Chapter 10
The Epidemiology of Diabetes Mellitus Among Adolescents from the Middle East and North Africa

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Abbreviations

DKA	Diabetic keto-acidosis
FPG	Fasting plasma glucose
GCC	Gulf Cooperation Council
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
NSPHUAE	National Study of Population Health in the United Arab Emirates
Pre-DM	Prediabetes mellitus
T1D	Type 1 diabetes
T2D	Type 2 diabetes
UAE	United Arab Emirates
WHO	World Health Organization

10.1 Introduction

The growing global burden of diabetes mellitus (commonly known as diabetes) has been illustrated repeatedly over the past two decades as one of the greatest health-care problems and challenges to human health in the twenty-first century (Zimmet et al. 2014). Over the course of the past decade, the estimated number of people (20–79 years) living with diabetes has increased by 62% (Saeedi et al. 2019; IDF

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2019). In fact, diabetes affects just under half a billion people worldwide (463 million), representing 9.3% of the population. This prevalence has significantly exceeded the predicted estimate for 2025 (300 million adults), (King et al. 1998), and is projected to increase by 25% in 2030 and 51% in 2045 (Saeedi et al. 2019). The changing behavioral dynamics of our society has played a contributory etiological role in the expression of this chronic disease, interactively with genetic and environmental risk factors, in both developed and developing countries (Saeedi et al. 2019; Zimmet et al. 2014). Particularly concerning is the increasing prevalence of juvenile diabetes (i.e., type 1 diabetes; T1D) and early-onset of type 2 diabetes (T2D), which has steadily contributed to this burgeoning epidemic across adolescents (10–19 years) (Guariguata and Jeyaseelan 2019).

Diabetes is a complex chronic disease influenced by a multitude of modifiable and nonmodifiable risk factors that can translate into a range of metabolic disorders characterized by high blood glucose levels affecting individuals as young as 6 months of age to individuals 65 years and older (Saraswathi et al. 2019; WHO 2016). T1D has been considered as one of the most common noncommunicable diseases diagnosed during the stages of childhood and adolescence (<19 years of age), with a peak incidence around puberty, and accounts for 5–10% of diabetes cases worldwide (Robert et al. 2018; Tuomilehto 2013). However, T2D, once considered an adult-onset disease, is also prevailing in many areas of the world among adolescents (Farsani et al. 2013), resulting in a shift in the epidemiological patterns of this disease once separated by its historical etiological tendencies. For example, recent national epidemiological studies suggest that the mean age of T2D diagnosis among adolescents is 13.7 years (Panagiotopoulos et al. 2018). According to the Global Burden Report (2019), diabetes affects more than 8.8. million children and adolescents (<20 years) worldwide. Recent prevalence estimates of T1D among adolescents from the International Diabetes Federation (2019) show that the worldwide annual incidence estimates were 98,200 and 128,900 new cases in the under 15-year and under 20-year age-groups, respectively (Patterson et al. 2019). Globally, 1.1 million children and adolescents are affected by T1D (IDF 2019). On the other hand, due to the recent recognition of T2D among adolescents, there is substantial variances and limited data available worldwide (Abuyassin and Laher 2016; Farsani et al. 2013).

Moreover, while the precise etiology and risk factors associated with T1D are not substantially characterized, nor presentably known, the progression from normality to T2D is more preventable. Specifically, T1D is a genetically induced auto-immune condition resulting in the slow destruction of insulin-secreting β cells that regulate glucose in the blood (Rasoul et al. 2016), while T2D is characterized by a progressive decline in insulin production and subsequent inefficiency of the body to utilize produced insulin due to developed resistance. T2D is considered a heterogenous disease, predominantly attributed to recent changes in behavioral and environmental conditions (e.g., urbanization and obesity) (Saeedi et al. 2019). Major risk factors such as reduced physical activity, poor nutritional practices, and in consequence, obesity, have been linked to T2D development in adolescents, as well as early expression in genetically susceptible individuals (Panagiotopoulos et al. 2018).

Certain populations, such as the Arab population, have been considered high risk for T2D. This may increase the risk of early-onset diabetes, given that T2D development is often correlated with a family history of T2D in a first-or second-degree relative (Panagiotopoulos et al. 2018; Zabetian et al. 2013).

10.1.1 A Regional Overview of the MENA

The Middle East and North Africa (MENA) region, widely considered as the "Arab World" has witnessed an increase in diabetes prevalence, aligned with the rapid growth of the region both economically and demographically (Al Makadma 2017; Zabetian et al. 2013). Specifically, the public health concern associated with the rising diabetes prevalence in the MENA region was brought to attention following the appearance of related risk factors associated with the demographic and geopolitical establishment of the region, which translated into changes in societal behaviors in lifestyle (e.g., nutritional practices and physical inactivity), and more positive associations, such as the decrease in perinatal mortality (Zabetian et al. 2013). According to the International Diabetes Federation (2019), the MENA currently has the highest world-age standardized diabetes prevalence (ages 20–79 years), accounting for 12.2% (CI 8.3–16.1) of the population (54.8 million people; CI 30.7–75.1) (Saeedi et al. 2019), a number that is quickly approaching the estimated prevalence expected for 2030 (59.9 million) (Whiting et al. 2011). Correspondingly, this projection may be accelerated due to the increasing prevalence of adolescent diabetes, and further exceed the prevalence in other regions worldwide.

In fact, high-income countries of the MENA region considered a part of the Gulf Cooperation Countries (GCC), such as, Kuwait have witnessed a prevalence much higher than that of Canada and the United States, of 34.9 per 100,000 among adolescents 6–18 years old for T2D (Moussa et al. 2008). Comparatively, in Canada, the national surveillance study demonstrated a minimum incidence of 1.54 per 100,000 in children and adolescents <18 years of age of T2D, while the states demonstrated an incidence of 8.1 per 100,000 person-years in the 10- to 14-year age group and 11.8 per 100,000 person-years in the 15- to 19-year age group (Panagiotopoulos et al. 2018). Moreover, the MENA region holds countries that are ranked among the top 10 for incidence rates of T1D in the 0- to 14-year age group. This includes Kuwait, Saudi Arabia, and Qatar, which also represent the highest prevalence for diabetes cases for individuals 0–19 years in the MENA region (Fig.10.1). Overall, the number of newly diagnosed cases for children and adolescents with T1D each year in the MENA region is 20,800, with currently 149,400 diagnosed (0–19 years) (IDF 2019). Correspondingly, the MENA is also represented as having the third largest estimated deaths in those with T1D (Patterson et al. 2019), indicating a dire neglect associated with diabetes management. This may be a consequence of limited health resources in some developing countries of the MENA such as Jordan, resulting in deterioration of metabolic control (Alassaf et al. 2019). In fact, acute complications, such as diabetic ketoacidosis (DKA)

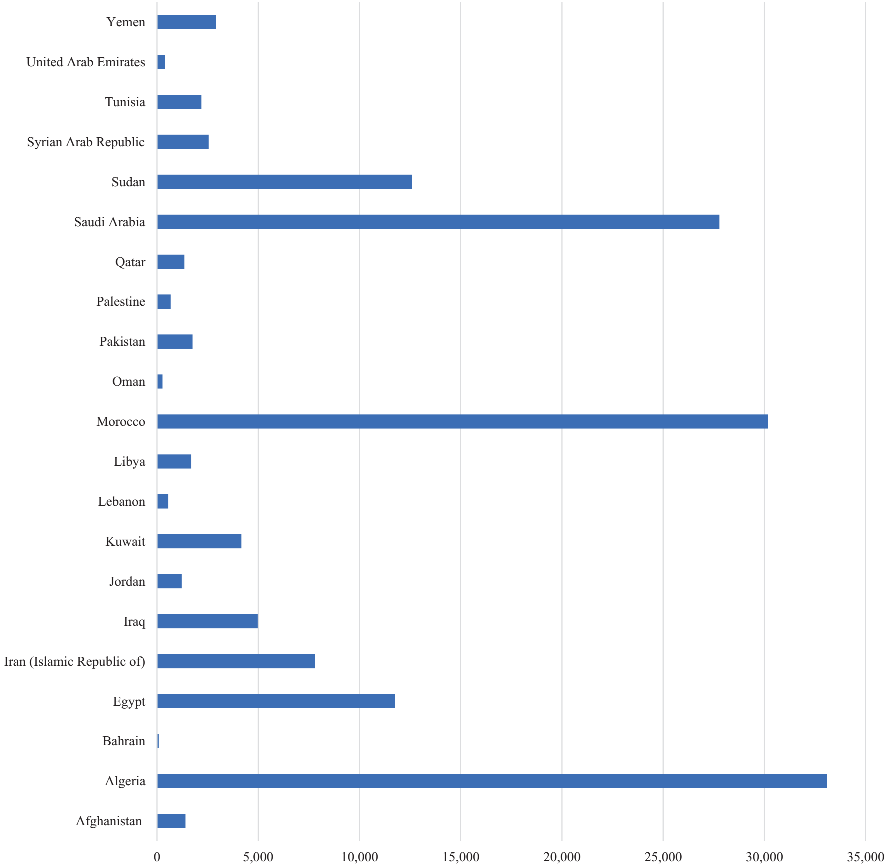

Fig. 10.1 Country-wise statistics for the prevalence of T1D in the Middle East and North Africa Region, represented as members of the International Diabetes Federation from IDF Diabetes Atlas: MENA 9th edition 2019

associated with T1D among adolescents due to lack of parental awareness, and delayed medical seeking, are common throughout the MENA, and may increase the risk of mortality (Cherian et al. 2010; Robert et al. 2018; Zayed 2016).

10.1.2 Living with Diabetes in Adolescence

Adolescence is recognized as a transitional period of life involving multifactorial changes that are controlled by biological and environmental (i.e., the social, cultural, and built environment) factors (Al Makadma 2017). These excessive and fundamental changes make this cohort vulnerable to the determinants of their social and physical environment, and act as predictors of positive development. Within this transitional phase, adolescents also experience the need for social success through acceptance and require a supportive family and social network to promote effective growth and health (Barakat and Yousufzai 2020). The success of these interactions and fulfilment of this desire may be dependent upon the health-related status of individuals.

Health conditions may negatively impact aspects of this period consisting of physical, emotional, and mental changes which coincide with hormonal shifts during puberty. Specifically, diabetes can have disrupting effects on young individuals during their most productive years, as their time becomes replaced by a rigorous regimen, and the possible emotional burden of coping with discrimination and stigmatization, and increase risk of decline in self-care (Elissa et al. 2017). Certain social and cultural contexts may also extenuate the burden and management of this condition for adolescents and lead to poor health outcomes, especially for those from the Arab culture.

Although feelings of alienation and stigmatization are common among adolescents living with diabetes from Western countries (e.g., the United States) (Buchbinder et al. 2005; Elissa et al. 2017), the experience of adolescents living with diabetes in the MENA region may be further magnified by traditional gender roles, societal norms, and misconceptions. For example, a study conducted in the West Bank of Palestine found that parent's concerns about their female children stemmed from lack of acceptance as a "suitable" wife and perceived inability to uphold traditional roles of Arabic women (e.g., taking care of children and household duties) as a result of their condition. In fact, lack of knowledge and misunderstandings about T1D in society have led to negative consequences like poorer adherence to management of diabetes, especially for females from trying to hide the condition from peers (Elissa et al. 2017). In addition, in some more religiously conservative areas throughout the MENA, social constraints related to physical activity may further restrict females from being able to control their diabetes and lead to increased health complications (Elissa et al. 2017). This may further facilitate differences in gender health outcomes and signifies the need for monitoring of this disease among vulnerable populations, as well as warranting the widespread knowledge of this disease for both parents and adolescents living in the MENA region, in order to mitigate misconceptions influenced by cultural perspectives.

Accordingly, due to the complexity of diabetes and its increasingly prevalent forms (i.e., T1D and T2D) among adolescents, and the lack of understanding on the etiological expression of this condition, more research is required to identify various risk factors that may contribute differently to the geographic variation in prevalence. While literature suggests a range of risk factors that may be correlated to the incidence of diabetes in adolescents, there are limited reviews examining the variation of these factors and related studies in relation to all countries of the MENA region (Saraswathi et al. 2019). Overview of trends in the incidence and prevalence of diabetes forms that may peak in adolescents in the MENA region is essential, given its large youth population and the region's dependence on this "youth bulge" for future development and prosperity. Furthermore, the increasing prevalence of associated modifiable risk factors for early-onset diabetes reinforces the need to create awareness about the formation of poor habits during this critical period.

10.2 Methods

This chapter focuses on the prevalence and predictors of diabetes by synthesizing evidence on literature published to date on adolescents (10–19 years) in the MENA region. The following countries identified as members of the International Diabetes Federation within the MENA region were inputted in the search: Afghanistan, Algeria, Bahrain, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Qatar, Sudan, Saudi Arabia, Syria, Tunisia, the United Arab Emirates, Pakistan, Palestine, and Yemen. A comprehensive search strategy was applied to search for all publications in five databases (OVID Medline, CINAHL, Google Scholar, Web of Science, and Scopus), from the year 2000 to 2020 of each database up to September 2020 limited to the English language. Boolean/phrase search was conducted using the following relevant search terms: “diabetes mellitus” OR “impaired glucose tolerance” OR “type 1 diabetes” OR “type 2 diabetes” AND Adolescen* OR Child* OR Youth AND “prevalence” OR “incidence” AND <country name> OR <region/continent> (e.g., “MENA” OR “Middle East” OR “North Africa” OR “GCC”).

The search of the five electronic databases in total yielded 572 results. Article titles and abstracts were downloaded in EndNote. A two-phase screening methodology to identify relevant articles was employed. In phase 1, the reference list was screened for duplicates and each article’s title and abstract for eligibility using the criteria described above was screened, resulting in 72 articles. Articles that were possibly relevant (not enough detail was provided to determine eligibility in the title and abstract) were further reviewed in phase 2. In phase 2, the full text of articles was reviewed to determine eligibility. Additional articles were identified based on references from other sources. Identified articles were iteratively screened for relevance regarding adolescents in relation to prevalence, incidence, predictors, and risk factors of diabetes among this population in the MENA region by article title, abstract, and full review of article.

In this chapter, adolescents are defined as the age group from 10 to 19 years old, in accordance with definitions from WHO (2020). However, multiple studies in this review include a wide age spectrum and population samples coinciding with the period of adolescence, which encompassed individuals from 0 to 19 years old (Table 1). Exclusion was based on studies that reported only on pediatric/child populations (<10 years of age), adult populations (>19 years), articles that were not written in English, and review articles. Although only one systematic review was found that specifically focused on childhood (ages 0 and 18 years) diabetes in the Middle East (Saraswathi et al. 2019). In total, 21 studies were eligible for inclusion.

Table 10.1 Summary of studies in relation to prevalence and incidence rate (IR) of type 1 and type 2 diabetes and other diabetic conditions among adolescents in the MENA region

	Author/year	Study design	Study population	Region	Diagnosis	Key findings
1	Aminzadeh et al. (2019)	Retrospective (2000–2015)	$N = 988$ Age: <15 years	Iran (Southwest)	T1D	Mean annual IR raised from 18 to 27 to 138 per year during 15 years Annual IR: 13.35/100,000
2	Moadab et al. (2010)	Cross-sectional	$N = 672$ Age: 6–19 years	Iran, Isfahan	IFG and T2D	Prevalence of IFG: 4.61% The prevalence of T2D was 0.1% ($n = 1$; age, 18.00 years old).
3	Al-Ghamdi and Fureeh (2018)	Retrospective	$N = 471$ Age: 0–19 years	Saudi Arabia, Al-Baha	T1D	Prevalence: 355/100,000 Prevalence was 57.5% vs. 42.5% ($p = 0.3$) for females and males, respectively, and the female/male ratio was 1.36 in favor of females
4	Al-Daghri et al. (2015)	Cross-sectional	$N = 2225$ Age:13–17 years	Saudi Arabia, Riyadh	T2D and prediabetes	Prevalence: 4.3% and 1.6% for males and females, respectively The prevalence of elevated fasting blood glucose levels was 20.5% for females and 17.7% for males ($p < 0.001$)
5	Al-Rubeaan (2015)	Observational cross-sectional	$N = 23$ Age: ≤18 years	Saudi Arabia	T1D, T2D, and IFG	Age-adjusted prevalence of T2D: 1/1000 Total prevalence: 105 participants (0.45%), of which 88 (0.38%) were T1D and 17 (0.07%) were T2D Of 17,207 (73.48%) participants aged 6–18 years who were tested for FPG, 1053 (6.12%) were IFG cases, and 735 (4.27%) were newly identified cases with diabetes totaling 10.39%
6	Al-Agha et al. (2012)	Retrospective cross-sectional study	$N = 387$ Age: 2–18 years	Saudi Arabia	Hyperinsulinism and T2D	Prevalence of hyperinsulinism: 44.7% Prevalence of T2D: 9.04%

(continued)

Table 10.1 (continued)

	Author/year	Study design	Study population	Region	Diagnosis	Key findings
7	Habeb et al. (2011)	Observational	*N* = 419 Age: 0–12 years	Saudi Arabia, Al Madinah	T1D	The mean annual age-standardized IR was 29.0 per 100,000 (95% CI: 26.0–32.0) 249 (59.4%) were females and 170 (40.6%) were males, giving a male to female ratio of 1.5:1
8	Abduljabbar et al. (2010)	Subpopulation-based observational incidence study (1990–2007)	*N* = 438 Age: <15 years	Saudi Arabia	T1D	The average IR was 27.52/100,000/year (95% CI: 26.72–28.32), increasing from 18.05/100,000/year in the first 9 years of the study period to 36.99/100,000/year in the last 9 years.
9	Al-Herbish et al. (2008)	Cross-sectional, case (2001–2007)	*N* = 45,682 Age: 5–18 years	Saudi Arabia	T1D	Fifty were identified as having T1D Prevalence rate: 109.5 per 100,000 Prevalence range by region: 48 (eastern) and 162 (central)/100,000 Children and adolescents were also grouped by age and prevalence rate: 5–6 (100), 7–12 (109), 13–16 (243), and 17–18 (150)
10	Shaltout et al. (2017)	Observational, case	*N* = 515 Age: 0–14 years	Kuwait	T1D	Crude IR: 40.9 (95% CI 37.4–44.6). Age standardized rate: 41.7 (95% CI: 38.1–45.4) per 100,000 per year IR males: 39.2 (95% CI: 34.6–44.4) IR females: 44.1 (95% CI: 39.0–49.7)
11	Moussa et al. (2008)	Cross-sectional, cohort	*N* = 128, 918 Age: 6–18 years	Kuwait	T2D	Prevalence of 34.9 per 100,000 [95% CI:24.7–45.1]
12	Shaltout et al. (2002)	Retrospective, case	*N* = 364 Age: 0–14 years	Kuwait	T1D	IR: 20.1 per 100,000 (95% CI: 18.0–22.1) Age-standardized rate: 20.9 (95% CI: 18.8–23.0) IR males: 21.1 per 100,000 (95% CI: 18.1–24.1) IR females: 19.0 per 100,000 (95% CI: 16.1–21.8)

	Author/year	Study design	Study population	Region	Diagnosis	Key findings
13	Barakat et al. (2021)	Cross-sectional	$N = 6329$ Age: 15–18 years	UAE	Diabetes (unspecified)	Prevalence: 0.9% (95% CI: 0.7–1.2) 1.5% (95% CI: 1.0–2.1) of males compared to 0.5% (95% CI: 0.3–0.8) of females reported a self-diagnosis of diabetes ($p < 0.001$)
14	Al Amiri et al. (2015)	Observational/ cross-sectional	$N = 1037$ Age: 11–17 years	UAE, Sharjah	Prediabetes and T2D	443 (43%) students had abnormal screening results. The prevalence of prediabetes and T2D was 5.4% and 0.87%, respectively, based on a standard oral glucose tolerance test
15	Punnose et al. (2005)	Case series/ retrospective	$N = 96$ Age: 0–18 years	UAE, Al-Ain	T2D	11 were identified as type 2
16	Punnose et al. (2002)	Retrospective analysis (1990–1998)	$N = 40$ Age: 0–18 years	UAE, Al-Ain	T1D and T2D	35 patients had T1D and five patients had features of early onset T2D
17	Alyafei et al. (2018)	Prospective cohort study	$N = 485$ Age: $0.5 \leq \text{age} \leq 14$	Qatar	T1D and T2D	T1D in this population over the period 2012–2016 was 28.39/100,000 (95% CI: 31.82–40.03). This was significantly higher compared to the unadjusted estimated incidence registered between 2006 and 2011 (23.15/100,000) The incidence of T2D increased from 1.82 per 100,000 in 2012 to 2.7 per 100,000 in 2016, with an incidence of T2D equal to 2.9/100,000 per year
18	Ali et al. (2013)	Comparative cohort study	$N = 210$ Age: 1–18 years	Egypt	T2D	Frequency: 28 (13.3%)
19	Osman et al. (2013)	Retrospective, descriptive hospital study (2006–2009)	$N = 958$ Age: 11–8 years	Sudan, Khartoum	T2D	Frequency: 38 (4%)

10.3 Results

The results section includes the prevalence and incidence rates for T1D and T2D from countries identified in Table 1. The most predominant risk factors and characteristics identified in studies for T1D and T2D development are also discussed, which include, pubertal onset, vitamin D deficiency, sex, obesity, and family history of diabetes.

10.3.1 Prevalence and Incidence Rates

T1D

Studies specifically reporting on the incidence and prevalence rates of T1D were conducted in Saudi Arabia (5), Kuwait (2), the United Arab Emirates (UAE) (2), Iran, and Qatar.

Saudi Arabia The incidence and prevalence of T1D was illustrated in five studies from Saudi Arabia and it shows an increasing trend over the years in prevalence and incidence rates for adolescents with T1D. Two observational case studies with a large study range period from 1990 to 2007 and 2004 to 2009 were conducted in Eastern Saudi Arabia and North-west Saudi Arabia, respectively. In the study conducted over a period of 18 years (1990 and 2007), a noticeable increase was found for incidence rate at an average increase of 27.52/100,000/year. The incidence rate was 36.99 per year compared to 18.05, in the first 9 years of study (100,000/year) (Abduljabbar et al. 2010). The second study, conducted over 5 years in Al-Madinah on children below 12 years of age, found a mean annual age-standardized incidence rate of 29 per 100, 000 (95% CI 26.0–32.0), although a significant annual increase in incidence rates was not found (Habeb et al. 2011). Prevalence rates were much higher for two other studies. A larger nationwide Saudi Arabian project conducted between 2001 and 2007 found that the overall prevalence rate was 109.5/100,000 and ranged between 48 and 162 (per 100,000) for individuals 5–18 years (Al-Herbish et al. 2008). The highest prevalence rate was reported for the most recent study conducted in the Al-Baha region in Saudi Arabia. This study found that over 10 years (2007–2016), the prevalence rate of T1D was 355/100,000 population of adolescents (0–19 years) (Al-Ghamdi and Fureeh 2018).

A large cross-sectional study ($n = 23,532$) reported on the prevalence of various diabetes diagnosis among adolescents (≤18 years), including T1D, T2D, and impaired fasting glucose (IFG). The age-adjusted prevalence of T2D in this study was 1/1000. Specifically, out of 105 adolescents diagnosed with diabetes, 0.07% were T2D and 0.38% were T1D (Al-Rubeaan 2015). However, in this study, more than 90% of the children and adolescents with diabetes were unaware of their disease, of which the known patients with T1D and T2D accounted for only 0.45%, while the newly identified cases with diabetes and IFG accounted for 10.39% (Al-Rubeaan 2015).

Kuwait In Kuwait, an increase in the incidence of T1D among children (<15 years) has been reported when comparing reports from 1980–1981 to 1992–1993, in which the incidence rate grew four times higher, from 3.96/100,000 person-years to 15.4/100,000 (Taha et al. 1983; Shaltout et al. 1995). Two studies reporting incident rates for Kuwait included in this review were conducted between 1992–1997 (Shaltout et al. 2002) and 2011–2013 (Shaltout et al. 2017). These studies reported data on newly diagnosed patients that were registered through the Childhood-Onset Diabetes e-Registry. The most recent study found that the incidence rate found in individuals (aged 0–14 years) was 40.9/100,000 per year from 2011 to 2013, which was 2.3 times higher (95% CI 1.9–2.7) than the incidence rate reported during 1992–1997 (17.7).

Iran A recent study from Iran also found that the annual incidence of T1D for children under 15 years of age, between the years 2000 and 2015, was 13.35/100,000 (Aminzadeh et al. 2019).

UAE One of the first studies to report on the patterns of diabetes incidence in adolescents from the UAE found that over 9 years (1990–1998), 40 adolescents (0–18 years) were diagnosed (Punnose et al. 2002). In this cohort, 35 individuals were diagnosed with T1D. A recent secondary analysis of data from the National Study of Population Health in the UAE, conducted between 2007 and 2009 (NSPHUAE 07–09), found that the prevalence of diabetes (not specified) based on self-reported diagnosis on a randomly selected stratified sample of 6329 school adolescents (15–18 years old) from 9 regions of the UAE was 0.9% (95% CI 0.7–1.2) (Barakat et al. 2021).

Qatar In a study conducted in Qatar, 440 youth with T1D (0.5–14 years) were identified from the registry of the National Pediatric Diabetes Centre. This study was a prospective cohort study which estimated the incidence and trend of T1D during the period between 2012 and 2016 and compared it to the incidence previously reported from 2006 to 2011. Results indicated that the inclusive unadjusted estimated incidence rates in this population was 28.39/100,000, which was significantly higher compared to the estimated incidence registered between 2006 and 2011 (23.15/100,000) (Alyafei et al. 2018). Equally, this study reported on the incidence of T2D, which also increased between 2012 and 2016 from 1.82 to 2.7 per 100,000.

T2D

The study from Qatar found that the overall incidence of T2D equated to 2.9/100,000 per year (Alyafei et al. 2018). The prevalence and characteristics of adolescents with T2D was also reported in Egypt (Ali et al. 2013), Sudan (Osman et al. 2013), Kuwait (Moussa et al. 2008), the UAE (Punnose et al. 2005), and Iran (Moadab et al. 2010). In a large cross-sectional study conducted in Kuwait, including 128,918 adolescents (6–18 years old) from 182 schools, the overall prevalence was 34.9/100, 000 (Moussa et al. 2008). A retrospective study from the Al-Ain hospital from the UAE characterized the features of T2D among 96 newly diagnosed children with diabetes, of which 11 were reported to have T2D (Punnose et al. 2005). In Egypt, a comparative cohort study found the prevalence of T2D to be 13.3% among adolescents diagnosed with diabetes (210) (Ali et al. 2013). In Sudan, the prevalence was lower, at 4%, based on the clinical records of 985 children attending a diabetic clinic for children and adolescents between 2006 and 2009. The lowest prevalence of T2D was reported by Moadab et al. (2010) in Iran, where the prevalence of T2D was 0.1% in a large cross-sectional study.

10.3.2 Risk Factors and Characteristics for T1D and T2D Among Adolescents

Pubertal Onset

The stage of adolescence is also known to coincide with the presentation of prediabetes symptoms, specifically, insulin resistance which is characterized by a lack of glucose uptake. Temporary insulin resistance is suggested to occur as a result of secretion of specific hormones (e.g., growth hormone) associated with development during puberty (Habeb et al. 2011). While decreased insulin sensitivity is normally compensated by an increase in insulin secretion, this period can make adolescents vulnerable to T2D development, which may be extenuated by the adverse effects of obesity (Kelly et al. 2011). Interestingly, one study from the UAE indicated that adolescents required an increase in insulin at the onset of puberty, and a peak incidence of T1D was in the 10–14 years age group (Punnose et al. 2002). These findings suggest that a critical factor to examine in relation to the incidence of T1D and T2D is the age of onset, and that adolescence may be a particularly vulnerable stage. Indeed, studies report a peak incidence of T2D representation during mid-puberty among adolescents (Arslanian 2000; Reinehr 2013). Similarly, many epidemiological studies have witnessed the disease onset of T1D to occur after the age of 15 years, coinciding with the years of adolescence rather than childhood (Tuomilehto 2013).

Pubertal onset was identified in a number of studies in relation to diagnosis of T2D. Two studies in particular indicated the association between T2D and pubertal onset (Punnose et al. 2005; Osman et al. 2013). In Sudanese adolescents, 92.1% had onset between 11 and 18 years of age and were all considered "pubertal" (Osman et al. 2013). In the study from the UAE, out of the identified adolescents with T2D, the mean age of diagnosis was 14.6 (SD 3.0) years, and 10/11 adolescents were considered to be portraying signs of puberty (Punnose et al. 2005). Similarly, a retrospective study in Saudi Arabia among adolescents with T2D indicated that the mean (SD) age of diagnosis was 13.1 ± 2.02, and 60% were considered pubertal

(Al-Agha et al. 2012). A study conducted in Kuwait indicated that a key pattern of prevalence of T2D in this study was the high percentage of children in the age group 14–18 years (57.8%), as the prevalence rate in this group was the highest (46.8 per 100,000) (Moussa et al. 2008). Conversely, two studies indicated that the highest T1D prevalence was for adolescents in the higher age groups; 13–18 years old (Al-Herbish et al. 2008), and 10–12 years old (Habeb et al. 2011) (Table 2).

Vitamin D Deficiency

Recent increase in vitamin D deficiency has been linked to a potential influence on several chronic diseases (Al-Daghri et al. 2015). The incidence and association with vitamin D deficiency and diabetes in particular has been a risk factor found among children and adolescents diagnosed with diabetes in Middle Eastern countries, despite the abundancy of seasonal exposure to sunlight (Al-Daghri et al. 2015; Robert et al. 2018). Vitamin D3 supplementation during the intrauterine period and early life may have a protective effect against autoimmune diseases (Cherian et al. 2010). For example, lack of sunlight in countries outside the MENA region, such as Finland, has suggested the relationship between lack of endogenous vitamin D production and exposure in pregnancy to the incidence of diabetes in offspring (Chakhtoura and Azar 2013). In one study from this review, in a sample of 2225 adolescents (13–17 years) from Riyadh with T2D, the difference between females and males with vitamin D deficiency (<25 nmol/L) was statistically significant (females: 47%; males:19.4%). However, vitamin D deficiency was significantly associated with T2D and prediabetes only in males. This indicates a sex-related disadvantage for males with low vitamin D status, and possible etiological differences associated with the incidence of T2D based on sex- and gender-related risk factors (Al-Daghri et al. 2015).

Sex-Related Prevalence

Studies show variability in the prevalence of diabetes diagnosis in females and males. The prevalence of diabetes diagnosis, specifically T2D, was significantly higher among males (47.3, 95% CI 28.7–65.8) than females (26.3, 95% CI 14.8–37.8) from a study in Kuwait of a randomly selected sample of school-going adolescents (Moussa et al. 2008). Similarly, results from the NSPHUAE show that 1.5% (95% CI 1.0–2.1) of males compared to 0.5% (95% CI 0.3–0.8) of females reported a self-diagnosis of diabetes ($p < 0.001$) (Barakat et al. 2021).

Conversely, a strong female preponderance among adolescents with a diabetes diagnosis has been found in five studies in this review. Two studies were from Saudi Arabia (Al-Ghamdi and Fureeh 2018; Habeb et al. 2011), and the rest were from the UAE (Punnose et al. 2005), Kuwait (Shaltout et al. 2017) and Egypt (Ali et al. 2013). Two studies found the prevalence of T2D to be higher among females. Specifically, Punnose et al. (2005) found that among adolescents from the UAE, the

Table 10.2 Association of risk factors and characteristics for T1D and T2D among adolescents residing in the MENA region

Author/year	Risk factors and characteristics
Al Amiri et al. (2015)	Adiposity, family history of T2D, employment and high levels of triglycerides were risk factors associated with abnormal glycemic testing Abnormal glycemic testing was 1.9 times more common among adolescents with a first-degree relative and 2.28 times more common among those with high levels of triglycerides
Al-Daghri et al. (2015)	Vitamin D deficiency was significantly associated with T2D [OR 3.47 (CI 1.26–5.55); $p < 0.05$] and pre-DM [OR 2.47 (CI 1.48–4.12); $p < 0.01$] in males
Ali et al. (2013)	There were significantly more females than males with T2D (64.3% vs. 58.2%) T2D patients had a highly significant higher waist circumference than T1D patients Obesity, female gender, and a positive family history were risk factors for T2D
Osman et al. (2013)	35 (92.1%) had T2D onset between 11 and 18 years of age and were all pubertal Thirty-five (92%) had family history of T2D Twenty-nine (76.3%) of the cases were obese, 8 (21.1%) overweight and only one (2.6%) had normal BMI
Al-Agha et al. (2012)	Among adolescents with T2D, 62.86% had a body mass index BMI ≥ 85th percentile, and 37.14% had a BMI ≥ 95th percentile Mean, SD, and median age of diagnosis: 13.1 ± 2.02 and 13.5 years 60% were pubertal
Habeb et al. (2011)	The incidence was significantly higher in the 10–12-year age group (46.5 per 100,000; 95% CI 38.9–55.2) than in younger children ($p < 0.001$) Incidence rate was significantly higher in females (33.0 per 100,000, 95% CI 29.1–37.3) than males (22.2 per 100,000, 95% CI 19.1–25.7; $p < 0.001$) More cases of T1D were diagnosed during autumn and winter months (249; $p = 0.002$) than during spring and summer (March–August: 170, 40.6%)
Cherian et al. (2010)	No etiological influences of maternal age at birth, birth order, birth weight, early introduction of cow's milk and cereals, infections, and vaccines as well as nitrate levels in drinking water were noted in 119 adolescents (<15 years) with T1D between 1980 and 2009 An association with cool months (November–February) was found for an increased incidence of T1D during 1990–1994 and 1995–1999
Moadab et al. (2010)	9.34% ($n = 706$) were overweight and 5.3% ($n = 403$) were obese Impaired glucose tolerance and insulin resistance were detected in three and six participants with IFG, who consisted 0.4% and 0.8% of total obese and overweight students, respectively
Moussa et al. (2008)	Significant difference in prevalence between males (47.3, 95% CI 28.7–65.8) and females (26.3, 95% CI 14.8–37.8) at $p = 0.05$ Significant trend for an increase in prevalence of T2D with age ($p = 0.026$). 6–9 (17.2); 10–13 (31.6); 14–18 (46.8) per 100,000 Adolescents with T2D had a significantly higher frequency (51.1%) of a positive family history of diabetes than those of a similar age without T2D (22.2%) ($p = 0.004$)

(continued)

Table 10.2 (continued)

Author/year	Risk factors and characteristics
Moussa et al. (2005)	Family history of T1D and T2D and thyroid disease was associated with T1D based on a pair-matched case-control study conducted in Kuwait (cases: 348; controls: 348) The risk for adolescents (6–18 years) with positive family history of T1D of becoming diabetic was 2.42 times higher than a child with no family history of diabetes (unadjusted odds ratio = 2.42, 95% CI = 1.62–3.67, $p < 0.001$) The risk for T2D was 2.83 times higher (unadjusted odds ratio = 2.83, 95% CI = 1.72–4.68, $p < 0.001$)
Punnose et al. (2005)	10 of the 11 patients diagnosed were female (M:F ratio 1:10) The mean age at diagnosis was 14.6 (SD 3.0) years (median 15 years, range 8–18 years) A positive parental history was obtained in 8 patients with 2 of them also having second-degree relatives with T2D The clinical characteristics were pubertal onset, female preponderance, obesity, and strong family history of T2D
Punnose et al. (2002)	Four (80%) were obese with a positive family history of Type 2 DM The mean age of onset of T1D: 9.2 ± 4.1 years with the peak incidence being in the 10–14-year age group
Shaltout et al. (2002)	Significant seasonal variation in the number of newly diagnoses cases of T1D was found among the total ($p < 0.001$), with an increase in autumn/winter and decrease in summer

female to male ratio of T2D diagnosis was 10:1. In Egypt, being female was suggested as a risk factor for T2D (Ali et al. 2013). This study found that among individuals diagnosed with T2D (13.3%), there was a significant difference in the prevalence of females (64.3%) diagnosed than their male counterparts (35.7%). In Saudi Arabia, T1D was also more common among females at 57.5% compared to 42.5% among males (Al-Ghamdi and Fureeh 2018). Similarly, an earlier study conducted in Saudi Arabia in Al-Madinah city found that the incidence of T1D was significantly high among females than in males (33.0 vs. 22.2 per 100, 000; $p < 0.001$) (Habeb et al. 2011). In Kuwait, although there were no significant differences, the standardized incidence rate for T1D was reported to be 44.1 for females compared to 39.2 for males (Shaltout et al. 2017).

Obesity

The steady decrease in age of onset of T2D beginning during adolescence rather than what has been previously considered as a risk factor correlated with adulthood, has been reflected as a consequence of rapid modernization with major lifestyle changes resulting in childhood obesity, and insulin resistance inducing glucose intolerance (Moussa et al. 2008). In this review, obesity was found as a characteristic and as an associated risk factor in five studies for T2D and prediabetes symptoms.

In one study from the UAE, 5.4% and 0.87% of 1034 overweight/obese Emirati students (11–17 years) had T2D and were positive for prediabetes, respectively

(Al-Amiri et al. 2015). A retrospective cross-sectional study conducted on Saudi overweight and obese adolescents (with body mass indexes of ≥85th and 95th percentile) found that the prevalence of T2D was higher at 9.04% in this population (Al-Agha et al. 2012). Among Saudi adolescents in Riyadh who were considered healthy, Al-Daghri et al. (2015) found that both the prevalence of obesity and elevated fasting blood glucose levels (equivalent to prediabetes; 5.6–6.9 mmol/L) were significantly higher among males than females, at 20.5% versus 17.7% ($p < 0.001$) and 17.8% versus 12.4% ($p < 0.003$), respectively. A large cross-sectional study that screened 672 overweight and obese school adolescents from Iran found that prediabetes symptoms (i.e., impaired glucose tolerance and insulin resistance) were detected in 0.4% and 0.8% of total obese and overweight students, and the overall prevalence of IFG was 4.61% (Moadab et al. 2010). The detection and prevalence of impaired glucose tolerance and insulin resistance among obese and overweight adolescents indicate the increased risk of T2D development in this cohort.

In Egypt, among adolescents <18 years, obesity was considered a risk factor for T2D, based on results showing that a significantly higher BMI and waist circumference centiles for age and sex was seen in adolescents with T2D than those with T1D (Ali et al. 2013). A study conducted in Sudan found that the appearance of obesity was also identified in 29 (76.3%) of the adolescent cases with T2D, while 8 (21.1%) were overweight, and only one (2.6%) had normal BMI (Osman et al. 2013). Most of the cases (86.8%) were coming from urban areas, and 55.3% of them were from high social class (Osman et al. 2013). Interestingly, this study also found that very obese children had earlier onset of T2D (8–11 years) in comparison to nonobese adolescents that had onset between 11 and 18 years. A family history of obesity was also found in this cohort.

Familial Disposition

Diabetes is a highly heritable condition for both T1D and T2D. In particular, literature suggest that 90% of children and youth affected by T2D have a first- or second-degree relative who also have T2D (Panagiotopoulos et al. 2018). Six studies (UAE:3; Egypt:1; Sudan:1; Kuwait:1) in this review reported family history of diabetes as a risk factor for T2D, while one study from Kuwait suggested a significant association for T1D (Al Amiri et al. 2015; Ali et al. 2013; Moussa et al. 2005, 2008; Osman et al. 2013; Punnose et al. 2002, 2005) (Table 2). Among overweight and obese adolescents from the UAE, family history of T2D was significantly associated with risk of abnormal glycemic testing (based on fasting blood glucose) (Al-Amiri et al. 2015). In Khartoum, Sudan, a large retrospective study found that out of adolescents that had T2D, 92% had a family history of T2D (Osman et al. 2013). A study of Kuwaiti adolescents with T1D matched by age and gender to nondiabetic controls suggested a family history of both T2D and T1D as significant associated factors for developing T1D, in which the risk for T1D was 2.42 times higher (95% CI:1.62–3.67) and T2D was 2.83 times higher (95% CI: 1.72–4.68) (Moussa et al. 2005). This study also indicated a 1.86 times higher risk of being diabetic for adolescents with a family history of thyroid disease (95% CI: 1.18–3.28) than those with no family history.

Other Factors

Few studies have looked at the role of causative environmental factors as possible contributors to the etiology of T1D incidence. One study in particular conducted in Saudi Arabia aimed to evaluate the role of multiple factors [i.e., maternal age at birth, birth order, birth weight, nutritional factors (cow's milk and cereals), infections and vaccines, as well nitrate levels in drinking water] in the rising incidence of T1D (Cherian et al. 2010). Although no significant associations were found, this study suggested a seasonal variation in T1D development in children during cool months (November–February) compared with warm months (June–September) (Cherian et al. 2010). These findings also aligned with an earlier study from Kuwait which indicated a significant seasonal variation in T1D diagnosis with an increase during autumn/winter (Shaltout et al. 2002), and the study conducted in Al Madinah, which found that 54.9% of adolescents were diagnosed with T1D during winter and autumn months (September–February) compared to 40.6% that were diagnosed during spring and summer (March–August) (Habeb et al. 2011). This seasonality effect could be linked to variability in vitamin D exposure and its immunomodulatory mechanisms in the prevention of T1D (Chakhtoura and Azar 2013).

10.4 Discussion

Diabetes mellitus is a noncommunicable disease which has become a major global public health issue. Some regions of the world have experienced greater challenges in controlling the spread of this epidemic, due to variations in health resources, and the influence of various environmental, behavioral, and genetic etiologies. The MENA region in particular is considered one of the highest risk regions for this chronic disease, which may be a result of the rapid changing demographic and recent transition from traditional to westernized nutritional practices, and an increase in sedentary behavior (Al Busaidi et al. 2019; Saeedi et al. 2019; Zabetian et al. 2013). In addition to the various environmental and behavioral factors that are widely known to contribute to diabetes prevalence worldwide, the expression of diabetes may be further influenced by certain social and cultural norms practiced throughout the MENA. Young individuals in particular are becoming targets of intervention as they are impacted by the most common forms of diabetes (T1D and T2D); however, many gaps maintain in the knowledge regarding the various etiology behind the rising epidemic of these diabetes forms.

Over the past two decades, there has been a noticeable increase in diabetes among adolescents throughout the region. In this review, studies from the MENA region that reported on the prevalence and risk factors of diabetes were related to

T1D and T2D. Accordingly, this chapter summarized epidemiological studies related to the prevalence, risk factors, or predictors of T1D and T2D among children and adolescents (0–19 years) from countries in the MENA region, including Saudi Arabia, the UAE, Kuwait, Qatar, Egypt, Iran, and Sudan. Studies from Saudi Arabia reported a significant increase in T1D among adolescents from 1990 to 2016, with incidence rates ranging from 18.05 per 100,000/year for adolescents <15 years old to a prevalence rate of 355/per 100,000 for adolescents 0–19 years old, respectively (Abdul-Jabbar et al. 2010; Al-Ghamdi and Fureeh 2018). In addition, incidence of T1D in Kuwaiti adolescents across two decades has been 4.1% annually, which aligns with international data, suggesting an average relative increase of 3–4% per calendar year worldwide (Patterson et al. 2019; Shaltout et al. 2017; Tuomilehto 2013).

Studies on the prevalence of T2D were limited and remain elusive. Nonetheless, these studies represent some of the predominant risk factors that may be associated with this growing prevalence in the MENA. In this review, factors associated with T2D and their characteristics were family history, sex, pubertal onset, vitamin D deficiency, and obesity. Few studies also reported that adolescents with T2D who were defined as obese also had a family history of T2D. Moreover, environmental and geographic related factors such as living in urban versus rural areas may have an effect on the risk of diabetes development, as suggested by the higher prevalence of people living with diabetes in urban areas (Saeedi et al. 2019; Osman et al. 2013). Geographic factors (e.g., harsh desert climate) coupled with cultural reasons in the MENA may contribute to poor vitamin D status and lead to clinical implications associated with T1D (Rasoul et al. 2016). In this review, vitamin D deficiency was more apparent in male adolescents with T2D, who also showed a high prevalence of prediabetes. This is despite research suggesting that Arab females are more likely to be deficient in vitamin D than Arab males, due to less physical activity outdoors, lack of exposure to sunlight, and are less likely to receive supplementation (Al-Daghri et al. 2015). These contradictory findings suggest that the influence of other gender-related behavioral factors, such as lack of physical activity and poor nutritional practices may be strongly correlated to the presentation of prediabetes symptoms among adolescent Arab males. Further research is required to characterize adolescents with T2D and the associated risk factors that may either initiate or accelerate the autoimmune process leading to pancreatic ß cell destruction (Weiss et al. 2017).

In obese adolescents and children, the risk of diabetes expression and transition from prediabetes symptoms to diabetes are faster than compared to adults, with deterioration of β cells occurring at 20–30% per year (Weiss et al. 2017). Accordingly, the early expression and onset of diabetes during adolescence provides a unique opportunity of intervention to mitigate the risk of development which is associated with many preventable behavioral practices. Specifically, sedentary behavior, nutritional habits consisting of high carbohydrate foods, and the subsequent development of obesity – a major predisposition for the transition from regular glucose metabolism to insulin resistance.

Moreover, the phenomenon of temporary insulin resistance and peak incidence of pubertal onset associated with T1D and T2D suggest homeostasis in glucose metabolism and insulin secretion are dependent upon healthy behaviors during adolescence, composed of balanced energy intake and expenditure involving health dietary behaviors and physical activity, to mitigate the risk of other predisposing factors. In addition, pubertal onset may also differentiate age of diagnosis for sex-related prevalence, as a reflection of differences associated with earlier onset of puberty in females than males (Habeb et al. 2011). In this case, it is critical to examine the earlier onset of symptoms in adolescent females, which may be accelerated in genetically susceptible individuals due to gender-related behaviors, and especially given the higher prevalence of both T1D and T2D among female adolescents found in this review.

The MENA region is composed mainly of Arab populations, which are considered a high-risk population for the development of T2D and T1D. This high-risk consideration stems from a range of epigenetic and genetic factors. Specifically, risk factors for the development of T2D in children and adolescents have been linked to a history of T2D in a first-or second-degree relative, which can also be further expressed throughout generations due to the high prevalence of consanguineous marriages in the region (Al-Amiri et al. 2015; Panagiotopoulos et al. 2018). The prevalence of these sociocultural norms (i.e., preservation of familial structure from unions formed between biologically related individuals) may also be associated with genetic dimorphisms resulting in the expression of risk alleles for T1D (Zayed 2016). The varied expression and contribution of genetic profiles of specific alleles leading to increased incidence of T1D in certain populations may explain the geographic variability in prevalence. This expression may be further initiated or accelerated by the effect of behavioral risk factors. However, further research is required to examine the underlying risk factors and epigenetic mechanisms that may be linked to this difference.

Studies have also illustrated the increase in obesity which has largely been linked to the development of T2D and as a risk factor for the development of gestational diabetes in childbearing women (15–45 years) in the MENA, which further compounds the intergenerational risk of diabetes in offspring (Al-Rifai et al. 2019; Al-Rubeaan, 2015). In fact, in the MENA region, 1 in 9 live births are affected by hyperglycemia in pregnancy (IDF 2019). The same predisposing risk factors have been shared among adolescents, and may be differentiated by gender-related social factors. For example, females face higher risk of sedentary lifestyles, as studies show that factors such as wearing sports clothing, safety concerns, or exercising outdoors for religious reasons are cultural barriers that affect females more than males from Arab nations (Barakat and Yousufzai 2020), which may indirectly contribute to the prevalence of overweight and obesity, and in translation increase the risk of developing T2D.

Overall, there are a limited number of studies reporting on the incidence of adolescent diabetes. In addition, although the countries of the MENA represent some of the highest numbers of T1D, overall this number may be underestimated as only 57% have incidence rates available from the MENA region reported by the IDF (Patterson et al. 2019). Multiple studies suggest the dire need of having a registry in each country with systemic coordination (Alassaf et al. 2019; Zayed 2016), as well as having research done in community-based settings, to further characterize the etiology, mortality, and complication of this serious disease (Saraswathi et al. 2019). Furthermore, multiple characteristics seem to be associated with early onset and diagnosis of diabetes in adolescents, and significant differences are seen between sexes and in relation to gender-related risk factors. Efforts need to be initiated to address prevention strategies and modifiable risk factors of diabetes in children and adolescents and to determine links between social, demographic, and economic contextual factors in developing countries.

Reflection Questions

1. What are the different forms of diabetes that may affect adolescents and how do they differentiate?
2. What countries have the highest prevalence rates of type 1 diabetes among adolescents in the MENA region?
3. What is the various risk factors that are prominent in the MENA region which may lead to the increased expression of diabetes during adolescence?
4. When do symptoms of type 1 diabetes become apparent among adolescents?
5. What is the key modifiable risk factors that can decrease the prevalence of diabetes and promote long-term positive health?
6. How can policies be tailored to ensure that all countries in the MENA are able to develop registries for diabetes, and why are registries important?

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