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Type 1 diabetes incidence in children and adolescents in Mexico: Data from a nation-wide institutional register during 2000–2018

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ABSTRACT

Aims: To describe the annual incidence of type 1 diabetes in children and adolescents insured by the Mexican Institute of Social Security, the main health provider in Mexico, during 2000–2018.

Methods: We conducted a secondary data analyses using the incidence registers from the Epidemiological Surveillance Coordination of the Mexican Institute of Social Security collected during 2000–2018. Incident type 1 diabetes cases (age 19 years old and below) were identified using ICD-10-CM E10 diagnostic codes. Age, sex, and geographical region and seasonal-specific incidence were calculated with their corresponding annual percentage change (APC) as well.

Results: In the period 2000–2018, the number of incident cases with type 1 diabetes decreased from 3.4 to 2.8 per 100,000 in insured for subjects below 20 years old. We observed an increase in the 2000–2006, followed by a decrease for the 2006–2018 period (APC +16.1 and −8.7 respectively). Females and children <5 years old had a significant decrease in the incidence rate, while inhabitants in Central Mexico showed a significant increase. No difference was found in incidence between seasons.

Conclusions: Our study describes significant fluctuations of the incidence of type 1 diabetes during the period 2000–2018, which appeared to correspond to influenza outbreaks, among Mexican children and adolescents.

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1. Introduction

Incidence of type 1 diabetes mellitus is growing worldwide [1–3], it varies greatly between countries, ranging from 57.6 per 100,000 person-years in Finland to almost 0.1 in some Caribbean countries. At the world level, it is estimated that there are 10–20 million cases. In the US, the prevalence is 0.2 to 0.4% of the general population under age 20 years, close to 1% of all ages; the total number of cases is close to 1.4 million.

Although the North America/Caribbean region has low incidence, Mexico is rated second in the area, surpassed only by the U.S. (U.S. = 169.86 vs Mexico = 26.60 cases in 1000 < 20 years of age) [1]. In Mexico, five nationwide population-based surveys have measured the diabetes prevalence in adults older than age 20 [4–8]. A remarkable growth in the incidence and the number of cases has been demonstrated in the past two decades. During the same time period, overweight and obesity tripled its prevalence in adolescents [9]. Despite that, scant amount of data exists about the prevalence or the incidence of type 1 diabetes. The DIAMOND project [3] reported a remarkably low incidence (0.6/100,000 inhabitants) in a city (Veracruz), located on the east coast of Mexico between 1990 and 1993 [10]. However, according to the weekly report of the Epidemiological Surveillance Coordination of the Mexican Institute of Social Security (IMSS), the incidence increased from 3.4 to 6.2 per 100,000 insured pediatric population during the 2000 to 2010 period [11]. This weekly reporting system is part of the National Surveillance System (SSA/DGE/SUAVE), which includes all the main health providers in Mexico (IMSS, ISSSTE, SSA, DIF, SEDENA, PEMEX, SEDEMAR and others). Currently, the Mexican Institute of Social Security (IMSS) system covers about 50% of the total Mexican population, which increased from 101.7 million in 2000 to 123 million in 2018.

Clearly, additional studies focused on type 1 diabetes are needed in Mexico and in any other country with increasing numbers of patients with diabetes. IMSS is the country's major social security institution. Therefore, the aim of this study was to describe the number of new cases with type 1 diabetes reported every year in children and adolescents (aged 19 years or younger) covered by IMSS during an 18-year period (2000–2018).

2. Methods

A secondary data analysis was conducted with children and adolescent type 1 diabetes cases.

Type 1 diabetes is diagnosed in accordance with criteria established by the American Diabetes Association Expert Committee, and all patients are treated with insulin [12]. New cases of type 1 diabetes are systematically reported in the national IMSS register. All medical units of the IMSS provide weekly reports of transmissible and non-transmissible diseases based on records generated by family doctors from outpatient visits. Data is collected by the Coordination of Epidemiological Surveillance and the information is reported regularly in a weekly bulletin, now edited by the National Epidemiological Surveillance System. Information is available from 2000 to 2018 in a webpage https://www.gob.mx/salud/, and annual reports by the General Office of Epidemiology, available at http://www.epidemiologia.salud.gob.mx/anuario/html/anuarios.html#. The information was combined with that contained in daily records, all of which was entered and coded by personnel from the areas of medical computers and clinical files of each unit offering care. This data was then used in the present study. Data on sex, age group, notification week and geographical region were obtained.

2.1. *Statistical analyses*

Data are presented as morbidity rates (cases per 100,000 subjects), calculated by dividing the total number of incident cases by the total insured population ≤ 19 years old in the correspondent year using the annual information as reference. The information was stratified by gender and age groups (5-year intervals). Trends over the study period were evaluated using annual percentage of change (APC) with the Joinpoint program desktop version 4.6.0.0 (available at https://surveillance.cancer.gov/joinpoint/). This program applies a regression model that breaks down the incidence trend into several different lineal segments, in this case sex, age groups and regions, connected together by "joinpoints", and calculates an APC for each segment and an average APC (AAPC) for the overall trend [13].

A multiple linear regression was also performed.

3. Results

IMSS provides primary and specialized care to workers nationwide. The number of insured population ≤19 years old that was treated in primary care units in 2000 was 10,642,811; by 2018, this number had almost doubled to 20,062,520.

During the years covered by this report, the number of new cases with type 1 diabetes decreased from 3.41 per 100,000 insured cases aged ≤19 years in year 2000 (95% CI 3.07–3.77) to 2.83 in 2018 (95% CI 2.60–3.07). Two peaks were registered in 2006 (8.72 (95%CI 8.20–9.27)) and in 2009 (7.72 (95%CI 7.23–8.23) (Fig. 1). In 2014, the rate had a gradual upsurge until 2017, which again decreased by 2018 (Table 1). In the Joinpoint analysis, we observed an increase in the 2000–2006, followed by a decrease for the 2006–2018 period (APC +16.1 and −8.7 respectively) (Table 2).

Data was stratified by age (5-year intervals) and gender. The age groups with the biggest increase in number of cases were the 10–14 years old and 15–19 years old. The patterns in incidence showed different trends, depending on the age group. The incidence in children under 5 years old peaked in 2005, and has been fairly steady since 2011. However, the 10–14 year olds peaked in 2009, before decreasing and reaching a very slight increase in 2017, while the 15–19 year old rate soared dramatically in 2006, peaking again in 2009 and 2016 (Fig. 2). Interestingly enough, these peaks corresponded to influenza outbreaks (2005–2006, 2008–2009, 2015–2016). The

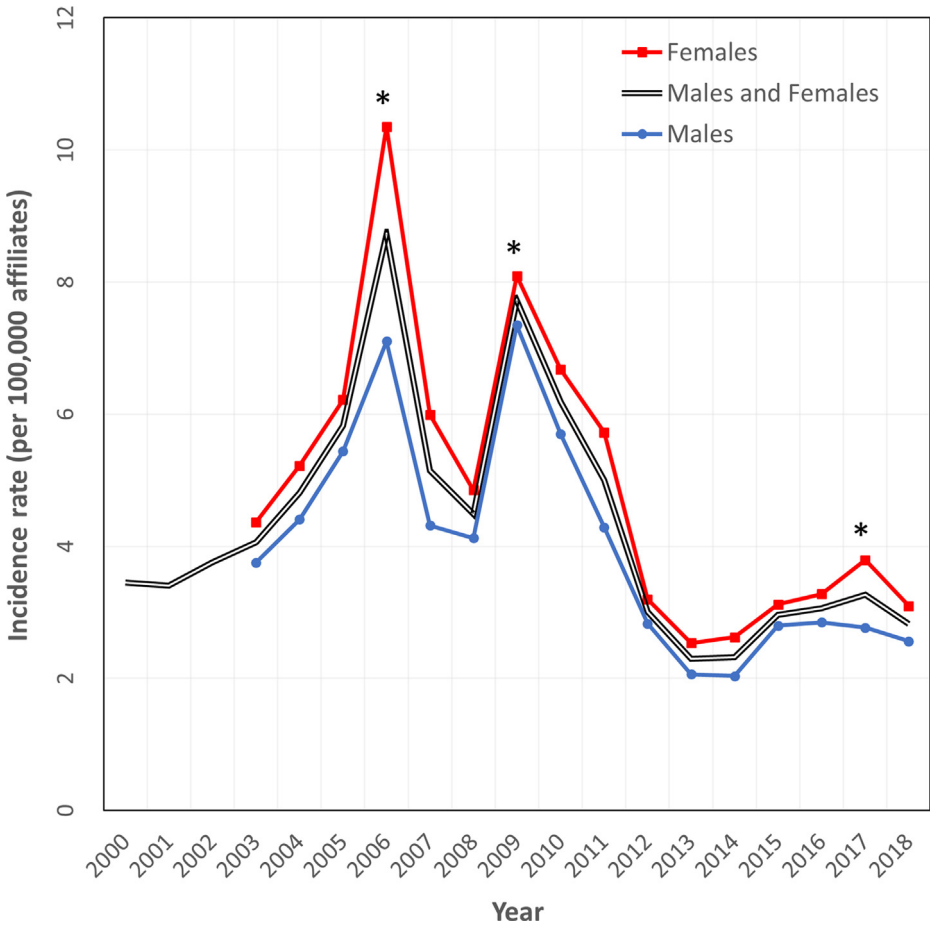

Fig. 1 – Incidence of type 1 diabetes in children and adolescents by gender in the Mexican Institute of Social Security (2000–2018). It should be noted that there were influenza outbreaks in 2005–2006, 2008–2009, and 2015–2016, which appear to correspond to the peaks in incidence of type 1 diabetes [14–16], as demonstrated by asterisks.

regions of Mexico with the greatest peaks appear to correspond to either avian or porcine industries [14–16]. This correspondence has not been studied to date in Mexico, although it has been suggested in other countries, such as Norway and Chile [17–20].

Before 2003 the data was not stratified by gender, as seen in Table 1. When the information became available by gender (2003–2018), an increase in the incidence rates was observed in both genders (Fig. 1). According to that information, the rate among males reached its peak in 2009, with 7.35 per 100,000 (95% CI 6.68–8.06), while in women the peak was achieved in 2006, with a rate of 10.36 (95% CI 9.55–11.22). In those younger than 5 years, incidence was higher in males than in females. On the other hand, in minors over 5 years of age, females had a consistently higher rate of incidence than males (Fig. 1, Supplementary Table 1). However, during the Jointpoint analysis, only females and age group <5 years old had a significant decrease in the type 1 diabetes incidence rate (Table 2).

When we look at geographical distribution, the northwest region of Mexico had the highest type 1 diabetes incidence rates, especially during the 2005–2006 peak, and followed by a significant decrease (APC +41.4 for 2001–2005 and APC −8.8 for 2005–2018) (Table 2, Fig. 3, Supplementary Fig. 1). Finally, no variation of new cases was found between seasons (Supplementary Fig. 2).

4. Discussion

In the past decade, an increase has been noted in the incidence of type 1 diabetes worldwide [1–3]. However, large differences exist between ethnic groups and regions (0.6 to 57.6 per 100,000) [3]. Sources of information are scant for this topic in many countries, including Mexico. Here, we report the number of new cases with type 1 diabetes occurring in the time period 2000–2018 among children and adolescents aged 19 years or younger that have access to the services provided by the largest Mexican insurer. This characteristic allows us to have national coverage and representativeness of a large proportion of the Mexican pediatric population. A growth in the incidence rates was observed in both genders, especially among subjects older than age 10. This report provides the first assessment of the incidence of type 1 diabetes over a long period of time in Mexico.

Mexico is considered among the countries with the lowest incidence of type 1 diabetes, on a par with Asian countries such as China (0.1 per 100 000) [3] and Japan (2.37 per 100,000) [21]. However, the evidence on which this assump-

Table 1 – Type 1 diabetes incidence rates in the population 19 years old and below in the Mexican Institute of Social Security 2000 – 2018.

Year	New cases	Population	Incidence Rate (95%CI)	RR (95%CI)
Total population ≤ 19 years[1]				
2000	367	10,642,811	3.45 (3.10–3.82)	Ref.
2001	369	10,834,298	3.41 (3.07–3.77)	0.99 (0.85–1.14)
2002	417	11,096,539	3.76 (3.41–4.14)	1.09 (0.94–1.26)
2003	452	11,134,292	4.06 (3.69–4.45)	1.18 (1.02–1.35)
2004	537	11,159,868	4.81 (4.41–5.24)	1.40 (1.22–1.60)
2005	667	11,443,886	5.83 (5.39–6.29)	1.69 (1.49–1.93)
2006	1024	11,739,112	8.72 (8.20–9.27)	2.53 (2.24–2.86)
2007	589	11,437,479	5.15 (4.74–5.58)	1.49 (1.31–1.71)
2008	513	11,433,088	4.49 (4.11–4.89)	1.30 (1.14–1.49)
2009	929	12,034,404	7.72 (7.23–8.23)	2.24 (1.98–2.53)
2010	698	11,284,768	6.19 (5.73–6.66)	1.79 (1.58–2.04)
2011	634	12,674,704	5.00 (4.62–5.41)	1.45 (1.27–1.65)
2012	566	18,803,594	3.01 (2.77–3.27)	0.87 (0.76–1.00)
2013	441	19,218,932	2.29 (2.09–2.52)	0.67 (0.58–0.77)
2014	450	19,363,213	2.32 (2.11–2.55)	0.67 (0.59–0.78)
2015	573	19,367,817	2.96 (2.72–3.21)	0.86 (0.75–0.98)
2016	571	18,668,316	3.06 (2.81–3.32)	0.89 (0.78–1.01)
2017	649	19,839,358	3.27 (3.02–3.53)	0.95 (0.83–1.08)
2018	567	20,062,520	2.83 (2.60–3.07)	0.82 (0.72–0.94)

Type 1 diabetes incidence rates per 100,000 affiliates 19 years old and below are shown.

CI 95%: Confidence Interval 95%; RR: Relative Risk.

Average annual percentage change (AAPC) for the period was −1.1 (CI95% −6.0, +4.1) for males and females; −2.6 (CI95% −11.9, +7.6) for males and −6.3 (CI95% −10.0, −2.5) for females.

[1] Before the year 2003, only totals were available, without separation by gender.

Table 2 – Type 1 diabetes incidence rates percentage change according to sex, age groups and regions. Mexican Institute of Social Security 2000 – 2018.

Cohort	Segment	Period	Estimates (95%CI)
National	1	2000–2006	APC 16.1 (0.6, 34.0)
	2	2006–2018	APC −8.7 (−12.6, −4.5)
	Full Range	*2000–2018*	*AAPC −1.1 (−6.0, 4.1)*
Males	1	2003–2009	APC 8.1 (−4.9, 23.0)
	2	2009–2013	APC −24.1 (−45.9, 6.4)
	3	2013–2018	APC 4.7 (−11.5, 23.9)
	Full Range	*2003–2018*	*AAPC −2.6 (−11.9, 7.6)*
Females	*Full Range*	*2003–2018*	*AAPC −6.3 (−10.0, −2.5)*
<5 years old	1	2001–2005	APC 47.5 (11.1, 96.0)
	2	2005–2018	APC −20.8 (−24.9, −16.5)
	Full Range	*2001–2018*	*AAPC −8.3 (−14.6, −1.6)*
5–9 years old	1	2001–2010	APC 6.7 (1.4, 12.2)
	2	2010–2013	APC −35.7 (−62.1, 9.1)
	3	2013–2018	APC 3.7 (−8.8, 18.0)
	Full Range	*2001–2018*	*AAPC −3.3 (−11.7, 6.0)*
10–14 years old	*Full Range*	*2001–2018*	*AAPC −0.2 (−3.3, 3.0)*
15–19 years old	1	2001–2006	APC 20.5 (5.2, 38.0)
	2	2006–2018	APC −6.1 (−9.0, −3.2)
	Full Range	*2001–2018*	*AAPC 1.0 (−3.1, 5.3)*
Northwest region	1	2001–2005	APC 41.4 (1.0, 97.8)
	2	2005–2018	APC −8.8 (−12.8, −4.6)
	Full Range	*2001–2018*	*AAPC 1.1 (−6.5, 9.4)*
Central region	*Full Range*	*2001–2018*	*AAPC 8.7 (4.2, 13.4)*
West region	*Full Range*	*2001–2018*	*AAPC 1.5 (−1.6, 4.6)*
Southeast region	*Full Range*	*2001–2018*	*AAPC 0.9 (−1.5, 3.3)*
East region	1	2001–2010	APC 9.0 (2.2, 16.4)
	2	2010–2018	APC −6.5 (−13.4, 0.8)
	Full Range	*2001–2018*	*AAPC 1.4 (−3.1, 6.1)*

CI 95%: Confidence Interval 95%; APC: annual percentage change; AAPC: average annual percentage change.

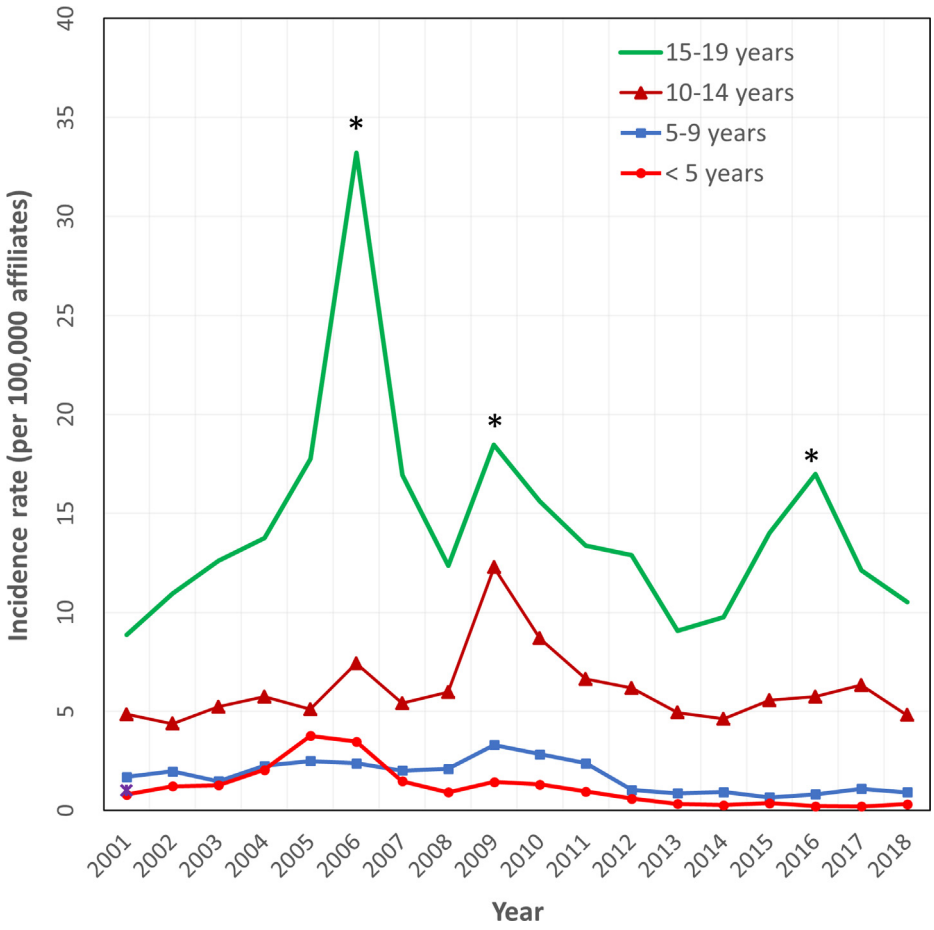

Fig. 2 – Incidence of type 1 diabetes according to the age group. It should be noted that there were influenza outbreaks in 2005–2006, 2008–2009, and 2015–2016, which appear to correspond to the peaks in incidence of type 1 diabetes [14–16], as demonstrated by asterisks.

tion is based is weak. In 1998, Aude Rueda et al. [9] measured the incidence of type 1 diabetes (1.15/100,000, 95% CI 0.75–1.70) in a register from 1978 to 1992 in only one Mexican state (Veracruz), which cannot be considered as representative of the country as a whole because that state typically has a very low incidence of type 1 diabetes (see supplementary Fig. 1). Previously, in 1993, the World Health Organization (WHO) reported 0.6/100 000 inhabitants in México [22]. By 2001, the WHO database was updated [15], based on the article by Aude Rueda and co-workers. The estimates presented here show that the Mexican pediatric population has an incidence rate similar to that found in Poland, Dominican Republic, Argentina, Brazil, Uruguay or Chile, where the incidence of type 1 diabetes was close to 6.58/100,000 inhabitants/year [23,24]. Nevertheless, the greatest incidences have been reported in Northern European countries and in the United States of America [17,18]. The incidence rates reported in our study sample are remarkably smaller compared to that reported in Germany (11.0), Canada (24.0), USA (15.0), Sweden (27.5) and Finland (36.5) in year 2001 [23]. In the US, the highest increase in rates of type 1 diabetes (2011–2012) were observed in Hispanic white youth (4.2% annual increase, vs. 1.2% in non-Hispanic whites) [18]. Thus, our data show that Mexico should be considered as a country with an incidence rate in the middle range.

Regrettably, changes in the incidence of type 1 diabetes have been the subject of very few reports. In countries such as Poland, Argentina and Brazil, that had an intermediate incidence, a significant increase was observed in the time period 2001–2004 (from 5.44 to 8.33 inhabitants/year, respectively, $p < 0.04$) [24]. In contrast, a survey done in the Madrid Region from 1997 to 2005 did not find changes in the annual incidence (15.9%/100 000 persons-years, 95% CI 15.0–16.8) [19]. The change in the incidence rate found in the pediatric Mexican population has a magnitude similar to that reported in other countries in the middle range of incidence worldwide, such as Germany (i.e. about 4% per decade, between 1996 and 2006) [20]. In some countries, like Norway, Chile and others, it has been suggested that there is an association between the presence of influenza and/or the application of vaccines with the risk of type 1 diabetes, although to date that association has not been corroborated [25–28]. Mexico also suffered influenza outbreaks in 2005–2006 and 2009, which supports the suggestion of this environmental factor as significant.

We looked for the age and gender groups that explained the growing incidence of type 1 diabetes in our study sample.

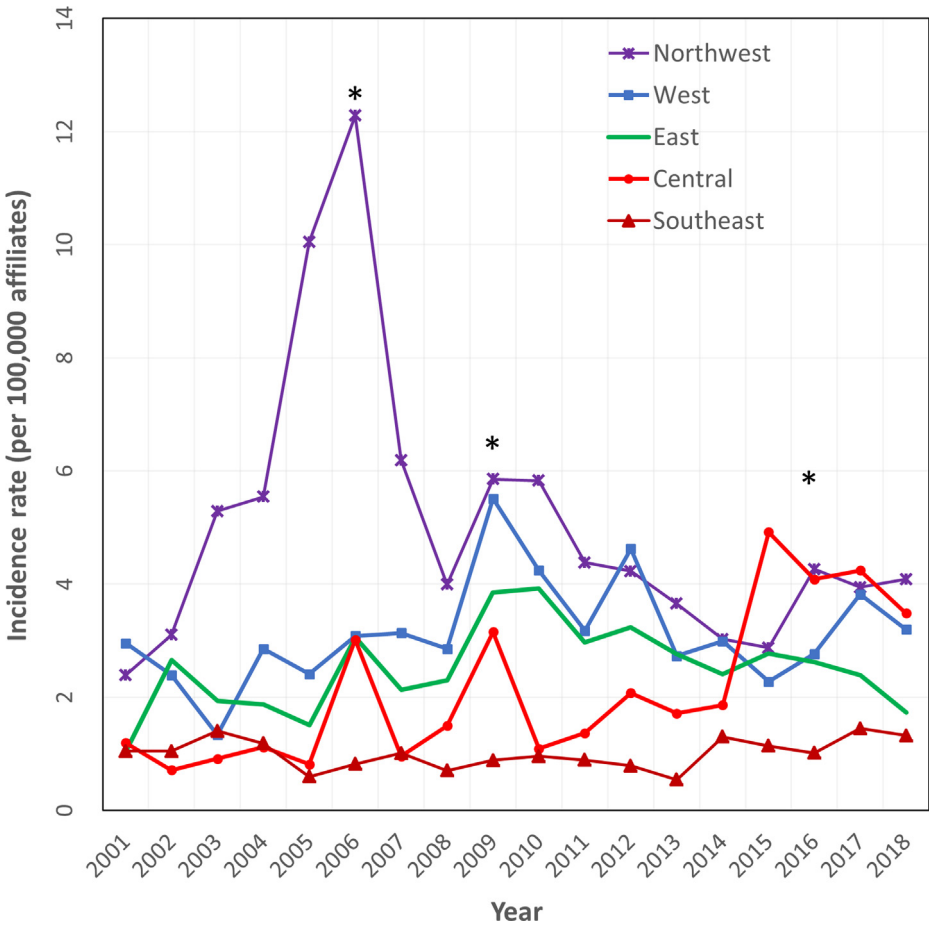

Fig. 3 – Type 1 diabetes incidence rates according to geographical region. It should be noted that there were influenza outbreaks in 2005–2006, 2008–2009, and 2015–2016, which appear to correspond to the peaks in incidence of type 1 diabetes [14–16], as demonstrated by asterisks.

Girls aged 10 or older was the group in which the largest increase was found. In children under age 5, males showed a greater incidence than females, while for those over 5 the females consistently showed greater incidence. In other parts of the world, such as France and Greece, males appeared to have a greater risk of diabetes type 1 [29,30]. However, in Latin America, in countries such as Argentina, Cuba, and Brazil, females are at greater risk [23,31].

Potential explanations for the increase of the incidence of type 1 diabetes include the well-known temporal variation of the occurrence of the disease and modifications in environmental factors. Peaks in the incidence occur every 5–6 years worldwide [32]. The pattern observed in our study sample (shown in Figs. 1 and 2) suggests that additional explanations should be sought, because the annual incidence rates peak at irregular intervals, affected by age and gender. However, the groups aged 10–14 and 15–19 showed the greatest variations and incidence. This may be explained by the fact that the physiological changes of puberty cause a worsening in insulin resistance, and insulin concentrations tend to peak during mid to late teenage years [33].

Social, economic and technological changes have occurred in the country, and the lifestyle of a great percentage of the population has been modified in the past few decades [34]. Changes in the humoral autoimmune response [35], a shorter duration of the sleep [36], perinatal infections, weight increase in the first months of life and increase in maternal age have become common in Mexicans; these factors have been associated with a higher risk for onset of type 1 diabetes [37–42]. Indeed, the risk of diabetes increases 43.2% for every 5 years of maternal age over 30 [43], but this association has not been confirmed in every population [44]. Additional studies are needed to identify with certainty the contribution of environmental factors to the changes in the incidence of type 1 diabetes observed in the Mexican pediatric population [45,46].

We must recognize that among the limitations of the study is that, as with other populations, the data presented depended on the diagnosis by the family doctor, and it is possible that, given the increase in the incidence of type 2 diabetes in children [47]' some cases were initially included as type 1, but in fact correspond to type 2 diabetes. Unfortunately, weight was not included in the registries utilized, so the possibility of obesity-related conditions was not considered. This is also true of the classification of newly-identified forms of monogenic diabetes, such as neonatal diabetes and maturity-onset diabetes of the young (MODY) [11]. Nevertheless, an exhaustive review of the clinical charts

and the necessary re-classifications were performed to correct for these errors.

In summary, this study demonstrates a substantial downward trend in diagnosed type 1 diabetes incidence during 2000–2018 among children and adolescents under 19 years of age in Mexico, with patterns depending on age.

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Contribution Statement: RAGD conceived the study question, carried out the study, analyzed results and wrote the manuscript. NHW analyzed results, contributed to discussion and reviewed and edited the manuscript. IDJAM and RARP carried out statistical analyses, interpreted the data and reviewed the manuscript. CAAS and VHBA contributed to the discussion and reviewed and edited the manuscript.

Declaration of Competing Interest

The authors state no conflicts of interest.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107949.

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