Received: 24 April 2023 | Revised: 3 October 2023 | Accepted: 11 November 2023

DOI: 10.1002/dmrr.3749

WILEY

RESEARCH ARTICLE

Incidence of type 1 diabetes mellitus in children and adolescents under 20 years of age across 55 countries from 2000 to 2022: A systematic review with meta-analysis

Ignacio Hormazábal-Aguayo[1] | Yasmin Ezzatvar[2] | Nidia Huerta-Uribe[1] | Robinson Ramírez-Vélez[1] | Mikel Izquierdo[1] | Antonio García-Hermoso[1]

[1]Navarrabiomed, Complejo Hospitalario de Navarra (CHN), Universidad Pública de Navarra (UPNA), Pamplona, Spain

[2]Department of Nursing, Universitat de València, Valencia, Spain

Correspondence
Yasmin Ezzatvar, Department of Nursing, University of Valencia, Valencia, Spain.
Email: yasmin.ezzatvar@uv.es

Abstract

Aims: The aim of this study was to determine the global incidence of type 1 diabetes mellitus (T1DM) in children and adolescents under 20 years of age from 2000 to 2022.

Materials and Methods: Two reviewers searched three electronic databases (PubMed, Web of Science, and CINAHL) for studies published between January 2000 and November 2022. Pooled estimates of T1DM incidence with a 95% confidence interval (CI) per 100,000 person-years were calculated by country/region, sex, age, and COVID-19 pandemic period (pre-COVID-19 and pandemic).

Results: The study included 126 studies from 55 countries and 18 regions. The incidence rate (IR) of T1DM from 2000 to 2022 was 14.07 (95%CI, 12.15–16.29) per 100,000 person-years. Finland and high-income North America had the highest IR, with 56.81 (95%CI, 55.91–57.73) and 28.77 (95%CI, 26.59–31.13) per 100,000 person-years, respectively. The IR was 13.37 (95%CI, 10.60–16.88) per 100,000 person-years in boys and 13.87 (95%CI, 11.51–16.70) per 100,000 person-years in girls. There were statistically significant differences among different age ranges: 0–4 versus 5–9 and 10–14 years old ($p < 0.001$); 5–9 versus 15–19 ($p < 0.001$) and 10–14 versus 15–19 years old ($p = 0.003$). Finally, during the pandemic period (2020–2022), the IR was 24.84 (95%CI, 17.16–35.96) per 100,000 person-years, which was higher but not significant compared with the prepandemic period (2017–2019) of 13.56 (95%CI, 7.49–24.56) per 100,000 person-years ($p = 0.090$).

Conclusions: The IR of T1DM in children and adolescents under 20 years of age is substantial, especially during the pandemic period, although it varies across regions. More reliable data from additional countries are needed to determine the worldwide incidence of T1DM.

KEYWORDS
epidemiology, incidence rate, insulin-dependent diabetes

1 | INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease that leads to the destruction of pancreatic beta cells, ultimately resulting in a complete deficiency of insulin production.[1] According to the International Diabetes Federation (IDF), Finland, Sweden, and Kuwait have the highest incidence rates (IRs) of T1DM in people under the age of 15 years, with 52.2, 44.1 and 41.7 per 100,000 person-years, respectively. In contrast, Rwanda, China, and Japan have the lowest IR, with 1.2,[2] 1.9[3] and 2.2[4] per 100,000 person-years, respectively. Furthermore, several studies have identified differences in T1DM incidence based on age.

The incidence peaks between 10 and 14 years old,[5–11] while a lower incidence is observed in the 0–4 years age group[5,12–17] and in those aged 15–19 years.[12,18] Additionally, sex differences in T1DM incidence have also been reported, with studies showing higher incidence in men than in women in European countries,[19–21] in comparison with Asian countries that show higher incidence in women than in men.[12–14]

To date, it has been estimated that more than 1.2 million children and adolescents worldwide have T1DM.[22] In 2021, the IDF estimated that there were 108,300 new cases of T1DM among children under 15 years of age, a number that increased to 149,500 when the age range extended to under 20 years. However, it remains unknown whether the incidence of T1DM has been affected by the recent pandemic caused by SARS-CoV-2. Several studies have analysed the incidence of T1DM during the pandemic period, but the results have been inconsistent.[23–27]

Previous studies have explored the incidence of T1DM among individuals under 15 years of age.[28–30] However, to date, no meta-analysis has been conducted to provide pooled estimates of T1DM among children and adolescents under 20 years of age, according to different age ranges and sex, and to investigate whether there is a difference between the prepandemic COVID-19 period and the COVID-19 pandemic period. Therefore, the aim of this study was to estimate the global IR of T1DM in children and adolescents below 20 years of age during the period 2000 to 2022 by conducting a systematic review and meta-analysis of observational studies.

2 | METHODS

The present systematic review and meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[31] and the protocol for this study was registered in the International Prospective Register of Systematic Reviews (ID: CRD42022330253). No funding was received for this study.

2.1 | Literature search strategy

In collaboration with a professional librarian, we conducted a search of three electronic databases (PubMed, Web of Science, and CINAHL) to identify articles published from 1 January 2000 to 15 November 2022. We used Boolean operators to identify records with terms "type 1 diabetes" OR "childhood diabetes" OR "juvenile diabetes" OR "diabetes" AND children OR adolescent OR infant AND incidence* OR registry* OR epidemiology and "observational studies" OR "cohort studies". A detailed description of the search strategy can be found in Electronic Supplemental Material (ESM) Methods 1. We did not apply any language restrictions.

2.2 | Study selection

Initially, we screened the titles and abstracts of all studies. Subsequently, two authors (IHA and AGH) screened the full texts of all eligible articles, and a final decision was made for each study. Disagreements were resolved by discussion between the reviewers. To be eligible for inclusion in the meta-analysis, studies needed to meet the following criteria: (i) individuals diagnosed with T1DM under 20 years of age; (ii) studies providing IR of observational studies (including cross-sectional, prospective and retrospective, surveys and cohort studies); (iii) studies reporting data by year or periods of time from 2000 to 2022; (iv) studies including IR and/or mean annual IR from population-based (national or regional), surveys, registries and 'whole of population' insurance-based data or hospital (i.e., not self-reported); (v) studies that did not report IR or confidence intervals (CIs), but instead presented data on the population at risk and new cases diagnosed to subsequently calculate the IR and CIs. If the studies were from the same country or city and the same range of years but were from different databases, we used both sources of information. Additionally, if there were two studies in the same country that used the same database, we took the study with the largest follow-up. Finally, when the study reported both crude and sex- or age-adjusted IRs, the unadjusted IR was chosen for analysis.

2.3 | Data extraction

Data were extracted from each included article using a standardized data extraction form. Data were extracted by one reviewer (IHA) and checked by a second reviewer (AGH). The following data were extracted from the studies: first author's name, publication year, the period of study, country/region, characteristics of the study population (sample size, age of participants, and sex) and outcomes (mean annual IR of T1DM). Then, we extracted the total incidence and categorised it by age, sex and age-sex combined, and analysed the data in different age groups, time periods and regions, if available.

2.4 | Study risk of bias assessment

The risk of bias was assessed using the critical appraisal quality tool for prevalence or incidence studies proposed by Loney et al.[32] The studies were scored on eight quality criteria items: (i) participants (random sample or population), (ii) use of an adequate sampling

method (e.g., random, cluster), (iii) adequate sample size (>300 subjects), (iv) appropriate diagnostic tools, (v) unbiased appraisal of the outcome, (vi) adequate response rate, (vii) subgroup analysis, and (viii) the detailed description of participants. Each item that was satisfied was awarded one point, with a minimum score of 0 and a maximum score of eight points. Two reviewers (IHA and AGH) independently assessed the risk of bias. Disagreements between the allocated scores were resolved through discussion.

2.5 | Statistical analysis

To calculate the pooled IR of T1DM, we used STATA (version 17.0, STATA Corporation, College Station, Tex). The effect size used was the IR per 100,000 person-years. The DerSimonian–Laird random-effects model was used to calculate the IR and 95% CI except in the following situations: (1) if multiple studies reported IR for the same country, the pooled estimate was taken, and (2) if IR was reported for a multiyear period, that multiyear period was analysed as a single pooled data. If the studies did not present the CIs, the calculation of the exact 95% CIs for incidence estimates was based on the number of events modelled as a Poisson variable for 100,000 person-years.[33]

We assessed the statistical consistency of the results using the I^2 statistic, where a value between 75% and 100% indicates considerable inconsistency.[34] We performed subgroup analyses by sex, age range (0–4, 5–9, 10–14, and 15–19 years old), and age plus sex. We also pooled the studies by country and subsequently into regions based on the Institute for Health Metrics and Evaluation (IHME).[35] Finally, we performed sensitivity analysis to compare results from studies reporting data prepandemic COVID-19 (i.e., from 2017 to 2019) versus the pandemic period (i.e., from 2020 to 2022). MapChart software was used to map the IR of T1DM in its respective quartiles.[36]

3 | RESULTS

3.1 | Search results

The initial search resulted in 7247 articles (Figure 1). After removing duplicates and excluding studies based on their abstracts or by examining their full texts, a total of 126 studies were included. The details of the included studies are presented in ESM Table 1. Likewise, excluded studies and reasons for exclusion are shown in ESM Results 1.

3.2 | Study characteristics

The studies included in this review reported 183,005 new cases of T1DM between 2000 and 2022 from 55 countries covering 18 of the

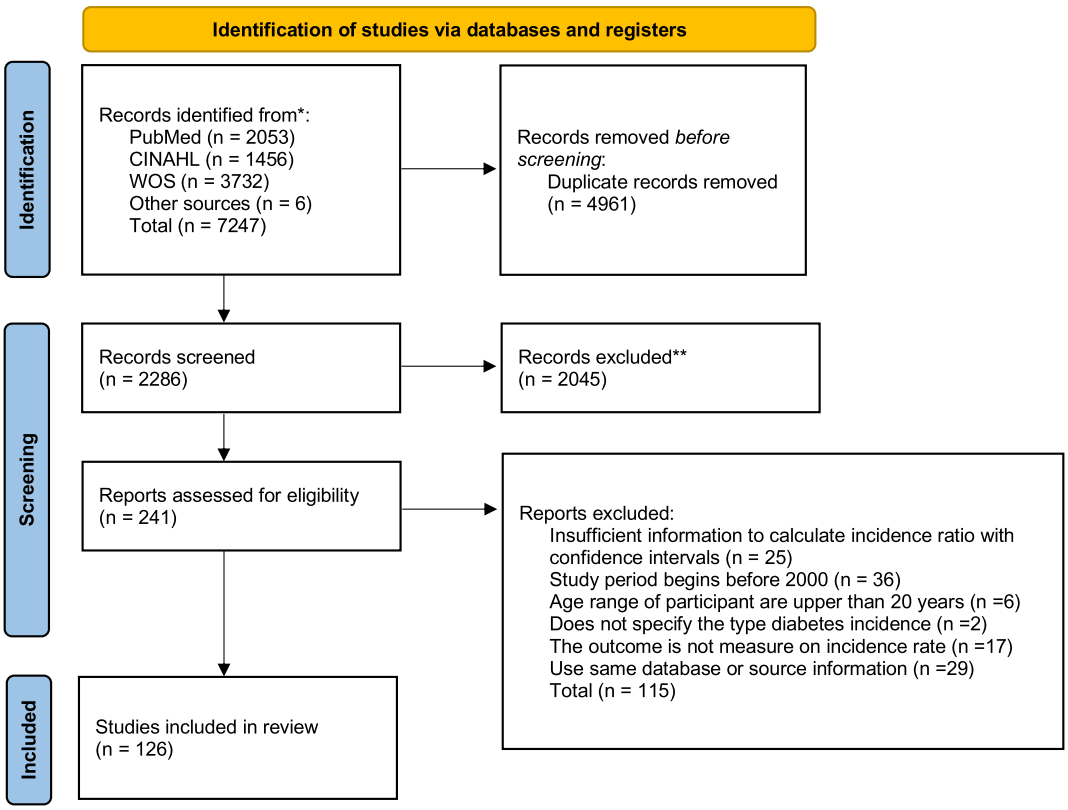

FIGURE 1 PRISMA flow-diagram.

21 regions. The regions include Australasia ($n = 2$), Caribbean ($n = 2$), Central Asia ($n = 1$), Central Europe ($n = 8$), Central Latin America ($n = 2$), East Asia ($n = 2$), Eastern Europe ($n = 1$), Eastern Sub-Saharan Africa ($n = 3$), High-income Asia Pacific ($n = 2$), High-income North America ($n = 2$), North Africa and Middle East ($n = 7$), Oceania ($n = 1$), South Asia ($n = 2$), Southeast Asia ($n = 1$), Southern Latin America ($n = 1$), Tropical Latin America ($n = 1$), Western Europe ($n = 16$), and Western Sub-Saharan Africa ($n = 1$). Western Europe, especially Italy and Spain, had a large number of studies, and the majority of new T1DM cases were reported from the United States of America ($n = 36{,}153$). In relation to the COVID-19 subanalysis, this review included 23 studies that encompassed both the prepandemic period ($n = 14$) and the COVID-19 pandemic period ($n = 8$).

3.3 | Participant characteristics

The studies were categorised based on reporting the general population ($n = 122$), sex ($n = 66$), age ranges from 0–14 years ($n = 65$) and 15–19 years ($n = 21$), and sex plus age ($n = 40$). For more detailed information about the characteristics of the participants, please refer to ESM Tables 3, 5, 7 and 9.

3.4 | Risk of bias in studies

The critical assessment of the 126 included studies are available in ESM Table 2. Of these, 50 articles met 100% of the quality criteria. The most common reason for not meeting the quality criteria was the lack of data on subgroup analysis. Overall, the risk of bias of the included studies was low.

3.5 | Incidence of T1DM

The average IR of T1DM per 100,000 person-years was 14.07 (95% CI, 12.15–16.29), with an I^2 value of 99.89%. Figure 2 shows the reported incidence of T1DM by region. Finland and high-income North America had the highest IR, with 56.81 (95% CI, 55.91–57.73) and 28.78 (95% CI, 26.60–31.14), respectively. In contrast, Mali and Sub-Saharan Africa West had the lowest IR of 0.66 (95% CI, 0.56–0.77) per 100,000 person-years because Mali was the only country in this subregion with reported information (ESM Table 4).

A worldwide map illustrating the geographic IR of T1DM by quartiles is provided in Figure 3.

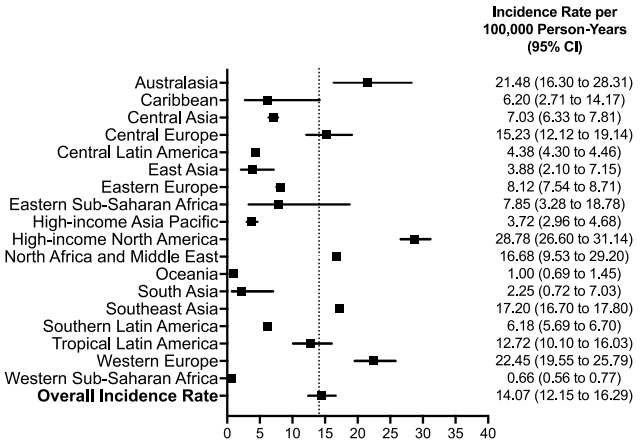

FIGURE 2 Incidence rate of type 1 diabetes mellitus by region.

3.6 | Subgroup analyses

Table 1 presents a summary of the higher and lower IR categorised by country and region, considering factors such as sex, age, sex plus age, and COVID-19 period categories.

Incidence of T1DM by sex. The IR of T1DM per 100,000 person-years for boys and girls was 13.37 (95% CI, 10.60–16.88) ($I^2 = 99.86\%$) and 13.87 (95% CI, 11.51–16.70) ($I^2 = 99.76\%$), respectively, without a difference between them ($p = 0.812$). ESM Tables 5 and 6 show the IR by sex and country/region.

Incidence of T1DM by age. During the study period, the overall IR for children and adolescents in age groups of 0–4, 5–9, 10–14, and 15–19 years old (per 100,000 person-years) were 9.66 (95% CI, 7.83–11.92) ($I^2 = 99.60\%$), 16.83 (95% CI, 13.88–20.41) ($I^2 = 99.72\%$), 18.96 (95% CI, 15.81–22.74) ($I^2 = 99.71\%$) and 7.05 (95% CI, 4.38–11.34) ($I^2 = 99.83\%$), respectively. There were significant differences between age ranges of 0–4 versus 5–9 ($p < 0.001$), 0–4 versus 10–14 years old ($p < 0.001$), 5–9 versus 15–19 ($p = 0.001$), and 10–14 versus 15–19 years old ($p < 0.001$). ESM Tables 7 and 8 show the IR by age range and country/region, respectively.

Incidence of T1DM by sex plus age range. There were no differences in the IR between sexes in the age groups 0–4 ($p = 0.996$), 5–9 ($p = 0.449$), 10–14 ($p = 0.507$), and 15–19 years old ($p = 0.678$). ESM Tables 9 and 10 show the IR by sex plus age range and country/region, respectively.

Incidence of T1DM during the prepandemic (2017 to 2019) and pandemic periods (2020 to 2022). The incidence of T1DM during the pandemic period (2020–2022) was higher than the prepandemic incidence (2017–2019). The IR was 24.84 (95% CI, 17.16–35.96) ($I^2 = 99.09\%$) per 100,000 person-years, compared to 13.56 (95% CI, 7.49–24.56) ($I^2 = 99.78\%$) in the prepandemic period, although the difference was not statistically significant ($p = 0.090$). Among the countries studied, Finland had the highest IR during the pandemic period, with 56.00 (95% CI, 45.22–69.34) per 100,000 person-years, while Turkey had the lowest IR, with 8.03 (95% CI, 6.18–10.41) per 100,000 person-years (ESM Table 11).

4 | DISCUSSION

This systematic review provides updated evidence on the incidence of T1DM in people under 20 years of age, with an IR of 14.07 per 100,000 person-years. Our study identified Finland and North

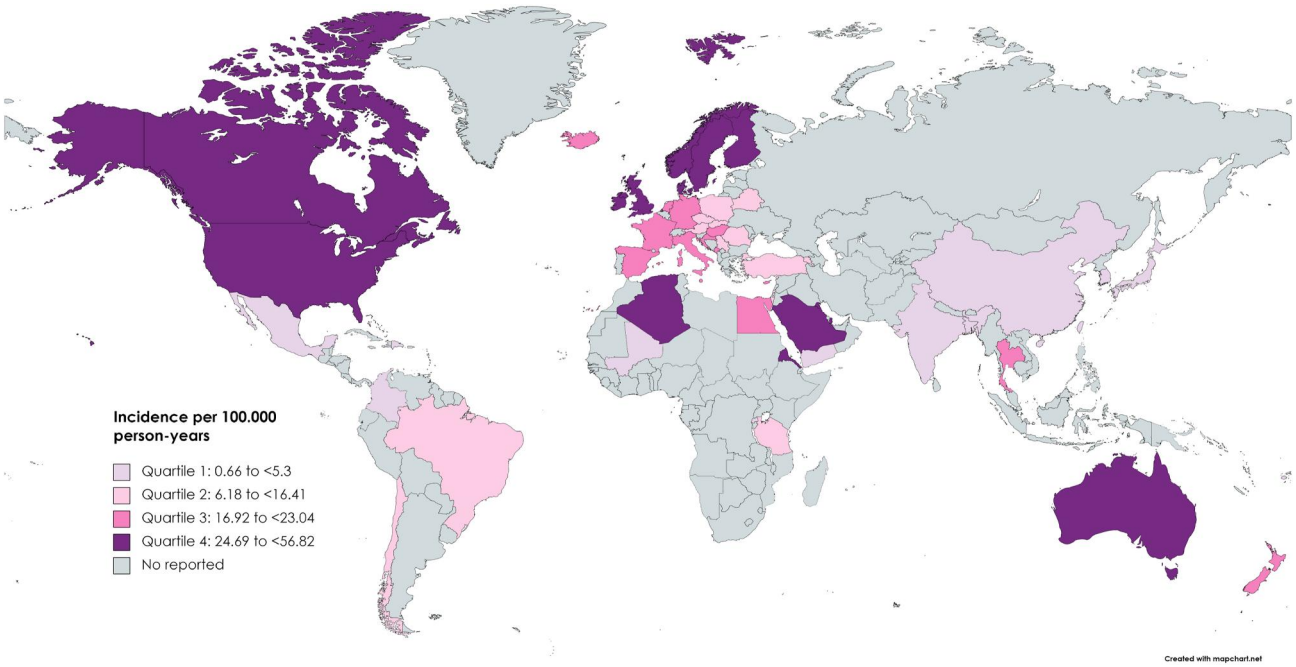

FIGURE 3 Worldwide map illustrating the geographic incidence rate of type 1 diabetes mellitus by quartile.

America as having the highest IR, while Mali and Sub-Saharan Africa had the lowest. We did not find any significant sex differences in the incidence of T1DM, but we did observe a higher IR in the 5–9 and 10–14 age groups than in the 0–4 and 15–19 age groups.

Our results are in contrast to previous studies such as Chen et al.,[37] who reported an IR of 11.43 per 100,000 person-years in people under 15 years old. Similarly, a multinational project focused on childhood diabetes (the Diamond Project Group),[38] which incorporated data from 50 countries during the years 1990–1999, revealed that Finland exhibited the highest IR of 40.9 per 100,000 person-years, while China had the lowest IR of 0.1 per 100,000 person-years. In our study, considering the period from 2000 to 2022, we observed a slight increase in the IR compared to the 1990–1999 period, with rates of 56.82 and 2.84 per 100,000 person-years in Finland and China, respectively. These substantial disparities among countries could be attributed to the ethnicity of children and adolescents. For example, a cohort study conducted by Guo et al.[39] demonstrated that the IR of T1DM was higher in Caucasians than in Asians, suggesting that Caucasians are more susceptible to the condition than Asians.

In addition to the T1DM incidence levels, the EURODIAB study conducted during 1999–2003 in Europe[40] found the highest IR in Finland with 54.5 and one of the lowest in Romania with 9.7 per 100,000 person-years. A possible explanation for Finland having the highest IR could be related to its location at higher latitudes, which leads to less ultraviolet radiation and vitamin D deficiency.[37,41] Vitamin D deficiency has been linked to insulin resistance and destruction of beta cells, both of which contribute to the onset of T1DM.[42]

When considering the incidence of T1DM according to sex, current evidence shows inconsistent results. For instance, a previous study that analysed data from 72 countries and patients younger than 19 years old from 1965 to 2012 reported no difference between sexes,[37] which is consistent with our findings. Conversely, other studies have reported a higher incidence in girls[43–45] or boys.[46] These differences have been observed depending on the country of origin of the patients. In Asian and African countries, the incidence is typically higher in girls than boys,[47] whereas in European[48,49] and Western countries, the opposite is true.[50] However, there is no clear explanation for this phenomenon. Previous studies have suggested that this difference could be due to a reduced development of T1DM in girls during puberty,[42,51] as girls have a more robust residual β-cell function than boys.[52] This suggests that the hormones produced by girls gonads could provide temporary protection against T1DM.

Our research also found that the incidence of T1DM was higher among individuals aged 5–14 years than among younger (i.e., 0–4 years old) and older individuals (i.e., 15–19 years old). Therefore, our findings further support the idea that incidence is lowest in people under 5 years old,[9] with an increase in incidence during the age range from 5 to 9 years and a peak of incidence during 10–14 years old, followed by a decline during the age range of 15–19 years old.[3,53] Regarding sex plus age ranges, no differences were observed between groups. The literature reports that boys are predominantly affected by T1DM after puberty (i.e., 15–19 years old).[54] Previous studies also show that in European girls, the highest incidence is found in the age group of 5–9 years, whereas in boys, the highest incidence was found in the age group of 10–14 years.[55,56]

Finally, our study examined the IR of T1DM during the COVID-19 pandemic period compared with the prepandemic period (2017–2019 vs. 2020–2022). Although the number of studies was limited and the results require caution in the interpretation, we found an increase in the incidence of T1DM among individuals under 20 years

TABLE 1 Highest and lowest incidence rates by country and region according to sex, age, sex and age, and COVID-19 period categories.

	Highest incidence rates		Lowest incidence rates	
Sub-analysis	**Country/Region**	**Incidence rate (95% CI)**	**Country/Region**	**Incidence rate (95% CI)**
By country				
Overall	Finland	56.82 (55.91–57.74)	Mali	0.66 (0.56–0.77)
Boys	Finland	62.66 (61.12–64.24)	China	2.17 (2.08–2.26)
Girls	Finland	50.98 (49.57–52.43)	China	3.06 (2.93–3.19)
0–4 years old	Finland	49.57 (48.05–51.13)	Yemen	0.54 (0.39–0.74)
5–9 years old	Finland	64.28 (62.57–66.04)	Yemen	1.51 (1.19–1.91)
10–14 years old	Finland	57.30 (55.73–58.92)	Yemen	2.23 (1.78–2.80)
15–19 years old	Eritrea	50.20 (43.50–57.70)	Bangladesh	1.25 (0.70–2.14)
Boys + 0–4 years old	Finland	51.42 (48.98–53.98)	Japan	1.31 (1.16–1.47)
Boys + 5–9 years old	Finland	69.08 (66.28–71.99)	Japan	1.70 (1.50–1.90)
Boys + 10–14 years old	Finland	67.67 (64.95–70.51)	Japan	2.70 (2.51–2.90)
Boys + 15–19 years old	Eritrea	56.70 (46.80–68.00)	China	2.52 (2.19–2.89)
Girls + 0–4 years old	Finland	45.90 (43.56–48.37)	China	1.21 (0.99–1.42)
Girls + 5–9 years old	Kuwait	61.40 (51.10–73.20)	Japan	2.78 (2.42–3.15)
Girls + 10–14 years old	Saudi Arabia	57.70 (46.20–71.30)	Japan	3.17 (2.77–3.56)
Girls + 15–19 years old	Eritrea	43.60 (34.80–53.90)	Serbia	3.42 (2.69–4.35)
Pre-pandemic	Finland	39.97 (33.43–47.80)	Bangladesh	1.21 (0.93–1.55)
Pandemic	Finland	56.00 (45.22–69.34)	Turkey	8.03 (6.18–10.41)
By region				
Overall	High-income North America	28.78 (26.60–31.14)	Western Sub-Saharan Africa	0.66 (0.56–0.77)
Boys	Australasia	25.30 (24.80–25.90)	High-income Asia Pacific	2.94 (1.81–4.77)
Girls	Eastern Sub-Saharan Africa	23.26 (19.87–27.24)	South Asia	4.10 (3.40–4.80)
0–4 years old	High-income North America	23.82 (14.74–38.49)	High-income Asia Pacific	1.55 (1.37–1.74)
5–9 years old	High-income North America	39.45 (20.21–37.61)	High-income Asia Pacific	2.67 (1.93–3.69)
10–14 years old	High-income North America	42.42 (33.64–53.48)	High-income Asia Pacific	3.65 (2.48–5.39)
15–19 years old	Eastern Sub-Saharan Africa	50.20 (43.50–57.70)	South Asia	2.01 (0.86–4.73)
Boys + 0–4 years old	High-income North America	19.53 (18.13–21.03)	High-income Asia Pacific	1.32 (1.18–1.47)
Boys + 5–9 years old	High-income North America	32.18 (30.46–33.99)	High-income Asia Pacific	2.12 (1.35–3.33)
Boys + 10–14 years old	High-income North America	36.86 (32.35–41.99)	High-income Asia Pacific	3.34 (2.18–5.09)
Boys + 15–19 years old	Eastern Sub-Saharan Africa	56.70 (46.80–68.00)	East Asia	2.52 (2.19–2.89)
Girls + 0–4 years old	High-income North America	19.38 (17.95–20.92)	East Asia	1.21 (1.00–1.46)
Girls + 5–9 years old	High-income North America	34.03 (30.51–37.94)	High-income Asia Pacific	3.17 (2.42–4.14)
Girls + 10–14 years old	High-income North America	32.73 (31.04–34.52)	High-income Asia Pacific	3.89 (2.60–5.83)
Girls + 15–19 years old	Eastern Sub-Saharan Africa	43.60 (34.80–53.90)	East Asia	3.48 (3.10–3.91)

of age during the pandemic period. However, we did not observe any significant difference between these two periods ($p = 0.090$). Some studies have suggested an increase in incidence during the pandemic, such as in Germany,[23] Finland,[24] Italy,[25] and Spain,[57] while others found no significant change during the pandemic compared to the prepandemic period in Kuwait[26] and Spain.[27] A recent meta-analysis assessed the impact of the first wave of the COVID-19 pandemic on the incidence of new-onset T1DM in pediatric patients, reporting an IR of 32.39 per 100,000 person-years,[58] which is higher than our results. These contrasting results may be due to methodological differences in the inclusion of the scientific articles. Our study only included articles reporting IR with their respective confidence

intervals or sufficient information to calculate these values. In contrast, the study by Rahmati et al.[58] did not consider this criterion, and thus, the result may have been overestimated. Although several hypotheses have been proposed for the association between COVID-19 and the higher IR of T1DM[59,60,] there is no solid evidence that SARS-CoV-2 causes T1DM itself. Therefore, the available data on T1DM incidence during the COVID-19 pandemic are inconsistent, and long-term follow-up studies are needed.[59]

This review has some limitations that should be considered when interpreting the results. First, the inclusion of studies was restricted to those reporting the IR of T1DM and providing sufficient data for calculation. Therefore, some countries were not included in this meta-analysis due to a lack of data, and several studies reporting the IR before 2000 were excluded. Second, not all countries in some regions provided data on T1DM incidence, which may have introduced bias at the regional level to underestimation or overestimation of the actual IR. Finally, the limited number of studies reporting T1DM incidence during the COVID-19 pandemic period may have influenced the incidence estimates during this period. Future studies should aim to report all possible data to obtain more accurate incidence estimates.

In conclusion, this meta-analysis offers updated estimation of the IR of T1DM among children and adolescents under 20 years of age across 55 countries. The IR was estimated to be 14.07 (95% CI, 12.15–16.29) per 100,000 person-years, with significant variability observed by country, region, and age group. Finland, high-income North America and the age range of 10–14 years had the highest IR. Further studies are needed to report the incidence of T1DM in countries with no official estimates to determine the true global IR.

AUTHOR CONTRIBUTION

Ignacio Hormazábal-Aguayo, Antonio García-Hermoso, Yasmin Ezzatvar, Nidia Huerta-Uribe, Robinson Ramírez-Vélez, and Mikel Izquierdo, developed the concept and draughted the manuscript. Ignacio Hormazábal-Aguayo, Yasmin Ezzatvar, and Antonio García-Hermoso prepared the tables and figures and completed the systematic review. Ignacio Hormazábal-Aguayo, Antonio García-Hermoso, Nidia Huerta-Uribe, and Mikel Izquierdo contributed to data preparation and modelling. All other authors provided data, developed models, reviewed results, provided guidance on methodology, or reviewed the manuscript, and approved the final version of the manuscript.

ACKNOWLEDGEMENTS

This study received no funding.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

ETHICS STATEMENT

This study did not involve human participants or animal research. This work was based on already produced and published data.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Ignacio Hormazábal-Aguayo https://orcid.org/0009-0002-7221-1731
Yasmin Ezzatvar https://orcid.org/0000-0002-9691-5998
Nidia Huerta-Uribe https://orcid.org/0000-0001-5443-5788
Robinson Ramírez-Vélez https://orcid.org/0000-0003-3075-6960
Mikel Izquierdo https://orcid.org/0000-0002-1506-4272
Antonio García-Hermoso https://orcid.org/0000-0002-1397-7182

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1002/dmrr.3749.

REFERENCES

1. Jasser-Nitsche H, Varga EM, Borkenstein HM, et al. Type 1 diabetes in children and adolescents is not associated with a reduced prevalence of atopy and allergic diseases. *Pediatr Diabetes*. 2017;18(8):890-894. https://doi.org/10.1111/pedi.12504
2. Marshall SL, Edidin D, Arena VC, et al. Prevalence and incidence of clinically recognized cases of Type 1 diabetes in children and adolescents in Rwanda, Africa. *Diabet Med*. 2015;32(9):1186-1192. https://doi.org/10.1111/dme.12701
3. Weng J, Zhou Z, Guo L, et al. Incidence of type 1 diabetes in China, 2010-13: population based study. *BMJ*. 2018:j5295. https://doi.org/10.1136/bmj.j5295
4. Onda Y, Sugihara S, Ogata T, Yokoya S, Yokoyama T, Tajima N. Incidence and prevalence of childhood-onset Type 1 diabetes in Japan: the T1D study. *Diabet Med*. 2017;34(7):909-915. https://doi.org/10.1111/dme.13295
5. Lu C-L, Shen H-N, Chen H-F, Li C-Y. Epidemiology of childhood type 1 diabetes in taiwan, 2003 to 2008. *Diabet Med*. 2014;31(6):666-673. https://doi.org/10.1111/dme.12407
6. Praveen PA, Madhu SV, Mohan V, et al. Registry of youth onset diabetes in India (YDR). *J Diabetes Sci Technol*. 2016;10(5):1034-1041. https://doi.org/10.1177/1932296816645121
7. Serban V, Brink S, Timar B, et al. An increasing incidence of type 1 diabetes mellitus in Romanian children aged 0 to 17 years. *J Pediatr Endocrinol Metab*. 2015;0. https://doi.org/10.1515/jpem-2014-0364
8. Sella T, Shoshan A, Goren I, et al. A retrospective study of the incidence of diagnosed Type 1 diabetes among children and adolescents in a large health organization in Israel, 2000-2008. *Diabet Med*. 2011;28:48-53. https://doi.org/10.1111/j.1464-5491.2010.03174.x
9. Spaans EAJM, Gusdorf LMA, Groenier KH, et al. The incidence of type 1 diabetes is still increasing in The Netherlands, but has stabilised in children under five (Young DUDEs-1). *Acta Paediatr*. 2015;104(6):626-629. https://doi.org/10.1111/apa.12949
10. Samuelsson U, Westerberg L, Aakesson K, et al. Geographical variation in the incidence of type 1 diabetes in the Nordic countries: a study within NordicDiabKids. *Pediatr Diabetes*. 2020;21(2):259-265. https://doi.org/10.1111/pedi.12943
11. Rojnic Putarek N, Ille J, Spehar Uroic A, et al. Incidence of type 1 diabetes mellitus in 0 to 14-yr-old children in Croatia - 2004 to 2012 study. *Pediatr Diabetes*. 2015;16(6):448-453. https://doi.org/10.1111/pedi.12197
12. Wu HB, Zhong JM, Hu RY, et al. Rapidly rising incidence of Type 1 diabetes in children and adolescents aged 0-19 years in Zhejiang,

China, 2007 to 2013. *Diabet Med*. 2016;33(10):1339-1346. https://doi.org/10.1111/dme.13010
13. Kim JH, Lee CG, Lee YA, Yang SW, Shin CH. Increasing incidence of type 1 diabetes among Korean children and adolescents: analysis of data from a nationwide registry in Korea. *Pediatr Diabetes*. 2016;17(7):519-524. https://doi.org/10.1111/pedi.12324
14. 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
15. Haynes A, Bulsara MK, Bergman P, et al. Incidence of type 1 diabetes in 0 to 14 year olds in Australia from 2002 to 2017. *Pediatr Diabetes*. 2020;21(5):707-712. https://doi.org/10.1111/pedi.13025
16. Flint SA, Gunn AJ, Hofman PL, et al. Evidence of a plateau in the incidence of type 1 diabetes in children 0–4 years of age from a regional pediatric diabetes center; Auckland, New Zealand: 1977–2019. *Pediatr Diabetes*. 2021;22(6):854-860. https://doi.org/10.1111/pedi.13236
17. Gyurus EK, Patterson C, Soltesz G. Twenty-one years of prospective incidence of childhood type 1 diabetes in Hungary - the rising trend continues (or peaks and highlands?). *Pediatr Diabetes*. 2012;13:21-25. https://doi.org/10.1111/j.1399-5448.2011.00826.x
18. Vukovic R, Jesic MD, Vorgucin I, et al. First report on the nationwide incidence of type 1 diabetes and ketoacidosis at onset in children in Serbia: a multicenter study. *Eur J Pediatr*. 2018;177(8):1155-1162. https://doi.org/10.1007/s00431-018-3172-4
19. Parviainen A, But A, Siljander H, et al. Decreased incidence of type 1 diabetes in young Finnish children. *Diabetes Care*. 2020;43(12):2953-2958. https://doi.org/10.2337/dc20-0604
20. 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*. 2014;57:57-62. https://doi.org/10.1007/s00125-013-3090-y
21. Kamrath C, Rosenbauer J, Eckert AJ, et al. Incidence of type 1 diabetes in children and adolescents during the COVID-19 pandemic in Germany: results from the DPV registry. *Diabetes Care*. 2022;45(8):1762-1771. https://doi.org/10.2337/dc21-0969
22. International Diabetes Federation. IDF Diabetes Atlas. Int. Diabetes Fed. 10th ed.; 2021:5.
23. Kamrath C, Mönkemöller K, Biester T, et al. Ketoacidosis in children and adolescents with newly diagnosed type 1 diabetes during the COVID-19 pandemic in Germany. *JAMA*. 2020;324(8):801. https://doi.org/10.1001/jama.2020.13445
24. Salmi H, Heinonen S, Hästbacka J, et al. New-onset type 1 diabetes in Finnish children during the COVID-19 pandemic. *Arch Dis Child*. 2022;107(2):180-185. https://doi.org/10.1136/archdischild-2020-321220
25. Passanisi S, Salzano G, Aloe M, et al. Increasing trend of type 1 diabetes incidence in the pediatric population of the Calabria region in 2019–2021. *Ital J Pediatr*. 2022;48:66. https://doi.org/10.1186/s13052-022-01264-z
26. Al-Abdulrazzaq D, Alkandari A, Alhusaini F, et al. Higher rates of diabetic ketoacidosis and admission to the paediatric intensive care unit among newly diagnosed children with type 1 diabetes in Kuwait during the COVID-19 pandemic. *Diabetes Metab Res Rev*. 2022;38(3). https://doi.org/10.1002/dmrr.3506
27. Nóvoa-Medina Y, Pavlovic-Nesic S, González-Martín JM, et al. Role of the SARS-CoV-2 virus in the appearance of new onset type 1 diabetes mellitus in children in Gran Canaria, Spain. *J Pediatr Endocrinol Metab*. 2022. https://doi.org/10.1515/jpem-2021-0727
28. Gomez-Lopera N, Pineda-Trujillo N, Diaz-Valencia PA. Correlating the global increase in type 1 diabetes incidence across age groups with national economic prosperity: a systematic review. *World J Diabetes*. 2019;10(12):560-580. https://doi.org/10.4239/wjd.v10.i12.560
29. Xia Y, Xie Z, Huang G, Zhou Z. Incidence and trend of type 1 diabetes and the underlying environmental determinants. *Diabetes Metab Res Rev*. 2019;35:e3075. https://doi.org/10.1002/dmrr.3075
30. 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
31. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *The BMJ*. 2021;372:n71. https://doi.org/10.1136/bmj.n71
32. Loney PL, Chambers LW, Bennett KJ, Roberts JG, Stratford PW. Critical appraisal of the health research literature: prevalence or incidence of a health problem. *Chronic Dis Can*. 1998;19:170-176.
33. Ulm K. Simple method to calculate the confidence interval of a standardized mortality ratio (SMR). *Am J Epidemiol*. 1990;131(2):373-375. https://doi.org/10.1093/oxfordjournals.aje.a115507
34. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Br Med J*. 2003;327(7414):557-560. https://doi.org/10.1136/bmj.327.7414.557
35. Global IHME. *Health Data Exchange (GHDx)*. Institute for Health Metrics and Evaluation (IHME); 2020.
36. Create MC. Your Own Custom Map. https://www.mapchart.net/index.html
37. Chen Y, Huang Y, Qiao Y, et al. Climates on incidence of childhood type 1 diabetes mellitus in 72 countries. *Sci Rep*. 2017;7:12810. https://doi.org/10.1038/s41598-017-12954-8
38. Karvonen M Incidence and trends of childhood Type 1 diabetes worldwide 1990-1999. *Diabet Med*. 2006;23(8):857-866. https://doi.org/10.1111/j.1464-5491.2006.01925.x
39. Guo Y, Luo R, Corsi DJ, Retnakaran R, Walker MC, Wen SW. Caucasian and Asian difference in role of type 1 diabetes on large-for-gestational-age neonates. *BMJ Open Diabetes Res Care*. 2020;8(2):e001746. https://doi.org/10.1136/bmjdrc-2020-001746
40. Patterson CC, Harjutsalo V, Rosenbauer J, et al. Trends and cyclical variation in the incidence of childhood type 1 diabetes in 26 European centres in the 25 year period 1989–2013: a multicentre prospective registration study. *Diabetologia*. 2019;62(3):408-417. https://doi.org/10.1007/s00125-018-4763-3
41. Mohr SB, Garland CF, Gorham ED, Garland FC. The association between ultraviolet B irradiance, vitamin D status and incidence rates of type 1 diabetes in 51 regions worldwide. *Diabetologia*. 2008;51(8):1391-1398. https://doi.org/10.1007/s00125-008-1061-5
42. Aljabri KS, Bokhari SA, Khan MJ. Glycemic changes after vitamin D supplementation in patients with type 1 diabetes mellitus and vitamin D deficiency. *Ann Saudi Med*. 2010;30(6):454-458. https://doi.org/10.4103/0256-4947.72265
43. Craig ME, Howard NJ, Silink M, Chan A. The rising incidence of childhood type 1 diabetes in new South wales, Australia. *J Pediatr Endocrinol Metab*. 2000;13(4). https://doi.org/10.1515/jpem.2000.13.4.363
44. Ionescu-Tirgovişte C, Guja C, Călin A, Mota M. An increasing trend in the incidence of type 1 diabetes mellitus in children aged 0-14 Years in Romania - ten years (1988-1997) EURODIAB study experience. *J Pediatr Endocrinol Metab*. 2004;17(7). https://doi.org/10.1515/jpem.2004.17.7.983
45. Crow YJ, Alberti KG, Parkin JM. Insulin dependent diabetes in childhood and material deprivation in northern England, 1977-86. *BMJ*. 1991;303(6795):158-160. https://doi.org/10.1136/bmj.303.6795.158
46. Casu A, Pascutto C, Bernardinelli L, Songini M. Type 1 diabetes among Sardinian children is increasing. *Diabetes Care*. 2004;27(7):1623-1629. https://doi.org/10.2337/diacare.27.7.1623

47. Soltesz G, Patterson C, Dahlquist G. Worldwide childhood type 1 diabetes incidence? what can we learn from epidemiology? *Pediatr Diabetes*. 2007;8(s6):6-14. https://doi.org/10.1111/j.1399-5448.2007.00280.x
48. Gonzalez ELM, Johansson S, Wallander M-A, Rodriguez LAG. Trends in the prevalence and incidence of diabetes in the UK: 1996-2005. *J Epidemiol Community Health*. 2009;63(4):332-336. https://doi.org/10.1136/jech.2008.080382
49. Bruno G, Maule M, Merletti F, et al. Age-Period-cohort analysis of 1990–2003 incidence time trends of childhood diabetes in Italy. *Diabetes*. 2010;59(9):2281-2287. https://doi.org/10.2337/db10-0151
50. Karvonen M, Pitkäniemi M, Pitkäniemi J, Kohtamäki K, Tajima N, Tuomilehto J. Sex difference in the incidence of insulin-dependent diabetes mellitus: an analysis of the recent epidemiological data. *Diabetes Metab Rev*. 1997;13(4):275-291. https://doi.org/10.1002/(sici)1099-0895(199712)13:4<275::aid-dmr197>3.0.co;2-v
51. NYSTRÖM L, Dahlquist G, Östman J, et al. Risk of developing insulin-dependent diabetes mellitus (IDDM) before 35 Years of age: indications of climatological determinants for age at onset. *Int J Epidemiol*. 1992;21(2):352-358. https://doi.org/10.1093/ije/21.2.352
52. Samuelsson U, Lindblad B, Carlsson A, et al. Residual beta cell function at diagnosis of type 1 diabetes in children and adolescents varies with gender and season. *Diabetes Metab Res Rev*. 2013;29:85-89. https://doi.org/10.1002/dmrr.2365
53. Szalecki M, Wysocka-Mincewicz M, Ramotowska A, et al. Epidemiology of type 1 diabetes in Polish children: a multicentre cohort study. *Diabetes Metab Res Rev*. 2018;34(2):e2962. https://doi.org/10.1002/dmrr.2962
54. Kyvik KO, Nystrom L, Gorus F, et al. The epidemiology of Type 1 diabetes mellitus is not the same in young adults as in children. *Diabetologia*. 2004;47(3):377-384. https://doi.org/10.1007/s00125-004-1331-9
55. Patterson CC, Dahlquist GG, Gyürüs E, Green A, Soltész G. Incidence trends for childhood type 1 diabetes in Europe during 1989–2003 and predicted new cases 2005–20: a multicentre prospective registration study. *Lancet*. 2009;373(9680):2027-2033. https://doi.org/10.1016/s0140-6736(09)60568-7
56. Harjutsalo V, Sjöberg L, Tuomilehto J. Time trends in the incidence of type 1 diabetes in Finnish children: a cohort study. *Lancet*. 2008;371(9626):1777-1782. https://doi.org/10.1016/s0140-6736(08)60765-5
57. Hernández Herrero M, Terradas Mercader P, Latorre Martinez E, Feliu Rovira A, Rodríguez Zaragoza N, Parada Ricart E. Nuevos diagnósticos de diabetes mellitus tipo 1 en niños durante la pandemia COVID-19. Estudio multicéntrico regional en España. *Endocrinol Diabetes Nutr*. 2022;69(9):709-714. https://doi.org/10.1016/j.endinu.2021.12.003
58. Rahmati M, Keshvari M, Mirnasuri S, et al. The global impact of COVID-19 pandemic on the incidence of pediatric new-onset type 1 diabetes and ketoacidosis: a systematic review and meta-analysis. *J Med Virol*. 2022;94(11):5112-5127. https://doi.org/10.1002/jmv.27996
59. Boddu SK, Aurangabadkar G, Kuchay MS. New onset diabetes, type 1 diabetes and COVID-19. *Diabetes Metab Syndr Clin Res Rev*. 2020;14(6):2211-2217. https://doi.org/10.1016/j.dsx.2020.11.012
60. Aabdi M, Aarab A, Es-Saad O, Malki K, Bkiyar H, Housni B. New-onset diabetes in children during COVID-19: clinical case report. *Case Rep Endocrinol*. 2021;2021:1-4. https://doi.org/10.1155/2021/6654019

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Hormazábal-Aguayo I, Ezzatvar Y, Huerta-Uribe N, Ramírez-Vélez R, Izquierdo M, García-Hermoso A. Incidence of type 1 diabetes mellitus in children and adolescents under 20 years of age across 55 countries from 2000 to 2022: A systematic review with meta-analysis. *Diabetes Metab Res Rev*. 2023;e3749. https://doi.org/10.1002/dmrr.3749