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Type 1 diabetes in pediatrics during the COVID-19 pandemic: Time from symptom onset and forms of presentation at a referral hospital

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ABSTRACT

Introduction. The COVID-19 pandemic impacted on the health care of patients with type 1 diabetes mellitus (DM1). An increase in diabetic ketoacidosis (DKA) as a form of diagnosis was reported.

Objectives. To assess whether there were changes in the time from symptom onset, the causes of hospitalization due to DM1, and the proportion of severe forms, and to describe SARS-CoV-2 infection in these patients.

Population and methods. Cross-sectional study in patients younger than 19 years hospitalized due to DM1 from March 2018 to August 2019 (pre-pandemic) and from March 2020 to August 2021 (pandemic).

Results. The assessment included 135 hospitalizations in the pre-pandemic period and 96 during the pandemic. The time from symptom onset during the pandemic in those with debut of diabetes was shorter than in the pre-pandemic period (18.8 ± 10.2 versus 52.1 ± 12.1 days, respectively; $p < 0.001$). Hospitalizations due to all forms of diabetes debut and debut with DKA were more common during the pandemic than before it (59.4% versus 39.3%; odds ratio [OR]: 2.3; 95% confidence interval [CI]: 1.3–3.8; $p = 0.003$ and 40.6% versus 20.7%; OR: 2.6; 95% CI: 1.4–5.2; $p = 0.006$, respectively). Severe forms of DKA did not change between both periods (48.1% versus 59.9%; $p = 0.3$). Only 6 patients developed SARS-CoV-2 infection; 3 were severe.

Conclusion. During the pandemic, the time from symptom onset decreased and the frequency of hospitalizations due to debut of DM1 increased. The proportion of severe forms of DKA did not change.

Keywords: *COVID-19 pandemic; type 1 diabetes mellitus; diabetic ketoacidosis.*

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INTRODUCTION

The COVID-19 pandemic caused rapid changes in the organization of health systems and public behavior. Several studies reported an increase in the frequency of diabetic ketoacidosis (DKA) and severe DKA as forms of type 1 diabetes mellitus (DM1) debut during the pandemic.[1–3] A quarter of healthcare providers reported delays in diagnosis and an increased rate of hospitalization due to DKA during the COVID-19 lockdown.[4]

Patients faced difficulties in accessing medical consultations due to the preventive and mandatory social isolation policy. Health systems were overwhelmed by the care required by COVID-19 cases, and many families feared visiting health centers due to the risk of exposure to the virus.[1–3] These barriers in access to health care and the lack of adequate follow-up may have increased the risk of onset of severe forms of DKA in this period.

The objective of this study was to determine the impact of the isolation policy established during the COVID-19 pandemic on hospitalized pediatric patients with DM1. Therefore, we set out to assess whether, during the COVID-19 pandemic, there were changes in the time from symptom onset to DM1 diagnosis, whether the reasons for hospitalization changed, and whether there was an increase in the proportion of severe forms as the debut of DM1. Finally, we described the presence of SARS-CoV-2 infection in patients hospitalized due to DM1 during the pandemic.

POPULATION AND METHODS

Design

This was a cross-sectional study.

Population

The medical records of all patients diagnosed with DM1, younger than 19 years, hospitalized in Hospital General de Niños Pedro de Elizalde in 2 similar periods: pre-pandemic (from 3-20-2018 to 8-31-2019) and pandemic (from 3-20-2020 to 8-31-2021) were included. Patients referred from other healthcare centers were excluded due to the possibility that they might have been given a treatment different from that administered at our center.

Predictive variable

Study period (pre-pandemic/COVID-19 pandemic).

Outcome variables

- Time from symptom onset: for patients hospitalized due to the debut of DM1, considering the number of days from the onset of compatible symptoms to the moment of hospitalization.
- Reason for hospitalization: 2 groups were considered.
  - Patients with previous diagnosis of DM1 (non-debut DM1): DKA/ketosis/other.
  - Patients with debut of diabetes: DKA/ketosis/status period.

DKA was defined as an acute decompensation of DM1 with a pH < 7.30 and/or bicarbonate level < 15 mEq/L; while severe DKA was defined as pH < 7.10 and/or bicarbonate level < 5 mEq/L.[5] Ketosis referred to an acute decompensation of DM1 with presence of hyperglycemia and ketonemia greater than 0.6 mmol/L without acidosis, and status period referred to a diagnosis of DM1 due to hyperglycemia without ketonemia.[6] The category "Other" included hospitalizations due to respiratory conditions, infections, etc.

Control variables

- Age at the time of hospitalization.
- Sex: male/female.
- Body mass index (BMI): based on the formula of BMI = weight (kg)/height (m^2).
- Bicarbonate (HCO_3): as determined by the acid-base status in venous blood upon admission.
- Glycated hemoglobin (HbA1c): latest HbA1c measured in the study period, expressed as a percentage.
- SARS-CoV-2 infection: defined by positive PCR for SARS-CoV-2 at the time of hospitalization.

Analysis

Categorical variables were described as absolute frequency and percent frequency (with their corresponding 95% confidence interval [CI]), while continuous variables (all adjusted to normality with the Kolmogorov-Smirnov test) were expressed as mean and standard deviation. The association among categorical variables was assessed using the χ^2 test and the contingency coefficient, while continuous variables were compared using the t test for independent samples. A value of $p < 0.05$ was considered significant. The SPSS 20.0 software was used.

Ethical considerations

All data were dissociated from any information related to the identity of the study subjects. The protocol was approved by the Research Ethics Committee of Hospital General de Niños Pedro de Elizalde (registration number: 6360).

RESULTS

A total of 238 hospitalizations were recorded across both periods. Seven cases were excluded due to missing data (4 in the pre-pandemic period and 3 during the pandemic). Finally, 231 hospitalizations of patients with DM1 were analyzed: 135 in the pre-pandemic period and 96 during the pandemic.

In the overall sample, 57.6% of patients were female (n = 133); patients' average age was 10.8 ± 3.9 years and their average body mass index (BMI) was 19 ± 4.7 (*Table 1*).

Table 2 shows a comparison of the clinical characteristics between both periods. The time from symptom onset in patients with debut of diabetes was shorter in the pandemic than in the pre-pandemic period: 18.8 ± 10.2 versus 52 ± 12,1 days, respectively; $p < 0.001$.

The most common reasons for hospitalization in the pre-pandemic period and during the pandemic were DKA in patients with non-debut DM1 in 38.5% and DKA as debut of DM1 in 40.6%, respectively (contingency coefficient: 0.2 $p = 0.02$).

Hospitalizations due to debut of diabetes (DKA;

Table 1. Characteristics of the population

	Total	Pre-pandemic	Pandemic	*p*
Number of subjects	231	135	96	NS
Age (years)*	10.8 ± 3.9	11.15 ± 3.74	10.4 ± 4.1	NS
Sex female/male**	133/98	79/56	54/42	NS
BMI*	19.2 ± 4.7	19.5 ± 4.8	18.7 ± 4.5	NS

** Mean ± standard deviation (t test for independent samples); ** χ^2 test; NS: not significant; BMI: body mass index.*

Table 2. Clinical and metabolic characteristics

	Total	Pre-pandemic	Pandemic	*p*
Number of subjects	231	135	96	
Reason for hospitalization*				0.02
DKA (non-debut)	79	52 (38.5%)	27 (28.1%)	
Ketosis (non-debut)	20	13 (9.6%)	7 (7.3%)	
Other (non-debut)	22	17 (12.6%)	5 (5.2%)	
Debut DKA	67	28 (20.7%)	39 (40.6%)	
Debut ketosis	37	21 (15.6%)	16 (16.7%)	
Debut with status period	6	4 (3%)	2 (2.1%)	
Disease course**				
Symptom onset (days)	23.4 ± 12.1	52.1 ± 12.1	18.8 ± 10.2	< 0.001
Hospitalization due to debut of DM1***				
Yes/no**	110/121	53/82	57/39	0.003
Severe forms of DKA***				
Yes/no**	52/96	25/55	27/41	NS
Lab tests*				
HbA1c	11.2 ± 2.4	11.1 ± 2.2	11.4 ± 2.5	NS
pH	7.1 ± 0.1	7.2 ± 0.1	7.1 ± 0.1	NS
HCO_3	12.2 ± 6.7	13.2 ± 11.1	11.1 ± 6.4	0.04

** χ^2 test for contingency; ** mean ± standard deviation (t test for independent samples);*

**** χ^2 test with odds ratio estimation.*

DKA: diabetic ketoacidosis; DM1: type 1 diabetes mellitus; NS: not significant, HbA1c: glycosylated hemoglobin; HCO_3: bicarbonate.

ketosis, and status period) were more common during the pandemic than in the pre-pandemic period: 59.4% versus 39.3%, respectively (OR: 2.3; 95% CI: 1.3–3.8; $p = 0.003$).

The proportion of severe forms of DKA did not significantly change between both periods (48.1% versus 59.9%; $p = 0.3$).

No differences between both periods were observed in HbA1c and pH values. However, lower HCO_3 levels were noted during the pandemic ($p = 0.04$).

Analysis of patients with SARS-CoV-2 infection

Out of 96 hospitalizations during the pandemic, 6 had a positive PCR for COVID-19; the reason for hospitalization was non-debut ketosis in 3 of these patients, DKA debut in 2, and ketosis debut in 1. The 2 cases with debut of DM1 and SARS-CoV-2 infection corresponded to severe forms of DKA and required mechanical ventilation.

DISCUSSION

This study found that, during the pandemic, the proportion of hospitalizations in children with DM1 due to debut of DKA doubled compared to the pre-pandemic period. Such change occurred in a context of low incidence of COVID-19 infections in the analyzed sample, so it can be assumed that COVID-19 infections had no influence on this result, which could be explained by changes in habits observed in the population during this period.

Our results are consistent with studies that reported a higher number of hospitalizations due to DKA as a form of debut of DM1 during this period,[7–9] and different hypotheses were put forward to explain such increase. Several studies suggest a delay in seeking medical care; this delay was attributed to the fear of contagion on the part of families, the cancellation of several medical services, or the closure of some health centers due to an increase in COVID-19 cases among healthcare staff and inpatients.[10,11] In the case of patients newly diagnosed with type 1 diabetes who presented with DKA, it is assumed that the delay in seeking medical care would be preceded by a longer duration of DM1 symptoms. However, in our study, the time from the onset of diabetes symptoms during the pandemic was shorter. Other studies reported similar results,[12,13] which contradicts the hypotheses suggesting that the increased frequency of DKA is due to a delay in DM1 diagnosis. These findings would support the presumption that the development of DKA results from a particularly aggressive disease rather than to a missed or delayed diagnosis.[13]

There is a limitation regarding the variable duration of symptoms, since it depends on the perception of patients and their families, but this finding may be supported by the unchanged HbA1c levels reported during the pandemic.[14,15]

When analyzing the reasons for hospitalization in both periods, we observed a significant increase in the proportion of debut forms of DM1 (DKA, ketosis, and status period) during the pandemic, with a resulting decrease in the proportion of hospitalizations of patients with a previous diagnosis of diabetes. The latter is possibly associated with greater parental supervision, stricter monitoring of blood glucose levels, greater use of technology for diabetes care, and access to online consultations with the possibility of being followed-up by the primary diabetes specialist. Several studies have observed an adequate blood glucose control in patients previously diagnosed with DM1 during the lockdown period, which may be due to close parental supervision, increased use of diabetes technology, fear of complications, and access to telemedicine.[16,17] For patients with a previous diagnosis of DM1, the pandemic allowed a new form of physician-patient relationship, which, together with technological advances, facilitated access to medical consultations.[18]

In our study, only 3 patients who debuted with diabetes were positive for COVID-19; of these, 2 had severe DKA and required high levels of insulin (greater than 2 U/kg/day), inotropic agents, and mechanical ventilation. This may be consistent with reports that suggested a direct effect of SARS-CoV-2 on glucose metabolism.[19,20]

Our study has some potential limitations. In the context of a retrospective study, it is likely that the time from symptoms onset prior to hospitalization in forms of DM1 debut was not very precise; however, it is consistent with what has been reported in other studies.[21,22] As for the other recorded data, objective variables with a low possibility of bias were used.

CONCLUSION

During the pandemic, the time from symptom onset decreased and the frequency of hospitalizations due to debut of DM1 increased, with a higher proportion of DKA. The proportion of severe forms of DKA did not change. ■

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