KJMS / OPEN ACCESS Print ISSN: 2790-0207 Online ISSN: 2790-0215

Case Report

New-Onset Diabetic Ketoacidosis Precipitated by COVID-19 in Children: A Case Report

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DOI: 10.32894/kjms.2022.174188

Abstract:

A 13-year-old girl presented with symptoms consistent with diabetic ketoacidosis, including polyuria, polydipsia, and lethargy. Notably, there was no history of obesity or other known risk factors for impaired glucose metabolism. Her condition was preceded by exposure to COVID-19, confirmed through RT-PCR testing despite the patient being asymptomatic. Both parents had documented COVID-19 infection. The patient responded well to standard treatment, including intravenous insulin and rehydration. By the fourth day of hospitalization, she was transitioned to subcutaneous insulin therapy along with education provided to the parents on therapeutic and nutritional management. This case highlights a rare presentation of new-onset type 1 diabetes mellitus triggered by COVID-19 infection. The potential relationship between COVID-19 and acute onset diabetes in children underscores the need for further research to understand the mechanisms involved and to optimize treatment strategies.

Keywords: Diabetic ketoacidosis, COVID-19, New-onset type 1 diabetes

INTRODUCTION

The clinical manifestations of coronavirus disease 2019 (COVID-19) range widely from mild symptoms to fatal outcomes. COVID-19 has demonstrated unpredictable effects across multiple organ systems, yet its impact on the endocrine system remains underexplored. In particular, the metabolic complications of COVID-19 are still not fully understood. Since the beginning of the pandemic, numerous scientific reports have consistently indicated that individuals with diabetes mellitus (DM) tend to experience more severe courses of COVID-19, often associated with higher mortality rates (1).

Globally, there has been a noticeable increase in cases of diabetic ketoacidosis (DKA) revealing previously undiagnosed type 1 diabetes mellitus (T1DM) in both pediatric and adult populations during or following COVID-19 infection. More recently, "new-onset" hyperglycemia and "new-onset" DM have emerged as potential sequelae of SARS-CoV-2 infection. These findings have led to the hypothesis that SARS-CoV-2 may contribute to beta-cell damage in the pancreas, thereby inducing diabetes, or that it may activate novel pathophysiological mechanisms contributing to glucose dysregulation (2). However, this hypothesis warrants confirmation through larger multicenter investigations.

Here, we present a case of a previously healthy adolescent girl who developed diabetic ketoacidosis as the initial presentation of newly diagnosed type 1 diabetes mellitus, potentially precipitated by asymptomatic COVID-19. She was treated accordingly and followed for four weeks to evaluate glycemic control. The case details include history, clinical findings, laboratory and imaging results, treatment, and follow-up.

Case Presentation

A 13-year-old girl with no significant past medical history was admitted to the hospital with a 6-day history of polyuria, lethargy, and somnolence. Her symptoms had been preceded by a mild flu-like illness accompanied by a low-grade fever. There was no family history of type 1 diabetes mellitus or autoimmune disorders. However, both her mother and sister had recently tested positive for COVID-19 via PCR testing.

Upon admission, the patient was hemodynamically stable, though mildly tachycardic and drowsy, without focal neurological deficits. She exhibited mild dehydration and tachypnea consistent with Kussmaul’s breathing, with an oxygen saturation of 98%. Her body temperature was 37.5°C, weight was 35 kg, and height was 140 cm. The remainder of the physical examination was unremarkable, with no clear source of infection identified.

Point-of-care testing revealed a capillary blood glucose level of 350 mg/dL. Urinalysis indicated 3+ glycosuria and 3+ ketonuria, suggestive of diabetic ketoacidosis. Initial laboratory investigations (Table

1) confirmed hyperglycemia and metabolic acidosis, with a normal complete blood count and negative C-reactive protein (CRP). The serum sodium level was 130 mEq/L, indicating hyponatremia. HbA1c was within normal limits, and testing for glutamic acid decarboxylase (GAD) antibodies returned positive. Chest X-ray findings were normal. Nasopharyngeal RT-PCR for SARS-CoV-2 and serology for COVID-19 antibodies were both positive. Interestingly, a urine analysis performed three days prior to admission had shown no glycosuria or ketonuria.

The patient was managed with intravenous fluids and insulin, alongside correction of hyponatremia and close clinical monitoring. Resolution of DKA was achieved within 48 hours of treatment initiation. On the second day, she experienced a transient decrease in consciousness, for which intravenous 20% mannitol was administered. She regained full consciousness by the third day, and a brain CT scan was reported as normal. Nutritional support was initiated on day four, and intravenous insulin therapy was transitioned to a basal-bolus regimen comprising glargine (Lantus) and insulin aspart (Novorapid). Blood glucose levels were closely monitored, and diabetes education was provided to her parents. No specific antiviral treatment for COVID-19 was administered. A repeat COVID-19 PCR test on day 10 of hospitalization returned negative. The patient was discharged after 12 days with a confirmed diagnosis of new-onset type 1 diabetes mellitus in the setting of COVID-19 infection.

Table 1: Main Biological Assessment

Measures	Reference Range	Case
White cell count (per µL)	4000–10,000	5000
Neutrophil count (per µL)	1500–8000	3000
Lymphocyte count (per µL)	1000–7000	1000
Platelet count (per µL)	150,000–450,000	200,000
Hematocrit (%)	F: 37–47	39%
HbA1c (%)	<6.5	6
Anti GAD ab	-	+ve
PCR of COVID-19	-	+ve
Blood urea (g/L)	15–45	Normal
Creatinine (mg/dL)	0.1–2.8	
SARS-CoV-2 antibody test	-	+ve
CRP	-	-ve

DISCUSSION

Globally, from the initial outbreak in December 2019 through January 1, 2021, the World Health Organization reported 81,658,440 confirmed COVID-19 cases and 1,802,206 deaths (3). In pediatric populations, COVID-19 generally manifests in milder forms than in adults. An epidemiological study from China indicated that 90% of 731 laboratory-confirmed COVID-19 cases in individuals under 18 were asymptomatic, mild, or moderate in severity (4). However, comorbid conditions such as type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and cardiovascular disease are associated with increased severity and mortality in COVID-19 infections (5).

Diabetic ketoacidosis (DKA), a life-threatening complication of diabetes, results from absolute or relative insulin deficiency (6). It is more commonly seen in younger children, particularly those under five years of age. Biochemically, DKA is defined by a venous pH of <7.3 or a serum bicarbonate level of <15 mmol/L, a serum glucose concentration >11 mmol/L (>200 mg/dL), along with ketonemia, glycosuria, and ketonuria (7).

Emerging data suggest an evolving link between COVID-19 and the onset of T1DM in children. In a retrospective Chinese study, 6.4% (42 patients) of those admitted with COVID-19 had ketosis, with only 35.7% (15 cases) having a prior diagnosis of diabetes (8). Similarly, a German study reported a significant rise in both the incidence and severity of DKA at the time of diabetes diagnosis among children and adolescents during the COVID-19 pandemic (9). This increase may be attributed to multiple factors, including reduced access to healthcare services and public fear of COVID-19 exposure in clinical settings (9).

Infections are widely recognized as common triggers of DKA in individuals with known diabetes. Additionally, some viral infections are thought to precipitate autoimmune diabetes in genetically susceptible individuals (10). New-onset hyperglycemia has also been observed in association with other viral infections, such as HIV (11). In a few cases, serological evidence and direct viral isolation from pancreatic tissue have supported the hypothesis of infection-induced diabetes (10, 12).

A potential mechanism for COVID-19–related DKA involves its interaction with the renin-angiotensin-aldosterone system (RAAS). Angiotensin-converting enzyme 2 (ACE2), which is highly expressed in pancreatic islets, may act as a receptor for SARS-CoV-2, facilitating viral entry into beta cells. This may result in direct cytotoxic damage and acute impairment of insulin secretion, precipitating hyperglycemia and potentially diabetes (13). Furthermore, aberrant immune responses induced by SARS-CoV-2 may trigger autoimmune destruction of pancreatic islet cells, resembling the pathophysiology of insulin-dependent diabetes (14).

Fluid management in such cases requires careful monitoring, as excessive fluid administration may exacerbate acute respiratory distress syndrome due to increased pulmonary vascular permeability mediated by angiotensin (15).

Additional evidence comes from a case series involving two toddlers who developed insulin-dependent diabetes and DKA several months after recovering from Kawasaki disease, further supporting a possible link between post-infectious COVID-19 inflammation and pancreatic endocrine dysfunction (16).

Nevertheless, it remains unclear whether COVID-19 directly induces diabetes or unmasks preexisting but previously undiagnosed glucose metabolism abnormalities. In our patient's case, regular subcutaneous insulin injections have been necessary for glycemic control for more than 18 months following her COVID-19 infection, indicating persistent diabetes (17).

In conclusion, it is crucial to promptly address metabolic disturbances, particularly hyperglycemia, in pediatric patients before the development of full-blown DKA. Early detection and intervention may significantly improve outcomes in children potentially affected by COVID-19–associated diabetes.

CONCLUSION

COVID-19 may exert a potential diabetogenic effect, either by directly contributing to the onset of diabetes or by unmasking preexisting but undiagnosed diabetes through the exacerbation of metabolic disturbances. In some patients, the physiological stress associated with severe illness may further aggravate glucose dysregulation. While current evidence supports this possibility, extensive further research is required to validate this hypothesis and elucidate the underlying mechanisms.

Ethical Clearance:

In accordance with the 2013 WMA Helsinki Declaration, all ethical aspects of this study were approved. Before enrolling the participants, an informed oral consent and signed agreement wwere obtained from their families. Additionally, approval from the hospital administrator was obtained.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest**.**

References

1. Caballero AE, Ceriello A, Misra A, et al. COVID-19 in people living with diabetes: an international consensus. *J Diabetes Complications*. 2020;34(9):107671.
2. Rubino F, Amiel SA, Zimmet P, et al. New-onset diabetes in COVID-19. *N Engl J Med*. 2020;383(8):789–790.
3. World Health Organization. WHO coronavirus disease (COVID-19) dashboard. [Accessed January 1, 2021]. Available from: https://covid19.who.int/
4. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics*. 2020;145(6):e20200702.
5. Holman N, Knighton P, Kar P, et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. *Lancet Diabetes Endocrinol*. 2020;8(10):823–833.
6. Roca-Ho H, Riera M, Palau V, Pascual J, Soler M. Characterization of ACE and ACE2 expression within different organs of the NOD mouse. *Int J Mol Sci*. 2017;18(3):563.
7. American Diabetes Association. Diagnosis and classification of diabetes: standards of medical care in diabetes—2018. *Diabetes Care*. 2018;41(Suppl 1):S13–S27.
8. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054–1062.
9. Kamrath C, Mönkemöller K, Biester T, et al. Ketoacidosis in children and adolescents with newly diagnosed type 1 diabetes during the COVID-19 pandemic in Germany. *JAMA*. 2020;324(8):801–804.
10. Jaeckel E, Manns M, Von Herrath M. Viruses and diabetes. *Ann N Y Acad Sci*. 2002;958:7–25.
11. Ursenbach A, Max V, Maurel M, et al. Incidence of diabetes in HIV-infected patients treated with first-line integrase strand transfer inhibitors: a French multicentre retrospective study. *J Antimicrob Chemother*. 2020;75(11):3344–3348.
12. Roivainen M, Rasilainen S, Ylipaasto P, et al. Mechanisms of coxsackievirus-induced damage to human pancreatic beta-cells. *J Clin Endocrinol Metab*. 2000;85(1):432–440.
13. 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(3):193–199.
14. Suwanwongse K, Shabarek N. Newly diagnosed diabetes mellitus, DKA, and COVID-19: causality or coincidence? A report of three cases. *J Med Virol*. 2021;93(2):1150–1153.
15. Guo J, Huang Z, Lin L, Lv J. Coronavirus disease 2019 (COVID-19) and cardiovascular disease: a viewpoint on the potential influence of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers on onset and severity of severe acute respiratory syndrome coronavirus 2 infection. *J Am Heart Assoc*. 2020;9(7):e016219.
16. Bhowmick SK, Estrada B, Rettig KR. Insulin-dependent diabetes mellitus in two male African American children after Kawasaki disease. *Pediatrics*. 2002;110(2):e27.
17. Pettitt DJ, Talton J, Dabelea D, et al. Prevalence of diabetes in U.S. youth in 2009: the SEARCH for Diabetes in Youth Study. *Diabetes Care*. 2014;37(2):402–408.