

## ORIGINAL RESEARCH

### Managing pediatric diabetes and other endocrine disorders in the midst of the COVID-19 pandemic presents a number of difficult challenges

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#### ABSTRACT

**Background:** It determined the frequency, dimensions, treatment, and results of the COVID-19 pandemic in children who had endocrine problems and diabetes.

**Methods:** A worldwide network of endocrine societies was sent an internet survey in the form of a cross-sectional questionnaire. The professional and practice characteristics of respondents, the size of their clinics, the nation in which they practiced medicine, and the influence that COVID-19 had on endocrine illnesses were explored.

**Results:** The study was completed by respondents from 134 pediatric endocrine institutions located in 51 different countries and across all seven continents. The majority of pediatric endocrinology clinics have made adjustments to their standard checkups as well as their educational programming. More than twenty percent of clinics reported experiencing a lack of availability of crucial supplies or drugs. Patients diagnosed with diabetes and COVID-19 needed therapy in an intensive care unit. It has been clearly stated that pediatric patients with endocrine abnormalities have alterations in their biopsychosocial functioning as well as their behaviors.

**Conclusions:** This extensive worldwide study was carried out during the COVID-19 pandemic, and its findings underscore the fact that diabetes is more difficult to control than any other juvenile endocrine illness, and it also carries a higher risk of morbidity. It is necessary to acknowledge and treat the psychological anguish that has been caused by COVID-19. Every patient ought to have easy access to medical supplies, and it is essential that they maintain frequent interaction with the medical staff who are responsible for their treatment.

**Keywords:** COVID-19, children, diabetes, obesity and metabolic syndrome, adrenal, thyroid, growth, puberty.

#### INTRODUCTION

Still having a significant influence on a worldwide scale is the COVID-19 pandemic, which was brought on by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (1). Even if there has been progress made in immunization, there is a good chance that there will be repeated "waves" of infection over the course of many years before the vast majority of the population either becomes immune via infection or through vaccination (1–4).

There have been isolated cases of a disease similar to Kawasaki disease that has been linked to SARS-CoV-2 infection. This disease is now recognized as a complication of COVID-19

[multisystem inflammatory syndrome (MIS) in children (MIS-C)]. Children in general have a milder form of the disease than adults (5–8). On the other hand, very little is known regarding the effects of COVID-19 on patients who have ongoing disorders such as endocrine diseases, particularly youngsters (9). The majority of contemporary research has focused on endocrine problems that affect adult populations (10–13). Despite the fact that healthcare professionals (HCPs) and families need guidance on the clinical management of children with endocrine disorders during the challenging circumstances of the COVID-19 pandemic, this is not the case. This is especially true for children who have suspected or confirmed cases of COVID-19.

The results of a worldwide survey of healthcare professionals who specialize in pediatric endocrinology and are registered in the database maintained by the International Consortium for Pediatric Endocrinology (ICPE) are shown here. We discuss the clinical features of patients who were handled throughout the pandemic, and we emphasize the knowledge and practice of healthcare professionals working in pediatric endocrinology, as well as the particular problems they have experienced during the epidemic. In addition, we discuss the gaps that were identified between a previous survey on diabetes that was conducted early on in the pandemic (9) and the current survey that was conducted to evaluate and explain the frequency, dimensions, management, viewpoints, and outcomes of the COVID-19 pandemic in children, adolescents, and young people who are living with chronic endocrine disease.

## **METHODS**

This was a digital cross-sectional survey that was carried out over the course of eight weeks, beginning on December 3, 2020 and ending on February 5, 2021. The survey was carried out with the assistance of Google Forms (Google LLC, Mountain View, California, United States), which enables results to be stored and then evaluated using a spreadsheet-based format. In a recent publication of ours, the methodology behind the data gathering and survey is broken out in detail (9).

The target population was determined with the help of a worldwide network of endocrine societies that operate under the auspices of the International Council for Pediatric Endocrinology (ICPE). This network includes the International Society for Pediatric and Adolescent Diabetes (ISPAD), the European Society for Pediatric Endocrinology (ESPE), the Global Pediatric Endocrinology and Diabetes (GPED), the Latin American Society of Pediatric Endocrinology (SLEP), the Australasian Pediatric Endocrine (RAE). Previous attendees of the conferences, training schools, or postgraduate courses hosted by the societies were also considered for inclusion.

Six pediatric endocrinologists were responsible for developing the survey questions, and ICPE members were provided with a direct online connection as well as the opportunity to provide their approval to take part in the poll by email and other social media platforms (Facebook, Twitter, and LinkedIn).

The questionnaire was broken up into fourteen different sections, each of which asked a different set of questions about the respondents' professional and practice profiles, the sizes of their clinics, the countries in which they practiced medicine, and how they managed the most common endocrine diseases.

The questions covered the practice and perceptions of HCPs in relation to the number of patients that were cared for, the organization of education sessions, the impact of the COVID-19 pandemic on daily routine, the availability of medications, the frequency of acute complications, delays to diagnoses, deterioration of disease control, and the psychological impact on patients and their families. We asked a few more detailed questions in order to define the profile of patients who tested positive for SARS-CoV-2 infection. These questions

focused on the patients' features, clinical presentation, diagnosis, and treatment options. Completing the survey required around thirty minutes of time.

STATA 14.0 for Windows was used to do the analysis on the data (College Station, TX, USA). One center served as the point of correspondence for the analytic unit. During the COVID-19 pandemic, descriptive statistics were used in order to display demographic data as well as analyze the level of knowledge, attitudes, and perspectives held by HCPs. Means and standard deviations (SD) were used to describe the quantitative variables, whereas numbers and percentages were used to describe the qualitative variables. Because participants may choose more than one answer to a question, the total number of replies was more than the sum of some of the findings. Some of the questions were open-ended, and their responses were examined using a coding method. In this method, answers that are quite close to one another are condensed and approximated into information that is very similar semantically (14).

## RESULTS

There were a total of 136 replies that were analyzed; during the course of the research project, a total of 134 pediatric endocrine centers from 51 different countries and across all continents took part in the gathering of data that was subsequently analyzed. Table 1 displays the respondent's countries of origin as well as their professional backgrounds, center settings, and sizes.

**Table 1: Endocrine clinical center characteristics and staff profiles.**

Characteristics (n respondents)	Respondent
<b>Centers by country</b>	
United States of America	12
Spain	10
Philippines	8
Germany	8
Egypt, Italy	6 each
Argentina, Brazil, United Kingdom	6 each
Canada, Greece	5 each
India, Japan, Netherlands, Portugal	3 each
Belgium, Bulgaria, Congo, Denmark, Indonesia, Iran, Malaysia, Mexico, New Zealand, Peru, Serbia and Montenegro, Sweden, Turkey	2 each
Australia, Austria, Bangladesh, Chile, Cyprus, Finland, Georgia, Hong Kong, Hungary, Iceland, Iraq, Ireland, Israel, Lebanon, Luxembourg, Malta, Netherlands Antilles, Poland, Romania, Slovenia, Sudan Taiwan, Ukraine	1 each
<b>Current clinical role (134)</b>	
Pediatric endocrinologist/diabetologist	110
Pediatrician with interest in endocrinology	16
Resident or fellow or trainee in pediatrics/pediatric endocrinology or diabetology or diabetes researcher	5
Adult physician looking after pediatric or adolescent patients	2
Nurse practitioner/registered nurse	1
<b>Clinical setting (134)</b>	
University/academic hospital or clinic	66
Public/governmental hospital or clinic	42
Private hospital or clinic	25
Primary care center	1
<b>Estimate case-mix, patients by endocrine disorders</b>	

Type 1 diabetes	
<100	50
100-250	40
251-500	15
>500	12
Type 2 diabetes	
≤50	47
51-100	2
>100	5
Other forms of diabetes	
≤50	40
51-100	1
>100	3
Obesity and metabolic syndrome	
≤50	39
51-100	9
>100	20
Hyperinsulinemichypoglycemia	
≤50	40
>50	2
Thyroid	
≤50	50
51-100	14
>100	25
Adrenal	
≤50	52
50-100	10
>100	4
Bone metabolism	
≤50	25
>50	5
Pituitary and other CNS disorder	
≤50	57
>50	5
Growth	
≤50	45
51-100	50
>100	15
Pubertal	
≤50	50
51-100	15
>100	5
Others: Gender dysphoria	
≤50	1
>50	1

During the COVID-19 pandemic, routine follow-up visits and education were modified in the majority of pediatric endocrine centers. Care and disease literacy were most commonly delivered face-to-face (F2F) while wearing appropriate personal protective equipment (PPE),

while telephone and video consultations were used in a less significant capacity. When it came to diabetic care, only one caregiver was allowed to provide F2F care. On the other hand, for hyperinsulinemic hypoglycemia (HH) and bone metabolism disorders, more than one fifth of centers continued to provide treatment in the same manner as before. It should come as no surprise that the families' own anxiety about COVID-19 prevented them from having much interaction with the diabetes or endocrine specialists in the majority of the centers.

**Table 2: Assessment of pediatric diabetes care during the COVID-19 pandemic by clinical centers.**

	<b>Type 1 diabetes</b>	<b>Type 2 diabetes</b>	<b>Other forms of diabetes</b>
<b>Estimate proportion of delayed diagnose due to COVID-19</b>	47%	18%	18%
<b>Estimate perception of worsening disease management</b>	30%	68%	30%
<b>Use of technologies among patients</b>			
• Insulin pump		N/A	N/A
○ Less than 10	40		
○ 10-25	15		
○ 26-50	25		
○ 51-75	24		
○ 76-100	10		
• CGMS		N/A	N/A
○ Less than 10	35		
○ 10-25	27		
○ 26-50	20		
○ 51-75	24		
○ 76-100	5		
• Flash GMS		N/A	N/A
○ Less than 10	35		
○ 10-25	30		
○ 26-50	20		
○ 51-75	21		
○ 76-100	10		
<b>Testing</b>			
• COVID-19 tests for newly diagnosed.	75	N/A	N/A
• Positivity			
○ No positives with standardized tests	55	N/A	N/A
○ Less than 25%	55		
○ 26-50%	1		
○ More than 75%	2		
• COVID-19 tests in DKA cases	80	N/A	N/A
• Positivity with standardized tests			
○ Less than 10%			
<b>Testing</b>			
• COVID-19 tests for newly diagnosed.	70	N/A	N/A
• Positivity			
○ No positives with standardized tests	50	N/A	N/A
○ Less than 25%	55		

○ 26-50%	1		
○ More than 75%	2		
• COVID-19 tests in DKA cases	80	N/A	N/A
• Positivity with standardized tests			
○ Less than 10%	75	N/A	N/A
○ 10-25%	5		
○ 26-50%	2		
○ More than 75%	2		
<b>Diabetic ketoacidosis episodes</b>			
• Increase of newly-onset cases	55	N/A	N/A
• Increase in established cases	35	N/A	N/A
• Proportion of DKA episodes			
○ 0-25%	65	N/A	N/A
○ 26-50%	15		
○ 51-75%	20		
○ 76-100%	13		
• Proportion of mild DKA		N/A	N/A
○ 0-25%	65		
○ 26-50%	35		
○ 51-75%	15		
○ 76-100%	5		
• Proportion of moderate DKA		N/A	N/A
○ 0-25%	70		
○ 26-50%	33		
○ 51-75%	10		
○ 76-100%	5		
• Proportion of severe DKA		N/A	N/A
○ 0-25%	85		
○ 26-50%	15		
○ 51-75%	15		
○ 76-100%	3		
• Perception of worsening episodes	50	N/A	N/A
<b>Severe Hypoglycemia episodes</b>			
• Increase of SH episodes	11	N/A	N/A
<b>Routine check-up</b>			
• As usual, no changes	20	10	9
• Sent SMS and emails for consultation.	35	10	14
• Apps	19	5	12
• Telephone consultations	75	25	25
• Video consultations	50	23	15
• Face to face consultation with appropriate personal protective equipment restricted to just one parent/caregiver	76	N/A	N/A
• Face to face consultation with appropriate personal protective equipment where all caregivers are allowed to attend	14	35	30
• No consultation during complete lockdown or postponing it to annual visits	3	1	0

• Limited contact with diabetes team because of COVID-19 fear	84	39	35
<b>Daily routine</b>			
• Maintenance of physical activity			
○ Less than 10%	25	N/A	N/A
○ 10-25%	45		
○ 26-50%	20		
○ 51-75%	15		
○ 76-100%	10		
• Worsening of dietary choices			
○ Less than 10%	25		N/A
○ 10-25%	30		
○ 26-50%	38		
○ 51-75%	10		
○ 76-100%	10	N/A	
• Increase of body weight			
○ Less than 10%	25		N/A
○ 10-25%	30		
○ 26-50%	35		
○ 51-75%	19		
○ 76-100%	10		
• Extra dose of insulin			
○ Yes	1		
○ No	N/A		
○ Not on insulin therapy		N/A	N/A
• Average glycemic control during pandemic			
○ Mostly improved	24		
○ Mostly maintained same level	58	34	
○ Mostly worsened	36		N/A
• Regular use of anti-hypertensive			
○ ACE inhibitor	N/A		
○ B-blocker			
○ Ca channel blocker	4	20	N/A
○ Control with salt-free diet		21	
○ None		15	
		N/A	
<b>School activities</b>			
• Parental concerns to return to school activities	75	15	N/A
• Specific school guidelines during pandemic	80		
<b>Patient and family education</b>			
• As usual, no changes	5	6	3
• By telephone	50	25	30
• Video consultations	50	21	20
• Apps/digital platforms	20	15	15
• Face to face education wearing appropriate personal protective equipment	95	40	40
<b>Supplies</b>			
• Refill prescription		N/A	N/A

○ Refill prescription every month	15		
○ Refill prescription every 3 months or less	50		
○ Refill prescription every 6 months or less	15		
○ Refill prescription every year or less	11		
○ As required by patient	15		
○ Automatic refill prescription from pharmacy	5		
○ I am not directly involved with prescription	5		
• Shortage of supplies			
○ Yes	24	7	5
○ No, everything was secured	75	33	35
○ I am not aware of situation	10	11	6
• Item under shortage			
○ Basal insulin	14	2	1
○ Bolus insulin	11	0	1
○ Glucose test strips	15	5	4
○ Blood glucose sensors	14	1	3
○ Insulin pump supplies	6	0	0
○ Ketone test strips	10	0	0
○ Oral medication	1	1	1
○ Genetic tests	0	1	2
<b>Characteristics of COVID-19 cases</b>			
• Estimate mean age, years	10.5	12.7	N/A
• Estimate % boys	50.1	52.1	
• Estimate % girls	52.1	40.1	
• Estimate mean duration of disease, years	4.0	1.5	
• Estimate mean HbA1c value, %	8.5	7.5	
• BMI, Kg/m <sup>2</sup>	N/A		
• <b>Presence of comorbidities</b>			
○ Asthma	30	15	5
○ Cancer	4	2	5
○ Obesity	45	50	10
○ Hypertension	20	25	1
○ Heart disease	3	0	2
○ Kidney disease	15	3	8
○ Neurological disease	2	0	2
○ Celiac disease	10	1	0
○ Hypothyroidism	7	0	0
○ Cystic fibrosis or bronchial dysplasia	10	2	11
○ Other: Allergy, other autoimmune disease, dyslipidemia, Polycystic ovary syndrome, Lupus, Anemia	4	2	2
○ No	35	5	20
<b>Psychological concerns</b>			
• Anxiety	70	35	25
• Parenting stress	65	25	15
• Depression	45	25	13
• Insomnia/hypersomnia or other sleep disruption	35	15	5
• Eating disorder	25	15	5

• Panic attacks	15	10	5
• Suicide attempt	5	2	1
• Patient or caregivers have improved the mood	4	0	1
• None have had psychological problems so far	31	17	20

Open in a separate window N/A, not applicable.

**Table 3: Assessment of pediatric endocrine care other than diabetes during COVID-19 pandemic by clinical centers.**

	<b>Obesity and Metabolic Syndrome</b>	<b>Hyperinsulinemic hypoglycemia</b>	<b>Thyroid disorders</b>	<b>Adrenal disorders</b>	<b>Bone metabolism disorders</b>	<b>Pituitary and other CNS disorders</b>	<b>Growth disorders</b>	<b>Pubertal disorders</b>
<b>Estimated proportion of delayed diagnoses due to COVID-19</b>	40.1	9.5	21.1	14.5	18.5	21.5	35.3	37.6
<b>Estimated proportion of increase in severity</b>	N/A	7.5	N/A	4.6%	N/A	N/A	N/A	N/A
<b>Estimate perception of worsening disease management</b>	85.2	23.1	20.3	33.1	32.1	27.4	35.5	34.5
<b>Patient and family education</b>								
• As usual, no changes	5	3	7	5	2	2	5	4
• By telephone	30	27	53	35	23	35	40	37
• Video consultations	20	10	28	25	11	25	25	15
• Apps/digital platforms	11	10	12	14	5	10	12	11
• Face to face education wearing appropriate personal protective equipment	45	35	68	55	15	50	55	59
<b>Supplies</b>								
• Shortage of supplies								
○ Yes	10	9	10	15	8	15	16	15
○ No,	50	31	75	45	21	45	55	48

everything was secured								
• Item under shortage								
○ Oral/nasal medications (e.g., metformin, diazoxide, levothyroxine, methimazole, hydrocortisone, fludrocortisone, calcitriol, desmopressin, estrogen)	5	8	7	15	5	10	1	1
○ Injectable medications (e.g., insulin, octreotide, glucagon, bisphosphonate, GnRHa, rhGHa)	4	2	1	2	2	2	10	2
○ Topic medications (e.g., estrogen)	0	0	1	0	0	1	0	0
○ Test strips	N/A	1	N/A	1	N/A	N/A	N/A	N/A
○ Syringe	0	2	0	0	0	0	1	0
○ Genetic testing /imaging	1	1	1	1	2	2	4	2
• <b>Presence of comorbidities</b>								
○ Asthma	25	3	17	5	1	4	20	4
○ Cancer	2	0	5	2	3	12	3	2
○ Obesity	1	5	25	5	10	24	20	21
○ Hypertension	35	1	3	3	0	2	3	1
○ Heart disease	2	1	5	2	1	3	11	2
○ Kidney disease	4	2	3	1	12	3	1	2
○ Neurological disease	0	2	1	0	1	0	0	2
○ No	10	25	44	38	40	25	32	30
<b>Use of medications</b>								
• <b>Anti-hypertensive</b>		N/A	N/A	N/A	N/A	N/A	N/A	N/A

○ ACE inhibitors I/II	22							
○ Beta-blocker	2							
○ Ca channel blocker	2							
○ Salt-free diet	2							
○ No treatment	21							
○ Continuation of anti-hypertensive	47							
○ No complication with anti-hypertensive use	45							
○ Maintenance of treatment during COVID19	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
• Management of adrenal crisis	N/A	N/A	N/A		N/A	N/A	N/A	N/A
○ Fluid and electrolyte resuscitation								
○ Ample doses of glucocorticoids		3		45				
○ Chronic glucocorticoid and mineralocorticoid replacement				5			4	
○ Treatment of the precipitating illness				1				

Table 2 shows the proportion of centers that had patients impacted by COVID-19 for all types of diabetes. Table 3 shows the percentage of centers that had patients affected by COVID-19 for other endocrine illnesses. Patients with diabetes were the most impacted by COVID-19, with more severe symptoms, perhaps owing to a larger proportion of comorbidities (Table 2) than patients with other endocrine disorders. Patients with diabetes also had a higher mortality rate than patients with other endocrine diseases (Table 3). It is important to highlight that individuals with bone metabolism problems seemed to have a greater susceptibility to COVID-19 infection owing to the fact that they had concomitant renal illness.

The majority of individuals diagnosed with COVID-19 either had no symptoms or had symptoms ranging from mild to severe (Tables 4). However, symptoms seemed to be more

common and severe in centers where patients with type 1 diabetes had a positive COVID-19 test than in centers where patients with other endocrine problems were treated (Tables 4). There were no documented fatalities associated with any endocrine disorder.

**Table 4: Symptoms, complications, and outcomes of pediatric diabetes cases during the COVID-19 pandemic by clinical center.**

	Type 1 diabetes	Type 2 diabetes	Other forms of diabetes
<b>Symptoms and/or complications among COVID-19 cases</b>			
• Asymptomatic			
○ None	70	32	31
○ 1-25%	20	5	2
○ 26-50%	10	2	3
○ 51-75%	5	4	5
○ 76-100%	11	5	5
• Fever			
○ None	25	35	31
○ 1-25%	21	6	8
○ 26-50%	15	5	5
○ 51-75%	10	5	5
○ 76-100%	15	0	1
• Cough			
○ None	31	33	21
○ 1-25%	30	4	7
○ 26-50%	25	12	5
○ 51-75%	15	4	2
○ 76-100%	10	5	2
• Pharyngeal erythema			
○ None	78	36	41
○ 1-25%	25	10	10
○ 26-50%	5	3	5
○ 51-75%	10	10	8
○ 76-100%	5	2	1
• Rhinorrhea			
○ None	55	35	40
○ 1-25%	21	10	10
○ 26-50%	21	5	5
○ 51-75%	15	6	6
○ 76-100%	10	1	3
• Shortness of breath			
○ None	80	45	42
○ 1-25%	31	6	4
○ 26-50%	5	3	1
○ 51-75%	2	3	0
○ 76-100%	2	1	2
• Headache			
○ None	55	40	40
○ 1-25%	34	10	5
○ 26-50%	6	5	3

○ 51-75%	10	7	4
○ 76-100%	6	0	0
• Myalgia			
○ None	55	35	40
○ 1-25%	43	12	7
○ 26-50%	15	5	6
○ 51-75%	8	8	1
○ 76-100%	9	0	4
• Hyperglycemia			
○ None	60	35	40
○ 1-25%	21	4	5
○ 26-50%	15	9	6
○ 51-75%	15	4	2
○ 76-100%	8	2	0
• Hypoglycemia			
○ None	110	45	45
○ 1-25%	15	6	4
○ 26-50%	0	1	0
○ 51-75%	3	0	0
○ 76-100%	0	0	1
• Diabetic ketoacidosis			
○ None	80	51	51
○ 1-25%	25	7	2
○ 26-50%	5	4	1
○ 51-75%	5	0	0
○ 76-100%	1	1	0
<b>Outcomes for COVID-19 cases</b>			
• Admission			
○ None	65	56	40
○ 1-25%	35	10	4
○ 26-50%	5	1	4
○ 51-75%	4	1	1
○ 76-100%	7	2	1
• Admission to intensive care unit			
○ None	70	51	45
○ 1-25%	20	5	2
○ 26-50%	2	0	3
○ 51-75%	5	3	3
○ 76-100%	5	0	0
• Need for bronchodilators and glucocorticoids			
○ None	87	45	48
○ 1-25%	25	8	2
○ 26-50%	5	0	2
○ 51-75%	0	4	0
○ 76-100%	0	0	0
• Need for oxygen			
○ None	55	43	45

○ 1-25%	20	7	6
○ 26-50%	10	5	1
○ 51-75%	1	0	1
○ 76-100%	3	1	0
• Need for intubation and ventilation			
○ None	110	50	41
○ 1-25%	15	6	1
○ 26-50%	1	0	1
○ 51-75%	0	2	0
○ 76-100%	0	0	0
• No need for specific treatments			
○ None	60	35	40
○ 1-25%	10	5	3
○ 26-50%	10	3	5
○ 51-75%	15	5	4
○ 76-100%	25	7	5
• Increased insulin dosage/other treatment adjustment			
○ None	45	35	40
○ 1-25%	20	8	9
○ 26-50%	24	5	5
○ 51-75%	5	1	4
○ 76-100%	20	2	5
• Need for antivirals			
○ None	115	55	45
○ 1-25%	7	5	4
○ 26-50%	0	0	0
○ 51-75%	0	0	0
○ 76-100%	0	0	0
• Need for anti-IL6 therapy			
○ None	115	55	45
○ 1-25%	2	0	0
○ 26-50%	0	2	0
○ 51-75%	0	0	0
○ 76-100%	0	0	0
• Need for hydroxychloroquine			
○ None	112	50	45
○ 1-25%	3	1	0
○ 26-50%	2	0	1
○ 51-75%	0	0	0
○ 76-100%	0	0	0
• Need for azithromycin			
○ None	85	45	45
○ 1-25%	7	3	1
○ 26-50%	11	1	1
○ 51-75%	5	3	1
○ 76-100%	5	0	1
• Average glycemc control during the			

pandemic			
○ Mostly improved	21	5	N/A
○ Mostly maintained same level	65		
○ Mostly worsened	43		

In most cases, it was not essential to treat COVID-19 with general treatment procedures. Patients did not need to be admitted to the hospital in the majority of centers, and the vast majority of them did not need beds in an intensive care unit (ICU), with the exception of patients who had diabetes. (Tables 4). In patients with type 1 diabetes, type 2 diabetes and obesity, the percentage of patients who required bronchodilators and glucocorticoids more often was greater than in individuals with other endocrine diseases who tested positive for COVID-19. They also required oxygen at a higher rate, non-invasive ventilation at a higher rate, intubation and ventilation at a lower rate, and other treatments (such as antibiotics and antiviral medicines more often than patients with other endocrine problems (Tables 4).

Although patients with COVID-19 only rarely required specific therapeutic measures for endocrine management, adjustments to the background treatment dose were common.

The proportion of centers reporting an increase in newly diagnosed cases of moderate to severe diabetic ketoacidosis (DKA) and new episodes in already established patients showed in (Table 2).

The majority of HCPs carried out COVID-19 testing on newly diagnosed patients (55%), as well as on existing patients (35%) for DKA episodes; (Table 2).

There was a delay in new diagnosis as well as a deterioration of the therapy for the vast majority of the endocrine illnesses that were evaluated. The majority of individuals who were diagnosed with COVID-19 either did not exhibit any symptoms or had symptoms ranging from mild to severe (Tables 3,4).

Surprisingly, individuals with obesity or metabolic syndrome were able to continue using ACE inhibitors, the antihypertensive medicine that was used the most, without interruption and without experiencing any consequences to this day. It is important to highlight that less than 10% of patients with HH reported having at least one episode of severe hypoglycemia.

There were two pediatric endocrine facilities that specialized in treating children and adolescents who struggled with gender dysphoria. The majority of patients received follow-up and education either via a telephone appointment or face-to-face interaction while wearing proper PPE. Because of the worry that the pandemic might spread, communication with the endocrine team was severely restricted at both locations. As a result, the diagnosis was sometimes delayed, but this did not seem to make the treatment any less effective. Patients diagnosed with gender dysphoria did not have an increased risk of suffering from COVID-19, contrary to what was seen for the majority of other endocrine diseases.

Lack of physical activity and inferior food choices were found, leading to a rise in body weight (25%) in these patients. Seventy-five percent of those who participated in the survey showed significant levels of parental worry on the return to school activities (Table 2). In spite of this troubling finding, it was heartening to see that the majority of schools, In addition, children diagnosed with pediatric endocrine disorders, which may include any and all types of diabetes, often report abnormalities in their overall psychosocial and behavioral functioning. Anxiety, sadness, the stress of parenthood, sleep disruptions, and eating disorders were indicated as being the most frequent types of difficulties. In point of fact, attempts at suicide were found in all conditions, with the exception of puberty problems (Tables 2,3).

## DISCUSSION

According to the results of this study, the percentage of children with endocrine abnormalities who tested positive for COVID-19 is sufficiently low that pediatric endocrine diseases should not be considered a risk associated with a poor prognosis for COVID-19. As was previously

documented, children and adolescents with any kind of endocrine disease did not have an elevated risk of contracting COVID-19 compared to children who did not have any type of endocrine condition (14,15). Comparing the proportion of patients with diabetes and COVID-19 in our previous survey with those reported here [only diabetes was assessed previously (9)], there was a significant increase in the number of children and adolescents with type 1 diabetes or other forms of diabetes who tested positive for COVID-19. This was the case despite the fact that only diabetes was evaluated in the previous survey (9). This is most likely attributable to the fact that much more COVID-19 testing was carried out as the epidemic proceeded as opposed to during the early stages of the pandemic (January-September 2020) and the reopening of schools in several nations.

Patients with type 1 or type 2 diabetes were not only more likely to suffer from COVID-19 but also experience moderate to severe symptoms, especially when other comorbidities were present. While the majority of pediatric patients with endocrine disorders affected by COVID-19 have asymptomatic or mild symptoms (16), it is important to note that patients with type 1 or type 2 diabetes were not only more likely to suffer from COVID-19 but also experience moderate to severe symptoms (17, 18). As a consequence of this, the number of diabetic patients admitted to the intensive care unit (ICU) also increased when compared to our previous survey (9), reaching a higher proportion of centers that reported intubation and ventilation in comparison to other endocrine conditions that were included in our survey. Diabetes and obesity are also risk factors for increased morbidity and mortality in adult patients with COVID-19 (19–21), although it is heartening that in individuals less than 25 years old, the mortality rate approaches zero even when diabetic or obese. So far, no fatalities have been documented.

Although there are some data on adult patients (10–13), very little is known regarding the influence of COVID-19 on other endocrine illnesses in the pediatric population. To the best of our knowledge, this is the first real-world and worldwide research that has been conducted on this subject. The present experiences of healthcare professionals who specialize in pediatric endocrinology imply that the treatment of diabetes is much more time-consuming and difficult than the management of other endocrine diseases. COVID-19 and diabetes mellitus are linked to one another in both directions. Diabetes that is not under control is associated with a more severe form of COVID-19 in adults. In addition, serious metabolic consequences, such as diabetic ketoacidosis (DKA), have been documented in individuals who had COVID-19, either at the outset (22, 23) of their diabetes or in patients who already had diabetes (24). Although it does not seem that pediatric patients with diabetes have an increased risk of SARS-CoV-2 infection, it is nonetheless important to avoid being infected and to take all preventative measures feasible (25). In addition to this, it has been postulated that SARS-CoV-2 could cause diabetes in and of itself, much as SARS-coronavirus 1 pneumonia does in its victims (26). On the other hand, this link has not yet been shown to exist, and further research in both adults and children is required.

According to the results of the current study, the COVID-19 pandemic was responsible for a delay in hospital admissions for diabetes and other endocrine illnesses, which led to a larger number of severe DKA patients, among other things, as has been documented elsewhere (22, 23, 27). It is essential to have a safe route that does not involve COVID-19 through pediatric emergency departments in order to assist and reassure parents who wish to bring their children to the hospital as quickly as possible in order to avoid needless complications in diabetes and other endocrine disorders (22).

Once endocrine illness has been diagnosed, it is essential to have an open line of communication with healthcare providers (HCPs), as is advocated by a multitude of endocrine organizations (9, 28, 29), particularly via the use of telemedicine so as to avoid congested waiting rooms. However, in the current survey, we found that despite the need to

reduce the number of unnecessary hospital visits during the pandemic by using dedicated platforms or video calls, text messaging, and emails, routine face-to-face visits remained the most common method of consultation. This was the case despite the fact that these methods were available. It is possible that an increase in awareness about telemedicine may assist patients and their families acquire confidence in this method of providing medical treatment. Complications in these patients may be avoided by giving priority to counseling on care management and accelerating innovation in telehealth. This is particularly important in situations where there are limited resources. Video platforms have been adopted at several institutions, particularly for educational purposes; however, not all of these institutions allow telehealth for inpatient care, and the usefulness of telemedicine for educational purposes is still up for debate [30-32].

During the COVID-19 pandemic, some parents were worried about the safety of returning their children who suffered from endocrine problems, most notably diabetes, back to school because they believed that these children had a larger probability of being infected with coronavirus. On the other hand, and this is reassuring, the vast majority of them were aware with the school's requirements and made sure that a disease care plan was in place (25, 30, 31).

It is of the utmost significance to have quick access to endocrine and diabetic care drugs and supplies, which was already a problem in a huge portion of the globe prior to the epidemic. Even though daily self-management, sick day management, and survival are all dependent on the availability of medical supplies, access issues have been exacerbated as a result of the pandemic. Important infrastructure, such as outpatient clinics and public transport, has been severely limited as a result of the pandemic. Fortunately, the current study found that a lack of supplies was reported by only a small percentage of centers (ranging from 6-22% depending on the kind of endocrine condition).

We made the observation that COVID-19 was associated with endocrine illness and comorbidities, with obesity and hypertension being the comorbidities that were reported the most often in relation to all endocrine disorders. Comorbidities were common among the children and adolescents who required acute medical care. As a result, it is of the utmost importance to have an understanding of which modifiable risk factors have the potential to play a part in enhancing the severity of COVID-19 (32–36). Comorbidities are less common in young patients than in adults, which may explain why children are less prone to COVID-19 but why some children still become critically sick. The reasons for why some children suffered from more severe COVID-19 are yet unknown. Because of the recent spike in the prevalence of type 2 diabetes and obesity in children and adolescents, it is possible that a considerable number of youngsters are at an increased risk.

Comorbidities in mental health have been made worse across the board as a result of the COVID-19 epidemic, particularly in people who suffer from diabetes and other endocrine illnesses (37,38). Children are at a greater risk of developing adverse health effects than adults because their neurological systems, endocrine systems, and hypothalamic-pituitary-adrenal axis are not fully matured. Children who are experiencing mental health issues often experience emotions of abandonment, hopelessness, incompetence, and tiredness, which may even increase the likelihood of their taking their own lives. Notably, the results of our study showed that children suffering from a broad variety of endocrine disorders had a much higher risk of attempting suicide during the pandemic. The provision of psychosocial support for children and their families is an essential component of both the health response to a catastrophe and the recovery from it. This is particularly true for families with children who suffer from chronic health disorders. Protective measures that are timely and adequate are required in order to forestall psychological and behavioral issues. It is possible that emerging digital applications and health services, such as telemedicine, social media, mobile health,

and remote interactive online education, can assist bridge the social distance and support the mental and behavioral health of children (39).

The SARS-CoV-2 virus has several pathophysiologic linkages with endocrine systems, and these interconnections have the potential to produce changes in pituitary, adrenal, and thyroid function, as well as mineral metabolism. The majority of the research done on the dangers of SARS-CoV-2 infection in people with underlying endocrine abnormalities has been done on adults (40). However, the limited data that are currently available are generally favorable in terms of the endocrine complications of COVID-19 in the pediatric population (41), as confirmed in our survey, where children with well-managed endocrine conditions did not seem to be at increased risk of getting infected with COVID-19 or becoming severely ill from the virus.

Previous research shown that the use of telemedicine for the treatment of juvenile obesity was effective; however, adapting this methodology to the use of telemedicine for the treatment of other endocrine diseases may be difficult (42).

At this time, there is no evidence to suggest that children and adolescents who have underlying thyroid abnormalities have an increased chance of getting SARS-CoV-2 infection or an altered illness course. It is essential to bear in mind, however, that individuals diagnosed with Graves' disease who are undergoing treatment with anti-thyroid medication run a significantly increased risk of developing agranulocytosis as well as secondary infections (43). This is of particular significance in light of the findings of a single research which indicated that one-half of those who did not survive COVID-19 also developed a subsequent infection (44). In addition, similar to other infections, COVID-19 has the potential to bring on a thyroid storm in individuals whose hyperthyroidism is not under adequate management (41). In individuals affected with COVID-19, an underlying thyroid condition, particularly hypothyroidism, does seem to be a risk factor for a more severe disease course (45–47). Children who suffer from metabolic bone disease or skeletal dysplasia, both of which may lead to respiratory insufficiency as a consequence of an altered chest wall structure, may have a higher risk of COVID-19 problems (48).

Due to the impaired natural immunity function that is characterized by a defective action of neutrophils and natural killer cells, which is known to be associated with primary adrenal insufficiency, patients with primary adrenal insufficiency (such as congenital adrenal hyperplasia) are slightly more susceptible to infections in general. This is because primary adrenal insufficiency is known to be associated with primary adrenal insufficiency (49). Additionally, susceptibility to infections may also be explained by an inadequate increase in the dose of hydrocortisone at the start of an illness. This may be the case if the dosage was not increased enough. According to the guidelines, therefore, children who are not experiencing any symptoms should continue to take their normal replacement doses of hydrocortisone rather than receiving higher dosages of the medication. If you have symptoms that might point to COVID-19, it is suggested that you immediately increase the dosages of hydrocortisone you are taking until the fever subsides, and then add an additional dose that is doubled.

Children who have been given a clinical diagnosis of hypopituitarism do not have an elevated risk for COVID-19. Due to the fact that a sizeable proportion of these individuals are suffering from secondary adrenal insufficiency, the same guidelines that are given to children who have adrenal insufficiency should be followed (50). In the case of COVID-19, the hyperinsulinemichypoglycemia side effects of the medications that are used to treat hyperinsulinemichypoglycemia (for example, diazoxide side effects include water retention and pulmonary hypertension; somatostatin analogues side effects include cardiac arrhythmias and cardiac conduction disorders) should be taken into consideration. The care of hypoglycemia in children should be followed throughout this pandemic. This includes close

monitoring of glucose levels, proper hydration, guaranteeing the availability of drugs, and an emergency protocol. However, it is comforting to know that survey statistics reveal that all of these endocrine problems did not create any significant discomfort to patients, and the only severe concern that patients will have to deal with is the possibility of a lack of medications and/or supplies.

The vast majority of endocrine data comes from guidelines for the treatment of juvenile endocrine problems that have been provided by a variety of health organizations and endocrine groups. These recommendations were produced throughout the pandemic. The majority of children with endocrine abnormalities do not constitute a high-risk group for contamination or severe manifestation of COVID-19; thus, according to the specified "sick day management standards" and seeking medical treatment without delay are only required in the majority of situations (51).

Although it is difficult to analyze the effects of COVID-19 on endocrine disorders in children due to a lack of studies and relatively less severe cases as compared to adults (52–54), it appears, looking at the data collected with the present survey, that diabetes is still more difficult to manage than any other pediatric endocrine disorder with an increased risk of morbidity. This is the case despite the fact that it is difficult to analyze the effects of COVID-19 on endocrine disorders in children.

There are a few problems with this research. In general, we obtained a lower response rate than we did in the last survey, which was centered on diabetes. We have a working hypothesis that health care professionals see COVID-19 as having a greater impact on diabetes, both directly and indirectly. Directly, diabetes is a risk factor for mortality and morbidity related to COVID-19. Indirectly, the pandemic can influence the management of diabetes and the availability of supplies. Other factors that may have contributed to the lack of responses include the pressures brought on by COVID-19, survey weariness brought on by the pandemic, an inadequate reach of potential participants by email, perceived stress, and burnout connected to job. Despite this, this is the first research ever conducted on a worldwide scale to investigate the effects of COVID-19 in any and all pediatric endocrinology problems. The majority of pediatric endocrinologists who participated in the study were located in nations that were badly damaged by COVID-19, and they were employed at academic or university facilities. This contributed to the reliability of the data as well as its worldwide reach.

### **Conclusion:**

In conclusion, the findings presented here demonstrate that diabetes posed a unique treatment burden during the COVID-19 pandemic and is associated with an elevated risk of morbidities, including diabetic ketoacidosis (DKA). It is vital to establish specific techniques in order to educate and reassure parents about the need of keeping in regular touch with their HCPs and promptly attending the emergency department in the event that their children develop symptoms that are unrelated to COVID-19. It is imperative that important medications continue to be available across the world. The use of telemedicine has to be improved and should become standard practice at all facilities. It is necessary to attend to the requirements of children and adolescents suffering from endocrine diseases in terms of their mental health. In order to lessen the severity of the effects that COVID-19 has on pediatric patients suffering from diabetes and other endocrine problems, guidelines at the international level must be developed with a particular focus on the psychological effects of the virus.

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