International Journal of Pediatrics and Adolescent Medicine 6 (2019) 125–130

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International Journal of Pediatrics and Adolescent Medicine

journal homepage: http://www.elsevier.com/locate/ijpam

Pediatric diabetes in Saudi Arabia: Challenges and potential solutions. A review article

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ARTICLE INFO

Article history:
Received 21 March 2019
Accepted 28 May 2019
Available online 28 May 2019

Keywords:
Type I diabetes
Type II diabetes
Diabetic ketoacidosis
Glycemic control
Pediatric
Saudi Arabia

ABSTRACT

Diabetes in children has increased globally, and the World Health Organization ranks Saudi Arabia 7th in prevalence and 5th in incidence of type 1 diabetes (T1D). Type 2 diabetes (T2D) in children and adolescents has been identified in Saudi Arabia but its prevalence is still unknown. Despite advances in diabetes management including new insulins, insulin delivery systems, glucose monitoring and easy access to media for disease awareness, diabetes in children continues to be challenging in many aspects. Problems include delayed diagnosis, suboptimal glycemic control, early and late disease complications, transition from pediatric to adult care and raising of obesity and T2D, poor psychological and school support. This review summarizes the pediatric and adolescent diabetes studies in Saudi Arabia to date and explores the country-specific treatment challenges and potential solutions.

1. Introduction

Type 1 diabetes (T1D) is an autoimmune disorder that is characterized by a relative or absolute deficiency of insulin [1]. It is one of the most common chronic diseases of childhood worldwide [2]. Studies have shown that T1D incidence is increasing by 3–4% every year and age at onset in children has become younger [3]. Saudi Arabia ranks 7th in global T1D prevalence and 5th in incidence. The exact cause of T1D and this trend in incidence is unknown [1], in contrast to T2D which has a strong relationship with obesity. T2D in children and adolescents has increased dramatically worldwide and studies have demonstrated higher mortality in T2D than in T1D [4]. Diabetes in children and adolescents is challenging in terms of delayed diagnosis, increasing prevalence, early and late complications, management in school settings, psychosocial issues and other factors that may interfere with glycemic control. Several smaller studies in Saudi Arabia have addressed these challenges and suggested possible solutions. This review explores and summarizes the challenges that may interfere with disease management in Saudi Arabia, and provides possible solutions based on international studies and guidelines. There is an urgent need to apply programs to address these country-specific challenges and to raise diabetes awareness among families and healthcare providers.

2. Materials and methods

Published studies in Saudi Arabia were reviewed by searching the medical database MEDLINE/PubMed under the terms: type 1 diabetes in Saudi Arabia, insulin-dependent diabetes mellitus (IDDM), Type 2 diabetes, and diabetes in children, adolescents or youth in Saudi Arabia. Studies that included patients outside Saudi Arabia or patients older than 19 years of age were excluded. The resulting studies were reviewed for trends in diabetic ketoacidosis (DKA) at new-onset diabetes mellitus (DM), comorbidities, and the prevalence of obesity and T2D in children and adolescents. Additionally, the main challenges to diabetes management have been explored and possible solutions have been provided based on international guidelines and recommendations.

3. Results and discussion

3.1. DKA at diagnosis of diabetes

Diabetic ketoacidosis is the leading cause of acute morbidity and mortality in children with T1D. It is a metabolic imbalance which is caused by a low level of insulin in the presence of increased counterregulatory hormones and characterized by hyperglycemia,

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Peer review under responsibility of King Faisal Specialist Hospital & Research Centre (General Organization), Saudi Arabia.

https://doi.org/10.1016/j.ijpam.2019.05.008

metabolic acidosis, and ketosis. In new onset T1D, DKA is caused by underlying progressive beta cell failure while in established patients, DKA occurs due to insulin omission, infection, gastrointestinal illness, stress, or pump failure. In T2D patients, DKA may occur during concomitant acute illness or the transition to insulin dependency [5].

In one study, Saudi Arabia had one of the highest rates of DKA at diagnosis of T1D (59%) beside other countries such as United Arab Emirates (80%), Romania (67%), and Taiwan (65%). In contrast, the lowest rates were in Sweden (14%), Canada (18.6%), Finland (22%) and Hungary (23%) [6]. In a study of American youth with T1D, 29–31% of patients <20 years of age presented in DKA at diagnosis [7]. An extensive review of national studies indicates that the DKA rate at diagnosis has decreased over the past 30 years in Saudi Arabia (Table 1).

Since Finland has ranked as the country with the highest prevalence of T1D with 54 cases per 100,000, the Type 1 Diabetes Prediction and Prevention Project (DIPP) was implemented. Thereafter, the prevalence of DKA at diagnosis decreased from 30% in 1982–1991 to 19% in 1992–2002. However, DKA at diagnosis remained high in children aged two years (39.1%–47.8%) [8]. According to the Diabetes Atlas (8th edition), Saudi Arabia ranked the 8th highest country for type 1 diabetes in those < 20 years of age, with an estimated 35,000 affected children and adolescents. Thus, in light of the significantly high incidence and prevalence of T1D, a structured program is required to decrease DKA at new-onset DM. This program should focus on increasing awareness of T1D signs and symptoms among both the public and health care providers, as patients with severe DKA are often seen earlier by healthcare providers who missed the diagnosis, particularly in the youngest children [7]. Moreover, the program should also include diabetes screening for family members of children with T1D.

3.2. Glycemic control

Hemoglobin A1c (HbA1c) is an important guide for the management, diagnosis, and prediction of complication in diabetes. HbA1c goals for children and adolescents with type 1 diabetes should be individualized based on hypoglycemia awareness, history of severe hypoglycemia, and more resource-limited environments. However, International Society for Pediatric and Adolescent Diabetes (ISPAD) and American Diabetes Association (ADA) HbA1c targets are <7% and <7.5% respectively. These targets were chosen to avoid long-term microvascular and macrovascular complications of diabetes and CNS complications secondary to severe hypoglycemia and hyperglycemia [20].

Based on 2015 T1D Exchange clinic registry data in the U.S., only 22–23% of children under 12 and 17% of children 13–17 years of age with T1D met the ADA target of <7.5%. Moreover, overall mean HbA1c was 8.3% in 2–4-year-olds, 8.1% at 7 years of age, and 9.2% in 19 year old [21]. In Saudi Arabia, a cross-sectional study of 239 children with T1D showed that the mean HbA1C level was 8.9% [22]. A study of 272 children and adolescents in Jeddah with T1D showed that 31.2% of children and adolescents with T1D were well controlled. However, the targeted HbA1c was based on 2011 ADA guidelines [23]. Another study in Jeddah on 228 children and adolescents with T1D showed that 30.4% of those <5 years old, 22.2–22.9% < 15 years old, and 19.2% > 15 years old met the ISPAD HbA1c target of <7%. Further, the overall mean HbA1c was 8.8% [24]. Based on prior studies, Saudi Arabian children have similar rates of overall glycemic control to U.S. T1D children and adolescents. However, these local studies may not accurately reflect the national glycemic control rates since they only included small samples. A national T1D registry in the kingdom would provide better data.

Additionally, more work needs to be done to achieve better glycemic control. Hypoglycemia in T1D is a well-known risk factor for poor diabetes management and glycemic control [25]. A cross-sectional study among 187 adolescents with T1D in Riyadh showed that a prior unpleasant experience of hypoglycemia was one of the major limiting factors of good glycemic control [26]. Additionally, Al Hayek et al. have shown that fear of self-injecting and self-testing were correlated with suboptimal diabetes control [27]. Two studies have demonstrated decreased episodes of hypoglycemia in patients using insulin pumps and continuous glucose monitors, compared to multiple daily injections or conventional therapy [28,29]. A study by Bin-Abbas showed a significant reduction in HbA1c, mean blood glucose level, total insulin requirement, rate of hypoglycemic episodes and frequency of DKA events during insulin pump therapy [29].

3.3. Acute and chronic complications of T1D

T1D may cause long-term microvascular, neurologic, and macrovascular complications. The most common are retinopathy, nephropathy, neuropathy, and cardiovascular disease. The Diabetes Control and Complications Trial (DCCT) confirmed that diabetic patients on intensive insulin therapy had better glycemic control and significantly lower complication rates than those on conventional therapy. Intensive therapy reduced retinopathy by 76%, microalbuminuria by 39% and neuropathy by 60% [30]. A cross-sectional study in Jeddah of 228 children and adolescents with T1D showed the association of dyslipidemia (8.3%) and microalbuminuria (16.2%) with poor glycemic control while retinopathy was not related to HbA1c (4.4%) [24]. Moreover, modestly impaired cognition, which is notable in patients who had severe hypoglycemia, has been linked to pediatric diabetes [31]. A study in Riyadh demonstrated lower academic performance in T1D patients

Table 1
Epidemiology of DKA among patients with newly diagnosed T1D in Saudi Arabia.

Study	Region	Study time	T1D No.	M: F	Mean age (Y)	DKA%	Study type
Salman H et al [9]	Riyadh	1985–1989	110	0.8:1.2	5.9	67%	Follow-up
Kulaylat et al [10]	Eastern	1986–1997	46	0.6:1.4	9	77%	Retrospective
Al-Magamsi et al [11]	Al-Madina	1992–2001	230	0.9:1.1	6.9	55.2%	Clinical
Habib [12]	Al-Madina	1992–2004	311	0.95:1.05	6.7	55.3%	Retrospective
Abduljabbar et al [13]	Eastern	1990–2007	438	0.8:1.2	6.7	40%	Observational
Abdulaziz M Al Rashed [14]	Jeddah	1993–2005	369	0.9:1.1	12.3	49.9%	Retrospective
Cherian et al [15]	Eastern	1980–2009	119	1.05:0.95	4.7	74%	Retrospective
Mohammad A. Al Qahtani [16]	Aseer	2006–2013	508		8.5	48%	Retrospective
A.M. Ahmed et al [17]	Northwest	2005–2014	541	0.93:1.06	5.5	44.9%	Retrospective
Ahmed H. Alghamdi [18]	Al-Baha	2007–2014	372	0.91:1.09	8.3	44.2%	Prospective
Al-Ghamdi [19]	Al-Baha	2006–2016	471	0.64:1.36	8.2	40.8%	Retrospective

T1D, Type 1 diabetes mellitus; M: F, male/Female; DKA%, Diabetes Ketoacidosis percent.

compared to healthy students and claimed that this was due to cognitive impairment secondary to DM, but further studies are required to confirm this finding [32].

The two main acute complications in T1D are DKA and hypoglycemia. One study found a 65.4% correlation between DKA and inadequate glycemic control and a 68.9% correlation between hypoglycemia episodes and poor glycemic control. However, hypoglycemia decreased with higher HbA1c [33]. DCCT also demonstrated that intensive therapy increases the chance of severe hypoglycemia by 2–3 fold compared to conventional therapy [34]. A study of 103 adolescents (aged 13–18 years) with established T1D in one center in Riyadh showed that 54.4% had one episode of DKA, 39.8% had two episodes, and 5.8% had three episodes [35]. Another cross-sectional study in Jeddah showed that DKA episodes occurred 1.64 times per year and were correlated with poor glycemic control [24]. Moreover, an increased frequency of DKA has been attributed to poor communication between the family and the care provider, inadequate compliance with a healthy lifestyle, and excess intake of sweets [23]. Additional factors are lipodystrophy and discontinuation of insulin treatment during sick days [35]. All of these factors are likely related to poor continuous teaching during provider visits and lack of psychosocial support. In fact, the mother's knowledge of T1D has specifically been shown to contribute to glycemic control in children, supporting the importance of training [36]. Long-term complications can be avoided or delayed by maintaining optimal glycemic control and increasing healthcare worker awareness of ADA based guidelines to look for complications in T1D [37].

3.4. Autoimmune disorders

As T1D is an autoimmune disease, patients with T1D have increased risk of developing other autoimmune diseases that may interfere with glycemic control [38]. Autoimmune thyroid disease is the most common associated autoimmune disease in T1D and occurs in 17–30% of patients [39]. Screening for thyroid disease is recommended at diagnosis of diabetes once clinically stable or after achieving glycemic control, then every 1–2 years or sooner if the patient develops symptoms suggestive of thyroid disorder such as thyromegaly, an abnormal growth rate, or an unexplained glycemic variation [37]. Local studies have found that the prevalence of thyroid antibodies in T1D patients is 8.1–16.3% [24,40,41,42].

The second most common autoimmune disorder is celiac disease, occurring in 1.6–16.4% of individuals with T1D compared with 0.3–1% of the general population. Screening for celiac disease is recommended at diagnosis and repeated at two and five years. Also, screening should be considered at other times in patients with symptoms suggestive of celiac disease [37]. In local studies, asymptomatic patients were seropositive for celiac disease at a rate of 7.1%–21.2%.; [24,40,43–45]. However, symptomatic celiac disease was reported in 7.3–11.3% [44–46].

3.5. Care in school settings

Because school-aged children spend a large portion of their day in school, expecting school personnel to become informed about diabetes is reasonable. The school can either present significant challenges or be a source of support to the child with diabetes [47]. The current standards of diabetes management reflect the need to maintain glucose control as near to normal as safely possible. To achieve this level of control, many children will be on intensified management. Intensified therapy requires one to three blood glucose checks during the school day and the use of continuous glucose monitoring, with smartphone and smartwatch applications or other technology, if applicable. In addition, good control requires checking urine ketones if blood glucose is high or during illness, insulin administration by injection or infusion pump, attention to food intake and carbohydrate content of foods, and knowledgeable school staff to observe for and treat hypoglycemia, including the administration of glucagon if recommended by the student's health care provider [48,49]. This requires flexibility and close communication among the child, parents, school personnel, and the healthcare team. A local study showed that only 26% of participants always have additional care at school, but details on management and staff at the school have not been reported [50]. Another study showed that 88.6% of schools had staff available to help in diabetes care; however, only 5% of them were nurses [51], who are considered the most appropriate staff to provide this care.

In the U.S., public schools must reasonably accommodate the special needs of children with diabetes. Also, each school year begins with a conference involving the child with diabetes, his or her parents, and school personnel to establish a plan of care and communication and to address important issues and concerns [48]. This is not well-established in all schools in Saudi Arabia.

3.6. Psychosocial issues in different age groups

Management of T1D in young children is challenging. The Impact of T1D on the psychological health of young children is not well reported; however, likely both T1D regimen demands and parent stress negatively impact the quality of life in these children [52]. Preschool children from age 3–5 tend to fear intrusive procedures and may act out their anxieties when insulin injections and blood testing are done. A preschoolers' appetite may be erratic and is often unpredictable which makes glucose control difficult for this age group. The responsibility of caring for a young child with diabetes and the fear of hypoglycemia is hugely stressful for families. Typical, erratic behavior in this age-group may mask hypoglycemic symptoms [53]. Therefore, pediatric health care providers, parents/guardians, and child care staff must work together to ensure that young children with diabetes are provided with the safest possible child care environment [49].

A school-age child (6–11 years old) is physically well-coordinated. They acquire strategies to keep from feeling different from their peers. One study reported a frequent association of mild depression and anxiety following the diagnosis of diabetes in this age group. Moreover, depression likely increased with the end of the honeymoon period, when children come to realize that the disease is permanent. Individual counseling or diabetes camps can be useful in assisting the child in resolving these feelings. Intervention should be initiated early and should be part of follow-up care [53].

The hallmarks of normal adolescence include difficulty accepting parental criticism, increased physical and social activity, increased independence in decision making, less social involvement with family and more with peers, and typical food-related behaviors including skipping meals and eating away from home [54,55]. Additionally, adolescents are known for disruption in communication between family members and providers, thereby compromising glycemic control. Educating adolescents about the impact of poor glycemic control on growth may motivate them in improving metabolic control [55]. In addition, psychological issues must be addressed and treated. Treatment regimens should be re-evaluated based on eating patterns. Moreover, technologies through smartphones have been shown to be a useful communication tool between adolescents and healthcare providers [56].

In Saudi Arabia, there have been few studies concerning the quality of life in T1D patients. A study conducted among adolescents (aged 13–18 years) with T1D reported that female gender, longer duration of T1D, multiple daily injections, DKA, and high

HbA1c levels were associated with reduced quality of life outcomes [57].

3.7. Transition from pediatric to adult care

Children with T1D require lifelong treatment and access to medical care, and the transition from pediatric to adult care is challenging and associated with worsening glycemic control [58]. This transition has not been well described or studied for adolescents with diabetes in Saudi Arabia. The challenges arise from the differences between the pediatric and adult approaches to diabetes; pediatric care is family-centered management while adult care is more focused on the patient alone. During transition to adult care, patients tend to lose follow-up. Moreover, acute complications such as DKA and hypoglycemia may increase due to loss of parental supervision of diabetes care and fewer diabetes clinic visits. In addition, psychosocial issues are commonly associated with diabetic adolescents in the form of depression, anxiety and eating disorders [59]. These challenges contribute to poor glycemic control, thus some transition models have been established in developed countries like the U.S., the U.K., Canada, and Australia. A proposed protocol includes assigning transition coordinators, and some programs included monthly visits for a few months in efforts to reduce loss to follow-up. Also, family physicians can continue follow-up during the transition period. ADA recommendations for transition care may reduce these challenges in order to maintain good glycemic control [59]. However, local research is required to explore local challenges and create appropriate models fitting the Saudi Arabia health system.

3.8. Rising obesity and T2D in children

Obesity and overweight in children and adolescents are defined as a BMI $\geq$95th percentile and $\geq$85th percentile, respectively, of the CDC growth charts [60]. According to the National Health and Nutrition Examination Survey, the prevalence of obesity among U.S. youth aged 2–19 years was 18.5% in 2015–2016 [61]. A recent national study (Jeeluna) in Saudi Arabia showed that 15.9% of adolescents were obese [62].

Obesity is a well-known risk factor in developing T2D. It has been shown that T2D in children and adolescents has increased dramatically throughout the world in recent years along with the rising incidence of obesity. The U.S. SEARCH study reported a T2D rate of 8.1/100,000 in 10–14-year-olds and 11.8/100,000 in 15–19-year-olds [63]. In contrast to T1D, which is an autoimmune disorder with antibodies destructing pancreatic beta cells [20], T2D in youth is characterized by insulin resistance signs such as acanthosis nigricans and possibly features of metabolic syndrome including hypertension, hyperlipidemia and fatty liver disease [63].

A study in Riyadh among children recently diagnosed with diabetes showed that 64% were overweight or obese, 34% had a sign of insulin-resistance such as acanthosis nigricans, 57% were found to have a family history of DM, and only 52% were shown to have positive pancreatic antibodies. Additionally, in follow-up, 46% of the patients were managed solely on metformin. All of these factors are likely to indicate T2D or double diabetes [64]. A cohort study in a screening for diabetes in 23,523 children 6–18 years of age from 2007 to 2009 demonstrated that 0.07% were known to have T2D while 4.27% were established incidentally to have diabetes based on fasting blood glucose >125 mg/dL. These cases were likely to be T2D based on associated findings such as overweight, family history, and signs of metabolic syndrome. The study was limited in that enrolled participants might not have adhered to the instructions of strict overnight fasting for the diagnostic blood glucose test [65].

In contrast to T1D in which chronic complications tend to occur after many years of suboptimal glucose control, youth with T2D are shown to have early signs of microvascular and macrovascular complications [66]. The U.S. multi-site TODAY trial demonstrated complications within two years of diagnosis of T2D in youth [7]. Moreover, these youths were estimated to have a loss of up to 15 years of life expectancy [67].

Since most T2D youths are obese at diagnosis [68], urgent obesity prevention, screening and early management programs are needed, in addition to early detection of T2D. The U.S. Preventative Services Task Force (USPSTF) recommended in 2010 that children should be screened for obesity by the age of six years and treatment including moderate to intense diet restrictions, physical activity, and behavioral modification should be offered [69].

4. Conclusion

A review of the T1D studies in Saudi Arabia reveals that the prevalence of the disease and DKA incidence at diagnosis are hugely variable in each region. Data on the prevalence and incidence of T2D in youth is very scarce. The main challenges in treating children and adolescents with diabetes in Saudi Arabia are a lack of patient and parent awareness of T1D and its complications, poor psychosocial support, limited resources for school support, and poor self-management techniques. An unknown percentage of patients utilize new technology in the form of pump therapy and continuous glucose monitoring. There are a lack of screening programs and programs to increase awareness of T1D, and a lack of clinical trials and multicenter research collaboration.

Potential solutions include collaboration of health and education ministries to implement educational programs to create awareness about T1D and its complications, as well as screening programs with testing of siblings of T1D patients prioritized. Parents should have access to healthcare providers with 24-h availability to answer questions or concerns regarding diabetes, and a nurse should be assigned to each school to manage diabetes and coordinate between families and healthcare providers. Finally, efforts should be made to ensure access to new technology in the form of continuous glucose monitoring, advanced insulin pumps, and closed-loop insulin delivery systems for better glycemic control.

Declaration of interest

None.

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The author is greatful to Dr.Ricardo Gomez for valuable comments on the manuscript.

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