Case Report

New-onset diabetes mellitus with COVID-19: Coincidence or cause

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A B S T R A C T

Diabetes mellitus (DM) was noted as the commonest comorbidity in the coronavirus disease 2019 (COVID-19) which contributed to worse prognosis in these patients. In some cases, we also noted new-onset DM detected during hospitalization for symptomatic COVID disease. We describe three such cases, where the patients presented with severe symptomatic hyperglycemia and ketoacidosis in two and hyperosmolality in one of them. Antibody to GAD-65 was negative and varying degrees of C-peptide secretion was noted after recovery in them. There was no clinical or biochemical evidence of exocrine pancreatic involvement noted during acute presentation or after the recovery. This interesting phenomenon of coexisting DM in symptomatic COVID-19 requires further studies to differentiate between coincidence or causation.

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Introduction

Coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, struck in the early months of 2020. In our tertiary care hospital, one of the largest COVID management centers in north India, we encountered diabetes mellitus (DM) as one of the commonest comorbidity and risk factor for adverse outcome in our patients.

In the background of the high genetic risk of type 2 DM in the population and the prevailing epidemic of the DM, which often gets unmasked during an infection like COVID-19, new onset of DM has also been increasingly noted. Often these patients present with severe symptomatic hyperglycemia with ketoacidosis or hyperosmolality as first presentation of DM.

We describe three patients with new-onset DM detected during hospitalization for symptomatic COVID disease. In all these three cases, the patients presented with severe symptomatic hyperglycemia and ketoacidosis in two and hyperosmolality in one of them.
Case report

Case 1

A 26-year-old female patient presented with low-grade fever, sore throat, and dry cough of 3 days’ duration. On screening, she was detected to have COVID-19 positive on reverse transcription polymerase chain reaction (RT-PCR) test. She was noted to have normal glucose levels (random plasma glucose 125 mg/dl). She was managed on standard lines for mild symptomatic COVID with Tab Paracetamol, Tab Vitamin C, and Zn supplementation over 1 week after which she recovered completely and was discharged. She remained asymptomatic for next 3 months, and then presented to hospital with significant weight loss (6 kg in 3 months), osmotic symptoms, and hyperglycemia (RBG 560 mg/dl, HbA1c 10.9%). Her pre-morbid BMI was 21.3 kg/m².

Ketoacidosis (urine ketones 3+, blood pH 7.1, HCO₃⁻ 10.1 mmol/l, potassium 4.8 mmol/l) was detected for which she was started on saline rehydration and insulin infusion to which she responded well. Screening test for COVID (RT-PCR) was negative. On recovery, she was started on premix insulin twice a day (total 36U per day) with good response. Over next 2 months, she had decreasing insulin requirement and presented with frequent hypoglycemic episodes, after which her insulin was discontinued and her blood glucose levels were monitored. Fasting blood glucose was 118 mg/dl and HbA1c 8.5%. She was advised diabetic diet and exercise, and initially started on Sitagliptin and Metformin which was discontinued due to symptoms of gastrointestinal intolerance. On review after 3 months of discontinuing insulin, she showed normal glucose tolerance (FBG 97 mg/dl, PPBG 141 mg/dl, HbA1c 6.8%).

Case 2

A 32-year-old male patient presented with complaints of weight loss, polyuria and increased thirst of 10 days, and low-grade fever of 2 days duration. There was no alteration in sensorium, breathing difficulty, or pain abdomen. There was no preceding history of pancreatic disease or steroid intake. On examination, his BMI was 20.4 kg/m², he had signs of dehydration, temp 100.2°F, pulse 96/min, regular, BP 130/70 mmHg and SPO₂ was 97% on room air. Chest was normal on examination. His random blood glucose at admission was 310 mg/dl and the HbA1c was 11.1%. Urine for ketones was mild positive and there was no metabolic acidosis on arterial blood gas (ABG) analysis. Chest radiograph was normal. Antibody to GAD-65 antibodies and plasma C-peptide levels are as mentioned in Table 1. Thyroid profile was normal. Urine protein and lipid profile was normal. Incidentally on USG abdomen, solitary right kidney was detected which showed compensatory hyperfunction on DTPA scan. All other hematological and biochemical parameters including liver functions, renal functions, and serum lipase and amylase were normal. He was detected to be positive for COVID-19 by RT-PCR. He was initially managed with hydration with normal saline and euglycemia was achieved on IV insulin infusion followed by subcutaneous basal-bolus insulin regimen. For mild symptoms of COVID (low-grade fever and sore throat), he received symptomatic therapy and remained afebrile after 3 days. He responded well to treatment and on follow-up after 6 weeks, he was asymptomatic and euglycemic on a total of 28 units of insulin in a basal-bolus regimen (FBG 108, PPBG 141 mg/dl, HbA1c 6.8%). Over next 4 weeks, he showed gradually decreasing insulin requirement and was started on metformin and vildagliptin along with 12U of basal insulin (Glargine).

Case 3

A 50-year-old male patient with no history of DM presented with unquantified weight loss, excessive thirst, and urination of one-week duration along with generalized weakness. There was no history of altered consciousness, breathing difficulty, pain abdomen, fever, cough, or sore throat. Screening before admission showed a random blood glucose of 580 mg/dl. At admission, he was lean (BMI 21 kg/m²), conscious, irritable, dehydrated, with low-grade fever 99.6°F, tachycardia 116/min, BP 110/60 mmHg, RR 18/min, SPO₂ 98% on room air, with a normal systemic examination. Rapid antigen test for COVID-19 was positive which was later confirmed on RT-PCR. Investigations revealed hyperglycemia, metabolic acidosis (pH 7.057, HCO₃⁻ 7.5 mmol/l) urine for ketones was strongly positive. HB was 10.8 g/dl, TLC 12000/ul, urea 80 mg/dl, creatinine 0.9 mg/dl, sodium 139 mmol/l, potassium 5.4 mmol/l. HbA1c was 9.8%. Radiograph of the chest was normal.

He was started on treatment on the lines of diabetic ketoacidosis. Over the next 48 hr, he was fully rehydrated and euglycemic. After recovery from COVID in the next 7 days, he was reviewed and found to have satisfactory glycemic control on a total of 54U of insulin.

Details of relevant investigations of these cases have been described in Table 1.

Discussion

Although mostly asymptomatic or mild disease, SARS-CoV-2 infection has the potential to develop into severe systemic inflammatory response syndrome, acute respiratory distress syndrome, multiorgan involvement, and shock. Co-existing DM puts the patients at higher risk for severe disease and mortality due to COVID-19.1

New-onset diabetes and severe metabolic complications of preexisting diabetes, including diabetic ketoacidosis and hyperosmolarity have been observed in patients with COVID-19.3

While a direct inflammatory damage to the β cells due to the virus leading to decreased insulin secretion is one of the likely mechanisms, stress-induced hyperglycemia and transient resistance to insulin action due to cytokines released as part of the inflammatory response are other mechanisms implicated in the pathogenesis of hyperglycemia in this setting.

The angiotensin-converting enzyme 2 receptor, a binding site for the SARS-CoV-2, is expressed in the pancreas (β cells). This viral binding to β cells could lead to initiation of
inflammatory cell damage and impaired insulin secretion. It is also postulated that there is a likelihood of SARS-CoV-2 exposure induced type 1 diabetes onset due to triggering of the autoimmune response.4

An increase in the number of new type 1 diabetes cases in children compared with a typical year, has been noted in the UK. An international group of diabetes experts announced the launch of CoviDIAB, a global registry of COVID-19-related diabetes which aims to unravel these potential mechanisms in the new onset diabetes and metabolic dysfunction in pre-existing patients with diabetes.5

All three of our patients presented with acute onset of severe hyperglycemia with ketoacidosis, suggesting severe insulin deficiency (Table 1). All of them were negative for GAD-65 antibodies, and did not demonstrate any other evidence of autoimmunity. None of them received glucocorticoids in any form as part of their therapy. Resolution of hyperglycemia in the first patient may be due to a transient pancreatic dysfunction having completely recovered. It could be due to stress-induced hyperglycemia, although the severity of hyperglycemia and presence of ketoacidosis was not commensurate with severity of symptoms of COVID disease in her. Other possible explanations for the remission could be a honeymoon phase of type 1 diabetes or a transient beta cell dysfunction due to viral infection—induced beta cell inflammation. She will need to be followed up closely for reappearance of hyperglycemia.

In the second patient, demonstration of adequate C-peptide secretion and gradual reduction of insulin requirement and response to oral antidiabetic drugs suggests significant residual beta-cell function, although in absence of family history of type 2 DM and features of insulin resistance, a close follow-up for insulin requirement and glycemic control is necessary to know the nature of DM in this patient.

In the third patient, more severe features of insulin deficiency and persistent insulin requirement in higher dosage with low C-peptide levels indicate greater degree of beta-cell damage. This could be explained by beta cell destruction by inflammation unmasking DM in this patient.

These three patients depict varying degree of beta-cell dysfunction in response to a documented mild COVID-19 disease. While the exact pathogenesis of diabetes in this disease is still not known, it will be interesting to understand the various mechanisms of causation as they might throw light on new molecular mechanistic pathways thus unraveling potential therapeutic targets.

Disclosure of competing interest
The authors have none to declare.

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