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ABOUT COVER

Editorial Board Member of *World Journal of Diabetes*, Guo-Xun Chen, PhD, Associate Professor, Director, Department of Nutrition, The University of Tennessee, Knoxville, TN 37909, United States. gchen6@utk.edu

AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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RESPONSIBLE EDITORS FOR THIS ISSUE

Observational Study

Prevalence of type 2 diabetes mellitus in the pediatric population of a third-level care hospital in Mexico City in 2013 and 2018

Jorge Mario Molina-Díaz, Blanca Estela Vargas-Terrez, Patricia Guadalupe Medina-Bravo, Antonia Martínez-Ambrosio, América Liliana Miranda-Lora, Miguel Klünder-Klünder

Jorge Mario Molina-Díaz, Department of Child Endocrinology, Children's Hospital Federico Gomez, Autonomous University of Mexico, Mexico City 06250, Mexico

Blanca Estela Vargas-Terrez, Faculty of Business, La Salle University, Mexico City 06250, Mexico

Patricia Guadalupe Medina-Bravo, Department of Endocrinology, Children's Hospital Federico Gomez, Mexico City 06720, Mexico

Antonia Martínez-Ambrosio, Department of Nursing and Endocrinology, Children's Hospital Federico Gómez, Mexico City 06720, Mexico

América Liliana Miranda-Lora, Epidemiological Research Unit in Endocrinology and Nutrition, Children's Hospital Federico Gomez, Mexico City 06720, Mexico

Miguel Klünder-Klünder, Division of Research, Children's Hospital Federico Gomez, Mexico City 06720, Mexico

Corresponding author: Jorge Mario Molina-Díaz, PhD, Doctor, Department of Child Endocrinology, Children's Hospital Federico Gomez, Autonomous University of Mexico, Mexico City 06250, Mexico. dereck79@live.com.mx

Abstract

BACKGROUND
Diabetes mellitus type 2 (T2DM) is a state of hyperglycemia due to a defect in the secretion and/or action of insulin, and it represents the most common form of diabetes worldwide. In Mexico, 10.3% of the adult population have been diagnosed with T2DM and it is expanding to the pediatric population.

AIM
To evaluate and compare the prevalence of T2DM in the pediatric population at the Children's Hospital, "*Hospital Infantil de México Federico Gómez (HIMFG)*", at two time periods: 2013 *vs* 2018.

METHODS
A comparison of two cross-sectional studies was done (2013 and 2018). The study population was comprised of children and adolescents 8-17 years old, from the

Diabetes Clinic at the aforementioned institution. A comprehensive interrogation regarding family history and perinatal antecedents was performed. Complete blood work after 12 h of fasting was obtained to determine serum levels of glucose, glycated hemoglobin, lipid profile, C-peptide, and insulin. The data were analysed using the statistical software package SPSS v. 23.0. A *P* value of < 0.05 was considered statistically significant.

RESULTS

A total of 151 patients were included: 47 from 2013, and 104 from 2018. There were age differences noted between the two periods with younger patients presenting T2DM in 2013. Also, T2DM predominated in the male sex in 55.36% in 2013 *vs* 32.7% in 2018. An increased prevalence of T2DM was noted from 2013 to 2018 (20.2% *vs* 33.0%, respectively), which was a statistically significant 12.8% increase (*P* < 0.0001). The illness phenotype was more aggressive in the 2018 group with the presence of a higher proportion of obesity, insulin resistance, and adverse lipid profiles.

CONCLUSION

The prevalence of T2DM at the *HIMFG* institution from 2013 to 2018 increased by 12.8% (20.2% *vs* 33.0%, respectively). The study results demonstrate the need for vigilance in T2DM trends, and to strengthen programs of healthy nutrition and physical activity as well as early detection and risk factors for obesity, data on insulin resistance, and metabolic syndrome, with the aim of preventing the development of T2DM.

Key Words: Diabetes; Children; adolescents; Epidemiology; Etiology; Risk factors and complications

Core Tip: Diabetes mellitus was a disease exclusive to the adult population; however, due to an increase in the prevalence of obesity, as well as genetic risk factors, this disease has increased in the pediatric population, having a different presentation, with the presence that causes micro and macrovascular complications at earlier ages. Therefore, it is necessary to think about this disease when faced with data of insulin resistance and identify complications early.

INTRODUCTION

In type 2 diabetes mellitus (T2DM), the state of hyperglycemia is due to a defect in the secretion and/or action of insulin which favor a decrease in the tissue response to the effect of insulin, leading to different abnormalities in the metabolism of carbohydrates, lipids, and proteins[1,2]. It is estimated that the function of the beta cells (β cells) of the pancreas is reduced by 20% per year in T2DM patients as a result of the compensatory hyperinsulinism secondary to insulin resistance (IR)[3]. The primary mechanisms that have been described for the development of T2DM are IR, and the deterioration of insulin secretion secondary to a progressive dysfunction of the β cells, which can vary between individuals and can convert to T2DM in an entity with an important heterogeneity[4].

T2DM is one of the primary chronic illnesses associated with high morbidity and mortality, and its incidence is increasing alarmingly worldwide. In 2011, it was estimated that there were about 366 million people with the disease; however, in 2030, the number of patients with T2DM could increased to more than 500 million[5]. Type 1 diabetes mellitus (T1DM) continues to be the most common form of diabetes in the pediatric population; however, the development of obesity has caused an increase in the percentage of cases, with reported rates of up to 45% in North America and 80% in Japan[6]. In the SEARCH study, an incidence of 9 cases/100000 to 12.5 cases/100000 in the population from 10-19 years old was demonstrated in the United States, with an important increase in all minority ethnic groups compared to the non-Hispanic Caucasian population[7,8].

In Mexico, according to the National Health and Nutrition Survey [*Encuesta Nacional de Salud y Nutrición* (*ENSANUT-2018*)], the prevalence of T2DM in people 20 years of age or older is 10.3%; in other

words, more than 8.6 million Mexicans suffer with this illness, yet there are no statistics about T2DM in Mexican children and adolescents[9].

The objective of this study was to evaluate and compare the prevalence of T2DM in the pediatric population of a tertiary care hospital at two time periods: 2013 *vs* 2018.

T2DM is a state of hyperglycemia as a result of an alteration in the secretion and/or action of insulin, and it is the main form of diabetes in about 90% of all cases of the condition. In Mexico, 10.3% of the population have been diagnosed with T2DM and it is expanding to the pediatric population due to the phenomenon of childhood obesity.

MATERIALS AND METHODS

Study design and location
This is a cross-sectional study of children and adolescents from the Diabetes Clinic at the Children's Hospital, "*Hospital Infantil de México Federico Gómez*", that compared the periods of January to December 2013 to January to December 2018.

Participants
Included were children and adolescents from 8-17 years of age of both sexes who met the diagnostic criteria for T2DM based on criteria from the American Diabetes Association, who had the clinical and biochemical phenotypes (obesity, acanthosis nigricans, and insulin resistance) and a diagnostic C-peptide level ≥ 0.45 ng/dL. Patients whose relatives presented with diabetes at an age younger than 25 years, leading to the suspicion of maturity onset diabetes of the young, were ruled out. In addition, study patients did not have a history of autoimmune disease or treatment that could alter glucose metabolism such as glucocorticoids or immunomodulators.

Anthropometric and biochemical measurements
Participants' height and weight were measured without footwear and wearing the least amount of clothing possible. Weight was determined using a digital scale (Seca® 884, Hamburgo, Alemania) with a precision of 0.1 kg. Height was measured using a stadimeter (Seca® 225, Hamburg, Germany) with a precision of 0.1 cm. The body mass index (BMI) was calculated using two measurements. Waist circumference was measured at the end of a respiratory expiration with a flexible, non-elastic measuring tape with a precision of 0.1 cm (Seca® 200, Hamburg, Germany) in a standing position, on the point mid-way between the most inferior rib and the top of the iliac crest. Arterial pressure was measured with a mercury sphygmomanometer on the right arm, sustained at the level of the heart, after 5 min of sedentary rest, using an arm band appropriate for the size of the patient. Three measurements were performed using the first and fifth Korotkoff sound with the reading closest to every 2 mmHg, ultimately using the calculated average of the three measurements.

Participants fasted for 12 h and then samples of peripheral blood (10 mL in total) were obtained for the evaluations of glucose (mg/dL, hexokinase Dimension RXL.MAX, Siemens®), insulin (mU/mL, chemiluminescence IMMULITE 1000, Siemens®, Euro, DPC, Llanberis, United Kingdom), C-peptide (ng/dL, chemiluminescence IMMULITE 1000, Siemens®, Euro, DPC, Llanberis, United Kingdom), hemoglobin A1c (HbA1c % and mmol/moL, Dimension RXL.MAX Siemens® immunoassay), total cholesterol, high density lipoprotein cholesterol (HDL-C), and triglycerides (Hitachi 902 analyzer®, Hitachi, LTD., Tokyo, Japan). The evaluation of LDL-cholesterol was calculated using the Friedewald formula (total cholesterol in mg/dL – HDL-C in mg/dL – triglycerides in mg/dL/5). The pancreatic reserve was evaluated using the HOMA-β index [(fasting insulin µUI/mL × 20)/(fasting glucose in mmol/L-3.5)].

Estimation of the subject's socioeconomic status (SES) was performed following the *AMAI-NSE8X7* model from the 'Mexican Association of Market Research and Public Opinion Agency, A.C'. This model classifies SES as lower, upper-lower, lower-middle, middle, upper-middle, and upper[10].

Statistical analysis
Descriptive statistics (measures of central tendency and dispersion) of the demographic, biochemical, and clinical variables were calculated. Variables with a normal distribution based on the Kolmogorov-Smirnov test are expressed as the mean and standard deviation, and variables not following a normal distribution are expressed as the median and interquartile ranges.

For the inferential analysis, the Student's *t* test was used for the continuous variables and the Pearson χ^2 test was used for the categorical variables, while medians were evaluated using the Mann-Whitney *U* test.

Logistic regression was used to determine the association between each of the variables and the presence of T2DM. The statistical package SPSS v. 23.0 was used for stastisical analyses, and a *P* value of < 0.05 was considered statistically significant.

RESULTS

A total of 151 patients with T2DM were included in the study: 47 patients from 2013, and 104 patients from 2018. The average age of the patients with T2DM in 2013 was 12.9 ± 1.9 years, and the average age in 2018 was higher (14.6 ± 1.9 years). The male sex predominated with 55.36% in 2013 *vs* 32.7% in 2018. The demographic, clinical, and biochemical data are shown in Table 1.

The prevalence of T2DM recorded was 20.2% and 33.0% for 2013 and 2018, respectively, with an observed increase of 12.8% (*P* < 0.0001). The T2DM first appeared in the 2013 group with clinical characteristics like obesity, acanthosis nigricans, polyuria, polydipsia, and unexplained weight loss in 36.2% of patients, while altered serum glucose in laboratory exams was the most frequent way that T2DM presented in the 2018 group. The presence of diabetic ketoacidosis has been reported in 22%-33% of T2DM cases; however, in 2013, diabetic ketoacidosis was the way in which the illness initially presented in 40.4% of cases, with the mild form being the most common in 21.3% of them. In 2018, diabetic ketoacidosis was the initial presentation in 28.8% of cases, with mild ketoacidosis being the most frequent in 13.5%.

Clinical and biochemical phenotypes also differed between the two periods; for example, the nutritional state of patients determined by the BMI showed a measurement of 25.3 ± 5.3 in 2013 *vs* 24.4 ± 6.7 in 2018, without statistically significant difference (*P* = 0.170). Nevertheless, on stratifying the groups according to the percentage of BMI with the Centers for Disease Control curves, a tendency to be more obese, and more morbidly obese, was observed in the 2018 group compared to the 2013 group (*P* = 0.297).

Antecedents of risk continue to be important in the manifestation of T2DM, as we can observe a greater increase in the prevalence of this illness when there was a first- or second-degree relative with diabetes, having demonstrated an exponential increase between the 2013 and 2018 groups. Similarly, the history of obesity in first- or second-degree family members demonstrated statistically significant differences between the two groups; with regard to birth weight, differences were also observed since the 2018 group presented lower birth weights compared to the 2013 group (Table 2).

Regarding SES, the 2013 group had a higher percentage of upper-lower and lower-middle SES levels (21.3% and 34%, respectively), and a lower percentage of patients with low SES. In the 2018 group, there was a significant increase of 26.9% in subjects with low and upper-lower SES compared to 2013, with the difference being statistically significant (*P* = 0.023) (Table 2).

The comorbidities associated with T2DM also differed between the two study groups: There was a higher percentage of hypertriglyceridemia, hepatic steatosis, and SAH in the 2018 group (21.2%, 75.0%, and 22.3%, respectively) and a lower percentage of hypercholesterolemia in the 2018 group compared to the 2013 group (27.9% and 46.8%, respectively) (Table 2).

DISCUSSION

Diabetes mellitus is one of the main chronic illnesses associated with high morbidity and mortality, and its incidence is increasing alarmingly around the world even in the pediatric population since more and more cases are being reported in children and adolescents, which concurs with the studies performed by Urakami and colleagues[11] where the incidence of T2DM in children in Tokyo was estimated at 2.6/100000/year, or two times higher than the reported incidence of T2DM. Therefore, in a short period of time, the prevalence of T2DM could surpass that of DM. In the United Kingdom, Candler also reported an increase in the incidence of T2DM between 2005 and 2015, which tended to be statistically significant with higher incidence among girls and among boys of the ethnic group belonging to South Asia[12].

In the present study, changes to the phenotypes were found since the tendency for the BMI to be higher was observed in the 2018 group, as well as more IR and less pancreatic reserve. In the TODAY study, Zeitler *et al*[13,14] described a more aggressive T2DM phenotype in the pediatric population, which predisposes to earlier dependency on insulin and a presentation of chronic complications in a shorter term[15].

Primary contact physicians in their daily practice should consider that T2DM can be present in children, and that it is related to the presence of overweight/obesity. Therefore, early screening is important in these types of patients who also present with a phenotype of IR, low birth weight, and a family history of diabetes.

The way in which T2DM first appears is variable; however, in 2013 more than 40% of cases presented with diabetic ketoacidosis, which was higher than the 22%-30% reported by Copeland and Dabela[16,17]. In the present study, in first- and second-degree relatives the history of diabetes was reported in 75.9%, and obesity in 80.7%, which was higher than that reported by other studies where only 40% of family members were affected. The antecedent of gestational diabetes was higher in the 2013 group, and this decreased to half in the 2018 group, which likely suggests better prenatal programs. Therefore, genetic, perinatal, environmental, dietary, and psychosocial factors play a role in the etiology of T2DM [17,18].

Table 1 Clinical and biochemical characteristics of patients with type 2 diabetes

Variable	Patients with T2DM (2013)	Patients with T2DM (2018)	P value
	n = 47	*n* = 104	
Sex [H (%)]	26 (55.3)	34 (32.7)	**0.009**
Age (yr)[a]	12.96 ± 1.9	14.6 ± 1.9	**0.000**
Weight (kg)	62.6 ± 20.4	62.8 ± 19.4	0.956
Height (cm)	157.5 ± 14.2	156.9 ± 11.9	0.773
BMI (kg/m^2)[a]	25.3 ± 5.3	24.4 ± 6.7	0.170
Waist (cm)[a]	84.7 ± 14.2	84.5 ± 19.2	0.905
Cholesterol total (mg/dL)	163.4 ± 33.1	172.5 ± 39.8	0.172
HDL-C (mg/dL)[a]	40.7 ± 12.1	44.1 ± 8.6	0.087
LDL-C (mg/dL)[a]	100.0 ± 25.3	95.9 ± 31.3	0.436
Triglycerides (mg/dL)[a]	136.7 ± 92.0	147.7 ± 64.9	0.412
AST (U/L)[b]	22.0 (11-143)	23.0 (11-89)	0.403
ALT (U/L)[b]	43.0 (23-139)	36.0 (11-79)	**0.005**
Fasting glucose (mg/dL)[a]	150.9 ± 88.1	189.0 ± 109.2	**0.038**
HbA1c (%)[a]	10.5 ± 3.9	8.9 ± 2.8	0.069
Fasting insulin (mUI/mL)[b]	11.2 (2-71)	11.2 (2-80)	0.902
C-peptide (ng/dL)[b]	2.0 (0.09-8.0)	1.5 (0.1-8.5)	**0.014**
SBP (mmHg)[b]	95.8 (70-130)	110 (90-150)	**0.004**
DBP (mmHg)[b]	62.8 (48-85)	70.0 (60-90)	0.005
HOMA-β[b]	135.9 (23-160.9)	50.2 (16-145)	0.183

[a]mean ± SD.

[b]Median (interquartile ranges).

T2DM: Type 2 diabetes mellitus; BMI: Body mass index; HDL-C: HDL cholesterol; LDL-C: LDL cholesterol; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; HbA1c: Hemoglobin A1c; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HOMA-IR: Homeostatic Model of Assessment-Insulin Resistance.

In the analysis of the results, there is a demonstrated relationship between SES and an increase in the prevalence of T2DM, with a significant increase in this disease observed in patients belonging to the lower and upper-lower classes. This is consistent with the finding of Agardh *et al*[19] that there was an increase in the incidence of the disease in individuals with a low and medium-low SES (relative risk = 1.41, 95%confidence interval: 1.28-1.51). Type 2 diabetes is a disease that is directly influenced by social and economic conditions that include risk behaviors, type of diet, physical activity, smoking, alcoholism, and high levels of stress[20]. There are several studies where the disease is concentrated in areas of greater poverty and in people with a low level of income as well as a low level of education. This association may be due to health care, disease prevention, health promotion measures, willingness to seek treatment, lack of access to health services, and unhealthy lifestyles that these people have, leading to a greater concentration of T2DM in marginalized groups that experience socio-economic and educational deprivation that leads to higher mortality[21,22].

LIMITATIONS AND STRENGTHS

One of the main limitations of the study is its design, which, due to its cross-sectional nature, can imply association but not causation. As such, the study design does not allow for a specific explanation as to how some variables may affect the prevalence of diabetes in the pediatric population. Also, the determination of pancreatic antibodies could not be performed in all patients, which could be a parameter to try to exclude patients with type 1 diabetes; although it is worth mentioning that a percentage between 20%-30% of patients with T2DM have positive pancreatic antibodies[23,24]. The size of the sample is another limitation, since it is unicentric and may not fully reflect the reality that is experienced in Mexico as a whole. Nevertheless, since the institution is a national reference center for tertiary level

Table 2 Family member and perinatal antecedents in the two study groups, *n* (%)

Variable	Patients with T2DM (2013)	Patients with T2DM (2018)	P value
	n = 47	*n* = 104	
History of T2DM, in relatives of 1° and 2° [*n* (%)]	24 (51.1)	79 (75.9)	**0.002**
Antecedent of obesity in relatives of 1° and 2° [*n* (%)]	31 (65.9)	84 (80.7)	**0.048**
Antecedent of DM [*n* (%)]	7 (14.9)	9 (8.7)	0.249
Weight at birth (kg)	3.31 ± 0.66	3.03 ± 0.44	0.005
Socioeconomic status[a,b]			
Upper	5 (10.6)	6 (5.8)	
Upper-middle	6 (12.8)	6 (5.8)	
Middle	6 (12.8)	18 (17.3)	**0.023**
Lower-middle	16 (34)	18 (17.3)	
Upper-Lower	10 (21.3)	28 (26.9)	
Lower	4 (8.5)	28 (26.9)	
Comorbidities			
Hypercholesterolemia [*n* (%)]	22 (46.8)	29 (27.9)	**0.023**
Hypertriglyceridemia	27 (57.4)	78 (75.0)	**0.030**
Hypoalphalipoproteinemia	19 (40.4)	16 (15.4)	**0.001**
Hepatic steatosis	6 (12.8)	22 (21.2)	0.219
Arterial hypertension	5 (10.6)	22 (22.3)	**0.021**

[a]AMAI/NSE 8 × 7 model.
[b]Pearson χ^2 test.
T2DM: Type 2 diabetes mellitus.

health care, a significant number of patients with this pathology could be obtained compared to other medical centers.

CONCLUSION

T2DM continues to be a public health problem in Mexico and the world, and its prevalence has augmented alarmingly in recent years. At the "*Hospital Infantil de México Federico Gómez*" Children's Hospital, the rates of T2DM increased significantly from 2013 to 2018, having an early onset in children and adolescents, as well as a more aggressive phenotype; in other words, patients tended to be more obese and have more lipid alterations, which can lead to worse metabolic control, greater chronic complications, and significantly higher risk of death due to cardiovascular causes or ischemic events. Therefore, T2DM in the pediatric population definitely presents with a more aggressive phenotype and worse prognosis over the long term. Hence, the results of the present study demonstrate the need for vigilance regarding the trend of T2DM, and the need to strengthen programs of healthy nutrition and physical activity along with early detection in confronting risk factors like obesity, IR, and metabolic syndrome, with the ultimate aim of preventing T2DM.

ARTICLE HIGHLIGHTS

Research background

This study is part of a line of research at the Federico Gómez Children's Hospital of Mexico on the behavior of type 2 diabetes in the child population.

Research motivation

Because Mexico is a country with a high prevalence of diabetes and obesity, which unfortunately

extends to the pediatric population, knowing the behavior of this disease in this specific age group will allow determining actions in clinical practice as well as in health policies.

Research objectives

To show the prevalence of type 2 diabetes in children and adolescents in two different time periods, as well as its clinical and biochemical characteristics.

Research methods

This is a cross-sectional study of children and adolescents from the Diabetes Clinic at the Children's Hospital, *Hospital Infantil de México Federico Gómez,* that compared two periods in the time.

Research results

An increase in the prevalence was observed, as well as a much more aggressive phenotype, which could lead to chronic complications in a shorter period.

Research conclusions

The rates of type 2 diabetes mellitus (T2DM) increased significantly from 2013 to 2018, having an early onset in children and adolescents, as well as a more aggressive phenotype; in other words, patients tended to be more obese and have more lipid alterations, which can lead to worse metabolic control, greater chronic complications, and significantly higher risk of death due to cardiovascular causes or ischemic events. Therefore, T2DM in the pediatric population definitely presents with a more aggressive phenotype and worse prognosis over the long term.

Research perspectives

We will continue with the follow-up of these patients to determine the behavior of the disease and have communication with the first and second level care centers to refer the patients in a timely manner.

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FOOTNOTES

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