

ORIGINAL ARTICLE

Debut and epidemiology of type 1 diabetes in pediatric patients

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ABSTRACT

Introduction: type 1 diabetes mellitus. It is one of the most prevalent chronic non-communicable diseases in the child population. Its incidence is variable. The causal multifactoriality is proposed where genetic, environmental and immunological factors are involved.

Objective: to characterize clinically and epidemiologically patients who debuted with type 1 diabetes mellitus in the child population of Villa Clara in the period from January 2007 to December 2016.

Methods: an epidemiological, observational, descriptive, retrospective longitudinal study was carried out at the José Luis Miranda Pediatric Hospital in Santa Clara. The population of 229 children diagnosed with the disease between 1/1/2007 and 12/31/2016 followed up at the institution was studied. Carrying out the review of medical records.

Results: 183 patients were identified, representing an average of 1.3/1,000 discharges/year. The absolute number of cases and their relationship with the number of discharges was variable (age, form of debut and sex). The average incidence was 13.12 cases per 100,000 pediatric population, with an average annual increase of 2.3 cases/year. The mean age at diagnosis was 9.74 ± 4.58 years, with greater frequency, respectively.

Conclusions: type 1 diabetes mellitus has a high incidence in Villa Clara, the debut occurs frequently between 5 and 14 years, without differences between the sexes, in the form of diabetic ketoacidosis and ketosis, with a very low frequency of complications. Some epidemiological characteristics were similar to those described in the literature.

Key words: type 1 diabetes mellitus; debut of the disease; risk factor; pediatric age

RESUMEN

Introducción: la diabetes mellitus tipo 1 es una de las enfermedades crónicas no transmisibles más prevalentes en la población infantil. Su incidencia es variable. Se plantea la multifactorialidad causal en la que están implicados factores genéticos, ambientales e inmunológicos.

Objetivo: caracterizar clínica y epidemiológicamente a pacientes que debutaron con diabetes mellitus tipo 1 en la población infantil de la Provincia de Villa Clara en el período comprendido de enero de 2007 a diciembre de 2016.

Métodos: se realizó un estudio epidemiológico, observacional, descriptivo, longitudinal retrospectivo en el Hospital "José Luis Miranda". Se estudió la población de 229 niños diagnosticados con la enfermedad entre el primero de enero de 2007 y el 31 de diciembre de 2016 seguidos en la institución. Se realizó la revisión de las historias clínicas.

Resultados: se identificaron 183 pacientes que representaron en promedio 1,3/1,000 egresos/año. El número absoluto de casos y su relación con el número de egresos fue variable (edades, forma de debut y sexo). La incidencia promedio fue de 13,12 casos por 100 000 habitantes pediátricos, con incremento promedio anual de 2,3 casos/año. La edad media al diagnóstico fue de 9,74±4,58 años con mayor frecuencia respectivamente.

Conclusiones: la diabetes mellitus tipo 1 tiene incidencia elevada en la Provincia de Villa Clara, el debut ocurre con frecuencia entre los cinco y los 14 años, sin diferencias entre los sexos, en forma de cetoacidosis diabética y cetosis, con muy baja frecuencia de complicaciones. Algunas características epidemiológicas fueron similares a las descritas en la bibliografía.

Palabras clave: diabetes mellitus tipo 1; debut de la enfermedad; factores de riesgo; edad pediátrica

INTRODUCTION

Type 1 diabetes mellitus (DM1) or insulin-dependent diabetes mellitus is the most frequent chronic endocrinological disease in the pediatric age group (more than 90% of cases). It is one of the most common chronic diseases in children and adolescents and represents a major health problem. The International Diabetes Federation (IDF) estimates that there are 490 100 children under 15 years of age with type 1 diabetes and that currently more than 200 children and adolescents in the world develop the disease every day and 77 800 new cases are diagnosed every year.⁽¹⁾

The incidence is increasing exponentially, with an average annual increase of 3%. It is projected that by 2020 it will double respected to the 2000 one. It varies up to 100 times between different countries, with the highest rates in Finland (52.6 per 100 000) and in northern Europe and Canada. They are very low in East Asia (Japan and China 2 and 3 per 100 000, respectively). In Spain the rate is intermediate (average 15 per 100 000), with significant variations between the different autonomous regions. In the countries of the African continent, rates range from 1.5 to 8.8 per 100,000 inhabitants.^(2,3)

In the United States it is 15 to 17 per 100,000 inhabitants, with 13,000 new cases diagnosed each year.⁽²⁾ In Central American countries the incidence is variable.^(3,4)

The incidence of type 1 diabetes shows an age-dependent pattern, with lower rates in children under four years of age and an increase with increasing age. The highest rates are found in the 10-14 years' age group. The relationship between the sexes shows no differences among those under 15 years of age; after puberty, males are more likely than females to develop type 1 diabetes.⁽⁵⁾

At present it varies between 427.5 per 100,000 inhabitants in Finland and 8.1 and 6.7 per 100,000 inhabitants in Mexico and Korea, respectively.^(1,5) In Cuba a study reveals an average annual incidence of 8.4 per 100,000 inhabitants.⁽⁴⁾ Because of its frequency and chronicity, DM1 is of great socio-health importance worldwide. Epidemiological studies are necessary to know the incidence and prevalence of the disease and to observe its evolution. It is of great importance to plan the health care resources dedicated to the disease and to study the possible etiological factors.^(1,4)

The study was carried out with the aim of describing the debut and epidemiology of type 1 diabetes mellitus in pediatric patients in Villa Clara Province in the decade 2007-2016.

METHODS

An epidemiological, observational, descriptive, retrospective, longitudinal and retrospective study was carried out at the "José Luis Miranda" University Pediatric Hospital of Santa Clara City, Villa Clara Province. The study population consisted of all children diagnosed with type 1 DM (229) who presented monitoring in the Endocrinology Consultations of the institution during the period from January 2007 to December 2016.

After establishing, intentionally (purposive, non-probabilistic sampling), the following criteria, no sample selection was performed because we worked with the totality of the aforementioned population.

The data were obtained from the medical records with the help of a document review guide prepared for research purposes and were exposed through different variables (years, age, age of debut, sex, personal pathological history, clinical forms of debut and complications). The data obtained were recorded in a statistical processor and the results were entered in tables and graphs according to the research objectives.

The annual incidence rates and the average incidence rates in the decade expressed per 100,000 inhabitants up to 19 years of age were calculated. The comparison of proportions test (Z statistic) and the comparison of means test (t statistic) were applied and the interpretation was made according to the significance (p) of the statistic in relation to the significance set for the tests $\alpha=0.05$.

The ethical standards established in the context and the bioethical principles of autonomy, beneficence, nonmaleficence, and justice were complied with. Because it is not a descriptive epidemiological investigation, no risk is exposed to the patient because only information about the disease is obtained. Absolute reliability of all data and of the individual results obtained was guaranteed.

RESULTS

In the period 2007-2016 in Villa Clara, the incidence of DM1 in children under 19 years of age averaged 13.12 per 100 000 inhabitants. An increase occurred from 7.85 per 100 000 children in 2007 to rate of 20.71 per 100 000 in 2016, with variation of 163.92% (Figure 1).

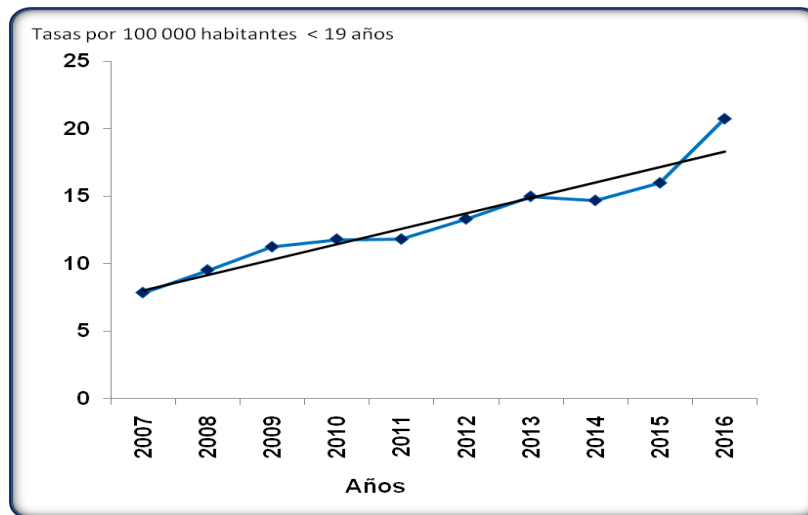


Figure 1. Incidence of type 1 diabetes mellitus in pediatric age

*Incidence rates per 100,000 population under 19 years of age

**Average incidence rate over 10 years (2007-2016)

Average population=174 495 inhabitants under 19 years of age

% change in incidence from 2007 to 2016=163.92%.

Average annual increase: 2.3 cases per year

At the end of the observed period, 115 were male, for 50.22%. The mean age of debut was 9±4.5 years, similar for both genders (Table 1). Approximately 65% of the children made their debut between 5 and 14 years of age. Although there was homogeneity between the groups compared, according to Goodman's and Kruskal's Tau test, as age increases the probability of disease debut increases in both sexes, with a maximum between five and 14 years of age.

Table 1. Debut age of type 1 diabetes mellitus according to gender

Debut age	Sexo				Total	
	Masculine		Feminine		No.	%
	No.	%	No.	%	No.	%
< 1	2	1.74	0	0.00	2	0.87
1 - 4	13	11.30	16	14.04	29	12.66
5 - 9	40	34.78	42	36.84	82	35.81
10 - 14	36	31.30	34	29.82	70	30.57
15 - 19	24	20.87	22	19.30	46	20.09
Total	115	100.0	114	100.0	229	100.0

*Percent per column

Goodman's and Kruskal's tau (columns/rows): 0.0007

$\chi^2=2.4989$; $p\chi^2=0.6448$

Mixed breastfeeding was the most frequent pathologic antecedent (58.08%). A history of diabetes mellitus in parents and grandparents was present in 35.37% and autoimmune diseases in relatives were identified in 63 cases (27.51%) -Figure 2-.

Diabetic ketoacidosis (94, 41.05%) and ketosis (91, 39.74%) were the most frequent forms of presentation. Hyperglycemia was present in 44 patients (19.21%) -Table 2-.

The form and age of diabetes debut were significantly related ($p=0.0000$) and, according to Goodman and Kruskal's Tau test, ages from 5 to 14 years are

predictive for ketoacidosis and ketosis and, as age increases, so does the probability of diagnosis through hyperglycemia.

Complications in pediatric patients with type 1 DM were neuropathy (2, 0.87%) and nephropathy (1, 0.44%)

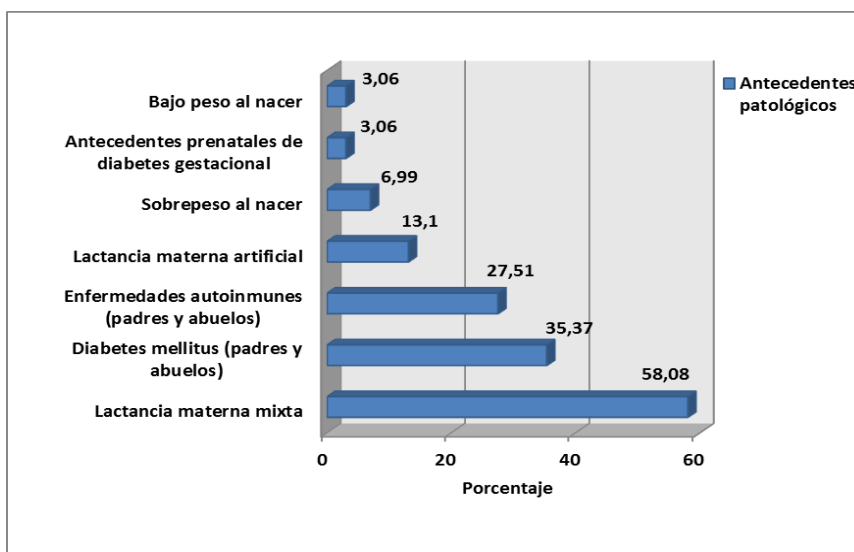


Figure 2. Pathologic history in pediatric patients with type 1 diabetes mellitus onset

Table 2. Clinical forms and age at patient debut

Age of debut (years)	Clinical forms of debut						Total	
	Diabetic ketoacidosis		Ketosis		Hyperglycemia		No.	%
	No.	%	No.	%	No.	%		
< 1	1	0.44	0	0.00	1	0.44	2	0.87
1 - 4	17	7.42	9	3.93	3	1.31	29	12.66
5 - 9	41	17.90	36	15.72	5	2.18	82	35.81
10 - 14	23	10.04	32	13.97	15	6.55	70	30.57
15 - 19	12	5.24	14	6.11	20	8.73	46	20.09
Total	94	100.0	91	100.0	44	100.0	229	100.0

*Percent per column
 Goodman's and Kruskal's tau (columns/rows): 0.0482
 $\chi^2=34.6006$; $p\chi^2=0.0000$

DISCUSIÓN

The Diabetes Mondiale project, sponsored by the World Health Organization, has proposed classifying rates into five groups according to incidence: very low (less than one case per 100 000 population), low (one to 4.99 cases per 100 000 population), intermediate (five to 9.99 cases per 100 000 population), high (10 to 19.99 cases per 100 000 population) and very high (greater than and equal to 20 cases per 100 000 population).⁽⁵⁾

In recent years, more cases of DM1 have been reported worldwide, with an annual increase of two to 3%.^(6,7,8,9,10) In addition, more young children, especially those under five years of age, were reported to be affected, accounting for 20 to 25% of the total. The increase in the incidence of DM1 appears to be greater than that of any other chronic noncommunicable disease.⁽¹⁰⁾ As genetic changes do not occur as rapidly, this increase suggests the involvement of environmental factors affecting subjects with genetic

susceptibility. The highest incidence rates of the disease were found in Europe and the United States. An overall increase in incidence rates of 2.8% per year was calculated, with a confidence interval (CI) of 2.4 to 3.2% and a significance of 95%; this increase is especially marked in Asia, Europe, and the United States. The increase in incidence rates was greater in younger age groups.

In Latin America, the highest incidence rates are reported by countries such as Uruguay and Brazil (higher than 5.0 per 100,000 inhabitants), while Peru and Venezuela (lower than 1.5 per 100,000 inhabitants) report the lowest rates of type 1 diabetes.^(2,9)

A Cuban study reports an increase in the incidence of type 1 diabetes mellitus at a rate of zero to one case/year in the first three years and 10 to 12 cases/year in the last three years of the study and emphasizes that this increase did not occur in a linear fashion, but that there were differences between the different time periods.⁽⁶⁾

According to these criteria, in Villa Clara Province the incidence is high (13.12 per 100,000 inhabitants in pediatric age), which is attributed to a higher detection of diabetes mellitus due to the structure of the Cuban Health System and to the surveillance of the disease in children under 19 years of age.

In the investigation, the distribution of the casuistry studied by age and sex, a similar distribution was found, without significant differences between males and females, with a discreet predominance of males (50.22%), and an average age of 9.74 ± 4.58 years. Patients were predominantly between five and nine years old and between 10 and 14 years old.⁽⁵⁾

Some studies suggest a relationship between the beginning of schooling and the consequent greater exposure to infectious agents, which favors the hypothesis that certain viral agents could be related to the production of damage to the pancreatic islets or at least to the triggering of DM1.^(1,4,7)

It is suggested that there is an increase in the beginning of DM1 at puberty because during this stage of life there is an increase in the secretion of growth hormones that antagonizes the action of insulin, together with the role of gonadal steroids and the psychic tensions that appear in this period.⁽⁸⁾

In the patients under study, a history of diabetes mellitus and autoimmune diseases in parents and grandparents and mixed breastfeeding (58.08%) are considered important. It is reported that the risk varies depending on whether the mother or father has the disease. When the mother has type 1 diabetes mellitus there is a two to 3% risk of developing the disease, and in children with a type 1 diabetic father the risk of developing the disease is five to 6%; when both parents are diabetic the risk increases to 30%. The risk for children of parents with type 1 diabetes mellitus is slightly higher if the diagnosis of the disease in the parents occurred before 11 years of age.⁽⁹⁾

DM1 is a multifactorial disease in which the type of feeding received in the first six months of life can condition its development, thus playing a protective role against the development of the disease. Mixed breastfeeding was the most frequent pathological antecedent (58.08%), 35.37% had a history of diabetes mellitus in parents and grandparents and autoimmune diseases in relatives were identified in 63 cases (27.51%). The absence or short period of breastfeeding may be a risk factor for the development of type 1 diabetes in later years.⁽¹⁰⁾

Diabetic ketoacidosis (94, 41.05%) and ketosis (91, 39.74%) were the most frequent forms of presentation. Hyperglycemia was present in 44 patients (19.21%). The form and age of diabetes debut were significantly related ($p=0.0000$) and, according to Goodman and Kruskal's Tau test, ages five to 14 years are predictive for ketoacidosis and ketosis and, as age increases, so does the probability of diagnosis through hyperglycemia. These results coincide with those of other studies consulted.^(5,6,9)

The literature refers that the main complications are given by acute metabolic disorders and long-term complications affecting small and large caliber vessels, resulting in retinopathy, nephropathy, neuropathy, ischemic heart disease and arterial obstruction with ischemia of the extremities.⁽⁷⁾ The scarce presence in the patients under study is considered related to the close follow-up by the medical team and the family in order to achieve adherence to treatment and prevent complications.

CONCLUSIONS

Type 1 diabetes mellitus has a high incidence in Villa Clara Province, with debut between 5 and 14 years of age, without differences between sexes, in the form of diabetic ketoacidosis and ketosis, with a very low frequency of complications.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTION OF THE AUTHORS

MRY: conceptualization, data curation, formal analysis, research, methodology, resources, validation, visualization, writing the original draft.

JGS: conceptualization, data curation, formal analysis, research, methodology, resources, validation, visualization, writing (review and edit).

EFM: formal analysis, research, resources, validation, writing (review and edit).

AINJ: resources, writing (review and editing).