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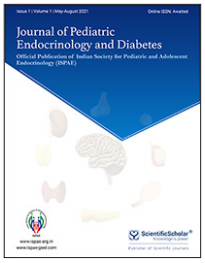

Original Article

Turkish children with new-onset type 1 diabetes mellitus had more severe clinical presentation during COVID-19 pandemic

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ABSTRACT

Objectives: The pandemic of coronavirus disease 2019 (COVID-19) seriously affected psychological, economic, and social aspects of life. We aimed to compare the clinical characteristics of children with new-onset type 1 diabetes mellitus diagnosed in the lockdown period with the profile of those diagnosed before the pandemic.

Material and Methods: The clinical features of 39 patients with new-onset type 1 diabetes diagnosed within 1 year starting from March 16, 2020, when schools were closed due to the COVID-19 pandemic in our country, were compared with the features of 27 patients with new-onset type 1 diabetes diagnosed in the previous year.

Results: Twenty-three (58.9%) of 39 patients presented with DKA in the pandemic group, while 7 (25.9%) of 27 patients presented with DKA in the pre-pandemic group ($P = 0.008$). A significant increase was also noted in the severe presentation in the pandemic group ($P = 0,019$). The decrease in HbA1C at the end of 3 months was significantly higher in the pandemic group.

Conclusion: Evaluation of patients with new-onset type 1 diabetes before and after pandemic showed a significant increase in the rates of severe DKA.

Keywords: Type 1 diabetes, Clinical presentation, COVID-19 pandemic, Children

INTRODUCTION

Type 1 diabetes mellitus is characterized by autoimmune beta-cell destruction, triggered by environmental factors in a genetically predisposed individual. Patients may progress to diabetic ketoacidosis (DKA) due to insulin deficiency. An infection, a serious lifestyle change, or a physical or emotional stress which is thought to accelerate this progression can often be found in the history. Studies supporting the higher incidences of type 1 diabetes after stressful events have been reported previously.[1,2]

The pandemic of coronavirus disease 2019 (COVID-19) affected psychological, economic, and social aspects of life. Schools were closed on March 16, 2020, after the first case was reported in our country. Strict measures were applied, both individually and socially. Within the scope of measures, it was recommended not to go to hospitals unless in a state of emergency. Total and partial curfews were applied for more than 1 year to the population under the age of 20.

In recent studies, a significant increase was found in DKA and severe ketoacidosis at presentation in children and adolescents during the COVID-19 pandemic.[3-8] Severity of the

clinical presentation is usually related with the duration of symptoms. An infection as the underlying trigger may also worsen clinical findings. The previous studies showed that mild DKA is more frequent than moderate and severe DKA in Turkish children with newly diagnosed type 1 diabetes.[9,10] However, during this period, we noticed that patients started to present with more severe clinical picture.

In this study, we aimed to compare the clinical characteristics of children with new-onset type 1 diabetes diagnosed in the lockdown period with of those diagnosed before the pandemic.

MATERIAL AND METHODS

The clinical features of 39 patients with new-onset type 1 diabetes diagnosed between March 16, 2020, and March 15, 2021, when schools were closed due to the COVID-19 pandemic in our country, were examined. Twenty-seven patients with new-onset type 1 diabetes diagnosed between the same dates of the previous year (March 16, 2019–March 15, 2020) were included as the control group. The group diagnosed during the pandemic was named "pandemic," and the control group was named "pre-pandemic." The study was approved by the ethics committee of our hospital and all authors accepted its compliance with the Helsinki II declaration (University of Health Sciences, Ümraniye Training and Research Hospital, Ethics Committee for Scientific Research; approval number-date: B.10.1.TKH.4.34. H.GP.0.01/351-20.12.2021).

The information on the duration of symptoms, hospital stay, signs of an infection, or other triggering factor were obtained from the medical records. Standard deviation scores of weight, height, and body mass index were calculated based on local reference data.[11,12] Pubertal development was evaluated according to the Tanner staging. Laboratory data at presentation, including venous blood gases, bedside blood ketone measurement, whole blood count, biochemical parameters, HbA1C, C-peptide, anti-glutamic acid decarboxylase, anti-insulin, and anti-islet cell antibodies, were recorded.

The epidemiological, anthropometric, and laboratory findings of patients in pandemic and pre-pandemic groups were compared. The distributions of patients according to the severity of clinical presentation among groups were evaluated in terms of difference. Correlations between epidemiological, anthropometric, and biochemical parameters were evaluated.

Statistical analysis

The data were analyzed using SPSS Statistics 22. In comparison of the distribution of patients among groups, Chi-square test was used. Independent samples *t*-test was used for the comparison of the normally distributed variables and Mann–Whitney U-test for non-normally distributed variables. The normally distributed data were shown as mean and standard deviation, while those that were not normally distributed were shown as median and interquartile range. $P < 0.05$ was considered statistically significant.

RESULTS

The mean age of 27 patients (14 boys and 13 girls) in the pre-pandemic group was 9.58 ± 4.57 years, 12 (44.4%) were pubertal, and 15 (55.5%) were prepubertal. The mean age of 39 patients (20 boys and 19 girls) in the pandemic group was 9.92 ± 4.36 years, 21 (53.8%) of them were pubertal, and 17 (43.5%) of them were prepubertal.

Epidemiological findings and anthropometric measurements were similar between the two groups [Table 1]. While seven of 27 patients presented with DKA before the pandemic, 23 of 39 patients presented with DKA during the pandemic ($P = 0.008$). Ten of 27 patients presented with hyperglycemia alone, ten with ketosis, three with DKA, and four with "severe DKA" in pre-pandemic group. Only four of 39 patients presented with hyperglycemia alone, 12 with ketosis, 14 with DKA, and nine with "severe DKA," during the pandemic period. The difference was statistically significant ($P = 0.019$) [Table 2].

The mean HbA1C was positively correlated with the pubertal stage in both groups (r = 0.429; $P = 0.026$; r = 0.399; $P = 0.013$) and positively correlated with age at diagnosis in the pandemic group (r = 0.419; $P = 0.08$). Those with longer duration of symptoms also had longer hospital stays (r = 0.319; 0.048). Ketone levels were significantly higher in the pandemic group ($P = 0.025$). The decrease in HbA1C in 3 months in the pre-pandemic group was 3.85 ± 2.5%, while 5.12 ± 1.8% in the pandemic group, which was significantly different ($P = 0.027$).

Three of our patients in the pandemic period had positive test results for COVID-19, but no symptom. One of them had severe DKA, one had ketosis with no acidosis, and one had only hyperglycemia.

DISCUSSION

In this study, it was determined that the patients diagnosed during the pandemic period were admitted with a more severe clinical presentation. Our study included two full-year periods, before and during the pandemic.

The study was designed to include patients diagnosed in two consecutive full-year periods to exclude seasonal differences. Several studies suggest a seasonality in the incidence of new-onset type 1 diabetes that peaks in the winter and troughs in the summer.[13] The frequency of new-onset diabetes in our pandemic group was significantly higher in winter. Infection remains the most common underlying trigger of diabetes

Table 1: Epidemiological and anthropometric findings of patients with type-1 diabetes diagnosed before the COVID-19 pandemic and diagnosed during the lockdown period.

Features	Pre-pandemic (*n*=27)	Pandemic (*n*=39)	*P*-value
Gender (F/M) *n* (%)	14 (51%)/13 (48%)	20 (51%)/19 (48%)	0.964
Age at presentation (year)	9.58±4.57	9.92±4.36	0.785
Duration of symptoms (day)	7.00 (2–90)	7.00 (2–60)	0.681
Duration of hospital stay (day)	9.00 (5–15)	10.0 (5–20)	0.435
Pubertal/prepubertal *n* (%)	12 (44%)/15 (55%)	21 (53%)/17 (43%)	0.390
Weight SDS	−0.36±1.00	−0.45±1.27	0.765
Height SDS	0.27±1.18	0.08±1.29	0.563
BMI SDS	−0.62±1.10	−0.27±3.39	0.555

BMI: Body mass index, SDS: Standard deviation score

Table 2: Clinical presentation of patients with type-1 diabetes diagnosed before the COVID-19 pandemic and diagnosed during the lockdown period.

Clinical presentation	Pre-pandemic *n*=27 (%100)	Pandemic *n*=27 (%100)	*P*-value
Hyperglycemia *n* (%)	10 (37.0)	4 (10.2)	**0.019***
Ketosis *n* (%)	10 (37.0)	12 (30.7)	
DKA *n* (%)	3 (11.1)	14 (35.8)	
Severe DKA *n* (%)	4 (14.8)	9 (23.0)	

**P*<0.05. DKA: Diabetic ketoacidosis

in children, occurring in 30–50% of cases.[14] However, we observed that none of our patients in the pandemic group had symptoms or signs of a triggering infection. In pandemic group, more patients were pubertal; more patients had difficulties in education and socioeconomic problems in the family. These made us think that puberty and emotional stress due to social and economic difficulties leading to psychological problems could be triggers.

The significant increase in the rates of DKA and severe DKA in the pandemic period was attributed to delayed diagnosis. This could be due to anxiety about going to hospital due to fear of COVID-19 disease, difficulty in reaching health-care centers, or relatively insidious occurrence of DKA since it was not triggered by an infection. In many children, the findings of this concomitant infection can provide earlier diagnosis before the acidosis worsens.

Similar studies were conducted in many centers by foreseeing these possibilities. First, Tittel *et al.* reported a multicenter study in Germany and compared the incidence of diabetes in the 2 months after the onset of the pandemic with the incidence of diabetes in the same months in the previous 10 years. They commented that the COVID-19 pandemic has no effect on the incidence in the short term, but that longer-term studies are needed.[15] Further studies from Germany, UK, Canada, Poland, Italy, Israel, and Brazil later showed increased frequency of DKA[3-8,16-19] The duration of hospital stay was longer in patients with more severe clinical findings. Clinical stabilization of the patient and cognitive and psychological readiness for education takes more time in patients presenting with DKA.

HbA1C, the marker of the level and the duration of hyperglycemia, was found to be higher in older patients and in advanced stages of puberty. One of the most interesting results of our study was that the decrease in HbA1C at the end of 3 months was significantly higher in the pandemic group than in the pre-pandemic group. Like ours, Praderi *et al.* also found improved glycemic control during lockdown in children and adolescents with type 1 diabetes.[20] This better glycemic control in the pandemic period made us think that the fear of more severe complications due to COVID-19 disease in patients with poorly controlled diabetes, fear of being again in a severe condition like DKA, and fear of having difficulty accessing healthcare could be effective. Besides, it was thought that adherence to treatment might have increased since the schools were closed, the stress of going to school, long lessons and examinations were less, and the patient had more time for self-care. It can also be attributed to the fact that parents were more at home, leading to healthier nutrition with home-made meals and more parental supervision.

CONCLUSION

In conclusion, the clinical presentation of patients with diabetes is more severe if the diagnosis is delayed, if the initial symptoms are insidious, and if it is difficult for people to reach health-care centers. Awareness about the signs, symptoms, and severity of diabetes under all circumstances is essential.

Author's contributions

Irmak Dicle Sargin: Study design, data collection, saving the data, writing, and revising the manuscript.

Heves Kırmızıbekmez: Diagnosis and follow-up of patients, study design, data collection, statistical analyses, writing, and revising the manuscript.

Gülcan Seymen: Diagnosis and follow-up of patients, data collection, and revising the final manuscript.

Esra Kutlu: Diagnosis and follow-up of patients, data collection, and revising the final manuscript.

Fatma Dursun: Diagnosis and follow-up of patients, data collection, and revising the final manuscript.

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

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Competing interests

The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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