Epidemiologic characteristics of Type 2 Diabetes in adolescents in Kazakhstan

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Abstract

The project focuses on analyzing epidemiologic characteristics of Type 2 Diabetes in adolescents between the ages of 10 and 17 in Kazakhstan, as incidence rate of this disease among younger generation has been growing progressively lately and its epidemiology has not been studied in-depth yet. The project will implement mainly descriptive statistics and use the Unified National Electronic Health System to provide the data. By examining the data from Kazakhstan and making comparison with the worldwide statistics, it will be possible to figure out the demographic situation and reasons of increased early Type 2 Diabetes occurrence. Moreover, it will provide the insight of how good Kazakhstani healthcare system at monitoring Type 2 Diabetes and what improvements can be done.

Introduction

Diabetes mellitus (DM) is a condition when there are high blood sugar levels (hyperglycemia) and damaged metabolism of such essential nutrients as carbohydrates, proteins and lipids, which can be caused by impaired insulin secretion. There are two types of diabetes: insulin-dependent diabetes mellitus (type 1 diabetes mellitus, T1DM) and non-insulin-dependent diabetes mellitus (type 2 diabetes mellitus, T2DM). The causes constitute the major difference between two forms of diabetes. T1DM develops when the immune system of a person starts attacking its own cells, to be more specific, the beta cells in the pancreas that are responsible for insulin production. Therefore, pancreas stops making enough insulin, which disturbs the regulation of glucose spikes in the blood. On the other hand, type 2 diabetes is associated with decreased insulin secretion and increased resistance of the cells to the insulin's action [Sanghera, Blackett, 2012].

Globally, it is reported that more than 90% of the cases is type 2 diabetes and the other 10% account for type 1 diabetes, so T2DM is more prevalent than T1DM. In general, T2DM is one of the most widespread diseases in the world that people develop during their lifetime. The most common reasons are poor diet, sedentary lifestyle, lack of exercise, work-related stress, such bad habits as smoking and alcohol consumption. According to the Worldwide Health Organization (WHO), excess weight and obesity are the major risk factors that lead to fast progression of T2DM. Moreover, consumption of processed foods and saturated fats, that are now more available than whole meals, increase the risk of developing the disease [Wu Y, Ding Y, et al., 2014]. However, people manifest the disease not only because of lifestyle-related and environmental factors. Research shows that multiple complex genetic causes are also involved in this case. Epigenetics that encompass such processes as DNA methylation and histone modification give insight into how genes can cause obesity and type 2 diabetes. Studies on target tissues such as pancreatic islets, skeletal muscles and adipose tissue of people with T2DM demonstrate that the cells of these tissues express increased DNA

methylation of crucial genes that are responsible for normal insulin secretion and glucose regulation because of elevated glucose levels and glycated hemoglobin [Ling, Ronn, 2019]. Furthermore, parental obesity or maternal diabetes can affect the child's metabolism and alter DNA methylation patterns leading to inheritance of the disease. Epigenetics also demonstrate a link between the environment and the genes. Investigation on how environmental factors influence gene expression allowed uncovering the methods of prevention and treatment. Thus, the good news about type 2 diabetes is that the most of the risk factors are modifiable unlike with type 1 diabetes. Patients with T1DM have to take injections of insulin to ensure their survival, but people with T2DM can achieve a more sustainable living by integrating healthier diet, starting to do exercises of moderate intensity, quitting such bad habits as smoking and alcohol consumption, and practicing quality sleep.

As it was mentioned, diabetes is one of the most widespread diseases and is the reason of many other medical conditions such as kidney failure, heart attacks, blindness and limb amputation. All mentioned complications lead to increased morbidity and mortality rates among affected individuals. This makes the disease even more dangerous and brings greater financial and emotional burdens to the families, as the treatment of the disease takes time, energy and involves huge expenditures. Only in 2017, 374 million people had impaired glucose tolerance (IGT) and the number of deaths because of diabetes reached 5 million. It was estimated that this number will go up to 587 million by 2045 [Cho, et al., 2018]. However, it seems that the world will amount to this number much earlier, because, according to the data of 2020, more than 460 million people already suffered from type 2 diabetes worldwide, which was about 6.8% of the world's population. Moreover, if in 1990s T2DM was on the eighteens place among the causes of death, now it is on the ninth place, leading to more than 1 million deaths each year [Khan, Hashim, et al., 2020]. The disease is getting more global and deadly each year, which raises significant concerns. It should be also taken into account that half of the adults with T2DM are undiagnosed and the number of affected people might be even higher than it was

previously estimated. Furthermore, undiagnosed and untreated diabetes can lead to even more severe complications and increased fatality rates. However, there is another concern related to the early-onset of T2DM. For many years T2DM was considered as an adult disease, as it develops due to a long-term insulin resistance and damaged insulin secretion, but now statistics demonstrate that the growing number of children and adolescents become affected by the disease. For instance, in the USA, the proportion of youth diagnosed with T2DM made up about 3% of all cases, but in the 2000s the percentage increased up to 20%, and reached 30% in the early 2010s [Ivy Lee Jia Jia, et al., 2024]. The prevalence of T2DM increased 2.5 fold between 2005 and 2010 in China and 10-fold between 2008 and 2019 in Israel. Such countries and regions as Canada, South Asia, Near and Middle East, South America and Australia report a similar concerning escalation in the number of cases among young generation [Bjornstad, Chao., et al, 2023]. This leads to the main question of why people acquire the disease at much earlier age than before.

Puberty is considered as one of reasons, as diabetes is more common in adolescents between the ages of 10 and 19, when they undergo puberty. During puberty adolescents experience hormonal changes: growth hormone, cortisol and such sex hormones as testosterone and estrogen rise and cause physiological insulin resistance which is actually a normal process during growth of a young organism. However, while the pancreas of healthy adolescents is able to produce more insulin in order to compensate the resistance, children with higher risks of developing T2DM, due to family history, particular medical conditions, obesity, demonstrate beta-cell dysfunction which prevents normal insulin compensation and leads to higher sugar levels in the blood. Nevertheless, recent rapid increase of type 2 diabetes among youth cannot be explained by the single factor of puberty or the factors related to genetics and sex. Rather, the environmental factor related to obesity plays even more important role. Harmful eating habits and lack of physical activity lead to accumulation of fat around internal organs (visceral fat). Visceral fat influences greatly regulation of hormones and metabolism

by releasing pro-inflammatory adipokines and inducing lipotoxicity [Ivy Lee Jia Jia, et al., 2024]. All these biological processes combined elevate insulin resistance and increase the risk of T2DM, which becomes especially evident during puberty.

It should be noted that there are differences of T2DM distribution not only by the age, but also by race, ethnic group, socio-economic status of the region. For instance, the vast majority of cases (79%) contribute to the low and middle income countries. The study on the global burden of T2DM published in 2017 demonstrates the disparities between the countries of Europe, Asia, America and Africa. According to their data, China (88.5 million individuals with type 2 diabetes), India (65.9 million), and the US (28.9 million) maintain the top positions due to the largest population sizes and rapidly developing fast-food industry. The European countries follow the list, because despite highly-developed healthcare system and high availability of medication, these countries demonstrate high level of urbanization associated with processed high-calorie foods and sedentary lifestyle [Khan, Hashim, et al., 2020]. Regarding youth population, the distribution shows similar patterns, as a greater number of young people with T2DM have African-American, Hispanic, Asian-Pacific, American-Indian roots. Specific parts of Canada and the US demonstrate higher incidence rates of diabetes among youth, as they contain larger proportion of Indigenous population. For example, average African-American child of 7 to 11 years old suffer from notably high insulin levels compared to their white peers [Reinehr, 2013].

Regarding the situation in Kazakhstan, the study on prevalence of T2DM in Kazakhstan based on random sampling and published in 2022 estimated that there were about 1.4 million Kazakhstani with T2DM, while the government estimated that there were only about 423 thousand people with the disease that year. The study reveals that the governmental estimations are quite low and that a large proportion of people in the country go undiagnosed which poses a great danger to their lives. Moreover, as the authors mention one of the greatest limitations in studying T2DM in Kazakhstan are

connected to the missing data about physical activity, dietary habits, and other medications of the participants, which complicates making final conclusions on the matter. In addition, the study compared rural and urban cases and confirmed that the fast urbanization in the cities is one of the leadings causes of growing obese population, as rural population is less likely to suffer from newly diagnosed T2DM [Orazumbekov, Issanov, et al., 2022]. Unfortunately, there are not enough papers and researches on epidemiology of type 2 diabetes among adults in Kazakhstan, let alone about children and adolescents. Therefore, it is even more crucial to study the cases of young population, as they are the future of the country and revealing the problem at its roots is essential to prevent the spread of the disease. Moreover, making comparisons between Kazakhstan and other countries might demonstrate what strategy the government and healthcare system should implement to improve the situation.

Specific aim(s):

1. To describe and assess incidence rate of Type 2 Diabetes in adolescents in Kazakhstan
2. To describe epidemiological characteristics of adolescence with T2DM in Kazakhstan
3. To describe comorbidities of Type 2 Diabetes in adolescents

Hypotheses:

1. Rising incidence rates of Type 2 Diabetes in adolescents in Kazakhstan is associated with the increasing prevalence of obesity, poor diet and sedentary lifestyle.
2. The incidence rate of Type 2 Diabetes among adolescents in Kazakhstan is lower than in the USA and China, but higher than in most European countries.

Methods and materials

Study population

This retrospective cohort study focused on Type 2 Diabetes mellitus in adolescents aged between 10 and 17 in Kazakhstan. The data was obtained from the Unified National Electronic Health System (UNEHC) and included socio-economic and clinical records of patients who registered in the UNEHC between 2014 (January 1) and 2021 (December 31). T2DM diagnoses were identified using the International Classification of Disseases, ICD-10 codes, specifically E11.x.

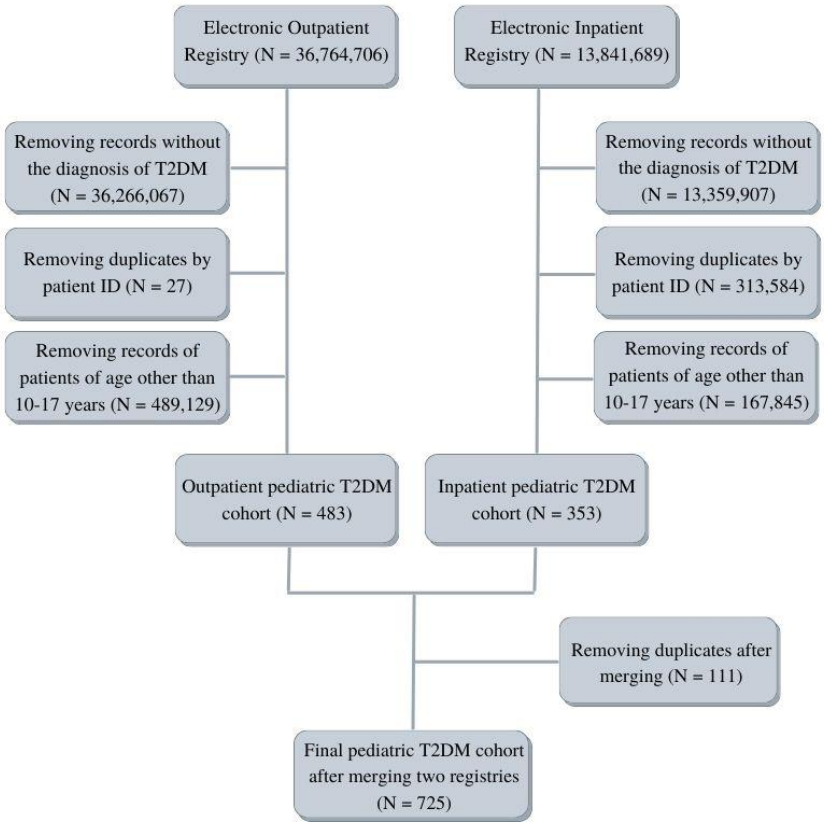

Figure 1. Flowchart of cohort selection of adolescents with T2DM registered in UNEHS in 2014-2021

As it is shown in Figure 1, the UNEHC data consisted of electronic outpatient registry and electronic inpatient registry, with 36,764,706 and 13,841,689 patients, respectively. After excluding records without a T2DM diagnosis, duplicates identified by patient ID and records of patients of age

other than 10-17 years old from each registry, two major cohorts were formed: the outpatient pediatric T2DM cohort and the inpatient pediatric T2DM cohort, with 483 and 353 patients, respectively. Then two groups were merged with consequent removal of duplicates which gave the final pediatric T2DM cohort consisting of 725 patients. Then this data was used to analyze the epidemiologic situation of T2DM among adolescents in Kazakhstan.

Exposures and covariates

Records of patients collected from the UNEHC database included the following information: birthdate, region, sex, age, dates of admission and discharge, date of diagnosis, ICD-10 codes for main diagnosis and comorbidities, and other data. Age was categorized into two groups: 10-13 years and 14-17 years. Ethnicity was classified as Kazakh, Russian, and Other (which included Uzbek, Ukrainian, Tatar, and more). The following comorbidities were included: coronary heart disease (CHD), arterial hypertension, stroke, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, neoplasms, diabetic foot, and amputations.

Statistical methods

For each year of follow-up between 2014 and 2021, incidence rates per 100,000 population were estimated for T2DM patients by dividing the number of incident cases in a year by Kazakhstan's total population of ages 10-17 years in that year. The population parameters of Kazakhstan were obtained from the Statistics Committee.

Categorical variables, including age category, sex, ethnicity, residence, all-cause hospitalizations, all-cause death, and complications were summarized as frequencies and percentages.

All statistical analyses were performed by using the software for statistical computations called IBM SPSS Statistics.

Results

Patients' characteristics

A cohort of 725 children and adolescents with T2DM during the given period was identified in the study. The frequencies and percentages of some descriptive characteristics are summarized in Table 1.

To be specific, sex distribution was nearly equal, 383 female and 342 male patients. The cohort was divided into two categories with the majority of patients belonging to the 14-17 age category. The minimum age was 10 years and the maximum was 17 years. In regards of ethnic distribution, the number of Kazakh people was the most prevalent, comprising 58.20% of the cohort, followed by the Russian group (19.20%) and Other ethnicities (22.60%). In terms place of residency, urban residents accounted for twice as many cases as those from rural areas. And place of residence of 50 patients remained unspecified.

The number of hospitalized patients was almost the same as the number of patients who were not admitted to the hospital, 357 and 368, respectively. The number of alive patients constituted 713 adolescents (98.30%), while the number of deceased patients was 12 (1.70%). Regarding the complications during T2DM, the most common were retinopathy (14.60%), neuropathy (12.10%), and diabetic foot (6.60%), while the least observed were neoplasms (2.60%) and stroke (0.30%).

Table 1. Baseline characteristics of adolescents with T2DM registered in UNEHS in 2014-2021

	Number of patients	*Percentage*
Total	725	100.00
Age category		
10-13 years	298	41.10
14-17 years	427	58.90
Sex		
Female	383	52.80
Male	342	47.20
Ethnicity		

Kazakh	422	58.20
Russian	139	19.20
Other	164	22.60
Residence		
Urban	465	64.10
Rural	210	29.00
Not specified	50	6.90
All-cause hospitalization		
No	368	50.80
Yes	357	49.20
All-cause death		
No	713	98.30
Yes	12	1.70
Complications		
Hypertension	30	4.10
Retinopathy	106	14.60
Nephropathy	35	4.80
Neuropathy	88	12.10
Diabetic foot	48	6.60
Neoplasms	19	2.60
Stroke	2	0.30
Amputations	0	0.00

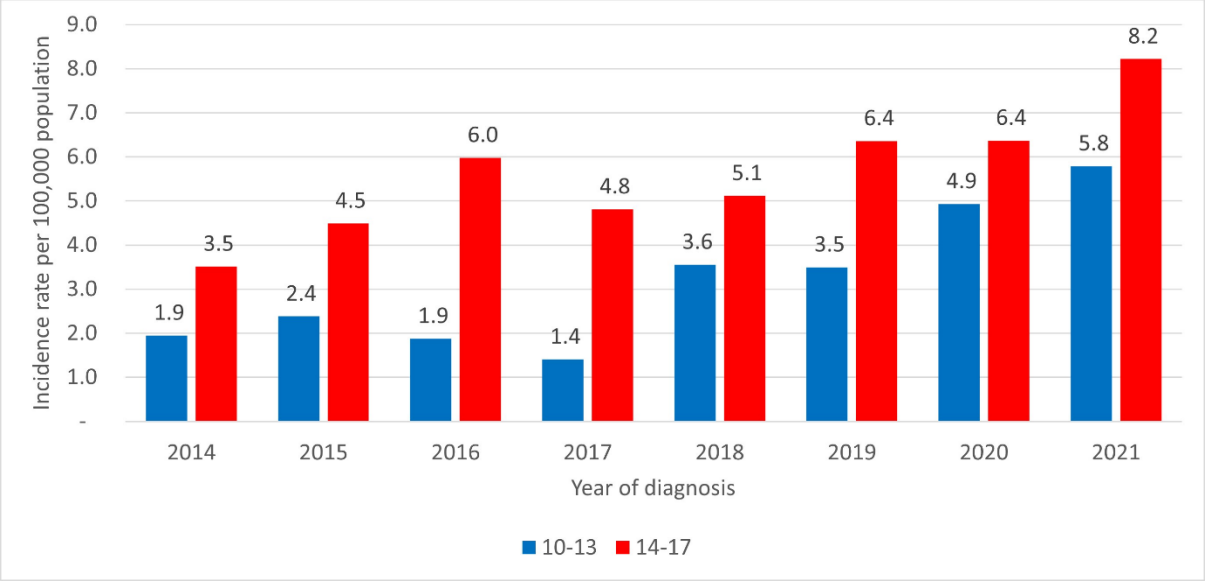

Figure 2. Incidence rates per 100,000 population stratified by age & year of T2DM diagnosis.

Over the study period, the general trend of the incidence rate stratified by age and year of diagnosis (Figure 2) implies increase from 2014 to 2021. The number of patients aged 14-17 had higher incidence rate than the patients aged 10-13 in all years of T2DM diagnosis. Notably, the incidence rate for the 14-17 age group increased drastically from 4.5 to 6 in 2016, but then suddenly decreased to 4.8 in 2017. The following years a continuous increase was observed, reaching the highest value of 8.2 in 2021. As for the 10-13 age category, the incidence rate was decreasing gradually from 2015 to 2017. However, after almost a double increase in 2018 from 1.4 to 3.6, the incidence rate only kept rising, reaching the highest value (5.8) as well in 2021.

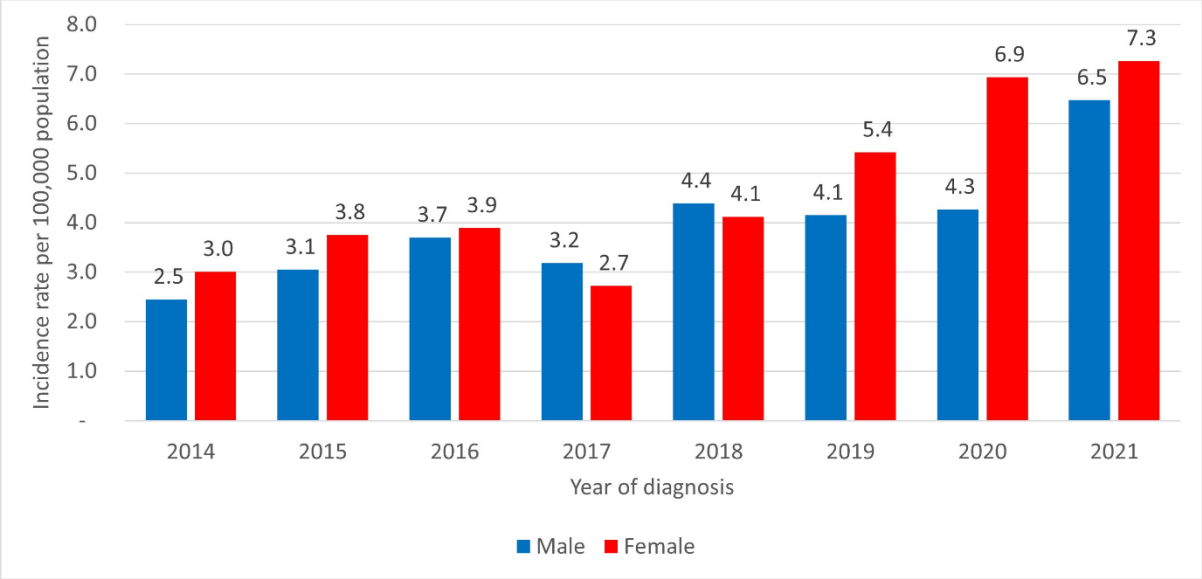

Figure 3. Incidence rates per 100,000 population stratified by sex & year of T2DM diagnosis.

According to the incidence rate stratified by sex and year of diagnosis (Figure 3), across almost all years, nearly equal proportion of males and females among adolescents were diagnosed with T2DM. The notable difference was observed in 2020, when the incidence rate for males was 4.1 and for females 6.9. It should be noted that most of the years the incidence rate for females was, albeit slightly, higher than that of males.

Discussion and conclusions

This capstone project analyzed the epidemiologic situation of type 2 diabetes mellitus (T2DM) in Kazakhstan among 725 adolescents aged between 10 and 17 years old by using national healthcare data of 2014-2021 period. It also examined the incidence rates stratified by age and sex, demographic factors, and comorbidities. The observed trends now will be compared to the global findings.

The average incidence rate of T2DM in Kazakhstan among adolescents of 10-13 years old between 2014 and 2021 was 3.2 cases per 100,000 population, which was significantly lower than among adolescents of 14-17 years (5.6 per 100,000). These findings align with the international data showing that the disease is more spread among older children due to puberty, lifestyle and physical changes.

In general, Kazakhstan fits into the middle range among other countries. For instance, Canada conducted a national surveillance study on the incidence rates of T2DM between April 2006 and March 2008. The survey showed that the minimum incidence rate of T2DM among children younger than 18 years was 1.54 cases per 100,000 population per year. Furthermore, in average, the incidence rate for Europe and the United Kingdom (UK) is 0.6 – 1.4 per 100,000 [Shah, Zeitler, et al, 2022]. On the other hand, the International Diabetes Federation reported that Near and Middle East region has the highest prevalence and incidence rates of T2DM. For example, Kuwait has the incidence rate of 8.0 cases per 100,000 people aged 10-14 years, which is significantly higher than the incidence rate in Kazakhstan in the same age category (3.2 cases). Libya demonstrates lower incidence rates in the same age group (1.8 per 100,000 people), but the incidence rate among 15-19 years old adolescents is almost the same (5.9 cases per 100,000) as in Kazakhstan [Bjornstad, Chao., et al, 2023]. Thus, these international values confirm that Kazakhstan's incidence lies between high-income Western countries and Middle Eastern areas with weaker economic growth.

Sex differences were not so evident in this study, but females demonstrated slightly higher results than males. The average incidence rate of T2DM was 3.9 cases per 100,000 for males and 4.6 cases per 100,000 for females. These findings are consistent with the data from Japan, where the prevalence ratio of girls to boys is 1.2:1. On the other hand, prevalence ratio of girls to boys among youth is 6:1 for First Nations in Canada, 5:1 for Pima Indian, and 3:1 for Mexican American [Shah, Zeitler, et al, 2022].

On the contrast to sex differences, there was an evident disparity between urban and rural disease reports. A higher percentage of T2DM cases in urban regions compared to rural areas might reflect the effect of urbanization, sedentary lifestyle, and availability of processed food, as studies conducted worldwide demonstrate similar observations. According to a 2015 study, the incidence rate of T2DM among children under 17 was 2.92 cases per 100,000 for Asian children, 1.67 for Black children, and 0.44 for White children [Bjornstad, Chao., et al, 2023]. In Kazakhstan, Kazakhs were the most affected population, followed by Russians and other ethnicities. Even if the data mostly reflects the ethnic composition of the country, it also shows to the global trend when Asians are more likely to develop T2DM. This suggests further need of examining the potential genetic risks of early onset of the disease.

Furthermore, it was found out that retinopathy (14.60%), neuropathy (12.10%), and diabetic foot (6.60%) were the most frequent comorbidities in the study, while worldwide studies show that T2DM patients are more prone to develop hypertension, cardiovascular complications, lipid disorders, and microvascular diseases. One of the key studies on youth-onset TDM on a global level was the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) trial. The study demonstrated that DM-related complications develop early and progress fast. Compared to T1DM the neuropathy scores and macrovascular complications were increased in young patients with T2DM. Moreover, the number of cardiovascular deaths was also increased. In general, all this data presents a poorer prognosis for patients with early-onset T2DM.

Despite the strengths of the study such as in-depth description of the demographic characteristics of youth-onset T2DM, one of the major limitations is that the data does not have laboratory findings and analyses. With more information about blood analyses, BMI and other biological tests, the study would be even more accurate in comparisons and estimations of the current situation. Thus, the reliance on secondary data, which lacked detailed information about physical activity, family history and dietary behavior, posed some challenges and made it impossible to prove or disprove one of the hypotheses stated in the beginning. The intention was to estimate the effect of the obesity and lifestyle behaviors on T2DM incidence. Moreover, some missing data in the UNEHC might have led to underestimation of the situation and incidence rates.

In conclusion, the increasing trend of T2DM among adolescents in Kazakhstan is a concerning issue that reflects one of the latest global patterns and requires further research and actions to prevent worse consequences. To reduce the early onset of DM-related complications and disparities in urban regions, public health organizations should stress the importance of early screening, health education, regulation of dietary habits and lifestyle patterns among adolescents. Future research should focus on evaluation of the effectiveness of different preventative methods.

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