alpha (HNF1α) (MODY1), hepatic nuclear factor 4 alpha (HNF4α) (MODY3) and insulin protein factor 1 (IPF1) (MODY4), hepatocyte nuclear factor-1β (HNF1β) (MODY5), and neurogenic differentiation factor (MODY6) (33). Each mutation results in specific clinical
and physiological characteristics of the disease making sub-type specific diagnosis important for the provision of optimal treatment (36).

The prevalence of MODY subtypes differs considerably across Europe (37-39) although MODY1 (HNF1α), MODY 2 (GCK) and MODY 3 (HNF4α) appear to be the commonest cause of defect. In the first U.K survey of type 2 and MODY diabetes in children, the crude minimum UK prevalence of MODY was found to be 0.17/100,000 in comparison to the prevalence of type 2 diabetes which was found to be 0.21/100,000 in children under 16 years of age (40). In a later study which aimed to compare the number of confirmed MODY cases across the U.K and to estimate the minimum prevalence, molecular genetic testing found the MODY 3 (HNF1α) and MODY 2 (GCK) mutations to be the most common; they estimated the minimal prevalence rate to be 10.8/100,000 in the population (34).

In Saudi Arabia, the prevalence of MODY was found to be approximately 1/2000, (50/100,000) (41). El-Haszmi et al found the prevalence rate of MODY diabetes in a sample of 8762 children under 14 years of age to be 0.148% (n=13). In Oman, a small sample (n=20) looking at patients with diabetes suggestive of MODY were tested for known mutations as well as the three most common MODY mutations recognized in Europe; the results of the study showed none of the patients to have the tested mutations including the common MODY mutations found in Europe suggesting that patients in that region may have a “novel” form of MODY (42).

MODY is a recognized type of DM and in Bahrain genetic testing allows these cases to be effectively identified; despite this, there remains a dramatic increase in children being diagnosed with T1DM in Bahrain. This rise in children being identified with T1DM has
consequently resulted in an increased workload on the pediatric endocrine clinic and an increase in hospital admissions incurring greater healthcare costs.

1.5.1 Pathogenesis of T1DM

Research into the possible pathogenesis and etiology of T1DM has been extensive and although the exact mechanism remains unknown there is a general consensus of the combined roles of both genetics and the environment (43-45).

1.5.1.1 Genetics

The development of T1DM has been linked to several genes; the most studied being perhaps the human leukocyte antigen (HLA) gene which is found in the major histocompatibility complex (MHC) and the insulin gene. The DR genes found in the HLA region, in particular the DR3 and DR4 alleles, have been associated with an increased risk of T1DM development (45). Certain alleles in the DQ gene also found in the HLA region confer an increased susceptibility. Interestingly different DQ and DR allele combinations can also confer a protective effect (43). In effect it seems that although genes found in the MHC have a key role in the pathogenesis of T1DM this phenotype requires the presence of other genes to appear (43).

Most human studies looking into the genetics of disease development come from twin studies. In a Finnish study of twin pairs the concordance for T1DM in monozygotic and dizygotic twins was found to be 42.9% and 7.4% respectively i.e. a higher disease concordance in monozygotic than dizygotic twins (46). Despite the strong evidence of genetics in the development of T1DM, the steady but rapid rise worldwide of the disease does not appear to be attributed to changes in the gene pool alone (27, 43). Possible explanations are environmental
triggers that instigate a cascade of events leading to the development of T1DM by either direct means, or indirect means, by interacting with already susceptible genes.

1.5.1.2 ENVIRONMENTAL FACTORS

Studies have shown that fetal exposure to maternal enterovirus is associated with an increased risk of T1DM development (47, 48). Congenital rubella is a virus known to directly cause T1DM in the afflicted offspring (49) and will be discussed further under viral and microbial infections (see section 1.5.1.3 p. 27). Maternal age, pre-eclampsia and blood group incompatibilities are also associated with an increased risk (50) as are caesarean section deliveries (51). It is hypothesized that infants born via C-section are not exposed to the natural bacteria found in the passage of the birth canal, which are involved in priming the immune system.

1.5.1.3 VIRAL AND BACTERIAL INFECTIONS

With improvements in sanitation and hygiene, there has been a dramatic decrease in communicable diseases but a rise in non-communicable diseases such as diabetes. It is hypothesized that viral infections may perhaps play a role in the development of the immune system and that, with improvements in hygiene and the use of vaccinations, the absences of immune stimuli weakens the body’s defense and decreases tolerance to beta cell antigens (43). Studies looking into the incidence rate of diabetes and child population density or urban/ rural status have found a higher incidence rate in areas of low child population density (52). The incidence rate was also found to be higher amongst firstborns and those with children with fewer siblings, both consistent with the “hygiene” theory (27).
It has long been speculated that viruses, in particular enteroviruses, are potential triggers of islet cell autoimmunity. Enteroviruses such as the Coxsackie B Virus (CBV) (53, 54), Epstein-Barr Virus (EBV) (55) and Cytomegalovirus (CMV) (56) have all been hypothesized to play a role in the development of diabetes. Islet cell antibodies (ICA) were detected in congenital rubella as well as in children with mumps (57). The seasonal variation in diabetes diagnoses, with a higher incidence reported in the winter months and a lower incidence in the summer, supports the argument that viral infections either trigger or accelerate the destruction of beta cells (27).

Early exposure to cow’s milk protein has long been postulated to have an etiological role in the development of T1DM (27, 43, 45, 50). It is hypothesized that cow’s milk protein exposure results in an immunological response to the protein and in particular to the bovine serum albumin (BSA) which in turn triggers autoimmunity. This is indicated by the presence of a higher level of BSA antibodies in newly diagnosed children compared to their healthy counterparts (43-45).

Many studies have looked into the association between T1DM and breastfeeding (58-62) although the results are inconclusive with some studies finding a protective effect (60) from breastfeeding, others have found no significant relationship (62). Rather than a direct effect of breastfeeding per se the association may be mediated by a protective effect of breastfeeding against enteroviruses (61) or because longer duration of breastfeeding is likely to also be a marker for delayed introduction of cow’s milk protein and/or gluten containing foods (59, 60). Some studies looking into the role of vitamin D and the risk of diabetes development have hypothesized that low levels of vitamin D in breast milk may be a potential risk factor perhaps explaining a negative association between this form of infant feeding and subsequent diabetes.
development and hence suggesting a potentially protective role for vitamin D supplementation in some mother-infant pairs (63).

The ‘accelerator’ theory postulates that the development of both type 1 and type 2 diabetes is a result of metabolic disturbances which leads to insulin resistance and autoimmunity, consequently causing beta cell insufficiency (64). The central concept of the accelerator theory is that an increased weight gain is associated with a greater risk of developing T1DM (65). In a large cohort study of 9,248 children (65) the BMI of diabetic children in all age groups was significantly higher as was the weight and BMI of newly diagnosed children with T1DM as compared to their healthy counterparts.

1.5.2 Diabetes and Vitamin D Deficiency

Vitamin D is often described as a fat soluble vitamin but it also exhibits hormonal properties in its active form acting via the vitamin D receptors which are found in most tissues in the human body (66). It plays an important role in the regulation of calcium and phosphorus for bone mineralization in the body (67) but more recently vitamin D has been recognized for its role in the immune function and modulation of cell growth as well as its role in the inflammatory process (68). Vitamin D deficiency has also been linked to cardiovascular diseases, diabetes mellitus, autoimmune disorders, and certain cancers (69, 70). There are two forms of vitamin D, which are of particular importance; vitamin D2 and vitamin D3. Vitamin D2, also known as ergocalciferol, is synthesized by plants whereas vitamin D3, known as cholecalciferol, is produced by the skin. Foods may be fortified with either vitamin D2 or D3 (71) although D2 is most commonly used in both food fortification and for prescription supplements. It is worthy to
note that few foods naturally contain vitamin D. Fatty fish and fish liver oils are a good source whereas eggs and cheese contain a small amount.

Vitamin D can be produced endogenously by the skin via photosynthesis using ultraviolet B light (UVb) which converts 7-dehydroxycholesterol (7-DHC) to pre-vitamin D₃. It can also be obtained from the diet or from a dietary supplement. Regardless of whether it is obtained from an endogenous or exogenous source, this form of vitamin D is inert and must undergo a series of hydroxylation reactions to convert it to its active form (49). Vitamin D is converted to calcidiol also known as 25-hydroxyvitamin D. This reaction occurs in the liver whereas the conversion of 25-hydroxyvitamin D to 1, 25-dihydroxyvitamin D occurs primarily in the kidney. Vitamin D in the form of 1, 25-dihydroxyvitamin D, also known as calcitriol, is the biologically active form of vitamin D. When measuring serum levels of vitamin D, 25(OH)D₂ (calcidiol) is measured and is considered a good indicator of vitamin D levels (72).

Studies have reported on the difference in bioavailability between vitamin D₂ and D₃ (73-76) with D₂ suggested to be a relatively lower potency than D₃. Houghton et al noted that vitamin D₃ appeared to be more efficient at raising serum vitamin D levels and at maintaining these levels (77), whilst Romagnoli noted that vitamin D₃ was twice as effective, whether administered orally or intramuscularly, at raising serum levels compared to D₂ (76). A review and meta-analysis of RCT’s showed that vitamin D₃ supplementation has a significantly greater effect on raising serum vitamin D levels in comparison to vitamin D₂ regardless of the dose administration, although the reason for this remains unclear and requires further investigation (78); Houghton et al speculate that vitamin D₃ metabolites may have a greater affinity to vitamin D-binding proteins than vitamin D₂.
In a large birth cohort study which involved over 12,000 infants born in 1966 and followed up until 1996, Hypponen et al found that children who were regularly supplemented with vitamin D in the first year of life had a reduced risk of developing T1DM (79). Data on the vitamin supplementation of those children within the first year of life was recorded as being regular, irregular or without supplementation and where supplementation had occurred, the dose was categorized as being either below, within, the recommended intake at the time (2000 IU). These results are supported by the EURODIAB sub-study group in which they also found a reduction in the risk of development of T1DM in reportedly supplemented children versus non-supplemented (80). This study involved seven European countries with access to registries of patients with T1DM and applied a case-control design to investigate risk factors for T1DM. In all, 820 patients with T1DM and 2334 controls were involved but the questionnaires and interviews used to gather data did not collect details on the form or level of supplementation that was given.

1.5.2.1 PROPOSED ROLE FOR VITAMIN D IN DIABETES DEVELOPMENT

As mentioned previously vitamin D is involved in the regulation of calcium metabolism along with the parathyroid hormone (PTH) that work both directly and indirectly to maintain calcium homeostasis. The presence of vitamin D receptors in the pancreas is believed to be a strong indicator of its role in insulin secretion and glucose tolerance (66). It is hypothesized that vitamin D influences insulin production by increasing intracellular calcium concentration which in turn results in the secretion of insulin from the beta cells (66, 67, 71). Vitamin D is also believed to mediate the activation of the calcium endopeptides which play a role in the conversion of proinsulin to insulin (66, 71). In addition a role has been hypothesized in the expression of insulin receptors which work to enhance insulin action (66).
**1.5.2.2. IMMUNE MODULATION**

Vitamin D receptors (VDR’s) have been identified on many of the cells of the immune system (66). As mentioned earlier, imbalances in inflammatory mediators, pro-/anti cytokines such as transforming growth factor beta 1 (TGF-b1), interferon gamma (INF-g), interleukin-1 receptor antagonist (IL-1ra), interleukin-1 alpha (IL-1a), interleukin-1b (IL-1b), IL-4, IL-6, IL-12 and tumor necrosis factor (TNF)-a have been implicated in the pathogenesis of T1DM (71). These inflammatory mediators and cytokines are produced by the immune system from activated T and B lymphocytes, dendric cells (DCs), natural killer cells (NK) and macrophages, all of which have VDRs (66, 71). Physiologically lymphocytes can be divided into two major subsets; T helper 1 (TH₁) and T helper 2 (TH₂). The function of TH₁ is mainly cell-mediated immune responses that produce inflammatory mediators, cytokines and produce IL-2, IFN-g, TNF-a and TNF-b. TH₂, on the other hand, acts as a mediator and activates beta-cells and antibody production and produces IL-4, IL-10, IL-13 and TGF-b which promote humoral immunity (71). Vitamin D acts to suppress the release of TH₁ causing a shift toward the production of TH₂. It also promotes the production of anti-inflammatory cytokine IL-4 and prevents beta-cell damage caused by the pro-inflammatory cytokines by acting as an inhibitor (71).

Studies on the NOD (non-obese diabetic) mouse models (considered highly relevant to models of human disease) have resulted in a wealth of information especially with regards to the role of the immune function in the development of T1DM (81). Enteroviruses as mentioned earlier, have been of focus for the past decade (82) and there is strong, albeit, circumstantial evidence for their role in the development of T1DM. Several reviews have stated convincing evidence that T1DM is linked to infection from enterovirus (83-86) and in particular the Coxsackie virus B1 (87, 88). A study conducted by Larrson et al, in which a prototype vaccine
against the Coxsackie virus B1 was developed and evaluated for safety resulted in protection from the virus without accelerating diabetes development (89). The development of diabetes was however, significantly earlier in mice that were not vaccinated and exposed to the virus compared to those that had been vaccinated although the vaccine did not prevent or delay progression of disease. More recently Yoon et al (90) tested a prototype vaccine with the aim of re-educating the immune system to insulin specific autoantigens; the results were promising as the vaccine was able to protect 40% of the vaccinated mice from developing diabetes compared to the control mice that all went on to develop diabetes (90).

1.5.2.3 **ANTIOXIDANT EFFECT**

Reactive oxygen species (ROS) can cause considerable damage at a cellular and nuclear level by destroying cell organelles and damaging DNA, leading to cell death by apoptosis (71). People with diabetes have been shown to have increased oxidative stress due to overproduction of ROS coupled with an impaired ability to neutralize their effects (71). Vitamin D may act as an antioxidant by scavenging different ROS and blocking cellular immunity mediated by TH1 (71).

1.6 **MANAGEMENT OF T1DM**

The findings of the Diabetes Control and Complication Trial (DCCT) conducted in 1994 became the cornerstone of diabetes management (91), showing that improved glycemic control in T1DM (via three or more daily injections of insulin a day, a minimum of 4 bloods glucose reading and dose adjustments for a target of 3.9 to 6.7 mmol per liter (70 to 120 mg per deciliter) pre-prandial and levels less than 10.0 mmol per liter (180 mg per deciliter) postprandial was significantly associated with a decrease in complications. The findings of the study
ultimately led to a change in policy and practice in the healthcare of people suffering from T1DM.

The DCCT trial examined the effect of intensive insulin treatment with the aim of maintaining blood glucose levels in the near normal ranges. The study, which ran over 6.5 years, compared a group of participants on intensive treatment and a control group that received standard care. In total 1441 patients were recruited from 29 centers between 1983-1989 across the United States and Canada. The results of the DCCT trial showed an approximate 60% reduction in the risk of developing diabetic retinopathy, nephropathy, and neuropathy (91). The benefits of intensive therapy not only delayed onset, but slowed down the progression of microvascular complications regardless of gender, age, and onset of diabetes. This prompted the American Diabetes Association to review its policy concluding that the primary treatment goal in T1DM should be to maintain tight blood glucose control using intensive therapy (IT) which can be achieved by using multiple daily injections (MDI’s) or continuous subcutaneous insulin infusion (92).

The DCCT trial was not without limitations; one of the main adverse events of the trial was a significant two-threefold increase in hypoglycemia attacks (93) and weight gain (94). Furthermore, the results of the trial failed to show a reduction in cardiovascular morbidity or mortality (95) although this was rationalized as being due to the fact that the participants recruited were young (13-39 years) hence less likely to demonstrate cardiovascular complications in the time-frame of the study.

In the United Kingdom, the United Kingdom Prospective Diabetes Study (UKPDS) found results similar to the DCCT trial but for people with T2DM. The trial was a multicenter
trial involving 23 clinics in the United Kingdom, recruiting 5,102 patients with newly diagnosed T2DM. The study, which ran for twenty years from 1977 to 1997, showed that intensive blood-glucose control (achieved by obtaining a fasting plasma glucose of less than 6 mmol/l in conjunction with either insulin or an antidiabetic drug) in T2DM could reduce and even slow the progression of microvascular complications but not macrovascular disease (96).

1.7 Structured and psycho-social education in the management of T1DM

In 1948 the definition of health by the World Health Organization as “being a complete state of physical, mental and social well-being, and not merely the absence of disease or infirmity (97)” revolutionized the way health care was perceived. Health was no longer to be viewed solely from a physical perspective but from a more holistic one that embraced the psycho-social wellbeing of individuals. Applying this to chronic conditions such as diabetes can be particularly challenging due to the potentially negative psycho-social conditions of managing a long term health issue. Diabetes management is particularly challenging for children and youths as they try to juggle the use of multiple daily injections, frequent blood glucose monitoring, balancing carbohydrates with insulin or managing their blood sugar whilst being physically active, travelling or when they fall ill. It is also challenging for the parents of those children whom often must assume the responsibility of such oppressive regiments.

There is a clear and documented link between diabetes and depression in adults (98, 99) which ranges in prevalence from 14.4% to 32.5% (100). Furthermore, depression in adults with T1DM also appears to increase the risk of diabetes complications (101) which in turn incurs greater health care costs (102). The psycho-social impact of diabetes extends beyond health to impact also on quality of life (QoL) and overall functioning (99, 103). The prevalence of
depression is believed to be two-folds higher in children and three folds higher in adolescents with diabetes compared to their healthy counterparts (104). Specifically, studies have identified a depression prevalence in children and adolescent with diabetes between 0.8% and 8.3% (105, 106) with a marked increase in adolescence due to the added burden associated with this age group as a result of attempts to gain autonomy from caregivers, adapting to body changes related to puberty and body image issues (107). Some documented consequences of depression in children or youth with diabetes include poor adherence to diabetes regimen, including poor compliance with insulin injections, dietary management and monitoring blood glucose (108, 109), as well as a poorer quality of life (110), and lower self-esteem (111). It has also been linked with an increased incidence of eating disorders (108) and suicide or suicidal thoughts (112) in this patient group.

Management of diabetes from a physical and medical perspective has come a long way was since the discovery of insulin by Banting and Best in 1921 (113). However from a psycho-social perspective, studies determining the effectiveness of psycho-social and educational interventions that seek to not only improve glycemic control but also outcomes such as QoL, diabetes self-efficacy, and stress in children and youths with T1DM are of great importance, especially in light of the real risk from co-morbidities such as suicidal thoughts and eating disorders (100). Although it appears that health-related QoL can be improved by such interventions, knowing which particular aspect of the intervention brings about the change is not always easy to measure. A systematic review of the most recent studies that seek to determine the effectiveness of educational and psycho-social interventions are further explored and described in Chapter 7.
1.8 Study Rationale

In conclusion, the increasing number of children being diagnosed with T1DM is of great concern and requires immediate attention from researchers and clinicians alike. As there are currently no studies, to the best of the author’s knowledge, aimed at identifying modifiable factors such as dietary intake, lifestyle or health-risk factors associated with the development of T1DM in the Kingdom, there is an urgent need for such research in this clinically significant population. By understanding the modifiable correlates of diabetes development alongside the user- and health care professional-identified needs in this population and in the region we can design a more effective tailored education package to address the current gaps in evidence-based practice. This will aim to optimize the management of those already living with type 1 diabetes in the region and inform the development of future preventative research and strategies to ultimately reduce the considerable social and economic burden conferred by this condition in the Kingdom.
2.0 AIMS AND OBJECTIVES

The overall aims of this program of work are:

Aim 1:
To investigate the lifestyle, dietary intake, and health risk factors associated with the risk of T1DM in children in the Kingdom of Bahrain.

Aim 2: To develop an educational package that specifically targets the needs of Bahraini children with diabetes and their families as informed by the needs of the healthcare workers and service-users.

The study will be conducted in FOUR phases:

PHASE I: CHARACTERIZING THE POPULATION – RETROSPECTIVE

This phase will involve the investigation of a cohort of children aged 6-12 newly diagnosed with diabetes in the years 2009 and 2010 in the Kingdom. A control group of children matched by age, and demographic location will be sought from primary health care centers. The specific aims and objectives of this phase will be:

Specific Aim 1: To describe the food habits/traditions of Bahraini children with and without diabetes.

Specific Aim 2: To determine if the nutritional intake of Bahraini children with diabetes meets the current recommended intake.
Specific Aim 3: To investigate the association between lifestyle factors, such as geographical location, activity levels, psychosocial issues, infant feeding habits and T1DM occurrence in a pediatric cohort.

Objectives:

- To extract relevant data from an existing internal registry.
- To recruit an appropriate control group.
- To analyze dietary intakes of children in the case and control groups via nutrition analysis software (Food Processor Software SQL version 10.70, ESHA Research).
- To assess the adequacy of their dietary intakes as compared to U.S. Recommended Dietary Intakes (RDA) as well as recommendations from the International Society for Pediatric and Adolescent Diabetes (ISPAD).
- To compare, using a statistical software package (SPSS version 21, SPSS Inc.) the health and dietary factors of children with T1DM with aged matched healthy comparators.

Objectives:

Phase II: Characterizing the Population - Prospective

In this phase, dietary intake as well as lifestyle factors will be investigated in more details. The serum vitamin D levels of a subgroup of children with diabetes will also be measured and compared to data on dietary intakes of vitamin D from a 24hr food recall. Cases will also be asked to provide information on diet and lifestyle factors relating to vitamin D status.
through completion of a food frequency questionnaire and lifestyle questionnaire. The specific aims and objectives of this phase are:

**Specific Aim 1:** To investigate in detail the dietary, lifestyle behaviors, and physiology of a small but representative sub-sample of newly diagnosed children aged 6-12 with diabetes.

**Objectives:**

- To prospectively recruit an appropriate sample of newly diagnosed children with T1DM
- To obtain and analyze the dietary intakes (three, 24-hr diet recalls) via region-specific nutrition analysis software.
- To administer a vitamin D specific FFQ questionnaire to all participants.
- To administer the Child Physical Activity Questionnaire (CPAQ) to all participants to assess activity level.
- To analyze all the data via statistical software package to assess any association between physiological factors such as body composition/vitamin D levels, or lifestyle factors such as activity levels/ frequency of sunlight exposure, and diabetes prevalence.

**Phase III: Development and testing of an education package**

This phase will involve the development of an educational package that specifically targets the needs of Bahraini children with diabetes and their families and care givers.

**Specific Aim 1:** To investigate the beliefs and attitudes of a representative sample of children with diabetes, their care givers and their families with respect to the etiology and management of diabetes in Bahrain.
Objectives:

- To conduct focus groups with the families of a sample of children with diabetes to investigate their beliefs/knowledge about the etiology and the management of T1DM including their perception of the admission, education, discharge and follow-up services provided as well as exploring recommendations.

- To conduct focus groups with the pediatric nurse educators and endocrinologist to investigate their role in the management of diabetes; perceived barriers to the education process as well as behavioral changes and future recommendations.

- To record and transcribe the focus groups so as to identify common themes.

Specific Aim 2: Undertake a review of the effectiveness of interventions conducted in clinical settings that seek to improve the management of children and adolescents with T1DM

Objectives:

- To conduct a search of reviews that have already addressed this topic to determine where there is a gap in knowledge to be addressed or present an update of new papers since last review published.

- To search electronic databases for new RCT’S conducted since last published review on MEDLINE, Psych INFO, PubMed, Embase, Scopus etc.

- To identify papers suitable for review, extract relevant data and synthesize to inform the development of the Bahraini education resource.
Specific Aim 3: To develop an evidence-based education package specifically targeting the needs of children with T1DM and their families and care givers.

Objective:

- To gather the findings of the qualitative study and the systematic review in order to inform the design of an education package for the local population.

Specific Aim 4: To assess the feasibility of implementing such an intervention.

Objectives:

- To present the proposed intervention to the pediatric nurse educators, endocrinologist and patients to obtain feedback on the feasibility of implementing the intervention in a real clinical setting.
- To design a pilot test protocol and parallel evaluation strategy for the implementation of the education package.

Phase IV: Dissemination

This phase involves disseminating the results of the studies to key stakeholders. During this phase preparation will be made for the publication of the studies.
3.0 CHILDREN WITH TYPE 1 DIABETES & THEIR HEALTHY COUNTERPARTS- A CASE-CONTROL STUDY

3.1 INTRODUCTION

In Bahrain’s largest serving hospital, the Salamiya Medical Complex, health statistics have revealed an increasingly alarming number of children being diagnosed with type 1 diabetes. Although there are no national registries that exist for children with diabetes in the Kingdom of Bahrain, an internal registry exits at the Pediatric Endocrine and Diabetes Unit in the Salamiya Medical Complex (SMC).

The aim of this study was to perform an audit of the Diabetes Registry Form (DRF) (Appendix 1) available at the Pediatric and Endocrine Diabetes Unit in the Salamiya Medical Complex and to compare lifestyle factors, psychosocial issues, infant feeding habits, dietary habits, childhood illness, and maternal pre and postnatal history of children with T1DM with age matched healthy comparators.

3.2 EXPERIMENTAL DESIGN & METHODOLOGY

ETHICS APPROVAL

This study was approved by the Salamiya Medical Complex Health Research Committee and the Primary Health Care Health Ethics Research Committee in Bahrain (Appendix 2). Data was collected from the existing DRF for the control groups whereas informed and signed consent was obtained from the parents or legal guardians of the control group prior to administering the similar questionnaire.
3.2.1 Experimental Design & Methodology-Case Group

Study Area/Setting:

The information was gathered from the Pediatric Diabetes Unit at the SMC complex where all completed Diabetes Registry Forms (DRF) for children with confirmed T1DM and T2DM are archived. The DRF is an existing data collection tool used to gather information on all patients with diabetes and includes information on:

- Demographic characteristics
- Current medical regimen (insulin)
- Infant feeding method
- Past medical history
- Family history of - diabetes and/or other diseases or known disorders
- Psychosocial issues
- Lifestyle habits which includes usual food intake

Study Subjects:

The study subjects were children aged 6-12 diagnosed receiving a confirmed diagnosis of T1DM informed by either antibody or genetic testing, and attending the Pediatric Endocrine Clinic in the years 2009 or 2010.

Study Design:

The study design was a descriptive study of children aged 6-12 with confirmed case of T1DM.

Inclusion Criteria:

The inclusion criteria for study subjects were as follows:
- The subject was registered as a confirmed case of T1DM at the Pediatric Diabetes Unit (PEU)
- The subject was between 6 and 12 years of age at diagnosis
- The subject was followed up at least once at the Pediatric Diabetes Unit
- The subject had a completed Diabetes Registry Form (DRF)

**Exclusion Criteria**

- Children with T2DM
- Children not having received a confirmed diagnosis of T1DM
- Children with an incomplete DRF
- Children not followed up at least once at the SMC
- Children not within the specified age group

**Data Collection Methods:**

The DRF for all subjects was obtained from the Pediatric Diabetes and Endocrine Unit. A 24 hour food recall gathered by a licensed dietitian or nutritionist at time of admission was also available for analysis; the results of which will be discussed in Chapter 4. All information was kept strictly confidential, with subjects allocated a unique identification number.

**3.2.2 Experimental Design & Methodology-Control Group**

**Study area/setting:**

A control group of children matched by age, sex, and demographic location were prospectively sought from Primary Care Centers, also known as Local Health Centers (LHC) from across the Kingdom. Subjects were selected based on whether they met all inclusion criteria
and were rejected if they met anyone of the exclusion criteria. Healthy controls were sought from LHC’s as opposed to children free from diabetes within the Salmaniya Complex so as to decrease any confounding effect that a chronic or acute disease may have on dietary and health factors.

**STUDY SUBJECTS:**

The criteria for the control group:

- Child between 6-12 years of age visiting LHC
- Free of any chronic diseases
- Accompanied by a legal guardian or parent

**DATA COLLECTION METHODS:**

Subjects were approached directly by interviewers. If the subjects met the age criteria, the parents were given a brief overview of the study and asked if they were interested in participating. If they agreed a letter was given to the parents or legal guardian with details regarding the study and informed signed consent was obtained prior to investigation.

The height and weight of the control group children was measured by a licensed dietitian using standardized methods. A 24hr food recall was obtained from the parents in the presence of the child by a licensed dietitian or nutritionist.

The DRF was modified, with any non-relevant information (i.e. type of diabetes, insulin regimen etc....) removed, and administered to the control group once consent was obtained.
Demographic, medical and other data was obtained directly from the parent or legal guardian (See Appendix 4).

3.3 Analysis

All data from the DRF for children with T1DM and data from the questionnaire obtained from healthy controls were entered into a spreadsheet and analyzed using SPSS version 21 (SPSS Inc.). Normality was tested for using the Kolmogorov-Smirnov test. Differences between subgroups were analyzed using Chi Square or independent t-test as appropriate. Logistic regression analysis was used to evaluate independent predictors of T1DM. A P value < 0.05 was considered significant.

3.4 Results

In total 59 children with T1DM met the criteria and were included in the study and compared to 53 healthy children. The case and control groups were matched for age, BMI, gender and geographic location. Demographic information (see Table 2) showed that children with T1DM were more likely to be Bahraini nationals (p<0.001) although there was no significant difference in self-reported race, with 95% of children being described as of Arab origin. A non-uniform distribution of subjects selected from different governorates, although non-intentional, reflects the more densely populated areas.
Table 2 Baseline characteristics of children recruited to the case-control study at the SMC.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Cases</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Age in years</td>
<td>9.02 (1.88)</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>BMI percentile</td>
<td>48.80 (35.76)</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bahraini</td>
<td>50</td>
<td>94.3</td>
<td></td>
</tr>
<tr>
<td>Non-Bahraini</td>
<td>3</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>24</td>
<td>45.3</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>29</td>
<td>54.7</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arab</td>
<td>53</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Non-Arab</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Religion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muslim</td>
<td>53</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Non-Muslim</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Governorate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muharraq</td>
<td>13</td>
<td>24.5</td>
<td></td>
</tr>
<tr>
<td>Capital</td>
<td>7</td>
<td>13.2</td>
<td></td>
</tr>
<tr>
<td>Northern</td>
<td>18</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>15</td>
<td>28.3</td>
<td></td>
</tr>
<tr>
<td>Southern</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>SD: Standard Deviation, <sup>a</sup>Mann Whitney, <sup>b</sup> Chi Squared, <sup>c</sup>Fisher Exact
Medical history, as shown in Table 3, revealed that children with T1DM were more likely to have suffered from an illness such as tonsillitis than healthy children (54.2% and 5.7% respectively; p< 0.001) or to have undergone surgery prior to diagnosis (23.7% and 3.8% respectively; p=0.001). Logistic regression analysis showed that children who reported suffering from an illness prior to diagnosis were approximately fifteen times more likely to develop diabetes [(OR 15.647) 95% CI, 4.075-60.07; P<0.001] than children who did not report an illness. However, logistic regression showed no significant relationship (p=0.096) between surgeries performed and the risk of developing diabetes. Other common diseases such as glucose-6-phosphate deficiency (G6PD), sickle cell disease/trait (SCD/SCT) and thalassemia were not found to be significantly associated with diabetes diagnosis.
### Table 3 Medical history of children with T1DM and healthy controls

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Control</th>
<th>P-value</th>
<th>OR (95% CI)</th>
<th>Logistic Regression P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td><strong>G6PD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>51</td>
<td>96.2</td>
<td>53</td>
<td>89.8</td>
<td>0.277(^{b})</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>3.8</td>
<td>6</td>
<td>10.2</td>
<td></td>
</tr>
<tr>
<td><strong>SCD/SCT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>45</td>
<td>84.9</td>
<td>55</td>
<td>93.2</td>
<td>0.155(^{a})</td>
</tr>
<tr>
<td>Yes</td>
<td>8</td>
<td>15.1</td>
<td>4</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td><strong>Thalassemia/ Trait</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>51</td>
<td>96.2</td>
<td>58</td>
<td>98.3</td>
<td>0.602(^{b})</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>3.8</td>
<td>1</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td><strong>Surgeries</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>51</td>
<td>96.2</td>
<td>45</td>
<td>76.3</td>
<td>0.003(^{a})</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>3.8</td>
<td>14</td>
<td>23.7</td>
<td></td>
</tr>
<tr>
<td><strong>Child Illness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>50</td>
<td>94.3</td>
<td>27</td>
<td>45.8</td>
<td>&lt;0.001(^{b})</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>5.7</td>
<td>32</td>
<td>54.2</td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\) Chi Squared, \(^{b}\) Fisher Exact

G6PD, Glucose-6-Phosphate deficiency; SCD/SCT, Sickle-cell disease/ Sickle-cell trait

Pre and post-natal history shown in Table 4 revealed that mothers of T1DM children were more likely to have had gestational diabetes (GDM) (p=0.053) and to have used medication during pregnancy than mothers with healthy children. Logistic regression analysis showed a significant but weak association (OR 1.7, 95% CI,(1.086-2.637)) between maternal use of medication and the risk of offspring’s developing diabetes; no significant relationship was found for mothers with GDM (p=0.065). Rates of pregnancy complications, gestational hypertension or prescribed drug use and exposure to toxins were not found to be significantly associated with diabetes diagnosis.
Table 4 Pre and postnatal maternal history

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th></th>
<th></th>
<th>P-Value</th>
<th>OR (95% CI)</th>
<th>Logistic Regression P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy Complications</td>
<td>Yes</td>
<td>7</td>
<td>13.2</td>
<td>11</td>
<td>18.6</td>
<td>0.984 (0.276-3.504)</td>
</tr>
<tr>
<td>Gestational DM</td>
<td>Yes</td>
<td>4</td>
<td>7.5</td>
<td>12</td>
<td>20.3</td>
<td>3.220 (0.932-11.127)</td>
</tr>
<tr>
<td>Gestational HTN</td>
<td>Yes</td>
<td>3</td>
<td>5.7</td>
<td>9</td>
<td>15.5</td>
<td>3.685 (0.774-17.53)</td>
</tr>
<tr>
<td>Medication use during pregnancy</td>
<td>Yes</td>
<td>12</td>
<td>22.6</td>
<td>8</td>
<td>13.6</td>
<td>1.704 (1.086-2.637)</td>
</tr>
<tr>
<td>Smoking/Drug use during pregnancy</td>
<td>Yes</td>
<td>1</td>
<td>1.9</td>
<td>2</td>
<td>3.4</td>
<td>0.868 (0.05-13.947)</td>
</tr>
<tr>
<td>Toxin/Radiation Exposure in pregnancy</td>
<td>Yes</td>
<td>1</td>
<td>1.9</td>
<td>3</td>
<td>5.1</td>
<td>2.400 (0.213-27.081)</td>
</tr>
</tbody>
</table>

"a Chi Squared, b Fisher Exact

DM, diabetes mellitus; HTN, hypertension

Investigation into the families past medical history identified children with T1DM to be more likely to have mothers with T2DM (p=0.053) as shown in Table 5, but a family history of T1DM was rarely reported in either group. There was a trend towards a significant relationship between maternal hypertension and diabetes (p= 0.095). However, logistic regression analysis did not reveal a significant and independent relationship between parental hypertension and diabetes.
Table 5 Parental history of diabetes and hypertension

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th></th>
<th>Cases</th>
<th></th>
<th>P-Value</th>
<th>Logistic Regression P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal Hx T1DM</td>
<td>No</td>
<td>53</td>
<td>100</td>
<td>59</td>
<td>100.0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Paternal Hx T1DM</td>
<td>No</td>
<td>52</td>
<td>98.1</td>
<td>58</td>
<td>98.3</td>
<td>1.000^b</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>1</td>
<td>1.9</td>
<td>1</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>Maternal Hx T2DM</td>
<td>No</td>
<td>53</td>
<td>100</td>
<td>53</td>
<td>91.4</td>
<td>0.058^b</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>8.6</td>
<td></td>
</tr>
<tr>
<td>Paternal Hx T2DM</td>
<td>No</td>
<td>47</td>
<td>88.7</td>
<td>51</td>
<td>86.4</td>
<td>0.781^a</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>6</td>
<td>11.3</td>
<td>8</td>
<td>13.6</td>
<td></td>
</tr>
<tr>
<td>Maternal Hx Hypertension</td>
<td>No</td>
<td>53</td>
<td>100</td>
<td>54</td>
<td>91.5</td>
<td>0.059^a</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>Paternal Hx Hypertension</td>
<td>No</td>
<td>53</td>
<td>100</td>
<td>57</td>
<td>96.6</td>
<td>0.497^b</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3.4</td>
<td></td>
</tr>
</tbody>
</table>

^aMann Whitney, ^b Chi Squared

Hx, history; T1DM, Type 1 Diabetes; T1DM, Type 2 Diabetes

No significant difference between children with T1DM and their healthy controls was found for infant feeding practices. Approximately 32.8% of the case group and 17% of the control children were breastfed beyond 18 months of age (see Table 6).
3.5 Discussion

This study is the first of its kind to report on the lifestyle and medical factors associated with T1DM in Bahrain. Although this study was unable to fully examine the role of genetics in the etiology of diabetes, it appears to support the role of infection as a potential trigger for T1DM, with just over half of the children with T1DM having reported suffering from an illness prior to diagnosis. The role of infection in the pathogenesis of T1DM has been studied extensively in both animal models (114-117) and in epidemiological studies (118, 119) (refer to Chapter 1, Environmental factors). In particular, certain enteroviruses have been found to cause...
beta-cell destruction (120) and can lead to T1DM. However caution is advised when interpreting the results of this study due to the relatively small sample size and potential bias introduced in the selection method.

The role of bacterial involvement either as a protective mechanism or an instigator in the development of T1DM has also been researched in recent years (121). The “hygiene theory” previously mentioned supports the notation that improper priming of the immune system as a result of decreased exposure to infections is correlated with a rise in T1DM, supported by studies that have shown a high incidence in first born children who are less exposed to infections than their siblings, and in rural, less crowded areas, as opposed to urban areas (52, 122). The “trigger theory” supports the notion that microbes trigger a cascade of autoimmune processes that ultimately leads to the destruction of beta-cells (121). The role of gut microbiota have also been investigated as a possible trigger with the proposed mechanism involving an interplay between three risk factors: abnormal intestinal microbiota, a leaky mucosal barrier also known as “leaky gut”, and alteration in intestinal immune response described by Vaarla and colleagues as being the “perfect storm” for T1DM development (123). Whilst the mechanism is unclear, changes in the microbiota appear to affect the development of T1DM as demonstrated in animal models (124-126) where the possible protective effect of certain gut microbes has also been shown. In particular studies on mice have shown that feeding the probiotic lactobacillus casei to non-obese mice prevented the development of diabetes and improved immune response (124). In a study conducted by Calcinaro et al, non-obese diabetic female mice were fed an oral dose of the probiotic VSL#3 three times a week from 4 weeks of age, which prevented the development of diabetes and was associated with an increase in the production of interleukin-10 (IL-10) (125). The probiotic induced IL-10 lymphocytes (an anti-inflammatory cytokine) which were
found in the spleen and the pancreas of the supplemented mice and appeared to confer a protective effect on the beta cells down regulating destructive autoimmune insulitis (125). Similar results were seen in rats fed lactobacillus casei and lactobacillus acidophilus with regards to the progression of induced T2DM against a background of a high fructose diet (126). In the latter study the authors were able to demonstrate a significant delay in the onset of glucose intolerance and hyperglycemia amongst other parameters tested (126).

The aforementioned ‘leaky gut’ is characterized by abnormalities in the intraepithelial junctions in the gastric mucosal barrier which are thought to allow the passage of antigens that are normally contained in the gut. It is hypothesized that these antigens, exposed to the intestinal immune system, trigger an autoimmune response that ultimately leads to the destruction of beta cells and development of T1DM (123). Interestingly, bovine serum albumin (BSA) found in cow’s milk protein (as mentioned in Chapter 1) is also hypothesized to trigger autoimmunity and studies on newly diagnosed children with T1DM have found a higher level of BSA antibodies compared to their healthy counterparts (43-45). The Trial to Reduce IDDM in the Genetically at Risk (TRIGR) study is currently investigating whether eliminating cow’s milk protein and weaning infants to a highly hydrolyzed formula can reduces the risk of T1DM later in childhood (127). The study is a double-blinded, prospective, placebo controlled intervention trial involving over 15 countries and 77 centers that commenced in 2007. It has recruited 2160 newborns with a first degree relative with T1DM. The study, which ends in 2017, is based on encouraging pilot test results which demonstrated a 50% reduction in cell autoimmunity in children who received the hydrolyzed formula as opposed to a cow’s milk formula (128).

Although children with diabetes in the current study were more likely to have undergone surgery, no details were given in the DRF as to the type of surgery performed limiting the
conclusions which could be drawn. Our findings contrast with those of Cardwell et al (129) who reported no increased risk of T1DM in children who had undergone tonsillectomies or adenoidectomies. The study gathered information from four hospital databases in Northern Ireland and included 25,488 children who had undergone either or both procedures (<15 years of age). Children who had undergone one or both of these surgical procedures, and who had a diagnosis of the T1DM, were identified to determine the incidence rate of diabetes. Standardized incidence ratios were then calculated which showed no significant association between those that have undergone either or both procedures and an increased risk in the development of T1DM. The authors acknowledge however, that the incidence rate of T1DM may have been underestimated since there is a possibility that not all the cases were correctly identified and not all possible confounding variables could be adjusted for via this design, perhaps contributing to the lack of association seen.

The existing relationship between the intrauterine environment and diabetes occurrence cannot be ruled out as mothers of children with T1DM in the current study were more likely to have T2DM, GDM, or a family history of GDM although it must be noted that far more mothers in the sampled cohort did not have gestational diabetes. Penderson (130) was the first to describe the association between infant birth weight and length, and maternal diabetes. Subsequent studies further examined the in-utero metabolic effects (130-132) suggesting that even minor changes in the equilibrium of the intrauterine environment, in particular maternal hyperglycemia, may have long-term effects extending beyond the perinatal period (133). Congenital rubella is the only known virus that directly causes T1DM in the offspring (134, 135) but studies have also implicated the Coxsackie B virus in the etiology of T1DM (47, 136).
There are several studies looking into the association of breastfeeding and development of T1DM (58, 59) although the high rates of breastfeeding across both groups (approximately 80% (n=112) of mothers breastfed for longer than 6 months) in the current study made it impossible to investigate any role for infant feeding in diabetes development in this sample. In the most recent study looking at the breastfeeding practices of women in Bahrain (137), they found the overall rate of breastfeeding, although not exclusive, in a sample of 408 children less than 2 years of age to be as high as 95% with a mean duration of 7.6± 5.4 months. A previous study found 34% of infants under the age of 4 months to have been exclusively breastfed in Bahrain (138). Such a high rate of breastfeeding is thus unlikely to be a discriminating factor in the development of T1DM in this specific population.

However in other populations where rates of breastfeeding are more variable both positive and negative associations have been suggested (58, 60, 62). Breastfeeding has been reported to confer a beneficial effect for T1DM development via mechanisms including protection against enteroviruses (60) or delayed introduction of cow’s milk protein and/or gluten containing foods with longer breastfeeding durations (58, 60) but other studies have found no significant relationship between breastfeeding and development of T1DM (62). In fact, some studies have hypothesized that since breast milk has low levels of vitamin D prolonged exclusive breastfeeding may represent a risk factor for diabetes development and that supplementation with vitamin D may be required to confer a protective effect (63). The retrospective nature of the current study meant that vitamin D levels from the mother and child were not available to allow the authors to further investigate the role of vitamin D and the risk of T1DM. However a recent study in Bahrain (19) (refer to Chapter 1; Common Nutritional Related Deficiencies) found 88.8% of the mothers and 90.3% of their newborns to have a vitamin D level below 50 nmol/l
In order to fill this gap in knowledge a prospective study of a small but representative sample of children was conducted and is described in Chapter 5.

3.5.1 LIMITATIONS OF THE STUDY

This study was limited in that data on the case group was collected retrospectively and therefore restricted to the routinely collected data available within the unit. No follow up of the children in the case group occurred and only some of the medical records were examined to obtain data that was incomplete in the DRF form. The control children were selected from LHC's on the basis that they were free of any chronic disease and essentially healthy. However, a control group could have been selected from within the hospital comparing the diets of children with T1DM to other children with chronic diseases excluding diabetes.

The relatively small sample size of the study population and the fact that no official sample size calculations were undertaken but instead selection was based on whether or not the children met the inclusion criteria does indeed limit any conclusions that may be drawn and can introduce bias. Hence, caution is required when generalizing these results due to the non-probability nature of the small sample size.

Although mothers of T1DM children appeared to have used more medication during pregnancy compared to mothers with healthy children, no detailed information as to the type of medication used was given limiting any conclusions that may be drawn. As a result the authors were not able to further investigate the role of genetics or environmental triggers in the development of diabetes. Similarly the role of breastfeeding, although previously postulated, could not be rigorously investigated due to the general high rates of prolonged breastfeeding in...
the cohort. The authors were also unable to investigate the possible link between vitamin D and risk of T1DM since this was not routinely measured in cases and controls at the time of the study.

3.5.2 AREAS OF FURTHER RESEARCH

The results of this study have laid the foundations for informing future prospective studies that aim to investigate the role that enteroviruses play in the development of T1DM as well as the potential protective role microbiota may play in the development of T1DM in Bahrain and in the Middle Eastern region. Furthermore, there is a need to investigate the intergenerational transfer of risk via maternal impaired glucose tolerance.

3.6 CONCLUSION

Children with T1DM were more likely to have suffered from an illness before diagnosis of T1DM than their healthy counterparts. This self-report analysis could not fully elucidate the role of genetics or environmental triggers in the development of diabetes nor were the authors able to expand on the role of infant feeding practices due to the high prevalence of breastfeeding in both groups. However, the preliminary findings have helped shed light on this underresearched population and highlighted the need for further work investigating the potential role infections and in particular gut microbiota play in the development of T1DM.
4.0 DIETARY INTAKE OF CHILDREN WITH T1DM & THEIR HEALTHY COMPARATORS

4.1 INTRODUCTION

There are no studies that have looked into the dietary intake of children with diabetes in Bahrain and only a few studies have examined the diet of children (139-143) and adolescents (141, 142, 144-147) with diabetes elsewhere, most of which are dated. The results of these studies, conducted primarily in Europe and the United States, showed that children with T1DM exceeded total fat recommendations, in particular saturated fat (139-142) and that children’s intakes of fiber were well below those recommended (140, 142). Some studies also found children to be consuming an insufficient amount of vitamin D (140, 141). Studies looking at the diet of adults with T1DM have shown similar trends, with these adults consuming a diet high in fat and in particular saturated fats coupled with a high intake of protein. Carbohydrate intake however was found to be lower than the recommended in one study of 571 adults with T1DM and 696 controls, aged between 19 to 56 years (148). According to the second National Health and Nutrition Examination Survey, NHANES II, in the United States, fiber intake in adults over 19 years of age (not specifically those with diabetes) was found to be below the recommendations with an average intake of approximately 11g/day (149). The report on the achievements of the American Diabetes Association recommendations for adults with diabetes for the years 1999-2002 based on the NHANE survey found that only 18.3% of adults with diabetes consumed the recommended amount of fiber (150).
T1DM is associated with an increased risk for the development of micro- and macrovascular complications like retinopathy, neuropathy, and nephropathy (151). People suffering from diabetes are also at a higher risk of developing cardiovascular disease than those without diabetes (152, 153). As such, compliance to dietary recommendations is especially important in children with diabetes as the development of atherosclerosis may begin in childhood and adolescence (154-157). The results of the DCCT trial showed a reduction in the risk of developing diabetic retinopathy, nephropathy, and neuropathy (91). The benefits of intensive therapy delayed and slowed down the progression of microvascular complications. (Refer to Chapter 1: Management of T1DM; p.33).

4.2 METHODS

4.2.1 STUDY DESIGN

The dietary intake of children from the same case-control study described in Chapter 3 was analyzed to allow the impact of disease to be investigated independently of other important factors like age and weight. A single 24 hour recall routinely collected for children with T1DM by a dietitian or nutritionist at the time of admission was made available for analysis. A 24 hour recall was prospectively taken by a dietitian from control children recruited at the LHC’s

4.2.2 INCLUSION CRITERIA

Refer to Chapter 3 for inclusion criteria (section 3.3.1 p. 46).
4.2.3 Analysis

The 24-hour recalls were analyzed using the Food Processor Software SQL version 10.70 (ESHA Research). Dietary intake was expressed as absolute nutrient intake and percent achievement of the U.S Recommended Dietary Allowance (RDA) (158) by age group. A comparison between the percent of cases and controls achieving the recommended dietary intakes (Acceptable Micronutrient Distribution Range (AMDR) established based on Dietary Reference Intakes (DRI)) and those meeting the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines are shown in Table 7. The data was statistically analyzed using SPSS version 21 (SPSS Inc.). Normality was tested for using Kolmogorov-Smirnov test and the independent T-tests and Mann-Whitney tests were used as appropriate to compare intakes between cases and controls. A P-value of less than 0.05 was considered statistically significant.

4.3 Results

In total, 50 children with T1DM (cases) and 55 healthy comparators (controls) were included. The median age was 9.5 (8.0-11.0) years and 9 (7.0-10.0) years respectively. The groups were matched for age, gender and BMI.
Table 7 Percent of cases and controls achieving the recommended dietary intakes for macro- and micronutrients and meeting the ISPAD guidelines

<table>
<thead>
<tr>
<th>Dietary Reference Intakes (RDA) or Acceptable Micronutrient Distribution Range (AMDR) where applicable (159)</th>
<th>% (n) of Cases within guidelines</th>
<th>% (n) of Controls within guidelines</th>
<th>P</th>
<th>ISPAD Guidelines (160)</th>
<th>% of Cases within guidelines</th>
<th>% of Controls within guidelines</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate, % 45-65 25-35 10-30</td>
<td>88 (44) 60 (30) 94 (47)</td>
<td>78(43) 55 (30) 89 (49)</td>
<td>0.182 0.573 0.369</td>
<td>50–55 30–35 10–15</td>
<td>24 (12) 32 (16) 62 (31)</td>
<td>22(12) 27 (15) 53(29)</td>
<td>0.790 0.919 0.338</td>
</tr>
<tr>
<td>Fat, % 7-10</td>
<td>32(16)</td>
<td>30 (16)</td>
<td>0.746</td>
<td>&lt;10</td>
<td>78 (39)</td>
<td>87(48)</td>
<td>0.322</td>
</tr>
<tr>
<td>Protein , % ≤ 10</td>
<td>100 (50)</td>
<td>100(55)</td>
<td>-</td>
<td>&lt;10</td>
<td>100 (50)</td>
<td>100(55)</td>
<td>-</td>
</tr>
<tr>
<td>Saturated fat and trans fatty acids, % 10-15</td>
<td>22 (11)</td>
<td>18 (10)</td>
<td>0.625</td>
<td>&gt;10 (up to 20 % total)</td>
<td>22 (11)</td>
<td>22(12)</td>
<td>0.616</td>
</tr>
<tr>
<td>Polyunsaturated fat, % 25 grams (children 4-8yrs) 31 grams (males, 9-13yrs) 26 grams (females,9-13yrs)</td>
<td>0</td>
<td>1.8 (1)</td>
<td>0.338</td>
<td>2.8–3.4 grams per megajoule*</td>
<td>0</td>
<td>1.8 (1)</td>
<td>0.338</td>
</tr>
<tr>
<td>Monounsaturated fat, % 1.2 g/day of sodium (children 4-8yrs) 1.5 g/day (males &amp; females, 9-13 yrs.)</td>
<td>26 (13)</td>
<td>29 (16)</td>
<td>0.723</td>
<td>&lt;6 g/day of sodium chloride (2400mg sodium)</td>
<td>68 (34)</td>
<td>82 (45)</td>
<td>0.101</td>
</tr>
</tbody>
</table>

*1 megajoule =239 Kilocalorie ¹ significance tested using Pearson chi-squared
ENERGY AND MACRONUTRIENT INTAKE

The age and gender appropriate estimated average requirement (EAR) for energy was met by 96% of the case group and 75% of the control group as shown in Table 8. Children with T1DM met their RDA for carbohydrates whereas healthy controls consumed 81% of their requirements (p<0.001). Both groups failed to meet the RDA values for dietary fiber intake but no significant difference was observed between mean intakes when expressed as a percentage of the recommendations (p<0.207). Children with T1DM consumed about 2.5 times their RDA for protein whereas their healthy counterparts consumed 2 times the RDA.

Table 8 Mean energy intakes and macronutrient distribution in children with (n=50) and without (n=55) T1DM

<table>
<thead>
<tr>
<th></th>
<th>Case</th>
<th>Control</th>
<th>P-Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean % RDA†</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Energy (kcals)</td>
<td>2023.16 (493.49)</td>
<td>96 (28)</td>
<td>1542.29 (505.22)</td>
</tr>
<tr>
<td>Calories from Fat (kcal)</td>
<td>622.32 (206.44)</td>
<td>108 (45)</td>
<td>437.58 (177.97)</td>
</tr>
<tr>
<td>Calories from Saturated Fat (kcal)</td>
<td>154.74 (69.13)</td>
<td>85 (49)</td>
<td>109.22 (66.54)</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>71.75 (21.37)</td>
<td>249 (112)</td>
<td>54.22 (23.74)</td>
</tr>
<tr>
<td>% energy, Protein</td>
<td>13.80 (13.65)</td>
<td>13.78 (3.08)</td>
<td></td>
</tr>
<tr>
<td>Carbohydrates(g)</td>
<td>300.22 (78.27)</td>
<td>103 (30)</td>
<td>225.87 (77.60)</td>
</tr>
<tr>
<td>% energy, Carbohydrates</td>
<td>55.84 (7.10)</td>
<td>57.70 (7.80)</td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>Control</td>
<td>P-Value†</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>---------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>Mean % RDA†</td>
<td>Mean (SD)</td>
<td>Mean % RDA†</td>
</tr>
<tr>
<td>Dietary fiber (g)</td>
<td>12.88 (5.26)</td>
<td>10.16 (5.71)</td>
<td>0.064a</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>69.15 (22.94)</td>
<td>48.93 (19.82)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>% energy, Fat</td>
<td>29.64 (20.68)</td>
<td>28.44 (7.64)</td>
<td>0.376b</td>
</tr>
<tr>
<td>Saturated Fat (g)</td>
<td>17.19 (7.68)</td>
<td>12.14 (7.39)</td>
<td>0.002a</td>
</tr>
<tr>
<td>% energy, Saturated Fat</td>
<td>7.68 (7.17)</td>
<td>7.09 (3.78)</td>
<td>0.280b</td>
</tr>
<tr>
<td>Monounsaturated Fats (g)</td>
<td>19.75 (8.08)</td>
<td>13.72 (8.21)</td>
<td>0.001a</td>
</tr>
<tr>
<td>% energy, Mono Fat</td>
<td>10.60 (8.09)</td>
<td>8.17 (4.24)</td>
<td>0.128b</td>
</tr>
<tr>
<td>Polyunsaturated Fats (g)</td>
<td>9.94 (4.23)</td>
<td>7.12 (4.24)</td>
<td>0.007a</td>
</tr>
<tr>
<td>% energy, Poly Fat</td>
<td>5.10 (4.10)</td>
<td>4.15 (2.05)</td>
<td>0.169b</td>
</tr>
</tbody>
</table>

SD Standard Deviation; °Mann Whitney; °T-test; †P-value for % mean RDA where available or mean absolute intakes; ‡Mean percent intake relative to Recommended Dietary Allowance (RDA);

The percent energy (% E) intake from protein, carbohydrate and fat for the two groups is also shown in Table 8. No significant difference was observed for intake of macronutrients (expressed as percentage of total energy intake) between the groups. Children with and without T1DM were within the AMDR range for macronutrients. The mean percent energy intake from
polyunsaturated fats was below the recommendation in both groups and the mean percent energy intake of monounsaturated fats was slightly higher than the recommendation in children with T1DM compared with healthy children. However when compared to the ISPAD guidelines specific to children and adolescents with T1DM, both children with T1DM and their healthy counterparts were found to consume more than the recommended percent energy intake from carbohydrates (50-55%) although they were within the recommendations for % E of fat and protein (158). The % E from saturated and polyunsaturated fats was also within the ISPAD guidelines. Children with T1DM achieved the recommended % E from monounsaturated fatty acids although the control group was found to consume less than the recommended proportion.

Under reporting of energy intake was assessed using Torun cutoffs (161). Table 9 shows the number and percent of children that were found to have under-reported energy intake. When under-reporters were excluded and data re-analyzed the results revealed similar trends in energy and macronutrient intakes (data not shown). Both children with T1DM and their healthy counterparts consumed an excess amount of sodium and protein but failed to meet vitamin D and calcium requirements. Furthermore, children with T1DM also consumed a significantly higher amount of energy and fat, including saturated, polyunsaturated, and monounsaturated fats than the control group. Both adequately reporting children with T1DM and adequately reporting healthy controls were within the % E of fat, carbohydrates and proteins when compared to the AMDR and were within recommendations for saturated, and polyunsaturated fatty acids. Similar to the results, for the whole sample children with T1DM slightly exceeded % E recommendations for monounsaturated fats as compared to the controls (10.63% vs. 8.10%).
Table 9 Number and percentage of cases and controls that under reported energy intake as assessed by the Torun Cutoffs (161)

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Control</th>
<th>Pearson Chi-Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate under-reporting</td>
<td>30</td>
<td>28</td>
<td>0.017</td>
</tr>
<tr>
<td>Under-reported</td>
<td>10</td>
<td>27</td>
<td></td>
</tr>
</tbody>
</table>

4.3.1 Vitamin Intakes

Vitamin intakes between the groups, shown in Table 10, revealed that children with T1DM consumed a significantly higher amount of vitamin B1 (p=0.034), vitamin B3 (p=0.016), vitamin B6 (p=0.006) and vitamin A (RAE) (p=0.007) as compared to healthy children but these differences were no longer significant when adjusted for energy intake. The vitamin A intakes, although highly variable, were a true reflection of the diversity of diets within this group and specifically the high intakes of vitamin A achieved by those children consuming liver; a common food for some families in the region. After adjusting for energy, vitamin K intake was found to be higher amongst healthy children as compared to those with T1DM (p=0.016). The foods contributing most to vitamin K intake appeared to be oils used in fried foods (e.g. French fries, potato wedges) and dairy products (milk, yogurt, cream cheese) as well as other miscellaneous foods like biscuits, chocolate spread etc... No significant difference was observed between children with T1DM and healthy control groups for vitamin D intake (unadjusted; p=0.061; energy adjusted p = 0.456, respectively) and both groups failed to meet the RDA requirements. Similarly no significant difference was observed between the groups for folate consumption (p=0.095) and again both groups failed to meet the recommended folate intake regardless of diabetes status requirements for vitamin C were met or exceeded (non-significant between groups with or without energy adjustment).
Table 10 Distribution of vitamin intakes* between children with and without T1DM (n=50 and n=55 respectively).

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Case Mean (SD)</th>
<th>Case % RDA†</th>
<th>Control Mean (SD)</th>
<th>Control % RDA‡</th>
<th>P-Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (RAE)</td>
<td>385.88 (768.88)</td>
<td>72</td>
<td>194.32 (238.47)</td>
<td>41</td>
<td>0.007a</td>
</tr>
<tr>
<td>Vitamin D (mcg)</td>
<td>0.74 (0.86)</td>
<td>15</td>
<td>0.55 (0.70)</td>
<td>11</td>
<td>0.061a</td>
</tr>
<tr>
<td>Vitamin E (mg)</td>
<td>2.02 (1.08)</td>
<td>21</td>
<td>1.68 (1.48)</td>
<td>19</td>
<td>0.122a</td>
</tr>
<tr>
<td>Vitamin K (mcg)</td>
<td>11.97 (13.06)</td>
<td>20</td>
<td>8.86 (19.15)</td>
<td>16</td>
<td>0.001a</td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>133.66 (119.7)</td>
<td>352</td>
<td>88.84 (92.18)</td>
<td>277</td>
<td>0.127a</td>
</tr>
<tr>
<td>Vitamin B1 (mg)</td>
<td>0.94 (0.46)</td>
<td>120</td>
<td>0.70 (0.42)</td>
<td>93</td>
<td>0.034a</td>
</tr>
<tr>
<td>Vitamin B2 (mg)</td>
<td>1.11 (0.70)</td>
<td>146</td>
<td>0.92 (0.85)</td>
<td>128</td>
<td>0.0877a</td>
</tr>
<tr>
<td>Vitamin B3 (mg)</td>
<td>13.43 (7.36)</td>
<td>127</td>
<td>9.20 (6.81)</td>
<td>95</td>
<td>0.016a</td>
</tr>
<tr>
<td>Vitamin B6 (mg)</td>
<td>1.35 (0.60)</td>
<td>163</td>
<td>0.94 (0.62)</td>
<td>121</td>
<td>0.006a</td>
</tr>
<tr>
<td>Vitamin B12 (mcg)</td>
<td>2.64 (3.57)</td>
<td>173</td>
<td>1.58 (1.86)</td>
<td>107</td>
<td>0.102a</td>
</tr>
<tr>
<td>Folate (mcg)</td>
<td>186.59 (107.63)</td>
<td>71</td>
<td>136.77 (95.73)</td>
<td>56</td>
<td>0.095a</td>
</tr>
</tbody>
</table>

*Vitamin intakes analysis did not include dietary supplements. SD Standard Deviation; aMann Whitney; bT-test cP-value for % mean RDA where available or mean absolute intakes; †Mean percent intake relative to Recommended Dietary Allowance (RDA).
Table 11 Distribution of Vitamin Intakes expressed per 1000 kcals in children with and without T1DM (n=50 & n= 55 respectively).

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Case Mean (SD)†</th>
<th>Control Mean (SD)†</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (RAE)</td>
<td>191.96 368.33</td>
<td>141.05 219.29</td>
<td>0.087 a</td>
</tr>
<tr>
<td>Vitamin D (mcg)</td>
<td>0.37 0.42</td>
<td>0.38 0.45</td>
<td>0.456 a</td>
</tr>
<tr>
<td>Vitamin E - Alpha Toco (mg)</td>
<td>1.03 .59</td>
<td>1.09 1.01</td>
<td>0.362 a</td>
</tr>
<tr>
<td>Vitamin K (mcg)</td>
<td>5.63 5.80</td>
<td>5.91 14.85</td>
<td><strong>0.016 a</strong></td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>65.02 55.45</td>
<td>55.78 51.03</td>
<td>0.223 a</td>
</tr>
<tr>
<td>Vitamin B1 (mg)</td>
<td>0.47 0.19</td>
<td>0.47 0.23</td>
<td>0.827 a</td>
</tr>
<tr>
<td>Vitamin B2 (mg)</td>
<td>0.56 0.34</td>
<td>.64 0.66</td>
<td>0.893 a</td>
</tr>
<tr>
<td>Vitamin B3 (mg)</td>
<td>6.72 3.61</td>
<td>6.00 3.40</td>
<td>0.326 a</td>
</tr>
<tr>
<td>Vitamin B6 (mg)</td>
<td>0.68 0.27</td>
<td>0.63 0.37</td>
<td>0.097 a</td>
</tr>
<tr>
<td>Vitamin B12 (mcg)</td>
<td>1.32 1.68</td>
<td>1.08 1.22</td>
<td>0.464 a</td>
</tr>
<tr>
<td>Folate (mcg)</td>
<td>91.63 46.98</td>
<td>93.30 60.64</td>
<td>0.985 a</td>
</tr>
</tbody>
</table>

†SD Standard Deviation; *Mann Whitney
4.3.2 Mineral Intakes

The mineral intakes of children with and without T1DM are shown in Table 12. It was observed that children with T1DM consumed significantly higher amounts of iron (p<0.001) and potassium (p<0.001) as compared to their healthy counterparts. The control group met the RDA for iron but children with T1DM consumed on average 1.5 times their requirement and potassium intakes were well below the requirements in both groups. After adjustment for energy intakes, the differences in potassium but not iron intakes remained significant (p=0.005 and p=0.773 respectively). A significant difference was observed between the groups for calcium intake (p=0.008) with children with T1DM consuming more compared with healthy children, however this difference disappeared after adjusting for energy (p=0.218). Children with T1DM and healthy controls exceeded recommendations for sodium by approximately 1.4 times and 1.1 times the RDA requirements respectively although no significant difference was noted between the groups (p=0.402) and this remained non-significant after adjusting for energy.
Table 12 Distribution of mineral intakes between children with (n=50) and without T1DM (n=55)

<table>
<thead>
<tr>
<th>Mineral (mg)</th>
<th>Case</th>
<th>Control</th>
<th>P-Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>% RDA†</td>
<td>% RDA†</td>
<td>% RDA†</td>
</tr>
<tr>
<td>Calcium</td>
<td>609.34 (266.33)</td>
<td>411.44 (237.31)</td>
<td>56 (27)</td>
</tr>
<tr>
<td>Iron</td>
<td>12.57 (5.57)</td>
<td>9.12 (4.97)</td>
<td>151 (65)</td>
</tr>
<tr>
<td>Magnesium</td>
<td>143.50 (76.70)</td>
<td>93.99 (53.08)</td>
<td>71 (44)</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>903.15 (272.26)</td>
<td>598.52 (261.31)</td>
<td>97 (45)</td>
</tr>
<tr>
<td>Potassium</td>
<td>1751.03 (859.98)</td>
<td>1025.22 (573.85)</td>
<td>40 (20)</td>
</tr>
<tr>
<td>Sodium</td>
<td>2390.15 (1394.55)</td>
<td>1851.60 (1261.08)</td>
<td>138 (97)</td>
</tr>
<tr>
<td>Zinc</td>
<td>6.14 (4.07)</td>
<td>4.12 (2.21)</td>
<td>90 (69)</td>
</tr>
</tbody>
</table>

SD Standard Deviation; ‡Mann Whitney

†P-value for % mean RDA where available or mean absolute intakes; †Mean percent intake relative to Recommended Dietary Allowance (RDA)
Table 13 Distribution of mineral intakes expressed per 1000 kcals between children with (n=50) and without T1DM (n=55)

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Case Mean (SD)</th>
<th>Control Mean (SD)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg)</td>
<td>308.61 (132.96)</td>
<td>281.33 (157.99)</td>
<td>0.218a</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>6.19 (2.30)</td>
<td>6.18 (2.67)</td>
<td>0.773a</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>69.93 (28.57)</td>
<td>64.15 (31.35)</td>
<td>0.100a</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
<td>458.02 (122.92)</td>
<td>408.66 (147.52)</td>
<td>0.048b</td>
</tr>
<tr>
<td>Potassium (mg)</td>
<td>861.53 (339.48)</td>
<td>690.83 (313.36)</td>
<td>0.005a</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>2390.15 (1394.55)</td>
<td>1851.60 (1261.08)</td>
<td>0.783a</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>2.99 (1.57)</td>
<td>2.72 (1.12)</td>
<td>0.468a</td>
</tr>
</tbody>
</table>

a SD Standard Deviation; "Mann Whitney"; b T-test.

4.4 DISCUSSION

This study is the first of its kind to evaluate the dietary intakes of Bahraini children with diabetes and compare them to those of matched children without the disease. The results of this study show some similarities with other work reporting the dietary intake of healthy school children in Bahrain (8-10). Of particular note children with T1DM consumed a significantly higher intake of energy and total fat including saturated, polyunsaturated and monounsaturated fatty acids, than children without T1DM. Excess intake of fat can lead to an acceleration of blood vessels damage, leading to the rapid progression of atherosclerosis and cardiovascular disease (162) and is of particular concern in children with diabetes since people with T1DM are thought to be 10 times more likely to develop cardiovascular disease as compared to an age matched healthy population (163, 164).
Both children with T1DM and healthy controls failed to meet fiber requirements, achievement of which is essential for maintenance of proper bowel health. An increased intake of fiber can help improve glycemic control and insulin sensitivity in individuals with diabetes (165). Studies have shown that an optimal fiber intake can also decrease the risk of heart disease, certain cancers and type 2 diabetes mellitus, with suboptimal intakes of fruits and vegetables, whole-grains, legumes and nuts in the U.S. population cited as impeding health promotion and chronic disease prevention (165, 166). The low fiber intakes in the Bahraini cohorts may be a result of their low intakes of fruits and vegetables as well as whole grains and their choices of foods rich in fats and refined sugars, common dietary patterns previously reported in this age group (8, 10, 17).

High protein intakes in children with T1DM and their healthy counterparts is not surprising and substantiated by several other studies looking into dietary intake of children with diabetes (139). Similarly in a cross-sectional study looking at the dietary intake of school children aged 7-10 years in Bahrain, protein intake was found to be 2.5 times more than the recommended (10). Approximately 75% of the male and 66% of the female children in that study reported consuming fish, meat or poultry on a near daily basis (5-7 times a week), as compared to only 9% of males and females reporting daily consumption of eggs and a mere 2.5 and 2.8% of males and females respectively contributing to their protein intake via daily (or near daily) consumption of legumes (10).

Kidney disease is a major risk factor for people suffering from diabetes (167) and therefore maintaining protein consumption within the recommendations is important because excessive intakes have been associated with worsening glomerular filtration rates (GFR) in
people suffering from chronic kidney disease (168). Furthermore, excessive intakes of protein may be converted to fat which could increase the risk of obesity later in life (169).

Vitamin D intakes were well below those recommended in both groups with no significant difference between the groups. Failure to find an association between vitamin D intakes and diabetes, as have been postulated previously, could be due to variations in study design and methodologies, differences in sample size or the sample population studied. Specifically the current study only assessed current intakes of vitamin D in children newly diagnosed with T1DM and their non-diabetic counterparts rather than attempting to quantify early-life exposure to vitamin D via diet or supplements or actual vitamin D status which may be influenced by factors other than diet alone. Vitamin D status of a sample of children with T1DM will be described in Chapter 5. The ISPAD does not recommend the routine supplementation of vitamins and minerals unless there is a confirmed deficiency, and supplementation of vitamin D for young children is left to the discretion of a country’s national guidelines (164). However in Bahrain there are currently no national guidelines or protocols that guide physicians on how to manage vitamin D deficiency and management is left either to the individual physician or is carried out in accordance with hospital policy if one is made available.

Both children with T1DM and their healthy counterparts consumed an excess amount of sodium and had potassium intakes well below recommended levels. High sodium, low potassium diets in early childhood have been linked to hypertension later in adulthood (170). Excessive intake of sodium coupled with low intake of potassium is of particular concern in children with T1DM as it increases the risk of vascular damage and diabetes related complications.
4.4.1 LIMITATIONS OF THE STUDY

The current study was limited by the use of a single 24-hour dietary recall to assess dietary intake. The possibility of underreporting of food consumption in 24-hour dietary recalls due to recall bias and the inability to reflect day-to-day variations in intakes may be a potential confounder (191). It is recognized that food intake at the time of diagnosis in children with T1DM could have been impacted by the symptoms of the disease itself which, aside from excessive urination, includes excessive thirst and appetite (26). The use of dietary supplementation was not included in the dietary analysis due to inconsistencies in the naming and dosage of supplements used. Furthermore, as children were selected based on inclusion/exclusion criteria, bias must be acknowledged. Also, the relative small purposive non-probability based sample size limits conclusions that may be drawn. Nonetheless, this study provides support for endorsing existing dietary guidelines (164) which promote increased intakes of dietary fiber, fruit and vegetables and limited intakes of fats and salt for children with T1DM and investigating the barriers to adherence with this existing advice.

4.4.2 AREAS OF FURTHER RESEARCH

Future work should focus on designing prospective and intervention trials to improve the diet and lifestyle behaviors of Bahraini children with and without T1DM since there appears to be widespread deviation from the recommendations in this age group.
4.5 CONCLUSION

Children with T1DM and their healthy counterparts in Bahrain consumed protein and sodium above the recommendation but fiber intakes fell short of requirements. Calcium and vitamin D intakes were also below the RDA recommendations in both groups. The diet of children with T1DM differed from healthy controls in that they consumed a significantly higher amount of dietary fat. The results of this study highlight the need to continue to recommend and promote adherence with the existing ISPAD nutritional guidelines for children and adolescents with T1DM (164).
5.0 PROSPECTIVE STUDY ON CHILDREN WITH T1DM

5.1 INTRODUCTION

The purpose of this study was to investigate in more details the dietary and lifestyle behaviors of a small sample of newly diagnosed children with T1DM in the SMC hospital. This sub-study aims to provide greater quality of data rather than quantity data to add to that already gathered and described previously in Chapters 3 and 4.

5.2 EXPERIMENTAL DESIGN & METHODOLOGY

Children admitted at the SMC with a confirmed diagnosis of T1DM meeting the selection criteria from January to March 2014 were invited to participate in this prospective study. In total a convenience sample of 20 children were recruited during this period. No differences were seen in terms of gender, race, age, or BMI between the prospectively recruited children with T1DM and those in the previous case-control study.

5.2.1 STUDY AREA/SETTING

Information was gathered from the Pediatric Diabetes Unit which holds the completed Diabetes Registry Forms of newly diagnosed children. A vitamin D specific food frequency questionnaire and lifestyle questionnaire (Appendix 5 and 6) were administered face-to-face by a licensed dietitian in either the Pediatric Diabetes Unit or at the patient’s bed side.

5.2.2 STUDY SUBJECTS:

The study subjects were children aged 6-12 years receiving a confirmed diagnosis of T1DM and attending the Pediatric Endocrine Clinic from January to March 2014. All newly
diagnosed children with T1DM diabetes during this time period that met the inclusion criteria were invited to participate. Subjects were recruited directly onto the study at the time of admission or once they were taken to the wards where written consent was obtained (see Appendix 7).

The inclusion criteria for study subjects were as follows:

- Newly diagnosed children aged 6-12 years with a confirmed case of T1DM
- Informed, written consent from parents or legal guardian
- Attended at least one follow up appointment at the Pediatric Endocrine Unit

Children were excluded if they had T2DM, did not give consent or were not planning on following up in the SMC.

5.3 DATA COLLECTION METHODS:

Information on the newly diagnosed children was gathered from the existing Pediatric Diabetes Registry Form (refer to Chapter 3 and Appendix 1).

5.3.1 ANTHROPOMETRIC DATA

Measurements were taken using standard techniques by a trained health professional which included:

- Weight
- Height
- Waist circumference
- Triceps skin-fold thickness
Height and weight were measured using standardized techniques (171). BMI was calculated by taking the weight of the subject in kilograms and dividing it by the square of their height in meters. Triceps skinfold thickness and BMI are often used in clinical and epidemiological studied to measure adiposity (172, 173). Triceps skinfold thickness and waist circumference, were also measured by the diabetes nurse educators using standardized techniques (174). The measurements were taken on the subject standing in a relaxed manner, usually on the right hand side, although no statistical difference between measurements on either side of the arm have been found (175). The posterior midline of the upper arm, halfway between the shoulder and the elbow was identified; a vertical skin fold was then pinched and a caliper used to measure the fat fold.

5.3.2 Dietary data

The vitamin D specific food frequency questionnaire (see Appendix 5) was administered before the patient was discharged. A 24-hour recall was obtained from parents or legal guardians at the time of admission with the child present and two other 24-hour recalls (including one weekend) were taken by phone one week after the patient was discharged. The subjects were interviewed using a reverse chronological order interview method with the interviewer prompting the subject to describe the previous night’s evening snack, dinner, working back to what the subject consumed at breakfast. The interview was directed at the parents in conjunction with the child. As food in Bahrain is traditionally eaten as a family from one common dish, the individuals were asked to describe portion sizes and preparation methods for the foods eaten using commonly available household food items such as a 180 gram yogurt cup container which is equivalent to a measuring cup (240ml). For example, when the subject described eating rice, the interviewer prompted the individuals to explain approximately how many yogurt cups’ full of
rice was eaten. Teaspoons and tablespoons, also common household items, were also used to estimate portion size. In the absence of these measuring spoons, qahwa cups (traditional Arabic coffee cups) which hold approximately 50ml were used to approximate quantity. For example when chai karak (tea with milk) was identified as a beverage consumed, the interviewer asked how many qahwa cups of milk or sugar was added to the water.

The dietary information obtained was analyzed using the Food Processor Software SQL version 10.70 (ESHA Research) to provide an estimation of usual intake of key micro- and macronutrients. Dietary intake for vitamins and minerals were expressed in absolute mean intake and in energy-adjusted mean intakes expressed per 1000kcals.

Vitamin D intakes were assessed by administering an existing food frequency questionnaire (Appendix 5) which was used determine calcium and vitamin D intake (21). The original questionnaire was previously validated however modified to reflect local food items known to contain vitamin D including locally eaten fish. Vitamin D values were based on information from the Food Composition Tables for Arab Gulf Countries (176) and the Food Composition Tables for the Kingdom of Bahrain (177). Values for non-local foods (e.g. tuna and salmon) were obtained from the US Department of Agriculture (159).

The initial questionnaire asked how often the respondents had consumed a specified serving size based on the exchange list for diabetes (e.g. 1 cup of milk or yogurt, ½ cup of ice cream or pudding, 1oz of cheese etc.….) or unit of food on daily, weekly and monthly basis. The intake of vitamin D was then calculated by multiplying the frequency of consumption of each unit of food by vitamin D content of the specified portions; hence the average daily intake was calculated.
5.3.3 Serum Vitamin D Levels

Serum levels of vitamin D were measured using an aliquot of blood taken from routine blood collection before the patient was discharged. The blood sample was sent to Al-Jawhara Center in Bahrain to be analyzed by Ultra-Pressure Liquid Chromatography/ Mass Spectrometry (UPLC/MSMS method) and compared to the Salmaniya Medical Complex laboratory via chemiluminescence.

5.3.4 Lifestyle and Sunlight Exposure Data

Environmental factors affecting vitamin D status were assessed by a lifestyle and sunlight questionnaire (see Appendix 6) which was administered by a licensed dietitian at the patient’s bedside or at the Pediatric Diabetes Unit. The questionnaire was specifically developed for this study with the purpose of addressing any gaps in the data regarding factors that can impact vitamin D intake from sunlight. It specifically explored:

i) Living conditions and whether or not the patients lived in a flat or house and if the children played in a garden or patio.

ii) Personal practices such as the use of a veil in females and the degree of body exposure to sunlight.

iii) Other factors such as the use of sunscreen, multivitamin use and if the patient had had a suntan in the past year.

Outdoor sunlight exposure was also investigated and an average daily and yearly sunlight exposure was calculated.
5.3.5 Physical activity

Physical activity levels were assessed using the Child Physical Activity Questionnaire (CPAQ) (see Appendix 8). The questionnaire was administered to the parents or legal guardian and asked about the physical activities their child had undertaken in the past 7 days. The number of minutes spent in sedentary, moderate and vigorous activity was then calculated for a 24hr period. Metabolic Equivalents (METs) were used to express the intensity of physical activities. One MET is defined as the energy cost of sitting which is equivalent to an energy consumption of 1kcal/kg/hour. A person's caloric consumption is three to six times higher when being moderately active (3-6 METs) and greater than six times higher when being vigorously active (>6 METs) compared to if they were sitting (178). Moderate intensity physical activity requires a moderate amount effort which results in a noticeable increase in heart rate. Examples of moderate physical activity include brisk walking, housework and domestic chores. Vigorous physical activity requires a large amount of effort that results in a significant increase in heart rate and rapid breathing which includes running, fast cycling, playing football or other competitive sports games.

5.4 Results

5.4.1 Baseline Characteristic

A total of 20 children were recruited for the purpose of this study with no subjects dropping out after consent. Table 14 shows the mean age of the children was 9.15 [SD2.16] years. There were no significant differences in terms of gender, race, age, or BMI between the recruited children with T1DM and those in the previous case control study (see Chapter 3).
Table 14 Baseline characteristic of children with T1DM in prospective study (n=20) compared to children with T1DM in case-control study (n=55)

<table>
<thead>
<tr>
<th></th>
<th>T1DM Children in Prospective Study</th>
<th>T1DM Children in Case Control Study</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>Mean [SD]¹</td>
<td>n (%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10 (50)</td>
<td>29 (49)</td>
<td>0.941</td>
</tr>
<tr>
<td>Female</td>
<td>10 (50)</td>
<td>30 (51)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arab</td>
<td>19 (95)</td>
<td>56 (95)</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-Arab</td>
<td>1 (5)</td>
<td>3 (5)</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>20(100)</td>
<td>9.15 [2.16]</td>
<td>59(100)</td>
</tr>
<tr>
<td>BMI², percentile</td>
<td>20(100)</td>
<td>53.08 [37.65]</td>
<td>59(100)</td>
</tr>
<tr>
<td>Waist Circumference, cm</td>
<td>20 (100)</td>
<td>67.7 [12.3]</td>
<td></td>
</tr>
<tr>
<td>TSF³, mm</td>
<td>20 (100)</td>
<td>17.4 [6.8]</td>
<td></td>
</tr>
</tbody>
</table>

¹SD: Standard Deviation, a Chi–Squared, b Fisher Exact, c T-test
²BMI: Body Mass Index, ³Triceps Skin Fold Thickness

There was a significant, positive correlation between BMI and TSF and between BMI and waist circumference as shown in Table 15. However, a negative, weak, and non-significant correlation was found between BMI and serum vitamin D status as assessed by UPLC/MSMS method.
Table 15 Pearson’s correlation coefficients (r) for the relationship between BMI and serum vitamin D (nmol/L), waist circumference and TSF in children with T1DM (n=20)

<table>
<thead>
<tr>
<th></th>
<th>Correlation Coefficient r ($r^2$) with BMI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSF (mm)</td>
<td>0.721 (0.52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>0.897 (0.80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>*Serum vitamin D levels</td>
<td>-0.298 (0.21)</td>
<td>0.229</td>
</tr>
</tbody>
</table>

2BMI: Body Mass Index; 3Triceps Skin Fold Thickness; *Sample n= 18

The mean total 25(OH) D levels for males was 58.0±14.2 and for females was 41.3±19.7; a difference approaching significance (p=0.056) although no statistically significant difference was found between males and females in the likelihood of being deficient (data not shown).

5.4.2 DIETARY INTAKE

5.4.2.1 ENERGY AND MACRONUTRIENT INTAKE

Age and gender appropriate estimated energy requirement (EER) (179) were used to calculate energy requirement. In total, 55% (n=11) of the children met 75% or more of their requirements, 30% (n=6) exceeded their requirements and 15% (n=3) of the children’s energy intake was less than 75% of EER. They met their RDA for carbohydrates but fell short in fiber intake consuming only half of the requirements (see Table 16). Protein intake was about 2.5 times the RDA values. The children in this study were within the AMDR range for macronutrients with a mean percent energy intake from polyunsaturated fats below the recommended.
### Table 16 Mean absolute (n=20) and adjusted (n=13) energy intakes and macronutrient distribution in children with T1DM (n=20)

<table>
<thead>
<tr>
<th></th>
<th>Absolute Mean (SD)</th>
<th>Absolute Mean % DRI</th>
<th>*Adjusted Mean (SD)</th>
<th>*Adjusted Mean % DRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (kcals)</td>
<td>1766.52 (303.16)</td>
<td>90.64 (16.85)</td>
<td>1896.65 (291.13)</td>
<td>98.57 (14.70)</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>76.77 (20.01)</td>
<td>250.08 (87.26)</td>
<td>83.77 (19.03)</td>
<td>287.16 (79.52)</td>
</tr>
<tr>
<td>%Kcal, Protein</td>
<td>16.01 (1.76)</td>
<td>16.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>258.43 (68.42)</td>
<td>102.81 (21.21)</td>
<td>284.18 (52.87)</td>
<td>106.82 (15.07)</td>
</tr>
<tr>
<td>%Kcal, Carbohydrates</td>
<td>55.91 (4.47)</td>
<td>56.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary fiber (g)</td>
<td>14.20 (5.40)</td>
<td>51.81 (19.83)</td>
<td>15.60 (6.09)</td>
<td>57.36 (21.71)</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>58.93 (12.77)</td>
<td>97.70 (24.25)</td>
<td>60.61 (13.14)</td>
<td>101.51 (23.48)</td>
</tr>
<tr>
<td>Fat (% of energy)</td>
<td>28.09 (4.58)</td>
<td>27.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated Fat (g)</td>
<td>16.32 (3.52)</td>
<td>85.28 (26.47)</td>
<td>16.76 (3.93)</td>
<td>89.01 (28.87)</td>
</tr>
<tr>
<td>Saturated Fat (% of energy)</td>
<td>7.97 (1.67)</td>
<td>7.61 (1.88)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monounsaturated Fats (g)</td>
<td>13.24 (3.82)</td>
<td>62.63 (23.90)</td>
<td>13.54 (3.45)</td>
<td>64.99 (23.85)</td>
</tr>
<tr>
<td>Mono Fat (% of energy)</td>
<td>6.43 (2.10)</td>
<td>6.19 (1.81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyunsaturated Fats (g)</td>
<td>8.73 (12.27)</td>
<td>30.87 (13.55)</td>
<td>10.34 (15.03)</td>
<td>31.64 (11.92)</td>
</tr>
<tr>
<td>Poly Fat (% of energy)</td>
<td>2.86 (1.22)</td>
<td>2.71 (0.86)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1SD: Standard Deviation; DRI: Dietary Reference Intake; *Adjusted mean intakes to account for over and under reporting using Torun Cut Offs (161).
5.4.2.2 Vitamin Intakes

Vitamin intakes are shown in Table 17. Intakes of vitamin E, D and K did not meet the recommended levels whereas the children met and exceeded levels for all B vitamins. Recommended intakes of folate were met by approximately 90% of the children. Micronutrients were expressed per 1000 kcal in order to adjust for the greater volume of food consumed by some children that may skew the results.

Table 17 Distribution of vitamin intakes in children with T1DM (n=20)

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Absolute Mean (SD)</th>
<th>*Adjusted Mean (SD)</th>
<th>Absolute Mean % DRI (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (RAE)</td>
<td>285.88 (668.88)</td>
<td>208.40 (335.25)</td>
<td>78.91 (56.19)</td>
</tr>
<tr>
<td>Vitamin D (IU)</td>
<td>43.07 (48.50)</td>
<td>24.38 (27.46)</td>
<td>16.21 (10.94)</td>
</tr>
<tr>
<td>Vitamin E - Alpha Tocopherol (mg)</td>
<td>1.38 (0.40)</td>
<td>0.78 (0.23)</td>
<td>15.28 (4.58)</td>
</tr>
<tr>
<td>Vitamin K (mcg)</td>
<td>6.62 (3.06)</td>
<td>3.75 (1.73)</td>
<td>11.49 (5.29)</td>
</tr>
<tr>
<td>Vitamin B1 (mg)</td>
<td>1.01 (0.27)</td>
<td>0.57 (0.15)</td>
<td>136.40 (39.36)</td>
</tr>
<tr>
<td>Vitamin B2 (mg)</td>
<td>1.37 (0.64)</td>
<td>0.76 (0.36)</td>
<td>178.24 (68.34)</td>
</tr>
<tr>
<td>Vitamin B3 (mg)</td>
<td>11.95 (3.91)</td>
<td>6.76 (2.21)</td>
<td>120.30 (43.60)</td>
</tr>
<tr>
<td>Vitamin B6 (mg)</td>
<td>1.12 (0.40)</td>
<td>0.63 (0.23)</td>
<td>143.24 (59.15)</td>
</tr>
</tbody>
</table>
5.4.2.3 MINERAL INTAKE

The iron intake of the children in this prospective study was approximately 1.6 times their requirement (see Table 18). Potassium and calcium levels were below the RDA values whereas sodium levels were in excess by approximately 1.5 times the RDA values.

Table 18 Distribution of mineral intakes in children with T1DM (n=20)

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Absolute Mean</th>
<th>*Adjusted Mean</th>
<th>Absolute Mean % DRI†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(SD)¹</td>
<td>(SD)¹</td>
<td>(SD)¹</td>
</tr>
<tr>
<td>Vitamin B12 (mcg)</td>
<td>2.98 (1.88)</td>
<td>1.69 (1.06)</td>
<td>207.29 (113.55)</td>
</tr>
<tr>
<td>Folate (mcg)</td>
<td>219.67 (67.29)</td>
<td>124.35 (38.09)</td>
<td>89.98 (29.73)</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>691.83 (215.97)</td>
<td>391.63 (122.26)</td>
<td>68.7 (26.78)</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>13.80 (4.89)</td>
<td>7.81 (2.77)</td>
<td>159.06 (65.60)</td>
</tr>
</tbody>
</table>
5.4.3 Vitamin D Intakes & Status (Food Frequency Questionnaire & Serum Levels)

Tables 19 and 20 show the top five foods that contributed to the highest and lowest dietary vitamin D intakes as assessed by the average of three food recalls and the vitamin D specific food frequency questionnaire.

According to the food records, the children that had the highest intakes of vitamin D commonly consumed milk and dairy products (cornflakes with milk, ice cream, yogurt, and flavored milks), eggs, fish, liver, rice and bread. Children with the lowest vitamin D intakes commonly consumed fried foods such as nuggets, fries, chips, hamburgers and pizza. They had a tendency to drink juices and sugary drinks several times a day. As with the children with the highest vitamin D intake, rice and bread were consumed on a daily basis in children with the lowest intake levels.

<table>
<thead>
<tr>
<th></th>
<th>Absolute Mean (SD)$^1$</th>
<th>*Adjusted Mean (SD)$^1$</th>
<th>Absolute Mean % DRI$^1$ (SD)$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium (mg)</td>
<td>1562.20 (625.06)</td>
<td>884.34 (353.84)</td>
<td>37.58 (14.86)</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>2520.51 (984.51)</td>
<td>1426.82 (557.32)</td>
<td>153.73 (68.61)</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>6.44 (2.87)</td>
<td>3.65 (1.62)</td>
<td>101.20 (47.82)</td>
</tr>
</tbody>
</table>

$^1$SD: Standard Deviation; $^1$DRI: Dietary Reference Intake; *Adjusted mean expressed per 1000kcals.
Table 19 Top 5 foods which contributed to vitamin D intake in children with highest vitamin D intake

<table>
<thead>
<tr>
<th>Food Recall</th>
<th>Food Frequency Questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cornflakes with milk</td>
<td>Milk</td>
</tr>
<tr>
<td>Cream cheese or cream cheese sandwich</td>
<td>Cornflakes with milk</td>
</tr>
<tr>
<td>Milk</td>
<td>Pasta with cheese</td>
</tr>
<tr>
<td>Egg</td>
<td>Ice cream</td>
</tr>
<tr>
<td>Buttermilk</td>
<td>Cream cheese</td>
</tr>
</tbody>
</table>

Table 20 Top 5 foods which contributed to vitamin D intake in children with lowest vitamin D intake

<table>
<thead>
<tr>
<th>Food Recall</th>
<th>Food Frequency Questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cream cheese</td>
<td>Milk</td>
</tr>
<tr>
<td>Tea with milk</td>
<td>Cornflakes with milk</td>
</tr>
<tr>
<td>Milk</td>
<td>Pasta with cheese</td>
</tr>
<tr>
<td>Egg</td>
<td>Beans</td>
</tr>
<tr>
<td>Liver</td>
<td>Pizza</td>
</tr>
</tbody>
</table>

Food intake of vitamin D was not normally distributed and hence non-parametric methods were used to compare the results from the FFQ and the FR. Spearman's rank correlation coefficient was also calculated. Table 21 shows the baseline dietary intakes calculated from the food frequency questionnaire (FFQ) (taken before the patient was discharged) and the average of
three 24hr food recalls (FR) (one taken at the time of admission and two by telephone one week after discharge).

Table 21 Baseline dietary intakes and serum vitamin D levels in children with T1DM (n=20)

<table>
<thead>
<tr>
<th></th>
<th>Dietary Vitamin D Intake (IU/day)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FFQ (Mean, SD)</td>
<td>FR (Mean, SD)</td>
</tr>
<tr>
<td>Vitamin D Intake</td>
<td>131.50 (95.86)</td>
<td>43.07 (48.50)</td>
</tr>
</tbody>
</table>

FFQ, food frequency questionnaire; FR, 24hr Food Recalls; SD, standard deviation

A Bland Altman plot (Figure 2) comparing the two methods shows poor agreement with the FFQ estimating higher intakes of mean vitamin D (131.50 [95.86]) compared to the FR (43.07 IU [48.50]). Dietary vitamin D as assessed by FFQ was moderately but significantly correlated with serum vitamin D levels (Spearman's rho = 0.547). However no association was found between serum vitamin D status and dietary intakes as assessed by the three FR’s.
Figure 2 Bland Altman plot showing the level of agreement between vitamin D intake (n=20) from the FFQ and the 24hr-FR. A statistically significant difference was shown between the two measurements (P=0.008) with the FFQ method estimating higher intakes than FR method.

A Bland Altman plot (Figure 2) comparing the two methods showed poor agreement with the FFQ estimating higher intakes of mean vitamin D (131.50 [95.86]) compared to the FR (43.07 IU [48.50]). The correlations between dietary vitamin D levels (as derived from the from the two different assessment methods) and serum vitamin D are shown in Table 22. Dietary vitamin D as assessed by FFQ was moderately but significantly correlated with serum vitamin D levels (Spearman's rho = 0.547). However no association was found between serum vitamin D status and dietary intakes as assessed by the three FR’s.
Table 22 Spearman’s Correlation $r (r^2)$ for the relationship between dietary Vitamin D (IU) intake levels and serum vitamin D (nmol/L) as measured by the UPLC-MSMS method in Children with T1DM (n=20)

<table>
<thead>
<tr>
<th></th>
<th>Correlation ($r^2$) with serum Vitamin D levels (nmol/L)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFQ</td>
<td>0.547(0.299)</td>
<td>0.013</td>
</tr>
<tr>
<td>FR</td>
<td>0.353(0.125)</td>
<td>0.126</td>
</tr>
</tbody>
</table>

FFQ, food frequency questionnaire; FR, 24hr food recall

5.4.4 Serum Vitamin D Levels

The mean 25-hydroxyvitamin D (25(OH)D) of the children was 49.65 [18.75] when analyzed using the ultra-pressure liquid chromatography mass spectrometry method (UPLC/MSMS) and 44.60 [13.20] when analyzed in the hospital laboratory using chemiluminescence immunoassays (CLIA) (see Table 23)
Table 23 Mean 25-hydroxyvitamin D (25(OH) D) values as assessed by two methods for Children diagnosed with Type 1 Diabetes Mellitus (T1DM) (n=18).

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VitaminD3+D2 UPLC-MSMS(^1)</td>
<td>49.65 (18.75)</td>
<td>18.10-78.30</td>
<td></td>
</tr>
<tr>
<td>Vitamin D CMIA(^2)</td>
<td>44.60 (13.20)</td>
<td>22.70-67.30</td>
<td>0.048</td>
</tr>
<tr>
<td>VitaminD3 UPLC-MSMS</td>
<td>49.10 (19.00)</td>
<td>16.80-78.3</td>
<td></td>
</tr>
<tr>
<td>VitaminD2 UPLC-MSMS</td>
<td>2.00 (2.00)</td>
<td>0.00-5.00</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Ultra-pressure liquid chromatography mass spectrometry (UP) LC MS/MS;
\(^2\) Chemiluminescence immunoassays (CLIA)

There was a statistically significant difference between the two assay methods (p= 0.048.)

The Bland and Altman plot (Figure 3) which shows the discrepancies between results for individual samples was used to reveal the differences between the two methods and clearly indicates that the CMIA method is biased compared to the UPLC/MSMS method. The CMIA overestimated insufficient values and underestimated deficiency as compared to UPLC/MSM.
As shown in Figure 4 below, 22% of the children analyzed using the UPLC/MSMS method, were classified as being deficient with a serum vitamin D level below 30nmol/L, 28% had insufficient vitamin D levels between 30-50nmol/L and 50% of the children had optimal levels of vitamin D above 50nmol/L. Analysis using CMIA on the other hand classified 11% of the children as being deficient, 61% as being insufficient and only 28% as having optimal levels of vitamin D.
Figure 4 Percentage of children with T1DM classified as being deficient, insufficient or having optimal serum levels of vitamin D using UP(LC)-MSMS (n=18) and using CLIA (n=18) assay methods. The difference in classification between the two methods was significant p=0.004 (Chi-squared).

5.4.5 LIFESTYLE AND SUNLIGHT EXPOSURE QUESTIONNAIRE

Table 24 shows the association of lifestyle factors with 25(OH) D levels (as measured by UPLC-MSMS). There was a trend towards an association between reported sunlight exposure and vitamin D with those exposed to more than 30 minutes per day having higher 25(OH) D levels (p=0.057) whereas no significant associations were shown between vitamin D levels and living conditions, veil use, playing outdoors, use of sunscreen or having had a suntan in the previous year.
Table 24 Association of lifestyle factors with 25(OH) D level measured by HPLC in children with T1DM (n=20)

<table>
<thead>
<tr>
<th>Lifestyle Factor</th>
<th>n</th>
<th>Vitamin D (nmol/L) Mean (SD)</th>
<th>P-Value T-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Living</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flat</td>
<td>10</td>
<td>44.88 (15.87)</td>
<td>0.261</td>
</tr>
<tr>
<td>House</td>
<td>9</td>
<td>53.99 (20.94)</td>
<td></td>
</tr>
<tr>
<td>Outdoor Patio/Garden</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>6</td>
<td>55.27 (19.85)</td>
<td>0.288</td>
</tr>
<tr>
<td>Patio or Garden</td>
<td>14</td>
<td>45.63 (17.27)</td>
<td></td>
</tr>
<tr>
<td>Play outdoor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>8</td>
<td>48.56 (18.59)</td>
<td>0.994</td>
</tr>
<tr>
<td>Yes</td>
<td>10</td>
<td>48.49 (18.63)</td>
<td></td>
</tr>
<tr>
<td>Veil use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>52.89 (16.14)</td>
<td>0.244</td>
</tr>
<tr>
<td>Yes</td>
<td>7</td>
<td>43.19 (19.89)</td>
<td></td>
</tr>
<tr>
<td>Suntan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>16</td>
<td>49.78 (18.53)</td>
<td>0.623</td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>43.50 (17.90)</td>
<td></td>
</tr>
<tr>
<td>Use of Sunscreen on Face</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18</td>
<td>48.91 (18.87)</td>
<td>0.784</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>45.05 (12.66)</td>
<td></td>
</tr>
<tr>
<td>Use of Sunscreen on Body</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>19</td>
<td>49.18 (18.37)</td>
<td>0.497</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>36.10</td>
<td></td>
</tr>
<tr>
<td>Average Daily Sunlight Exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 30 mins/day</td>
<td>14</td>
<td>43.53 (19.07)</td>
<td>0.057</td>
</tr>
<tr>
<td>More than 30 mins/day</td>
<td>6</td>
<td>60.17 (8.35)</td>
<td></td>
</tr>
</tbody>
</table>

1SD: Standard Deviation
Table 25 shows the association between annual sunlight exposure and vitamin D levels as assessed by a questionnaire with scores ranging from 4 to 24 and where 4 reflected a higher exposure and 24 a low exposure.

Table 25 Association between annual sunlight exposure score with 25(OH) D level (n=20) which approached significance at p=0.062.

<table>
<thead>
<tr>
<th>Annual Sunlight Exposure score &amp; 25(OH) D Level</th>
<th>Pearson’s Correlation (r²)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-0.424 (0.180)</td>
<td>0.062</td>
</tr>
</tbody>
</table>

1Assessed via questionnaire with a possible score ranging from 4 to 24 where 4 = high exposure and 24 = low exposure

5.4.6 Physical Activity (C-PAQ Questionnaire)

Table 26 shows the association between physical activity levels (expressed in mean number of minutes spent doing moderate or vigorous activity per day) as assessed by the Children’s Physical Activity Questionnaire (C-PAQ) with 25(OH) D levels. This shows that there was no significant association between activity levels (as expressed by mean time spent in moderate and vigorous activity) and adequacy of vitamin D status. In fact the time spent in moderate or vigorous activity was lower for those with adequate vitamin D status although there was substantial variation within the group.
Table 26 Association between mean time spent in moderate and vigorous activity and 25(OH) D Level (n=20)

<table>
<thead>
<tr>
<th>Time spent in moderate and vigorous activity, minutes</th>
<th>Less than 50nmol/L serum Vitamin D</th>
<th>More than 50 nmol/L serum Vitamin D</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median [IQR]</td>
<td>25.71 [26.43]</td>
<td>17.14 [42.50]</td>
<td>0.759a</td>
</tr>
</tbody>
</table>

Table 26 shows the correlation between the physical activity level in percentage as assessed by the CPAQ questionnaire and serum vitamin D levels. It shows a negative, non-significant and weak association (Pearson’s rho=-0.133; p=0.577) between the percent of physical activity levels and 25(OH) D level as assessed by HPLC assay method.

Table 27 Pearson’s correlation between percentage of time spent doing moderate and vigorous physical activity and 25(OH) D level (n=20)

<table>
<thead>
<tr>
<th>Physical Activity Level as expressed in % &amp; 25(OH) D Level</th>
<th>Pearson’s Correlation (r2)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson’s Correlation (r2)</td>
<td>-0.133 (0.018)</td>
<td>0.577</td>
</tr>
</tbody>
</table>

Table 27 shows the correlation between the percentage of time spent doing moderate and vigorous physical activity and 25(OH) D level (n=20).

Figure 5 shows the time children with T1DM (n=20) reported spending in moderate and vigorous activity in a 24 hour period. The current physical activity guidelines recommend that children and adolescents spend at least 60 minutes (1 hour) of moderate to vigorous activity daily.
(180). Only twenty percent of the children in the sample met the minimum requirements for physical activity.

Figure 5 Time children with T1DM (n=20) spent in moderate to vigorous physical activity

Figure 6 shows the percent of time that children with T1DM (n=20) spent doing moderate and vigorous activity from total reported time. A mere 4 children (20%) spent 50% or more of the reported total time doing moderate and vigorous activity.
Figure 6 Percent of time the children with T1DM (n=20) spent doing moderate and vigorous activity from total reported time.

5.5 Discussion

The aim of this study was to provide more in-depth data on a smaller group of children seen within the unit to add to that previously gathered and to assess in detail the dietary and lifestyle behaviors of a small sample of newly diagnosed children with T1DM in the SMC hospital.

The results of this prospective study showed a significant correlation between BMI and TSF as well as waist circumference. Measurement of waist circumference is a simple tool for screening body fat and in particular is a good indicator of abdominal fat, especially intra-abdominal fat in children (181, 182). Furthermore, waist circumference appears to be a better predictor of the risk of cardiovascular disease than BMI and waist to hip ratio (183). Most of the studies looking at adiposity as measured by BMI, waist circumference and/or skinfold thickness
measurements were limited to children with type 2 diabetes (184, 185). No significant correlation was found between BMI and serum vitamin D levels although some studies have found a relationship between insufficient vitamin D status and increasing BMI in otherwise healthy children (186-189). Perhaps one of the reasons we were unable to find a relationship between increasing BMI and vitamin D insufficiency is due to the relatively small sample size.

5.5.1 Dietary Intake

No significant differences were seen in terms of gender, race, age, or BMI between the recruited children in this small prospective study and those recruited in the larger study described in Chapter 3, suggesting that the in depth cohort were representative of the wider T1DM population seen in the unit and therefore that the results of the current study are generalizable within the SMC.

The dietary intake of the children with T1DM in this prospective study showed similar trends to the intake of children with T1DM in the case-control study described in Chapter 4, confirming the issues highlighted with respect to the quality of the diets consumed.

Protein intake was similar to the protein intake of T1DM children in the larger group study with both groups consuming approximately 2.5 times the RDA. The mean percent energy intake from polyunsaturated fats was below the recommendation, although iron intake was in excess by approximately 1.6 times; again following the same dietary trend as the children with T1DM in the case-control study (see section Chapter 4: Mineral Intakes; p. 72).

Averages of three 24-hour diet recalls were used to assess the nutritional intake of the children. A diet recall is a quantitative method used in nutritional assessment which asks the subject to recall foods and beverages consumed the previous day or the previous 24 hours. A
single 24 hour recall is not considered representative of an individual’s habitual diet; however, it is considered representative when surveying a large group or mean intakes. Studies looking at the effectiveness of a 3 day multiple-pass recall in young children found them to be sufficient for group estimates but not at an individual level for energy intake (190, 191).

Dietary intake in this study was assessed using the traditional 24-hr recall method with a reverse chronological order to obtain information on what was consumed the previous day. In recent years, the USDA’s five-step multiple-pass method for dietary recall has become a popular and accurate method of performing food recalls (190, 192) and it may be that given greater time during clinical consultations this could be adopted to provide more accurate representation of the children’s intakes.

Dietary intake was taken from the parent or legal guardian in the presence of the child as this has been found to produce more accurate recalls (193). Children’s ability to recall food varies widely as demonstrated in a study of 203 children aged 5 to 7 years to determine the accuracy of lunch time meal recall during school (194). However, their ability to recall food increases after the age of 8 years (195). The preferred chronological order of recall in children remains unclear (196).

Children with T1DM in this study were found to consume a greater amount of protein than RDA requirements (although comparable to results of healthy Bahraini children (10)) and to consume an excess amount of sodium. Furthermore, potassium and calcium levels were well below the recommended RDA values along with fiber intake. The results of this study reinforce the need to find ways to implement and encourage compliance with the available general population dietary guidelines.
5.5.2 Validation of Vitamin D Specific FFQ

In this study a vitamin D specific FFQ and the three 24hr food recalls were used to assess dietary vitamin D intake alongside measurement of serum vitamin D levels. Sub-analysis of the children that consumed a higher amount of vitamin D rich foods as reported by the FFQ identified dairy products and in particular daily milk consumption as a key contributor to overall higher intakes. This was verified by scrutinizing the FFQ’s of children with the lowest levels of vitamin D intake who were found not to consume milk on a daily basis. Despite some children eating fish four times a week, it did not appear to be as large a contributor as milk to total vitamin D, suggesting that strategies to promote milk and work to identify barriers to milk consumption may be most effective in increasing vitamin D intakes in this population.

Dietary intakes vary from day to day for many individuals. Variations in meal patterns may be due to food availability, whether an individual is eating at home or outside the home, and working/education patterns to name just a few examples. Capturing an individual’s habitual food habits can be assessed by a food diary or repeated 24 hour recalls only if sufficient days of intake are assessed. In order to obtain a representative reflection of an individual’s usual intake, the more days that can be recorded the better although in practice this is cumbersome and can affect recruitment and compliance. The review by Bingham in 1987 is still used for guidance on the number of days that are sufficient to assess intake depending on nutrient. Although vitamin D was not one of the nutrients analyzed, Bingham recommends 12 days of repeated recalls or the equivalent amount of information from a food diary to capture iron intake ± 10% of the average; she recommends 19 days for riboflavin and 36 days for vitamin C (197). Macronutrients tend to require fewer recording days than micronutrients especially those that are found in a limited number of foods such as vitamin A and the wider the within individual nutrient variation the
greater the number of days that will be required to study a particular nutrient (197). The advantage of a FFQ is its’ ability to capture these specific food items which are good dietary sources but may not be consumed on a daily basis (198). Furthermore, the FFQ being specific to vitamin D containing foods would be expected to be a better indicator of intake than the average of three day FR. In the UK, the National Diet and Nutrition Survey was reduced from 7 days to 4 days so as to improve recruitment. No difference was found in nutrient intake when a four food diary versus a 4 day 24hr food recall was used (199).

Bahrain’s market is saturated with imported milk from Saudi Arabia which claims to be fortified with 400 IU of vitamin D per liter of milk. Despite this claim, a study conducted by Sedrani and colleagues, looking into the fortification of milk in Saudi Arabia (200) found that as much as 57% of the sampled fortified milk in Saudi contained undetectable levels of vitamin D, 28.5% contained vitamin D exceeding the 400 IU and the remaining 14.5% contained approximately 250 IU of vitamin D per liter. In light of this study the results of our FFQ analysis, which assumes the fortification of foods, must be interpreted with caution since they may have consistently overestimated true vitamin D intakes. Furthermore, given the prevalence of Saudi dairy products within the Bahrain market, assuming poor or erratic fortification suggests that the results of the FFQ are not representative of true intake as levels may not be constant across the population.

In the United States fortification of milk began in the early 1930’s with the aim of preventing rickets (201). Today, fortification of foods with vitamin D is voluntary in the United States with the exception of foods that claim to be fortified with vitamin D (202). Foods voluntarily fortified are strictly regulated in order to avoid over-fortification (203). Most of the
milk in the U.S is fortified although not all dairy products such as cheese are fortified; it is not uncommon to see vitamin D fortified breakfast cereals, soy milk and even orange juice in the U.S (203).

Canada on the other hand mandates the fortification of milk to provide 180 IU/250mL as well as milk alternatives and margarine with 530 IU/100gm (203). Fortification of other foods is permitted although strictly regulated, with the exception of the fortification of ready-to-eat cereals with vitamin D which is considered illegal in Canada, unlike in the U.S (203). Australia mandates the fortification of edible oils spreads such as margarine although fortification of other foods is voluntary (204). Fortification of vitamin D in Europe varies significantly; the United Kingdom fortify edible spreads and cereals (205) and Norway fortifies spreads such as margarine and dairy products (206).

As there are no mandates for the fortification of foods in Bahrain, the results of our study highlights the need to consistently fortify dairy and milk products as they were the main foods that contributed to vitamin D intake (if fortification at reported levels is achieved). This has been suggested previously in a study looking at the vitamin D intake of women in labor and their partners (21) in Bahrain. Furthermore, in light of the study conducted by Sedrani et al, there needs to be strict quality control implemented to assure that content of vitamin D in fortified foods is homogenous.

Assuming that a stronger correlation of dietary vitamin D with serum levels can be interpreted as an indication of greater validity, it would appear that the vitamin D specific FFQ produces more valid estimates compared to the three 24hr food if we are to assume that food fortification is indeed consistent as a significant positive moderate correlation ($r=0.547; p=0.013$) was found between the FFQ and serum vitamin D levels. However, as mentioned earlier,
interpretation of the results of the FFQ should be made with caution and may indicate a ‘best case’ scenario given the tendency to overestimate intakes via FFQs (207, 208) and the known inconsistencies in fortification of products.

It is worthy to note that the food composition of specific Bahraini dishes included all major macronutrients but data on micronutrient, and in particular on vitamin D was limited to the typical fish consumed in Bahrain (177), possibly underestimating vitamin D intake from other locally eaten dishes. The two assessment measures also have common error sources such as their reliance on memory (209) and estimation of portion sizes (210). Although both methods were interviewer based, the FFQ relies on long-term memory whereas the FR relies more on short-term memory.

When assessing vitamin D, it is important to note that body status is not affected by diet sources alone and more than 90% of the vitamin D requirement for most people is believed to come from casual exposure to sunlight (70, 211, 212). This may provide some basis for the generally low correlation between intake and status. It is important to recognize and acknowledge that relatively few foods naturally contain vitamin D and therefore diet contributes only minimally to overall vitamin D requirements in many people. It is the author’s opinion that safe sun-exposure in children with T1DM, as well as healthy children, should be recommended especially since sunlight is plentiful all year around in Bahrain. Holick recommends sun exposure 2 or 3 times per week for approximately 5–10 minutes and specifically exposing the arms and legs or hands, arms, and face between 10:00 to 15:00hrs (69). A suggestion would be to integrate this recommendation into the physical activity lessons of school children. As children are required to have two 45min sessions a week of physical activity, the last 5-10 minutes of class could focus on “getting our vitamin D” allowing children to expose arms and legs or hands,
arms and face. Furthermore, as schools in the Kingdom segregate males and females, the cultural issues of body exposure would not be an issue for the females.

**5.5.3 LIFESTYLE AND SUNLIGHT EXPOSURE**

Vitamin D can be produced endogenously by the skin via photosynthesis using ultraviolet B light (UVb) which converts 7-dehydroxycholesterol (7-DHC) to pre-vitamin D₃. It can also be obtained from the diet or from a dietary supplement. As previously mentioned few foods naturally contain vitamin D with the exception of fatty fish and fish liver oils which are a good source; eggs and cheese and meats contain a small amount (213). However, the results of this study have shown that milk (if presumed fortification levels are achieved) contributed most to dietary vitamin D intake in the sampled children.

Whilst likely to represent the greatest contributor to vitamin D status, cutaneous synthesis itself is subject to a range of factors affecting extent and efficacy namely latitude, altitude, time of day and season (214, 215). Environmental factors also need to be considered such as air pollution, cloud cover and ozone levels which affect U.V ray absorption (216). Cutaneous vitamin D synthesis is impacted by clothing (217), sunscreen (218), and skin pigmentation (219) with darker skin colored people synthesizing less vitamin D.

Although there was a trend towards an association between sunlight exposure and vitamin D in the current study, with the children exposed to more than 30 minutes per day having higher 25(OH) D levels (p=0.057), no significant associations were shown between vitamin D levels and lifestyle and living conditions as described previously. In the study conducted by Mahroos et al, looking into the role of lifestyle and sunlight exposure in serum vitamin D levels in pregnant women and their partners, the results showed veil use and living conditions to be
significantly associated with 25 (OH) D deficiency (19). Of the females in the current sample 8 (80%) were veiled but no association was found between veil use nor living conditions in this study perhaps due to the small sample size of the study population or because veil use in young female girls is not as strict as it is in older women and therefore is unlikely to exert such a great or consistent effect on sun exposure and therefore vitamin D status.

5.5.4 Serum Vitamin D Levels

An increased interest in the role vitamin D plays in health and in particular recognition of the non-bone effects has led to an increase in the frequency of vitamin D status testing in recent years (220). Variations in measured circulating 25(OH) D levels between assay methods and inter-laboratory measurements can however confound the diagnosis of hypovitaminosis D (221). The results of the current study, put into clinical context, suggest that (if we assume any newly diagnosed child with T1DM with a 25(OH)D of less than 50 nmol/l were indicated for supplementation) 50% of the children would require supplementation according to UPLC/MSM measurements as compared to 72% of children according to CMIA measurements. Previous work (222) has cited an approximate 20% misclassification rate between samples assessed using chemiluminescence immunoassay and LC-MS/MS with 57% and 41% respectively being classified as deficient using a cut-point of 50nmol/l.

There is currently no consensus amongst clinicians as to the optimal reference to classify moderate to severe insufficiency in children and adults and this may be in part due to inter-method bias (223). Furthermore, there is no consensus on the amount of vitamin D intake required for optimal health despite a substantial number of published literature and studies conducted trying to determine what constitutes an adequate intake. The U.S Institute of Medicine’s (IOM) recommend an intake of 600 IU of vitamin D in children one year of age and
older in order to achieve a 25(OH)D level of 50nmol/l to meet the requirements of 97.5% of the healthy population (224). There has been however, recent controversy regarding the accuracy of this estimation (225, 226) with authors Veuglers and colleagues claiming that over 8000 IU of vitamin D is a more accurate estimation of the needs of 97.5% of a healthy population (225). Furthermore, the study by Heaney and colleagues supported these findings and put forth the argument that a total intake of close to 7000 IU per day is a more accurate recommendation.

Studies comparing commercially available assays using CLIA or RIA assay methods to HPLC have found low inter-assay agreement (223, 227, 228). Farrell and colleagues (228) describe the variability in results of vitamin D in automated immuno-assays including the Abbott (Architect) that is currently used in our facility. The Abbott Architect automated immunoassay in Farrell’s study showed the greatest deviation of all assays when compared to the LC-MS/MS. Detection of 25(OH)D appears to be method-dependent (228, 229), although the precision of immunoassays as well as HPLC, LC-MS/MS are comparable in detecting severe vitamin D deficiency (230).

Deciding on which assay method to use depends on balancing out many factors. Firstly, laboratories that test on a frequent basis and that require a higher output may benefit more from a commercially available kit (231), similar to the one used at the SMC hospital laboratory. However, inexperienced users of such commercial kits may introduce more assay variability (221). Secondly, one must take into consideration the commercial assays that discriminate between D₂ and D₃ which may result in an underestimation of vitamin D. Thirdly, cost is another factor to consider as the cost of running vitamin D assay using HPLC method is currently three times the cost of the CMIA assay method used in the hospital laboratory.
In light of the multifactorial issues surrounding diagnosis and treatment of hypovitaminosis D, we should exercise prudence when assessing a single 25 OH D value (221) especially when the "gold standard" assay method is not feasible. Since vitamin D is believed to be implicated in a number of disorders, the wider implication of inaccurate readings in the management of hypovitaminosis D is not limited to children with T1DM.

5.5.5 Physical Activity

Physical activity is related to many important health benefits; in fact studies looking at the health benefits of physical activity of school-aged children found a dose-response relationship between physical activity and health with increasing physical activity providing greater health as assessed by biochemical markers and anthropometric measurements (232). There are several studies that have examined the impact of physical activity in children with T1DM and its impact on cardiovascular function (233-235). In a Swiss studying examining specific markers of atherosclerosis in children and adolescents aged 6-17 years with T1DM, those patients who practiced more than 60 min/day of moderate-to-vigorous physical activity were found to have improved vascular function (233). Other studies found similar results whereby the children and adolescents who engaged in moderate to vigorous physical activity for more than five days in the week had lower triglyceride levels and better metabolic control than inactive patients (234). Better glycemic control with increasing physical activity was also reported (235) in another multicenter European study.

In this study only 20% of the sampled children that completed the CPAQ questionnaire met the current recommendation. It is important note that the CPAQ questionnaire is self-reported and tends to overestimate activity level and so this evaluation is likely to be the ‘best
case’ scenario for the assessed sample. Other studies found a generally low adherence to recommendation of physical activity with only 38.5% of T1DM children meeting the recommendations (236).

Whilst investigating the impact of physical activity and serum vitamin D levels, no significant association between mean time spent in moderate and vigorous activity and adequacy of vitamin D status was found. Surprisingly, the more time the children spent in moderate and vigorous activity, the lower their vitamin D levels were. The investigators rationalized that the climate in Bahrain being hot and humid for a majority of the year, could possibly impact outdoor physical activity. Hence, the more physical activity the children are engaged in, the more likely it would be done indoors to avoid the hot climate. This highlights the need to be cognizant of environmental factors and the need for novel approaches to the communication of recommendations where these may otherwise be inadvertently counterproductive.

5.5.6 LIMITATIONS OF STUDY

One of the limitations of this study is the small number of children sampled and therefore interpretation of the results and estimation of the true effects of the variables must be done with caution. Furthermore as participants were selected as a convenience sample, selection bias cannot be ruled out.

Diet recalls were obtained using the traditional method instead of the five-step multiple pass recall which is thought to be more accurate and reflective of habitual dietary intake. The use of household items is not a reliable method of estimating portion sizes and thus could have introduced bias. Another limitation was that the FFQ were based on the assumption that foods such as milk were fortified although in reality, the consistency of fortification in Bahrain is
questionable. Furthermore, accuracy of vitamin D intake from the FFQ cannot be generalized with such a small sample size thus limiting any conclusions that may be drawn.

Establishing vitamin D status in the SMC is based on the hospital immunoassay results and existing cut-offs and although experienced users are employed to run the immunoassays the level of accuracy cannot be confirmed.

5.5.7 AREA OF FURTHER RESEARCH

Larger more adequately powered confirmatory studies need to be designed to investigate the relationship between dietary intakes of vitamin D, sunlight exposure, and exercise on children with T1DM as compared to healthy children. The development of public health campaigns which encourage sensible sun exposure as a health recommendation should be explored especially in light of the abundance of sunlight that Bahrain enjoys. Finally, studies looking at the feasibility of fortifying flour with vitamin D as has been previously done for iron in Bahrain to prevent anemia in the National Flour Fortification Program, should be explored.

5.6 CONCLUSION

In conclusion, the results of this prospective study has shown that dietary intake, sunlight exposure and physical activity may to some extent impact the vitamin D status of children with T1DM but that the relationships do not always follow previously reported patterns perhaps in part to environmental influences. Children with T1DM were found to consume a greater amount of protein than the RDA requirements and an excess amount of sodium. Furthermore, potassium and calcium levels were well below the recommended RDA values as was fiber intake; similar to the results of the previous case-control study. There was a trend towards an association between reported sunlight exposure and vitamin D with those exposed to more than 30 minutes per day
having higher 25(OH) D levels. Greater time spent doing moderate and vigorous activity appeared to be associated with lower vitamin D levels. This study has highlighted the wider implication of inaccurate readings of serum vitamin D as assessed by different techniques in the management of hypovitaminosis D.
6.0 QUALITATIVE PEDIATRIC DIABETES STUDY (QualPDS)

6.1 INTRODUCTION

In order to further investigate the beliefs and attitude of a sample of children with diabetes and their care givers in relation to the etiology and the management of their diabetes, focus groups were set up. In qualitative research the quality rather than the quantity of the sample is paramount. Qualitative research aims to generate data for analysis from direct observations that involve open-ended and documented interviews (237). The aim in doing so is to generate in depth narrative descriptions that will yield themes (237). Qualitative data is becoming increasingly recognized as a valuable research method and using both qualitative and quantitative data has the potential to generate a wealth of information that neither could produce alone (238).

The systematic review undertaken by the Health Technology Assessment (HTA) of the most effective educational or psycho-social intervention for improving metabolic control of children and adolescents with T1DM, identified the need for more rigorously designed studies and demonstrated a lack of clear evidence by the studies reviewed (239). Since then, the HTA as well as the National Institute for Health Research (NIHR) have adopted evidence-based approaches to allow the participation of key and lay stakeholder including service users in the development of interventions (240). More and more funding bodies now require the involvement of stakeholders which reflects the growing focus on service users and public involvement in the research process stages (240, 241). Involving such participants in the research process is a means by which the researchers can address the validity of the research intervention (242, 243). The DEPICTED (Development and Evaluation of A Psycho-social Intervention in Children and
Teenagers Experiencing Diabetes) Study was developed with the active participation of children and teenagers with diabetes as well as their parents or caregivers (244) (Refer to Chapter 7 for more details of the DEPICTED study). The lay participants, as described, played a crucial role in helping the research team to design the intervention tool and inform guideline development. Interesting to note is that none of these stakeholders, parents and children with T1DM, withdrew from the DEPICTED study’s development phase which the authors rationalized as being due to the value placed on being able to influence improvements in services (244).

6.2 Experimental Design & Methodology

Study Area/Setting:

   The study recruited from within the patient, relative and staff populations at the Salmaniya Medical Complex.

Study Subjects:

i) Parents of children who are newly diagnosed with T1DM and admitted to the Salmaniya Medical Complex.

ii) Health professionals working with children with diabetes and their families (doctors and nurses).

Sample Size:

   In total, the families of 5 children out of 20 approached agreed to participate in the focus group. All three of the diabetes nurse educators and two of the three endocrinologists at SMC also participated in the staff focus groups. The focus groups for parents, nurses and physicians were conducted separately. No difference was observed in terms of the nationality, religion, race,
geographic location or gender of the child whose caregivers’ participated in the focus groups versus those that did not (see Appendix 9).

**DATA COLLECTION METHODS:**

The focus groups were recorded and transcribed verbatim before undergoing systematic qualitative analysis. Focus groups lasted between 30 and 45 minutes and were facilitated by the principal investigator who used a prepared set of open-ended questions to facilitate the discussions (see Appendix 10). Although the children themselves were invited to participate only one child accompanied his parents to the focus group session.

The focus groups for the parents aimed to explore the following areas of discussion:

- Perceptions of the disease prior to and after admission
- Evaluation of the hospital stay and whether it was considered a good or bad experience
- Evaluation of the education received during the hospital admission period
- Evaluation of the follow-up system at the pediatric diabetes clinic
- Exploring recommendations for future support programs

The focus groups of the pediatric nurse educators aimed to explore the following areas of discussion:

- Barriers to the education process and behavioral changes
- Evaluating the role of the health care workers in educating the family post diagnosis.
- Exploring recommendations for future educational programs
The focus group of the pediatric endocrinologist aimed to explore the following areas of discussion:

- Evaluating the role of the health care workers in educating the family post diagnosis
- Evaluating barriers to education process and behavioral changes
- Recommendations for future educational programs

6.3 RESULTS

Figure 7 shows the process of admission, education, discharge and follow-up of children with T1DM at the Salmaniya Medical Complex (SMC).

6.4 PARENTS OF CHILDREN WITH DIABETES AND THEIR FAMILIES FOCUS GROUP

6.4.1 FAMILY FOCUS GROUPS

6.4.1.1 PERCEPTIONS OF THE DISEASE PRIOR TO AND AFTER ADMISSION

Knowledge of the disease prior to diagnosis Most focus group members had a pre-conceived notion about diabetes prior to their child being diagnosed. Their knowledge of the disease seemed largely dependent on whether or not they had a family member or relative with diabetes. One group member stated “I just knew what it was because my mother had it” whilst another parent stated “I had no clue what it was because no one in our family has it.” When probed further about the type of diabetes one parent replied: “The type that requires taking injections.” Other group member’s replied simply “It was high”
Breaking news and diagnosis of the diabetes Some group members explained that the news of the disease was broken to them by the attending physician at their local health center whilst others had the news broken to them at the emergency department in the hospital by the consultant endocrinologist. However, all group members expressed their sense of shock when they discovered their child had diabetes. One group member explained, “Diabetes to me was a shock…it was a shock when I found out it was diabetes “another member stated “I was surprised he was diagnosed with diabetes” and “it took me a month to come to terms with the disease…” One mother reported that she did not know about the disease before her child was diagnosed and “that it had not even passed [her] mind that she could have this illness.”

Social and future concerns All group members expressed either social or future concerns in regards to their child’s diabetes. Many of the members had concerns about the side effects of the disease as expressed by one mother “I am worried their blood sugar will be very high and that it will affect part of their body negatively” or as another mother explains who already has a child with kidney failure “I fear the side effects of diabetes like kidneys and kidney problems because I hear a lot of people talk about this. People say for example that they got kidney failure from diabetes…”

When asked about other concerns asides from physical side effects, one mother explains:

Well I am worried it will impact his studies, and I think about when he is older and starts to work, will he be able to lead a normal life?! I am thinking even about when he marries. That’s what I think about.

Particularly interesting in the above statement is this mother’s concern about the far-reaching impact of her child’s diabetes on their ability to get married or any marriage itself. This concern
was shared by other parents regardless of whether the child diagnosed was male or female. For example another parent explains

“Me too, I have many concerns... in terms of people’s perception... because she is still young. I am worried about when she gets older when she marries..."

Many of the parents also expressed concerns about their child’s schooling and the social stigma of diabetes. For example one mother states:

Yes and many families they hide the fact that their children have diabetes one child in my son’s school they found out he had diabetes and the father wouldn’t give him his insulin injection at school because he felt ashamed to give it to him for people to know and the school discovered only after my son was also diagnosed.

The reaction of their child's school to the diagnosis was also discussed by parents with one mother reporting that her daughter’s school were “very concerned and they offered to switch her class so she would be closer to the nurse.” However their experiences were not always so positive with one member believing that “…the schools should understand when my son asks to go to the washroom, you know because of his condition.”
Figure 7 Processes of admission, education, discharge and follow-up of children with type I diabetes at the Salmaniya Medical Complex (SMC)
6.4.1.2 Evaluation of the Initial Hospital Stay

Admission process Most group members explained that they were diagnosed at their local health center (LHC) before being transferred to the hospital for admission and education. One family member explains the process:

“We were taken by ambulance from the local health center...everything went smoothly a couple of hours later we were in the wards.”

Other members describe their experience at the LHC:

M was first diagnosed at the local health center where they referred us to the Salmaniya Medical Complex Accident and Emergency and a week later his sister exhibited same symptoms so I also took her to the local health center and we were again referred to the Accident and Emergency. But M didn’t need to be admitted as her brother was diagnosed a week before and I knew what to do.

Hospital experience and length of stay Several members explained that they felt more comfortable when they were in the wards; “it was more relaxed upstairs.” All of the group members were given a private room with the exception of one who was initially admitted in the pediatric intensive care unit after which she was moved to a private room in the general pediatric wards. One group member explained that the nurses in the wards were “better than the nurses in the Accident and Emergency”, they were “more caring” and “…in the wards there was no shortage.” Linked to this, another parent reported that staff in the Accident and Emergency “…were under a lot of pressure” suggesting that requiring newly diagnosed children with diabetes to be admitted via A&E may not be the most practical or acceptable approach.
All of the group members felt that the length of stay was adequate and they expressed their comfort in the private room as one member expressed “it was a nice room.”

6.4.1.3 Evaluation of the Education Received During the Hospital Admission Period

Role of nurse educators’ One common element in many of the focus groups was the emphasis on the importance of the role of the nurse educators at the time of admission. They described them as having done “their job well” and “…no one can fault them… they were excellent.”

One group member described her experience with the nurse educators:

“…after we left the ICU and were admitted in a private room in a general ward, the nurse educators were there for us immediately and the nurse educator sat with me and H’s father for a long time and explained to us to give insulin and injection site rotations.”

Length of education All group members expressed satisfaction at the length of the education as one member describes:

“…I feel that she went at the pace that I wanted and you know my son didn’t want to stay long so as long as I understood the essentials and was able to give the injections that was enough to be discharged.”

As highlighted in the above statement and reinforced by other parents is the fact that the nurse educators were able to match their pace to the needs of the families in terms of education, spending a longer or shorter time according to their receptiveness: “She sat with us several hours a day and devoted her entire attention to us.” This was further highlighted by comments from group members acknowledging that “…the time was enough and they were very clear” and “It was a good time” or “Yes, I agree she moved at our pace…”
Education materials When asked about the educational materials used one group member responded “Oh it was excellent, very complete.” This was the general response across all focus groups. One parent explains further:

“I liked the drawings [the nurse educator] used to explain my child’s condition. I mean even at home when I was trying to become more knowledgeable about my son’s condition I would go back to the drawings.”

Dietician role All group members learnt how to carbohydrate count and although many of the members knew about healthier food options, this was not always applied prior to diagnosis. One focus group members explains that prior to her child’s diagnosis she “…didn’t know about portions and now I have to give meals at specific time and quantity and it should be healthy.” One group member describes what she learnt from the dietitian:

“I learnt that I could give my son everything but within the portions allowed. He wasn’t deprived of anything…but he could eat at specific times. I also learnt that if his sugar is high I shouldn’t give him foods that will make it even higher and you know I knew about healthy eating and portions before but I didn’t apply it, now I am…”

Another member describes similar experience:

“I learnt about the healthy and unhealthy foods. I have applied this with all my children not just M. We stopped the sugar and the sweets. His brothers are the same.”

One group member explains that although she “found it difficult to plan meals to calculate carbohydrates” she now feels “… it’s not so bad, he isn’t being denied from anything I just make sure that his food is healthy and within the amount of carbohydrates.”
It is evident from the statements above that after sitting with the dietician the families made an effort to make healthier food choices for the entire family and not simply for their child with diabetes.

**Endocrinologist role** A majority of the focus group members describe their encounter with the consultant endocrinologist as being "once" and "briefly." When asked about if the endocrinologist had answered any questions or concerns the members may have had, one parent explained:

*No but to be frank I didn’t really ask him.... The nurses had answered all my questions.*

Others describe a similar experience with regards to the endocrinologist’s role:

"...[The endocrinologist] didn’t sit down with us, he just passed by. I would have liked it if he stayed longer to answer some of our questions."

In contrast one mother whose child was admitted to the Pediatric Intensive Care Unit describes much more input from the endocrinologist and explains that “I saw him three times in H’s admission period” and “He explained everything to us....” suggesting that their input is largely driven by the child’s condition on admission and therefore the care setting in which they are initially seen.

**6.4.1.4 Evaluation of the follow-up system at the pediatric diabetes clinic**

**Voicemail** Approximately two thirds of the members of the focus group explained that their preferred method of following up is with the voicemail. One member states “Ohhhh I always use the voicemail” and “If I need anything I leave a message for the nurses.” They explained that the nurse educators will respond “within the same day or next day.” However one parent described a negative aspect of using the voicemail:
“They are good but at times when I call they won’t respond till next day maybe it’s because they are very busy. So it’s late. That’s the only negative point.”

Another focus group member describes the same experience:

“….but if I call at 1:30 or 2pm they won’t respond till next day.”

**Hotline use** All of the group members describe depending on the hotline mostly “Just in the beginning...” When asked what reason would prompt them to use the hotline, one member explains that she would use it “when she gets hypoglycemia...” Another explains:

“Well his sugar was always high and he would be lethargic and I would get worried and call.”

In terms of promptness of response, one mother explains that “…they pick up immediately.”

Some group members explained that they try to deal with events of hyper or hypoglycemia and that they “…try to deal with this myself first before calling the nurses.”

**Supply issue** Half of the group members complained about insufficient supply of blood glucose strips, needles, and other supplies. One member explains:

“Yes we don’t get enough strips...sometimes I need to check his blood sugar more than the times given but maybe because he complains of a headache or stomachache so I check his sugar again but they give us a limited supply.”

Another focus group member describes a similar complaint:

“The only issue I personally have with is the supplies and obtaining enough supplies.”

[Note: Upon discharge from the hospital, patients are given a 6 months prescription for insulin and supplies such as needles, glucometer strips, alcohol swabs etc…. These can be obtained
either from the SMC pharmacy or from the pharmacy at the local health center. The prescription is renewed at their next follow up visit.

**Improvements** A common comment from group members was that that the clinic area itself “*It needs to be bigger!*”

**6.4.1.5 Exploring Recommendations for Future Support Programs**

**Future program** When parents in the focus groups were asked what types of programs they would like to see for their children, the majority exclaimed that they wished their child could meet other children with diabetes “…*so that they don’t feel like they are in this alone*” and “*so that psychologically they feel better.*” Others voiced similar concerns stating:

“*Yes especially if they could mix with children with the same condition they will feel that they are not all alone.*”

Psychological support was requested by approximately half the members with one parent stating:

“*I would like to address their attitudes; you know everything changes when they start insulin. So yes yes…psychologically.*”

One parent explained that they wished that the initiative be taken by the diabetes clinic in order to avoid parent-child clashes stating: “*but I want it to be through the clinic through you guys, they listen to you.*”

The rest of the members requested more trips and social gatherings for the children.
6.4.2 Pediatric Nurse Educators Focus Group

6.4.2.1 Barriers to Education

**Social barriers** When exploring some of the main barriers to education from the point of view of the pediatric diabetes nurse educators (PDN), familial social problems was one of the main themes which resonated throughout the focus group as an obstacle to education. One nurse described it in the following way:

“Sometimes social problems, it will be the main our main uh problem with the patient. Uh like if the patients uh uh parents are divorced sometimes or uh if they are non-educated ah well so it will be very difficult for us for education.”

Another diabetes nurse educator agreed that “social problems some psychiatric issue” are barriers to education and follow-up.

**Logistical barriers** Another barrier to education as identified by the PDN’s are logistical issues such as “shortage of staff” They reported finding it difficult to juggle the influx of outpatients coming for follow-ups post discharge or for review of blood logs resulting in long waiting times due to limited working space as highlighted in the following passage:

“Sometimes for example for walk in patients on Wednesday we are taking patients without any appointments. If there are so many patients and want to review for them umm some educational material and there is standing outside patients and we are only three and the place for education only here for outpatient. This suggests that the issues were a combination of inadequate space and staff combined with unpredictable nature of the caseload.

It would appear that one of the impacts of this shortage is the loss of patients to follow up appointments as explained in by one educator:
“...because of the shortage the shortage of the staff and in between the patient will be missing even if they are new patients because of the shortage of the staff. So imagine that we are three of us ah doing all this job...”

When asked about the length of education time, the nurses explained that although the average inpatient education time was two days, they moved at the pace the patient was most comfortable with as described:

“Some families they need one or two days according to their education, according to their response to the pathways.”

Facilities The lack of adequate facilities such as space is a theme that was echoed throughout the focus group. One nurse explains:

“Sometimes we are also arranging for re-education here for outpatient department and we don’t have rooms.”

Another nurse explains how the limited space available impacts education:

“The limitation of the place it is one effect and the ahhh the time the time that we are spending for the outpatient re-education, whatever we will give in three days maximum staying at home need to be reviewed.”

The nurses all agreed that if logistical problem were to be resolved that the time spent educating would be reduced and education could be completed within a 24hr period. One nurse explains it in this way:

“If we are crossing these problems yeah, it will be in one day the patient will be discharged.”

Relationship with patients Clearly the nurses develop a close relationship with the patients and this relationship has an impact on education and the willingness of families to undergo
behavioral changes. One of the main concerns of the nurses is what they describe as the abuse of the 24hr hotline. One nurse gives more details:

“Any time they are calling for silly things, silly silly things for nothing. We are with our children ahh praying or our special work we have it is not their business in between also they are shouting to us even and even emergency they don’t want from us anything and they are going on calling us so…”

The above passage highlights the frustration the nurses feel in relation to the 24hr hotline and its infringement on their personal time with their families. It also highlights the fact that some patients are using the emergency line for non-urgent matters and at times these patients can be, as put by the nurses, impolite.

The 24hr hotline was described as being an additional work pressure as described by this one educator:

“...the call that is 24 hours call the hotline this is too much pressure for us.”

6.4.2.2 BARRIERS TO BEHAVIORAL CHANGE

Treatment The treatment of diabetes was described as one of the main barriers to behavioral changes and in particular “the injection itself.” One nurse explains it in the following way:

“The injection and accepting that their son or their daughter has diabetes and this disease will be long life. It is very difficult to tell you that your son or your daughter is diabetes and this is his life and he should give this injection in all of his life. That’s the complication.”

Factors affecting acceptance Accepting the disease itself either by the child or their family, appeared to be a significant determinant of willingness to undergo the necessary behavioral
changes. Several themes were highlighted that relate to acceptance. One such factor is the family’s personal beliefs. One nurse described it in the following way:

“Also the belief, the belief of the family ahhh that this ahh disease will go. Always they are thinking that for type 1, temporary.”

From the statement above it is evident that there are overt misunderstandings amongst parents as to the pathophysiology of the disease and that this then impedes behavioral changes and even education process.

Whereas the impact of education level had appeared more clear cut earlier in relation to disease acceptance this did not seem to be the case as one nurse replied:

“It’s random... so you will have very highly educated families unable to accept....”

**Effect of Religion on acceptance** Religion was described by the nurses as having a “positive” impact on accepting the disease. One nurse states:

“The religion also itself it is affecting in the accepting.”

Another nurse further explains:

“Uhh, like what we are getting....uhh what are getting most of our patients what we are getting is something from the God and we will get some benefit in in...”

The above statement highlights how some families believe that this illness is a test from God and hence a challenge to their faith that should not be viewed negatively. This belief gives them “strength to cope.”
Social factors  Some social factors, according to the nurses, also have an impact on the acceptance of the disease such as “...the social also life of the family’ or “the surrounding.” However these were not expanded on and so did not appear to be major influences

Knowledge/family history  Having a family history of the disease or prior knowledge appears to have an impact on accepting the disease. One nurse explains:

“Especially if they are having family history; so that’s means they will accept their daughter or son to be diabetes.”

However the social stigma of the disease remains a concern of the families according to the nurses negatively impacting on their acceptance of their child’s condition. This was highlighted in the following statement:

“But here the society is having bad uhhh..you know anybody is knows that you, that your son is having diabetes that means that is very big big problem, its huge problem, it’s the main problem in your life...you cannot live with this problem. This is what they are thinking.”

6.4.2.3 ROLE OF PEDIATRIC DIABETES NURSE EDUCATORS

Treatment  One of the main roles of the PDN’s is in the active treatment of the disease which as described by the nurses involves “adjusting the blood sugar” and “increase and decrease insulin with doctors...” The nurses explained that during the admission period the physician will adjust the dose but that post-discharge if necessary they will make adjustments without referring back to the primary consultant. They did acknowledge however the need to refer back to the physician when a difficult case presents stating that “Sometimes yes, sometimes we need our doctors.”

Their role is also to “review the information” and as one nurse explains:
“...will review whatever they have problems at home even diet sometimes we are giving advice and we are adjusting the glucose also and we are repeating education for some patients.”

**Support** The PDNs also felt that they had a significant support role for families “because at first they will be in shock.” And when asked if emotional support takes up a major part of their time one nurse replied:

“Yes yes... it will take a big big part of our management.”

Besides emotional support, the nurses are also there to guide the patients on how to manage diabetes post-diagnosis advising them on the support options available as explained by one nurse in this statement:

“...to serve the patients ahh at home how to manage diabetes ahhh and the follow up system by either telephone, fax or walk in patients ummm”

**Education** Another major role is to “To start education,” “Educate, re-education” and “Modeling...” One nurse explains:

“We are following the patients uhh uhhh during three days after diagnose.. after discharge in 24hours hotline so any problem they are calling us ahhh anytime we are covering ,and the readings should be followed every day for three days...”

The above statement shows the close follow up the nurses provide post-discharge and in particular in the days after diagnosis in providing support by being available if needed 24hrs a day to adjusting blood sugar readings. Besides educating the patients and their families, the nurses are also involved in training other nurses or educating medical students with regards to the treatment and management of diabetes. One nurse explains:
“... the medical students also sometimes in between they are coming for us for teaching them and some of the staff also coming in between for us to take our service from us or ahh any information and they are coming for us students to train them in between.”

Management The nurses also have a managerial role in the department which involve reporting on statistics, administrative issues, and are involved in liaising with the Diabetes Society and their activities such as the annual diabetes camp, and other activities organized by the society:

“...management job we are doing and we have to uhh cover the society also the activities of the society”

6.4.2.4 Future Recommendations to Strengthen the Education Program

Several ideas were identified by the nurse educators that they felt would help improve and strengthen the education program they are currently delivering.

Logistics There is a basic need for more educational materials as one nurse states:

“we need educational materials to develop educational materials”

Equipment There is a need for equipment “like colored printer” and as one nurse states:

“We need telephone we don’t have telephone, telephone hotline we don’t have it, we need camera we need laptop we need educational materials to develop educational materials.”

Facilities As mentioned earlier, there is a need for more space to accommodate the patients.

Age-specific support The nurses highlighted the need to focus on “adolescents” with diabetes as they described them as being in a “crisis age” and “lost.” They highlight that this population in particular requires more of their attention as they will be moved from the pediatric clinic to the adult clinic. One nurse explains more:
“Ahh this period is very crisis period for the children. That they are newly diagnosed in this period they are teenagers they are not accepting sometimes. They are doing so many many things false from the disease. So they need support they need very strong support so the patients when they are transferred to adult they are coming back to us because nobody is there for them.”

Another nurse expands further:

“Because they are in between pediatric and adult and pediatric and adult some they will go into pediatric and some year they want to go into adult and this area they need a transitional clinic. This clinic is supposed to be for adolescents and there will be pediatric nurse and adult nurse and even the consultant they can match in this idea.”

Social Support All of the nurses agreed and recognized that there should be more of an initiative to provide social support for families. One nurse explains

“We need support for so many things to give the patients to encourage the patients in so many things.”

They focus on the need to provide a strong social support group for parents of very young children:

“They need to see be socials relationship especially for small, small, kids the parents will be very effective.”

Finally the nurses underline the need to engage key stakeholders along with the Diabetes Society to provide activities and support groups for the families and the children:

“For the society what they are doing, only the camping and now they are starting summer activities only that things but the children themselves they need more. For the whole of the year they need somebody to support continuous support continuous activities.”
**Finance** Financial constraints are identified as being a major barrier to providing better education. One nurse explains:

“We have also the proposal for the diabetes center it is still not done because of the economy…”

So although a proposal has been in place for a diabetes center the “financial problem” according to the nurses is hindering the development of the center which they hoped would resolve all logistical problems.

**Staffing** The nurse educators recognized many of their weaknesses and wanted to implement changes but due to the shortage of staff and limited work space they felt they were unable to do this as explained by one diabetes nurse educator:

"...and we don’t have the place to meet them together or the people to work on them we are only three of us we cannot do all of this. We have the ideas but we cannot do it because of the shortage.

**Education for PDN** Finally, the nurses stress the importance of educational courses and updates on diabetes in order for them to be able to provide the most up to date materials and education. They stress that “updates in diabetes should be yearly.” The nurses voiced the need for taking courses in dietary management in order to better understand the impact of nutrition and insulin as well as courses in psychology and counseling as this takes up a major part of their management. To sum up one nurse states:

“We should go for further study... for the diabetic educator course that we went it is not enough with our practice.... It is OK but we need more life is changing day by day.”
6.4.3 Physician Focus Groups

6.4.3.1 Role of Health Care Workers in Education Post-Diagnosis

Whilst evaluating the role of the health care workers in educating families post diagnosis from the perspective of the physicians several themes were highlighted.

Reliance on teamwork The physicians voiced strongly the importance of teamwork and their reliance on the nurse educators and dietician. When asked who they rely most on one replied “All of them!”

And another physician exclaimed:

“Well yes I cannot do my job without the diabetes nurse educators or the dietitians. They are all equally important.”

Role of physician at time of diagnosis The role of the physician at the time of the diagnosis is to break the news if this was not done so previously and explain to the parents about diabetes, its treatment and management. As one physician recounts:

“Well I go to see the patient whether they are admitted in the ward or if they are in the emergency and I explain to them about the disease and about the management and I address any concerns they may have”.

Another physician explains:

First of all I think I have to sit with the parent and explain what is diabetes so they understand what is the problem exactly and then after introducing after discussing what is diabetes is, I try to calm them down and tell them that there is a team that is going to take care of you so you are not alone. The team consists of the following and they will come and sit with you they will
discuss with you what is diabetes in details with you. Whatever you need from diabetes they will help you to understand to learn how to manage and we will be there for you.

**Breaking news** The physicians recount that most of the families they see have already been told about the diagnosis either “From the local health center” or when at the pediatric emergency department. When it comes to breaking the news one physician states:

“It is our job but most of the time when we see the patient they already know as the news was broken to them from the health center or in emergency or even some parents when they see blood sugar is high they know immediately that is diabetes.”

**Patient visit during admission period** It would seem that that although the physicians do daily rounds on their patients, as noted earlier their presence is more prominent in the severe cases that present with diabetic ketoacidosis and those that require pediatric intensive care. One physician explains:

“It depends on the condition if they are admitted with DKA usually I go frequently and make sure the acid-base balance in correcting. Once the acute management is done then daily I need to see them once or twice.”

**Patient knowledge of disease prior to diagnosis** The physicians explained that “almost all of them they know what is diabetes before” but most will have only a superficial knowledge of the disease. The physician explained in more details:

“Well...let's put it this way, they have all heard of diabetes but we explain to them in more detail and we explain the management.”

Often, the knowledge they have of the disease comes from their family members with the disease or from their community:
“Ya, so they relate it to the people they know and one more thing is the beliefs in the community”.

**Parental concerns at time of diagnosis** The physicians had varying views about what most concerned the parents at the time of diagnosis. One physician states:

“...from what I hear, parents are always concerned about the diabetes complications. So once they hear about the diagnosis they are afraid of the complications.”

The physician explains further:

“In the beginning yes maybe the injection but once we sit with them and start the uh treatment they find that that the blood glucose is coming down. I feel most of them... number one is the complication cause they are afraid from what happened to their grandma or grandpa because they have confusion they don’t know what is type 1 and type 2, so they are always confused with the types of diabetes.”

One physician explains that initially they will start to worry about the treatment about the injection and that they many have queries regarding “the food.” The physician elaborates:

“Yes they are so worried about what their child can and cannot eat and how they will be able to handle this...I tell them don’t worry our dietician will sit with you and explain about the diet. I reassure them that they can eat everything but in quantities prescribed by the dietician.”

**Physician role in post-discharge follow-ups** The role of the physicians as explained by one doctor “is to follow up with patient, to adjust insulin to check rotation site…” The physician explains in more details:

“What happens uh during their hospital stay, uh, I trust my team so I don’t interfere in uhh, the knowledge that they give to them but post discharge I ask my patients a few questions just to...
make sure that they grasped the information, they understood the information, they are comfortable with the information they got.”

**Role of the nurse educators** The physician’s explained from their point of view the role of the nurse educators:

“The nurses in my team they explain again what is diabetes in their way, their own way, then they sit with the parent and try to calm them down try to make them feel better and then they go into the diabetes education…”

And,

“So, usually they go into the details of acute complications, chronic complications, how to manage sick days, how to manage school days, how to manage parties, how to manage picnics…”

Another physician acknowledged that families tend to have a closer relationship with the nurses and explains further:

“Well the nurses they have closer contact with the patients. Whereas they will see us once every 4 months, they have access to the nurse daily…and if there are any serious concerns about the patient the nurse educators will come and discuss with us.”

**Role of the dietician** The role of dietician is “very important” as exclaimed by one physician as “many times the first things the parents ask us is what can our child eat.” Another physician explains the role of the dietician further:

“My dietician, my dietician also sits with the patient and will go into the details of the diet and uh try also to clear the things for them and try to give them clear information and tell them that type 1 diabetes is different in children than type 2 and she goes into the details of the dietary
management what is allowed and what is not allowed and how to balance the diet and the insulin requirements in relation to activity and in relation to sick days. So almost she is covering everything in relation to diabetes and the diet.”

One physician explains the need to have one dietician to focus on just the children with diabetes and states:

“Because she is the one dietician to cover all of pediatrics so she does not have enough time...”

And

“We need our own dietitian....”

**Referral to other consultant** The physicians explained that they do not often refer to other consultants as one states:

*Sometimes yes, most of the times it is with the nephrologist but it is very rare.*

Another physician reiterates:

“...it does but rarely like to a nephrologist if we suspect that there is kidney damage....but not often.”

They do acknowledge the need to refer to the psychiatrist although as one physician states:

“...we need a psychologist. But the doctor working with us is a psychiatrist”

And another physician states:

“...we refer to a psychiatrist a lot also....for families or children themselves having difficulty psychologically dealing with illness.”
6.4.3.2 **Barriers to education process**

**Limited resources/ Limited Facilities** One of the main barriers to educating as described by the physicians were limited facilities such as workspace and shortage of staff. One physician states:

“We are short staffed..... the diabetes nurse educators...we don’t have enough and no proper room or space.”

Another physician expands further:

“Yah I think there is uh, I mean what we have now, we are trying to cope with because usually we are trying to do our best even with the minimal as a team I mean. With the minimal available resources... but I think if we have a well-organized diabetic unit a place where we can either me or the dietician or the educators somewhere where we can sit in a calm quiet place with the parents and try to give them the information in a clear way in a suitable situation quiet...”

From the statement above, it is interesting to see that the physician recognizes the difficulty faced by the team and acknowledges that they do their best with the limited resources they find themselves confronted with.

**Lack of awareness/knowledge** Another barrier to education perceived by the physicians is the lack of knowledge of the disease and the family’s reliance on word of mouth with regards to the management and even complications of the disease. As one physician states

“They don’t have awareness; they don’t read other than their uhhh fields... So when you come to them they really know nothing. The knowledge they have is just the knowledge that is spread in the community. What everyone else knows they know. Whether they are educated or not educated it is the same for everyone...”
It would appear from the above statement that the physicians feel that dealing with educated families is not necessarily synonymously with the successful management of diabetes.

Another physician states in agreement:

“No I don’t think it is making a difference…. Sometimes I get illiterate people and umm they want to put more effort and do good for their kids and they do very well…”

6.4.3.3 Barriers to Behavioral Health Related Changes

Misinformation/ lack of Awareness Again, the theme of misinformation and lack of awareness of the disease were highlighted by the physicians as being a barrier to behavioral health changes. They reported that families sourced information from their surroundings and from their community which were not necessarily reliable sources.

One physician states:

“Ya, so they relate it to the people they know and one more thing is the beliefs in the community.”

Difficult age group The physicians’ state that specific age groups are also a barrier to behavioral changes:

“Adolescents and infants so those are the two groups you feel there needs to be more focus on them...”

Another physician states:

“I face the greatest difficulty with the adolescents. The young children they are easy to control. The older ones we have difficulty. They don’t want to take injection sometimes or sometimes they
don’t want to check blood sugar. They also want to eat at any time like their friends.... They are very difficult. You know it is the age”.

The physician went on to say:

“They need for us to spend more time with them, to try and deal with all these issues....you know especially when they transition to adult clinic they will feel lost because there they have no time to do this.”

6.4.3.4 RECOMMENDATIONS FOR FUTURE EDUCATIONAL PROGRAMS

When asked about future recommendation and suggestions for improvement, one physician states:

“I think we are providing an excellent job and service educating the families especially when they have been admitted. We admit for an average of 2 days only...”

And another confirms:

“We have an excellent team but most of the things we are doing it’s on a personal effort basis...”

It is interesting to see from the above statements that before elaborating on the needs for improvement, both physicians began by commending their team’s effort and achievements.

Facilities/limited resources The physicians explained the need to provide more adequate facilities and resources as explained by one:

“So if it done in an organized way and the people get what they deserve and the Ministry of Health try to help us in having a really well organized unit with all the facilities that we need I think that we can give more.”
Finance The doctors agreed strongly with the need to provide more financial support in order to update everyone on the current management and practices regarding diabetes. As they state:

“We especially need to send the nurses, the dietitians and even ourselves to conferences and we do not have the financial support.”

Training or educational courses The physician also stressed the need to train the entire team and “even after finishing the training we need updates” Another physician explains:

“All of us including the doctors, I think we need updates. Like the things that we saw 10 years back it was amazing and I don’t think that things are the same. We are reading we are attending conferences, but working with the right people also makes a difference.”

Shortage of staff The shortage of staff is a theme that consistently arises throughout the focus groups and the physicians were equally concerned:

“We need more staff more diabetes nurse educators and we need more dieticians one is not enough to cover the whole hospital. We need time more for the patient. They should come for 2 or more sessions as outpatient.”

6.5 DISCUSSION

This study aimed to gain a better understanding and insight into the relationship between healthcare providers and caregivers of children newly diagnosed with diabetes. In particular we aimed to explore the process of admission and education and the characteristics of the exchanges between various health care providers (HCP’s) and caregivers. Furthermore we wished to investigate processes which caregivers felt were conducive to successfully managing diabetes and those that imposed barriers. Finally we aimed to get an overview of the perceived roles of HCP’s in relation to each other and in relation to the caregivers of children with diabetes.
The themes highlighted from the focus groups have given invaluable insight and information with regards to the views of the families of children with diabetes and health care workers in this field. Perhaps one of the most beneficial insights gained from the focus groups is the way in which a lack of proper awareness and knowledge of diabetes prior to diagnosis can impact on treatment of the disease. As highlighted by the physicians and nurses alike, and confirmed by the families themselves, most of the awareness and information regarding the disease is obtained from their immediate community or from family members. Furthermore, this problem was identified as being non-discriminating of the social and educational strata but was “random.” This is contrary to some studies which have shown that lower socioeconomic status and educational level are contributing factors to health knowledge regarding diabetes care (245). Studies have shown that greater diabetes knowledge is associated with better adherence outcomes (245, 246), lower hemoglobin A1c (247) and fewer family conflicts (246). Furthermore, some studies suggest that better glycemic control can be achieved by improving health literacy, in particular the numerical skills of the caregivers of children with T1DM (248, 249), and can result in better adherence to insulin regimen (250). The authors of these studies suggest developing educational programs that address the issue of diabetes health care literacy (245) and intensive diabetes education for parents with low health literacy (250) and, although health literacy per say was not directly assessed in the current study, this approach would be expected to also help tackle the general misinformation identified amongst our population.

Another interesting insight from the focus group was the identification of future concerns of the families and the perceived concerns reported by the nurses and the physicians. Although the physicians felt that complications of the disease were the most dominant concern for parents of children with diabetes, the group members themselves also voiced concerns such as the fear of
social stigma of the disease and fear of their child being treated differently or concerns about when and if their child marries. Although these concerns are not medical, it is important that they be recognized and addressed by the healthcare workers as a means to influence change. The reports of concern regarding future complications and overall control of diabetes are consistent with the findings of Faulkner et al (251). The parents of children with diabetes in their study “reminisced”(251) about the events that led up to the hospitalization and voiced their sense of shock and denial, as did the parents in our study. Also consistent with the findings of Faulkner et al are the reports of changes in diet subsequent to the diagnosis of diabetes. The admission process and hospital stay was deemed by group members in the current study as being a positive experience. Most focus group members’ children were diagnosed at local health centers and then referred to the Salmaniya Medical Complex center physician or at the emergency department in the hospital (see flowchart in Figure 7).

In the most recent publication by the American Diabetes Association on the standards of medical care in diabetes (252), they state that diabetes education should be a collaborative partnership between the multidisciplinary healthcare team and the patients themselves. Treatment of patients should be tailored to their individual needs and should adopt diabetes self-management education (DSME) which is aimed at empowering patients to self-manage their illness (252). Application of this systematic educational program, DSME, in the United States has resulted in improvement in A1C levels (253, 254). In the United Kingdom, the Dose Adjustment For Normal Eating curriculum (DAFNE) is recommended for all adults with T1DM (255) and is a validated reproducible education program used to empower patients to take control of their disease (256) and which has shown to improve glycemic control and quality of life (257). The Kids in Control OF Food (Kick-Off) program adapted from the DAFNE curriculum targets
children aged 11-16 years (258). Pilot studies of the program are on-going but show promising results especially in improving quality of life (259). In Bahrain the current care models for diabetes management are based on acute care management and the reactive management of individual problems as they arise, instead of using a more proactive form of management. Such health care management is not sustainable in the long-term and can be taxing on health care systems and facilities (260). According to the American Diabetes Association, diabetes care should follow the chronic care model (CCM) (252) which has been shown to be effective in improving quality of care (261). The CCM has six main evidence based components which are (262) 1) delivery system design 2) self-management 3) decision support, 4) clinical information 5) community resources and 6) health systems. Hence, diabetes health care services in Bahrain may benefit from a shift which results in the increased use of primary and preventive care and a decrease in the use of acute tertiary hospital care (252).

In recent years several studies (263-267) have looked into the management of non-acutely ill newly diagnosed children with diabetes at home versus hospital care setting and have found a lower healthcare cost (265, 267) and increased overall satisfaction (264, 266) associated with home care. Home care is started by a pediatric diabetes nurse (PDN) who visits the home to educate the parents on the management of diabetes in practical terms (268). Depending on the pediatric diabetes center the patient is affiliated with, home care could mean the complete avoidance of hospital care (269, 270) or a short hospital stay (271) followed by home care management. The application and feasibility of a home-based healthcare approach in the Bahraini context could be further investigated as a means to decrease work load in hospital settings, and healthcare costs, whilst continuing to provide satisfactory education.
In the current study the roles of the health care workers as described by the families and the healthcare workers themselves generated some interesting themes. The role of the pediatric nurse educators was expressed as being central to the educational process both during and after admission. Their role was felt by many of the group members as being significant and they appreciated the time spent on education and the individualized pace at which the nurses took this. This is consistent with the study conducted by Howe et al (272) examining parental expectations of diabetes health care providers, in which group members also expressed their appreciation of health care provides that were “present for them” and “mindful in their interactions” despite having a busy clinic and suggests it may be the interactions of the HCP rather than their specific job title which is most important in effecting a satisfactory relationship. Furthermore, Howe et al found that parents in their study expressed their desire for the provision of practical individualized solutions to diabetes care, and they also voiced their desire for visits to be “efficient, convenient, and comfortable (272).” Despite the satisfaction of the parents or legal guardians, the current model of educating does not conform to the best practice as described by the literature stated above. The focus group members in our study expressed their appreciation of the health care providers but voiced their concerns about the difficulty in obtaining medical supplies from the hospital pharmacy due to issues with shortage of supply.

The physician’s role became more dominant during acute management such as when the patient was admitted with ketoacidosis. The physicians acknowledged the closer relationship and contact between the nurse educators and the patients. The dietician’s role was described as being very important and central to meal planning and carbohydrate counting. It was evident from the focus group that there was a strong reliance and sense of teamwork. The physicians had trust and confidence in the management of their healthcare team.
In terms of the follow-up and post discharge education, the majority of the focus group members expressed overall satisfaction at the services available. Most used the voicemail system to review blood sugar levels. They appeared satisfied with this although some parents acknowledged that if the readings were sent at the end of the day the response would not be received until the following day. It was interesting to note the high levels of dissatisfaction the nurses felt with regards to the 24hr hotline and what they believed was its infringement on their personal lives. They felt this system was abused, although most of the focus group members interviewed described their limited use of the hotline and its use only in times of real urgency. In a study conducted by Chiari et al (273), that looked at the effectiveness of an emergency hotline for children and adolescents with T1DM in Italy, they found that only 24% of the phone calls received were considered real emergencies. Furthermore, they also found in that 5 year retrospective analysis, that the real emergency phone calls came from parents of younger children with a shorter duration of diabetes and that the phone calls were often during the weekends or holidays (273). Perhaps in the future, an audit of the voicemail and hotline usage in the pediatric diabetes clinic in the SMC could help in defining where there is an issue and how these issues can be resolved.

In a recent review by Balkhi et al (274), on the impact of telehealth interventions to reduce management complications in T1DM, they state that one of the main challenges to telehealth is the provision of financial compensation and reimbursement to skilled staff delivering this service (274). Although the nurse educators did not highlight financial reimbursement as an issue in our focus group, it is worthy to note that the provision of the hotline is in effect only possible due to what one physician describes as a “personal effort basis;” of these nurses who in fact are not paid for the provision of this service. This could explain the
frustration that was exemplified in the focus group session by the nurses and should be an area of further exploration.

Several issues were identified by healthcare workers and focus group members as being barriers to education and behavioral changes. One of the main barriers from the point of view of the healthcare workers is dealing with the misconceptions and preconceived notions of the disease followed by social and psychological issues related to the acceptance of the disease. Several reviews have been published in the past decade looking at the impact of interventions on children with T1DM (275-281). These studies have shown that psychosocial interventions demonstrate greater efficacy than educational interventions alone in improving glycemic control as well as secondary outcomes such as quality of life, reduction in stress and family conflict. Furthermore it has been established that theory-based interventions appear to be more effective in achieving positive outcomes than interventions that are not built on the basis of a theoretical model (277, 281). Hence, family and child education should be supported by systematic, theory-based psychosocial interventions (281).

The focus group interviews allowed us to gain more insight into what the families and healthcare workers would like to improve and their future recommendations. Families stated that they would like to see the problem of lack of adequate supply of medication and strips resolved. They would also appreciate the nurse educators having a larger room to work in. Beside improvements in facilities and services, parents wanted to see more socialization and in particular social gatherings used as a platform for children with diabetes to meet and interact. The physicians and nurse educators also agreed that there is a need for more social support services for the families and in particular for very young children and the adolescents who are in
need of a transitional clinic. They expressed the need for psychological support especially at time of diagnosis when the family is in shock.

Adolescents with diabetes were highlighted as a significant yet under treated group which require more focus and attention. This is in agreement with previous research which has deemed adolescents with diabetes to be a high risk group with these emerging adults being prone to deteriorating diabetes control (282). Worsening of metabolic control in this vulnerable age group is due to multiple factors which include insulin resistance due to hormonal changes (282, 283) and growth (283) and psychosocial issues (282) coupled with poor decision making and impulsivity (284). It has been well established that parenteral involvement in collaboration with health care professionals during this critical period is associated with improved glycemic control (285-287).

The healthcare providers in our study underlined the need for continuous updates and education on the diabetes management. Furthermore, there is a need to engage key stakeholders in order to provide awareness campaigns that aim to differentiate between the various forms of diabetes and disseminate fact from fiction in the community. The healthcare workers recognize the weaknesses in their service but state limited resources and facilities as the main barrier to making improvements. The healthcare workers also describe the need to improve facilities and update their knowledge on a continuous basis by being provided with the opportunity to undergo more training and update courses and conferences.

6.5.1 LIMITATIONS OF STUDY

A limitation of this study is the very small number of subjects who voluntarily participated in the focus groups introducing a potential bias. Because there was only one
parent/child focus group, one nurse/educator focus group and one physician focus group making it difficult to make generalizations in regards to the results. Another limitation of this study is that we only assessed opinions, which can be subjective as opposed to outcomes, which are more objective and measurable. Furthermore, although families seemed to be overall happy with the educational process, which focuses on acute care management, there is now a general trend towards more of a preventative and primary care focused health care management as a more sustainable means of healthcare. This approach was not discussed with the current sample nor was a sample of families exposed to such an approach available for comparison meaning that the strengths and benefits of such an alternative approach in this population can only be hypothesized at the current time.

6.5.2 AREAS OF FURTHER RESEARCH

Further work needs to be undertaken investigating the usage of the voicemail and hotline, the feasibility of putting into place a structured psychoeducational program for adolescents, and the delivery of partial home care as opposed to complete hospital care at diagnosis. Finally, parental concerns besides the evident complications of the disease should be explored and used as a means to help bring about positive behavioral changes.

6.6 CONCLUSION

These focus groups were unique in providing an all-around and in depth insight into the beliefs and attitudes of children with diabetes and healthcare workers on topics ranging from the admission and educational process, to barriers to change and future recommendations. Overall the educational process and services were described positively although these did not conform to current best practice as described in the international literature. All stakeholders agreed with the
need to make improvements to facilities and to solve logistical issues in order to provide better services. Finally, the focus group highlighted the need to provide specialized care to adolescents in order to tackle the particular issues of this challenging group.
7.0 SYSTEMATIC REVIEW OF RANDOMIZED CONTROL INTERVENTIONS IN CHILDREN & ADOLESCENTS WITH T1DM

7.1 INTRODUCTION

Diabetes has been on the rise worldwide (281, 288). In the United States, the incidence rate of diabetes in youth was expected to increase by 23% between 2010 and 2050 and in the United Kingdom the incidence rate in children and adolescents under 16 is also on the rise (289). Bahrain has not escaped this increase with a reported incident rate of T1DM in children of 8 per 100,000 in 1995 increasing to nearly 30 per 100,000 in 2014 (290).

Maintaining good glycemic control is critical in preventing complications of the disease; nonetheless this can be a difficult task especially for children and adolescents as it requires the careful balancing between the daily insulin regimen, frequent blood glucose monitoring, diet and exercise (291, 292) all set against a background of usually reducing parental control and increasing patient autonomy as the child gets older. The current target for glycemic control in children is a HbA1c of < 7.5% (58 mmol/mol) without frequent hypoglycemia (293). Despite the importance placed on obtaining good glycemic control, studies have shown that children and adolescents are having difficulty achieving this in practice (294). However, according to the National Pediatric Diabetes Audit report in 2013-14, in the United Kingdom 18.4% of children and youths were achieving an HbA1c of less than 7.5%, a significant increase from the 2012/13 statistics in which only 15.8% of youths were achieving this target. Furthermore, the percentage of children and youth with an unacceptable level above 9.5% (80 mmol/mol) also decreased from 25.8% in 2012/13 to 23.9% in the most recent report (295). The audit also reports on variables affecting diabetes control which include ethnicity, with white ethnic groups achieving
better control than non-white ethnic groups, and socioeconomic status, with those living in deprived areas having poorer outcomes (295).

Although increasing knowledge of diabetes and its management are core components in diabetes education programs, as previously discussed there is a growing focus on the psycho-social aspects of disease management as well, which encompasses the acquisition of coping skills and positive family relationships (281). A systematic review published by the National Health Service Technology Assessment in 2000 (NHS HTA) (239) looking at the effectiveness of psycho-educational interventions in adolescents identified the need for more rigorously designed studies as those reviewed had several methodological flaws. Since then, there have been a number of reviews published that have looked at the effectiveness of these interventions in children (275-281, 296, 297). The reviews found little evidence to support educational intervention alone and identified the combination of psycho-social interventions with education as having more favorable outcomes (281). Furthermore, studies with a theoretical basis to their interventions appear to be more effective (277, 281). However the diversity of the studies and their inherent interventions makes interpretation difficult, with reviewers highlighting the need for randomized control trials of good quality undertaken in accordance with the CONSORT standards (278). In 2010, Savage et al (281) reviewed randomized control trials of interventions for children with T1DM, acknowledging the great advancement made in the development of psycho-social interventions since earlier reviews; however the authors again highlighted the need for greater scientific rigor in the assessment of interventions and a more systematic approach so as to establish effective interventions.

The results of the focus groups discussed in Chapter 5 have highlighted the need locally in Bahrain, as described by the healthcare team and the parents of children with diabetes, to
focus on adolescents and to assess the feasibility of putting into place a structured intervention program that is translatable into routine care.

7.2 SEARCH METHODS

7.2.1 DATA SOURCES

The following electronic databases were searched from January 2008-February 2015: MEDLINE, Psych INFO, Child Development and Adolescent Studies, CINAHL, British Education Index, Psychology and Behavioral Sciences Collection, PsycARTICLES, Centers for Reviews & Dissemination (CRD), SCI-EXPANDED, PubMed, Embase, and Scopus.

The search terms used were synonyms of the following: type 1 diabetes AND children AND educational interventions/programs. For example the synonyms used for diabetes included “type 1 diabetes” OR “diabetes mellitus” OR “insulin dependent diabetes”. The synonyms used for young people were “children/ child OR teen/teenager OR youth OR adolescent/adolescence.” Educational interventions or programs was more broadly defined and included psycho-social education or support or training including individual or family counseling (Table 28). The search terms were used as text words and any potential papers with full text were assessed for eligibility.

Inclusion Criteria

The inclusion criteria were randomised control trials (RCTs) that involved an intervention for managing any aspect of T1DM for a sample of children or youths aged between 6-18 years of age and/or their families. Only trials in the English language were included. Furthermore, although databases were searched from Jan 2008-Feb 2015, only studies from Jan
2010 to June 2015 were included in this review as the last published review in this subject was in 2010 (281).

Studies were excluded if they were not RCT’s or pilot studies and were excluded if they did not have an educational, psycho-social or family component to the intervention. Studies that looked solely at carbohydrate counting were also excluded as were interventions that involved technology such as telehealth.

Table 28 List of search terms used in systematic review

<table>
<thead>
<tr>
<th>Education Programs</th>
<th>Type 1 Diabetes</th>
<th>Children</th>
<th>Interventions</th>
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<td>Education*(al)</td>
<td>T1D*(M)</td>
<td>Child*(ren or hood)</td>
<td>Intervention*(s)</td>
</tr>
<tr>
<td>Program*(s or mes)</td>
<td>Type I Diabetes</td>
<td>Young*(er) person</td>
<td>Psychological</td>
</tr>
<tr>
<td>Package*(s)</td>
<td>Insulin-dependent</td>
<td>Young*(er) people</td>
<td>Psychosocial</td>
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<td>Toolkit</td>
<td>IDDM</td>
<td>Youth</td>
<td>Family therapy</td>
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<tr>
<td>Teach* (ing)</td>
<td></td>
<td>Adolescent*(s)</td>
<td>Behavioural/</td>
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<td>Train*(ing)</td>
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<td>Adolecetence</td>
<td>behavioral</td>
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<td>Teen</td>
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<td>Juvenile</td>
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<td>Puberty</td>
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<td>Boy(s)</td>
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<td></td>
<td></td>
<td>Girl(s)</td>
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7.2.2 Search Outcomes

The initial search identified 2269 electronic records after removal of duplicates. After screening the title and abstracts only 22 papers were found suitable for inclusion. An additional search for related papers in June 2015 yielded a further 5 papers. In total 17 studies were found to be suitable for review. Figure 8 summarizes the search process and output which includes the reason for the exclusion of papers.
Figure 8 Flow Diagram of search process and output
7.3 **RESULTS**

The studies included in the review were categorized according to whether they were i) educational based, ii) psycho-social or iii) family interventions. As shown in Table 29, two of the studies were education based studies alone (298, 299), five were psycho-social interventions (300-304) all aimed at adolescents alone, and ten studies involved a family intervention (291, 305-313). All of the family interventions had a psycho-education aspect although some had an education component as a control (308, 311, 314). A meta-analysis could not be undertaken as the studies and outcome data did not provide sufficient homogeneity to allow for such an analysis.

7.3.1 **STUDY CHARACTERISTICS**

Seventeen RCT’s conducted over a 5-year period were analyzed. Collectively, these studies recruited a total of 2936 participants. Two interventions were educational (n=428), five were psycho-social (n=614), and ten family interventions (n=1453) (see Table 29). Four interventions were web-based (n=502), four studies were integrated in the hospital diabetes clinics (n=390) and six studies were conducted within the hospital premises (n= 1239) but did not explicitly state where in the hospital e.g. in- or outpatient setting. Three studies (n=530) did not explicitly state where the intervention took place. Three studies exclusively involved a parent(s) of children with T1DM (305, 306, 314) as opposed to solely focusing on the child or on the child and parent together.

The studies took place in the United States, United Kingdom, Canadian, Australian, Irish and Danish jurisdictions with the majority based in the U.S (n=8) followed by the United
Kingdom (n=5) and Australia (n=2). The majority involved multiple centers (291, 298, 299, 302, 311-314) with two studies (308, 309) involving only two centers.
Table 29 Systematic review of studies investigating the differential effects of education programs on various outcomes related to T1DM

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Christie et al. | 2014 | UK      | CASCADE Study (291)      | 362 8-16yrs               | **Type of Study:** Cluster randomized controlled trial  
**Intervention:** (n=70)  
**Description:** Structured Diabetes Education Program consisting of 12 hours of education over 4 weeks in 3 hourly interactive group based sessions with 3-4 families  
**Theory/general principle (if provided):** Interactive group education  
**Duration:** 4 weeks  
**Control:** (n=65)  
**Description:** Standard diabetes care | **Outcome measures:** HbA1c  
**Secondary outcome measures:** hypoglycemic episodes, hospital admissions, diabetes regimen, knowledge and skills of diabetes management, responsibility, compliance, clinic utilization, emotional and behavioral adjustment, diabetes specific quality of life.  
**Findings:** Intervention had no effect on HbA1c at 12 months (p = 0.584) or 24 months (p = 0.891).  
Half (50%) of the young people in the Intervention group reported that the groups had made them want to try harder and that they had carried on trying at 24 months.  
Intervention group parents at 12 months and young people at 24 months had higher scores on the diabetes family responsibility questionnaire.  
Young people reported reduced happiness with body weight at 12 months  
**Notes:** Only 68% of groups were run.  
Of the 180 families recruited, only 53% attended at least one module. |
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<tr>
<th>Author Year</th>
<th>Country</th>
<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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</table>
| Coates et al. 2013 | Northern-Ireland | CHOICE Study (299) | 135 13-19yrs | Type of Study: Randomized controlled trial  
Intervention: (n=70)  
Description: Structured diabetes education (12 hours education over 4 weeks, in 3 hourly interactive, group based sessions).  
Theory/general principle (if provided): Interactive group education  
Duration: 4 weeks  
Control: (n=65)  
Description: Routine care – 3 month review at clinic using a problem-solving approach. | Outcome measures: HbA1c  
Secondary outcome measures: BMI, hyper/hypoglycemia, dietary adherence  
Findings:  
Significant difference in HbA1c at 24 months (Intervention 81mmol/mol vs. control 75mmol/mol).  
The mean BMI remained the same in the intervention and Control groups from baseline to 6 months.  
No difference in reported hyper or hypoglycemic episodes.  
Better dietary adherence at 1, 3 and 6 months in the Intervention group but return to baseline at 24 months. |
| Doherty et al. 2013 | UK | (305) | 79 Parents of 11-17yrs | Type of Study: Randomized controlled trial  
Intervention: (n=42)  
Description: Web-based, self-directed Teen Triple P (positive parenting program) workbook (10 x 1 hr modules) plus chronic illness tip sheet  
Theory/general principle (if provided): Social learning principle  
Duration: 10 weeks  
Control: (n=37)  
Description: Usual care | Outcome measures: diabetes-related conflict, parental stress  
Secondary outcome measures: parental perceptions of child’s behavior, feelings about parent, parenting style  
Findings: The Intervention group showed significantly improved diabetes-related conflict ( p=0.008) but not parental stress when compared to Control group.  
 Significant improvement in the Intervention group for disruptive behavior problems, productive parenting strategies and self-confidence in parenting skills.  
Notes: All outcome measures were self-reported.  
Subject retention was 68%. |
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<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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</table>
| Gregory et al.         | 2011 | UK      | DEPICTED STUDY (313)     | 693 (657 had follow-up analyses) children and 1 of their carers 4-15yrs | **Type of Study**: Cluster randomized controlled trial  
**Intervention**: (n=318)  
**Description**: “Talking diabetes” psychosocial intervention delivered by trained healthcare professional which involves flexible consultation styles, balancing multiple health behaviors, negotiating behavior change, targeting interventions to individual needs  
**Theory/general principle (if provided)**: Behavior-change theory  
**Duration**: regular appointments over 12 months  
**Control**: (n=339)  
**Description**: Standard care delivered by non-“Talking-diabetes”-trained healthcare professional  
**Notes**:  
Phase 1 – Training of health-care staff  
Phase 2 – Trial of training program | **Phase 2 Outcome measures**: HbA1c over 12 month study period  
**Secondary outcome measures**: Patient - Quality of life, BMI and psychosocial measures, self-care activities, service usage measures  
Carer – Quality of life  
Professionals – performance of training techniques  
**Findings**:  
HbA1c levels increased by a similar amount from baseline to follow-up in intervention and control arms.  
A non-significant 1% increase occurred in HbA1c levels in the intervention arm compared to Control group.  
There was no effect of healthcare professionals’ training on HbA1c level in patients attending their services \(p = 0.5\).  
Intervention group experienced a loss of confidence in their ability to manage diabetes.  
Controls showed reduced barriers \(p = 0.03\) and improved adherence \(p = 0.05\).  
Patients in intervention arm reported short-term increased ability to cope with diabetes \(p = 0.04\).  
Carers in the intervention arm experienced greater excitement about clinic visits \(p = 0.03\) and improved continuity of care \(p = 0.01\). |
<table>
<thead>
<tr>
<th>Author Year Country Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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</table>
| Grey et al. 2011 USA (314)                 | 181 Up to 12 years       | **Type of Study:** Randomized controlled trial  
**Intervention:** (n=75)  
**Description:** Coping skills training – six 1.5hr interactive sessions delivered by a health professional, each focusing on a coping skill delivered to groups of 2-5 and parents were encouraged to attend  
**Theory/general principle (if provided):** Social cognitive theory  
**Duration:** Six sessions  
**Control:** (n=106)  
**Description:** Group education – equal attention group education providing updates in care of T1DM focusing on insulin regimens, carb counting, sick days, sports | **Outcome measures:** HbA1c, parental coping, quality of life, parental responsibility (proxy for child responsibility level), diabetes-related conflict.  
**Findings:** There were no significant treatment effects on any outcome variable.  
When rates of change over time were examined across both groups, there was improvement in parental coping (p < 0.001) and quality of life (p = 0.005).  
Significant decrease in parental responsibility for diabetes-related tasks over 12 months (p<0.001) in intervention and control arms.  
Significant increase over time in children’s HbA1c levels in intervention and control arm (p<0.001).  
No significant changes in diabetes-related conflict.  
**Notes:** Number of sessions attended was not related significantly to changes in outcomes. |
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Grey et al.</td>
<td>2013</td>
<td>USA</td>
<td>(302)</td>
<td>320 11-14yrs</td>
<td>Type of Study: Multisite randomized parallel group trial</td>
<td>Outcome measures: HbA1c and quality of life Secondary outcomes: Stress and coping, self-efficacy, self-management, social competence, family conflict</td>
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<td>Program 1: (n=42) Description: Internet coping training skills program (TeenCope) used characters whom had T1DM in videos to model problematic social situations and coping skills Theory/general principle (if provided): Social cognitive theory Duration: 5 weeks</td>
<td>Findings: Stable quality of life and minimal increases in HbA1c levels over 12 months in program 1 and 2 and no significant differences between the groups. After 18 months, those who completed programs 1 and 2 had lower HbA1c (p=0.04), higher QOL (p=0.02), social acceptance (p=0.01), and self-efficacy (p=0.03) and lower perceived stress (p=0.02) and diabetes family conflict (p=0.02) compared with those who completed only program 1 OR 2.</td>
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<td>Program 2: (n=41) Description: Internet diabetes health education program (Managing Diabetes) problem solving program using visuals and an interactive interface to teach youth about healthy eating, physical activity, glucose control, sick days and diabetes technology</td>
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<td>Program 1 followed by 2: (n=65) Program 2 followed by 1: (n=57) Program 1 OR 2 completed only: (n=83)</td>
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<td>Author</td>
<td>Year</td>
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| Holmes et al.   | 2014 | USA     |                          | Families of 226 11-14yrs  | **Type of Study:** Randomized clinical trial  
**Intervention** (n=137 enrolled, 80 in final assessment)  
**Description:** Four brief family teamwork  
**Theory/general principle (if provided):** Coping skills training  
**Duration:** 18 months  
**Control:** (n=89 enrolled, 56 in final assessment)  
**Description:** Diabetes education in addition to quarterly medical appointments | **Outcome measure:** Glycemic control  
**Findings:**  
Both treatment groups prevented deterioration in adolescent disease care and improved quality of life in adults and adolescents without an increase in family conflict.  
Over the 3-year follow-up period, the Control group improved disease adherence and glycemic control more effectively than the Intervention group. |
<table>
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<tr>
<th>Author Year Country Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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</thead>
</table>
| Husted et al. 2014 Denmark (309)            | 71 13-18yrs              | **Type of Study:** Randomized clinical trial  
**Intervention:** (n=37)  
**Description:** Guided self-determination in youth - 8 sessions scheduled over an 8-12 month period involving 18 semi-structured reflection sheets to be completed by the child using their own words or drawings, 5 sheets for the parents and 6 if the child was visiting a dietitian to be completed between sessions  
**Theory/general principle (if provided):** Self-determination theory  
**Duration:** 8-12 months  
**Control:** (n=34)  
**Description:** Treatment as usual | **Outcome measure:** HbA1c measured at baseline and every 3 months  
**Secondary measures:** Multiple measures indicating development of life-skills  

**Findings**  
Intervention had no significant effect on HbA1c (p=0.85). Intervention significantly reduced the lack of motivation for diabetes self-management after adjusting for the baseline value (p=0.001).  
Compared with the Control group, the intervention time to completion was longer in the Intervention group (p<0.001) and had a higher rate of non-attendance (p=0.01).  
Intervention group parents participated in fewer of the adolescents’ visits (p=0.05) compared with control parents.  
**Notes:** 80% completed the trial, and 75% completed a six-month post-treatment follow-up. |
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<th>Author</th>
<th>Year</th>
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<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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| Katz et al. | 2014 | USA | (310) | 153 8-16yrs | **Type of Study**: Randomized clinical trial  
**Intervention 1**: (n=52)  
*Description*: monthly outreach by a care ambassador whose role included outreach to families to schedule clinic appointments or to relay family concerns to medical providers  
**Intervention 2**: (n=50)  
*Description*: Monthly outreach by a care ambassador plus a quarterly clinic-based 30 minute psychoeducational intervention also delivered by the care ambassador who facilitated problem solving and role-play exercises  
**Duration**: 2 years  
**Theory/general principle (if provided)**: Care ambassador  
**Control group** (n=51)  
*Description*: Standard care | **Outcome measures**: HbA1c  
*Findings*: No differences in HbA1c were detected among the three groups at 2 years.  
Intervention 2 was effective in maintaining or improving HbA1c and parent involvement in children with suboptimal baseline glycemic control. |
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<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Mulvaney et al.</td>
<td>2010</td>
<td>USA</td>
<td>(303)</td>
<td>72</td>
<td>13-17yrs</td>
<td><strong>Type of Study:</strong> Randomized controlled trial</td>
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<td><strong>Intervention:</strong> (n=34)</td>
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<td><strong>Description:</strong> Usual care plus intervention support in the form of six multi-media stories accessed via the “YourWay” website, focusing on psychosocial barriers to self-management, coping and problem-solving. (There is also access to personalized homepage, multimedia presentations, social networking via a forum and help from experts and weekly emails)</td>
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<td><strong>Theory/general principle (if provided):</strong> Learning, social-cognitive and self-determination theories</td>
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<td><strong>Duration:</strong> 11 weeks</td>
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<td><strong>Control:</strong> (n=18)</td>
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<td></td>
<td><strong>Description:</strong> Usual care</td>
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<td><strong>Outcome measure:</strong> HbA1c, self-management, problem-solving</td>
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<td><strong>Findings:</strong> Using intention-to-treat analyses, group differences were not significant, however using as-treated analyses, the Intervention group significant improved in self-management (p=0.02), and showed some improvements in problem-solving (p=0.23)</td>
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<td>Unlike the Control group whose mean HbA1c increased, the Intervention group remained constant HbA1c (p=0.27).</td>
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<td>Author Year Country Study name (if provided)</td>
<td>Number randomized and age</td>
<td>Study details (n=number allocated)</td>
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</table>
| Murphy et al. 2012 UK FACTS (311)         | 305 11-16yrs              | **Type of Study**: Randomized clinical trial  
**Intervention**: (n=158, however only 75 attended sessions)  
**Description**: Families and Adolescents Communication and Teamwork Study (FACTS) education program (6 90 minute sessions for parents and adolescents per month focusing on skills training and teamwork)  
**Theory/general principle (if provided)**: Skills training  
**Duration**: 6 months  
**Control**: (n=147)  
**Description**: Conventional clinical care | **Outcome measure**: HbA1c, parental input  
**Findings**: All biomedical and psychosocial outcomes were comparable between groups.  
At 18 months HbA1c was not significantly different in either group or between groups over time.  
At 12 months, adolescents did not perceive any changes in parental input.  
**Notes**: Session attendance was poor: 30.4% families did not attend any sessions and 47.5% families attended 4 or more group sessions. |
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>Nansel et al.</td>
<td>2012</td>
<td>USA</td>
<td></td>
<td>390 families 9-14.9yrs</td>
<td>Type of Study: Randomized clinical trial – multicenter parallel group study</td>
<td>Outcome measure: Glycemic control</td>
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<td>Intervention: (n=201)</td>
<td>Findings: The intervention had a significant effect (p=0.03) on glycemic control from baseline to 24 months. Participants aged 12-14 decreased their HbA1c significantly (p=0.009) over 24 months from baseline but no such effect was seen in those aged 9-11yrs. Adherence was not affected by the intervention.</td>
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<td>Description: Clinic-integrated behavioral intervention focusing on family management of diabetes - “WE-CAN manage diabetes”</td>
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<td>Theory/general principle (if provided): Social cognitive theory, self-regulation models and systems theory</td>
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<td>Duration: 2 years</td>
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<td>Control: (n=189)</td>
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<td>Description: Standard care</td>
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<tr>
<td>Nicholas et al.</td>
<td>2012</td>
<td>Canada</td>
<td></td>
<td>31 families 12-17yrs</td>
<td>Type of Study: Randomized controlled trial</td>
<td>Outcome measures: Social support</td>
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<td>Intervention: (n=15)</td>
<td>Findings: The intervention lead to social support benefits approaching statistical significance.</td>
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<td>Description: Web-based intervention comprised of diabetes-based information, interactive learning activities and relevant discussion topics whereby patients accessed the internet every day for 2 hours per day (on average)</td>
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<td>Theory/general principle (if provided): Web-based peer support and McCracken’s** (long interview) approach</td>
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<td>Duration: 8 weeks</td>
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<td>Control: (n=16)</td>
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<td>Description: Had access to the website following trial completion</td>
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<tr>
<td>Author Year Country Study name (if provided)</td>
<td>Number randomized and age</td>
<td>Study details (n=number allocated)</td>
<td>Outcomes</td>
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| Noyes et al. 2014 EPIC UK (298)             | 293 6-18yrs               | **Type of Study:** Randomized controlled trial  
**Intervention** (n=223, 190 analyzed)  
**Description:** Age-appropriate Evidence into Practice Information Counts (EPIC) Diabetes diaries and information packs to support decision-making and self-care.  
**Theory/general principle (if provided):** Social learning theory and developmental theory  
**Duration:** 6 months  
**Control:** (n= 114, 103 analyzed)  
**Description:** Routine clinical practice | **Outcome measure:** Diabetes self-efficacy and quality of life (via PedsQL).  
**Secondary measure:** HbA1c  
**Findings:**  
No significant difference was found in the mean quality of life scores between groups at baseline, 3 or 6 months for either the child-reported or parent-reported measure.  
These values were also similar across all three time points within the Intervention group and within the Control group.  
Both groups had a range of recorded HbA1c levels, which required improvement to reach levels recommended by the Institute for Health and Care Excellence guidance.  
**Notes:** This study was the third stage of a four-stage study. |
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Serlachius et al. | 2014 | Australia/New Zealand (300) | 147 13-16yrs | **Type of Study:** Randomized controlled trial  
**Intervention** (n=73 intent-to-treat, 30 analyzed)  
Description: 5 2 hour sessions carried out over 5 weeks of Best of Coping (BOC) cognitive behavioral therapy involving coping strategies, goal setting, self-talk, problem solving and conflict resolution  
Theory/general principle (if provided): Cognitive behavioral therapy  
Duration: 5 weeks  
Control: (n=74)  
Description: Standard care | **Outcomes**  
**Outcome measure:** HbA1c at 3 and 12 months  
**Secondary outcome measures:** stress, self-efficacy, quality of life  
**Findings:**  
HbA1c - little evidence of a group difference at 3 months or 12 months via intent-to-treat or per protocol analysis.  
Stress – at 3 months, significantly less stress in Intervention group than Control group (p=0.0.019) however this was not sustained at 12 months.  
Self-efficacy - consistently higher in Intervention group compared to Control group (p<0.05) at 3 and 12 months.  
Quality of life – better in Intervention group at 3 months (p=0.008) but not maintained to 12 months. |
| Wang et al.     | 2010 | USA (301)     | 44 12-18yrs | **Type of Study:** Randomized controlled trial  
**Intervention 1:** (n=21)  
Description: Motivational interviewing at baseline and 3 months.  
Theory/general principle (if provided): Motivational Interviewing  
Duration: 3 months  
**Intervention 2:** (n=23)  
Description: Structured diabetes education at baseline and 3 months. | **Outcome measure:** HbA1c  
**Findings:**  
The intervention 2 group over the 6 months of follow-up had lower adjusted mean HbA1c levels than the intervention 1 group (p = 0.03).  
There were no differences in any of the psychosocial measures. |
<table>
<thead>
<tr>
<th>Author Year Country Study name (if provided)</th>
<th>Number randomized and age</th>
<th>Study details (n=number allocated)</th>
<th>Outcomes</th>
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</thead>
</table>
| Westrupp et al. 2014 Australia (306)       | 76 4-12 yrs.               | **Type of Study**: Randomized controlled trial  
**Intervention**: (n=38)  
**Description**: Ten 1h weekly sessions with a clinical psychologist. Triple-P teaches 17 strategies some of which promote children’s competence and development and some of which help behavior management. Two books were given – a workbook and a parenting advice book. All parents received standard diabetes care.  
**Theory/general principle (if provided)**: Social learning principle  
**Duration**: 3 months  
**Control**: (n=38)  
**Description**: Standard diabetes care | **Outcome measures**: Child internalizing and externalizing behavior problems measured at 3 and 12 months.  
**Secondary outcome measures**: glycemic control, parent mental health, parenting skills, family function.  
**Findings**: At three months, parental mental health, parenting skills and family function significantly improved (p<0.05) following the intervention.  
Child mental health and glycemic control showed very little change at 12 months.  
Child mental health, parent mental health, parenting skills and diabetes family conflict in children or families of children with pre-existing internalizing or externalizing behavior problems showed greater improvements at 3 months (p<0.05) however parenting self-efficacy worsened. Parent mental health and parenting competency improvements were sustained over 12 months in this group. |


7.3.2 Theoretical Components

The majority of the studies in the review were explicitly theory based (n=12). Four studies were based on social cognitive theory (SCT) (302, 308, 312, 314) with one study being based on both social cognitive and self-determination theories (303). One study was based on cognitive behavioral therapy (CBT) (300), two based on social learning theory (SLT) (305, 306) in the context of the Teen Triple P (positive parenting program). One study was exclusively based on the self-determination theory (309), two involved motivational interviewing (MI) (301, 313) and one structured educational program involved both motivational interviewing and solution focused brief therapy (SFBT) (291).

Fidelity to theory was evident in most of the theoretical based interventions between the outcomes and underpinning theories. In the “WE CAN manage diabetes” Nansel et al’s intervention was designed to help families improve diabetes management by improving self-efficacy underpinned by social cognitive theory. One education based intervention explicitly stated the dominant ‘normalization’ theory underpinning the Evidence into Practice Information Counts (EPIC) packs and diabetes diaries (298).

7.3.3 Effectiveness of Intervention and Outcome Measures

Outcomes were measured at several points in most of the trials ranging from 3 months to 24 months (see Table 30). All the studies, with the exception of two (304, 305), reported on HbA1C as an outcome measure. In fact HbA1C was the primary outcome measured across thirteen of the studies and was a secondary outcome in three of the studies (298, 306). A significant improvement in HbA1C was reported in four of the studies, one was a structured
educational program (299), one was a family intervention (312) and two were psycho-social interventions (301, 302). Nansel et al (312) examined the effect of a clinic-integrated behavioral intervention focusing on family management of diabetes and found a significant improvement in glycemic control with improvement in mean HbA1c (0.44 in intervention group and 0.76 in usual care group; p=0.03) from baseline to 24 months in the intervention arm group. Wang et al compared motivational interviewing to structured diabetes education in adolescents with HbA1C of ≥9%. They had hypothesized that lack of motivation rather than a lack of knowledge is what hinders good glycemic control however, they found a significant improvement in adjusted mean HbA1C in the group randomized to the structured diabetes education (p=0.03) (301). The authors conclude that motivational interviewing in the absence of previously establishing education level does not improve metabolic control but rather continuous education or re-education for children with poor control may have a beneficial impact on glycemic control (301).

The study conducted by Grey et al (302) was a study comparing the effect of two internet based psycho-educational programs: TeenScope (program 1) which was designed based on cognitive-social learning principals and Manage Diabetes (program 2), a diabetes education and problem solving program designed as a control. The study also looked at the combined effect of the programs with the adolescents invited to go on to complete the program they had not completed at the end of the first study phase. After 18 months the study results showed that those who completed both programs had a lower HbA1C (p=0.04) and higher quality of life scores (p=0.02), self-efficacy (p=0.03) social acceptance (p=0.01) and lower perceived stress (p=0.02) and diabetes family conflict (p=0.012) compared to those that completed either program alone. No significant difference was found between groups for satisfaction, or attendance and contrary to the authors’ hypothesis there were no significant difference between
the two groups for any of the primary outcomes after 12 months using intent-to-treat analysis. HbA1c levels increased though not significantly in both groups. The group that had completed the Manage Diabetes program had less family conflict (p=0.02) than those in the TeenCope program.

A decline in metabolic control is not surprising during pre-adolescents and adolescents and has previously been described (315). Two studies reported an increase in HbA1c (313, 314) and although the studies conducted by Mulvaney and Holmes et al show no improvement in glycemic control, they make the argument that their interventions nonetheless prevented deterioration of diabetes care. Hence, no deterioration in glycemic control can be considered as a success.

Quality of life (QoL) was the second most frequent outcome to be measured. It was measured in eight of the studies in the review (298, 300-302, 308, 310, 313, 314). No significant difference over time was found in the mean quality of life scores in the studies reported by Noyes, Gregory, Wang and Katz (298, 301, 310, 313). Serlachius et al reported a significant improvement in QoL at 3 months (p=0.008) but this was not maintained after one year (300). In the study reported by Holmes and colleagues participants were randomized into either an intervention group that included 4 quarterly coping skills sessions or a diabetes education session either prior to or after their regular quarterly medical visits. Those in the diabetes education arm of the study performed just as well or even better in quality of life improvements over time as those in the coping sessions. Furthermore, the education group adhered more to the follow-ups (p=0.014) compared to the coping group. The authors suggest that both basic education and coping skills may be needed to improve blood sugar control (308). Studies conducted by Grey and colleagues (302, 314) both reported on significant and positive changes in QoL: one study

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which used the internet as a medium to run two programs (Internet coping skills program (TeenCope) and an internet diabetes health education program (Managing Diabetes) resulted in a higher QoL (p=0.02) after 18 months in the participants that had completed both the internet programs compared to those that did not complete both programs. The earlier study conducted by Grey and colleagues (314) involved training parents to use coping skills which resulted in an improvement in quality of life (p=0.005). Self-efficacy, family conflict, and parental stress, coping and parental skills, hyper/hypoglycemia’s and BMI were some other outcomes measured.

At the endpoint measurements (which ranged from 3 to 24 months), nine out of the ten family focused interventions demonstrated a positive effect on some outcomes with only one study conducted by Murphy et al (311) not showing any positive effects on any of the outcomes measured. Poor session attendance (30.4% of the families did not attend any session) and difficulty scheduling sessions were cited as possible reasons for the negative outcomes (311). One of the two education interventions showed a positive effect on the outcomes measured (299). Specifically, Coates and colleagues reported a significant difference in HbA1C between the intervention group that received structured diabetes education as opposed to those in the control arm receiving usual care (299). No difference in mean BMI or reported hypo or hyperglycemia were shown although those in the intervention group had better dietary adherence for up to 6 months post intervention (299); four (300-304) of the five psycho-social interventions showed significantly positive outcomes on some measurements.

Wang et al (301) report on a lower adjusted mean HbA1c in the group receiving structured diabetes education as compared to those receiving motivational interviewing whilst Mulvaney et al reported (303) a significant improvement in self-management (p=0.02). The fifth
study conducted by Nicholas et al reported improvements in the quality of relationships outside the family circle although this did not reach significance (304).
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<th>Structured Educational Intervention</th>
<th>Psychosocial Intervention</th>
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<td><strong>Family Outcomes</strong></td>
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A Noyes; B Coates; C Serlachious; D Wang; E Grey’13; F Mulvaney; G Nicholas; H Doherty; I Westrupp; J Grey’11; K Holmes; L Husted; M Katz; N Murphy; O Nansel; P Christie; Q Gregory

✓ Grey shading indicates significantly positive outcome(s)
*significant improvement in QoL at 3 months but this was not maintained after one year
** Significant improvement in those that completed both coping and education session together;
†Significant improvement after using as treated analysis;


7.3.4 Quality of Randomized Control Trials

One educational study (298) and three family therapy interventions were developed from pilot studies (277, 291, 313). The use of manuals, in which written protocols and education material are available to guide the intervention, were reportedly used in both of the structured educational interventions (298, 299) and five of the family interventions (291, 305, 306, 311, 313). Training of the interventionist or care provider was reported in eight of the interventions (291, 299, 301, 309-311, 313, 314) and continued supervision of interventionist in all but three studies which did not explicitly state this (299, 309, 311). Nine of the studies used the Consolidated Standards of Reporting Trials (CONSORT) diagram for reporting flow of participants thorough the trial (291, 298, 302, 305, 306, 308, 311, 313, 314).

Quality of the studies were assessed using the Cochrane Collaboration's tool for assessing risk of bias (316) which rates the risk of bias based on seven main criteria: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome measures; incomplete data, selective reporting and any other perceived bias (see Table 31). The studies are rated as being low risk, high risk or unclear risk of bias based on whether or not they have met certain criteria described in the assessment tool. All of the educational and family interventions (see Table 31) explicitly reported on attrition compared to only 2 of the psycho-social interventions (300, 302). Most of the studies used block randomization (299, 303, 308, 309, 312, 314). Doherty and Serlachius et al (300, 305) used computer generated block randomization. Two other studies used a computerized allocation system to generate sequences but they did not report using blocks (302, 311). Noyes et al (298) reported using a web-based
randomized service. Wang et al (301) report randomizing based on a sex-stratified schedule, no further details were given.

For allocation concealment measurements, six of the studies reported using sealed envelope techniques (300, 303, 306, 309, 312, 314). In terms of implementation, seven studies explicitly reported blinding of research assistants or the use of an independent statistician in randomization (291, 300, 301, 305, 306, 311, 312, 314). Gregory et al (313) report that although they aimed to recruit subjects before the allocation of centers was revealed, this was not always possible.
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<th>Structured Educational Intervention</th>
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<td>Other bias</td>
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**UR unclear risk; LR low risk**

A Noyes; B Coates; C Serlachious; D Wang; E Grey; F Mulvaney; G Nicholas; H Doherty; I Westrupp; J Grey; K Holmes; L Husted; M Katz; N Murphy; O Nansel; P Christie; Q Gregory
7.4 Discussion

It has been well documented that theory based studies appear more effective than non-theoretical based interventions. Four (299, 304, 310, 311) of the studies reviewed here did not explicitly document a theory behind the intervention of which only one study by Coates et al (299) reported positive changes in any of the outcomes measured. Of the remaining 13 studies whose intervention was theory based, three studies (291, 298, 306) did not report positive changes in any of the outcomes measured. The majority of the selected theories in this review were based on Albert Bandura’s work on social learning principals and social cognitive behavior which clearly underpinned the components of the interventions. Self-determination theory, motivational interviewing and solution-focused brief therapy were other theories applied in the studies reviewed.

7.4.1 Main Theories in Reviewed Studies

The social learning principals promoted by Albert Bandura postulate that learning is a cognitive process that occurs through direct observation in a social context (317). In his famous studies, known as the Bobo doll experiments, which took place between 1961 and 1963, he observed children watching an adult model aggressive behavior towards a doll, and demonstrated the powerful effect modeling has on the ability to acquire a particular behavior, whether positive or negative (317). In 1977, Bandura expanded on this early work to develop the concept of social learning theory (318), positing a direct relationship between an individual’s perceived self-efficacy and behavioral change (318). In 1986, Bandura renamed his original theory to what is today known as the social cognitive theory (319) where he claims that behavior is influenced by personal, behavioral and environmental factors (319). Interestingly, the studies in this review
with the greatest significantly positive outcomes were those in which social cognitive theory was the underlining theory (302,305, 314). In 2001, Bandura identified “symbolic modeling” as a process that could influence learning, motivation and personal actions (320). It is Bandura’s article on “Principals of Behavioral Modifications” (321) that set the foundation for what has ultimately became known as cognitive behavioral therapy (322).

Cognitive behavioral therapy (CBT) is a form of psychotherapy that focuses on problem solving in order to change an individual’s negative pattern of thinking (323). It has been used for over 50 years to treat a number of mental health disorders ranging from phobias to alcoholism (324). CBT therapy can be applied in an individual or group setting with lessons lasting for approximately 60 minutes. The aim of the therapy is to aid the recipient of the treatment to acquire skills that can be applied in daily life to tackle problems and negative thoughts (325).

One of the earliest forms of CBT was the Rational Emotive Behavioral Therapy (REBT), developed by Albert Ellis using an ABC model approach (326, 327) to exemplify how our beliefs influence our emotions and our behavioral response to an outside stimulus. A- is the activating agent or an external stimuli that triggers and emotion; B- is our beliefs regarding the situation; C- are the consequence or the emotional reaction to that belief. Whilst using the ABC model for CBT, it has been expanded to include D for discussing ways in which negative beliefs and reactions can be changed into a desired effect known as E, which leads to less negative behaviors by acquiring effective coping skills (325).

Self- determination theory (SDT) simply put is a theory about human motivation. SDT evolved from a study (328) looking at how external (extrinsic) factors such as money and internal (intrinsic) factors such as self-satisfaction, independence or the thirst for knowledge
motivate the human being. However, it was not until the works of Edward Deci (329) and Richard Ryan (330) that the theory gained popularity and acceptance. According to Deci and Ryan, there are three innate psychological needs that people need to experience in order to be self-determined and to be intrinsically motivated to change and these include a sense of competence, autonomy, and relatedness or a sense of belonging or attachment (331).

SDT is believed to provide the theoretical framework for motivational interviewing (MI) (332) with a patient-centered focus that attempts to motivate a patient to change. It was initially used to treat addictions (333) although it is now widely used for a range of problems.

Solution focused brief therapy (SFBT) is a form of psychotherapy that relies on focusing on trying to find solution rather than on problem solving. It was developed at the Brief Family Therapy Center in Milwaukee, in the United States by Steve de Shazer in 1986 (334). It has been reportedly used effectively in addressing a range of issues including substance/ drug abuse and mental health issues (335, 336).

### 7.4.2 Review of Study Findings

Previous systematic reviews have highlighted the need to improve the quality of randomized control trials of interventions (239, 278). They also highlighted the need for RCT’s to adhere to the Consolidated Standards of Reporting Trials (CONSORT) statement and to assess the scientific development of the interventions (281). The CONSORT statement is a set of evidence-based recommendations which includes a flow diagram and a checklist (updated in 2010) for reporting on RCT’s. Its main purpose is to allow for transparent and complete reporting in order to facilitate interpretation and critical appraisal of studies (337). The checklist requires scientific background and explanation of rational; an explicit description of the trial;
details on the intervention, the comparator, and a description of the intervention components; detailed description of randomization methods, including sequence generation and allocation concealment and implementation methods (338). The CONSORT diagram specifies enrollment, allocation, follow-up and analysis in a standardized method. In this review an improvement in the quality of RCT’s has been noted, of which more than half of the studies adhered to, greatly facilitating their interpretation.

Half of the studies in the current review had manuals or protocols to guide the interventions. The development and use of manuals in interventions helps ensure intervention fidelity (339) and strengthens the impact of the study. In fact well developed manuals or protocols are considered the gold standard of any intervention therapy (340). The manuals should contain clear objectives, content, and information about the sessions as well as the time allotted per session; a process evaluation of strategies used to test knowledge transfer or understanding or role-play behavior should be mentioned (339).

Research funders, grant providers, and even taxpayers are increasingly looking for quality assurance and cost effectiveness of potential research. Process evaluation, although not a new concept, has gained momentum in the past two decades as a means of evaluating whether a program intervention is successful by looking to explain the how and why of any of these outcomes (341). In particular the growing number of complex, multiple cited studies require a thoughtful process evaluation to explain the results achieved especially in regards to interventions with positive and significant outcomes (341). Clinical trials that fail to include details of processes and mechanisms obscure critical appraisal of the research study (342). In the UK, the Medical Research Council framework was developed to address precisely such issues (343, 344). The context of the environment in which the intervention occurs has been cited as
being critical to determining intervention design (341, 342). Linnan and Steckler determined that the process evaluation should contain at least four main domains which include data to determine the context, the reach, the dose of the intervention i.e. who should deliver and who are the intended recipients, as well as the fidelity of the intervention (341). By fidelity to the intervention, the authors refer to it as being the quality of the implementation and although this may seem straightforward, fidelity is not easy to measure or calculate (341). Developing checklists, or a list of minimum requirements may help to increase the fidelity of an intervention (345) or by observing the intervention using structured guidelines (346). In this review two major studies the DEPICTED study (313) and the EPIC (298) study followed the MRC framework for designing complex interventions which included a comprehensive process evaluation. Unfortunately, none of these studies described in Table 29 resulted in significant improvements although patients in the intervention arm of the DEPICTED study did experience greater excitement about their clinic visits (p=0.03), improved continuity of care (p=0.01) and short term increased ability to cope with diabetes (p=0.04).

7.4.3 Differences from Previous Reviews

This review clearly highlights the shift from purely educational and psychosocial intervention to interventions that encompass the family as a whole. Recent interventions have integrated either an educational, psychosocial, or both components in their study design. More than half of the studies in this review were family focused as opposed to only three studies in the last review by Savage and colleagues (281).

The management of children with diabetes is a triad involving the child, the child’s parent(s), and the health care workers. Psycho-social and family based interventions appear to
improve glycemic control, self-efficacy in management and family relationships (347, 348). Earlier work by Laffel et al has shown an increase in family involvement and prevention of the deterioration of glycemic control in a family focused teamwork intervention (349). Studies by Murphy et al have shown the potential benefits of parental involvement on metabolic control (350) although the integration of the program into a real clinical setting proved to be a challenge (311). De Wit and colleagues also demonstrated improvement in psycho-social well-being, mainly behavioral after clinic integrated consultations on health related quality of life. De Wit and colleagues did not however find a significant difference in HbA1c (351) although studies by Wysocki (279, 352, 353) looking at the impact of behavioral family systems therapy were able to show a significant decrease in HbA1C. However, the study by Ellis and colleagues looking at a multi-systemic therapy intervention were not able to maintain initial post-treatment improvement in HbA1c (354) when the participants were followed up at 6 months post completion of the intervention.

Although most studies have previously focused on face-to-face intervention, this review has highlighted the increasing importance of utilizing alternative methods of intervention delivery, namely online and via websites. All but one web-based study in this review resulted in significant improvements in on or more outcome measurement(s) with one further study approaching significance for the change in quality of relationships with those other than family members (304). Grey et al were able to demonstrate a significant decrease in HbA1C as well as an increase in quality of life in participants that completed both of their online programs (302).

The advantages of internet based intervention are numerous and include an increase in accessibility to a potentially diverse number of children with diabetes and their families and it can prove to be a more efficient means of utilizing resources as geographic boundaries and
scheduling no longer pose barriers. Previous psycho-educational studies that have used the Internet have shown some promising results in children of varying ages and health conditions (355-357). Access to internet has increased drastically in the past decade with its use in the home, at school and in libraries as well as on smartphones. In the United States approximately 95% of teenagers access the Internet on a regular basis (358) and in Canada 24% of teenagers report on average spending 3 hours online each day (359). Furthermore, in a study looking at Internet use in children and adolescents with diabetes, 42% reported searching for diabetes information on the Internet (360). In Bahrain, the Internet World Stats reports that 96.4% of the population had access to the Internet in the year 2015, the highest rate of access compared to other Middle Eastern regions (361). Hence the Internet presents an attractive platform from which such interventions can be developed as the program can easily be updated, modified and standardized via a website. The downside of the Internet is that access is still not universal and information conveyed in this way is open to misinterpretation although again as the technology advances the opportunities for content tailored to the individual are growing.

### 7.4.4 Limitation of Study

The lack of homogeneity in the studies and their outcomes made it difficult to undertake a meta-analysis. This was due to the large differences in the type and quality of the studies reviewed including the cultural and environmental context, as well as the varying sample sizes and types of interventions.
7.5 CONCLUSION

This review was helpful in identifying some of the facilitators of successful interventions aimed at children and adolescents with T1DM. Theoretical based interventions appear to demonstrate more effectiveness as highlighted by more positive changes to outcome measures and as such this should be considered in the development of an intervention. The theory behind the intervention, whether it is based on social cognitive theory, cognitive behavioral therapy or motivational interviewing should be left at the discretion of the researchers, ideally in conjunction with key stakeholders. A combination of both educational and psycho-social family targeted intervention need to be further researched. The use of web-based interventions is an attractive and promising alternative which can help improve adherence and reduce scheduling conflicts.

A key barrier identified is the real-life integration of such interventions which, when piloted show positive results, but in actual clinical and wide-spread settings fail to do so. The key unresolved issue remains what would in reality work to improve children’s HbA1C and diabetes self-management. Interventions with an integrated process evaluation therefore remain important in identifying features that contribute to the success or failure of interventions and further work is required focusing on intervention cost-effectiveness and sustainability alongside clinical effectiveness.
8.0 DEVELOPMENT AND FEASIBILITY STUDY FOR A TRANSITIONAL CARE PROGRAM FOR ADOLESCENTS WITH T1DM

8.1 INTRODUCTION

This chapter reports on the development of a structured transition care program for adolescents with T1DM and the proposed feasibility testing of this within the SMC hospital. In a country that ranks 5th worldwide for diabetes prevalence (3), foresight into future health care provision of this population that will ultimately spill into an already taxed adult care service, is urgently required. The results of a qualitative study detailed in Chapter 5 have highlighted the need, both globally and more locally, to provide more specialized care to adolescents, which are considered a challenging group, prior to transitioning to adult diabetes clinic. Currently, children at the pediatric clinic at the SMC are transferred to the adult clinic at the age of 14 years; no transition support is provided.

8.1.2 SYSTEMATIC REVIEW OF RANDOMIZED CONTROL TRIAL INTERVENTIONS FOR CHILDREN AND ADOLESCENTS WITH T1DM

The results of a systematic review of randomized control interventions for children and adolescents with T1DM described in Chapter 7 has shown that theoretically based interventions appear to be more efficacious and hence should be considered in the development of any intervention. Furthermore, the combination of both educational and psycho-social interventions that targets the family group rather than the individual alone show promising results. Developing interventions with an integrated process evaluation is essential component for identifying features that contribute to the failure or success of the proposed intervention (341).
8.1.3 Review of transitional programs for adolescents with T1DM

8.1.3.1 Guidelines for the transition of adolescents and youths from pediatric to adult services

In the United States, a consensus on health care transition for young adults with special health care needs was approved as a policy by the American Academy of Pediatrics, the American Academy of Family Physicians, and the American Society of Internal Medicine in 2002. The goal of this policy was to have implemented, by 2010, a structured plan for health care transition for young adults from the pediatric to adult care so as to “maximize lifelong functioning and potential through the provision of high-quality, developmentally appropriate health care services that continue uninterrupted as the individual moves from adolescence to adulthood” (362). In 2002, the International Society for Pediatric and Adolescent Diabetes (ISPAD), in their consensus guideline for the management of T1DM in Children and Adolescents (160) recommended joint adolescent or young adult clinics between pediatric and adult care providers before transition (160).

In March 2010 The American Diabetes Association (ADA), in collaboration with experts and individuals with diabetes, put forth a set of evidence-based recommendations for the care of emerging adults with T1DM in transit from pediatric health care to the adult health care services (363). Amongst other recommendations, they advocated for: a gradual shift of responsibility from parents to the adolescents; information on differences between the pediatric and adult services; written medical summary which includes medication used, glycemic control, and self-diabetes care. In 2014, the ADA’s position statement on standards of care in diabetes recommended that both pediatric and adult care health providers provide support and resource links to young adults who are in transit (252).
In the U.K the National Institute for Healthcare and Excellence (NICE) 2015 guidelines for the management of diabetes in children and young adults (364, 365) recommended age specific protocols for the transfer from pediatric to adult clinics and the use of evidence of physical development and maturity level to decide on the age to transfer. They also recommend that young adults and their families become familiar with the transfer process as a means to increase attendance post-transfer.

8.1.3.2 Transitioning from Pediatric Care to Adult Care

There have been a number of reviews published recently on the transitioning of adolescents and young adults with T1DM from pediatric to adult healthcare (366-371). Blum describes the period of transition as “purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented health care systems” (372). The transition period can be a turbulent one as it is a period in which adolescents are emerging as young adults struggling to define their identity and balancing the need for independence and dependence from their parents (373); dealing with a chronic illness complicates matters further. The age at transition from a pediatric health care system to an adult health care system varies from country to country and between institutions largely due to institutional policies or even state legislature which dictate age of transfer (374). In a review by Fegran et al (366) examining the transition experience of adolescents moving from pediatric to adult care, the average age of transfer varied from 14-22 years.
8.1.3.3 Outcomes of Adolescent Transitioning to Adult Care Services

Attendance Rate

One of the greatest challenges faced by healthcare professionals is maintaining a good attendance rate post-transfer as this has been found to decrease after transition (375-377). When patients achieve a good attendance rate at a specialist center for T1DM studies have shown a decrease in frequency of hospitalization and diabetic ketoacidosis (378, 379). Furthermore, studies have demonstrated that a higher rate of attendance whilst under pediatric care often correlates with a good attendance rate in adult care services (380, 381).

A study in the United Kingdom looking at the transfer mode of young people with T1DM into adult services demonstrated a higher rate of clinic attendance in young people that had had the opportunity to meet with an adult diabetes consultant prior to transfer and who had attended a joint adult/pediatric clinic before transfer to an adult clinic (375). The mean HbA1c levels during the 2 years prior to transfer was significantly higher in those that did not attend hospital clinic visits in the 2 years after the transfer compared to those regularly attending clinic. It has been well documented that adolescents with higher HbA1C levels prior to transitioning are also less likely to attend adult clinic care (377, 382). Furthermore, some studies report that adolescents who did not receive adequate support or information prior to the transitioning were unlikely to attend diabetes adult clinic (276, 379, 383, 384).

As a result of the shift of parental responsibility of clinic attendance to the adolescents, a decline in clinic attendance can occur due to this change in supervision (385); nonetheless, promoting a routine of regular attendance supervised by the parents whilst under the pediatric care can aid in maintaining attendance rates in subsequent adult clinic (386).
**Glycemic Control**

The transition’s impact on glycemic control has shown mixed results. Sparud-Lundin and colleagues conducted a retrospective longitudinal study of adolescents (n=104) during transition to adult care and reported a decrease in HbA1c in females (p=0.004) but not in males (385). The higher frequency of visits by the females to the adult clinic may be a contributing factor however the authors conclude this gender difference warrants further investigation (385).

Some studies have reported no significant change in HbA1c during this period (378, 380, 387, 388) whilst the SEARCH for Diabetes in Youth group reported that a higher HbA1c level prior to transition predicted poor glycemic control in the adult care setting (389). In fact, the study describes 2.5 times greater odds of having poor glycemic control after transition to adult care if levels were higher during the pre-transition period (389). However when viewed prospectively the changes appear less dramatic with one study which followed the glycemic control of 82 adolescents with T1DM finding no significant change in HbA1c pre- to post transition (390). This was confirmed by another study which found no significant change in HbA1c post transfer (374). Despite these potentially positive findings, a recent systematic review assessing the impact of transitioning from pediatric to adult clinics once again reported mixed results for studies of glycemic control as assessed by HbA1c. Of the 24 studies included in the review, 19 assessed the impact of transition on HbA1c levels. From nine observational studies, 5 reported no change in HbA1c and only the study conducted by Sparud-Lundin (385), as mentioned previously, reported a change in females but not males. Of the remaining 10 studies that specifically examined transitional programs or an intervention, 6 reported improvement in HbA1c and 4 reported no change (369).
Follow-Up Losses

Studies reporting on potential reason for losing patients to follow up cite relocation, transfer to a different center and follow-up by a general practitioner or at an obstetrics clinic (391). In a more recent prospective study conducted by Mistry and colleagues which included 136 participants and explored the predictors of successful transition, high HbA1c levels were found to be predictive of poor follow up (381). Loss to follow up was also more prevalent within that cohort if the adolescents were diagnosed before the age of 12, if they were using multiple daily injections or if they were on a pump, and in those who had fewer visits to the pediatric endocrinologist prior to the transition (381). The authors did however identify that older children who had met with the adult physician prior to transitioning were less likely to be lost to follow-up.

In a retrospective study conducted by Bryden et al, following adolescents and young adults who had transitioned to adult care, the authors identified that 75% were attending specialist care, 19% were being followed by a general physician and 3% were not receiving any form of follow-up (392). Northam et al found that 38% of individuals with T1DM, after 12 years of diagnosis, (n=110; mean age of 20.7 years) were not receiving any specialist care (393).

8.1.3.4 Feedback from Adolescents and Youths on What is Wanted from a Transition Program

Several studies have reported on the experiences, either via focus groups or questionnaires, of adolescents undergoing service transition from pediatric to adult care (382, 394-400). Table 32 highlights some of the factors within the transition process that appear to impact on a successful transition according to the adolescents themselves. Youth often describe
a feeling of unpreparedness for the focus on an older population and describe a sense of “shock” and “surprise” at the unexpected difference between the pediatric and adult setting (400).

Table 32 Feedback from adolescents and youths of the facilitators of the transitioning process

<table>
<thead>
<tr>
<th>Facilitators of Transition Process</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early preparation for transfer</td>
<td>(399, 400)</td>
</tr>
<tr>
<td>Provision of transition specific information</td>
<td>(394, 395, 397, 400)</td>
</tr>
<tr>
<td>Continuity of provider care during the transfer process</td>
<td>(396)</td>
</tr>
<tr>
<td>Meeting with adult provider whilst under pediatric care</td>
<td>(399, 401)</td>
</tr>
<tr>
<td>Organized transition process</td>
<td>(395, 397, 398)</td>
</tr>
<tr>
<td>Flexible</td>
<td>(382, 398)</td>
</tr>
<tr>
<td>Short waiting periods</td>
<td>(394, 395)</td>
</tr>
<tr>
<td>Support scheduling and re-scheduling appointments</td>
<td>(400)</td>
</tr>
</tbody>
</table>

8.1.4 Predictors of successful transitioning

8.1.4.1 Familiarity with the adult clinic and physician

Kipps and colleagues were the first to describe a higher rate of clinic attendance in young people who had the opportunity to meet with the adult diabetes consultant prior to transfer (375). This was followed by a large retrospective cohort study (n=1507), conducted by Nakhla et al who described the different methods of transfer of care and their impact on health outcomes. The results of that study revealed that those who transferred with no change to the physician
were 77% less likely to be hospitalized as compared to those who were transitioned with a new physician (402).

### 8.1.4.2 Transition Coordinator

Holmes-Walker and colleagues (378) introduced a transition coordinator in a transition support program for youths (n=191) attending a specialist clinic with the aim of improving metabolic control and rate of hospitalization with diabetic ketoacidosis (DKA). The role of the transition coordinator or diabetes educator was to arrange booking and re-booking of appointments and to provide phone support service after working hours. The results were promising as there was a significant reduction in DKA related hospitalization (p=0.05) and HbA1C significantly improved (p < 0.001), with the greatest improvement seen in those with an HbA1c > 11% (−2.5 ± 2.3%, p< 0.001). Furthermore, there was an 82% attendance rate which was deemed as ‘good’ 6 months after the initiation of the program. Interestingly, the cost saved from repeated admissions was used to cover the cost of the program itself. A major limitation of the study however, is the absence of a comparison group which makes it difficult to determine which components of the program contributed to the positive outcome and to what extent the changes seen were a result of the intervention itself.

### 8.1.4.3 Transfer to Adult Clinic in the Same Hospital

Transfer of children to adult clinics within the same hospital depends largely on the availability of this service. In Bahrain, for example, transition to adult clinic occurs within the same hospital although this varies not only across countries but even within different provinces, states, or jurisdictions. In the United States young people may continue to see their pediatric
endocrinologist well into their early adulthood whereas transfer is usually mandated in other countries by 18 years of age (369).

Vanelli and colleagues report on a retrospective study over an 8 year period which studied the effect of a structured transition process in which the transition of adolescents (n=73) occurred in the same hospital (403). The adolescents in the uninterrupted process had a clinic attendance rate which ranged between 92 and 100% although there was no control or comparator group. Cadario and colleagues (388) describe an observational study of adolescents (n=62) over 10 years in which a structured transition process was put into place and led by a transition coordinator. The transition coordinator followed the adolescents in the pediatric clinic during the patient’s last year after which a provider sent a letter informing the adolescent about the transition at the second last pediatric visit; the last pediatric and first adult visit was run jointly between the pediatric and adult endocrinologists in the presence of the parents. The results for the participants (n=30) in the transition program revealed a higher rate of attendance in the adult clinic (80% vs. 57 p<0.05), a shorter mean review time between last pediatric and first adult clinic (0.8 years vs 4.6 years p< 0.001), and a lower HbA1c level after one year as compared to those that did not participate (n=32) in the program.

8.1.4.4 Young adult diabetes clinic

Several studies have reported on the experience of a ‘young adult’ diabetes clinic as an interim phase between the standard pediatric and adult settings (380, 387, 404, 405). In Belfast, Ireland, the Young Persons’ Clinic, setup to facilitate the transfer of adolescents with T1DM from pediatric to adult services, was audited. Attendance was rated as good in only 36% of the participants (n=33) with 6 of the participants having attended all scheduled appointments over
the two year period (380). Attendance was rated as being moderate in 33% and poor in 30% and the percentage of those with good attendance prior to transfer also had the highest attendance rate after transfer compared to those with poor attendance prior to transfer (380). The authors did not find a relationship between glycemic control and attendance rate and state that although they were not surprised by the results obtained, they were disappointed considering the great effort that was needed to set up these clinics. They conclude that possible factors contributing to the disappointing results could have been the lack of flexibility in clinic timings, the need to target more socially deprived patient as well as the relatively late age of transfer (mean 17 years) (380).

In a more recent observational study conducted by Johnson and colleagues in the UK involving two diabetes clinics for young adults the authors reported improved screening rates and lower non-attendance. However, mean HbA1c of participants in this study, which were compared to a previous audit of the centers by Wills et al (406), remained higher than recommended (< 58 mmol/mol or 7.5%) (405) suggesting that, whilst the special clinic may improve engagement and subsequently screening for complications in this high risk population, it has yet to translate into significantly improved metabolic outcomes.

8.1.4.5 NEW APPROACHES AND TECHNOLOGIES

“Maestro” is an innovative systems navigator service developed with the aim of increasing medical contact with youths transferring from pediatric to adult care. (383). Maestro was developed in Canada by the Winnipeg Regional Health Authority and the Child Health Program in 2002. A report released by Health Canada in 2008 placed the development of a transition care strategy for children with chronic disease from pediatric to adult clinic as one of the top priorities for the national public policy (407). Maestro keeps a log of the telephone and
e-mail contact of youths so as to provide support in accessing healthcare service. Resources within this novel approach include provision of a comprehensive website, newsletter, announcement of casual group and educational events. In total, 64 participants and 101 controls have been involved in pilot testing to date. The results revealed no statistically significant difference in hospitalization for DKA or severe hypoglycemia; however, only 11% of system users versus 40% of the controls dropped out of adult care. After having been given access to the Maestro services, the control group increased their use of the healthcare services from 59.4% prior to Maestro to 73.3% after being given access to Maestro.

8.2 Development of Proposed Intervention

The current intervention was borne out of discussions with service users and service providers as discussed in Chapter 6 and was developed based on the results of the systematic review described in Chapter 7 and the evidence review of transition programs for youths with T1DM moving from pediatric to adult clinic described above. Specifically, the intervention was based on cognitive behavioral therapy, as interventions with an explicit theoretical basis have been found to be more effective as mentioned in the systematic review. Elements of what youths themselves have found to ease transition were included such as preparation for transition one year prior, provision of transition specific information, scheduling appointments and setting up a framework for an organized transition process by means of a transition coordinator as a facilitator. Lesson plans such as those focused on managing blood sugar, coping with diabetes on a day to day basis, and effectively managing diabetes are all topics that are regularly taught as part of the current education received. However, unlike the current structured education the patients receive, this intervention uses a psycho-social approach. Family support, conflict and
communication, although subjects frequently discussed during routine visits, are not part of the structured education and were therefore made explicit within the suggested transition program. Cognitive behavioral therapy, which stems from Albert Bandura’s social learning principal theory, was selected as the form of psychotherapy as it focuses on problem solving in order to change negative thoughts or actions into positive or desired effects (323). It also aims to engage the patient directly giving them a sense of autonomy whilst encouraging them to assume responsibility and control of their condition (325).

The intervention will be led by a pediatric nurse educator whose role includes the following:

- Meeting quarterly with the patient and parent(s) or legal guardian during routine visits to the endocrinologist for a period of 15 months or 4 visits (see figures 9 and 10).
- Conducting psycho-educational sessions with adolescents in the presence of their parent or legal guardian before/after medical appointments for a period of approximately 30 mins at a time. Four separate sessions have been designed:
  i) How to manage blood sugar for the long term
  ii) How to manage diabetes effectively
  iii) How to cope with diabetes day-by-day
  iv) Family support, conflict and communication

The content of these sessions can be viewed in Appendix 13 and are based on the A-B-C Model of Cognitive Behavior Therapy. After each visit, families will receive a brochure summarizing the major session points to reinforce the verbal education and act as a resource for the future.
The proposed primary outcomes measures will be improvements in quality of life and problem areas that adolescents face with managing their diabetes; a secondary outcome measure will be improvement in HbA1c levels. Pre-existing questionnaires from The Diabetes Attitudes, Wishes, and Needs (DAWN) Study will be used to assess these outcomes (Appendix 11 & 12) and HbA1C levels routinely tested in the hospital laboratory will be used.

8.3 PHASE I: FEASIBILITY AND ACCEPTABILITY OF PROPOSED INTERVENTION

8.3.1 INTRODUCTION

Prior to commencing any study it is crucial to assess the feasibility issues affecting the full study and to determine if the proposed intervention is relevant and sustainable in the given environment. Many highly controlled, well designed, randomized control trials allow researchers’ to draw out causal inferences; however such interventions often fail in real-world settings because the focus on internal validity reduces the relevance of the intervention in a particular setting (408). Furthermore, the growing financial and resource constraints means that not all interventions will have sufficient funding to be tried.

8.3.2 FEEDBACK FROM PEDIATRIC NURSE EDUCATORS & ADOLESCENTS WITH TIDM ON CONTENT, FEASIBILITY AND ACCEPTABILITY OF PROPOSED INTERVENTION

Feedback from the pediatric nurse educators was overall positive. In terms of the content of the material used and the lesson plans, they felt that the material and the CBT questions were very relevant and appropriate to the adolescents in the clinic. In principal they agreed with the proposed lesson plans but did not rule out the possibility of making changes largely dependent on the results of the feasibility assessment. With regards to the use of a discharge summary chart
before transitioning, the nurses felt that it was a very essential and something they wished to implement immediately after obtaining approval from the pediatric diabetes consultants.

As for the feasibility of the program, they voiced their concerns regarding the time proposed to be spent with youths and preferred it be cut down from the proposed 30-45 mins to 20 mins with 5-10 mins in the end to allow the patient to fill out the questionnaires. They also voiced concerns regarding the additional work load this would be on just one nurse and felt that perhaps dividing the workload amongst the three nurses would decrease the load. They felt that ideally the implementation of the program would require the undivided attention of just once nurse whose role was to act as a transition coordinator; however they acknowledged that due to the less than ideal circumstances and financial restraints this would not be possible initially.

Finally, when asked about whether they felt that the program would be accepted by the patients, the nurses stated that in their opinion the integration of the program into clinic setting would be appreciated as would the extra attention focused on the adolescents. They felt that the adolescent as well as their caregivers are more likely than not to appreciate the extra time and information they will receive to help the transition.

Feedback from a couple of adolescents with T1DM was encouraging as they showed keen interest in participating in such a program. The content of the program they felt was relevant to their real life struggles with diabetes. However, one adolescent expressed his wish that more time be focused on the CBT subjects rather than the educational aspect which in his opinion he has “all heard before” and felt it to be redundant. Both adolescents appreciated that the program was integrated into clinical setting which meant that they did not need to miss out
on school time and were quite happy to stay an additional 30 minutes with the designated transition coordinator during their routine visits.

8.4 PROTOCOL FOR FULL FEASIBILITY TESTING

8.4.1 INTRODUCTION:

As there is currently no transitional care program available for children with T1DM in the Salmaniya Medical Complex prior to transitioning into adult health care services within the hospital, a transition care program was developed. Thus the aim of this study is to assess the feasibility and acceptability of the proposed program.

8.4.2 SPECIFIC AIMS OF THE STUDY:

1. To assess the ease and efficacy of integrating the proposed transition care program into routine clinical setting.

2. To assess the patient and healthcare workers acceptability of such program.

8.4.3 STUDY AREA/SETTING:

The proposed transition program with the use of a newly defined ‘transition coordinator’ will be conducted in the out-patient pediatric clinic in the Pediatric Endocrine and Diabetes Clinic of SMC. The parent(s) or legal guardian of adolescents will be approached for consent four months prior to their entering the final year in pediatric care. For those who agree to participate, baseline demographic information will be collected prior to commencement of the intervention.
8.4.4 Study subjects:

Study subjects will be children with diabetes aged 13 years of age. This age group was deemed appropriate since children are transferred to the adult clinic in SMC once they turn 14 years and one day.

The inclusion criteria are the following:

- Children with T1DM entering their final year in the pediatric diabetes care

Exclusion Criteria

- Children with T1DM with a history of psychiatric disorders
- Children with T1DM being followed by a psychologist or psychiatrist
Recruitment of volunteer adolescents 4 months prior to entering final year in Pediatric Clinic (PC)

Scheduling of appointments by transition coordinator:
- Appointments q 4 months in PC (3 appointments)
- First appointment post-transfer in Adult Clinic (AC)

1st appointment in final year of PCC
- Meet with Endocrinologist as usual
- Meet with PDN as usual
- Introduction to Transition Coordinator (TC) (20-30 mins)

Reminder of appointment by TC one week prior

After 4 months

1st appointment in Adult Clinic
- TC facilitates meeting with Adult Endocrinologist and nurse educator
- TC hands over patient summary file
- Brief meeting with TC after 1st AC appointment (20-30 mins)

Reminder of appointment by TC one week prior

Follow up Phone Call after 6 weeks

3rd appointment in final year of PCC
- Meet with Endocrinologist as usual; obtain summary file
- Meet with PDN as usual
- Meet with TC (20-30 mins)

After 4 months

2nd appointment in final year of PCC
- Meet with Endocrinologist as usual
- Meet with PDN as usual
- Meet with Dietician
- Meet with (20-30 mins)

After 4 months

Referral to other healthcare providers if needed

PCC: Pediatric Clinic Care
AC: Adult Care
PC: Pediatric Clinic
PDN: Pediatric Nurse Educator
TC: Transition Coordinator

Figure 9 Flow diagram of proposed intervention for adolescents in final year of pediatric diabetes care
8.4.5 Recruitment:

The Pediatric Nurse Educators will submit a list of patients that meet the criteria. These children and their parent(s) will be approached for consent to participate in the feasibility study.

8.4.6 Sample size:

Approximately 10-15 adolescents are transferred yearly according to the pediatric diabetes nurse educators as official statistics on transfer number are currently not available at the pediatric diabetes clinic in the SMC (409). A convenience sample of participants will be recruited to assess the feasibility of implementing the intervention.

8.4.7 Data Collection Methods:

Upon obtaining consent, demographic information will be collected as well as anthropometric measurements such as the child's weight, height, BMI, and waist circumference (see Figure 10). Participants will also be asked to complete at baseline and at every visit the Diabetes Quality of Life Youth Questionnaire (DQOLY) (Appendix 11) and the Problem Areas in Diabetes Questionnaire (PAID) questionnaire (Appendix 12). The DAWN Study was initiated in 2001 by the pharmaceutical company Novo Nordisk and the International Diabetes Federation with the purpose of improving diabetes care at an International level (410). The aim of the DAWN qualitative study was to explore the attitudes of people with diabetes as well as their care providers towards health care provision and to identify their needs and wishes (410). The study involved 13 countries and over 5000 participants with type 1 and type 2 diabetes and was overseen by an international expert panel (411). Since the initial study, the DAWN project has expanded considerably with the aim of implementing best practices in the management of
diabetes at a global level and has partnered with the ISPAD to develop the DAWN youth program. This initiative stems from a qualitative study looking at the attitudes, wishes, and needs of young people with diabetes, their parents, and healthcare providers (412). In an effort to improve the standards of care for youths with T1DM, the DAWN youth project uses the Diabetes Quality of Life Youth Questionnaire (DQOLY) to assess QoL (413). QoL has been recognized as a central outcome of health care (414) and has been associated with lower HbA1c in adolescents with T1DM (415). The PAID questionnaire which will also be used has been found to not only correlate with the youths health beliefs’, depression, social support and coping style (416, 417) but it can also be used to predict future blood glucose control (418). Response from these questionnaires at each interval of the transition program can help the clinicians assess improvements in the specified outcomes as a result of the proposed intervention. It can also be used to allow the healthcare providers to identify problem areas adolescents so as to tailor the most appropriate intervention such as the need for more individual vs. family centered intervention or even the need to refer to other healthcare professionals.

### 8.4.8 Data Management and Analysis Plan:

The Diabetes Quality of Life Youth Questionnaire (DQOLY) and the Problem Areas in Diabetes Questionnaire (PAID) questionnaire will be completed prior to commencing the study as well as at the end of each visit to serve as a control. The time taken at each visit and with the nurses, physicians, and transition coordinator will be noted as will the time taken to complete the questionnaires. Any difficulties or challenges that are faced by either the transition coordinator, the participants themselves or the physicians will be noted at each visit. At the end of the intervention, focus groups will be planned for the participants to obtain feedback on the program and areas of perceived strengths and areas where there is a need for improvement. Separate focus
groups will be planned for the healthcare members that participated including the transition coordinator. Themes produced from these focus groups as well as the notes taken during the intervention program itself will be used to help further develop the intervention program.
Once volunteers identified:
- TC Schedules appointments by block
- Check to see pt. has a completed diabetes Registry Form (if not complete by phone)
- Complete DQOLY and PAID questionnaire prior to commencing study

1st appointment with TC in PC
- Complete Consent Forms
- Explain role of TC and purpose of study
- Record anthropometric measurements such as the child’s weight, height, BMI, and waist circumference
- Record BG readings
- **Lesson 1: How to manage blood sugar for the long term**
- Conclude and gather data DQOLY and PAID questionnaire

2nd appointment with TC in PC
- Record Anthropometrics/BG readings
- Review previous session discussions
- **Lesson 2: How to cope with diabetes effectively**
- Conclude and gather data DQOLY and PAID questionnaire

3rd appointment with TC in PC
- Complete and have signed pt. summary file
- Record Anthropometrics/BG readings
- Review previous session discussions
- **Lesson 3: How to cope with diabetes on a day to day basis**
- Conclude and gather data from DQOLY and PAID questionnaire
- Give Pt tour of AC and appointment desk

4th appointment with TC in AC
- Accompany Pt to first AC clinic
- Handover summary file
- Record Anthropometrics/BG readings
- Review previous session discussions
- **Lesson 4 Family support, conflict and communication**
- Conclude and gather data from DQOLY and PAID questionnaire

Call after 6 weeks to FUP

After 4 months

Pt: Patient
AC: Adult Care
PC: Pediatric Clinic
TC: Transition Coordinator
BG: Blood Glucose

Figure 10 Summary of Transition Coordinator’s role throughout the intervention
8.5 Discussion

The best practice approach to addressing the transitioning of adolescents and youths to adult clinics has come predominantly from professional bodies and is based primarily on expert opinion or consensus (252, 362-364). There is a consensus that a transition program should be well structured and well planned (368) but the details of the transition currently remain at the discretion of the institution or center.

There is currently no transition program established at the Salmaniya Medical Complex and no formal information is given to the patient or their caregivers on the transition process. Qualitative data from focus groups has highlighted the demand for the development and implementation of a transition program from the perspective of the health care professionals as well as the parents of children with diabetes. One physician explains:

“They need for us to spend more time with them, to try and deal with all these issues….you know especially when they transition to adult clinic they will feel lost ...”

The pediatric diabetes nurses have also highlighted the need to focus on adolescents with diabetes as they described them as being at a “crisis age” and “lost.” One nurse explains the dilemma they face when transferred adolescents want to return to pediatric diabetes care because of the lack of a structured support:

“Ahh this period is very crisis period for the children. That they are newly diagnosed in this period they are teenagers they are not accepting sometimes. They are doing so many many things false from the disease. So they need support, they need very strong support so the patients when they are transferred to adult they are coming back to us because nobody is there for them.”
The program was designed so as to be integrated into routine clinical setting to facilitate implementation and acceptability and to be cognizant of limited facilities and finances. The intervention was designed so as not to require additional staff or manpower; is applicable in clinical settings, and can be sustained without additional funds to maximize practicality although these factors will all be objectively assessed via the proposed feasibility study to assess whether this has been achieved.

8.6 Conclusion

There is both a service-user demand from the families of children and adolescents with diabetes and a professional demand from the HCPs managing their care for such a program. Although the acceptability of the program has yet to be tested, the development of the program was based on evidence from the systematic review of interventions on children with T1DM and the literature review on the facilitators of successful adolescent and young adult transition programs. A feasibility study has been designed to ensure objective testing of the implementation and evaluation process, as well as the appropriateness of the program content to allow robust evaluation and ongoing development of the program.
9.0 CONCLUSION

9.1 INTRODUCTORY COMMENTS

Diabetes has become a worldwide epidemic with the Middle Eastern and North African Region reporting some of the highest prevalence rates with far-reaching global and economic consequences (3). Bahrain, a small country in the heart of the Middle East has not escaped this burden. More alarming is the rise in T1DM in the pediatric population in the Kingdom.

Within this context, this PhD program has comprised two key approaches to extending the knowledge base:

1. Investigating the association between lifestyle, diet, and medical factors and the risk of T1DM in children in the Kingdom of Bahrain.

2. Designing and developing an educational program for children with T1DM in Bahrain informed by an investigation of the local needs of the healthcare workers and families of children with T1DM and an assimilation of the evidence base.

To the author's best knowledge, this study is the first of its kind to give insight into the lifestyle, dietary and medical factors associated with pediatric T1DM in the Kingdom. This study provides a platform for facilitating the implementation and adoption of existing international guidelines for children with T1DM (164) and for heeding the call for action made by the International Diabetes Federation (419).
The findings are summarized below with concluding remarks:

1. Audit of a Pediatric Diabetes Registry available at the Salmaniya Medical Complex. (420)

The Diabetes Registry Forms of 55 children with T1DM in the year 2009 and 2010 were audited to investigate whether any medical or lifestyle factors were associated with T1DM occurrence. The results showed that children with T1DM were significantly more likely to be Bahraini nationals than controls although there was no significant difference in self-reported race. Children with T1DM were significantly more likely to have suffered from an illness, than control children and significantly more likely to have undergone surgery prior to diagnosis than controls. Prenatal history identified mothers of T1DM children to be significantly more likely to have gestational diabetes with a trend towards greater maternal T2DM too. With prolonged breastfeeding prevalent in the Kingdom no association between reported infant feeding practices and T1DM was seen.

In summary, whilst this audit could not prove causation due to the aforementioned limitations of the study design, they nonetheless appear to align with the infection hypotheses of T1DM pathophysiology as indicated by greater rates of early childhood illness and surgery in cases compared to non-diabetic controls. The preliminary findings have helped shed light on this under-researched population and have highlighted potential avenues for future country-specific prevention research.
2. Dietary intake of children with T1DM compared to healthy children as assessed by a single 24 food recall (421).

The analysis of a 24-hr food recall revealed that children with T1DM consumed significantly more calories than the healthy controls. They also had significantly higher carbohydrate, fat and protein intakes when expressed as percentage of the RDA. Both children with T1DM and healthy controls consumed excess protein and sodium whereas fiber intake was below the RDA requirements as were the intakes of calcium and vitamin D.

This study revealed that the diet of children with T1DM does appear to differ in some ways from that of apparently healthy (or at least diabetes-free) controls although both healthy and diabetic children of this age in the Kingdom are failing to meet many of their age and gender appropriate nutrient recommendations. This emphasizes the importance of continuing to promote adherence to existing ISPAD nutritional guidelines for children and adolescents with T1DM and perhaps highlights the need for a more general targeting of dietary intakes in school aged children in Bahrain.

3. Vitamin D status of a small but representative sample of children with T1DM (422)

Given the mounting evidence in regards to the link between vitamin D deficiency and the risk of developing T1DM, the authors investigated prospectively the vitamin D status of 18 newly diagnosed children with T1DM. Serum vitamin D levels were assessed using both the CLIA assay method and UPLC/MSMS. The results revealed that between 50% (UPLC/MSMS)
and 72% (CLIA) of the children had suboptimal levels of serum vitamin D according to accepted cutoffs. There was a statistically significant difference between the two assay methods (p=0.048.) and a poor agreement, with the CLIA assay method overestimating insufficiency.

This study is the first of its kind to assess the vitamin D status of children with T1DM and has highlighted that, in line with previous studies in healthy children and adults in the Kingdom, suboptimal vitamin D levels are also common in children with T1DM. In light of the few but significant studies that have shown early childhood supplementation with vitamin D to reduce the risk of developing T1DM, vitamin D supplementation presents itself as potential prophylaxis against the development of T1DM. However, despite the subsequent interest in assessing and managing vitamin D levels in clinical populations, including those with diabetes, this study has highlighted the practical issues surrounding implementation in countries such as Bahrain, particularly limited access to robust screening methods and the potential methodological bias, and therefore misdiagnosis associated with some cheaper techniques. It is therefore essential that both resource issues and clinical efficacy are considered before implementing any new screening or supplementation program in the Kingdom to maximize impact.

4. Prospective in-depth study on a small representative sample of children with T1DM

Having identified potential lifestyle features associated with pediatric T1DM in the Kingdom, including differing dietary intakes, a more in depth prospective study was undertaken to confirm and hopefully extend these findings. In particular the study aimed to assess the dietary
intake of vitamin D as assessed by a vitamin D specific food frequency questionnaire and the
average of three 24hr food recalls. Dietary intakes revealed similar trends to those described in
the larger case-control study. Intake of dietary vitamin D as reported by a FFQ and 24hr food
recalls were not sufficient to meet the requirements. A lifestyle and sunlight questionnaire
revealed a trend towards an association between reported sunlight exposure and vitamin D with
those exposed to more than 30 minutes per day having higher 25(OH) D levels (p=0.057). The
children were not achieving the physical activity guidelines as assessed by the CPAQ
questionnaire.

It would appear that factors such as dietary intake, sunlight exposure and physical
activity may to some extent impact the vitamin D status of children with T1DM. Dietary
intake of vitamin D alone does not appear sufficient to meet the recommended RDA values
and in light of the suboptimal serum vitamin D levels of a significant number of children in
this cohort, there is an urgent need for consensus guidelines and recommendations
specifically targeted for children with T1DM that encourages outdoor activity and sunlight
exposure as well as a unified policy on vitamin D supplementation.

5. Qualitative pediatric diabetes study

Focus groups were set up in order to further investigate the beliefs and attitude of a sample of
children with diabetes and their care givers in relation to the etiology and the management of
their diabetes. With an overarching aim of this PhD being to improve diabetes services in the
clinic it was felt essential to place the service-users at the center of the project and to seek their
views before deciding on the focus of any service developments. Topics ranging from the
admission and educational process, to barriers to change and future recommendations were discussed yielding a number of key themes including fears of social stigma, impact of their condition on future marriage, and the fear of complications. Overall the educational process and services were described positively although these did not conform to current best practice as described in the international literature. Healthcare providers as well as the caregivers themselves highlighted the need for more support especially during adolescence and when transitioning to adult care services.

These focus groups were unique in providing an in depth insight into the beliefs and attitudes of children with diabetes and their carers (both family members and professionals). All stakeholders agreed with the need to make improvements to facilities and to solve logistical issues in order to provide better services. Finally, the focus group highlighted the need to provide specialized care to adolescents in order to tackle the issues of this challenging group, directing the remaining research within this PhD.

6. Systematic Review of Randomized Control Interventions in Children and Adolescents with T1DM

A systematic review of interventions conducted in clinical settings seeking to improve the management of children and adolescents with T1DM was undertaken to further inform the service development work. This included papers published between January 2010 (when a previous review was published) and June 2015. In total 17 studies were included with the suggestion that study quality has improved from previous reviews and a clear shift towards more family focused interventions, and the use of the Internet to deliver interventions. Theoretical
based interventions were identified as being more effective and so this approach was adopted along with other positive factors in the subsequent program design phase.

In summary, a combination of both educational and psycho-social family targeted intervention appear promising in this age group and warrant further research. The use of web-based interventions is an attractive and promising alternative, which can help improve adherence and scheduling conflicts. A key barrier identified is the real-life integration of such interventions which, when piloted show positive results, but in actual clinical and wide-spread settings fail to do so. The key unresolved issue remains what would consistently improve children’s HbA1C and diabetes self-management. However facilitators of successful transitional programs such as early preparation for transfer and provision of transition specific information have been identified as key in any transitional program and will be incorporated into the planned service developments.

7. Development of transition care program for children with T1DM

An intervention package was developed and a transition care program designed to incorporate key characteristics of successful interventions informed by the literature and cognizant of the needs assessment and client needs identified earlier in the project. Specifically the intervention package was based on a series of psycho-educational sessions grounded on cognitive behavioral theory. The design of the package offers a structured program that aims to prepare the adolescents to transition to adult services by providing transition specific information, continuity of care, a health summary sheet, and an opportunity to tour the adult clinic prior to the transition.
In summary, a transition care program has been developed as a direct result of an identified local demand from the service users (children and adolescents with diabetes and their families) and healthcare workers and grounded in the existing evidence base. A protocol for feasibility testing has been developed to assess acceptability and implementation of the program for the SMC pediatric endocrine outpatient clinic.

9.2 Future research

Future work should focus on redesigning the study using a probability sample that is adequately powered and that involves multiple centers. There is also a need to design prospective and intervention trials that aim to improve the diet and lifestyle behaviors of Bahraini children with and without T1DM since there appears to be widespread deviation from the recommendations in this age group. Furthermore, there is a need for larger more adequately powered confirmatory studies to investigate the relationship between dietary intakes of vitamin D, sunlight exposure, and exercise on children with T1DM as compared to healthy children. The development of public health campaigns which encourage sensible sun exposure as a health recommendation should be explored especially in light of the abundance of sunlight that Bahrain enjoys. A larger mother and child cohort should be sought. Although no strong conclusion can be made in regards to the potential role of infection as a possible trigger or accelerator of T1DM development in high risk children, the results of our study warrant further investigation especially in light of the substantial evidence and the current research into potential vaccines which aim either to procure immunity against suspect viruses or by means of immunomodulation.
In relation to practical service delivery further work needs to be undertaken investigating the usage of the existing voicemail and hotline systems, the feasibility of putting into place a structured psychoeducational program for adolescents, and the delivery of partial home care as opposed to complete hospital care at diagnosis. There is also a need to acknowledge and address parental concerns besides the evident complications of the disease and use these to help leverage positive behavioral changes in the patients and their families as a whole.

Assessing the feasibility of implementing the proposed transition program by involving key and lay stakeholders is a top priority. Including a process evaluation is critical in order to explain the results achieved especially in regards to positive and significant outcomes.

9.3 CONCLUDING REMARKS

This thesis investigates the dietary, lifestyle and health risk factors of children with T1DM in the Kingdom of Bahrain. Children with diabetes do appear to differ from age matched controls with respect to medical history and socio-demographic characteristics. Larger confirmatory studies should be of importance as the Kingdom struggles with the health impact of the diabetes epidemic both in children and adults. In the shorter term an evidence and needs-based development of the diabetes service is being implemented and evaluated with the express aim of improving management and specifically transitioning of adolescents with T1DM in the Kingdom.
10.0 REFERENCES

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11.0 APPENDICES

11.1 LIST OF APPENDICES

1. Diabetes registry form (DRF)
2. Ethic approval for case-control study
3. Ethics approval for prospective study
4. Questionnaire for control group
5. Vitamin D food questionnaire
6. Sunlight exposure & lifestyles questionnaire
7. Consent form for prospective study
8. Child Physical Activity Questionnaire (CPAQ)
9. Focus group participants data
10. Focus group open-ended questions
11. Diabetes Quality of Life Youth Questionnaire (DQOLY) from Dawn Youth Study
12. Problem Areas in Diabetes Questionnaire (PAID) questionnaire from Dawn Youth Study
13. Proposed transition program for adolescent with T1DM
# Pediatric Diabetes Registry Form

**Date:**

**Patient Name:**

**Unit Number:**

**Age:**

**Sex:** □ Male □ Female

**Nationality:** (ID Sticker)

---

## Demographic Data & Current Medical Hx

1. **Birth Date:** ______/_____/______  **Place of Birth:** Country:_______ Area:______
2. **Race:** □ Arab:________________ □ None-Arab:________________
3. **Religion:** □ Muslim □ Christian □ Jewish □ Hindu □ Other:________________
4. **Date of Diagnosis:** ______/_____/______  **Age at Diagnosis:** ______ years
5. **Diagnosis:** □ Type 1 Diabetes □ Type 2 Diabetes □ Drug Induced
   □ Iron Overload Associated Diabetes □ CF-Related Diabetes
6. **Presentation at Diagnosis:** □ DKA □ None-DKA
7. **Rx Regimen at Diagnosis:** □ NPH+R □ L+R □ L+Novo □ L+Apidra □ OGA (Tab.)
   □ Carb. Count □ Fixed Carbs □ Other:________________
8. **Other Diagnosis:** □ Hypothyroidism □ G6PD Act. □ Celiac Disease □ PCOS
   □ SCD □ Thalassemia □ Malignancies □ Nephrotic Syndrome
   □ Obesity □ Acanthosis: Location:________________
   □ Others:________________
9. **Allergies:** □ Unknown □ Yes,________________
10. **Health Care Providers:**
    
    **Endocrinologist:** Dr. AJ – FJ – MR – __________ **Hospital:** SMC – __________
    
    **Ped. Diabetes Nurse:** EO – AA – ________ **Dietician:** JJ – FH – __________
    
    **Health Center:** __________ **Pediatrician:** __________
11. **Main Family Care Givers:**

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<th></th>
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<th>Relationship</th>
<th>Contact Number</th>
<th>Notes</th>
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<tbody>
<tr>
<td>1</td>
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<td>Father</td>
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<tr>
<td>2</td>
<td></td>
<td>Mother</td>
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<tr>
<td>3</td>
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</tbody>
</table>
12) Address: Villa / Flat: _______________ Road: _______________.
Area: _______________ Block: _______________.
Telephone: Residence: _______________ Patient M: _______________.
13) Health Insurance: □ No □ Yes, Specify, ________________________________
14) School: Attends School: □ Yes □ No, explain ________________________________
School: _______________________________ Telephone: _______________________________
School Nurse: _______________________________ Telephone: _______________________________
Social Worker: _______________________________ Telephone: _______________________________

Past Medical History

15) Prenatal Hx:
a. Pregnancy:
   i. Complications: □ Yes, ________________________________ □ No
   ii. Gestational Diabetes: □ Yes, treatment ________________________________ □ No
   iii. HTN: □ Yes □ No
b. Use of medications/hormones: □ Yes, ________________________________ □ No
c. Use of illicit drugs/alcohol/smoking: □ Yes (circle substance) □ No
d. Exposure to toxins/radiation: □ Yes, ________________________________ □ No

16) Peri/Postnatal Hx:
a. Labor onset: □ FT □ Premature
   b. Delivery: □ NVD □ C-section □ Forceps/vacuum extraction
   □ Complications: ________________________________
   c. Birth Weight: _______________ kg Height: _______________ cm
d. Condition at Birth: Complications: □ No □ Yes, ________________________________

17) Concerns about Growth & Development: □ No □ Yes, ________________________________

   □ Mix-Breast Fed & Bottle Fed

19) Illness: □ Yes, ________________________________ □ No

20) Psychosocial Issues: □ Yes, ________________________________ □ No

21) Surgeries: □ Yes, ________________________________ □ No

22) Injuries: □ Yes, ________________________________ □ No
23) Medication Taken: □ Yes, ___________________________ □ No
24) Immunization: □ Up-to-date □ Defaulter

### Family History

25) Family Hx of Type I Diabetes:
   a. Immediate Family: □ Mother □ Father □ Sibling □ Identical Twin □ None
   b. Maternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None
   c. Paternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None

26) Family Hx of Type II Diabetes:
   a. Immediate Family: □ Mother □ Father □ Sibling □ Identical Twin □ None
   b. Maternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None
   c. Paternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None

27) Family Hx of Gestational Diabetes: □ Mother □ None

28) Other Family Hx:

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DS/PEDT/PDRF/7/2009. 3 of 5
Psychosocial History

29) Support System:
   - Lives with both parents: □ Yes □ No, explain ____________________________
   - Total number of siblings: _______ Brother(s) _______ Sister(s) ____________
   - Economic Situation: ____________________________

30) Household Members:

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31) Significant Others (who may be involved in the child’s care):

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32) Parents & Child’s Acceptance of Diagnosis/Coping/Readiness to Learn:

33) Social/Cultural/Religious Considerations:

DS/PEDT/PDRF/7/2009.
Healthcare Habits

34) Current Healthcare Habits:
   a. Sleep Schedule: Schooldays: _____ pm - _____ am  Holidays: _____ pm - _____ am
      Naps: ______________________
   b. Exercise/activity: _______________________________
   c. Safety: ________________________________
   d. Healthcare visits: ☐ When needed  ☐ Routine

35) Nutritional Habits:
   e. Weight: ______ Kg  Height: ______ cm  BMI: ______
   f. Current Meal Schedule:
      | Time | Meal/ Snack | Examples |
      |------|-------------|----------|
      |      | Breakfast   |          |
      |      | Snack       |          |
      |      | Lunch       |          |
      |      | Snack       |          |
      |      | Dinner      |          |
      |      | Snack       |          |
   g. Water Intake: ______ glasses/day
   h. Milk/Dairy Products Intake: __________________________
   i. Fiber Intake: __________________________
   j. Fruit Intake: __________________________
   k. Dietary Concerns: ☐ No ☐ Yes, __________________________

36) Other Issues & Concerns:

DS/PEDT/PDRF/7/2009
To: Fatima Al-Hadad  
Senior clinical dietitian  
SMC, Ministry of Health

Subject: Dietary intake and lifestyle habits of children with diabetes in the Kingdom of Bahrain

Dear Fatima,

This is to inform you that the research committee at Salmaniya Medical Complex has reviewed, approved and supports your research study titled “Dietary intake and lifestyle habits of children with diabetes in the Kingdom of Bahrain”. We are very interested in your research efforts that might help us understand the lifestyle of children suffering from diabetes mellitus in Bahrain.

It is our understanding the project will commence in a time frame not exceeding one year from the date of approval.

Thank you for giving us the opportunity to review this excellent research.

If you have any questions or need further assistance, please do not hesitate to contact me at 17284205 / 39739344.

Best regards,

Sincerely,

Qasim Omran MD, ABIM, CABM, MS, FCCP  
Chairperson, Committee of secondary care medical research  
Salmaniya Medical Complex  
Ministry of Health.
Ms. Fatima Al Hadad
Sr. Clinical Dietitian
Dietetic Unit
Salmaniya Medical Complex
Kingdom of Bahrain

Dear Ms. Fatima Al Hadad

Subject: Dietary Intake and Lifestyle habits of Newly Diagnosed Children with Type 1 Diabetes: A Prospective Study

This is to inform you that the Research Committee at Salmaniya Medical Complex has reviewed support and approved your research proposal which satisfy the criteria of the ethical and research guidelines of the ministry of health.

We are very interested in your research efforts that may help us to improve our knowledge to the dietary intake and recognize the lifestyle habits of diabetic children.

It is our understanding that project will commence in a time frame not exceeding one year from the date of approval.

Thank you for giving us the opportunity to review this excellent research proposal. For our records I would highly appreciate if you could inform us once the manuscript of this research accepted for publication.

If you have any questions or need further assistance, please do not hesitate to contact me.

Best regards,
Sincerely,

Dr. Ebtisam Al-Alawi, FRCS(Glasg,Ed), MRCOphth, Do
Senior Consultant Pediatric Ophthalmology & Anterior Segment Surgeon
Chairperson, Secondary Care Medical Research Subcommittee
Ealawi@health.gov.bh,
17279775, +97317741707
Control Group Questionnaire Form

Local Health Center:
CPR:
Age:
Sex: □ Male □ Female
Nationality:

Demographic Data & Current Medical Hx

1) Birth Date: _____/____/____ Place of Birth: Country:___________ Area:_____

2) Race: □ Arab: ______________________ □ None-Arab _______________________

3) Religion: □ Muslim □ Christian □ Jewish □ Hindu □ Other: ___________________

4) Diagnosis of: □ Hypothyroidism □ ↓G6PD Act. □ Celiac Disease □ PCOS
   □ SCD/trait □ Thalassemia □ Malignancies □ Nephrotic Syndrome
   □ Obesity □ Acanthosis: Location:________________________
   □ Others: _______________________________________________

5) Allergies: □ Unknown □ Yes, _______________________________________________________________________

6) Address: Area: ___________________ Block: ________

7) Health Insurance: □ No □ Yes, Specify,__________________________________________
8) **School:** Attends School: □ Yes □ No, explain ____________________________

Grade _____

### Past Medical History

9) **Prenatal Hx:**
   a. **Pregnancy:**
      i. Complications: □ Yes, ________________________________ □ No
      ii. Gestational Diabetes: □ Yes, treatment_________________________ □ No
      iii. HTN: □ Yes □ No
   b. **Use of medications/hormones:** □ Yes, __________________________ □ No
   c. **Use of illicit drugs/alcohol/smoking:** □ Yes (circle substance) □ No
   d. **Exposure to toxins/radiation:** □ Yes, __________________________ □ No

10) **Pre/Postnatal Hx:**
   a. **Labor onset:** □ FT □ Premature
   b. **Delivery:** □ NVD □ C-section □ Forceps/vacuum extraction □
      Complications: ________________________________________________
   c. **Birth Weight:**__________ kg  Height:__________ cm
   d. **Condition at Birth:** Complications: □ No □ Yes, __________________________

11) **Concerns about Growth & Development:** □ No □ Yes, __________________________

12) **Breast Feeding Hx:** □ Exclusively Breast Fed for _____ wks/months □ Bottle Fed
    □ Mix-Breast Fed & Bottle Fed

13) **Illness:** □ Yes, _____________________________________________________ □ No

14) **Psychosocial Issues:** □ Yes, _____________________________________________ □ No

15) **Surgeries:** □ Yes, _____________________________________________________ □ No

16) **Injuries:** □ Yes, _____________________________________________________ □ No
17) Medication Taken: □ Yes, ________________________________ □ No

18) Immunization: □ Up-to-date □ Defaulter

**Family History**

19) **Family Hx of Type I Diabetes:**
   a. Immediate Family: □ Mother □ Father □ Sibling □ Identical Twin □ None
   
   b. Maternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None
   
   c. Paternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None

20) **Family Hx of Type II Diabetes:**
   a. Immediate Family: □ Mother □ Father □ Sibling □ Identical Twin □ None
   
   b. Maternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None
   
   c. Paternal: □ G-Mother □ G-Father □ Aunt □ Uncle □ Cousin □ None

21) **Family Hx of Gestational Diabetes:** □ Mother □ None
### Other Family Hx:

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<tr>
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<td>Obesity</td>
<td></td>
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<tr>
<td>Hyperthyroid</td>
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<tr>
<td>Hypothyroid</td>
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<tr>
<td>Celiac Disease</td>
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<tr>
<td>Alopecia</td>
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</tr>
<tr>
<td>Vitiligo</td>
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<tr>
<td>Addison's Disease</td>
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<tr>
<td>Hypertension</td>
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</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD/Angina/MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney Disease</td>
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<td></td>
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</tr>
<tr>
<td>Psychiatric</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substance Abuse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(drug/alcohol)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others:</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>□</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Psychosocial History

#### Support System:
- **Lives with both parents**: □ Yes □ No, explain ____________________________
- **Total number of siblings**: ______Brother(s) _______ Sister(s) _________
- **Economic Situation**: _______________________________________________
24) **Current Healthcare Habits:**

   a. **Sleep Schedule:** School days: _____ pm - _____ am  Holidays: _____ pm - _____ am

   Naps: ____________________

   b. **Exercise/activity:** ____________________________

   c. **Safety:** ____________________________

   d. **Healthcare visits:** ☐ When needed  ☐ Routine ____________________________

25) **Nutritional Habits:**

   e. **Weight:** ________ Kg   **Height:** ________ cm   **BMI:** ________

### 24 hour Food Recall

<table>
<thead>
<tr>
<th>Time</th>
<th>Meal/Snack</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Breakfast</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Snack</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lunch</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Snack</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dinner</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Snack</td>
<td></td>
</tr>
<tr>
<td>Calcium and Vitamin D Frequency Questionnaire</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Vit D (IU)</strong></td>
<td><strong>Ca+ (mg)</strong></td>
<td><strong>Food</strong></td>
</tr>
<tr>
<td>92.4</td>
<td>300</td>
<td>Milk (wht, LF, skim, choc, soy)</td>
</tr>
<tr>
<td>46.4</td>
<td>150</td>
<td>Milk over cereal</td>
</tr>
<tr>
<td>11.6</td>
<td>35</td>
<td>Milk Creamer</td>
</tr>
<tr>
<td>2</td>
<td>275</td>
<td>Laban (Buttermilk)</td>
</tr>
<tr>
<td>0.8</td>
<td>435</td>
<td>Yogurt (Plain or fruited)</td>
</tr>
<tr>
<td>6.4</td>
<td>95</td>
<td>Ice cream / ice milk / Ice cream bar / Frozen yogurt</td>
</tr>
<tr>
<td>3.0</td>
<td>135</td>
<td>Processed Cheese Slice / Hard cheese (cheddar, swiss, cheddarale)</td>
</tr>
<tr>
<td>3.2</td>
<td>25</td>
<td>Cream Cheese</td>
</tr>
<tr>
<td>25</td>
<td>175</td>
<td>Macaroni and cheese, lasagna</td>
</tr>
<tr>
<td>3.6</td>
<td>280</td>
<td>Cheese pizza (large)</td>
</tr>
<tr>
<td>44.4</td>
<td>125</td>
<td>Custard / Mahlabia / Pudding</td>
</tr>
<tr>
<td>11.6</td>
<td>75</td>
<td>Muffins</td>
</tr>
<tr>
<td>20.4</td>
<td>145</td>
<td>Biscuit</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>Beans (Red beans, pinto, lima, black-eye)</td>
</tr>
<tr>
<td>26</td>
<td>25</td>
<td>Eggs</td>
</tr>
</tbody>
</table>

How many times do you eat fish? (90 grams/3oz)

What type of fish consumed?

<table>
<thead>
<tr>
<th><strong>Safi (medium size)</strong></th>
<th><strong>Yes</strong></th>
<th><strong>No</strong></th>
<th><strong>90 grams</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>15.3</td>
<td>42</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3.9</td>
<td>64</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>15.3</td>
<td>22</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3.9</td>
<td>13</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>30</td>
<td>33</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>15.3</td>
<td>21</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>N/A</td>
<td>16</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>15.3</td>
<td>32</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3.9</td>
<td>23</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>193</td>
<td>350</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Other Fish</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For Dietitian Use Only

Subtotal Calcium (food only) /day
Subtotal Vit D (food only) /day
Total Calcium Food and Supplement
Total Vit D Food and Supplement
Sunlight Exposure & Lifestyle Questionnaire

Living Conditions

1. a) Do you live in a flat or house?
   
   Flat □ House □

If living in a house:

1. b) Does it have a garden or patio (حوش) □
   
   Garden □ Patio □ None □

1. c) Does your child play in the patio or garden in your home?
   
   Yes □ No □

Personal Practices

2. a) Does your child wear a head veil or scarf (حجاب) □
   
   Yes □ No □

2. b) When going outdoors which part of your child’s body is exposed and how often?

<table>
<thead>
<tr>
<th>Are the following body parts exposed</th>
<th>Always</th>
<th>Often</th>
<th>Sometimes</th>
<th>Rarely</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>Yes</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Hand</td>
<td>Yes</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Arms</td>
<td>Yes</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Legs</td>
<td>Yes</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>
2. c) Does your child use sunscreen on their face?
   □ Always
   □ Often
   □ Sometimes
   □ Rarely
   □ Never

2. d) Does your child use sunscreen on their body?
   □ Always
   □ Often
   □ Sometimes
   □ Rarely
   □ Never

2. e) Does your child take a multivitamin
   
   Yes □ No □

   If taking a multivitamin....

2. f) How many times per day?
   _________________________________

2. g) What is the brand name used?
   _________________________________

Outdoor Exposure

3. a) How much time on average is your child exposed to sunlight between the hours of 10 am and 4pm?
   
   □ None
   □ Less than 30 minutes
   □ 30 to 59 minutes
   □ 1 to 2 hours
   □ More than 2 hours
3. b) During the following months how often does your child go outdoors for at least 15 minutes?

<table>
<thead>
<tr>
<th>Months</th>
<th>several times a day, every day</th>
<th>once a day, every day</th>
<th>3-5 days a week</th>
<th>0-2 times a week</th>
<th>once a week</th>
<th>less than once a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>June to August</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
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<td>[ ]</td>
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<tr>
<td>September to November</td>
<td>[ ]</td>
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<td>[ ]</td>
</tr>
<tr>
<td>December to February</td>
<td>[ ]</td>
<td>[ ]</td>
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<tr>
<td>March to May</td>
<td>[ ]</td>
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<td>[ ]</td>
<td>[ ]</td>
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<td>[ ]</td>
</tr>
</tbody>
</table>

3. c) In the past 12 months has your child had a suntan?

Yes □
No □
Informed Consent Form for Parents and Staff participants in the Focus Groups

You are being invited to take part in a research study. Before you decide to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and do not hesitate to ask us if there is anything that is not clear or if you would like more information. Feel free to talk to others about the study and take time to decide whether or not you wish to take part.

Name of Principle Investigator:
Mrs Fatima Al-Haddad. Email: FHaddad@health.gov.bh
Dr Kathryn Hart, University of Surrey. Tel. +44 1483 686438; Email: k.hart@surrey.ac.uk

Name of Organization: Arab Center For Nutrition, Salmaniya Medical Complex, Ministry of Health & University of Surrey, UK
Name of Project and Version: Diet and lifestyle behaviours in Bahraini children with and without diabetes.

This Informed Consent Form has two parts:
- Information Sheet (to share information about the study with you)
- Certificate of Consent (for signatures if you agree that you will participate)

You will be given a copy of the full Informed Consent Form

Part I: Information Sheet
Introduction

I am Fatima Al-Haddad, and I work at the Salmaniya Medical Complex as a Pediatric Dietitian. I am doing some research which might help shed light on the influence of diet and lifestyle factors in childhood diabetes. This involves talking to children with and without diabetes as well as their parents and the medical team that may be involved in their care. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me or of another researcher.

Purpose

We invite you to kindly participate in a focus group which will provide invaluable insight into the treatment and management of newly diagnosed children with diabetes in the Salmaniya Medical Complex. The aim of the focus groups is to identify key topics of concern and areas of existing good practice. The types of things that we might discuss are your perceptions of the disease and its prognosis and your experience of any existing diabetes education and care packages.

Selection of Participants

We would like you to participate in this focus group as we believe that your contribution, as a parent of a child with diabetes or as a medical professional working with this group, will provide us with important information that can be used to improve future educational programs.
Voluntary Participation

You can choose to say no and any services that you and your family receive at this centre will not change. You may ask as many questions as you like and we take the time to answer them. If you do decide to take part any answers you give will be recorded anonymously and will not affect the care you or your family receive in the future.

Procedure

You will be asked along with 6 to 8 other individuals to participate in the focus group which will take place in the diabetes clinic. We ask you to speak as freely as possible and to know that the information recorded is confidential, and no one else except myself and those involved in the study will have access to them. Anonymous quotes from the focus groups may be used in reports arising from the study to illustrate the discussions had however it will not be possible to identify an individual participant from such information.

Duration

The focus group will require approximately 40 minutes of your time.

Benefits

There will be no immediate and direct benefit but your participation is likely to help us find out more about the educational and health needs of girls and boys with diabetes and we hope that these will help the local clinics and hospitals to meet those needs better in the future.

Reimbursements

You will not be provided with any payment to take part in the research.

Confidentiality:

We will not be sharing information outside of the research team. The information that we collect from this research project will be kept confidential. Information collected from the focus group will be stored securely and no-one but the researchers will be able to access it. You will be assigned an identification number and this will be used in all records to maintain anonymity. No individual will be identifiable from any reports arising from the study. The coding list will be stored securely by the principle investigator.

Complaints:

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

If you have a concern about any aspect of your participation, please raise this with me Fatima Al-Haddad (+973 17284022) or Dr Kathryn Hart who will do their best to answer your questions (+44 1483 686438).

Sharing of Research Findings

At the end of the study, we will be sharing what we have learnt with the participants and with the community. We will do this by meeting first with the participants and then with the larger community. Although quotes from the focus groups may be used to illustrate our findings these
will be completely anonymous and you will not be identifiable from these. We will also publish the results in order that other interested people may learn from our research.

Right to refuse or withdraw
You may choose not to participate in this study. Choosing to participate or not will not affect your future treatment at the Centre here in any way. You may stop participating in the discussion/interview at any time that you wish without losing any of your rights.

Research review:
This study was given a favourable ethical opinion by the Research Committee at Salmaniya Medical Complex and the University of Surrey Research Ethics Committee. If you agree to take part in the study you will keep a copy of this information sheet and a signed consent form.

Who to Contact
If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following:
Fatina Al-Haddad Email: Flhaddad@health.gov.bh Tel: +97317284022
Dr Kathryn Hart, University of Surrey. Tel. +44 1483 686438. Email: k.hart@surrey.ac.uk

PART II: Certificate of Consent
Certificate of Consent

- I, the undersigned voluntarily consent to participate in the focus group.
- I have read and understood the Information Sheet provided. I have been given a full explanation by the investigators of the nature, purpose, location and likely duration of the study, and of what I we will be expected to do. We have been given the opportunity to ask questions on all aspects of the study and have understood the advice and information given as a result.
- I agree to comply with any instruction given to me during the study and to co-operate fully with the investigators.
- I consent to the use of the information obtained and as outlined in the accompanying information sheet, being used for the research project detailed in the information sheet, and agree that data collected may be shared with other researchers involved in this study. I understand that all personal data relating to volunteers is held and processed in the strictest confidence, and in accordance with the Data Protection Act (1998).
- I understand that I am free to withdraw from the study at any time without needing to justify our decision and without prejudice.
- I confirm that I have read and understood the above and freely consent to participate in this study. I have been given adequate time to consider our participation and agree to comply with the instructions and restrictions of the study.
Print Name of Parent or Staff

Signature of Parent of Staff

Date ______________________
Day/month/year

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the parent or hospital staff member, and to the best of my ability made sure that the person understands their participation in this focus group.

I confirm that the parents or staff member was given an opportunity to ask questions about the study, and all the questions asked by him/her have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Print Name of Researcher/person taking the consent

Page 4
CHILDREN’S PHYSICAL ACTIVITY QUESTIONNAIRE (C-PAQ)

Parent Questionnaire

Your child’s name: .................................................................................................................
Your child’s date of birth (dd/mm/yy): .......... / ............... / .................
Are you the child’s: mother / father / guardian / other

Please note: - this questionnaire will take approximately 10 minutes to complete
- please answer the questions in relation to the child named above
- please complete every line in the questionnaire

For further information, please contact:
Which of the following PHYSICAL activities did your child do in the PAST 7 DAYS?

Please complete this questionnaire for the following days: .................................. to ..................................

<table>
<thead>
<tr>
<th>Did your CHILD do the following activities in the past 7 days?</th>
<th>MONDAY – FRIDAY</th>
<th>SATURDAY – SUNDAY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>How many times Mon-Fri?</td>
<td>Total hours/minutes Mon-Fri?</td>
</tr>
<tr>
<td>EXAMPLE: Bike riding</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>SPORTS ACTIVITIES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerobics</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Baseball/softball</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Basketball/volleyball</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Cricket</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Dancing</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Football</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Gymnastics</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Hockey (field or ice)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Martial arts</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Netball</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Rugby</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Did your CHILD do the following activities in the past 7 days?</td>
<td>MONDAY – FRIDAY</td>
<td>SATURDAY – SUNDAY</td>
</tr>
<tr>
<td>-------------------------------------------------------------</td>
<td>-----------------</td>
<td>------------------</td>
</tr>
<tr>
<td></td>
<td>How many times Mon-Fri?</td>
<td>Total hours/minutes Mon-Fri?</td>
</tr>
<tr>
<td>Running or jogging</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Swimming lessons</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Swimming for fun</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Tennis/badminton/squash/other racquet sport</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>LEISURE TIME ACTIVITIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bike riding (not school travel)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Bounce on the trampoline</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Bowling</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Household chores</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Play in a play house</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Play on playground equipment</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Play with pets</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Rollerblading/roller-skating</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Scooter</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Did your CHILD do the following activities in the past 7 days?</td>
<td>MONDAY – FRIDAY</td>
<td>SATURDAY – SUNDAY</td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
<td>-----------------</td>
<td>------------------</td>
</tr>
<tr>
<td></td>
<td>How many times Mon-Fri?</td>
<td>Total hours/minutes Mon-Fri?</td>
</tr>
<tr>
<td>Running or jogging</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Swimming lessons</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Swimming for fun</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Tennis/badminton/squash/other racquet sport</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>LEISURE TIME ACTIVITIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bike riding (not school travel)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Bounce on the trampoline</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Bowling</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Household chores</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Play in a play house</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Play on playground equipment</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Play with pets</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Rollerblading/roller-skating</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Scooter</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Activity</td>
<td>MONDAY-FRIDAY</td>
<td>SATURDAY-SUNDAY</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>---------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Watching TV/videos</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Art &amp; craft (e.g. pottery, sewing, drawing, painting)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Doing homework</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Imaginary play</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Listen to music</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Play indoors with toys</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Playing board games / cards</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Playing computer games (e.g. playstation / gameboy)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Playing musical instrument</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Reading</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sitting talking</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Talk on the phone</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Travel by car / bus to school (to and from school)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Did your CHILD do the following activities in the past 7 days?</td>
<td>MONDAY-FRIDAY Total hours/minutes</td>
<td>SATURDAY-SUNDAY Total hours/minutes</td>
</tr>
<tr>
<td>-------------------------------------------------------------</td>
<td>-----------------------------------</td>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Using computer / internet</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Watching TV/videos</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Other (please state):</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Focus group participants versus non-participants

<table>
<thead>
<tr>
<th></th>
<th>Focus Group Participants</th>
<th>Non-Focus Group Participants</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nationality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bahraini</td>
<td>4</td>
<td>13</td>
<td>0.601b</td>
</tr>
<tr>
<td>Non-Bahraini</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Child gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3</td>
<td>7</td>
<td>0.267a</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arab</td>
<td>5</td>
<td>14</td>
<td>1.000b</td>
</tr>
<tr>
<td>Non-Arab</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Religion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muslim</td>
<td>5</td>
<td>14</td>
<td>1.000b</td>
</tr>
<tr>
<td>Non-Muslim</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Economic Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>5</td>
<td>11</td>
<td>1.000b</td>
</tr>
<tr>
<td>High</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Governorate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muharraq</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Capital</td>
<td>2</td>
<td>0</td>
<td>0.223a</td>
</tr>
<tr>
<td>Central</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Chi Squared,
Focus Group for parents of children with diabetes and their families

Some possible topics of interest that will be explored are as follows:

Introductory topics/ ‘warm up’

- When was your child diagnosed with diabetes
- What was your initial reaction/feeling?
- How do you feel now towards your child's condition?
- Evaluating their perceptions of the disease prior to and after admission
  - Did you know what diabetes was prior to your child's diagnosis?
  - Do you feel that you have a clearer understanding or the disease now or are some things still vague?
  - How do you feel he will cope with the disease in the future?
- Evaluating whether the hospital stay was considered a good or bad experience and what could have been done to improve the stay.

➤ Upon arrival at the hospital did you feel that the admission procedure went smoothly or was it hectic?
➤ Who was the person that broke the news of your child's condition?
➤ Where you placed in a private or public room? Where you comfortable?
➤ What did you think of the nurses that were taking care of your child in the wards?
➤ Overall do you feel that your hospital stay was a good or bad experience
➤ What could have been done in your opinion to improve the stay?
• Evaluating any education received during the hospital admission period (i.e. its strengths & weaknesses,)

• What did you think of the education you received from the diabetes nurse educator?
  Was it clear? Was there too much material or too little material covered?
• Do you feel that the time spent on education was sufficient?
• Where the nurses reassuring? Confident? Competent?
• Did you feel that the dietician explained clearly the exchanges and dietary management? Did she spend sufficient time with you?
• Did you feel that the consultant was clear in his explanation of the disease? Do you feel he spent sufficient time at the initial diagnosis and during his follow-up visits?
• What suggestions do you have or comments for the physician/ the diabetes nurse educator/dietician?
• What do you feel were the diabetes teams’ strength and what were their weaknesses?
• Evaluating the follow-up system at the pediatric diabetes clinic

➡ What do you think of the follow up system available? The voice mail, fax and 24hour emergency line?
➡ Do you feel that the follow appointment time given with the physicians is suitable?
➡ Do the nurse educators give you sufficient time or do you feel hurried?
➡ What do you think of the diabetes clinic itself? Do they have sufficient place and space?
• Exploring recommendations for future support programs
➡ In the future what support or educational programs would you like to have?
Focus Group on staff working with children with diabetes and their families

Some possible topics of interest that will be explored are as follows:

- Evaluating barriers to education process and behavioral changes
  - What do you feel are some of the barriers to educating parents and/or child? i.e. educational materials, other resources, finances, time etc.…
  - Is time spent on education an issue? i.e. too long too short
  - What do you consider is the ideal amount of time required to cover the material?
  - From your experience what are the greatest barriers to behavioral health related changes? i.e. accepting diagnosis, willingness to administer insulin, willing to check BG by HgT, willing to make changes to diet.

- Evaluating the role of the health care workers in educating family post diagnosis.
  - What is your role in education at time of diagnosis?
  - What is your role in post-discharge follow-ups?

- Exploring recommendations for future educational programs
  - What would be needed in your opinion to strengthen the educational program? (time, money, resources)
  - Would you benefit from more educational resources and if so what kind?
  - Do you feel you need more training or educational courses
Focus Group on staff working with children with diabetes and their families

Some possible topics of interest that will be explored are as follows:

Introductory topics/ ‘warm up’

- Number of years spent working with diabetes
- Time spent currently working with diabetes
- Evaluating the role of the health care workers in educating family post diagnosis.

⇒ Who is part of your diabetes team?
⇒ Who do you work closest to?
⇒ What is your role at time of diagnosis? Whose job is it to break the news to the family?
⇒ What is your role in post-discharge follow-ups?
⇒ What is the role of the nurses in your team
⇒ What is the role of the dietician?
⇒ Do you refer your patients to other consultants and why?

Evaluating barriers to education process and behavioral changes

⇒ What do you feel are some of the barriers to educating parents and/or child? i.e. educational materials, other resources, finances, time etc….
⇒ From your experience what are the greatest barriers to behavioral health related changes? i.e. accepting diagnosis, willingness to administer insulin, willing to check BG by HgT, willing to make changes to diet.
Do you think that certain groups are more/less receptive to education – if so who?
(e.g. different age groups/parents versus children/with or without good family support)

- Exploring recommendations for future educational programs

- What would be needed in your opinion to strengthen the educational program? (time, money, resources)
- Would you benefit from more educational resources and if so what kind? Face to face, online?
- Do you feel you need more training or educational courses?
The following questions are about how you see your life with diabetes. Circle the number that gives the best answer for you. Please provide an answer for each question. Please bring the completed form with you to the next consultation where it will form the basis for a dialogue about how you are coping with your diabetes.

<table>
<thead>
<tr>
<th>Patient name:</th>
<th>Completion date:</th>
<th>Interview date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact of symptoms relating to diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How often do you...</td>
<td>Never</td>
<td>Very</td>
</tr>
<tr>
<td>1. Feel physically ill?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2. Have a bad night's sleep?</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3. Miss school because of your diabetes?</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

| Impact of treatment | | |
| How often do you... | | |
| 4. Do you feel pain associated with the treatment? | 0 | 1 | 2 | 3 | 4 | 0-20 |
| 5. Does diabetes interfere with your family life? | 0 | 1 | 2 | 3 | 4 | 0-12 |
| 6. Do you feel restricted by your diet? | 0 | 1 | 2 | 3 | 4 | 0-12 |

| Impact on activities | | |
| How often do you... | | |
| 7. Limit your social relationships and friendships? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 8. Prevent you from blushing or using a machine (e.g., a computer)? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 9. Interfere with you exercising? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 10. Interrupt your leisure time activities? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 11. Prevent you from doing activities at school? | 0 | 1 | 2 | 3 | 4 | 0-28 |

| Parent issues | | |
| How often do you feel that your parents... | | |
| 12. Are too protective of you? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 13. Worry too much about your diabetes? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 14. Act like diabetes is their disease, not yours? | 0 | 1 | 2 | 3 | 4 | 0-28 |

| Worries about diabetes | | |
| How often do you worry about whether... | | |
| 15. You will get married? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 16. You will have children? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 17. You will not get a job? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 18. You will faint or pass out? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 19. You will be able to complete your education? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 20. Your body looks different because of diabetes? | 0 | 1 | 2 | 3 | 4 | 0-28 |
| 21. You will get complications? | 0 | 1 | 2 | 3 | 4 | 0-28 |

| Health perception | | |
| Compared with others your age, would you say your health is... | Excellent | Good | Fair | Poor | 0-4 |

Thank you for your help!
The “quality of life for youth” questionnaire

The achievement of good metabolic control is difficult in children, and particularly in adolescents. Having diabetes requires a complex, intrusive and highly demanding daily programme for families, which may have a negative effect on Quality of Life (QOL). Good Quality of Life is associated with better metabolic control.

Why use the “quality of life for youth” questionnaire?

It is vital that clinicians are able to assess QOL and identify issues which may affect it, particularly as these issues may not be obvious during the clinical consultation. The “quality of life for youth” questionnaire is a valid assessment that enables the identification of specific issues which are negatively affecting QOL. It provides an opportunity for enhanced communication between the patient, family and diabetes care team, and also an opportunity to resolve these negative issues.

How to use the “quality of life for youth” questionnaire

The questionnaire can be used as part of any routine diabetes consultation. The young person can be asked to complete the form at home or in the waiting room prior to the consultation. The completed form should be reviewed in the consultation by the nurse, diabetologist or psychologist, together with the child/adolescent. It can be used to identify issues that may be interfering with daily diabetes management and quality of life and can help prompt a dialogue about issues of particular concern for the young person with diabetes. The questionnaire can be used to obtain a reliable quality of life score that can be used to monitor changes over time and individual response to changes in therapy.

To further enhance the focus on the young person's own agenda, an additional question can be added at the end of the form as follows: "Which topic would you most like to discuss with your diabetes care team today? (e.g. treatment related issues, school, home, sport or other areas)". This question is not to be scored but can help facilitate dialogue.

What is the “quality of life for youth” questionnaire?

The “quality of life for youth” questionnaire was developed from the revised 52 item DCCT Diabetes QOL for Youth Questionnaire (*1). This shorter form is a more precise version with improved construct validity and with items known to be associated with metabolic control. It has been validated for children and adolescents aged 10-18 years and has been translated into 16 languages to date (*2). The questionnaire is quick and easy to score and allows comparisons across countries and cultures.

Scoring of the questionnaire

Each item has five possible scores with a value from 0 to 4, with 0 representing 'never' and 4 'all the time'. Higher scores indicate a more negative impact of diabetes and poorer QOL, and lower scores indicate greater QOL. The scoring of each subscale is done separately by summation of scores for each item within the subscale. Emphasis on a score for each subscale, as opposed to a total score, puts a greater emphasis on each item and subscale and thus highlights a problem in a single area.

For ongoing monitoring and comparison to normative scores, standardised scores with a range from 0-100 can be calculated as follows:

- Total QOL impact score: 100 * (raw total score - 21) / 84
- Impact of symptoms: 100 * (raw score – 3) / 12
- Impact of treatment: 100 * (raw score – 3) / 12
- Impact of activities: 100 * (raw score – 7) / 28
- Parent issues: 100 * (raw score – 3) / 12
- Worries about diabetes: 100 * (raw score – 5) / 20
- The self-rated health perception question is treated separately and standardised to 1-100 as follows: Score= 100 * (raw score-1)/3

A high score indicates a high negative impact on QOL.

Questionnaire availability

The questionnaire is available in many languages from the Hvidere Study Group on Childhood Diabetes (*2). Please contact questionnaire administrator Mette Bauditz, Corporate Responsibility, Novo Nordisk, to obtain a user agreement form for research purposes and further information. E-mail: mtb@novonordisk.com.

Further information about the Hvidere Study Group on Childhood Diabetes: hvideregroupp.org

The quality of life for youth questionnaire was developed with the Hvidere Study Group on Childhood Diabetes. The questionnaire is now being used to implement evaluation of QOL in diabetes treatment as part of DAWN Youth, a global Novo Nordisk initiative in partnership with the International Diabetes Federation (IDF) and the International Society for Paediatric and Adolescent Diabetes (ISPAD).

The DAWN Youth initiative seeks to improve psychosocial support for young people with diabetes and their families through promotion of evidence-based tools and strategies for paediatric psychosocial diabetes management.

For more information, please access dawnyouth.com


*2) Copies of the questionnaire are available in the following languages: Danish, Dutch, English (North American and UK), Finnish, French, German, Italian, Japanese, Macedonian, Norwegian, Portuguese, Spanish and Swedish.
**Problem Areas in Diabetes Questionnaire (PAID) questionnaire from Dawn Youth Study**

<table>
<thead>
<tr>
<th>Patient name:</th>
<th>Completion date:</th>
<th>Interview date:</th>
</tr>
</thead>
</table>

**INSTRUCTIONS:** Which of the following diabetes issues are currently a problem for you? Circle the number that gives the best answer for you. Please provide an answer for each question. Please bring the completed form with you to your next consultation where it will form the basis for a dialogue about how you are coping with your diabetes.

<table>
<thead>
<tr>
<th>Question</th>
<th>Not a problem</th>
<th>Minor problem</th>
<th>Moderate problem</th>
<th>Somewhat serious problem</th>
<th>Serious problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Not having clear and concrete goals for your diabetes care?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Feeling discouraged with your diabetes treatment plan?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Feeling scared when you think about living with diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Uncomfortable social situations related to your diabetes care (e.g., people telling you what to eat?)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Feelings of deprivation regarding food and meals?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Feeling depressed when you think about living with diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Not knowing if your mood or feelings are related to your diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Feeling overwhelmed by your diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Worrying about low blood sugar reactions?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Feeling angry when you think about living with diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Feeling constantly concerned about food and eating?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Worrying about the future and the possibility of serious complications?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Feelings of guilt or anxiety when you get off track with your diabetes management?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Not &quot;accepting&quot; your diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Feeling unsatisfied with your diabetes physician?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Feeling that diabetes is taking up too much of your mental and physical energy every day?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17. Feeling alone with your diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18. Feeling that your friends and family are not supportive of your diabetes management efforts?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19. Coping with complications of diabetes?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20. Feeling “burned out” by the constant effort needed to manage diabetes?</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Problem Areas in Diabetes Questionnaire (PAID)

Ways to Identify patient emotional distress
Diabetes can be demanding and cause emotional distress. It is vital that clinicians are able to identify diabetes-related emotional distress in their patients. Validated practical strategies are available to promote an open dialogue and help to flag when serious emotional distress exists.

One tool that has proven very helpful to healthcare professionals is the Problem Areas in Diabetes (PAID) scale, a simple, one-page questionnaire.

Why the PAID scale?
PAID has high acceptability and scientific validity as evidenced by more than 60 scientific papers and scientific research abstracts.

The PAID measure of diabetes related emotional distress correlates with measures of related concepts such as depression, social support, health beliefs, and coping style, as well as predicts future blood glucose control of the patient.

The questionnaire has proven to be sensitive to detect changes over time following educational and therapeutic interventions.

What is the PAID scale?
The PAID is a self-report pencil and paper questionnaire that contains 20 items that describe negative emotions related to diabetes (e.g., fear, anger, frustration) commonly experienced by patients with diabetes. Completion takes approximately five minutes.

Scoring of the questionnaire
Each question has five possible answers with a value from 0 to 4, with 0 representing "no problem" and 4 "a serious problem". The scores are added up and multiplied by 1.25, generating a total score between 0 – 100. Patients scoring 40 or higher may be at the level of "emotional burnout" and warrant special attention. PAID scores in these patients may drop 10-15 points in response to educational and medical interventions.

An extremely low score (0-10) combined with poor glycaemic control may be indicative for dental.

How to use the PAID scale?
In a clinical setting, the PAID can be administered routinely (e.g. annual review) and/or ad hoc as a diagnostic tool.
The patient can be asked to complete the questionnaire before consultation (waiting room) or at the beginning of the consultation. Together with the patient, the clinician can calculate the total score and invite the patient to elaborate on problem areas that stand out (high scores) and explore options for overcoming the identified issues. This may include referral to a mental health specialist.

Novo Nordisk 2006. Adapted from DAWN Interactive 2. Text by Frank Snoek and Garry Welch.
Proposed transition program for adolescent with T1DM

Lesson Plan 1:

**Introducing yourself as a Transition Coordinator**

My name is ________ I am a pediatric diabetes nurse, I will be your transition coordinator.

My role will be to facilitate your transfer to adult clinic in one year’s time.

Part of my job will be to:

- Meeting with you and your parent(s) before or after your routine visit with your endocrinologist for a total of 4 visits. (3 in pediatric clinic and 1 in adult clinic)
- Each meeting will include a lesson plan for a period of approximately 30 minutes
- After the lesson plan I will be asking you to fill out 2 questionnaires.
- I will also be calling in between visits to remind you of appointment schedule, help you with questions, solve problems or help with any resources needed.
Managing diabetes for the long-term

Activity #1

- Use the “my blood sugar” tool to guide this section.
- Ask them to communicate what the latest readings for long term blood sugar show? What does it tell them about their sugar control?

```
<table>
<thead>
<tr>
<th>Long-term blood sugar [HbA1c]</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.5</td>
</tr>
<tr>
<td>48</td>
</tr>
</tbody>
</table>
```

- Ask them to identify on a scale of 0-10 how concerned they are about their blood sugar

```
On a scale of 0 to 10, where 0 is 'Not at all' and 10 is 'Very'
```

Complications:

- Discuss importance of maintain good HbA1c control
- Discuss consequences of poor control in terms of damage to the large blood vessels heart attacks and stroke: having diabetes increases your risk of having a heart attack or stroke, kidney disease, blindness and even amputations.
- Clarify that in adult care unlike in pediatrics, they may see patients with these conditions

Activity # 2:
Activating Agent

I don’t like checking my blood sugar

Beliefs: What do you think or tell yourself

Consequences: How do you feel? What did you/didn’t you do

Discussion: Is it helpful or unhelpful, will it help me reach my goals

Effect: How would you like to feel? What would you ideally do?
Complete Brochure of Points of Focus

Lesson One Focus Points

5 mins
Lesson Plan 2

How to manage diabetes effectively

Re-assure patient that you are here to guide and support them along the path so as to maximize their health potential.

Review the following points making sure to engage patient and actively listen:

**Treatment of Hypo-glycaemia (hypo)**

- Explain that while hypo-glycaemia occurs when your blood glucose levels drop (usually below 4.0mmol/L) Hypos can be caused by missing a meal, not eating enough carbohydrates for a given dose of insulin, unplanned.
- Explain or ask patient to explain how to treat a hypo
- Review use of glucagon injection

**Treatment of Hyper-glycaemia:**

- Hyper-glycaemia occurs when the levels are too high (usually above 15mmol/L).
- Review causes of hyperglycemia
- Review injection site rotation
- Explain or ask patient to explain how to treat a hypo
- Review importance of checking blood sugar

CBT-Therapy activity
I have a high blood sugar reading

Activating Agent

Beliefs: What do you think or tell yourself

Consequences: How do you feel? What did you/didn’t you do

Discussion

Consequences: How do you feel? What did you/didn’t you do
Complete Brochure of Points of Focus

Lesson Two Focus Points

5 mins
Lesson 3:
Coping with Diabetes Day-by-Day

Explain how these daily factors can affect blood sugar; engage patient and actively listen

- **Exercise:**
  i. Exercise brings down blood glucose levels.
  ii. Explain how different kinds of exercise affect insulin and carbohydrate balance.
  iii. Explain how to avoid hypos whilst exercising (i.e. a snack prior to exercise or starting with higher levels than usual can help to avoid having a hypo)

- **Diet:**
  i. Importance of eating healthy low fat foods
  ii. Balancing carbohydrate with insulin

- **Hormones**
  i. Puberty hormones can impact blood sugar causing hyperglycemia

- **Illness:**
  i. It is important to have a sick plan in place to help manage your diabetes during times of illness.
  ii. Review sick days rules
  iii. Review when to contact diabetes educator and when to go to the hospital/emergency

Activity # 2 CBT-Therapy
I want to eat whenever and whatever I want

Beliefs: What do you think or tell yourself

Consequences: How do you feel? What did you/didn’t you do

Discussion

Effect: How would you like to feel? What would you ideally do?
Complete Brochure of Points of Focus

Lesson Three Focus Points

5 mins
Lesson 4: Family support, conflict and communication

- Ask patient what he/she sees; actively listen
- Use the children’s circle tool to explain to patient how diabetes is different when you are a child. Focus on the child being within the family circle and the child’s surroundings
- Explain that transitioning into adult care means that you will gradually be moving out of the family circle (overlapping and sharing responsibility at one point) but your family and friends will still be there to support you.
- Explain briefly the difference in communication between pediatric and adult care (i.e. pediatric care, the healthcare provider will communicate with you and your parents; but in adult care, they expect to be communicating with you.)

Children’s Circle Tool (DAWN-2)

Activity # 2 CBT-Therapy
Activating Agent

My parent(s) upset me when...

Beliefs: What do you think or tell yourself

Consequences: How do you feel? What did you/didn’t you do

Discussion

Effect: How would you like to feel? What would you ideally do?
Lesson Four: Focus Points

5 mins
11.2 List of abstracts and oral presentations


3. Al-Haddad F. Oral Presentation College of Health Sciences, Kingdom of Bahrain February 25, 2014


Type 1 Diabetes in Children: The Bahraini Dilemma.

By K Hart, Y Nicolaoud, A Musaiger, SM Alqallaf, F Al-Haddad

1Department of Nutritional Science, University of Surrey, Guildford, GU2 7XH, 2Bahrain Centre for Studies and Research,
Manama, Bahrain and 3College of Health Sciences, Bahrain.

Summary:

- Diabetes represents a significant and growing public health challenge in the Middle East with the increases in pediatric Type 1 Diabetes (T1DM) of particular concern since these do not appear to mirror the trends seen elsewhere.
- As part of a larger study attempting to characterize the Bahraini pediatric T1DM population, differences in socioeconomic and medical history were identified between children with T1DM and healthy age and weight matched controls, specifically in relation to prior childhood illness and infections and maternal medical history.

Introduction:

- In the Middle East approximately one in four adult deaths is attributed to diabetes.
- Bahrain specifically has experienced a doubling of rates of childhood Type 1 diabetes mellitus (T1DM) in the past ten years.
- Whilst a healthy diet and lifestyle is recognized as central to maintaining good blood glucose control and preventing long-term complications, little or no data exists on the dietary intake or lifestyle of children living with T1DM in Bahrain.

Aim:

- To undertake an observational case-control study to compare the social and medical history of children with and without T1DM living in Bahrain, in an attempt to elucidate the potential etiologies of the disease.

Methods:

- Ethical approval was received from the Health Ethics and Research Committee in the Samaanyaa Medical Complex (SMC), Bahrain.
- Cases: all children aged 6-12 years receiving a confirmed diagnosis of T1DM in SMC in the years 2009 and 2010.
- Controls: an age matched group of children recruited from primary health care centres in Bahrain.
- Data for cases was extracted from the Diabetes Registry Forms (DRF) completed for all newly diagnosed cases. These records the family’s sociodemographic status, mother’s pre and postnatal history, infant feeding practices, and the child’s past medical history and family history of diabetes matched controls, specifically in relation to prior childhood illness and infections and maternal medical history.
- Comparative data for cases was collected using an adapted version of the DRF administered by the local researchers.
- Height and weight of all children were measured using standardized methods of diagnosis/registration.
- PANW (y/o) was used to compare the characteristics of the cases and controls using independent t-tests, Mann Whitney U tests and Chi Squared analysis as appropriate. Statistical significance was assumed at p<0.05.

Results:

Sample

- The data for 59 cases and 60 controls were available for analysis.
- The cases and controls were well matched for age, gender, and BMI (see Table 1).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases (n=59)</th>
<th>Controls (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y/o)</td>
<td>9.66±1.72</td>
<td>8.67±2.01</td>
</tr>
<tr>
<td>Male (% female)</td>
<td>49.1%</td>
<td>48.5%</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>16.9±5.1</td>
<td>17.3±4.7</td>
</tr>
</tbody>
</table>

Socioeconomic factors

- A significant association between economic situation and diabetes diagnosis was identified (p=0.046) but this was due more to cases reporting their income as ‘moderate’ rather than a skew towards the ‘high’ or ‘low’ income bands (see Fig 1).

Results (continued):

- Children with diabetes were less likely to be Bahraini nationals (p=0.001) but there was no significant difference in self-reported race with the majority of all children (94.5%) described as of Arab origin.

Family medical history

- A family history of T1DM was rarely reported (Total sample: mothers: n=0; fathers: n=0; sibling: n=1).
- Cases were more likely to have a mother with T1DM, gestational diabetes and gestational hypertension (see Fig 2).

Child medical history

- Prior to diabetes diagnosis, cases were more likely than controls to have suffered from other childhood illnesses (54% and 10% respectively; p<0.001), most commonly tonsillitis (56% and 0%) or to have undergone surgery (17% and 3% respectively; p=0.006).

Infant feeding

- No significant association between T1DM diagnosis and infant feeding was seen.
- Over 90% of all children had received some breast milk and 55% and 65% of cases and controls respectively were reported to be still receiving breast milk beyond 6 months.

Discussion:

- The etiology of T1DM may involve an interaction between genetic and environmental factors.
- Although this analysis was unable to fully interrogate potential genetic differences it does support the role of infections as an environmental trigger for T1DM.
- The importance of infant feeding practices cannot be confirmed, however the analysis of dietary intakes and Vitamin D status in this population group are ongoing and will further inform the development of effective prevention and management strategies to tackle paediatric T1DM in the Middle East.

References:

11.3 List of publications


Children with Type 1 Diabetes

Farima Ahmed Al-Haddad, MSc, RD, LD* Abdulrahman Musaiger, PhD (Nutrition)**
Mahmood Al-Qallaf, PhD*** Kathryn Hart, RD, PhD, SCEPTre Fellow****

Background: The prevalence of diabetes in the Middle East is amongst the highest worldwide; Bahrain ranks amongst the top 10 countries. In particular, increasing number of children are being diagnosed with type 1 diabetes mellitus (T1DM) posing a significant public health concern.

Objective: To evaluate the magnitude of type 1 diabetes in Bahrain.

Design: A Case-Control Retrospective Study.

Setting: Pediatric Diabetes and Endocrine Clinic and Local Health Centers (LHC).

Method: Fifty-nine cases and 53 controls were included in the study. Data from the Diabetes Registry were recorded for subjects meeting the inclusion criteria and questionnaire was administered to healthy controls. Chi Square or Student’s t-test was used as appropriate. Logistic regression analysis was used to evaluate independent predictors of T1DM.

Result: Fifty-nine children aged 6-12 years diagnosed with T1DM in the years 2009 and 2010 were compared to 53 healthy controls. Children with T1DM were more likely to have suffered from a pre-diabetes illness such as tonsillitis 32 (54.2%) compared to controls 3 (5.7%), and have undergone a surgery prior to diagnosis 14 (23.7%), and to have mothers with T1DM or family history of GDM. No significant difference in infant-feeding practices was observed between children with type 1 diabetes and the healthy controls.

Conclusion: Children with T1DM were more likely to have suffered from other infectious illnesses before the diagnosis was established. Whilst unable to fully investigate any potential genetic differences between cases and controls, this study provides support for the theoretical role of infections as a trigger for T1DM.

* Sr. Clinical Dietician, Salmaniya Medical Complex
** Director Arab Center for Nutrition, Head of Nutrition and Health Studies Unit, University of Bahrain
*** Associate Professor, University of Bahrain College of Health Sciences
**** Lecturer in Diabetics, University of Surrey Department of Nutritional Sciences School of Biosciences and Medicine
Email: Farima.alhaddad@gmail.com
The prevalence of diabetes in the Middle East and the North African region is considered among one of the highest worldwide. Bahrain ranks amongst the top 10 countries for prevalence of diabetes, and therefore faces economic and health-care burden imposed by this disease. The World Health Organization (WHO) estimates that approximately one in four adult deaths is attributed to diabetes in the Eastern Mediterranean region, with diabetes-related deaths in Bahrain increasing from 9% in 2002 to 12% in 2010.

The increasing number of children diagnosed with type 1 diabetes mellitus (T1DM) in Bahrain is alarming; it has more than doubled in the past ten years. In Bahrain, little or no data is currently available on the lifestyle, dietary, or the role of infection or childhood illnesses on the risk of T1DM. Most studies have focused only on the lifestyle and dietary intake of healthy Bahraini children.

Although no national registry exists for children with diabetes, an internal registry exists at the Pediatric Endocrine and Diabetes Unit in the Salmaniya Medical Complex (SMC).

The aim of this study is to evaluate the magnitude and risk factors of type 1 diabetes in Bahrain.

METHOD

The study subjects were children aged 6 to 12 years diagnosed with T1DM from 2009 to 2010 in the Salmaniya Medical Complex, Bahrain. The inclusion criteria were as follows:

- Registered as a confirmed case of T1DM at the Pediatric Diabetes Unit (PEU).
- 6-12 years of age at diagnosis.
- Followed up at least once at the Pediatric Diabetes Unit.
- Had a completed Diabetes Registry Form (DRF).

DRF includes personal characteristics, psychosocial, and health-related information.

Control subjects were recruited from local Health Centers across the country. Fifty-three children were selected to match the cases for age, sex, and geographic location and were randomly selected. The majority of the control group selected had either the common cold or was accompanying their parents to appointments.

All data analyzed using SPSS version 21; all information was kept strictly confidential. Differences between subgroups were analyzed using Chi Square or Student’s t-test as appropriate. Logistic regression analysis was used to evaluate independent predictors of T1DM. P value < 0.05 was considered significant.

RESULT

Fifty-nine children met the criteria and were included in the study, compared to 53 healthy controls, see table 1. The mean age of the control group was 9.02±1.88 years and the mean age of the case group was 9.66±1.72 years. The mean BMI for the control was 48.80±35.76 and case group was 43.73±37.31. Children with T1DM were more likely to be Bahraini nationals (p=0.001) although there was no significant difference in self-reported race, with 95% of children being described as of Arab origin, see table 1. A significant association was identified between economic status and diabetes diagnosis (p=0.028) as shown in table 2.
Table 1: Baseline Characteristic of Case-Control Study

<table>
<thead>
<tr>
<th></th>
<th>Control 53</th>
<th></th>
<th>Case: 59</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number and</td>
<td>Mean (SD)</td>
<td>Number and</td>
<td>Mean (SD)</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>Percentage</td>
<td></td>
<td>Percentage</td>
<td></td>
<td>Value</td>
</tr>
<tr>
<td>Age in years</td>
<td>53</td>
<td>33 51 (1.88)</td>
<td>59</td>
<td>51 45.73 (3.31)</td>
<td>0.005</td>
</tr>
<tr>
<td>BMI percentile*</td>
<td>42.80 (31.76)</td>
<td>43.76 (33.76)</td>
<td>45.73 (33.31)</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balanini</td>
<td>30 (94.3%)</td>
<td>37 (62.7%)</td>
<td>0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Balanini</td>
<td>3 (5.7%)</td>
<td>22 (37.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>34 (48.2%)</td>
<td>29 (49.2%)</td>
<td>0.682*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>25 (51.8%)</td>
<td>30 (50.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arab</td>
<td>53 (100%)</td>
<td>56 (94.9%)</td>
<td>0.245*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Arab</td>
<td>0 (0.0%)</td>
<td>3 (3.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Religion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muslims</td>
<td>53 (100%)</td>
<td>56 (94.9%)</td>
<td>0.245*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Muslim</td>
<td>0 (0.0%)</td>
<td>3 (3.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Governorate**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mohammar</td>
<td>13 (24.5%)</td>
<td>7 (12.1%)</td>
<td></td>
<td></td>
<td>0.088</td>
</tr>
<tr>
<td>Capital</td>
<td>7 (13.5%)</td>
<td>13 (22.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northen</td>
<td>18 (34%)</td>
<td>12 (20.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>15 (28.3%)</td>
<td>25 (43.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southern</td>
<td>0 (0.0%)</td>
<td>1 (3.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Economic Status of Children with TIDM and Healthy Controls

<table>
<thead>
<tr>
<th></th>
<th>Control 53</th>
<th></th>
<th>Case: 59</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Number and</td>
<td>Mean (SD)</td>
<td>Number and</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Percentage</td>
<td></td>
<td>Percentage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Economic Situation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>13 (24.9%)</td>
<td>7 (13.3%)</td>
<td>0.028</td>
<td>0.375 (0.175-0.802)</td>
<td>0.11</td>
</tr>
<tr>
<td>Medium</td>
<td>34 (64.2%)</td>
<td>46 (83.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>6 (11.9%)</td>
<td>1 (1.9%)</td>
<td></td>
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</tbody>
</table>

Medical history revealed that children with TIDM were more likely to have suffered from an illness such as tonsillitis than healthy children, 32 (54.2%) and 3 (5.7%) respectively; p<0.001 or to have undergone surgery prior to diagnosis, 14 (23.7%) and 2 (3.8%) respectively; p=0.001, see table 3. Furthermore, logistic regression analysis revealed that children who were suffering from an illness were approximately fifteen times more likely to develop diabetes [(OR 15.647) 95% CI 4.075-60.07; p<0.001] than other children. Logistic regression showed no significant relationship (p=0.096) between surgery performed and the risk of developing diabetes. Other common diseases such as glucose-6-phosphate deficiency (G6PD), sickle cell disease (SCD/SCT) and thalassemia were not found to be significantly associated with diabetes diagnosis.
Table 3: Medical History of Children with TIDM and Healthy Controls

<table>
<thead>
<tr>
<th></th>
<th>Controls 53</th>
<th>Cases 59</th>
<th>P-value</th>
<th>OR (95% CI)</th>
<th>Logistic Regression P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G6PD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>51 (96.2%)</td>
<td>52 (98.8%)</td>
<td>0.277</td>
<td>8.656 (0.342-218.56)</td>
<td>0.190</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (3.8%)</td>
<td>1 (1.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCD/SCC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>45 (84.9%)</td>
<td>35 (95.1%)</td>
<td>0.155</td>
<td>0.454 (0.099-2.308)</td>
<td>0.341</td>
</tr>
<tr>
<td>Yes</td>
<td>8 (15.1%)</td>
<td>4 (4.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalassemia/ Trait</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>31 (96.2%)</td>
<td>38 (98.8%)</td>
<td>0.602</td>
<td>0.058 (0.002-1.694)</td>
<td>0.109</td>
</tr>
<tr>
<td>Yes</td>
<td>1 (3.8%)</td>
<td>1 (2.2%)</td>
<td></td>
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</tr>
<tr>
<td>Surgeries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>51 (96.2%)</td>
<td>45 (97.9%)</td>
<td>0.003</td>
<td>4.687 (0.761-28.36)</td>
<td>0.096</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (3.8%)</td>
<td>1 (2.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child Illness</td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
<td>15.847 (4.075-60.074)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>50 (94.3%)</td>
<td>47 (93.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (5.7%)</td>
<td>3 (6.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Chi Squared, Fisher Exact; G6PD: Glucose-6-Phosphate dehydrogenase; SCD/SCC: Sickle-cell disease/Sickle-cell trait

Mothers of TIDM children are more likely to have had gestational diabetes (GDM) (P=0.053) and to have used medication during pregnancy than mothers with healthy children, see table 3. Logistic regression analysis showed a significant but weak association [OR 1.7, 95% CI (1.086-2.637)] between maternal use of medication and the risk of offspring’s developing diabetes; also no significant relationship was found for mothers with GDM (P=0.055). Pregnancy complications, gestational hypertension or prescribed drug use and exposure to toxins were not found to be significantly associated with diabetes diagnosis, see table 4. Family history of TIDM was rarely reported in either group. No significant and independent relationship between parental hypertension and diabetes, see table 5.

Table 4: Pre and Postnatal Maternal History

<table>
<thead>
<tr>
<th></th>
<th>Control 53</th>
<th>Cases 59</th>
<th>P-value</th>
<th>OR (95% CI)</th>
<th>Logistic Regression P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy Complications</td>
<td>Yes</td>
<td>7 (12.2%)</td>
<td>1 (18.2%)</td>
<td>0.434a</td>
<td>0.964 (0.274-3.594)</td>
</tr>
<tr>
<td>GDM</td>
<td>Yes</td>
<td>4 (7.5%)</td>
<td>12 (20.3%)</td>
<td>0.058a</td>
<td>3.220 (0.932-11.127)</td>
</tr>
<tr>
<td>HTN</td>
<td>Yes</td>
<td>3 (5.7%)</td>
<td>9 (15.3%)</td>
<td>0.095a</td>
<td>3.651 (0.774-17.33)</td>
</tr>
<tr>
<td>Medication use during pregnancy</td>
<td>Yes</td>
<td>12 (22.6%)</td>
<td>8 (18.3%)</td>
<td>0.034a</td>
<td>1.754 (1.066-2.837)</td>
</tr>
<tr>
<td>Smoking/Drug use during pregnancy</td>
<td>Yes</td>
<td>1 (1.9%)</td>
<td>2 (3.4%)</td>
<td>1.000b</td>
<td>0.868 (0.035-13.947)</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td>Yes</td>
<td>1 (1.9%)</td>
<td>3 (5.1%)</td>
<td>0.620b</td>
<td>2.400 (0.213-27.081)</td>
</tr>
</tbody>
</table>

*Chi Squared, Fisher Exact
Table 5: Parental History of Diabetes and Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Control 53</th>
<th>Cases 59</th>
<th>P-Value</th>
<th>Logistic Regression P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Hx</td>
<td>No</td>
<td>53 (100.0%)</td>
<td>59 (100.0%)</td>
<td>-</td>
</tr>
<tr>
<td>T1DM</td>
<td>Yes</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Paternal Hx</td>
<td>No</td>
<td>52 (98.1%)</td>
<td>58 (98.3%)</td>
<td>0.058*</td>
</tr>
<tr>
<td>T1DM</td>
<td>Yes</td>
<td>1 (1.9%)</td>
<td>1 (1.7%)</td>
<td>0.781*</td>
</tr>
<tr>
<td>Family Hx</td>
<td>No</td>
<td>53 (100.0%)</td>
<td>59 (100.0%)</td>
<td>0.059*</td>
</tr>
<tr>
<td>T1DM</td>
<td>Yes</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0.497*</td>
</tr>
</tbody>
</table>

*Mann Whitney, *Chi Squared, *missing one

No significant difference between children with T1DM and their healthy controls was found for infant-feeding practices, see table 6.

Table 6: Infant Feeding History of Children with T1DM and Healthy Controls

<table>
<thead>
<tr>
<th></th>
<th>Control 53</th>
<th>Cases 59</th>
<th>Chi-Square P-Value</th>
<th>OR (95% CI)</th>
<th>Logistic Regression P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bottle Fed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed feeding (breast &amp; bottle)</td>
<td>4 (7.5%)</td>
<td>3 (5.2%)</td>
<td>0.769</td>
<td>0.755-1.115</td>
<td>0.389</td>
</tr>
<tr>
<td>EBF - 6 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-12 months</td>
<td>5 (8.5%)</td>
<td>5 (8.5%)</td>
<td>0.918</td>
<td>0.755-1.115</td>
<td>0.389</td>
</tr>
<tr>
<td>Breastfed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-18 months</td>
<td>9 (17.0%)</td>
<td>10 (17.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥18 months</td>
<td>22 (41.3%)</td>
<td>19 (32.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Missing data

DISCUSSION

The exact mechanism remains unknown, there is a general consensus that both genetics and the environment play a role. Despite the strong evidence of genetics in the development of T1DM, the steady and rapid rise of the disease does not appear to be solely attributed to changes in the gene pool. A possible explanation is environmental triggers that instigate a cascade of events leading to the development of T1DM either by direct or indirect means or by interacting with existing susceptible genes.

This study supports the role of infection as a potential trigger for T1DM because over half of the children with T1DM have suffered from an illness prior to diagnosis. Seasonal variation in diabetes diagnoses revealed higher incidence in the winter months which supports the premise that viral infections either trigger or accelerate the destruction of beta cells. Although children with diabetes were more likely to have undergone a surgery, no details were given as to the type of surgery performed. Cardwell et al found no increased risk of T1DM in children who had tonsillectomy or adenoidectomy.
REFERENCES


Dietary Intake of Children with Type 1 Diabetes in Bahrain: A Case-Control Study

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Abstract: Background & Objective: Bahrain is reported to rank amongst the top 10 countries for diabetes prevalence worldwide. In particular, growing numbers of children are being diagnosed with Type 1 diabetes mellitus (T1DM). The objective of this study was to describe the dietary intake of Bahraini children with T1DM as compared to a sample of healthy counterparts and to determine whether the nutrient intakes of Bahraini children with T1DM meet the current recommendations.

Design & Setting: This was a case-control study. Dietary intake, estimated using 24-hour dietary recall, for the cases was gathered from the Pediatric Endocrine and Diabetes Unit at the Salamiya Medical Complex and compared to the 24-hour recalls of children without diabetes recruited from local Health Centers.

Patients & Methods: 50 children aged 6-12 years receiving a confirmed diagnosis of T1DM in the years 2009 and 2010 compared with 55 healthy comparators.

Results: Children with T1DM consumed significantly more calories than controls (p<0.001) and significantly more protein relative to their RDA (p<0.029). Both groups failed to meet the RDA values for dietary fiber and for Vitamin D. Sodium intakes were in excess of RDA values although no significant difference was observed between groups (p=0.433).

Conclusion: The diets of both children with and without T1DM were found to contain excess protein and sodium and inadequate fiber, vitamin D and calcium. Children with T1DM also appeared to consume excess energy and fat. There is a need to endorse existing dietary guidelines for children with T1DM.

Keywords: Type 1 diabetes mellitus (T1DM), Children, Bahrain, Healthy diet.

BACKGROUND

Diabetes has become one of the main public health problems in the Middle East, including Bahrain. It was reported that Bahrain ranks among the top ten countries worldwide for diabetes prevalence [1]. In Bahrain, the number of children diagnosed with Type 1 diabetes mellitus (T1DM) is also on the rise having more than doubled in the past ten years, with 25 new cases of pediatric Type 1 diabetes diagnosed per 100,000 population in 2010 [2]. It is well known that cardiovascular disease (the main cause of death in Bahrain) is more prevalent among patients with T1DM than among those without diabetes [3, 4]. This is placing a significant economic burden on the health services provided by the Ministry of Health.

Type 1 diabetes is associated with an increased risk for the development of micro and macro vascular complications such as retinopathy, neuropathy, and nephropathy [5]. Managing diabetes with good nutrition by maintaining ideal body weight, optimal growth, and development can help prevent such complications [6]. Investigations in Western countries showed that children with T1DM have unhealthy dietary habits, with high intake of energy, carbohydrates, fat and low intake of several micronutrients, compared to healthy children [7-9]. Studies of the dietary intakes of children with T1DM in the Middle East are limited with most research in the region focusing on the dietary habits of those with type 2 diabetes [10].

A few studies have attempted to assess the dietary habits of children and adolescents in Bahrain [11-15], finding that these habits are characterized by low intakes of dietary fiber, milk, vegetables and fruit; and high intakes of fat, fast food and sugar-sweetened beverages. Breakfast was skipped by more than 50% of Bahraini children. However, none of these studies examined the dietary habits of children with T1DM alone or in comparison to those of healthy children. Understanding the current eating behaviors of children
with T1DM in Bahrain is vital to inform the development of culturally appropriate education programs for this population yet this data is currently lacking. This study aimed to describe the dietary intake of Bahraini children with T1DM as compared to a sample of healthy counterparts and to determine if the nutrient intakes of Bahraini children with T1DM meet the current age and gender specific recommended intakes.

METHODS

This was a case-control study designed to assess the dietary intakes of newly diagnosed children with a confirmed diagnosis of T1DM in the years 2009 and 2010 in the Pediatric Endocrine Unit at the Salimaniyah Medical Complex (SMC), the main governmental hospital in Bahrain. These children were compared to healthy controls recruited from local Health Centers across the country to allow the impact of disease to be investigated independently of other important factors like age and weight. The Health Research Committee at the Salimaniyah Medical Complex and the Research Committee at Primary Health Care in Bahrain gave ethical approval for the study.

The inclusion criteria for case subjects were: The subject was registered as a confirmed case of T1DM at the Pediatric Diabetes Unit (PEU) at SMC; the subject was between 5 and 12 years of age at diagnosis; the subject was seen by a dietitian/nutritionist at the initial visit and had completed a 24-hour dietary recall (taken from the child in the presence of a parent or legal guardian); the subject was followed up at least once at the Pediatric Diabetes Unit, and the subject had a completed Diabetes Registry Form (DRF).

The control subjects were selected from 5 health centers. They were matched with case subjects by age, gender, BMI, and geographic location (Table 1). The total samples comprised 50 cases and 55 controls.

The 24 hr recall was taken before commencing nutrition education and carbohydrate counting so that the diet recall was reflective of previous dietary habits and not of diet intake subsequent to diet education. Dietary Intake was estimated using the 24-hour dietary recalls, which were analyzed using the Food Processor Software SQL version 10.70 (ESHA Research). Dietary intakes were expressed as absolute nutrient intakes and compared to the U.S Dietary Reference Intakes (DRI) [14]. Energy requirements were calculated based on the children’s age, gender, height, weight, and activity level. The percent energy intake from macronutrients was compared to the Acceptable Macronutrient Distribution Range (AMDR) established based on U.S Dietary Reference Intakes (DRI) [14]. The data were then statistically analyzed using SPSS version 21 (SPSS Inc.) to compare intakes between cases and controls, using independent t-tests and Mann-Whitney tests as appropriate. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

Energy and Macronutrient Intake

The energy and macronutrients intake of children with and without T1DM are presented in Table 2. Overall 96% of the case group and 75% of the control group met their energy requirements when compared to their estimated total energy expenditure (TEE).

<table>
<thead>
<tr>
<th>Table 1: Baseline Characteristics of Children with Type 1 Diabetes (n=60) and Healthy Control Group (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
</tr>
<tr>
<td><strong>Median (IQR)</strong></td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Gender, %</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>BMI, percentile</td>
</tr>
<tr>
<td>49.90 (22.40)</td>
</tr>
<tr>
<td>15.05 (6.98)</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
</tr>
<tr>
<td>Geographic Location by Governorate</td>
</tr>
<tr>
<td>Muharraq</td>
</tr>
<tr>
<td>Capital</td>
</tr>
<tr>
<td>Northern</td>
</tr>
<tr>
<td>Central</td>
</tr>
<tr>
<td>Southern</td>
</tr>
</tbody>
</table>

Table 2: Energy Intakes and Macronutrient Distributions in DM Children (n=60) and Non-DM Children (n = 66) Expressed as Mean of Absolute Intake and Mean Percent Intake Relative to Age and Gender Recommended Dietary Allowance

<table>
<thead>
<tr>
<th></th>
<th>T1DM</th>
<th>Healthy controls</th>
<th>P-Valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (kcal)</td>
<td>2023 [493.49]</td>
<td>1542 [26]</td>
<td>&gt;0.001*</td>
</tr>
<tr>
<td></td>
<td>622 [206.44]</td>
<td>438 [45]</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Calories from Fat (kcal)</td>
<td>155 [89.13]</td>
<td>109 [46]</td>
<td>0.002*</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>71.75 [21.97]</td>
<td>54.22 [112]</td>
<td>0.018*</td>
</tr>
<tr>
<td>% of energy from protein</td>
<td>13.80 [13.65]</td>
<td>13.78 [3.08]</td>
<td>0.002*</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>300.22 [78.27]</td>
<td>225.87 [30]</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>% energy from carbohydrates</td>
<td>55.84 [7.10]</td>
<td>57.70 [7.80]</td>
<td>0.106*</td>
</tr>
<tr>
<td>Dietary fiber (g)</td>
<td>12.88 [5.26]</td>
<td>10.16 [16]</td>
<td>0.064*</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>89.15 [22.04]</td>
<td>48.93 [44]</td>
<td>&gt;0.001*</td>
</tr>
<tr>
<td>% energy from fat</td>
<td>26.64 [20.68]</td>
<td>28.44 [7.64]</td>
<td>0.376*</td>
</tr>
<tr>
<td>Saturated Fat (g)</td>
<td>17.19 [7.66]</td>
<td>12.14 [45]</td>
<td>0.002*</td>
</tr>
<tr>
<td>% energy from saturated Fat</td>
<td>7.68 [7.17]</td>
<td>7.09 [3.78]</td>
<td>0.280*</td>
</tr>
<tr>
<td>Monounsaturated Fat (g)</td>
<td>19.75 [8.08]</td>
<td>13.72 [36]</td>
<td>0.001*</td>
</tr>
<tr>
<td>Polyunsaturated Fat (g)</td>
<td>9.94 [4.23]</td>
<td>7.12 [47]</td>
<td>0.007*</td>
</tr>
</tbody>
</table>

Children with T1DM consumed significantly more calories than controls (p<0.001). They also consumed a significantly higher number of calories from fat (p<0.001) and saturated fat (p=0.002) than healthy children. Children with T1DM consumed about 2.5 times their RDA for protein, whereas their healthy counterparts consumed approximately twice the RDA (p=0.018).

On average children with T1DM met their RDA for carbohydrates whereas healthy controls consumed a mean of 81 [SD 29] % of their requirements (p<0.001). Both groups failed to meet the RDA values for dietary fiber intake but no significant difference was observed between mean intakes when expressed as a percentage of the recommendations (p=0.564).

The percent energy (% E) intake from protein, carbohydrate and fat for the two groups is also shown in Table 2. No significant difference was observed for percent energy intake of macronutrients between the groups. Children with T1DM and healthy controls were
within the AMDR range for macronutrients. The mean percent energy intake from polyunsaturated fats was below the recommendation in both groups and the mean percent energy intake of monounsaturated fats was slightly higher than the recommendation in children with T1DM.

Vitamin Intakes

The vitamin intakes of children with and without T1DM are presented in Table 3. Children with T1DM consumed a significantly higher amount of vitamin B1 (p=0.034), vitamin B3 (p=0.016), vitamin B6 (p=0.006) and vitamin A (RAE) (p=0.007) as compared to healthy children but this difference was no longer significant when adjusted for energy intake. Although the range of vitamin A intakes is wide, this is a true reflection of the diversity of diets within this group and specifically the high intakes of vitamin A achieved by those children consuming liver, a common food in the region. After adjusting for energy vitamin K intake was found to be higher amongst healthy children as compared to those with T1DM (p=0.016). No significant difference was observed between the two groups for vitamin D intakes, with both groups falling to meet the RDA. Both groups also failed to consume the recommended folate intake, whilst they met or exceeded requirements for vitamin C (non-significant between groups with or without energy adjustment).

Mineral Intakes

The mineral intakes of children with and without T1DM are given in Table 4. Children with T1DM had a significantly higher intake of iron (p=0.001) and potassium (p=0.001) as compared to their healthy counterparts. After adjusting for energy intakes, iron intake was no longer significant (p=0.773) although potassium intake remained significant (p=0.005). The control group met the RDA for iron but children with T1DM consumed on average 1.5 times their requirement. Potassium intakes were well below the requirements in both groups. A significant difference was observed between the groups for calcium intake.

Table 3: Distribution of Vitamin Intakes between Children with and without DM (n=60) and Non-DM (n=66) Group

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>T1DM</th>
<th>Healthy Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean [SD]</td>
<td>Mean % DR²</td>
</tr>
<tr>
<td>Vitamin A (RAE)</td>
<td>795 [788.88]</td>
<td>54 [34]</td>
</tr>
<tr>
<td>Vitamin B1 (mg)</td>
<td>0.74 [0.86]</td>
<td>15 [17]</td>
</tr>
<tr>
<td>Vitamin K (mg)</td>
<td>11.97 [10.6]</td>
<td>20 [22]</td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>133.66 [119.7]</td>
<td>352 [357]</td>
</tr>
<tr>
<td>Vitamin B1 (mg)</td>
<td>0.94 [0.48]</td>
<td>120 [69]</td>
</tr>
<tr>
<td>Vitamin B2 (mg)</td>
<td>1.11 [0.70]</td>
<td>148 [95]</td>
</tr>
<tr>
<td>Vitamin B3 (mg)</td>
<td>1.43 [7.9]</td>
<td>127 [70]</td>
</tr>
<tr>
<td>Vitamin B6 (mg)</td>
<td>1.35 [0.60]</td>
<td>183 [43]</td>
</tr>
<tr>
<td>Vitamin B12 (mcg)</td>
<td>2.64 [3.57]</td>
<td>173 [211]</td>
</tr>
<tr>
<td>Folate (mcg)</td>
<td>187 [107.6]</td>
<td>71 [42]</td>
</tr>
</tbody>
</table>

SD: Standard Deviation; *Mean percent intake relative to Dietary Reference Intake (DR); #Mean Whiffen; *T-test; P-value for % mean RDA where available or mean absolute intake.
Table 4: Distribution of Mineral Intakes between Children with (n=60) and without DM (n=60)

<table>
<thead>
<tr>
<th></th>
<th>T1DM</th>
<th>Healthy Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean [SD]</td>
<td>Mean % RDA*</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>609 [268.33]</td>
<td>56 [27]</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>143 [76.70]</td>
<td>71 [44]</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
<td>603 [272.26]</td>
<td>97 [46]</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>2590 [1394.55]</td>
<td>138 [97]</td>
</tr>
</tbody>
</table>

SD Standard Deviation; *Mean percent intake relative to Dietary Reference Intake (DRI); **Mann Whitney; P-value for % mean RDA where available or mean absolute intake.

(p=0.008) with children with T1DM consuming more compared with control children, however this difference disappeared after adjusting for energy Intake (p=0.218). Sodium Intake was in excess for both groups although no significant difference was noted between the groups (p=0.402).

DISCUSSION

This study attempted to address the gap in knowledge with regards to the current dietary intakes of children with and without T1DM in Bahrain in order to inform age and culture appropriate education packages for this significant clinical population. The diets of both children with and without T1DM were found to contain excess protein and sodium and inadequate fiber, vitamin D and calcium. Children with T1DM also appeared to consume excess energy and fat compared to their healthy counterparts.

Bahrain has experienced a rapid change in socio-economic status over the past decades leading to a substantial transformation in dietary habits and lifestyle. Traditional diets which consisted of fish, vegetable, legumes and brown bread have changed to more westernized dietary patterns associated with low intakes of dietary fiber and high intakes of fat, salt and sugar [15-17]. Bahraini children are not immune to these societal shifts becoming significant consumers of fast foods and sugar-sweetened beverages, but low consumers of fruit and vegetables [11-13]. Previous researchers attempting to investigate dietary differences between children with and without diabetes in Europe have identified lower intakes of sugar-sweetened soft drinks and higher intakes of fruit and vegetables among non-diabetic children compared to diabetic children [7], whilst Abdulian et al. [16] have postulated that changes in dietary habits, low intakes of foods rich in vitamin D and low breastfeeding rates, might play a role in the high incidence of T1DM in Arab countries.

The results of this study show higher intakes of energy and fat among the children with T1DM, when compared with non-diabetic children. These finding are in agreement with findings from Western countries [7, 8, 19]. Excessive dietary fat is of particular concern in children with diabetes as studies have shown that people with T1DM are 10 times more likely to develop cardiovascular disease as compared to an age matched healthy population [6, 20]. Furthermore, excess intakes of fat can lead to an acceleration of blood vessel damage and a subsequent rapid progression of atherosclerosis and cardiovascular disease [21].

Fiber intake was well below the recommended RDA values in both groups. Optimal fiber intakes have been found to decrease the risk of heart disease, certain cancers and type 2 diabetes mellitus [22]. Increasing
fiber intake can help lower blood pressure, serum cholesterol levels, and has been found to be of benefit in gastrointestinal disorders such as gastroesophageal reflux disease, duodenal ulcer, diverticulitis and constipation [23]. Furthermore, an increased intake of fiber can help improve glycemic control and insulin sensitivity in individuals with diabetes [23]. The average protein intake of both children with T1DM and their healthy counterparts was higher than the requirements. Kidney disease is a major risk factor for people suffering from diabetes [24]. Consumption within the recommended dietary allowance for protein is important as an excessive intake has been associated with worsening glomerular filtration rates (GFR) in people suffering from chronic kidney disease [25]. In addition excess intakes of protein may be converted to fat which could increase the risk of obesity later in life [26].

Both groups of children had a low intake of vitamin D and no significant difference was found between the two groups. This is not consistent with the findings of Benet et al., [27] who found that vitamin D deficiency was higher in children with T1DM than non-diabetic children in Qatar. Some studies have specifically linked low 25-hydroxycholecalciferol levels with the increased incidence of diabetes [29-30] with the presence of vitamin D receptors in the pancreas cited as a strong indicator for its role in insulin secretion and glucose tolerance [31]. It is hypothesized that vitamin D has an effect on insulin production by increasing intracellular calcium concentration which results in the secretion of insulin from the beta cells [31-33]. In a large birth cohort study, Hyponen et al. found [28] that children who were regularly supplemented with vitamin D in the first year of life had a reduced risk of developing T1DM [29]. These results are supported by the EURODIAB sub-study group which found a reduction in the risk of development of T1DM in supplemented children versus non-supplemented [30]. However, in contrast, another study [29] found no association between vitamin D supplementation during the first year of life or maternal supplementation and risk of T1DM development.

Failure to find an association could be due to variations in design methodologies, differences in sample size or sample population studied. Specifically the current study only assessed current intakes of vitamin D in children newly diagnosed with T1DM and their non-diabetic counterparts rather than attempting to quantify early-life exposure to vitamin D via diet or supplements or actual vitamin D status which may be influenced by factors other than diet alone. Children in both groups consumed excess sodium and had potassium intakes well below recommended levels—a combination which, in early childhood, has been linked to hypertension later in adulthood [34]. This is of particular concern in children with T1DM as raised blood pressure increases the risk of vascular damage and diabetes related complications.

The current study was limited by the use of a single 24-hour dietary recall to assess dietary intake. The authors acknowledge the possibility of under or over reporting of food consumption in 24-hour dietary recalls due to recall bias and the inability to reflect day-to-day variations in intakes. The authors also recognize that food intake at the time of diagnosis in children with T1DM could have been impacted by the symptoms of the disease itself which, aside from excessive urination, may include excessive thirst and appetite.

CONCLUSION

This study provides support for continuing to endorse the existing dietary guidelines [20] which promote increased intakes of dietary fiber, fruit and vegetables and limited intakes of fats and salt for children with T1DM. The findings of this study should be used to inform the design of future prospective and intervention trials that focus on improving the diet of both healthy children and children with T1DM. Further in-depth investigation of the factors associated with the food habits of diabetic children in the Middle East and how these may change during their disease ‘journey’ is urgently needed.

COMPETING INTERESTS

No competing interests to declare.

REFERENCES


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Assessment of vitamin D levels in newly diagnosed children with type 1 diabetes mellitus comparing two methods of measurement: a facility’s experience in the Middle Eastern country of Bahrain

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S Mahmood Al-Qallaf1
Abdulrahman O Musaiger1
Kathryn H Hart2

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Background: The number of children being diagnosed with type 1 diabetes mellitus (T1DM) is on the rise and has more than doubled in the past 10 years in Bahrain. Some studies have linked low vitamin D levels with an increased risk of diabetes. There are concerns regarding the variations in circulating 25(OH)D levels measured by different laboratories and by using different analytical techniques.

Objective: The aim of this study was to evaluate the vitamin D levels of newly diagnosed children with T1DM using the "gold standard method" with high-pressure liquid chromatography-tandem mass spectrometry methods compared to the chemiluminescence micro-particle immunoassay (CMIA) used in a hospital laboratory.

Subjects: Eighteen children, aged 6-12 years, who received a confirmed diagnosis of T1DM in 2014 were chosen as subjects.

Methods: Serum vitamin D levels were assessed in a hospital, while an extra aliquot of blood collected during routine blood collection after acquiring informed written consents from the subjects, and sent to Princess Al-Jaudara Center for Molecular Medicine and Inherited Disorders to be analyzed by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS).

Results: The mean age of the study group was 9±2 years. The mean total of 25(OH)D levels (D3 and D2) assessed by UPLC-MS/MS was 49.7±18.8, whereas the mean total of 25(OH)D levels obtained from the CMIA assay was 44.6±13.20. The difference in classification between the two methods was found to be statistically significant (P=0.004). A Bland–Altman plot showed a poor level of agreement between the two assay methods. The CMIA overestimated insufficient values and underestimated deficiency, when compared to UPLC-MS/MS.

Conclusions: There was a statistically significant difference between the two assay methods with CMIA overestimating vitamin D insufficiency. Clinicians should be prudent in their assessment of a single vitamin D reading, when the gold standard method is not available or feasible.

Keywords: type 1 diabetes, children, vitamin D, Middle East

Introduction
A large number of studies have reported a relationship between vitamin D levels and the risk of osteoporosis, diabetes, cancer, multiple sclerosis, and rheumatoid arthritis. Some studies have also linked low vitamin D levels with an increased risk of diabetes, while other studies have found that children who were regularly supplemented with vitamin D in the first year of life had a reduced risk of developing type 1 diabetes mellitus (T1DM).
T1DM in children is on the rise worldwide. The number of children being diagnosed with T1DM is also on the rise in Bahrain. The number of those newly diagnosed victims has more than doubled in the past 10 years with 25 new cases diagnosed per 100,000 population in 2010.

Vitamin D is often described as a fat-soluble vitamin, but it also exhibits hormonal properties in its active form through its action via vitamin D receptors found in most tissues in the human body. More than 90% of the vitamin D requirement for most people is believed to come from casual exposure to sunlight. vitamin D is produced endogenously by the skin via photosynthesis using ultraviolet B light, which converts 7-dehydrocholesterol to pre-vitamin D3. It can also be obtained from the diet or from a dietary supplement; fatty fish and fish liver oils are a good source of the vitamin.

This research is a substudy of a larger study undertaken by the author to explore dietary and health risk factors of T1DM in children. The objective of the larger study was to evaluate the association between physiological factors, such as vitamin D levels and lifestyle factors (eg, activity levels and frequency of sunlight exposure) and diabetes prevalence in a small, but representative sample of newly diagnosed children. In this regard, the ideal assay method for determining serum vitamin D levels in this sample of children was subject to considerable debate; hence, this study reports on the experience of assaying vitamin D levels using two different methods to help inform future practice.

Vitamin D levels are tested as part of the routine blood workup for all newly diagnosed children with T1DM admitted at the Salmaniya Medical Complex (SMC), the main governmental hospital in Bahrain. Currently, the hospital laboratory uses an automated chemiluminescence micro-particle immunoassay (CMIA) kit (ARCHITECT; Abbott Laboratories, Abbott Park, IL, USA) to test vitamin D levels. Serum 25(OH)D (25-hydroxy vitamin D), known as calcidiol, is considered a good indicator of vitamin D levels. However, concerns remain regarding the variations in circulating 25(OH)D levels measured by different laboratories and by different analytical techniques as highlighted by Binkley et al. Some of the commonly used alternate assays include radioimmunoassay (RIA), enzyme-linked immunosorbent assay, high-performance liquid chromatography (HPLC), liquid chromatography coupled with mass spectrometry (LC-MS), and automated assay using chemiluminescence immunoassay (CLIA).

HPLC is considered as the gold standard assay method for the detection of 25(OH)D levels. It is a technique that requires pumps to pass a pressurized liquid solvent, which contains a blood sample mixture through a column filled with a solid adsorbent material. The constituents of the sample mixture pass through the pumps and interact differently with the adsorbent material, thus resulting in varying flow rates and the ultimate separation of the components. Following HPLC, quantification of vitamin D is made possible by UV detection at 264 nm. The absorption spectrum is then computed as a chromatogram with retention time being used as a means to identify the compound. This process is fully automated and has the ability to separately assay vitamins D3, D2, and D1 metabolites. CLIA, on the other hand, involves the attachment of highly specific proteins to magnets in a competitive binding protein assay reaction, which causes the chemical substrate to produce light that is detected and measured. A blood sample is combined with anti-human vitamin D coated micro-particles, which causes the vitamin D to disassociate from its binding protein, thus allowing it to bind to these micro-particles. A conjugate is then added, which produces a chemiluminescent reaction with the antibodies bound to these micro-particles, producing light that can be measured. Although studies have compared commercially available assays using CLIA or RIA methods to HPLC, no studies, to the best of the author’s knowledge, have assessed vitamin D levels of children with T1DM comparing these two methods. In light of the growing evidence of the importance of vitamin D in relation to diabetes, the reliability of 25(OH)D measurements should be evaluated, as these results will ultimately inform the management of those who are found to be insufficient. The aim of this study was to investigate whether there is a significant difference in vitamin D levels in newly diagnosed children with T1DM as measured by the gold standard method using high-performance liquid chromatography tandem mass spectrometry when compared to the CLIA method currently used in the SMC.

Methods

Recruitment and data collection took place from mid-January till the end of March; months considered to be cooler although it should be noted that Bahrain enjoys sunlight all year around with a monthly average of 7 hours of sunlight over the year. The inclusion criteria for study subjects were as follows:

- Newly diagnosed children aged 6–12 years with a confirmed diagnosis of T1DM
- Informed, written consent from parents or legal guardian
- Patients were being followed up at the Pediatric Endocrine Unit in the SMC hospital.

The study subjects were 18 (nine males and nine females) children newly diagnosed with T1DM, aged 6–12 years, and admitted to the SMC. This study was approved by the Salmaniya Medical Complex Health Research Ethics
Committee. Informed, written consent was obtained from the parents or legal guardian and all children were followed up at the Pediatric Endocrine Unit in the SMC. Vitamin D levels were measured as part of the routine blood collection and analyzed by CMIA at the SMC laboratory; however, an extra blood sample was collected from the study subjects and sent to Princess Al-Jawhara Center for Molecular Medicine and Inherited Disorders in Bahrain to be analyzed by ultra-Performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS).

SPSS Statistical package Version 22 was used for data entry and analysis. A paired t-test was performed as a measure of assay association. Chi-squared tests were used to compare the sufficiency classifications of the group between the two methods and Bland–Altman analysis (constructed using MedCal software Version 14.10.2) was used to measure assay agreement. A P-value < 0.05 was considered as significant.

Results
The mean age of the study group was 9.12 years with a mean body mass index (BMI) percentile of 54.3±36.9 as shown in Table 1. The mean total 25(OH)D levels (D3 and D2) assessed by UPLC-MS/MS was 49.7±18.8, whereas the mean total 25(OH)D levels assessed by CMIA assay was 44.60±13.20 (see Table 2). The mean total 25(OH)D levels for males was 58.0±14.2 and for females was 41.3±19.7, which is a difference approaching significance (P=0.056). According to the cutoff values set by the author to define hypovitaminosis, 22% of children analyzed using the UPLC-MS/MS method were classified as being deficient with a serum vitamin D level below 30 nmol/L, 28% had insufficient vitamin D levels between 30 and 50 nmol/L and 50% of the children had optimal levels of vitamin D, which is >50 nmol/L as shown in Figure 1. Analysis using CMIA, on the other hand, classified 11% of the children as being deficient, 61% as being insufficient, and only 28% as having optimal levels of vitamin D. The difference in classification between the two methods was found to be statistically significant (P=0.004); there was also a statistically significant difference in the mean vitamin D measurements between the two assays (P=0.048).

A Bland–Altman plot, which shows the discrepancies between results for individual samples, was used to reveal the differences between the two methods. The Bland–Altman plot with linear regression analysis with 95% confidence limits is presented in Figure 2. It clearly shows that the CMIA is biased when compared to the UPLC-MS/MS method. CMIA overestimated insufficient values and underestimated deficiency, when compared to UPLC-MS/MS.

Discussion
Variations in circulating 25(OH)D levels between assay methods and interlaboratory measurements can potentially confound the diagnosis of hypovitaminosis D.17 There is currently no consensus on the optimal reference to classify moderate to severe insufficiency among clinicians and this may be, in part, due to an inter-method bias.23,24 Furthermore, there is currently no consensus on the vitamin D intake required for optimal health, despite a substantial number of published studies, which aim to determine what constitutes an adequate intake. Many of these studies have unfortunately had mixed outcomes and were lacking in the robust designs needed to develop dietary guidelines.13

The USA Institute of Medicine’s (IOM) most recent recommendation is a recommended dietary intake of 600 IU of vitamin D in children, who are 1 year old and more in order to achieve a 25(OH)D level of 50 nmol/L which, according to IOM, meets the requirements of 97.5% of the healthy population.24 However, there has been recent controversy regarding the accuracy of this estimation.25-28 Indeed, Veugelers and Ekwaru argue that over 8,000 IU of vitamin D is a more accurate estimation of the need of 97.5% of a healthy population in order to achieve a serum value of 50 nmol or above.29 Furthermore, the study by Heaney et al corroborated these findings and put forth the argument that a total intake of close to 7,000 IU per day is a more accurate
recommendation than the 600 IU intake currently suggested by the IOM.

There are a limited number of studies that have looked into the vitamin D levels of children in the Middle Eastern region\(^\text{27-30}\) and research on the vitamin D status of children with T1DM in the Middle East is even scarcer. In fact, only one study by Benet et al\(^\text{31}\) exclusively looked at children with T1DM, concluding that vitamin D deficiency was significantly higher in children with T1DM, when compared to healthy controls.

Several studies that have compared commercially available assays using CLIA or RIA methods to HPLC have found low inter-assay agreement.\(^\text{13,21,22}\) Farrell et al\(^\text{32}\) describe the variability in results of vitamin D in “state of the art” automated immuno-assays including the ARCHITECT (Abbott Laboratories) (currently used in our facility), which showed the greatest deviation of all assays when compared to the LC-MS/MS. Detection of 25(OH)D levels appears to be largely method-dependent.\(^\text{33,34}\) Wallace et al in their review of the measurement procedures and limitations of vitamin D assays, conclude that the precision of immunoassays as well as HPLC and LC-MS/MS were comparable in detecting severe vitamin D deficiency, nonetheless the authors highlighted the need for a standard reference method.\(^\text{35}\)

Putting the results of this study into clinical context, we can conclude that (assuming any newly diagnosed child with T1DM with a 25(OH)D level of <50 nmol/L was indicated for supplementation) 50% of the children would require supplementation according to UPLC-MS/MS measurements, when compared to 72% of children according to CMIA measurements. Other studies\(^\text{36}\) cite an approximate 20% misclassification rate between samples assessed using CLIA and LC-MS/MS with 57% and 41%, respectively, being classified as deficient using a cut-point of 50 nmol/L.

However, deciding on which assay method to use depends on balancing out many factors. First, laboratories that test on a frequent basis and require a higher output may benefit more from a commercially available kit.\(^\text{37}\) However, it is important to take into consideration that inexperienced users of such commercial kits may introduce more assay variability.\(^\text{38}\) Furthermore, one must also take into consideration the commercial assays that discriminate between \(D_2\) and \(D_3\), which may result in an underestimation of vitamin D levels. Second, the cost of the assays is another factor to consider; the cost of running vitamin D assays using HPLC method is currently three times the cost of the CMIA method used in the hospital laboratory.

Since vitamin D levels are implicated in a number of disorders, the wider implication of inaccurate readings in the management of hypovitaminosis D is not limited to children with T1DM. Hence, in light of the multifactorial issues surrounding diagnosis and treatment of hypovitaminosis D,
the authors of this paper support the recommendation that clinicians be prudent in their assessment of 25(OH)D measurements as variations exist between the assay methods.\(^\text{15,28}\)

**Conclusion**

There was a statistically significant difference between the two assay methods with CMIA overestimating vitamin D insufficiency. Clinicians should take care in their assessment of a single vitamin D reading in the treatment of hypovitaminosis D when I-HPLC, which is considered as the gold standard assay method, is not available or feasible to use.

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**Disclosure**

The authors report no conflicts of interest in this work.

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