CASE REPORT

New onset of diabetes in a child infected with COVID-19: a case report

Mahtab Ordooei1,2 · Nasrin Behniafard1,2 · Fahimeh Soheilipour3 · Elahe Akbarian1

Received: 3 May 2021 / Accepted: 11 September 2021 / Published online: 17 September 2021
© Springer Nature Switzerland AG 2021

Abstract
Background Diabetic ketoacidosis (DKA) is a serious complication of type 1 diabetes. A few studies have reported that COVID-19 is associated with the development of new-onset diabetes. Here, we present an infected child with new onset diabetes leading to DKA.
Case presentation A 10-year-old patient with respiratory distress admitted to the Emergency Department of our center. The patient’s COVID-19 Polymerase Chain Reaction (PCR) test was positive and also biochemical analyses confirmed that he had DKA. Despite standard initial treatments, ketoacidosis remained resistant; hence we prescribed oral bicarbonate (40 cc every 8 h) to treat the patient’s refractory acidosis. Due to the patient’s improvement, he was discharged after 10 days (7 days in the PICU), receiving outpatient enoxaparin (for a week) and ongoing subcutaneous insulin.
Conclusion We report an interesting case of a child with COVID-19 infection precipitating presentation with new onset diabetes. Due to refractory acidosis, starting oral bicarbonate treatment after 2 days improved acidosis and tachypnea in the patient. The patient’s medical team suggest close biochemical monitoring, prescribing enoxaparin for high level of D-dimer, and ordering oral bicarbonate acidosis persists.

Keywords COVID-19 · New Onset · Diabetes · Children · Ketoacidosis · Oral Bicarbonate

Introduction
In late December 2019, the novel coronavirus was discovered in Wuhan City, which is the 11-million-population capital of Hubei Province, China [1]. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the disease called as COVID-19 by the World Health Organization [2]. A number of previous studies reported a bidirectional relationship between SARS-CoV-2 and the onset of diabetes [3]. Although diabetes is prevalent worldwide, healthcare professionals are worried about this new pandemic’s consequences regarding diabetes [4]. While it has been shown that persons with diabetes (PWD) are considered as high risk population for developing complications [5]; herein, we presented a young patient with new onset diabetes after SARS-CoV-2 infection.

Recently, evidence showed that an association may exist between diabetes and higher risk of COVID-19 infection and the increased mortality rate [6]. On the other hand, in some people infected with COVID-19, new-onset diabetes has been reported and in some others, severe metabolic complications occurring in PWD have been observed [7–9]. Therefore, it can be said that there is a bidirectional relationship between diabetes and COVID-19. Herein, we presented a child with new onset diabetes infected with COVID-19.

Case report
A 10-year-old male patient with respiratory distress was admitted to the Emergency Department (ED), Shahid Sadoughi Hospital, Yazd. In his medical history, polyuria and polydipsia were reported since ten days before the admission time. Moreover, he had vomiting since three days prior to the admission. In his family history, his mother’s COVID-19 PCR test was reported as positive two weeks ago and she had a history of hypothyroidism and gestational diabetes.
mellitus. Of note, the patient’s other family members had no history of type 1 diabetes mellitus (T1DM), coeliac, thyroiditis or other associated autoimmune diseases. He was referred to the ED due to tachypnea, deep breathing, drowsiness, and no response to dextrose saline serum as the outpatient therapy. As well, clinical examinations and vital signs were as follows: RR: 55, PR: 80, BP: 95/45, T: 37.8, O₂ Sat: 97%, weight: 52 kg, height: 135 cm, and body mass index (BMI): 28.53 kg/m². All the physical examinations were normal except the chest exam. The patient had tachypnea with deep respiration, and he was using his respiratory accessory muscles. Of note, chest auscultation and other physical examinations were normal. Chest X-ray showed no abnormality. The patient was admitted under the impression of diabetic ketoacidosis (DKA). The initial laboratory data (with normal range in parenthesis) showed a high Blood Sugar level (BS): 487 mg/dL (<140), HbA1c: 7.2% (<6.5%), pH: 6.7 (7.35–7.45), Bicarbonate (HCO₃): 4.2 mEq/L (22–26), Anti GAD65: negative, Insulin Antibody (Ab): negative, Carbon Dioxide (pCO₂): 21.7 mmHg (30–50), Urine Ketone: 1+, Sodium (Na): 128 mEq/L (134–145), Potassium (K): 2.5 mEq/L (3.5–5.5), WBC: 11,400 /µL (3500–10,000), RBC: 6,100,000 /µL (3,600,000–6,100,000), Hemoglobin: 15 gr/dL (11.5–18.8), PLT: 354 /µL (150–450), CRP: negative, Magnesium (Mg): 2.2 mg/dL (1.5–2.3), Phosphorus (P): 1.7 mg/dL (3.9–7.7), Blood Urea Nitrogen (BUN): 90 mg/dL (5–18), and Creatinine (Cr): 0.6 mg/dL (0.7–1.4). Additionally, due to the patient’s contact with his mother, all the laboratory workups related to COVID-19 were done.

Based on the performed tests, diagnoses of both DKA and COVID-19 were confirmed. Initial normal saline serum (10 cc/kg/h) was applied to the patient at the admission time to the ED. Thereafter, he was transferred to the PICU. Considering receiving an outpatient serum, a 36-h serum (half saline) was calculated and then applied due to the patient’s dehydration. In addition, the patient received serum K (50 mEq/L). Insulin (0.1 unit/kg/h) was also started from the second hour of his admission to the PICU. Despite expecting an increase in HCO₃, the acidosis did not change during the first 4 h; therefore, the patient’s IV line was checked again and a new vein was taken. After 8 h, acidosis was still observed to be resistant, so we decided to take the central vein for the patient. By passing 4 h, Cr began to increase and was reported as 2.5 (mg/dL). Despite the increase in Cr, the patient’s urine output remained normal (1.5 to 2 cc/kg/h). Next, Remdesivir was suggested in the initial infectious consultation, but due to the increased level of Cr and glomerular filtration rate (GFR) disorder, this medication was not given to him. D-dimer at the admission time was 9 (µg/mL), so considering the positive result of COVID-19, enoxaparin was started at 20 mg/bd for the patient. D-dimer was checked every 48 h, which reached 7 (µg/mL), 3 (µg/mL), and finally 2 (µg/mL). Because of hypophosphatemia, phosphorus therapy was started for the patient. During the control phase, P and K did not fall below 2.5 and 3.5 (mEq/L), respectively. Moreover, Cr reached 2.5 (mg/dL), increased up to 3 (mg/dL), and then decreased to 2 (mg/dL) after 3 or 4 days. Within 36 h, despite performing fluid and insulin therapy, the acidosis still continued (pH: 7.2, HCO₃: 9 (mEq/L)). Due to refractory acidosis and a low level of bicarbonate, we decided to give him oral bicarbonate (at amount of 40 cc every 8 h). Consequently, it caused an increase in HCO₃ up to 12 (mEq/L) within 24 h. When pH increased up to 7.3, insulin was converted to subcutaneous (Sc). By passing 24 h from per-oral order, the patient’s serum was discontinued and only Sc insulin plus enoxaparin were given to him. After 48 h from the start of oral bicarbonate, HCO₃ reached 15 (mEq/L) and oral bicarbonate was discontinued. Due to microscopic hematuria, a decreasing trend was observed in platelets during the course of the disease, as well as a decrease in GFR and increase in urea, creatinine, and D-dimer levels. So, for rolling out renal thrombosis, renal vascular Doppler sonography was requested, which was normal.

The patient was hospitalized for 10 days (7 days at PICU and 3 days at ward). Due to the good condition and proper control of BS, the patient was then discharged under stable condition with no fever and good oral tolerance. At the time of discharge, Cr and d-dimer were calculated as 2 (mEq/L) and 2 (µg/mL), respectively, and the patient received outpatient enoxaparin and Sc insulin. After one week follow up, d-dimer fell into 0.5 (µg/mL) and Cr into 0.7 (mEq/L), so enoxaparin was discontinued for him. It is noteworthy that the level of C-peptide was in the normal lower limit, which may cause a possible damage to the pancreas, so it was recommended to continue insulin subcutaneous and follow up for longer time.

Discussion

COVID-19 has increased mortality and morbidity rates in individuals with comorbidities, including diabetes mellitus (DM) [6]. Previous experiences during the severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) endemic showed that DM is frequently observed in patients with no history of both DM and glucocorticoid [10]. Moreover, new emerging evidence showed that exposure to COVID-19 may be associated with new-onset DM and DKA in those individuals with no susceptibility to the impaired glucose metabolism [11, 12].

To the best of our knowledge, this is the first case of new onset diabetes and DKA in a child infected with COVID-19 in Iran. Abdi et al. in their study described new-onset diabetes with symptoms of DKA in a 3-year-old Moroccan child infected with COVID-19. Similarly,
in their study, it was indicated that COVID-19 might be associated with atypical symptoms, including new-onset diabetes and DKA. Accordingly, they recommended that clinicians must be aware of that in children with blood glucose and HbA1c at the time of their admission during COVID-19 pandemic [13]. Moreover, a multicenter retrospective cohort study conducted in Saudi Arabia revealed that the implemented lockdown was significantly associated with an increased frequency of new-onset T1DM and DKA in the population [14]. However, Salmi et al. in a cohort on Finnish children showed that the higher frequency of new-onset T1D likely arises from the delays in its diagnosis, not because of SARS-CoV-2 infection [15]. Moreover, Ebekozien et al. in a multicenter study on 64 T1DM patients who were confirmed or suspected cases of COVID-19, have reported that six patients presented with new-onset T1DM [16]. In another study by Unsworth et al., it was indicated that there is a considerable increase in the incidence of new T1DM in comparison with the condition before the COVID-19 pandemic [17]. Angiotensin-converting enzyme 2 (ACE2) receptors are known to be expressed in organs and cells, especially in pancreatic β-cells. Therefore, these receptors might be helpful in understanding the mechanism of SARS-CoV-2 in new onset diabetes cases [18]. Of note, the pleiotropic alteration of glucose metabolism caused by SARS-CoV-2 is not unexpected. Accordingly, this can consequently lead to new mechanisms of diabetes or complicate the pathophysiology of preexisting diabetes. According to a previously performed research, COVID-19 can cause ketoacidosis [8]. In this regard, evidence related to the viral cause of ketosis-prone diabetes, including another type of Coronavirus, reported that patients with SARS-COV-1 pneumonia considerably presented fasting glycaemia and acute-onset diabetes compared to those with non-SARS pneumonia [19]. Previous literature have shown that the SARS-CoV-1 virus may have passed into pancreatic islet cells through the ACE2 receptors, leading to β-cell damage and new-onset of diabetes. Thus, it is supposed that COVID-19 virus may infect the human pancreatic beta cells through the ACE2 receptors [20]. As well, a recent study reported that COVID-19 precipitate insulin resistance in patients, causing chronic metabolic disorders that did not exist prior to their infection 21.

In our patient, due to negative autoantibodies and a normal lower limit of C-peptide, damage to the pancreas β-cells induced by the entrance of SARS-CoV-2 in pancreatic islet cells via the ACE2 receptors seems possible. So, the autoimmune mechanism possibility is ruled out. Besides, insulin resistance caused by COVID-19 infection is not unexpected in the affected patients. However, further studies are needed to confirm the mechanisms of the effect of COVID-19 on the development of diabetes or its complications among positive cases of COVID-19.

**Conclusion**

Herein, this is the first reported case of new onset diabetes and DKA in a child infected with COVID-19 in Iran. In this case, refractory acidosis was treated with serum, insulin, and oral bicarbonate therapy. Due to the fact that bicarbonate treatment in DKA causes cerebral edema, bicarbonate was not started for the patient within the first 48 h. But, due to refractory acidosis, by starting oral bicarbonate treatment after 2 days, acidosis and tachypnea have improved in the patient. The patient’s medical team proposed ions monitoring and control, prescribing enoxaparin in the case of high level of D-dimer, as well as ordering oral bicarbonate if the patient's acidosis still persisted. According to our report, oral bicarbonate can be useful in the treatment of refractory acidosis among patients with DM who do not respond to the routine treatments during the pandemic.

**Declarations**

**Ethics approval** This study was approved by Shahid Sadoughi University of Medical Sciences’ ethics committee (ethics certificate number: IR.SSU.REC.1400.050).

**Consent to participate** A written informed consent was obtained from the patient’s parents for this manuscript.

**Conflicts of interest/Competing interests** The authors declare that they have no conflict of interest.

**References**

1. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, Abbasi H, Mirjalili SR, Behforouz A, et al. Vertical transmission of coronavirus disease 19 (COVID-19) from infected pregnant mothers to neonates: a review. Fetal Pediatr Pathol. 2020;39:246–50.
2. Jarahzadeh MH, Asadian F, Farbod M, Meibodi B, Abbasi H, Jafari M, et al. Cancer and coronavirus disease (COVID-19): comorbidity, mechanical ventilation, and death risk. J Gastrointest Cancer. 2021;52:80–4.
3. Rubino F, Amiel SA, Zimmet P, Alberti G, Bornstein S, Eckel RH, et al. New-onset diabetes in Covid-19. N Engl J Med. 2020;383:789–90.
4. Dastgheib SA, Najafi F, Shajari A, Bahrami R, Asadian F, Sadeghizadeh-Yazdi J, et al. Association of plasminogen activator inhibitor-1 4G5G Polymorphism with risk of diabetic nephropathy and retinopathy: a systematic review and meta-analysis. J Diabetes Metab Disord. 2020;19:2005–16.
5. Malek M, Hosseinpahah F, Meybodi HRA, Jahed SA, Hadeegh F, Sharghi S, et al. Diabetes management during the COVID-19 pandemic: An Iranian expert opinion statement. Arch Iran Med. 2020;23:564–7.
6. Mirjalili H, Dastgheib SA, Shaker SH, Bahrami R, Mazaheri M, Sadr-Bafghi SMH, et al. Proportion and mortality of Iranian diabetes mellitus, chronic kidney disease, hypertension and cardiovascular disease patients with COVID-19: a meta-analysis. J Diabetes Metab Disord. 2021;1–13.

7. Chee YJ, Ng SJH, Yeoh E. Diabetic ketoacidosis precipitated by Covid-19 in a patient with newly diagnosed diabetes mellitus. Diabetes Res Clin Pract. 2020;164:108166.

8. Li J, Wang X, Chen J, Zuo X, Zhang H, Deng A. COVID-19 infection may cause ketosis and ketoacidosis. Diabetes, Obes Metab. 2020;22:1935–41.

9. Ren H, Yang Y, Wang F, Yan Y, Shi X, Dong K, et al. Association of the insulin resistance marker TyG index with the severity and mortality of COVID-19. Cardiowasc Diabetol. 2020;19:58.

10. Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med. 2006;23:623–8.

11. Papachristou S, Stamatiou I, Stoian AP, Papanas N. New-onset diabetes in COVID-19: time to frame its fearful symmetry. Diabetes Ther. Adis; 2021;461–4.

12. Reddy PK, Kuchay MS, Mehta Y, Mishra SK. Diabetic ketoacidosis precipitated by COVID-19: a report of two cases and review of literature. Diabetes Metab Syndr. 2020;14:1459–62.

13. Aabdi M, Aarab A, Es-Saad O, Malki K, Bkiyar H, Housni B. New-Onset Diabetes in Children during COVID-19: Clinical Case Report. Case Rep Endocrinol. 2021;2021:6654019.

14. Alaqeel A, Aljurairah F, Alsuhaihani M, Huneef M, Alsheel A, Dubayee MA, et al. The impact of COVID-19 pandemic lockdown on the incidence of new-onset type 1 diabetes and ketoacidosis among Saudi children. Front Endocrinol (Lausanne). 2021;12:669302.

15. Salmi H, Heinonen S, Hästbacka J, Liääperi M, Rautiainen P, Miettinen PJ, et al. New-onset type 1 diabetes in Finnish children during the COVID-19 pandemic. Arch Dis Child. 2021;archdischild-2020-321220.

16. Ebekozien OA, Noor N, Gallagher MP, Alonso GT. Type 1 diabetes and covid-19: Preliminary findings from a multicenter surveillance study in the U.S. Diabetes Care. 2020;43:e83-5.

17. Unsworth R, Wallace S, Oliver NS, Yeung S, Kshirsagar A, Naidu H, et al. New-onset type 1 diabetes in children during COVID-19: Multicenter regional findings in the U.K. Diabetes Care. 2020;43:e170-1. American Diabetes Association Inc.

18. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003;426:450–4.

19. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol. 2010;47:193–9.

20. Müller JA, Groß R, Conzelmann C, Krüger J, Merle U, Steinhart J, et al. SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas. Nat Metab. 2021;3:149–65.

21. Govender N, Khaliq OP, Moodley J, Naicker T. Insulin resistance in COVID-19 and diabetes. Prim Care Diabetes. 2021;15:629-34.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.