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Original article

Examining 25-year trends of type 1 diabetes incidence in pediatric population aged 0-14 in Republic of Srpska

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Summary

Introduction. Data on newly diagnosed cases of type 1 diabetes and the incidence of this disease are very significant. Studies like this one, with an analysis of incidence over the past 25 years, help not only locally but also globally.

Methods. The primary source of data is hospital records from hospital centers in Republic of Srpska. The secondary, confirmatory source, is the data from the Health Insurance Fund of Republic of Srpska through which all newly diagnosed patients receive insulin and blood glucose testing strips.

Results. The average incidence for the entire period was 12.8/100,000 (95% CI: 10.40–15.22), with a total of 527 cases, of which 265 (50.3%) were boys. Positive linear trend was observed (R=0.747, R^2=0.558, p=0.000018). The annual increase was 0.59 (95% CI: 0.37– 0.82) or 29.06%. There was no difference between sexes, and the highest incidence, number, and growth were in the age group of 10–14 years.

Discussion. Compared to the period 2001–2016 (11/100,000) and to the period 1998–2010 (7.5/100,000), there was the increase in incidence. Significant increase in incidence was observed in the period 2017–2022. There is no difference from the rest of the world regarding incidence by sex, but there is regarding age group, with the highest incidence in the 10–14 age group.

Conclusion. This research provides a good basis for future studies on the impact of environmental, medical, and other factors on the onset of type 1 diabetes, as well as potential local, national, and global diabetes prevention programs.

Keywords: type 1 diabetes, incidence trend, pediatric patients

Introduction

According to the latest data and analyses from 2021, diabetes exhibited an average incidence of 19.6 per 100,000 individuals and ranked as the 10th leading cause of death globally. This incidence has evolved over time; in 1990, it held the 14th rank with the incidence of 18.2 per 100,000, whereas by 2019, it rose to the 8th position with the incidence of 19.8 per 100,000 [1]. These statistics highlight the enduring impact of diabetes on global mortality, with relatively stable mortality rates observed over the years.

Data from the Institute of Public Health of Republic of Srpska indicate the mortality incidence of 88.7 per 100,000 for endocrine gland diseases in 2022. Concurrently, there have been 71 429 newly diagnosed cases of diabetes mellitus since the introduction of registry in Republic of Srpska more than 20 years ago, with significant majority attributed to type 1 diabetes mellitus [2]. It is noteworthy that these figures are estimated, as reported by the institute, due to irregular reporting of newly diagnosed cases.

In 2021, the number of newly diagnosed cases of diabetes among children reached 355,900 (95% CI: 334,200–377,300), projecting an alarming annual increase of 100,000 cases by the year 2050 [3]. This underscores the significance of tracking and addressing newly diagnosed cases of type 1 diabetes to develop preventive strategies and mitigate its projected impact on mortality.

Type 1 diabetes mellitus stands as the predominant metabolic and endocrine disorder in the pediatric population [4]. This autoimmune condition, characterized by insulin deficiency resulting from pancreatic beta cell destruction, necessitates lifelong insulin replacement therapy [5]. The incidence and prevalence of diabetes in children hold substantial implications for healthcare systems, necessitating robust planning for staff, resources, and comprehensive support structures.

Studies conducted in Republic of Srpska [6–8], in the neighboring countries [9–12] and globally [13, 14] indicate an upward trend in the number of affected individuals in the 0–14 age group, reflecting a broader phenomenon observed in neighboring regions and worldwide. Discrepancies in reported incidence rates, such as those highlighted by the International Diabetes Federation atlas for Bosnia and Herzegovina, underscore the need for detailed analyses and data consolidation to refine global diabetes statistics [15].

Research endeavors like the present study, which amalgamate data from prior studies and offer in-depth analyses spanning multiple decades, play a crucial role in refining global diabetes data and informing targeted interventions at local and global levels.

Methods

In Bosnia and Herzegovina, including Republic of Srpska, the absence of a national diabetes patient registry is a notable gap, as evidenced by research indicating its critical importance in accurately determining incidence rates and devising effective treatment strategies. The data presented in this study were sourced from two primary avenues. First, hospital records from tertiary and secondary healthcare facilities in Republic of Srpska provided information on newly diagnosed cases of type 1 diabetes among individuals aged 0–14 years. Second, corroborative data were obtained from the Health Insurance Fund of Republic of Srpska, where all newly diagnosed diabetes patients receive insulin and blood glucose testing strips.

An additional crucial aspect of this study pertains to the reliance on official data from the most recent census conducted in Bosnia and Herzegovina, inclusive of Republic of Srpska, in 2013. These census figures serve as the foundational data in this research, with subsequent population estimates for each year derived from statistical yearbooks published by the Statistical Office of Republic of Srpska. The methodology utilized for population estimation employs the ponder method, utilizing the 2013 census data as reference values to determine the number of children in each age group.

The diagnostic criteria adhered to in this study align with the EURODIAB guidelines for identifying newly diagnosed cases of diabetes. These criteria stipulate that individuals must be citizens of Republic of Srpska at the time of diagnosis, fall within the age range of 0–14 years, have received a diabetes diagnosis from a pediatric endocrinologist, undergone insulin treatment during the diagnostic period, and utilized

self-monitoring devices procured from authorized institutions, such as the Health Insurance Fund of Republic of Srpska, between January 1, 1999, and December 31, 2023. The estimation methodology employed the capture-recapture method, yielding a result demonstrating a 99% concordance.

Statistical Analysis

Incidence was calculated as the number of children per 100,000 total children as well as for each age group or sex. As mentioned in the methods, the reference values for the total population and for each category were from the 2013 census, while values for other years were calculated using the ponder method based on the reference year and the estimated population from the Statistical Yearbook of the Statistical Office of Republic of Srpska [16]. The data were grouped as frequencies and percentages for categorical variables, and as measures of central distribution and variability for numerical variables. Poisson regression, linear regression, t-test, and Chi-square test techniques were used. A 95% confidence interval was used for all analyses, and statistical significance was set at $p<0.05$.

Results

During the period from 1999 to 2023, a total of 527 children aged 0 to 14 were diagnosed with type 1 diabetes in Republic of Srpska. Of these, 265 (50.3%) were boys, and 262 (49.7%) were girls. The average age at the time of diagnosis was 7.09 ± 3.75 years. The average incidence for the entire period was 12.8 per 100,000 (95% CI: 10.40–15.22). The lowest incidence was 4.7 per 100,000 in 2002, while the highest incidence was in 2020 with 28.7 per 100,000, coinciding with the first year of the global COVID-19 pandemic. Figure 1 shows the annual variability of the incidence during this period.

Linear regression model indicates a positive linear trend ($R=0.747$, $R^2=0.558$, $p=0.000018$). The annual increase was 0.59 (95% CI: 0.37–0.82), translating to the average annual increase of 29.06% over this period when expressed in percentages. Table 1 provides the numbers of newly diagnosed cases by year and sex, as well as the incidence for the entire period.

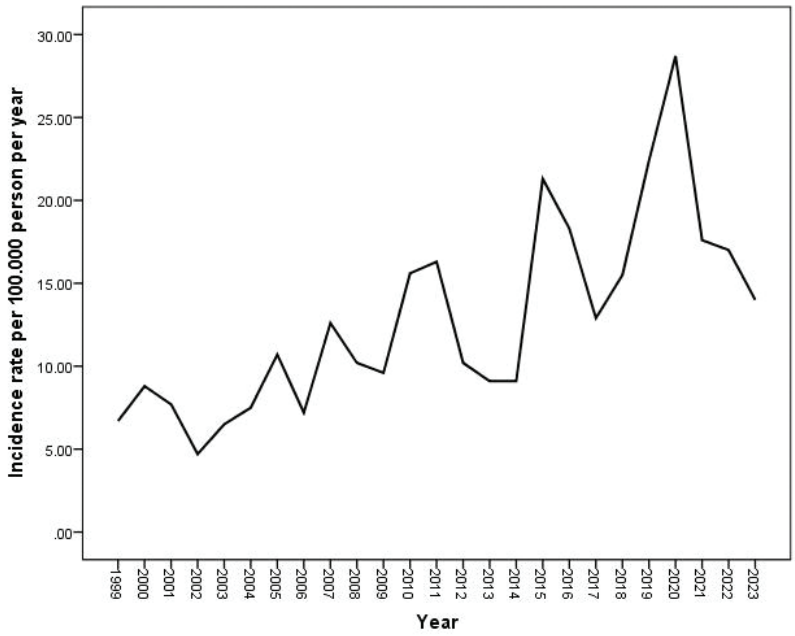

Figure 1. Annual variability of the incidence during the observed period. The graph shows significant variability in incidence, with years or periods of sharp increases and decreases.

Table 1. Incidence of newly diagnosed cases of type 1 diabetes per 100,000 people for the period 1999–2023, by sex

Year	Number of newly diagnosed cases			Incidence/100,000		
	Male	Female	Total	Male	Female	Total
1999	3	9	12	2,5	9,8	6,7
2000	9	7	16	10,1	7,5	8,8
2001	5	8	13	5,4	8,7	7,7
2002	4	4	8	4,3	4,4	4,7
2003	7	4	11	7,5	4,4	6,5
2004	7	6	13	7,5	6,5	7,7
2005	8	10	18	8,6	10,9	10,7
2006	5	7	12	5,4	7,6	7,2
2007	9	12	21	9,7	13,1	12,6
2008	4	13	17	4,3	14,2	10,2
2009	10	6	16	10,7	6,5	9,6
2010	10	16	26	10,7	17,5	15,6
2011	18	9	27	19,3	9,8	16,3
2012	9	8	17	9,7	8,7	10,2
2013	7	8	15	7,5	8,7	9,1
2014	8	7	15	8,6	7,6	9,1
2015	16	19	35	17,2	20,4	21,3
2016	21	9	30	22,6	9,8	18,3
2017	14	7	21	16,8	8,8	12,9
2018	13	12	25	15,7	15,3	15,5
2019	14	22	36	17	28,1	22,4
2020	22	24	46	26,8	30,8	28,7
2021	19	9	28	23,3	11,6	17,6
2022	14	13	27	17,2	16,8	17
2023	9	13	22	11,1	17,1	14

The average incidence for boys is 11.98 ± 6.54 (95% CI: 9.28–14.68), while for girls, it is 12.18 ± 6.68 (95% CI: 9.42–14.94). The minimum incidence among boys was 2.5/100,000 in 1999, while among girls it was 4.4 in 2002 and 2003. The maximum incidence in both sex groups corresponded to the maximum overall incidence in 2020, with 26.8 for boys and 30.8 for girls. There is a positive linear trend observed in both groups. For boys, the average annual increase is 0.667 ($p<0.001$), or 29.66%, while for girls, it is 0.55 ($p=0.001$), or 13.91%. Although girls have a higher maximum incidence, the statistical annual increase in incidence among girls is significantly lower than among boys, so the overall increase of 24.39% is mainly influenced by the increase in incidence among boys.

The paired sample t-test does not show statistical significance for sex groups in relation to overall incidence. The correlation of boys' incidence with overall incidence is 88.6%, but $t=-1.36$ ($p=0.185$), while for girls, the correlation is 87.2%, with a t statistic of -0.953 ($p=0.350$). Therefore, we can conclude that there are no significant differences in incidence between boys and girls, and neither of these incidences predominantly affects the overall incidence of the group.

Table 2 shows the number of newly diagnosed cases by age groups, along with the incidence for each age group and the overall incidence.

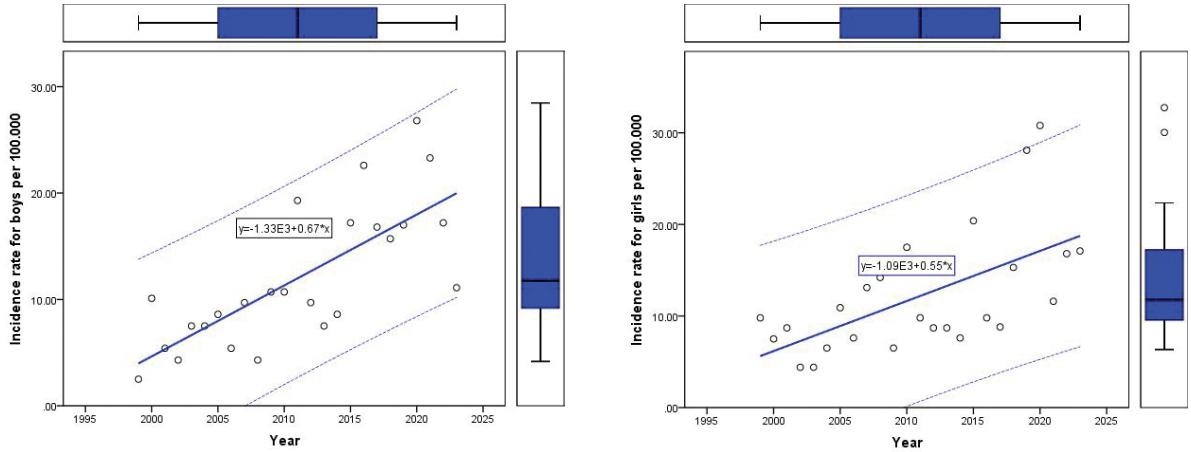

Figure 2. Linear regression of incidence with 95% CI (dotted lines) for boys (left) and girls (right)

Table 2. Number and incidance of newly diagnosed cases by age group over the years

Year	Number of newly diagnosed cases by age group over the years				Incidance of newly diagnosed cases by age group over the years			
	0–4	5–9	10–14	Total	0–4	5–9	10–14	Total
1999	2	6	4	12	4.8	8.9	5.6	6.7
2000	3	8	5	16	7.1	11.8	6.9	8.8
2001	1	9	3	13	1.8	16.3	5.1	7.7
2002	3	1	4	8	5.5	1.8	6.8	4.7
2003	3	7	1	11	5.5	12.7	1.7	6.5
2004	1	2	10	13	1.8	3.6	17	7.7
2005	3	7	8	18	5.5	12.8	13.6	10.7
2006	0	5	7	12	0	9.1	11.9	7.2
2007	1	9	11	21	1.8	16.5	18.8	12.6
2008	1	9	7	17	1.9	16.5	12	10.2
2009	6	6	4	16	11.1	11	6.9	9.6
2010	9	10	7	26	16.7	18.4	12	15.6
2011	4	13	10	27	7.4	24	17.2	16.3
2012	3	7	7	17	5.6	12.9	12	10.2
2013	4	3	8	15	7.5	5.6	13.8	9.1
2014	4	6	5	15	7.5	11.1	8.6	9.1
2015	4	11	20	35	7.5	20.5	34.7	21.3
2016	3	12	15	30	5.7	22.5	26.2	18.3
2017	4	6	11	21	7.6	11.3	19.5	12.9
2018	6	6	13	25	11.5	11.3	23.1	15.5
2019	8	12	16	36	15.3	22.7	28.6	22.4
2020	11	15	20	46	21.2	28.6	35.9	28.7
2021	6	9	13	28	11.7	17.3	23.5	17.6
2022	4	10	13	27	7.8	19.2	23.5	17
2023	5	9	13	22	9.8	17.4	14.6	14
TOTAL	99	198	235	532	7.6 (5.5–9.4)	13.7 (11.0–16.4)	15.4 (11.4–19.3)	12.8 (10.4–15.2)

The highest number of cases and consequently the highest incidence is in the age group of 10–14 years. The increase per year was 12.08% (0.40; p=0.002), 8.7% (0.47; p=0.007), and 30.3% (0.98; p=0.000013) in each respective age group. Therefore, the highest and statistically most significant increase is in the 10–14 age group. Figure 3 shows the incidences by age groups, indicating that the slope in the 10–14 age group is the highest, corresponding to the highest increase in incidence over the years in this age group.

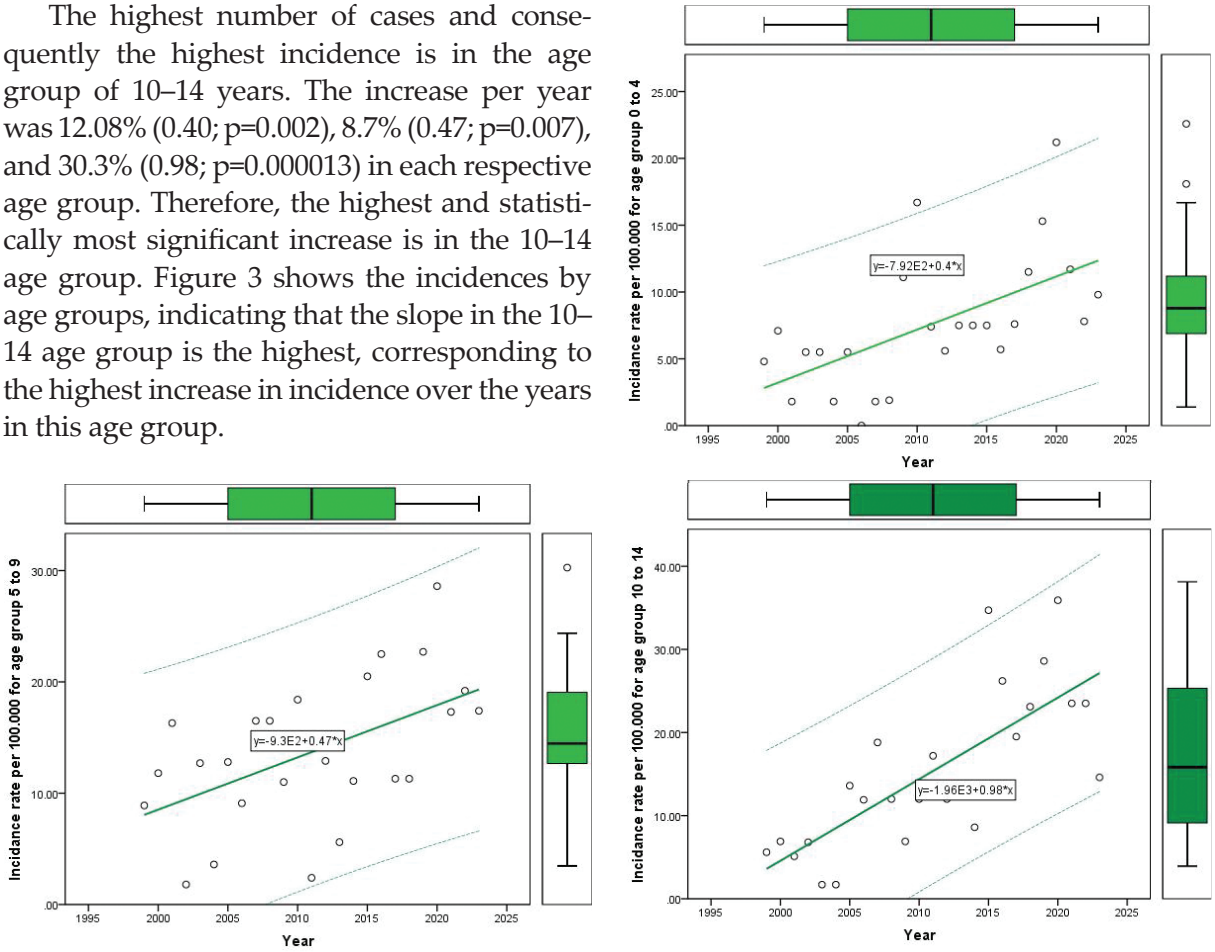

Figure 3. The linear trend of incidence growth by age groups with a 95% confidence interval (dotted line) is as follows: A. Age group 0–4; B. Age group 5–9; C. Age group 10–14. It is noticeable that the slope in the age group of 10–14 is the highest, corresponding to the highest increase in incidence over the years in this age group.

Discussion

The results demonstrate a notable average incidence of type 1 diabetes in Republic of Srpska over the past 25 years, at 12.8/100,000 (95% CI: 10.4–15.1). Comparing with previous reports [6–9], a slight increase is observed compared to the period 2001-2016 (11/100,000), and a significant increase compared to the period 1998–2010 (7.5/100,000). However, this period has notably fewer cases than the period 2017–2022 (19/100,000). Similar to England and Wales following their diabetes audit, the increase in incidence was noticed in the years 2018–2021 [17], coinciding with the global COVID-19 pandemic that influenced the spike in 2020. Encouragingly, there has been the decrease in the incidence of type 1 diabetes after 2020, with the incidence in 2023 recorded at 14/100,000.

In comparison to Sweden, which recently published results from 40 years of monitoring, the increase in diabetes across age groups over the years is significantly lower here [18]. Their investigation into the impact of increasing migration on the occurrence of type 1 diabetes in children did not find a drastic effect from migration, a hypothesis somewhat supported by our

research due to the decrease in the local population over the years alongside the increase in incidence. This suggests other environmental factors contributing to the rise, including socioeconomic aspects, genetics, lifestyle habits [19], and potentially stress, with the COVID-19 virus possibly acting as an accelerator in the first year of the pandemic [20]. The recent decrease in incidence hints at potential positive effects from increased intake of supplements, vitamins, and minerals during the pandemic, a topic warranting further research on their impact on diabetes onset.

Similar to global trends, there is no sex difference in incidence; boys and girls are equally affected [21]. However, a unique aspect observed here is the age at which symptoms occur, with the highest incidence shifting to the 10–14 age group, differing from European 5–9 age group peak in 2020 [9–12]. This shift aligns with patterns seen in Montenegro and neighboring countries, suggesting an area for further investigation.

The importance of this research lies in providing a robust foundation for healthcare authorities to develop prevention and education programs aimed at early symptom recognition and reducing acute complications in diabetes. It offers insights for projecting healthcare system expenditures for treating this population in long-term. Internationally, the correction of IDF data places us in the cohort of countries monitoring this phenomenon, contributing to potential global diabetes prevention initiatives in these age groups.

Conclusion

There has been an observed increase in new cases of type 1 diabetes in children aged 0 to 14 in Republic of Srpska over the past 25 years. The highest increase was in 2020, the first year of the global COVID-19 pandemic, indicating that the virus, in combination with psychological stressors, acted as the accelerator of diabetes onset that year. The declining trend observed in the last three years is encouraging, but the cause of this decline still needs to be investigated. This research serves as the solid foundation for future studies delving into the factors highlighted in this work. It also paves the way for the development of local, national, and global prevention and education programs targeting type 1 diabetes in pediatric population.

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Ethical approval. The Ethics Committee of the University Clinical Center of Republic of Srpska (protocol number: 01-19-82-2/23 from March 22, 2023), Republic of Srpska, Bosnia and Herzegovina, approved the study and informed consent was obtained from all individual respondents. The research was conducted according to the Declaration of Helsinki.

Conflicts of interest. The authors declare no conflict of interest.

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Pregled 25-godišnjeg trenda incidencije tipa 1 dijabetesa u Republici Srpskoj u pedijatrijskoj populaciji uzrasta od 0 do 14 godina starosti

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Uvod. Podaci o broju novootkrivenih slučajeva tipa 1 dijabetesa i incidenciji ove bolesti postaju veoma značajni. Studije kao što je ova, koje sumiraju podatke iz prethodno objavljenih radova o 25 godina incidencije tipa 1 dijabetesa su veoma značajne ne samo lokalno već i globalno.

Metode. Primarni izvor podataka su bolnički kartoni iz bolničkih centara u Republici Srpskoj o broju novooboljelih od dijabetesa tipa 1 u dobi 0–14 godina. Sekundarni, potvrdni izvor su podaci Fonda zdravstvenog osiguranja Republike Srpske preko kojeg svi novooboljeli pacijenti dobijaju insulin i trakice za mjerenje glukoze u krvi.

Rezultati. Prosječna incidencija za cijelo razdoblje bila je 12,80/100 000 (95% CI: 10,40–15,22), s ukupno 527 slučajeva, od čega 265 (50,3%) dječaka. Uočen je pozitivan linearni trend (R=0,747, R^2=0,558, p=0,000018). Godišnje povećanje iznosilo je 0,59 (95% CI: 0,37– 0,82) ili 29,06%. Nije bilo razlike među polovima, a najveća incidencija, brojnost i rast bili su u uzrasnoj grupi 10–14 godina.

Diskusija. U odnosu na razdoblje 2001–2016. (11,0/100 000) i razdoblje 1998–2010. (7,5/100 000) bilježi se porast. Međutim, značajan porast incidencije uočen je u razdoblju 2017–2022. Ne postoji razlika u odnosu na svijet u pogledu incidencije prema polu, ali je primjetna razlika u incidenciji prema uzrasnim grupama, s najvećom incidencijom u uzrasnoj grupi od 10 do 14 godina.

Zaključak. Ovo istraživanje pruža dobru osnovu za buduće studije o uticaju faktora sredine, medicinskih i drugih faktora na nastanak dijabetesa tipa 1, kao i za potencijalne lokalne, nacionalne i globalne programe prevencije dijabetesa.

Ključne riječi: tip 1 dijabetesa, trend incidencije, pedijatrijski pacijenti