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Epidemiological criteria and risk factors for type two diabetes mellitus (T2DM) in children and adolescents: Can we modify them?

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Abstract

Type 2 Diabetes Mellitus (T2DM) has become an increasingly important public health concern globally among children and adolescents. The unique features of T2DM in children are the rapidly progressive decline in β-cell function and accelerated development of complications. Important proven environmental risk factors for developing T2DM include, prediabetes (high blood glucose short of T2DM definition), obesity, inactivity, family history of T2DM, being a member of a high-risk ethnic group, and poverty.

The estimated T2DM prevalence per 1000 youths aged 10 to 19 years increased significantly in many countries in the past 20 years. T2DM impacts more specific ethnic groups compared to children of other ethnicities.

This search reviews the literature about epidemiological data on T2DM in children and adolescents and the different interventions adopted for its prevention and management.

Epidemiological evidence indicates that T2DM in youth is different from type 1 Diabetes Mellitus (T1DM) and T2DM in adults. Many research articles showed that screening for abnormal blood glucose (prediabetes and diabetes) in high-risk children and adolescents represents an effective population intervention method for the early diagnosis and management of prediabetes and T2DM. The use of lifestyle intervention programs (LSI), *applied* successfully in the US, and many European countries, have shown some success in reversing glucose abnormalities and preventing the progression to T2DM decreasing cardiovascular risk factors.

In conclusion, Proper screening, and the wide application of LSI programs in selected high-risk populations are expected to have good preventive outcomes reducing the incidence and complications of T2DM in children and adolescents.

Keywords: Type 2 Diabetes Mellitus*; Children; Adolescents;* Epidemiology*;* Risk factors

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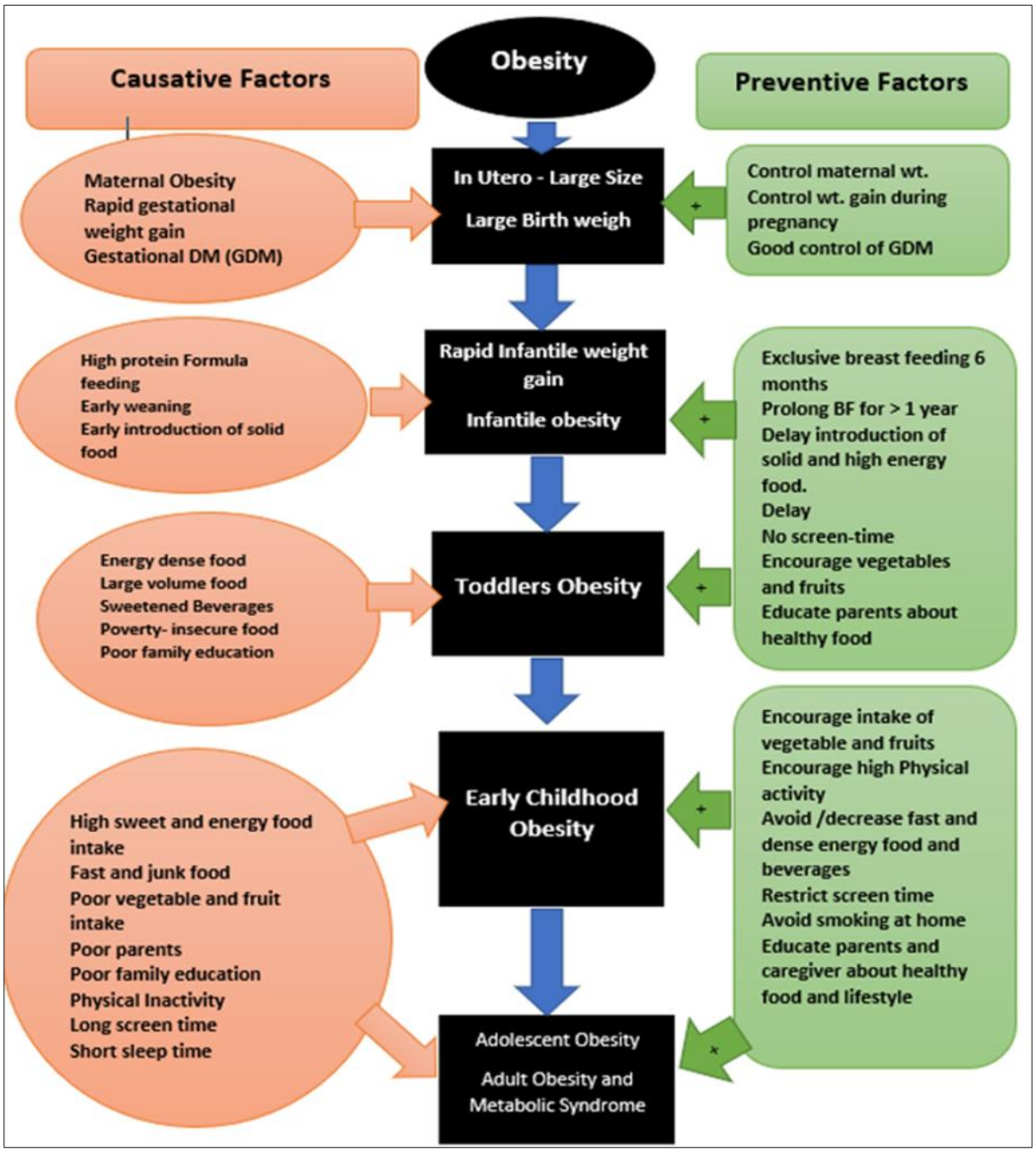
Graphical Abstract



1. Introduction

Since the early 1990s, the incidence of type 2 diabetes mellitus (T2DM) among children and adolescents has increased globally and this problem is tightly connected to the rise in childhood obesity. Type 2 Diabetes Mellitus (T2DM) is characterized by hyperglycemia, insulin resistance, and relative insulin deficiency. Its comorbidities are risk factors for many diseases affecting many organs and systems and can affect nearly every major organ in the body, including the blood vessels, nerves, eyes, and kidneys. The increasing incidence and the high prevalence of T2DM and its complications make this disease a major public health problem. Certain factors have been identified as increasing the risk to develop T2DM. These risk factors include overweight and obesity, prediabetes state, inactivity, family history of T2DM, low birth weight and prematurity, being born to a mother who had gestational diabetes (GD) during the pregnancy, and poverty. (1)

The long-term complications of T2DM develop gradually over many years. Ultimately, its complications may be incapacitating or even life-threatening. These include hypertension, hyperlipidemia, cardiovascular morbidities, stroke,

renal impairment and failure, neuropathies, and retinopathies. However, not all populations are equally affected, and T2DM impacts specific racial and ethnic groups to a greater extent. American Indian/Alaska Native (AI/AN) children in the United States of America (US) and Canada have a higher rate of this disease than do children of other ethnicities. Latinos and African American children in Canada and the US are also at increased risk for T2DM. In US children and adolescents, the prevalence of T2DM is expected to exceed that of T1DM within 10 years (around 2032).

There is a compelling need for additional research, primary and secondary prevention efforts, and evidence-based treatment for children and youth with T2DM. (2) Therefore, health care providers must understand the epidemiology of this disease, including predisposing factors experienced by different populations, to advance prevention efforts, early identification of the disease, and proper treatment options for children and adolescents with this disorder in order to avoid the devastating long-term complications.

This review provides a summary and a clarification on the different epidemiological characteristics of this developing epidemic in children globally and enlighten some evidence-based methods for prevention and management.

2. Methods

Epidemiological and clinical data of the developing epidemic of T2DM and prediabetes in children and adolescents are developing since 2000. Different new aspects including the natural history of the disease, short and long-term complications, and factors increasing the risk of developing the disease have been studied in various parts of the world. In addition, studies are investigating the possible beneficial effects of using intervention programs to prevent and/or reduce the incidence of T2DM at this early age. This review aimed at summarizing these important epidemiological and clinical data to clarify the different aspects of the disease and its precipitating factors that are necessary for the prevention, early detection, and proper management to prevent complications. The literature was searched including PubMed, Google Scholar, and Research Gate, for research articles related to T2DM in children and young children, including prevalence, trends, and possible factors that may increase the risk of T2DM in children in the US. Search keywords included the following: "Type 2 diabetes mellitus", And prediabetes , And Obesity, And Metabolic Syndrome (MetS), "Children, Adolescents, Youth, Epidemiology, And Incidence, And Prevalence, And Trend, And gender, And ethnicity, And minority groups And Diet, And Lifestyle intervention, And the US. . All articles with publication dates before 2000 and health-related topics not listed in the inclusion criteria were excluded from the search. Additionally, all other forms of diabetes mellitus in children (Type 1 Diabetes Mellitus (T1DM), cystic fibrosis-related DM, and genetic syndromes with DM) and adults were excluded unless needed for comparison.

3. Review

3.1. Definition and diagnostic criteria of Prediabetes in children and adolescents in the US

Diabetes mellitus is a group of metabolic diseases characterized by high blood glucose in the blood due to decreased insulin secretion and/or action. Diagnostic criteria for diabetes are based on blood glucose measurements and the presence or absence of symptoms. (3) These criteria are important for differentiating prediabetes from diabetes state required by health caregivers as well as for educating people at risk.

Table 1 Criteria for the diagnosis of diabetes mellitus from CDC (4)

Results	HbA1C	Fasting glucose	Glucose tolerance test	Random blood glucose
Diabetes	6.5% or above	126 mg/dL or >	200 mg/dL or >	200 mg/dL or >
Prediabetes	5.7 – 6.4%	100-125 mg/dL	140-199 mg/dL	N/A
Normal	Below 5.7%	99 mg/dL or <	140 mg/dL or <	N/A

>= above, < = below

T1DM is due to a deficiency of insulin secretion whereas T2DM results from a combination of resistance to insulin action and a defective insulin secretory response. The characteristic features of youth onset T2DM in comparison with T1DM are shown in Table 2.

Table 2 Clinical characteristics of T2DM in comparison to T1DM in children and adolescents. (5, 6)

	Type 1 Diabetes	**Type 2 Diabetes**
Onset	Acute-symptomatic	Slow- may be asymptomatic
Clinical picture	Weight loss, Polyuria, polydipsia	Obese, Family history of T2DM-Obesity, high prevalence in certain ethnic groups, Acanthosis nigricans, PCOS
Ketosis	Almost always present C-peptide negative ICA positive Anti-GAD positive ICA 512 positive	Usually absent C-peptide positive ICA negative Anti-GAD negative ICA 512 negative
Therapy	Insulin invariably	Oral hypoglycemic agents
Associated autoimmune diseases	Yes	No

ICA= islet cell antibody, anti-GAD =Antibodies to glutamic acid decarboxylase, PCOS = Polycystic ovary syndrome.

Prediabetes is a form of higher blood glucose (sugar) levels than normal—but not high enough to be diagnosed as DM. Prediabetes can progress to T2DM and it is the most common form of glycemic abnormality. Prediabetes is a state of high risk to develop T2DM and can lead to heart disease and stroke. Its early recognition and management in a population, especially those who have a high prevalence of obesity and DM, may prevent the progression of diabetes state.

In the US, Andes LJ, et al (2016) reported the overall prevalence of prediabetes in youth 12 to 18 years of age to be 18%. The prevalence was significantly higher (26%) among those with obesity and in males (22.5%) versus females (13.4 %). This considerably high prevalence of prediabetes in children and adolescents makes its early recognition and management a public health priority to decrease the occurrence of DM. (7,8)

3.2. Pathogenesis of T2DM and its characteristics in children

T2DM is characterized by high blood glucose levels due to decreased insulin action and a relative deficiency in insulin secretion. The etiology is affected by genetic (inherited) and physiologic (environmental) components. The environmental component includes lifestyle factors such as excess fat intake, insufficient physical activity, and increased sedentary behavior. Associated comorbidities include obesity, high blood lipids, and hypertension. (5-7)

T2DM in youth is clinically characterized by obesity, decreased insulin action (insulin resistance), and other clinical features known as metabolic syndrome (MetS). Adults with the Mets have a five-fold higher risk to develop T2DM and a two-fold higher risk to develop cardiovascular complications and strokes. Children and adolescents with the MetS have an even higher risk to develop these complications earlier during their longer life expectancy. The early development of the components of MetS in children and adolescents appears to accelerate the occurrence of high blood pressure, high blood lipids, cardiac attacks, and fatty liver disease. (8) There is a strong epidemiologically proven clinical association between prediabetes and T2DM with obesity. Obesity leads to a marked decrease in insulin action (insulin resistance). The pancreas increases insulin secretion to compensate for this decreased insulin action, but this ends up in exhaustion and failure of insulin secretion. Adolescents usually have lost approximately 80 % of their pancreatic beta-cell function before the diagnosis of T2DM. (3)

3.3. Epidemiological characteristics of Prediabetes and T2DM in children and adolescents

Studying the epidemiological characteristics can guide the best way/s to be adopted for effective prevention of T2DM, especially in the high-risk population. As previously mentioned, T2DM disproportionately affects youth of ethnic and racial minorities and can occur in complex psychosocial and cultural environments. These conditions may make it challenging to maintain healthy lifestyle changes and self-management behaviors required for treatment. (9) One-third of children with T2DM have been identified by screening in the absence of symptoms. The families of adolescents with T2DM often have lifestyle risk factors leading to obesity. These factors include regularly eating high-calorie foods, lack of exercise, being a member of a family of overweight/obese people, living under personal, parental, and/or family stress, and/or living in some communities which have limited resources (poor) and limited access to healthy food. (10)

3.4. Epidemiology (incidence, prevalence, and trends) of T2DM globally: relation to racial differences, genetics, and epigenetics

The global incidence of T2DM in youth has increased dramatically over the past 20 years. T2DM now accounts for 8-45% of all new cases of diabetes reported among children and adolescents in the US. (11) In the US, among youths 19 years or younger, 588 out of 1.73 million had T2DM in 2001, 814 of 1.85 million had T2DM in 2009, and 1230 of 1.85 million had T2DM in 2017. The estimated T2DM prevalence per 1000 youths aged 10 to 19 years increased significantly from 0.34 (95% CI, 0.31-0.37) in 2001 to 0.46 (95% CI, 0.43-0.49) in 2009 to 0.67 (95% CI, 0.63-0.70) in 2017, an absolute increase of 0.32 per 1000 youths (95% CI, 0.30-0.35) and a 95.3% (95% CI, 77.0%-115.4%) relative increase over 16 years. (5) The greatest absolute increases were observed among non-Hispanic Black (0.85 per 1000 youths [95% CI, 0.74-0.97]) and Hispanics (0.57 per 1000 youths [95% CI, 0.51-0.64]) (5).

In a recent overview of country-specific differences in epidemiology data of T2DM, the highest reported prevalence rates of youth-onset T2DM in China (520 cases/100,000 people) and the USA (212 cases/100,000) and the lowest in Denmark (0.6 cases/100,000) and Ireland (1.2 cases/100,000). Nevertheless, the peak incidence rates were found in Taiwan (63 cases/100,000) and the UK (33.2 cases/100,000), with the lowermost in Fiji (0.43 cases/100,000) and Austria (0.6 cases/100,000). These differences in epidemiology data may be partly explained by variations in the diagnostic criteria used within studies, screening recommendations within national guidelines, and race/ethnicity within countries. (9) The global trend of age-standardized of T2DM from 1990 to 2017 in 195 countries, increased from 228.5 (213.7–244.3) to 279.1 (256.6–304.3) for incidence, from 4,576.7 (4,238.6–4,941.9) to 5,722.1 (5,238.2–6,291.0) for prevalence respectively. (12) In addition, the trends of the incidence rate of T2DM are rapidly increasing in Brazil, Russia, India, China, and South Africa (BRICS). (1990: 2015) (13)

The SEARCH study is a national multi-center study in the US using 5 search study Centers, each located in one of five states (CA, CO, OH, SC, and WA) (2002-2014) reported the different incidences in variable ethnic groups. The incidence rates in 2012 were 3.9 per 100,000 for non-Hispanic White youth, 32.6 per 100,000 for non-Hispanic Black youth, 18.2 per 100,000 for Hispanic youth, 12.2 per 100,000 for Asian/Pacific Islander youth, and 46.5 per 100,000 for Native American youth. (5) The greatest adjusted annual increases were among Asian/Pacific Islander youth (8.5 %) and Native American youth (8.9 %), although there were significant increases in incidence rates from 2002-2003 through 2011-2012 among all groups except for non-Hispanic White youth. American Indians have the highest rates of youth-onset T2DM in the US. (14)

In 2020, according to the Centers for Disease Control (CDC), among US children and adolescents aged 10 to 19 years, the overall incidence of T2DM significantly increased between 2002 and 2015 period. During the 2002–2010 and 2011–2015 periods, changes in the incidence of T2DM were consistent across race/ethnic groups. Specifically, the incidence of T2DM remained stable among non-Hispanic whites and significantly increased for all others, especially non-Hispanic African Americans. (15,16)

In addition, it has been demonstrated that Hispanic American children demonstrated early risk factors for metabolic syndrome (MetS), including high levels of body mass index, insulin, glucose, triglycerides, and systolic blood pressure, as well as lower HDL cholesterol. African American children had a greater risk for T2DM, with lower insulin sensitivity and higher insulin secretion than White children, after controlling for body mass index and/or visceral fat accumulation. (17)

Data from the UK indicated the importance of racial and ethnic differences as the incidence of T2DM in black children and adolescents in England was higher (3.9 per 100,000) versus whites (0.35 per 100,000) based on data from 2004-5. (18, 19) In Canada, a total of 396 adolescent participants representing 3 ethnic groups were screened for prediabetes and T2DM (European, Filipino, and Indigenous). The study indicated statistically significant differences in terms of ethnicity. The adolescents from the Filipino group had increased HbA1c levels and were 3.13 times higher compared to the Indigenous group *and* 7.50 times higher than the European group. (20)

In Australia, Australia's Aboriginal and Torres Strait Islander children and young people are at much higher risk of T2DM than non-Indigenous children and young people. Studies in WA and NSW have reported the incidence of T2DM in Indigenous children and adolescents to be more than 6 times that in the non-Indigenous population. In NSW in 2001–08, the incidence of T2DM among Indigenous people 10–18-year-old was 13 per 100,000. (21)

3.5. Epidemiology of factors associated with higher risk to develop dysglycemia

3.5.1. Family History (genetics versus environmental effects)

Children with a family history of T2DM have a disproportionately higher prevalence of T2DM. (22) One-half to three-quarters of children and adolescents with T2DM have at least one affected parent. Data from the TODAY study (a multicenter, randomized clinical trial for investigating Treatment Options for T2DM in Adolescents and Youth) showed that 60% of study participants had a positive family history of diabetes in a first-degree relative, while 89% had a positive family history of diabetes with the addition of grandparents. (23) Genetic predisposition, as well as aging, contribute to epigenetic variability, and several environmental factors, including exercise and diet, further interact with the human epigenome. The reversible nature of epigenetic modifications holds promise for future therapeutic strategies in obesity and T2DM. (24)

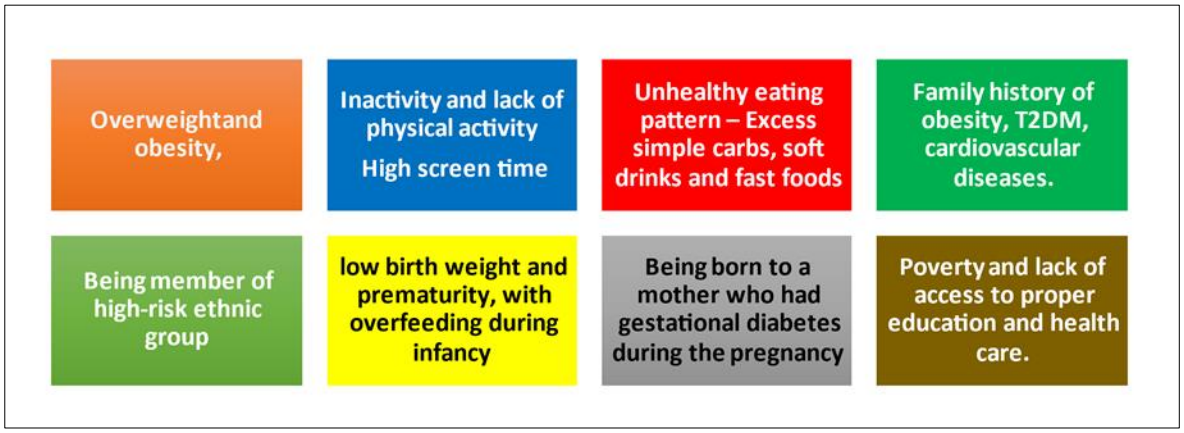


Figure 1 Risk factors That markedly increase the risk to develop T2DM

3.6. Overweight and Obesity: link with prediabetes and T2DM

Between 2017-2018, the prevalence of Childhood Obesity in the US was 19.3% and affected about 14.4 million children and adolescents. Obesity prevalence was 13.4% among 2- to 5-year-olds, 20.3% among 6- to 11-year-olds, and 21.2% among 12- to 19-year-olds. (25) T2DM is frequently linked to obesity, and its increasing prevalence has grown in parallel with the global childhood obesity epidemic. In a registry study from the US, nearly 80 percent of youth with T2DM were obese and an additional 10 percent were overweight. (8) Being overweight and obese are major acquired contributors to the development of T2DM due to their association with impaired insulin action. A longitudinal study on 547 children and adolescents with prediabetes found a linear relationship between worsening BMI and progression to T2DM. (26) On the other hand, in high-risk patients with prediabetes and/or metabolic syndrome, weight loss effectively improves blood glucose levels, prevents progression to T2DM, and improves cardiovascular risk factors. (27) In addition, people with T2DM who decrease their BMI to be within a moderate range can reverse their diabetes by losing weight. Two-thirds of the participants found that their T2DM went into remission and could stop taking their medication. (28) The association between obesity and T2DM is even stronger in youth than in adults because during puberty the tissues have more resistance to insulin actions. (29)

In the US, the prevalence of prediabetes state was assessed in a multiethnic cohort of 167 obese children and adolescents. Prediabetes was present in 25 percent of the 55 obese children (4 to 10 years of age) and 21 percent of the 112 obese adolescents (11 to 18 years of age). (30) In a large cohort multicenter European observational study on obese children and adolescents (n = 4932*, males* = 2481*, mean* age 12.9 ± 2.7 years), the prevalence of prediabetes and T2DM was 11.9%. (31) Another study on obese children in the Arab Gulf area (n = 748, aged 11–17 years) showed a prevalence of prediabetes in 5.7% and T2DM in 1.1 % of them. (32) In a large Cohort study from India, the prevalence of pre-diabetes/diabetes was 12.3% and 8.4% among adolescent boys and girls, respectively. In adolescents, the two most important predictors of prediabetes were body mass index and Subscapular skinfold thickness.

Collectively, these data support the strong epidemiological link between obesity, prediabetes, and T2DM in children and adolescents. (33) However, the available epidemiological data suggested that the overall incidence of T2DM in adolescents had not increased as sharply as the increases in obesity in the same age group. This can be explained by a substantial latency period between the onset of obesity and the related risk for T2DM. Consistent with this theory, studies have shown sharp increases in T2DM among young adults. Thus, the rates of obesity among adolescents may

cause a modest increase in T2DM but a more substantial increase in T2DM when the cohort reaches adulthood. (34) In conclusion, appropriate and early detection, prevention, and management of childhood obesity appears to be one of the most important targets that can greatly decrease the risk of adolescent and adult obesity and T2DM.

3.7. Gender and age effects

In the US, females are 1.3 to 1.7 times more likely than males to develop T2DM during adolescence. This may be related to an increased risk of insulin resistance during adolescence. (35) In a study from the US, (2013-14, n = 500 under the age of 25) T2DM occurred more in females (60-70%). (36) However, in China no statistically significant difference in incidence was found between boys and girls (37). Many patients with pediatric T2DM present at the onset of puberty (mean age of 13.5 years), a stage of development when there is physiologic insulin resistance as well as increased weight. Approximately 40 % of pediatric cases occur between 10 and 14 years of age and the remaining 60 % are between 15 and 19 years. (38) Therefore, it is important to give special interest to age and gender during screening for prediabetes and T2DM.

3.7.1. Socioeconomic status, income, and education level

Socioeconomic factors are important factors linked to obesity, physical inactivity, smoking, and low birth weight, that represent risk factors for T2DM. (39-44) The Socioeconomic status (SES), as determined by income, education, and employment among other factors, is the primary social determinant of health impacting youth and families living with T2DM.

Globally, many populations at high risk for youth-onset T2DM also have high rates of poverty and low parental educational attainment. Youths who experienced poverty at some point from childhood through adolescence were 1.67 times (95% CI = 1.27, 2.20) more likely to become obese for the first time by age 15.5 than those who were not poor during this period. (39) A negative association between parental education and child physical activity was detected in lower economic status countries. Children who had a parent with a high school education or less and were either overweight or obese were 80% more likely to develop overweight or obesity compared with children whose parents did not meet these criteria (OR = 1.8, 95% CI, 1.37-2.37). (40)

In Western cultures, these factors (poverty, lack of education, unemployment) are related to low socioeconomic status. Thus, an inverse relationship would be expected between the prevalence of T2DM and socioeconomic status. (12) A large study described a significant inverse relation between glucose intolerance and grade of employment. (41)

On the other hand, in the Middle East, T2DM in youth has a considerably high incidence in countries with considerably high income (oil-rich countries). In Kuwait, the incidence rate of T2DM in youth was 2.65 per 100,000 and in Qatar, the incidence rate was 2.72 per 100,000 in 2016. These can be due to the sedentary lifestyle, high incidence of obesity in adults, bad dietary habits, and big consumption of high-calorie fast food, in children and adolescents in these countries. (45, 46)

In summary, T2DM is now considered a disease initiated by environmental factors in a genetically susceptible host. The environmental triggers appear to be obesity, the worldwide epidemic of modern living, leading to insulin resistance, and unmasking of genetic or acquired defects in the complex machinery of normal insulin secretion which led to relative insulin deficiency inadequate to overcome the degree of resistance, but which respond to various oral agents. (7,17)

3.8. Screen time

In adults, higher screen time is related to a higher risk to develop T2DM. In children, a large cohort (4495 children aged 9–10 years) compared an hour or less screen time daily to those reporting screen time over 3 hours. The latter group had higher skinfold thickness (4.5%, 0.2% to 8.8%), fat mass index (3.3%, 0.0% to 6.7%), leptin (9.2%, 1.1% to 18.0%) and insulin resistance (10.5%, 4.9% to 16.4%). These data suggested that reducing screen time could facilitate early T2D prevention. (47)

3.9. Birth size: Link to obesity, MetS and obesity

Children born small for gestational age (SGA) are known to have a higher risk to develop T2DM in later life. (48-50) Studies showed a link between fast postnatal catch-up growth in weight and length and higher risk of developing T2DM later in life. (50-53)

On the other hand, children who were born large for date (LGA) have significantly a higher risk to develop obesity and MetS in early childhood, especially those born to mothers with gestational diabetes or pre-existing T2DM. In these

children breast-feeding was associated with a lower risk of being overweight/obese in childhood in most children. (53-55)

3.10. Relation between Diet and T2DM in children

A strong association was suggested between the occurrence of T2DM and the high intake of carbohydrates and fats. Several studies have reported a positive link between increased intake of sugars and development of T2DM. (56)

Ludwig et al investigated more than 500 ethnically diverse schoolchildren for 19 months. They found that for each additional serving of carbonated drinks consumed, the frequency of obesity increased, after adjusting for different parameters such as dietary, demographic, anthropometric, and lifestyle. (57) A link between the intake of soft drinks with obesity and diabetes, was explained by the large amounts of high fructose corn syrup and glycated chemicals used in the manufacturing of soft drinks, which raises blood glucose levels, insulin resistance and BMI to the unsafe levels. (57, 58) In a Japanese study, a large intake of rice was associated with a higher risk to develop T2DM. (59)

A systemic review summarized (53 studies) the evidence of associations between dietary factors and incidence of T2DM. They reported that the quality of evidence was rated high for an inverse association for T2DM incidence with the increased intake of whole grains (for an increment of 30 g/day, adjusted summary hazard ratio 0.87 (95% confidence interval 0.82 to 0.93)) and cereal fiber (for an increment of 10 g/day, 0.75 (0.65 to 0.86). Quality of evidence was also high for the association for increased incidence of T2DM with higher intake of red meat (for an increment of 100 g/day, 1.17 (1.08 to 1.26)), processed meat (for an increment of 50 g/day, 1.37 (1.22 to 1.54)), bacon (per two slices/day, 2.07 (1.40 to 3.05)), and sugar-sweetened beverages (for an increase of one serving/day, 1.26 (1.11 to 1.43)). (60)

In overweight and obese adolescents, seven dietary interventions were randomly assigned to participants based on weekly or bi-weekly dietary counseling sessions over a 12-24-week period. Four interventions, with energy restriction and/or change to carbohydrate consumption, showed significant reductions in fasting insulin and insulin resistance levels relative to baseline concentrations ranging from 26 to 50%. (61).

4. Interventions based on epidemiological data:

These epidemiological data necessitate an urgent need for active national and international evidence-based intervention methods for preventing T2DM. These interventions start with screening, especially in the high-risk groups to detect obesity, prediabetes, and asymptomatic T2DM. (36, 62,63) This shall be followed by a population-based approach for prevention and management of these 3 conditions including the application of lifestyle intervention programs, following well-studied guidelines for pediatric nutrition, physical activity, and screen time published by the different scientific bodies (CDC, ADA, IDF, and American Academy of Pediatrics (AAP). (38, 64-69) Proper antenatal care for mothers and control of gestational diabetes and weight gain during pregnancy can decrease the occurrence of LGA and SGA. (69) Appropriate nutritional management of children born SGA to prevent rapid catch-up may decrease the risk of developing obesity and MetS later in life. (49-51) Encouraging breast-feeding and prevention of infantile and early childhood obesity can reduce adolescent and adulthood obesity and dysglycemia. (70-73) There is good evidence that signifies the preschool years as an important opportunity to prevent overweight or obesity. (74) In addition, encouraging and increasing health education programs (families, schools, social clubs, and media) to raise the consciousness of healthy diet and lifestyle patterns in children and adolescents is an important step to prevent obesity and T2DM. (75)

5. Genetic variants associated with T2DM

Utilizing genetic variants as instrumental variables for an exposure, Mendelian randomization (MR) analysis can strengthen the causal inference on an exposure–outcome association. (76) A wide-angled Mendelian randomization (MR) study was conducted to identify the causal risk factors for T2DM. The authors made a metanalysis and identified 97 risk factors with available genetic instrumental variables which were included in MR analyses. After Benjamini–Hochberg adjustment, among these exposures they detected that 11 were associated with an increased risk of T2DM. Among these factors were childhood, increased BMI, body fat percentage, visceral fat mass, systolic BP, insomnia, dietary sodium intake, smoking, insomnia and short sleep duration and poor sleep quality, plasma, and liver alanine aminotransferase. Eight exposures were inversely associated with T2DM (protective). Among them were high education level, birthweight, adulthood height, HDL- and total cholesterol. (77).

6. Conclusion

Incidence and prevalence rates of T2DM in children and adolescents have increased over the past 20 years and are commonly associated with obesity. The increasing prevalence of T2DM paralleled increases in the worldwide childhood obesity epidemic. Both obesity and prediabetes are two major risk factors for developing T2DM. T2DM in youth is characterized by rapid progression with early occurrence of related complications compared to adults. It often occurs in overweight or obese patients and from a minority group (Native Americans, Blacks, and Pacific Islanders). It is asymptomatic in a third of adolescent patients. Adolescents and children with T2DM often have other existing co-morbidities such as high blood pressure, high blood lipids, and fatty liver which markedly increase the cardiovascular risk in these patients. The families of adolescents with T2DM often have lifestyle risk factors leading to obesity. Early detection of obesity and prediabetes especially in high-risk populations is highly recommended through proper screening. Intervention studies in obese infants and children and those with prediabetes proved partially successful in reducing the incidence of developing T2DM. Over the coming years, randomized controlled trials are needed to test the effects of different forms of lifestyle intervention (as the primary preventive measure) with and without the help of new medications in the prevention of T2DM or reducing its incidence.

Compliance with ethical standards

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Disclosure of conflict of interest

Authors have no conflict of interest with products that compete with those mentioned in their manuscript.

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