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Research Article

A Long-Term Comparison of Presenting Characteristics of Children with Newly Diagnosed Type 1 Diabetes Before and During the COVID-19 Pandemic

Kaya et al. Characteristics of Children with Type 1 Diabetes Before and During the COVID-19 Pandemic

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What is already known about this topic
The limited use of healthcare services due to fear of COVID-19 transmission during the pandemic has raised concerns of delays in T1D diagnosis, among other diseases. This study investigates the presenting characteristics of newly diagnosed T1D patients assessed in our clinic during the pandemic and compares them with the pre-pandemic period.

What this study adds to the literature
Our study provides an additional contribution to the literature in its coverage of the one-year period during the pandemic and its comparison with the previous three years.

Abstract
Objective: Diabetic ketoacidosis (DKA) – a potentially preventable complication of Type 1 diabetes (T1D) – is one of the most common chronic childhood diseases, and is associated with a significant risk of morbidity and mortality. The limited use of healthcare services due to fear of COVID-19 transmission during the pandemic has raised concerns of delays in T1D diagnosis, among other diseases. This study investigates the presenting characteristics of newly diagnosed T1D patients assessed in our clinic during the pandemic and compares them with the pre-pandemic period.
Materials and Method: For the purpose of this study, the first year of the pandemic is referred to as the "pandemic period", and the previous three years as the "pre-pandemic period". Patient files were reviewed retrospectively, the demographic and clinical characteristics and laboratory findings of the patients were recorded, and the findings from both periods were compared.
Results: The number of patients diagnosed with T1D was 44 in the pandemic period, and 39 in 2017, 22 in 2018 and 18 in 2019 in the pre-pandemic period. The two groups were noted to have similar age, sex, pubertal stage and anthropometric characteristics ($p > 0.05$). Regarding the type of presentation, the frequency of DKA was significantly higher in the pandemic period (68.2%) than in the pre-pandemic period (40.5%) ($p = 0.006$), and this difference was also observed in the comparison by years ($p = 0.016$). The duration of symptoms (16.5±10.7 vs. 23.5±17.6 days) and the length of hospital stay (10±3.9 vs. 15.2±5.5 days) were significantly shorter in the pandemic period ($p = 0.032$, and $p < 0.001$, respectively). There was no difference in the frequency of severe DKA between the pandemic (46.7%) and the pre-pandemic (37.5%) periods ($p > 0.05$). However, pH (7.17±0.16 vs. 7.26±0.14) and bicarbonate (12.8±6.3 vs. 16.6±6.3) levels were significantly lower in the pandemic period ($p < 0.005$). Additional signs of infection on admission were less frequent in the pandemic period (9.1%) than in the pre-pandemic period (27.8%) ($p = 0.027$). The groups did not differ in terms of HbA1c, C-peptide, concurrent thyroid autoantibodies and tissue transglutaminase antibodies ($p > 0.05$). The rate of anti-GAD positivity was higher in the pandemic period (73.8% vs. 39.2%) ($p = 0.001$) while the frequency of other diabetes-associated autoantibodies was similar between the groups ($p > 0.05$). The PCR test for COVID-19 was negative in six patients with a history of contact.
Conclusion: We observed an increased frequency and severity of DKA in children with newly diagnosed T1D in the pandemic period, and our findings justify our concerns related to the diagnosis of other diseases during the pandemic. Studies to raise awareness of diabetes symptoms during the pandemic should be continued regularly to reach all segments of society. Our study provides an additional contribution to the literature in its coverage of the one-year period during the pandemic and its comparison with the previous three years.
Keywords: COVID-19, type-1 diabetes, diabetic ketoacidosis, child

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Introduction

The novel coronavirus disease (SARS-COV-2, COVID-19) was first reported in late 2019 in Wuhan in the Hubei province of China (1). The virus spread rapidly all over the world, and the World Health Organization and the Center for Disease Control and Prevention declared COVID-19 a pandemic on March 24, 2020 (2). The first case of COVID-19 in Turkey was reported

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on March 11, 2020 (3). Most of the hospitals in our country were assigned as referral hospitals, where among the applied restrictions were the postponement of outpatient appointments. In the first year of the pandemic, Turkey imposed social distancing restrictions from time to time to varying degrees (3). The limited use of healthcare services and the fear of contracting COVID-19 infection in hospitals have led to concerns about delays in the diagnosis of serious diseases.
The early diagnosis of type-1 diabetes (T1D) and metabolic control
are known to prevent many of the associated acute complications. T1D patients mostly present with such symptoms as polyuria, polydipsia, enuresis and weight loss (4). Diabetic ketoacidosis (DKA) is the most severe life-threatening acute complication of T1D. At the onset of newly diagnosed T1D in childhood, the reported frequency of DKA is 15–70% in various regions around the world (5).
The increased presentation of severe DKA among children in the diagnosis of T1D during the COVID-19 pandemic is a major concern**.** Severe DKA is not only life-threatening but also leads to the use of intensive care beds and resources during a period of potentially high demand. The limited studies of this issue conducted during the pandemic report different findings regarding the frequency of DKA on admission (6-13). The present study compares the clinical and laboratory characteristics of pediatric patients with newly diagnosed T1D during the pandemic with those of the three pre-pandemic years to identify the factors affecting the results, and makes recommendations in this regard.

Materials and Methods

This study included 123 newly diagnosed T1D patients aged 0–18 years who were followed up in the Pediatric Endocrinology Clinic and Pediatric Intensive Care Unit of the Karadeniz Technical University Faculty of Medicine. The collected data were analyzed in two groups. For the purpose of this study, the first year of the pandemic (February 1, 2020–January 31, 2021) was considered the "pandemic period" and the previous three years (February 1, 2019–January 31, 2020; February 1, 2018–January 31, 2019; and February 1, 2017–January 31, 2018) were considered the "pre-pandemic period". A retrospective review was made of the file records of the patients, comparing the age and date of diagnosis, sex, family history of diabetes, symptoms on admission to the outpatient clinic (polyuria, polydipsia, enuresis, vomiting, altered consciousness, fever, signs of infection, increased appetite, weight loss, Kussmaul breathing), duration of symptoms, body weight, body mass index [BMI = body mass (kg)/height (m2)], pubertal status, venous blood gas [pH, partial pressure of carbon dioxide (PCO2), bicarbonate (HCO3)], hemogram, biochemistry [glucose, blood urea nitrogen, creatinine, corrected sodium, potassium, chloride, amylase, calcium, phosphorus, alkaline phosphatase], hemoglobin A1c (HbA1c), preprandial-postprandial C-peptide, 25-hydroxyvitamin D (25 OH vitamin D), parathormone, insulin autoantibodies (IAA), islet-cell antibodies (ICA), glutamic acid decarboxylase antibodies (anti-GAD), anti-tissue transglutaminase antibodies (anti dTGA), thyroid function tests (TSH, fT3, fT4), anti-thyroid peroxidase (TPO), anti-thyroglobulin (anti-TG) and length of hospital stay.
HbA1c was measured by spectrophotometric method, and C-peptide levels were estimated by electrochemiluminescence (ECLIA). The presence of AIA, ICA, and GADA was determined by chemiluminescence immunoassay (CLIA). The electrochemiluminescence immunoassay method was used to analyze parathormone, 25-OH vitamin D, TSH, fT3, fT4, TPO and anti-TG.
DKA was diagnosed and classified at the time of admission in accordance with the ISPAD 2018 guidelines (5). Unlike in literature, our study also included cases with a history and clinical presentation compatible with T1D, but without positive diabetes-associated autoantibodies. Patients with positive IAA, ICA or anti-GAD were classified as type 1a while antibody-negative patients were classified as type 1b. Cases with a random blood glucose value of >200 mg/dl, pH of <7.30 and HCO3 of <15 mmol/l in blood gas, and positive urine ketones in a urine analysis were considered DKA. Patients diagnosed with DKA were divided into mild, moderate and severe groups according to their blood gas results. Cases with a blood gas pH of <7.3 or HCO3 of <15 mmol/l were considered mild DKA; while a pH of <7.2 or HCO3 of <10 mmol/l indicated moderate DKA; and a pH of < 7.1 or HCO3 of <5 mmol/l indicated severe DKA (5).
The data were analyzed using IBM SPSS Statistics (Version 23.0. Armonk, NY: IBM Corp.). Descriptive statistics were presented as numbers and percentages for categorical variables, and mean, standard deviation, minimum and maximum for quantitative variables. A Kolmogorov-Smirnov test was used to test the normality of continuous variables; quantitative variables were compared between two independent groups using the Student's t-test or the Mann-Whitney U test; and differences in the rates of categorical variables were analyzed using a Chi-square test. The level of statistical significance (alpha) was considered $p < 0.05$. A Fisher's exact test and an ANOVA were used to analyze the differences between the pandemic and pre-pandemic groups.
The study was initiated upon the written approval by the clinical research ethics committee of Karadeniz Technical University Faculty of Medicine (2021/210).

Results

The number of patients with newly diagnosed T1D was higher in the pandemic period (44) than in the three pre-pandemic years (39, 22 and 19, respectively). Demographic, clinical and laboratory data of the groups according to the pre-pandemic-pandemic period and years are presented in Tables 1 and 2. Autoantibody data of pre-pandemic period and pandemic period groups are presented in Table 3. The age, sex, pubertal stage and anthropometric characteristics of the groups were similar ($p > 0.05$). Regarding the type of presentation, the frequency of DKA was significantly higher in the pandemic period (68.2%) than in the pre-pandemic period (40.5%) ($p = 0.006$), and the difference in the frequency of DKA was also observed in a comparison by years ($p = 0.016$). The duration of symptoms (16.5±10.7 vs. 23.5±17.6 days) and the length of hospital stay (10.0±3.9 vs. 15.2±5.5 days) were shorter in the pandemic period ($p = 0.032$, and $p < 0.001$, respectively). There was no difference in the frequency of severe DKA between the pandemic (46.7%) and the pre-pandemic (37.5%) periods ($p > 0.05$). However, the pH (7.1±0.1 vs. 7.26±0.1) and bicarbonate (12.8±6.3 and 16.6±6.3) levels were significantly lower in the pandemic period ($p < 0.005$). Additional signs of infection (mostly tonsillitis) on admission were less frequent in the pandemic period (9.1%) than in the pre-pandemic period (27.8%) ($p = 0.027$). The groups did not differ in terms of HbA1c, C-peptide, concurrent thyroid autoantibodies and tissue transglutaminase antibodies ($p > 0.05$). The rate of anti-GAD

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positivity was higher in the pandemic period (73.8% vs. 39.2%) (p = 0.001) while the frequency of other diabetes-associated autoantibodies was similar between the groups (p > 0.05).
Furthermore, 17 (42.5%) of the 40 patients in the pandemic period, and similarly 28 (37.3%) of the 75 patients in the pre-pandemic period had a 25-OH vitamin D level of < 15 µg/L; and 23 (57.5%) of the 40 patients in the pandemic period and similarly 47 (62%) of the 75 patients in the pre-pandemic period had a 25-OH vitamin D level of < 20 µg/L. PCR tests were administered to six patients with a history of contact, revealing no COVID-19-positive case.

Discussion

In our study the number of patients with newly diagnosed T1D was higher in the pandemic period than in the three pre-pandemic years. The incidence of T1D worldwide has been increasing over the recent years (4). In addition, only one other hospital has a Pediatric Endocrinology Clinic in our city. As that hospital worked as a pandemic hospital during the study period, all patients with T1D were referred to our center, which is the reference hospital. Therefore, it could be an explanation for the higher number of patients during the pandemic period than the pre-pandemic period.
In the present study, significant increases were identified in the frequency (68.2% vs. 40.5%) of children presenting with DKA, the severity of DKA [(pH: 7.17±0.16 vs. 7.26±0.14), and bicarbonate levels (12.8±6.3 vs. 16.6±6.3)] at the onset of newly diagnosed T1D during the COVID-19 pandemic when compared to the pre-pandemic period. While the frequency of severe DKA increased in the pandemic period when compared to the pre-pandemic period, the difference was insignificant (46.7% vs. 37.5%).
The results of other studies conducted during the COVID-19 pandemic regarding DKA and severe DKA in children with T1D at the time of diagnosis support our findings. A previous study of Canadian children found the presentation of DKA to be higher during the pandemic than in the pre-pandemic period (55% vs. 36.4%), and the same study also established an increased presentation of hospital admissions with severe DKA (48.3% vs. 33.3%) (6). In Australia, a study reported the frequency of DKA in children to be significantly higher during the pandemic than in the pre-pandemic period (73% vs. 26%), and again, the results on the frequency of severe DKA were similar (45% vs. 5%) (7). In a study in Germany, an increase in DKA (23.5% vs. 44.7%) and severe DKA (13.9% vs. 19.7%) were identified during the COVID-19 pandemic, with those under the age of 6 years being at greater risk (8). A study of children in the United Kingdom reported a high rate (70%) of children presenting with DKA during the pandemic, with severe DKA being identified in more than half (52%) (9). In contrast, a study from Poland reported no increase in DKA during the pandemic when compared to the previous year, but identified an increased frequency of severe DKA (10). A multicenter study of children in Saudi Arabia reported a higher rate of DKA in those newly diagnosed with T1D during the pandemic (26%) compared to the pre-pandemic year (13.4%), with the frequency of severe DKA being similar in both years (11). In a study in Italy, fewer pediatric cases of newly diagnosed T1D by 23% and an increased frequency of severe DKA were reported during the pandemic when compared to the same period the previous year (44.3% vs. 36%) (12). A study in Turkey reported the rate of DKA in children with newly diagnosed T1D to be higher during the pandemic (91.9%) than in the pre-pandemic year (58.7%), while the frequency of severe DKA was similar in both years (13).
Compared to the pre-pandemic period, the pH and bicarbonate levels on admission were significantly decreased during the pandemic, in line with the increased frequency of DKA. In contrast, there was no statistically significant increase in the **frequency** of severe DKA. Social isolation and fear of exposure to COVID 19 might have led families to hesitate in referring to hospitals. Although there are reduced restrictions today, the pandemic continues, highlighting the significance of our findings.
In newly diagnosed T1D, the risk factors for DKA on admission include age <2 years, ethnic minority, low BMI, delayed diagnosis and low socioeconomic status, while the presence of a first-degree relative with T1D, a parent with a high level of education and a high incidence of T1D in the community are protective factors (14,15,16). No difference in anthropometric characteristics or the presence of T1D in relatives was identified between the pandemic and pre-pandemic groups in the present study, although the duration of baseline symptoms was found to be shorter in the pandemic period than in the pre-pandemic period (16.5±10.7 vs. 23.5±17.6 days). Similarly, Dżygało K. et al. (10) also identified no significant difference in the family history of T1D between the pandemic and pre-pandemic groups. A previous study ın the United Kingdom reported a short duration of symptoms with an increased frequency of severe DKA during the pandemic (9), which may be attributed to the fact that the parents were unaware of the typical symptoms of hyperglycemia during the lockdown restrictions.
Although literature lacks data on additional infections on admission, the rate of additional infections was lower in the pandemic period than in the pre-pandemic period in the present study (9.1% vs. 27.8%). In our country, education was provided through distance learning during the pandemic, except for certain age groups. Previous studies reported a decrease in the incidence of respiratory syncytial virus, parainfluenza viruses, human metapneumovirus, enteroviruses, adenoviruses and influenza viruses during the pandemic in Europe and Australia when compared to the previous years (17,18). We believe that during the pandemic, children were less exposed to infections due to the need to wear masks, the greater attention paid to hygiene, the limitations on social interactions and the closure of schools during lockdown.
In the present study, the rate of anti-GAD positivity was higher in the pandemic period than in the pre-pandemic period (73.8% vs. 39.2%), and similarly, Dilek et al.(13) reported a higher rate of anti-GAD positivity in the pandemic period than in the pre-pandemic period (45.9% vs. 19.6%). Anti-GAD positivity was found to be at a high rate as a risk factor for autoimmune type-1 diabetes in the young children of families exposed to psychosocial stress factors (19). The inability to go to school at all and the limitations on social interactions during the pandemic can be interpreted as psychosocial stress factors. We believe that more detailed studies are required to better clarify the relationship between COVID-19 and anti-GAD positivity.
The length of hospital stay was shorter in the pandemic period than in the pre-pandemic period (10±3.9 vs. 15.2±5.5 days), which is a natural consequence of the fact that most hospitals were assigned as referral hospitals, and beds were reserved mostly for COVID 19 patients during the pandemic.
It has been reported that vitamin D deficiency is common at onset of T1D in children (20). In our study, 42.5% of the 40 patients in the pandemic period, and similarly 37.3% of the 75 patients in the pre-pandemic period had a 25-OH vitamin D

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level of < 15 µg/L; and 57.5% of the patients in the pandemic period and similarly 62% of the patients in the pre-pandemic period had a 25-OH vitamin D level of < 20 µg/L. We found no evidence of increased frequency of vitamin D deficiency or insufficiency associated with inadequate outdoor activities and reduced sunlight exposure due to pandemic restrictions in children with T1D. We could not find any other study examining the frequency of vitamin D deficiency or insufficiency during the COVID-19 pandemic in T1D children.

Our work has some limitations and strengths. It adds to the limited existing literature describing DKA frequency in children during the COVID-19 pandemic. Moreover, while most of the studies conducted during the pandemic included short-term (average three-month) comparisons**,** our study covered a one-year period during the pandemic and compared the findings with those of the previous three years, making an additional contribution to literature. The main limitation of our study is that it is a single-center study. However, our center provides care for all children with T1D over a large geographic region, being a reference center. We also could not perform PCR testing for COVID-19 on all patients participating in the study due to the absence of associated symptoms.

In conclusion, we observed an increased incidence and severity of DKA in children with newly diagnosed T1D in the pandemic period. Our findings justify the concerns about the diagnosis of other diseases during the pandemic. To enhance physician and social awareness of T1D symptoms during the pandemic, diabetes awareness campaigns should be continued to reach all segments of society.

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	PRE-PANDEMİC PERİOD n=79	PANDEMİC PERİOD n=44	Total	p
Age at T1D onset (years)	8,13±4,75	8,48±4,37	8,26±4,60	0,572
Sex				1,000
Female	46,8% (37)	45,5% (20)	46,3% (57)	
Male	53,2% (42)	54,5% (24)	53,7% (66)	
Pubertal stage				0,326
Prepubertal	69,6% (55)	59,1% (26)	65,9% (81)	
Pubertal	30,4% (24)	40,9% (18)	34,1% (42)	
Weight_SDS	-0,15±1,32 (79)	-0,10±1,28 (44)	-0,13±1,30 (123)	0,852
Height_SDS	0,39±1,44 (79)	0,49±1,12 (44)	0,42±1,33 (123)	0,681
BMI_SDS	-0,51±1,72 (79)	-0,63±1,55 (44)	-0,55±1,66 (123)	0,724
Family history				1,000
Negative	81,0% (64)	79,5% (35)	80,5% (99)	
Positive	19,0% (15)	20,5% (9)	19,5% (24)	
Duration of symptoms (days)	23,51±17,60 (79)	16,54±10,73(44)	21,02±15,81 (123)	0,032
Hospitalization duration (days)	15,20±5,53(79)	10,02±3,89(44)	13,35±5,58(123)	0,000
Additional infections*				0,027
Negative	72,2% (57)	90,9% (40)	78,9% (97)	
Positive	27,8% (22)	9,1% (4)	21,1% (26)	
DKA at presentation				**0,006**
No DKA	59,5% (47)	31,8% (14)	49,6% (62)	
DKA	40,5% (32)	68,2% (30)	50,4% (61)	
Presentations by severity				0,662
Mild DKA	37,5% (12)	36,7% (11)	37,1% (23)	
Moderate DKA	25,0% (8)	16,7% (5)	21,0% (13)	
Severe DKA	37,5% (12)	46,7% (14)	41,9% (26)	
Creatinine (mg/dl)	0,56±0,184 (79)	0,56±0,18 (44)	0,56±0,18 (123)	0,920
Calcium (mg/dL)	9,57±0,57 (79)	9,51±0,46 (42)	9,55±0,53 (121)	0,583
Phosphorus (mg/dL)	4,33±1,22 (79)	4,34±0,74 (43)	4,33±1,07 (122)	0,626
ALP (U/L)	245,73±126,40 (74)	202,65±78,69 (41)	230,37±113,28 (115)	0,070
25 OH VİTD (µg/L)	19,00±10,12 (75)	17,36±9,11 (40)	18,43±9,77 (115)	0,538
PTH (ng/L)	20,44±13,00 (75)	25,00±15,68 (41)	22,11±14,14 (112)	0,101
TSH (mIU/L)	2,77±1,73 (79)	2,61±1,74 (43)	2,71±1,73 (122)	0,635
sT4 (ng/L)	1,08±0,32 (79)	1,03±,57 (43)	1,06±0,42 (122)	0,179
sT3 (ng/dL)	3,16±0,82 (52)	3,35±0,99 (36)	3,24±0,90 (88)	0,306
pH	7,26±0,14 (78)	7,17±0,16 (44)	7,23±,15± (122)	**0,002**
PCO2	31,20±10,88 (78)	25,95±10,28 (43)	29,33±10,92 (121)	**0,010**
HCO3 (mmol/L)	16,62±6,30 (78)	12,77±6,28 (44)	15,23±6,53 (122)	**0,003**
HbA1c (%)	11,91±2,60 (79)	12,26±2,57 (43)	12,03±2,58 (122)	0,479
Preprandial C-peptide (µg/L)	0,42±0,40 (77)	0,81±2,73 (42)	0,56±1,65 (119)	0,736
Postprandial C-peptide (µg/L)	0,68±0,60 (69)	0,62±0,56 (37)	0,66±0,58 (106)	0,464

Table 1. Demographic, clinical and laboratory results of pre-pandemic and pandemic patients.
TSH: Thyroid stimulating hormone, PTH : Parathormone, ALP: Alkaline phosphatase, 25 OH VİTD: 25-hydroxyvitamin D,
*Additional infections: 70% tonsillitis

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Table 2. Demographic, clinical and laboratory results of patients by years.

	2017 (N=39)	2018 (N=22)	2019 (N=18)	2020 (N=44)	Total (N=123)	p
Age at T1D onset (years)	7,57±4,40	8,52±4,88	8,85±5,42	8,48±4,37	8,26±4,60	0,778
Sex						0,848
Female	51,3% (20)	45,5% (10)	38,9% (7)	45,5% (20)	46,3% (57)	
Male	48,7% (19)	54,5% (12)	61,1% (11)	54,5% (24)	53,7% (66)	
Pubertal stage						0,355
Prepubertal	76,9% (30)	63,6% (14)	61,1% (11)	59,1% (26)	65,9% (81)	
Pubertal	23,1% (9)	36,4% (8)	38,9% (7)	40,9% (18)	34,1% (42)	
Height_SDS	0,17±1,39	-0,36±1,23	-0,58±1,16	-,10±1,28	-,13±1,30	0,168
Weight_SDS	0,65±1,20	0,11±1,68	0,15±1,57	,49±1,12	,42±1,33	0,351
BMI_SDS	-0,30±1,56	-0,57±1,60	-0,90±2,19	-,63±1,55	-,55±1,66	0,636
Family history						
Negative	92,3% (36)	81,8% (18)	55,6% (10)	79,5% (35)	80,5% (99)	
Positive	7,7% (3)	18,2% (4)	44,4% (8)	20,5% (9)	19,5% (24)	
Duration of symptoms (days)	25,6±20,2	20,727±15,9	22,2±12,9	16,5±10,7	21,0±15,8	0,143
Hospitalization duration (days)	14,8±5,6	15,5±5,4	15,5±5,6	10,0±3,8	13,3±5,5	0,000
Additional infections*						
Negative	69,2%(27)	77,3% (17)	72,2% (13)	90,9% (40)	78,9% (97)	
Positive	30,8% (12)	22,7% (5)	27,8% (5)	9,1% (4)	21,1% (26)	
DKA at presentation						0,016
No DKA	66,7% (26)	50,0% (11)	55,6% (10)	31,8% (14)	49,6% (61)	
DKA	33,3% (13)	50,0% (11	44,4% (8)	68,2% (30)	50,4% (62)	
Presentations by severity						
Mild DKA	23,1% (3)	27,3% (3)	75,0% (6)	36,7% (11)	37,1% (23)	
Moderate DKA	15,4% (2)	36,4% (4)	25,0% (2)	16,7% (5)	21,0% (13)	
Severe DKA	61,5% (8)	36,4% (4)	0,0% (0)	46,7% (14	41,9% (26)	
Creatinine (mg/dl)	,58±,18	,55±,16	,52±,19	,56±,18	,56±,18	0,616
Calcium (mg/dL)	9,54±,53	9,69±,59	9,50±,64	9,51±,46	9,55±,53	0,470
Phosphorus (mg/dL)	4,31±,93	4,36±,97	4,36±1,93	4,34±,74	4,33±1,07	0,770
ALP (U/L)	249,74±131,65	260,72±135,25	218,05±104,39	202,65±78,69	230,37±113,28	0,191
25 OH VİTD (µg/L)	19,85±10,60	18,01±11,71	18,30±6,42	17,36±9,11	18,43±9,77	0,598
PTH (ng/L)	23,32±11,13	17,03±17,05	19,22±8,95	25,00±15,68	22,11±14,14	0,040
TSH (mIU/L)	2,81±1,50	2,73±2,35	2,71±1,38	2,61±1,74	2,71±1,73	0,733
sT4 (ng/L)	1,13±0,32	0,96±0,27	1,11±0,35	1,03±0,57	1,06±0,45	0,141
sT3 (ng/dL)	3,55±0,73	2,78±0,84	2,91±0,69	3,35±0,99	3,24±0,90	0,018
pH	7,27±0,15	7,22±0,16	7,29±0,07	7,17±0,16	7,23±0,15	0,008
PCO2	31,12±10,74	29,01±11,68	33,92±10,20	25,95±10,28	29,33±10,92	0,030
HCO3 (mmol/L)	17,07±6,58	15,16±6,67	17,36±5,18	12,77±6,28	15,23±6,53	0,014
HbA1c (%)	11,74±2,69	12,32±2,59	11,75±2,50	12,26±2,57	12,03±2,58	0,735
Preprandıal C-peptide (µg/L)	0,43±0,34	0,49±0,59	0,34±0,23	0,81±2,73	0,56±1,65	0,923
Postprandial C-peptide (µg/L)	0,71±0,56	0,69±0,75	0,64±0,49	0,62±0,56	0,66±0,58	0,766

TSH: Thyroid stimulating hormone, PTH : Parathormone, ALP: Alkaline phosphatase, 25 OH VİTD: 25-hydroxyvitamin D,
*Additional infections: 70% tonsillitis

Uncorrected proof

	PRE-PANDEMİC PERİOD N=79	PANDEMİC PERİOD N=44	TOTAL	p
ICA (IU/mL)				0,546
Negative	35,4% (28)	42,9% (18)	38,0% (46)	
Positive	64,6% (51)	57,1% (24)	62,0% (75)	
anti GAD (IU/mL)				**0,001**
Negative	%60,8 (48)	%26,2 (11)	%48,8 (56)	
Positive	%39,2 (31)	%73,8 (31)	%51,2 (62)	
IAA (IU/mL)				0,213
Negative	87,3% (69)	95,2% (40)	90,1% (109)	
Positive	12,7% (10)	4,8% (2)	9,9% (12)	
anti-TPO (IU/mL)				1,000
Negative	87,2% (68)	88,1% (37)	87,5% (105)	
Positive	12,8% (10)	11,9% (5)	12,5% 8 (15)	
anti-TG (IU/mL)				1,000
Negative	97,3% (71)	97,6% (40)	97,4% (111)	
Positive	2,7% (2)	2,4% (1)	2,6% (3)	
anti-tTGA				0,108
Negative	93,2% (69)	82,5% (33)	89,5% (102)	
Positive	6,8% (5)	17,5% (7)	10,5% (12)	
type 1b	26,6% (21)	14,3% (6)	22,3% (27)	0,188
type 1a	73,4% (58)	85,7% (36)	77,7% (36)	

Table 3. Autoantibody results of pre-pandemic and pandemic-period patients

Table 3. Autoantibody results of pre-pandemic and pandemic-period patients.

ICA: Islet cell autoantibody, IAA: Insulin autoantibody, anti-GAD: Glutamic acid decarboxylase antibodies, anti-TPO: Anti-thyroid peroxidase, anti-TG: Anti thyroglobulin, anti-tTGA: Anti-tissue transglutaminase antibodies, type 1a: Positive diabetes-associated autoantibodies, type 1b: Negative diabetes-associated autoantibodies

uncorrected proof