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Original article

COVID-19 outbreak and pediatric diabetes: perceptions of health care professionals worldwide

Running title: COVID-19 and pediatric diabetes

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Abstract

Background: COVID-19 is an infectious disease that started in Wuhan, China in late 2019 and later spread around the world. Diabetes has been recognized as a possible risk factor for COVID-19 complications.

Objective: ISPAD investigated perceptions, challenges and experience of healthcare professionals (HCP) taking care of children and young people with diabetes world-wide during COVID-19 pandemic.

Methods: From 21st April to 17th May 2020, during COVID-19 pandemic, a web-based survey was sent to ISPAD members and former participants of ISPAD conferences by email.

Results: Responders from 215 diabetes centres from 75 countries completed the survey. Majority were from UK (35; 16.3%), USA (20; 9.3%) and India (15; 7%). HCP were mostly pediatric endocrinologists (64%). During COVID-19 pandemic, 16.5% of responders continued face-to-face consultation while most changed to telephone (32%) or video (18%) consultations. 19% reported a shortage of medical supplies. 22% reported a delay in diagnosis of patients with new-onset diabetes, while 15% reported a higher incidence of DKA. 12% reported having one or more patients with COVID-19. Most of the 86 children and adolescents with diabetes and COVID-19 had only mild/moderate symptoms, while 5 required admission to an intensive care unit. No deaths were reported.

Conclusions: This large global survey during COVID-19 pandemic showed that many HCP adapted to the pandemic by resorting to telemedicine. One fourth of HCP reported delays in diagnosis and an increased rate of DKA. The emergence of COVID-19 pandemic had an important impact on family's behaviour that might have led to increase in DKA presentation.

Keywords: COVID-19, Children, Diabetes, Diabetic ketoacidosis, Telemedicine.

Introduction

Coronaviruses are a large family of viruses that can cause disorders ranging from a mild cold to severe diseases. In December 2019, a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused an outbreak of COronaVirus Disease (COVID-19). Typical symptoms of COVID-19 include fever, cough, shortness of breath, and muscle pain [1]. In the time frame studied, a large cohort with COVID-19 from China showed that illness severity can range from mild (81%), severe (14%) to critical (5%). All deaths occurred among patients with critical illness and the overall case fatality rate was 2.3% [2]. Moreover, pooled rates of ICU admission, acute respiratory distress syndrome and mortality reported in another systematic review and meta-analysis were 10.9%, 18.4% and 4.3%, respectively [3].

Several data suggest that most people with COVID-19 may have comorbidities, the most prevalent of which are diabetes, cardiovascular disease, and hypertension [4]. In England, a nationwide analysis demonstrates that all types of diabetes are independently associated with a significant increased risk of in-hospital death with COVID-19 [5].

However, it is reassuring to hear that, at least according to some reports, young people, with or without diabetes, are coping better with COVID-19 infection [6]. Of 2,572 laboratory-confirmed cases aged 18 years or younger in the US, none had type 1 nor type 2 diabetes but had other condition such as chronic lung disease and cardiovascular disease [7] or no chronic conditions at all [8].

COVID-19 pandemic has forced dramatic changes in the delivery of healthcare landscape, and healthcare professionals (HCP) are making unprecedented modifications to healthcare systems, social services as well as attitude and management of children living with diabetes. To the best of our knowledge, we do not have established guidelines for managing COVID-19 in children, adolescents and young adults with diabetes. Therefore, we conducted this survey to gain an understanding of the patterns of practice of HCP registered in the database of the International Society for Pediatric and Adolescent Diabetes (ISPAD), who are likely to be taking care of children and adolescents with diabetes. This survey should help to identify different management strategies, challenges, knowledge and practice of HCP caring for pediatric patients with diabetes during COVID-19 pandemic so we can guide our future educational activities toward improving the management in this area.

Methods

Study setting and design

This is a cross-sectional electronic survey conducted over a four-week period from 21st April to 17th May 2020 under the auspices of ISPAD. The answers were entered into a web-based commercial software (Google Forms, Google LLC, California, United States) which is a collaborative web survey software created by Google. A Google Form is automatically connected to a spreadsheet, responses can be saved there and subsequently analysed.

The target population was identified from the ISPAD HCP database (ISPAD members and former participants of ISPAD conferences and post-graduate courses). Respondents were asked to describe themselves concerning specialties, and volume of practice. They all received an initial invitation by e-mail that explained the rationale and what was required from the responders, followed by two reminder e-mails over 3 weeks for non-responders. If responders belong to the same centre, this was considered as a single response. All subjects provided explicit informed consent electronically to voluntary participate before they could proceed to the survey questions. The voluntary nature and the strict confidentiality in which data were analysed and reiterated. Responses were collected automatically, stored electronically, and interpreted via linkage to spreadsheet. Summary statistics were prepared for responses to each question.

The survey

The survey questions were developed by six pediatric endocrinologists. The survey was sent to about 2,300 HCP. A direct electronic link of the survey and consent was sent to the HCP by email and also via social media platforms (Facebook, Twitter, and LinkedIn). The completion of the survey took no more than twenty minutes. It was created in an online format with 47 questions divided into five sections. The first section concerns targeted HCP consent to participate in the survey and confirm their voluntary participation, and the following section included responders' professional and practice profiles. Three questions were aimed to define the professional profile of the responders, size of their clinic and their country of practice. To further understand challenges and changes that HCP have had to make in caring for children and adolescents with diabetes during the pandemic, the next section included a set of questions focused on diabetes management. The questions covered the HCP's perceptions and practices including medication prescriptions, their availability, how they managed education sessions, acute complications seen, special considerations on use of concomitant drugs, blood glucose measurement, parents' beliefs and psychological aspects faced. The last two sections included questions sought to characterise the profile of patients who tested positive for SARS-CoV-2 virus, including their characteristics, clinical presentation, diagnosis and treatment (the full version of the survey is available as a supplemental material).

Statistical analysis

Analysis of data was performed using Google Sheets. Descriptive statistics were used to present demographic data and to evaluate knowledge, attitudes and perceptions of HCP during COVID-19 pandemic. Quantitative variables were described in the form of mean and

standard deviation, and qualitative variables were described as number and percentage. Some questions were open-ended questions.

Results

Responders' professional and practice profiles

In total we received 303 responses to the survey. Since for some center more than one response was received, we merged all the responders from the same center and considered it as one response. A convenient sample of 215 diabetes centers from 75 countries participated in the study. The majority of participants were from UK (35; 16.3%), followed by US (20; 9.3%) and India (15; 7%). Among the responders 193 (64%) were pediatric endocrinologists, 46 (15%) pediatricians with interest in diabetes, 26 (9%) nurse practitioners. The remaining were dietitians, trainee, diabetes educator and adult physicians. Majority of the participants (72.5%) had clinic size of more than 100 children with diabetes [Table 1].

Perceptions and practices of HCP towards diabetes during COVID-19

During COVID-19 pandemic, face-to-face consultation has been maintained by 16.7% of responders, and only once adequate personal protective equipment has been provided. Most of the HCP offered only phone call (32%) and video consultations (18%) for existing patients. However, for patients with new onset diabetes, a majority of HCP (38%) offered face-to-face education wearing appropriate personal protective equipment followed by phone calls (25.5%) and video consultations (22%) [Table 1].

We asked if any shortage of supply has been perceived as a result of COVID-19 where there previously had not been shortages. There is very wide variation in insulin and supply refill prescription duration, varying from 1 month to always [Table 1]. Scarcity of any diabetes supply has been observed only by 19%, while 65% had not had any shortage of supplies, and

16% of them were not aware of any challenging situation. Main shortage of diabetes care supplies have been glucose test strips (26%), basal and bolus insulins (22% each), glucose sensors (10.5%).

Immune stimulants have been prescribed only by one fourth of the responders, most of them, however, at less than 50% of their pediatric diabetes population [**Table 1**].

General management practices of diabetes care during COVID-19

Twenty-two percent of responders reported a potentially delayed diagnosis of children with new onset diabetes mellitus during the pandemic and 15% reported a higher incidence of DKA in their practice. [**Table 2**].

Coming to the potential fear of COVID-19, most participants (68%) had the feeling that caregivers/families avoided contact with the diabetes team during pandemic because of this fear.

Management of children and young people with diabetes mellitus that were COVID-19 positive

Twelve percent of HCP reported caring for one or more patients with COVID-19 [**Table 2**].

Most of responders reported using RT-PCR SARS-CoV-2 as method to confirm the diagnosis (78%), using both nasal (56%) and oropharyngeal (37%) swab, while serologic tests and bronchi alveolar lavage were used in very few patients [**Table 2**].

Only a small number of pediatric patients with positive testing for COVID-19 were reported in this global survey: 61 with type 1 diabetes mellitus and 25 with type 2.

Their clinical characteristics and symptoms (generally mild or moderate, with just 5 patients admitted to ICU) have been summarized in [Table 2]. No deaths were reported.

Most of them reported a contact with family member with a confirmed positive test, or clinical suspicion (50%), while in 12.5% of cases the caregiver was a healthcare worker confronted with a positive case. In 7.5% travel or residence in a location reporting cases during the last 2 weeks was described. In 30% of COVID-19 positive patients the source of contagion remains unknown [Table 2].

During the COVID-19 outbreak paracetamol was the most antipyretic drug used (81%), while very few used ibuprofen (4%) or a combination of both (12%).

The responders reported that majority of patients did not observe false readings with continuous glucose monitoring (CGM) (93%). Among the ones who reported false readings, the most used intermittent scanned or real time CGM was FreeStyle Libre™ (43%), followed by Dexcom G6™ (27%) and Dexcom G5™ (24%) respectively.

Regarding continuing to use of angiotensin-converting enzyme inhibitors (ACEi) drugs in patients with nephropathy and/or hypertension, only 25% of people using the drug (about 50% of the sample), have been advised to interrupt the ACEi. Patients (12%) who continued ACEi did not report any complications.

Anxiety and parental stress were the most reported psychological problems faced so far (31% and 24%, respectively) while few patients (15%) did not face any.

Discussion

This is the first study to quantitatively investigate the perceptions, challenges and experience of HCP for children and adolescents with diabetes mellitus during COVID-19 pandemic.

Since its outbreak in Wuhan, China, in December 2019 COVID-19 has spread to more than 200 countries and has been labeled as pandemic [9]. Epidemiologic studies have consistently demonstrated that children are at lower risk of developing severe symptoms or critical illness compared with adults [10,11]. Despite many uncertainties, the COVID-19 pandemic recommendations in most countries include people with diabetes within the ‘at risk’ population. ISPAD guidance for HCP reassured people from anecdotal reports coming from Wuhan, China, and Italy, stating that children with diabetes have not shown a different disease pattern compared to their peers and that children in general had less severe clinical manifestations than adults [12].

Diabetic ketoacidosis is an acute, major, life-threatening complication of diabetes. Early diagnosis of type 1 diabetes is essential to allow treatment to start as soon as possible.

Although, 15% of responders reported increased incidence of DKA in children in their centers, delayed diagnosis and admission to hospital were seen in 22% of the centers. This would suggest that for a significant number of centers, newly diagnosis of type 1 diabetes would be postponed, and possibly they would be facing a similar rate of DKA during the pandemic, but with more severe DKA due to the delay of the diagnosis. In the midst of the COVID-19 pandemic, people are sheltering in place and practicing social distancing. Parents and caregivers are delaying seeking emergency help out of fear of being infected in the

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hospital or due to the reduced service for non-COVID-19 care. Moreover, delayed diagnosis of new cases of type 1 diabetes could be due to the front-line health workers focusing on respiratory symptoms of the unwell child (with DKA), without considering type 1 diabetes as a potential diagnosis. Thus, anecdotal reports have suggested that as a result of delay in seeking medical attention, affected individuals have presented with more severe DKA [13]. The importance of following public health measures of containment in addition to standard diabetes mellitus care and, whenever needed, the sick day management guidelines of ISPAD should be emphasized [14]. Emergency department doctors should remember general pediatric evaluation in the time of a pandemic, such as recently observed, to avoid the need for hospitalization and emergency. Pediatric diabetes teams should be informed immediately to avoid complications; recommendations should be produced as soon as possible to allow appropriate treatment to start [12]. We recommend that every opportunity should be taken to raise awareness of the symptoms of diabetes amongst parents, caregivers, school staff, and the general population. It is the role of HCP to urge experiencing symptoms to seek care for these life-threatening events.

COVID-19 pandemic has forced a majority of the diabetologists to adapt to providing diabetes mellitus care remotely through telehealth. However, healthcare disparities continue to challenge availability of diabetes technologies for underprivileged communities. In a recent two case series, DKA was prevented via telemedicine by shared glucose data through Clarity™ or the share feature of CGM, and frequent insulin dose adjustments. Clinical outcomes were similar without any hospital admissions, thus saving significant cost [15]. Telemedicine and digital medicine also offer critically important approaches to improve

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access, efficacy, efficiency, and cost-effectiveness of medical care for people with diabetes. It will be important to include these measures as well after the pandemic. Telemedicine, technology and digital healthcare have demonstrated their role in diabetes mellitus care during a period of crisis, and this experience may be used to convince payers and policy makers of the lasting benefits for this high-risk population, and to systemize them [16]. It is strongly encouraged to upgrade telehealth services by institutions to continue caring for patients, as well as protect the healthcare workers and community.

Face-to-face consultation, with appropriate personal protective equipment, was used at 16.5% of the centers. This pandemic is bringing healthcare systems worldwide to the brink of collapse based on the rapidly increasing number of new severe infections, including the high rate of infections among frequently exposed healthcare professionals. Telemedicine or another virtual diabetes clinic can be a useful tool to ease data exchange between patients and HCP, as well as to reduce the number of physician-patient contacts. However, it is of note that even for newly diagnosed patients (for whom usually the face-to face education is the gold standard) more than 50% of patients received education via telehealth systems.

Consequences of the lockdown for persons with diabetes could be absent or major, based on less exercise, changes in dietary habits (e.g., increased snacking, consumption of ‘comfort’ dense-calorie foods), restrictions in routine visits to the physician, and decreased availability of insulin and/or oral hypoglycemic agents. Although HCP kept insulin available for almost three months ahead and all insulin and technology companies announced that they did not anticipate disruptions of the medical supply line, 19% of responders had shortage in basic diabetes supplies: blood glucose test strips, basal and bolus insulins, as well as sensors for

CGM. This is an alarming fact that might lead to uncontrolled glycemia or worsening status of comorbid diseases in some region of the world. It should be emphasized to urge companies on providing all diabetes medical supplies around the globe. A link to their on-line shop for supplies should also be provided. Telehealth consultations should be supported, and virtual training sessions should be readily available.

In our survey, 12% reported on COVID -19 positive patients. These were mainly type 1 and type 2 diabetes patients. In type 1 diabetes patients mean HbA1c was 7.6%, diabetes duration range 1-5 years, while for type 2 was 7.8% and diabetes duration range 3-10 years. It seems that most of cases were well controlled with standard therapy, and just few needed ICU admission; two adolescents with type 2 diabetes admitted to ICU required intubation and ventilation. Fortunately, no death was reported. A study from China reported that adults with diabetes had a significantly higher risk than people without, of severe pneumonia, release of tissue injury-related enzymes, excessive uncontrolled inflammatory responses, and hypercoagulable state associated with dysregulated glucose metabolism [17]. A recent study reported that a higher HbA1c level is associated with inflammation, hypercoagulability, and low oxygen saturation in COVID-19 patients, leading to a higher mortality rate [18].

As cardiovascular diseases and diabetes are strongly associated with elevated adipose tissue mass and low grade inflammation, a higher body mass index might be an important risk factor for a more severe course of the disease, particularly of pneumonia, in these people [19]. It is notable that the only ones who underwent intubation and ventilation were 2 adolescents with type 2 diabetes. Knowledge about insulin resistance is also important, because it is among the strongest determinants of impaired metabolic health and cardiac

dysfunction. Measurement of anthropometrics and metabolic parameters is crucial as both might be useful in a hospital setting to assess the risk of a complicated course of disease in patients with positive COVID-19 tests [20].

Current knowledge suggests the virus can be transmitted through droplets, direct contact and aerosols. Droplets transmission may occur when respiratory droplets of an infected person, are ingested or inhaled by individuals nearby [21]. This is also been reported in our survey, as 50% of respondents reveal direct contact with confirmed case among family members in previous two weeks. Though, 30% responded that the source of infection was unknown. Fecal shedding may be another source of transmission [22].

The clinical spectrum of COVID-19 is very heterogeneous. The most commonly reported symptoms were fever, cough, and hypo/hyperglycemia. However, shortness of breath, headache, myalgia, upper respiratory symptoms (e.g., sore throat and rhinorrhea) and gastrointestinal symptoms (e.g., nausea and diarrhea) can also occur, as recently reported [4,23]. Caution should be taken to potential hypoglycemic events either from severe illness and lack of food intake, ibuprofen should be handled with care as it could increase the hypoglycemic effect of insulin [24] and with the use of chloroquine in these subjects. Patient tailored therapeutic strategies, rigorous glucose monitoring and careful consideration of drug interactions seem to reduce adverse outcomes [25].

Another issue during this COVID-19 pandemic has been the use of immunostimulants to help preventing the disease. To date there is insufficient evidence to conclude that children with type 1 diabetes are immunocompromised. The evidence indicates that an immunocompromised state occurs only in the context of poor glycemic control and/or with

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severe complications, such as DKA or in adults with vasculopathy and chronic kidney disease [26]. The link between catching COVID-19 infection and diabetes was explored in this survey and 75% of HCP responded that parents did not ask for immunostimulant treatments. Interestingly, about the 25% who were asked for immunostimulant supplement, there is not a specific region of the world where this habit is consistent, but it was spread in several countries. It is important to note that immune supporting effects of supplements and vitamins, in the context of the COVID-19, are not proven. Furthermore, attention to nutrition, protein intake and vitamin status is important for individuals with diabetes at any time and thus as well during this pandemic [1]. Although a few studies recommend vitamin C supplementation as an antioxidant [27] and higher doses of vitamin D in elderly in the first few weeks of COVID-19 infection [28] or those with vitamin deficiency[29], neither vitamin D nor vitamin C supplementation appears to have any effect in protecting from COVID-19. Of all respondents 81% used paracetamol as antipyretic, in line with some non-confirmed recommendations which hypothesized that ibuprofen or other non-steroidal anti-inflammatory drugs could be harmful for patients with COVID-19 [30].

A low percentage of responders reported false positive elevated CGM reading (7%), especially among FreeStyle Libre™ users, perhaps due to acetaminophen interference [31]; this kind of interference has been previously reported for several CGM systems, including FreeStyle Libre™ [32].

In the lower respiratory tract, it appears that decreased angiotensin-converting enzyme 2 (ACE2), which binds to the receptor binding domain of SARS-CoV-2 virus, could portend a higher risk of developing severe acute respiratory distress and lung injury [5,33]. For this

reason, 25% of responders advised their patients to interrupt ACEi in advance. No substantial increase in the likelihood of a positive test for COVID-19 or in the risk of severe COVID-19 was reported in association with five common classes of antihypertensive medications [34]. In fact, the American Heart Association and other major associations recommend their continued use [35]. Achieving glycemic targets should be the goal, no matter which drugs are being used.

Anxiety and parenting stress were the most commonly seen psychological problems among our responders. Living with diabetes and managing the condition on a day-to-day basis are associated with heightened levels of anxiety and distress [36, 37]. In a recent study, 25% experienced diabetes distress at the beginning of the COVID-19 pandemic, which corresponds to what is found under normal circumstances [38-40]. A Danish study showed that people with diabetes have COVID-19-specific worries related to their disease which is associated with poorer psychosocial health. These worries should be addressed through support targeting specific questions and needs of individuals with diabetes as well as frequent updates on new knowledge regarding COVID-19 and diabetes mellitus [38].

It is important to prioritize mental health in these stressful days for both patients and their families, which can have a big impact on diabetes control and blood glucose levels. People with diabetes are two to three times more likely to have depression. Use of technology to stay connected to friends and family; trying an online meeting or calling a friend may lessen the stress patients might experience.

Strengths of our study are the global sourcing (215 centers in 75 countries) among HCP with a focus on pediatric diabetes and the timeliness of the survey, which was initiated very

shortly after substantial lockdown in most countries due to the COVID-19 pandemic.

Although SARS-CoV-2 infection in adults includes persons with diabetes in the vulnerable, high risk population, our report suggests that children with diabetes do not belong to the high risk group. This might have some important implications for children with diabetes and the restart of school, since does not seem they have to be more cautious than their healthy peers. Limitations of the survey may be that we present observational data from some countries but not all where COVID-19 spread out, even if the most interested ones (by numbers of infected people and deaths) are all represented. While 15% reported a higher incidence of DKA, only registry data prospectively will show accurately any impact on the rates of DKA presentation. However, we acknowledge that the missed countries could have had different experience or knowledge in handling these patients. Relating to this issue we would like also to highlight that out of approximately 2300 emails sent, we received only 303 responses (13%). Even if in line with the answer rate to similar surveys, these low numbers could be due either to the pandemic itself and much less time to manage usual daily workload, and the fact that some of the email addresses could have been changed or not active anymore.

Follow up survey could be of utmost importance to improve our knowledge and to evaluate the effects of COVID-19 over time.

In conclusion, this large global survey, done with HCP coming from centers treating children and adolescents with diabetes, showed how HCP adapted their current practices during COVID-19 pandemics. Social isolation highly influenced patients care around the world, favoring remote consultation through telehealth/telemedicine as an option to maintain

assistance to patients with diabetes, in comparison to traditional face-to-face consultation.

The great majority of centers did not have diabetes children COVID-19 positive, and from those who had, the majority had just mild/moderate disease course. The emergence of COVID-19 pandemic had an important impact on family's behavior that might be associated with increase in DKA at diagnosis and delaying new onset diagnosis.

References

1. Gupta R, Ghosh A, Singh AK, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. *Diabetes Metab Syndr*. 2020 May - Jun;14(3):211-212.
2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA* 2020.
3. Zhang JJY, Lee KS, Ang LW, Leo YS, Young BE. Risk Factors of Severe Disease and Efficacy of Treatment in Patients Infected with COVID-19: A Systematic Review, Meta-Analysis and Meta Regression Analysis. *Clinical Infectious Diseases*. 2020
4. Chen Y, Gong X, Wang L, Guo J. Effects of hypertension, diabetes and coronary heart disease on COVID-19 diseases severity: a systematic review and meta-analysis. *medRxiv* 2020; published online March 30; DOI:10.1101/2020.03.25.20043133 (preprint).
5. Barron E, Bakhai C , Kar P, Weaver A, Bradley D, Ismail H, et al. Type 1 and Type 2 diabetes and COVID-19 related mortality in England: a whole population study. version posted 19th May 2020[Internet] .Available from: <https://www.england.nhs.uk/publication/type-1-and-type-2-diabetes-and-covid-19-related-mortality-in-england/>
6. CDC COVID-19 Response Team Coronavirus disease 2019 in children—United States, February 12–April 2, 2020.*MMWR Morb Mortal Wkly Rep*. 2020; 69: 422-426
7. Danne T. COVID-19, type 1 diabetes, and technology: why paediatric patients are leading the way. *Lancet Diabetes Endocrinol* 2020 Published Online May 5, 2020 [https://doi.org/10.1016/S2213-8587\(20\)30155-8](https://doi.org/10.1016/S2213-8587(20)30155-8)
8. Oberweis ML, Codreanu A, Boehm W, Olivier D, Pierron C, Tsobo C et al. Pediatric Life-Threatening Coronavirus Disease 2019 With Myocarditis [published online

- ahead of print, 2020 May 11]. *Pediatr Infect Dis J*. 2020;10.1097/INF.0000000000002744. doi:10.1097/INF.0000000000002744
9. Ghosh A, Gupta R, Misra A. Telemedicine for diabetes care in India during COVID19 pandemic and national lockdown period: Guidelines for physicians. *Diabetes Metab Syndr*. 2020 Apr 4;14(4):273-276. doi: 10.1016/j.dsx.2020.04.001. [Epub ahead of print].
10. Y. Dong, X. Mo, Y. Hu, Xin Q, Fang J, Zhongyi J, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China .*Pediatrics* (2020), 10.1542/peds.2020-0702
11. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study [published online ahead of print, 2020 Mar 25]. *Lancet Infect Dis*. 2020;S1473-3099(20)30198-5. doi:10.1016/S1473-3099(20)30198-5
12. International Society of Pediatric and Adolescent Diabetes (ISPAD). Summary of recommendations regarding COVID-19 in children with diabetes: Keep Calm and Mind your Diabetes Care and Public Health Advice. *Pediatr Diabetes*. 2020; 21: 413-414.
13. Cherubini V, Gohil A, Addala A, Zanfardino A, Iafusco D, Maahs D. Unintended consequences of COVID-19: remember general pediatrics. *J Pediatr* 2020. doi: 10.1016/j.jpeds.2020.05.004.
14. Laffel LM, Limbert C, Phelan H, Virmani A, Wood J, Hofer SE. ISPAD Clinical Practice Consensus Guidelines 2018: Sick day management in children and adolescents with diabetes. *Pediatr Diabetes*. 2018 Oct;19 Suppl 27:193-204.
15. Peters AL, Garg S. The Silver Lining to COVID-19: Avoiding Diabetic Ketoacidosis Admissions with Telehealth. *Diabetes Technol Ther*. 2020 May 5. doi: 10.1089/dia.2020.0187. [Epub ahead of print]
16. Garg SK, Rodbard D, Hirsch IB, Forlenza GP. Managing New-Onset Type 1 Diabetes During the COVID-19 Pandemic: Challenges and Opportunities. *Diabetes Technol Ther*. 2020 Apr 17. doi: 10.1089/dia.2020.0161. [Epub ahead of print]

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17. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, Qin R, Wang H, Shen Y, Du K, Zhao L, Fan H, Luo S, Hu D. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes Metab Res Rev*. 2020 Mar 31:e3319. doi: 10.1002/dmrr.3319. [Epub ahead of print]
 18. Wang Z, Du Z, Zhu F. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. *Diabetes Res Clin Pract*. 2020 May 13:108214. doi: 10.1016/j.diabres.2020.108214. [Epub ahead of print].
 19. Stefan N, Birkenfeld AL, Schulze MB, Ludwig DS. Obesity and impaired metabolic health in patients with COVID-19 [published online ahead of print, 2020 Apr 23]. *Nat Rev Endocrinol*. 2020;1-2. doi:10.1038/s41574-020-0364-6
 20. Bornstein SR, Dalan R, Hopkins D, Mingrone G, Boehm BO. Endocrine and metabolic link to coronavirus infection. *Nat Rev Endocrinol*. 2020;16(6):297-298. doi:10.1038/s41574-020-0353-9
 21. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infect Dis Poverty*. 2020;9(1):29. Epub 2020/03/19. doi: 10.1186/s40249-020-00646-x.
 22. Hindson J. COVID-19: faecal-oral transmission?. *Nat Rev Gastroenterol Hepatol*. 2020;17(5):259. doi:10.1038/s41575-020-0295-7
 23. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. Epub 2020/01/28. doi: 10.1016/S0140-6736(20)30183-5.
 24. Coronavirus and Type 1 Diabetes: What You Need to Know [Internet]. 2020 [Updated 2020 May 18]. Available from: <https://www.jdrf.org/coronavirus/>
 25. Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: Knowledge in progress. *Diabetes Res Clin Pract*. 2020;162:108142. doi:10.1016/j.diabres.2020.108142
 26. Mustapha S, Sellers E, Dean H. Are children with type 1 diabetes immunocompromised? *CMAJ*. 2005 Aug 16;173(4):341.

27. Carr AC. A new clinical trial to test high-dose vitamin C in patients with COVID-19. *Crit Care*. 2020 Apr 7;24(1):133. doi: 10.1186/s13054-020-02851-4
28. Grant, W.B.; Lahore, H.; McDonnell, S.L.; Baggerly, C.A.; French, C.B.; Aliano, J.L.; Bhattoa, H.P. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths. *Nutrients* 2020, 12, 988.
29. Zhang, L, Liu, Y. Potential interventions for novel coronavirus in China: A systematic review. *J Med Virol*. 2020; 92: 479– 490
30. Beth Russell, Charlotte Moss, Anne Rigg, Mieke Van Hemelrijck. COVID-19 and treatment with NSAIDs and corticosteroids: should we be limiting their use in the clinical setting? *Ecancer medical science*, 2020; 14 DOI: 10.3332/ecancer.2020.1023
31. Calhoun P, Johnson TK, Hughes J, Price D, Balo AK. Resistance to Acetaminophen Interference in a Novel Continuous Glucose Monitoring System. *J Diabetes Sci Technol*. 2018;12(2):393-396. doi:10.1177/1932296818755797
32. Basu A, Slama MQ, Nicholson WT, Langman L, Peyser T, Carter R, Basu R. Continuous glucose monitor interference with commonly prescribed medications: a pilot study. *J Diabetes Sci Technol*. 2017;11(5):936-941.
33. Pal R, Bhadada SK. Should anti-diabetic medications be reconsidered amid COVID-19 pandemic? *Diabetes Res Clin Pract*. 2020 Apr 10;163:108146. doi: 10.1016/j.diabres.2020.108146. [Epub ahead of print]..
34. Reynolds HR, Adhikari S, Pulgarin C, Troxel AB, Iturrate E, Johnson SB, et al. Renin-Angiotensin-Aldosterone System Inhibitors and Risk of Covid-19 [published online ahead of print, 2020 May 1]. *N Engl J Med*. 2020;NEJMoa2008975. doi:10.1056/NEJMoa2008975
35. American College of Cardiology. HFSA/ACC/AHA statement addresses concerns re: using RAAS antagonists in COVID-19. ACC News Story. 2020 Mar 17. (<https://viajwat.ch/2REZU2H>)
36. Fisher L, Hessler D, Polonsky W, Strycker L, Masharani U, Peters A. Diabetes distress in adults with type 1 diabetes: prevalence, incidence and change over time. *J Diabetes Complications* 2016; 30: 1123–1128.

37. Young-Hyman D, de Groot M, Hill-Briggs F, Gonzalez JS, Hood K, Peyrot M. Psychosocial care for people with diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2016; 39: 2126–2140.
38. Joensen LE, Madsen KP, Holm L, Nielsen KA, Rod MH, Petersen AA, et al. Diabetes and COVID-19: psychosocial consequences of the COVID-19 pandemic in people with diabetes in Denmark-what characterizes people with high levels of COVID-19-related worries? [published online ahead of print, 2020 May 11]. *Diabet Med*. 2020;10.1111/dme.14319. doi:10.1111/dme.14319
39. Perrin NE, Davies MJ, Robertson N, Snoek FJ, Khunti K. The prevalence of diabetes-specific emotional distress in people with type 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2017; 34: 1508–1520.
40. Sturt J, Dennick K, Due-Christensen M, McCarthy K. The detection and management of diabetes distress in people with type 1 diabetes. *Curr Diab Rep* 2015; 15: 101.

Table 1: Clinical profile, centre characteristics and patients feature during COVID19 pandemic

Characteristics (number of responses)	Responses (%)
Centres by country (215) ^a	
United Kingdom	35 (16.3)
United States	20 (9.3)
France	15 (7.0)
Canada, Italy	9 (4.2) each
Australia, Belgium	7 (3.3) each
Denmark, Spain	5 (2.3) each
Brazil, Germany, Netherlands, Portugal, Sweden	4 (1.9) each
Argentina, Austria, Egypt, Greece, Ireland	3 (1.4) each
Participants' clinical role (303)	

Pediatric Endocrinologist/diabetologist	193 (64)
Pediatrician with interest in diabetes	46 (15)
Nurse practitioner/registered nurse	26 (9)
Resident/fellow/trainee in Pediatrics/Pediatric endocrinology or diabetology/ Diabetes researcher	13 (4)
Diabetes educator	7 (2)
Dietitian	6 (2)
Primary care practitioner/family doctor with interest in diabetes	5 (2)
Adult physician looking after pediatric or adolescent patients	4 (1)
Mental health professional	3 (1)
Children and young people aged 0-18 years with diabetes being looked after (301)	
Less than 100	83 (27.5)
100-200	83 (27.5)
201-500	97 (32)
More than 500	38 (13)
Current routine check-up (832) ^b	
Telephone consultation	266 (32.0)
Video consultation	150 (18.0)
Face to face consultation with appropriate PPE	139 (16.5)
Sent SMS, use of cross-platform messaging (e.g. WhatsApp®) and emails for consultations	128 (15.5)
Apps or Patient Portal	79 (9.5)
Only newly diagnosed patients or patients in a complex social system visit our center	45 (5.5)
As usual, no changes	16 (1.9)
HbA1c drive through staff in PPE but not at hospital site	8 (1.0)
I am retired and no longer evaluate patients	1 (0.1)
Multidisciplinary team deliver education to patients with new onset type 1 diabetes (565) ^b	

Face to face education wearing appropriate personal protective equipment (PPE)	214 (38)
By Telephone	144 (25.5)
Video consultation	126 (22)
Via application	37 (6.5)
As usual, no changes	44 (8)
Refill prescription period (303)	
Every month	44 (14.5)
Every 3 months or less	129 (43)
Every 6 months or less	35 (11.5)
Every year	27 (9)
Automatically from pharmacy	13 (4)
As required	15 (5)
Refill prescription is not allowed	3 (1)
I am not directly involved with prescription	37 (12)
Shortage of any diabetes medical supplies (303)	
Yes	57 (19)
No, everything was secured	198 (65)
I was not aware of situation	48 (16)
Main shortage of diabetes supplies (134)	
Glucose test strips	35 (26)
Basal Insulin	30 (22)
Bolus Insulin	30 (22)
Blood glucose sensors	14 (10.5)
Ketone strips	13 (10)
Pump supplies	9 (7)
Alcohol wipes	2 (1.5)
Syringe and needles	1 (1)

Adaptations on blood or sensor glucose monitoring (237)	
No changes from usual practice	104 (44)
Monitor blood glucose and review CGM data more frequently	100 (42)
Check sick day management with diabetes team	12 (5)
Review CGM data more frequently	8 (3.5)
Change to CGM, when available	7 (3)
Monitor blood glucose more frequently	2 (1)
Strict hand hygiene	2 (1)
Check ketones more frequently	1 (0.5)
Most used antipyretics (118)	
Paracetamol (acetaminophen)	96 (81)
Combination of both ibuprofen and paracetamol	14 (12)
Ibuprofen	5 (4)
None	2 (2)
Metamizole (dipyrone)	1 (1)
Aspirin	0
Report of more falsely elevated CGM readings (193)	
Yes	13 (7)
No	180 (93)
CGM sensor affected during pandemic (37)	
Freestyle Libre	16 (43)
Dexcom G6 System	10 (27)
Dexcom G5	9 (24)
Verisense	1 (3)
Medtronic Enlite	1(3)
Prescription of immunostimulants (301)	
None	225 (75)

Less than 10%	54 (18)
Around 25%	12 (4)
Around 50%	6 (2)
More than 75%	4 (1)
Recommendations of use of ACEi in patients with diabetic nephropathy/hypertension during pandemic (101)	
Yes	76 (75)
No	25 (25)
Complications of using ACEi during pandemic (61)	
No patient with nephropathy or on ACEi	28 (46)
No complications	17 (28)
Patients on ACEi have not had COVID19	16 (26)
Most reported psychological effects (491) ^b	
Anxiety	151 (31)
Parental stress	118 (24)
None have had psychological problems so far	73 (15)
Depression	40 (8)
Insomnia/hypersomnia	33 (7)
Eating disorder	31 (6)
Panic attacks	20 (4)
Patient or caregivers have improved the mood	18 (3.5)
Denial	3 (0.5)
Slight terror	2 (0.5)
Suicide attempt	2 (0.5)

PPE: personal protective equipment; CGM: continuous glucose monitor; ACEi: Angiotensin-converting-enzyme inhibitors

^a Remaining countries that contributed with two or less centers: Bulgaria, Chile, Indonesia, Japan, Liberia, Mexico, New Zealand, Nigeria, Norway, Poland, South Africa, Turkey, Algeria,

Bangladesh, Barbados, Burma, Cameroon, Colombia, Congo, Costa Rica, Cote D'Ivoire, Croatia, Czech Republic, Ecuador, Estonia, Ethiopia, France, Georgia, Ghana, Haiti, Iraq, Kenya, South Korea, Kuwait, Luxembourg, Macedonia, Malawi, Malaysia, Malta, Mauritius, Nepal, Pakistan, Peru, Philippines, Romania, Russia, Saudi Arabia, Serbia and Montenegro, Slovenia, Switzerland, Tanzania, Tunisia, Ukraine, United Arab Emirates, Vietnam, Zambia.

^b number of responses are over of number of participants due to multiple-choice selection

Table 2: Reported effects among patients with diabetes during COVID19 pandemic

Characteristics (number of responses)	Responses (%)
Delayed diagnosis of diabetes during pandemic (301)	
Yes	65 (22)
No	236 (78)
Increase of new onset diabetes with DKA (297)	
Yes	44 (15)
No	253 (85)
Feeling that caregivers/families avoid contact with diabetes team during pandemic (300)	
Yes	203 (68)
No	97 (32)
Any patient with diabetes that experienced COVID19 infection (303)	
Yes	37 (12)
No	266 (88)
Method of diagnosis (78)	
RT-PCR SARS-CoV-2	61 (78)
Serologic tests	5 (6)
Other (presumptive positive)	12 (15)
Sample that confirmed diagnosis (113)	
Nasal swab	63 (56)
Oropharyngeal swab	42 (37)
Bronchoalveolar	3 (3)
Blood	5 (4)
Exposed history (40)	
Any family member as a confirmed or probable case in the last 14 days	20 (50)
Caregiver is a health care worker where a case had been diagnosed	5 (12.5)

History of travel to or residence in a location reporting cases during the last 14 days	3 (7.5)
Unknown source	12 (30)
T1D patients that experienced COVID19 (61)	
Age (years)	
0-5	3 (9)
6-10	8 (23.5)
11-16	16 (47)
16-18	7 (20.5)
Reported gender	
Boys	14 (34)
Girls	28 (66)
Duration of disease (years)	
New onset	3 (10.5)
Less than one	2 (7)
1-5	8 (29)
5-10	12 (43)
More than 10	3 (10.5)
Main symptoms	
Fever	29
Cough	28
Hypoglycemia	>23
Myalgia	16
Rhinorrhea	15
Headache	15
Pharyngeal erythema	11

Hyperglycemia	>10
Gastrointestinal symptoms	9
Diabetic ketoacidosis	>8
Shortness of breath	6
Mean HbA1c, % (SD; range min-max)	7.6 (1.6; 5.7-13.0)
Therapies required	
Admission to hospital	
Admission to ICU	>15
Oxygen	2
Bronchodilators and glucocorticoids	1
Noninvasive ventilation	0
Intubation and ventilation	0
Antibiotics	0
Antipyretics	2
Antihistamine	3
DKA management	1
Dextrose	2
	1
T2D patients that experienced COVID19 (25)	
Age (years)	
0-5	0
6-10	0
11-16	4 (57)
More than 16	3 (43)
Reported gender	

Boys	6 (54)
Girls	5 (46)
Duration of diabetes (years)	
Less than 3	3 (50)
3-10	3 (50)
More than 10	0
Symptoms	
Hyperglycemia	
Hypoglycemia	>10
Diabetic ketoacidosis	>6
Fever	4
Cough	3
Shortness of breath	3
Myalgia	3
Pharyngeal erythema	3
Rhinorrhea	1
Hyperglycemic hyperosmolar state	1
Respiratory failure	1
Headache	1
Gastrointestinal symptoms	0
	0
Mean HbA1c, % (SD; range min-max)	7.8 (1.3; 5.8-9.9)
Therapies required	
Admission to hospital	5
Admission to ICU	3

Oxygen	3
Bronchodilators and glucocorticoids	2
Noninvasive ventilation	2
Intubation and ventilation	2
Pressor drugs	2

DKA: Diabetic ketoacidosis; RT-PCR SARS-CoV-2: Reverse-Transcription-Polymerase Chain Reaction for detecting Severe acute respiratory syndrome coronavirus 2; SD: Standard deviation; ICU: Intensive care unit