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Epidemiology of type 1 diabetes mellitus in children in Kazakhstan: Data from unified national electronic health system 2014-2021

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ABSTRACT

The epidemiology of type 1 diabetes mellitus (T1DM) in children aged 0-17 in Kazakhstan was explored using aggregated large-scale healthcare data from the unified national electronic health system (UNEHS) in 2014-2021. Incidence, period prevalence, and mortality rates per 100,000 population at risk were calculated. Cox proportional hazards regression modelling and Kaplan-Meier methodology were used. The follow-up period was from the initial date of T1DM until death or the end of the follow-up (31 December 2021). Among the 11,088 patients, the incidence rate of T1DM decreased from 28.1 to 24.5 per 100,000 population, whereas the period prevalence rate increased from 48.8 to 179.1, and the mortality rate rose from 0.18 to 0.67. Diagnosis at age 0-1 years (hazards ratio [HR] 4.42), presence of nephropathy (HR 8.94) or neoplasms (HR 1.64) were associated with a higher risk of death, while the presence of retinopathy (HR 0.31) was associated with a lower risk of death.

Keywords: epidemiology, Kazakhstan, pediatric, type 1 diabetes mellitus

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is one of the most common chronic diseases in children with an estimated global incidence of 149,500 cases within the age range 0-19 diagnosed in 2021 [1]. In addition to the impact on the life quality of patients, T1DM predisposes to acute and chronic complications, such as diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, cardiovascular alterations leading to coronary artery disease, cerebrovascular diseases, and others [2].

However, in T1DM children the most fearful situations are related to the inappropriate and/or delayed recognition and/or management of this disease, which can result in acute metabolic complications, such as diabetic ketoacidosis (DKA) and severe hypoglycemia [3].

The annual incidence rate of T1DM in children and adolescents under 15 varies between 0.1 and 57.6 documented cases per 100,000 population, with the lowest rates being found in Fiji and China, and the highest–in Finland [4]. However, a global increase of approximately 3-5% per year in the incidence and prevalence of T1DM has been reported [5-7].

Data on mortality in pediatric T1DM populations has been lacking in recent years [8]. However, a systematic review based on the data from the late 20th century shows a great variation yet consistent higher mortality rates when compared with the general population, with a maximum standardized mortality ratio (SMR) reaching 854 in Cuba [9]. Notably, the majority of deaths tend to occur in low- and middle-income countries due to lower availability of appropriate medical care and/or access to diagnostic and therapeutic resources [8].

There is a lack of clinical and epidemiological studies on pediatric chronic disorders from Kazakhstan (and, in general, Central Asia), including T1DM. A few cross-sectional observational studies investigating the general epidemiology of diabetes mellitus in Kazakhstan have been previously published [10-13]. However, they tend to have a smaller scale, or focus on adult populations.

Kazakhstan has a well-developed electronic healthcare system named the unified national electronic health system (UNEHS), established in 2014, which allows the use of medical records for research. These records are aggregated from different electronic data sources such as inpatient electronic registries of hospitalized patients, outpatient electronic registries of dispensary patients and many others, which are implemented across all medical organizations in the country.

The establishment of UNEHS in Kazakhstan created an unprecedented possibility to study the epidemiology of a wide variety of health conditions in Kazakhstan on a national scale, including diabetes mellitus. Therefore, through the analysis of UNEHS, which provides comprehensive data from hospitals from all regions of Kazakhstan, we aimed to investigate the incidence, prevalence, and all-cause mortality of pediatric T1DM in the country from 2014 to 2021.

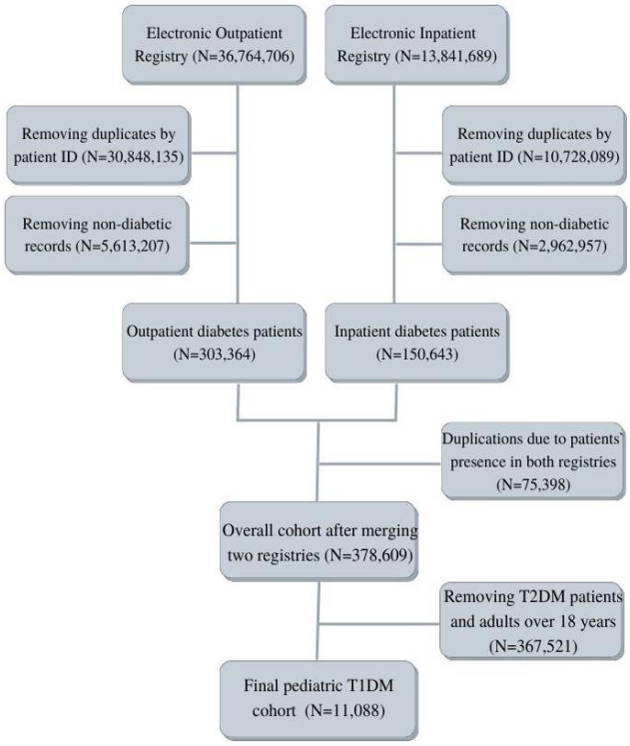

Figure 1. Cohort selection flowchart of pediatric T1DM patients registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

METHODS

Study Population

This is a retrospective cohort study, which included patient records of T1DM children aged 0-17 years at diagnosis, who were registered in UNEHS, between 1 January 2014 and 31 December 2021. UNEHS database aggregates individual patient records and provides socio-demographic and clinical diagnoses according to the international classification of diseases 10 (ICD-10) coding system. T1DM patients were identified using ICD-10 code E10 (**Appendix A**). The follow-up period was defined as the period from the date of T1DM diagnosis to 31 December 2021, or until the date of death. The cohort selection flowchart presented in **Figure 1** depicts each step of the process.

The sample is non-random, assembled with the aim of covering as many documented pediatric T1DM patients in the country as possible. UNEHS database is organized into inpatient and outpatient electronic registries. The entire database consisted of 50,606,395 records for the period between 2014 and 2021 of which 13,841,689 are inpatient, and 36,764,706 are outpatient. The final cohort of children aged 0-17 with T1DM consisted of 11,088 patients.

Exposures and Covariates

Patients' records extracted from UNEHS database contained the following information: sex, ethnicity, date of birth, date of death, date of diagnosis, ICD-10 codes for main diagnosis and comorbidities, dates of admission and discharge, and anonymized population registry number (RPN). RPN is a unique patient identification number used exclusively within the healthcare records systems. Where applicable, the information on the date of death was obtained through linkage with the population registry through RPN. Age was divided into three categories: 0-1 years, 2-11, and 12-17 [14]. Ethnicity was divided into Kazakh, Russian, and others (including Uzbek, Ukrainian, Tatar, and more). The following comorbidities were included: coronary heart disease (CHD), arterial hypertension, stroke, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, neoplasms, celiac disease, and thyroid diseases. These diagnoses were cross-referenced across the database for each patient using their RPN ID to ensure maximum capture. This was done to account for the database being divided into sections, such as the inpatient and the outpatient registries. RPN IDs are unique and consistent throughout the database and allow to gather data that could be present in one section of the database, but not the other for maximum capture.

Outcome Assessment

Incidence, period prevalence, and all-cause mortality were evaluated for pediatric T1DM patients for each year between 2014 and 2021. Incidence rate per 100,000 population was calculated by dividing the number of incident cases within a year by the average total population of ages 0-17 in Kazakhstan within that year. Similarly, period prevalence and mortality rates were calculated per 100,000 population by dividing the total number of patients alive at the end of a year, or number of deaths in that year by the average of the total population at risk, respectively. Population statistics were obtained from the National Statistical Bureau of the Agency of Strategic Planning and Reforms of the Republic of Kazakhstan [15].

Statistical Methods

Categorical variables were summarized as frequencies and percentages. Continuous variables were summarized as medians and interquartile ranges (IQR). For survival analysis, cox proportional hazards regression modelling and the Kaplan-Meier method were used. After checking for the assumptions, cox modelling was used to obtain crude and adjusted hazard ratios (HR) with 95% confidence intervals (CI). Adjustment was made for age at diagnosis, sex, ethnicity, CHD, hypertension, stroke, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, neoplasms, and thyroid diseases. The Kaplan-Meier method was used to estimate and graphically depict survivor functions for D1TM patients based on age at diagnosis, sex, residency, and ethnicity. The significance of the difference between the survival curves was estimated using the log-rank test.

All statistical analyses were performed using STATA 15 MP2 version (STATA Corporation, College Station, TX). p-values are two-sided and reported as statistically significant at ≤0.05 for all analyses.

RESULTS

Patients' Characteristics

A cohort of 11,088 children diagnosed with T1DM was identified during the study period. The descriptive statistics regarding the general demographic and clinical characteristics of these T1DM children are summarized in **Table 1**.

In detail, the gender distribution was substantially equal; the median age of diagnosis was 9.87 years (IQR 6.12-13.28). As regards the ethnic distribution, 44.44% were Kazakhs, 16.28% were Russians, other ethnicities represented the remaining 17.57%. In terms of comorbidities, retinopathy (11.43%),

Table 1. Descriptive statistics of pediatric T1DM cohort registered in UNEHS in 2014-2021

Characteristics	Patients
Total, n (%)	11,088 (100)
Age when diagnosed (years), median (IQR)	9.87 (6.12-13.28)
Age at the time of death (years), median (IQR)	9.41 (4.51-16.26)
Years of follow-up, median (IQR)	3.85 (1.80-6.12)
Age group when diagnosed, n (%)	
0-1	535 (4.83)
02-11	6,699 (60.42)
12-17	3,854 (34.76)
Sex, n (%)	
Female	5,566 (50.20)
Male	5,522 (49.80)
Ethnicity, n (%)	
Kazakh	4,927 (44.44)
Russian	1,805 (16.28)
Other	1,948 (17.57)
Missing	2,408 (12.72)
Residency, n (%)	
Urban	6,431 (59.41)
Rural	4,393 (40.59)
Comorbidities, n (%)	
CHD	537 (4.48)
Hypertension	350 (3.16)
Stroke	196 (1.77)
Retinopathy	1,267 (11.43)
Neuropathy	783 (7.06)
Nephropathy	195 (1.76)
Neoplasms	1,183 (10.67)
Celiac disease	21 (0.19)
Thyroid diseases	79 (0.71)
Outcome	
Alive	10.896 (98.27)
Dead	192 (1.73)

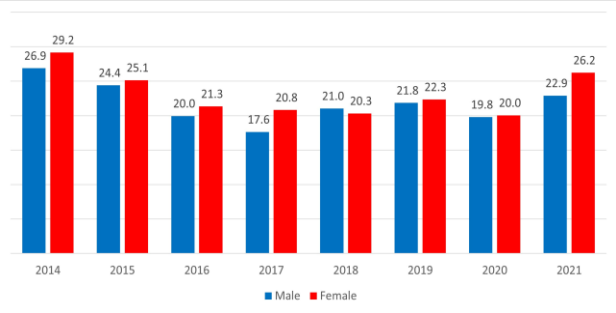

Figure 2. Incidence rate per 100,000 population at risk aged 0-17 stratified by sex & year of diagnosis for pediatric T1DM cohort registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

neoplasms (10.67%), neuropathy (7.06%), and CHD (4.48%) were the most observed. All-cause mortality by the end of the follow-up period reached 1.73%, which corresponds to the overall mortality rate of 17.3 per 1,000 patients in this cohort.

Incidence, Prevalence, and Mortality Rates

During the study period, the incidence rate of T1DM decreased from 28.1 (year 2014) to 24.5 (year 2021) cases per 100,000 population at risk, with the average of 22.5 (**Figure 2**).

T1DM prevalence increased from 48.8 to 179.1 cases per 100,000 persons over the study period, with the average of 116.0 (**Figure 3**). Both incidence and prevalence were slightly, yet consistently higher among girls.

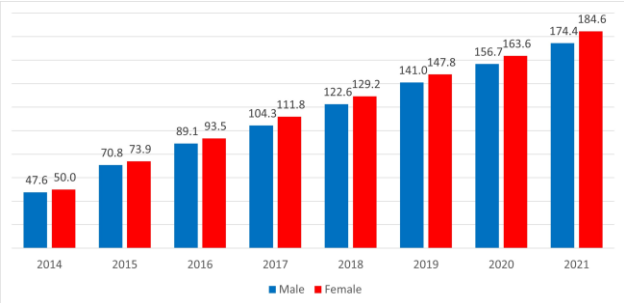

Figure 3. Prevalence rate per 100,000 population at risk aged 0-17 stratified by sex & year of diagnosis for pediatric T1DM cohort registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

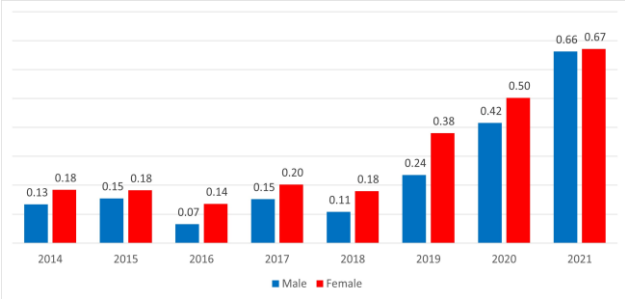

Figure 4. Mortality rate per 100,000 population at risk aged 0-17 stratified by sex & year of diagnosis for pediatric T1DM cohort registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

The mortality rate rose from 0.18 to 0.67 per 100,000 people in the at-risk population during the study period, with the average of 0.32 (**Figure 4**).

Survival Analysis

Figure 5, **Figure 6**, **Figure 7**, and **Figure 8** depict survivor function plots constructed using the Kaplan-Meier method with the p-values from the log-rank test, indicating the significance of the difference between the survivor curves.

Differences in survival are significantly different among age and ethnicity groups. Patients diagnosed with T1DM at age 0-1 years demonstrate lower survival rates than those diagnosed later in life. Survival was also found to be significantly lower among males and rural residents.

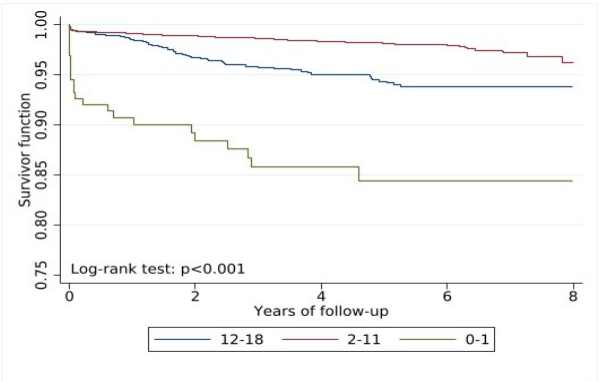

Figure 5. Kaplan-Meier plot of survivor function on age at diagnosis & adjusted for residency, sex, & ethnicity for pediatric T1DM cohort registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

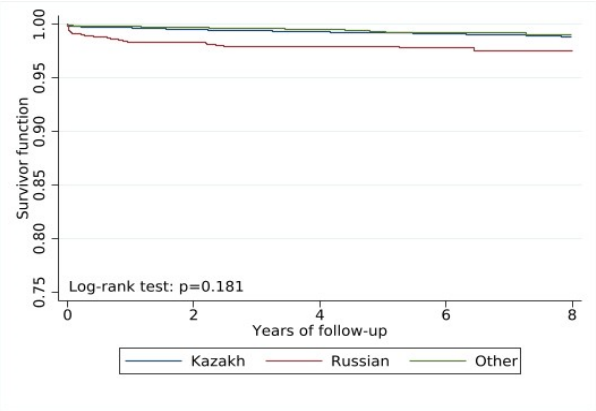

Figure 6. Kaplan-Meier plot of survivor function on ethnicity & adjusted for residency, sex, & age at diagnosis for pediatric T1DM cohort registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

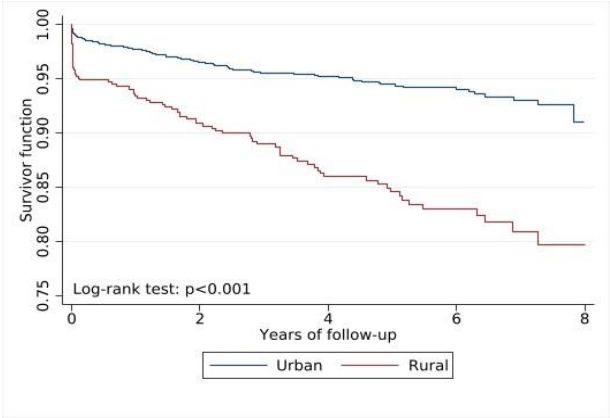

Figure 8. Kaplan-Meier plot of survivor function on residency & adjusted for sex, ethnicity, & age at diagnosis for pediatric T1DM cohort registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

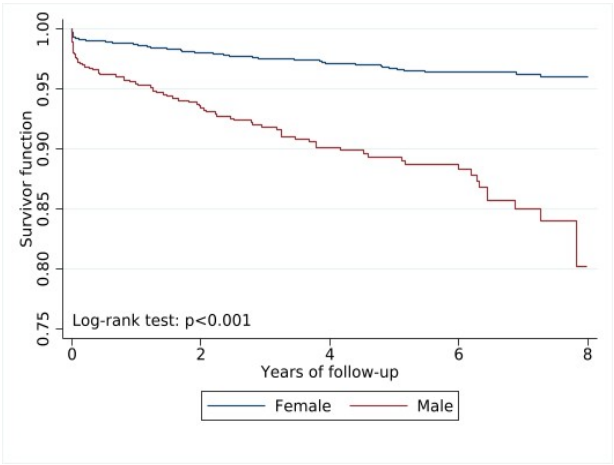

Figure 7. Kaplan-Meier plot of survivor function on sex & adjusted for residency, ethnicity, & age at diagnosis for pediatric T1DM cohort registered in UNEHS in 2014-2021 (Source: Authors' own elaboration)

In **Table 2**, hazards ratios (HR) with 95% confidence intervals (CI) and p-values corresponding to associations between risk of death and demographic characteristics, are reported. Among T1DM patients, those diagnosed at age 0-1 years exhibit almost 4.5-fold higher risk of death (HR 4.42 [95% CI: 2.69-7.26] compared to 12-17 age group at diagnosis. No significant relations were found in terms of sex and ethnicity.

Table 3 lists HRs based on presence of diagnosed comorbidities and their association with the risk of death.

Among T1DM patients, three types of comorbidities were significantly associated with a change in the risk of death after full adjustment: nephropathy was associated with an 8.9-fold higher risk of death (HR 8.94 [95% CI: 5.27-15.18]), neoplasms– with a 64% higher risk of death (HR 1.64 [95% CI: 1.13-2.40]), and retinopathy was associated with a 69% lower risk of death (HR 0.31 [95% CI: 0.17-0.57]).

DISCUSSION AND CONCLUSIONS

In this study, we investigated the epidemiology of pediatric T1DM in Kazakhstan for the period of 2014-2021 using large-scale administrative health data. We described incidence, prevalence, mortality, and survival of pediatric T1DM patients and investigated demographic factors and DM-related comorbidities. We found that retinopathy, neoplasms, and neuropathy are the most common comorbidities, documented for 11.4%, 10.7%, and 7.1% of the cohort, respectively. The average incidence rate of T1DM was 22.5 cases per 100,000 population at risk. Period prevalence rate reached 179.1 cases

Table 2. Cox proportional hazards regression models of associations between risk factors & risk of all-cause death for pediatric T1DM cohort registered in UNEHS in 2014-2021

	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Sex				
Male	Ref.		Ref.	
Female	1.15 (0.85-1.55)	0.379	1.16 (0.85-1.57)	0.344
Age when diagnosed				
12-17	Ref.		Ref.	
2-11	0.87 (0.63-1.22)	0.424	1.09 (0.78-1.53)	0.594
0-1	3.00 (1.84-4.90)	<0.001	4.42 (2.69-7.26)	<0.001
Ethnicity				
Kazakh	Ref.		Ref.	
Russian	0.64 (0.41-0.99)	0.043	0.66 (0.43-1.03)	0.066
Other	0.90 (0.61-1.34)	0.605	0.90 (0.60-1.33)	0.587
Residence				
Urban	Ref.		Ref.	
Rural	1.15 (0.85-1.56)	0.366	1.21 (0.90-1.65)	0.211

Note: Adjusted for age at diagnosis, sex, ethnicity, and residency

Table 3. Cox proportional hazards regression models of associations between comorbidities & risk of all-cause death for pediatric T1DM cohort registered in UNEHS in 2014-2021

	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
CHD	1.04 (0.56-1.92)	0.901	0.52 (0.17-1.62)	0.258
Hypertension	1.22 (0.62-2.39)	0.569	1.70 (0.50-5.76)	0.396
Stroke	1.67 (0.74-3.77)	0.219	1.61 (0.67-3.83)	0.286
Retinopathy	0.54 (0.31-0.93)	0.027	0.31 (0.17-0.57)	<0.001
Neuropathy	0.93 (0.55-1.59)	0.794	0.77 (0.43-1.39)	0.378
Nephropathy	5.81 (3.60-9.38)	<0.001	8.94 (5.27-15.18)	<0.001
Neoplasms	1.77 (1.22-2.56)	0.002	1.64 (1.13-2.40)	0.010
Thyroid diseases	0.66 (0.09-4.69)	0.675	0.68 (0.09-4.87)	0.701

Note. Adjusted for age at diagnosis, sex, ethnicity, residency, CHD, hypertension, stroke, retinopathy, neuropathy, nephropathy, diabetic foot, neoplasms, & thyroid diseases

per 100,000 population at risk in 2021. The average mortality rate was estimated at 0.32 deaths per 100,000 population at risk. Children diagnosed before at age 0-1 year were at a 4.5-fold higher risk of all-cause mortality compared to those diagnosed at the age 12-17. The presence of neoplasms and nephropathy corresponded to 64% and 794% higher risk of all-cause mortality, respectively, while presence of retinopathy was associated with a 69% lower risk of death.

The estimated average incidence rate of 22.5 cases of pediatric T1DM per 100,000 population is consistent with the data published by the International Diabetes Federation for the Central Asian region in 2019 [16].

A recent study reported incidence rates of pediatric T1DM at 5.1-8.9 cases per 100,000 population for the world, and 16-24 for Europe and Central Asia in 2021 within the 0-19 age group [17]. In North America the incidence ranged from 16 to 34 cases per 100,000 population, in Latin America and Caribbean–from 8 to 11, in Middle East and North Africa–from 11 to 23, in Sub-Saharan Africa– between two and three, in South Asia, East Asia, and Pacific–between four and six cases per 100,000 pediatric population [17, 18].

Period prevalence rate of T1DM reached 179.1 cases per 100,000 population in 2021 in Kazakhstan, compared to 152.5 cases per 100,000 population in 2020 in Italy [19], 247.1 per 100,000 in 2020 in Germany [20], 17.6 per 100,000 in 2015 in Thailand [21], and 2.05 per 100,000 in 2016 in Mali [22]. Based on these estimates, Kazakhstan appears closer to higher income European countries, which may indicate improved recognition, diagnostic capacity, and detection rate of chronic conditions, such as T1DM, compared to lower income developing nations.

All-cause mortality rate was estimated to be 1.73% in this cohort, and 0.32 per 100,000 population at risk per year. Research on mortality among pediatric T1DM patients has been scarce in recent years. In a study conducted in Australia between 1997 and 2010, overall mortality rate reached 7.0%, however, this study included patients of all ages [23].

Prevalence of diabetic retinopathy (DR) was 11.4% in this cohort, which is lower than the estimates from the US [24], where 20.1% of youths with T1DM developed DR over 3.2 median years of observation; and the estimates from the UK, where 37.4% had DR at first screening [25]. Prevalence of diabetic nephropathy (DN) was 1.8%, which is considerably lower than the estimated 15-20% DN development rate among T1DM youths [26, 27]. Celiac disease was found only in 0.2% of the patients in this cohort, which is significantly lower than the estimated 4-11% prevalence in T1DM populations [28]. This may indicate that these types of comorbidities are significantly underdiagnosed in Kazakhstan. Prevalence of hypertension in this cohort reached 3.2%, which is within 2-4% range determined by American Academy of Pediatrics in 2017 [29].

We found a significantly higher risk of mortality among children diagnosed with at age 0-1 years, 4.5 times higher, compared to those diagnosed at age 12-17. A similar trend was found in a study conducted in Sweden, which showed that mortality rate among children diagnosed within the first two years of life is considerably higher, compared to those diagnosed later in life [30]. Nephropathy and neoplasms were significantly associated with 8.9- and 1.6-times higher risk of death, respectively. In the [31], all-cause mortality risk has been estimated to be up to 30 times higher in T1DM patients with diabetic nephropathy, compared to T1DM patients without it. T1DM is also associated with higher risk of development of certain cancer types [17]. Interestingly, diabetic retinopathy is associated with a 69% lower risk of all-cause mortality. This unexpected inverse relationship, observed in our study, aligns with the concept of reverse epidemiology [32]. Diabetic retinopathy is the most common complication in children with type 1 DM, therefore, patients might be receiving more intense medical care and higher quality treatment. However, due to the lack of data on the specifics of the treatments, we could not explore this association further. However, it has also been documented that the risk of mortality due to DR increases with the duration of this condition, suggesting that longer-term complications of DR may contribute to poorer health outcomes [33].

There are several strengths to this study. Firstly, to our knowledge, this is the first study into the epidemiology of pediatric T1DM in Kazakhstan using aggregated data from the nationwide digital healthcare registries for the entire population, which allows a more complete assessment of the epidemiology of pediatric T1DM in the country. Secondly, this retrospective cohort study uses data collected continuously over the period of eight years, which made the analysis of trends over time comprehensive. Thirdly, the outcome data of patient mortality was obtained through linkage to the population registry, which helped ascertain cases of death outside of in-hospital mortality.

The study also has a number of limitations. Firstly, reliance on secondary data poses certain challenges, although efforts were made to ensure reliability and accuracy of the data. The data were originally collected for purposes other than the specific research questions of this study. This mismatch in data collection objectives and methodologies may have resulted in certain variables being unavailable or not aligned precisely with the research aims. Secondly, lack of laboratory data further limited the variety of analytical procedures that could be employed, thus preventing us from studying the

epidemiology of T1DM from a greater number of perspectives. Thirdly, the data on mortality are from all causes, with no cause specification. This limited our ability to analyze the relationships between the risk factors and cause-specific mortality. Consequently, the interpretation of the observed associations should be made with caution due to the observational nature of this study. Lastly, while efforts were made to control for potential confounders, it is acknowledged that there may be residual confounding due to unmeasured or unknown factors. Despite these limitations, this study provides valuable insights into the epidemiology of pediatric T1DM in Kazakhstan and sets the stage for further research to address these limitations and strengthen our understanding of topic.

Based on the findings of this research, several recommendations can be made. Diabetic retinopathy, neoplasms, and neuropathy were found to be the most commonly documented comorbidities, which warrants further research into these conditions in pediatric T1DM populations. In terms of policy, despite the decreasing incidence trend, continued longitudinal surveillance and research with the aim of monitoring the evolving patterns of pediatric T1DM might help ensure that healthcare policies remain responsive to the changing epidemiological trends. Additionally, further research into the risk factors, such as diabetic nephropathy and neoplasms, could guide the development of targeted interventions and more efficient efforts aimed at reducing mortality among pediatric T1DM patients. In terms of clinical practice, early diagnosis and management of T1DM and relevant complications is essential for improving health outcomes. Continuous monitoring of patients and a smooth transition from pediatric to adult care are needed, ensuring that they are well equipped with the necessary self-management skills and resources to continue effective care. Finally, UNEHS database, while being an exceedingly useful source of data for various research purposes, could be improved further by increasing the breadth of documented information, such as laboratory and treatment details.

Author contributions: All authors have sufficiently contributed to the study and agreed with the results and conclusions.

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Ethical statement: Authors stated that Nazarbayev University Institutional Research Ethics Committee (NU-IREC) approved this project to be exempt from further NU IREC oversight (NU-IREC 505/06122021). The study was performed according to both international local ethics guidelines and regulation as well as declaration of Helsinki.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Ogle GD, James S, Dabelea D, et al. Global estimates of incidence of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Atlas, 10th edition. Diabetes Res Clin Pract. 2022;183:109083. https://doi.org/10.1016/j.diabres.2021.109083 PMid: 34883188
2. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: A review of current evidence. Diabetologia. 2019;62(1):3-16. https://doi.org/10.1007/s00125-018-4711-2 PMid:30171279
3. Cengiz E, Xing D, Wong JC, et al. Severe hypoglycemia and diabetic ketoacidosis among youth with type 1 diabetes in the T1D exchange clinic registry. Pediatr Diabetes. 2013;14(6):447-54. https://doi.org/10.1111/pedi.12030 PMid:23469984 PMCid:PMC4100244
4. Craig ME, Hattersley A, Donaghue KC. Definition, epidemiology and classification of diabetes in children and adolescents. Pediatr Diabetes. 2009;10(Suppl 12):3-12. https://doi.org/10.1111/j.1399-5448.2009.00568.x PMid: 19754613
5. Barkai L, Kiss Z, Rokszin G, et al. Changes in the incidence and prevalence of type 1 and type 2 diabetes among 2 million children and adolescents in Hungary between 2001 and 2016–A nationwide population-based study. Arch Med Sci. 2020;16(1):34-41. https://doi.org/10.5114/aoms.2019.88406 PMid:32051703 PMCid:PMC6963129
6. Harjutsalo V, Sund R, Knip M, Groop P-H. Incidence of type 1 diabetes in Finland. JAMA. 2013;310(4):427-8. https://doi.org/10.1001/jama.2013.8399 PMid:23917294
7. Skrivarhaug T, Stene LC, Drivvoll AK, Strøm H, Joner G. Incidence of type 1 diabetes in Norway among children aged 0-14 years between 1989 and 2012: Has the incidence stopped rising? Results from the Norwegian childhood diabetes registry. Diabetologia. 2013;57(1):57-62. https://doi.org/10.1007/s00125-013-3090-y PMid:24149838
8. Patterson C, Guariguata L, Dahlquist G, Soltész G, Ogle G, Silink M. Diabetes in the young–A global view and worldwide estimates of numbers of children with type 1 diabetes. Diabetes Res Clin Pract. 2014;103(2):161-75. https://doi.org/10.1016/j.diabres.2013.11.005 PMid: 24331235
9. Morgan E, Cardwell CR, Black CJ, McCance DR, Patterson CC. Excess mortality in type 1 diabetes diagnosed in childhood and adolescence: A systematic review of population-based cohorts. Acta Diabetologica. 2015;52(4):801-7. https://doi.org/10.1007/s00592-014-0702-z PMid:25585594
10. Poddighe D, Turganbekova A, Baymukasheva D, Saduakas Z, Zhanzakova Z, Abdrakhmanova S. Genetic predisposition to celiac disease in Kazakhstan: Potential impact on the clinical practice in Central Asia. PLoS One. 2020;15(1):e0226546. https://doi.org/10.1371/journal.pone.0226546 PMid:31895924 PMCid:PMC6939901
11. Orazumbekova B, Issanov A, Atageldiyeva K, et al. Prevalence of impaired fasting glucose and type 2 diabetes in Kazakhstan: Findings from large study. Front Public Health. 2022;10:810153. https://doi.org/10.3389/fpubh.2022.810153 PMid:35284393 PMCid:PMC8907545
12. Galiyeva D, Gusmanov A, Sakko Y, et al. Epidemiology of type 1 and type 2 diabetes mellitus in Kazakhstan: Data from unified national electronic health system 2014-2019. BMC Endocr Disord. 2022;22(1):275. https://doi.org/10.1186/s12902-022-01200-6 PMid:36368961 PMCid: PMC9650815
13. Supiyev A, Kossumov A, Kassenova A, et al. Diabetes prevalence, awareness and treatment and their correlates in older persons in urban and rural population in the Astana Region, Kazakhstan. Diabetes Res Clin Pract. 2016;112:6-12. https://doi.org/10.1016/j.diabres.2015.11.011 PMid: 26706921
14. Job KM, Gamalo M, Ward RM. Pediatric age groups and approach to studies. Ther Innov Regul Sci. 2019;53(5):584-9. https://doi.org/10.1177/2168479019856572 PMid: 31311309

15. National Statistical Bureau. Taldau statistics. Available at: https://www.taldau.stat.gov.kz (Accessed: 27 August 2022).
16. IDF Diabetes Atlas 2019. Available at: https://www.diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf (Accessed: 27 August 2022).
17. Gregory GA, Robinson TI, Linklater SE, et al. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: A modelling study. Lancet Diabetes Endocrinol. 2022;10(10):741-60. https://doi.org/10.1016/S2213-8587(22)00218-2 PMid:36113507
18. Gomber A, Ward ZJ, Ross C, et al. Variation in the incidence of type 1 diabetes mellitus in children and adolescents by world region and country income group: A scoping review. PLOS Glob Public Health. 2022;2(11):e0001099. https://doi.org/10.1371/journal.pgph.0001099 PMid:36962669 PMCid:PMC10021400
19. Maffeis C, Mancioppi V, Piona C, Avossa F, Fedeli U, Marigliano M. Type 1 diabetes prevalence and incidence rates in the pediatric population of Veneto Region (Italy) in 2015-2020. Diabetes Res Clin Pract. 2021;179:109020. https://doi.org/10.1016/j.diabres.2021.109020 PMid:34437942
20. Baechle C, Stahl-Pehe A, Prinz N, et al. Prevalence trends of type 1 and type 2 diabetes in children and adolescents in North Rhine-Westphalia, the most populous federal state in Germany, 2002-2020. Diabetes Res Clin Pract. 2022;190:109995. https://doi.org/10.1016/j.diabres.2022.109995 PMid:35853531
21. Rittiphairoj T, Owais M, Ward ZJ, Reddy CL, Yeh JM, Atun R. Incidence and prevalence of type 1 diabetes and diabetic ketoacidosis in children and adolescents (0-19 years) in Thailand (2015-2020): A nationwide population-based study. Lancet Reg Health West Pac. 2022;21:100392. https://doi.org/10.1016/j.lanwpc.2022.100392 PMid:35169761 PMCid:PMC8829760
22. Sandy JL, Besançon S, Sidibé AT, Minkailou M, Togo A, Ogle GD. Rapid increases in observed incidence and prevalence of type 1 diabetes in children and youth in Mali, 2007-2016. Pediatr Diabetes. 2021;22(4):545-51. https://doi.org/10.1111/pedi.13191 PMid:33586301
23. Huo L, Harding JL, Peeters A, Shaw JE, Magliano DJ. Life expectancy of type 1 diabetic patients during 1997-2010: A national Australian registry-based cohort study. Diabetologia. 2016;59(6):1177-85. https://doi.org/10.1007/s00125-015-3857-4 PMid:26796634
24. Wang SY, Andrews CA, Herman WH, Gardner TW, Stein JD. Incidence and risk factors for developing diabetic retinopathy among youths with type 1 or type 2 diabetes throughout the United States. Ophthalmology. 2017;124(4):424-30. https://doi.org/10.1016/j.ophtha.2016.10.031 PMid:27914837 PMCid:PMC5728116
25. Rafferty J, Owens DR, Luzio SD, Watts P, Akbari A, Thomas RL. Risk factors for having diabetic retinopathy at first screening in persons with type 1 diabetes diagnosed under 18 years of age. Eye (Lond). 2021;35(10):2840-7. https://doi.org/10.1038/s41433-020-01326-8 PMid:33262478 PMCid:PMC8452782
26. Bogdanović R. Diabetic nephropathy in children and adolescents. Pediatr Nephrol. 2008;23(4):507-25. https://doi.org/10.1007/s00467-007-0583-2 PMid:17940807
27. Karguppikar M, Oza C, Shah N, Khadilkar V, Gondhalekar K, Khadilkar A. Prevalence of nephropathy in Indian children and youth with type 1 diabetes mellitus. J Pediatr Endocrinol Metab. 2022;35(5):585-92. https://doi.org/10.1515/jpem-2021-0644 PMid:35304981
28. Camarca M, Mozzillo E, Nugnes R, et al. Celiac disease in type 1 diabetes mellitus. Ital J Pediatr. 2012;38:10. https://doi.org/10.1186/1824-7288-38-10 PMid:22449104 PMCid:PMC3348012
29. Bell CS, Samuel JP, Samuels JA. Prevalence of hypertension in children. Hypertension. 2019;73(1):148-52. https://doi.org/10.1161/HYPERTENSIONAHA.118.11673 PMid:30571555 PMCid:PMC6291260
30. Dahlquist G, Kallen B. Mortality in childhood-onset type 1 diabetes: A population-based study. Diabetes Care. 2005;28(10):2384-7. https://doi.org/10.2337/diacare.28.10.2384 PMid:16186267
31. Sagoo MK, Gnudi L. Diabetic nephropathy: An overview. Methods Mol Biol. 2020;2067:3-7. https://doi.org/10.1007/978-1-4939-9841-8_1 PMid:31701441
32. Kalantar-Zadeh K, Block G, Humphreys MH, Kopple JD. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. Kidney Int. 2003;63(3):793-808. https://doi.org/10.1046/j.1523-1755.2003.00803.x PMid:12631061
33. Frith E, Loprinzi PD. Retinopathy and mortality. Diabetes Spectr. 2018;31(2):184-8. https://doi.org/10.2337/ds17-0010 PMid:29773939 PMCid:PMC5951238

APPENDIX A

Table A1. Codes

	ICD-10 diagnosis	ICD-9 procedures
CHD	I20-I25	00.66 & 36.00-36.99
Hypertension	I10-I16	
Stroke	I60-I66	00.61, 00.62, 00.64, & 00.65
Retinopathy	E10.3, E11.3, E12.3, E13.3, E14.3, H25-H26, H28, H30-H36, H43.1, & H54	
Nephropathy	E10.2, E11.2, E12.2, E13.2, E14.2, N17-N19.9, & Z99.2	55.6
Neoplasm	C00-D49	
Neuropathy	E10.4, E11.4, E12.4, E13.4, E14.4, G63.2, & G62.9	
Celiac disease	K90.0	
Thyroid disease	E00-E07	
Type 1 diabetes mellitus	E10	