

A Report of Three Cases of Acute Hyperglycemic Crises in Asymptomatic COVID-19 Infection

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Abstract

Introduction: Recently emerging data suggests a direct correlation detected between elevated glucose levels and coronavirus infection. The parallel occurrence of these two disease entities calls for further probe in order to define investigation protocols and management strategy. **Cases:** In this review we report three coronavirus patients who presented with new onset diabetes and ketoacidosis. The reports and biochemical markers of these patients were recorded and evaluated. **Results:** Two of the three patients were newly diagnosed both for SARS-COV-2 and diabetes mellitus. The third patient was a known case of diabetes mellitus and had presented with diabetes ketoacidosis. All these patients responded well to the treatment and were discharged in a stable condition. **Conclusion:** These cases suggest a strong interplay between glucose metabolism and coronavirus infection. A thorough understanding of this mechanism is crucial in the management of such patients especially those with asymptomatic coronavirus infection.

Keywords: Ketoacidosis; Coronavirus; Hyperglycemia

Introduction

Diabetes has emerged as a major contributing factor in the pandemic of COVID-19. Given the insidious nature of this metabolic disorder, it may lead to certain fatal complications like diabetic ketoacidosis if not managed efficiently. The fatality of these complications is even more in a COVID-19 patient.

A considerable number of COVID-19 patients have been found to have diabetes mellitus as a co-morbidity. ^[1] Diabetes mellitus has a multifaceted link with COVID-19. On one hand, it predisposes an individual to coronavirus infection and on the other, it increases the mortality and morbidity ratio in a COVID-19 positive patient. ^[2]

Also, there have been instances where acute hyperglycemia has been reported in newly diagnosed COVID-19 patients. The aim of this article is to explore the correlation between diabetes mellitus and COVID-19 and suggest a pathophysiological mechanism with reference to three clinical cases with simultaneous occurrence of diabetes mellitus and COVID-19.

Subjects and Methods

Patient 1

An 18 year old obese male presented with fatigue and polyuria for fifteen days. He had a strong family history of diabetes, with both his parents, elder brother, and paternal grandparents diagnosed with type 2 diabetes mellitus.

Clinical findings: The patient also had markers of insulin resistance in the form of acanthosis nigricans and abdominal obesity with Waist Hip Ratio (WHR) of 1.0 and Body Mass Index (BMI) of 26.2 kg/m². Screening for SARS-COV-2 RT PCR returned positive.

Diagnostic assessment: His Glucose Tolerance Test (GTT)

showed severe hyperglycemia and serum ketones were normal. C peptide and fasting insulin levels were also assessed. The details are mentioned in Table 1.

Therapeutic intervention: He was managed as a newly diagnosed case of type 2 diabetes mellitus, with asymptomatic COVID-19. He was treated with split mixed insulin injection in addition to hydration and supportive care. He did not receive any specific treatment for COVID. His blood sugars improved and the patient did not develop any pulmonary symptoms at any time.

Patient 2

A 30 years old previously healthy male presented with a one week history of polyuria, polydipsia, and weight loss of 4 kg-5 kg. He was afebrile with the absence of any pulmonary symptoms.

Clinical findings: He had tachycardia with a heart rate of 110 per min, tachypnoea (RR 28/min) with Kussmaul's breathing, and an oxygen saturation of 98%. His blood pressure and body mass index were 130/80 mmHg and 22.6 kg/m² respectively.

Diagnostic assessment: His GTT showed severe hyperglycemia. Urinalysis showed large amounts of sugar and ketones. Serum β hydroxybutyrate levels were elevated at 37.17 mg/dl. The Arterial Blood Gas (ABG) report showed severe metabolic acidosis with a wide anion gap. RT PCR for COVID-19 was positive.

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Therapeutic intervention: He was treated with oxygen, IV normal saline infusion, insulin infusion with continuous glucose monitoring, and electrolyte replacement. He made a satisfactory recovery and was discharged with a subcutaneous insulin regimen.

Patient 3

A 65-year-old male, presented with extreme exhaustion and polyuria of about 10 days duration. He was a known case of type 2 diabetes mellitus, on treatment for more than 6 months.

Diagnostic assessment: His fasting blood sugar was 326mg% and post prandial blood sugar was 481mg%. Urine acetone was strongly positive. ABG showed metabolic acidosis. RT PCR for COVID was positive.

Therapeutic intervention: He was managed with Intra Venous (IV) fluids and insulin infusion. He showed symptomatic improvement and was discharged in a stable condition.

Results and Discussion

It is well established that diabetes worsens the prognosis for a COVID-19 patient. [3] However, asymptomatic novel coronavirus patients presenting new onset diabetes has opened up a new gambit to research for the medical fraternity. [4,5]

In this case report, three patients had presented with the primary symptoms indicating diabetes mellitus with a parallel asymptomatic coronavirus infection. There was an acute surge in the glycemic index in all the three patients, of which one was a known case of diabetes while the other two had experienced the symptoms for the first time. The metabolic profile of two

out of the three patients also showed evidence of Diabetic Ketoacidosis (DKA). The chest X rays of all these patients were normal besides showing no pulmonary symptoms whatsoever. These three patients responded well to the prevalent triad treatment protocol consisting of administration of IV fluids, insulin infusion and electrolyte replacement.

Several mechanisms have been proposed to correlate the simultaneous occurrence of diabetes and COVID-19. The interference of coronavirus with the Renin Angiotensin Aldosterone System (RAAS) is one of the suggestive mechanisms. The conversion of angiotensin II to angiotensin I occurs with the help of Angiotensin Converting Enzyme 2 (ACE2) which is highly expressed in the lungs, pancreas, and intestines. These organs may serve as an entry point for the virus complex to enter the body that may hamper the normal functioning of beta cells of the pancreas, thereby leading to depletion of the insulin levels. [5] The decreased insulin levels promote the utilization of the free fatty acids that further results in the formation of ketone bodies. These ketone bodies being acidic in nature lead to ketoacidosis [Figure1].

In a recent study, majority of patients (62%) with COVID-19 have diabetes mellitus and 23.9% were pre diabetics with increased fasting blood glucose levels. [3,6] The SARS-Cov-2 infection was associated with new onset diabetes and diabetic ketoacidosis in those with diabetics. The details of various other published reports regarding the association of COVID-19 and DKA or DM have been summarized in Table 2.

These three cases have also shown that a COVID-19 patient can also present with acute hyperglycemia, besides presenting with

Table 1: Laboratory results for patient 1,2,3.

Parameter	Patient 1	Patient 2	Patient 3	Reference range
Glucose tolerance test (mg/dl)				
Fasting	470	339	326	60-100
1/2 hr	556	398		
1 Hour	682	489		<200
1 1/2 hours	607	535		
2 hours	549	541	481	<140
Insulin (mU/L)	7.58			8-Mar
Serum hydroxybutyrate	-	37.17		0.2-2.81
HbA1c (%)	15.7	12.4	9.8	<6
C Peptide (ng/ml)	1.85	0.03	1.5	0.5-2.0
Urine analysis	Ketones +	Ketones ++, Sugar +	Acetones +	
Body mass index (kg/m ²)	26.2	22.6	21.4	18.5-24.9

Table 2: The summary of previously published cases of DKA in COVID-19 patients.

Case Report	Age	New onset diabetes/known case of diabetes	Presenting features	Co-morbidities	DKA
Palermo et al. (2020)	2 patients 1st: 53 years 2nd: 45 years	1st: known case of diabetes 2nd: new onset diabetes	1st: dyspnea, fever, anorexia 2nd: fatigue, polyuria, polydipsia	1st: hypertension, hyperlipidemia 2nd: None	1st: Yes 2nd: No
Chee et al. (2020)	37 years	new onset diabetes	fever, vomiting, polydipsia and polyuria	None	Yes
Li et al. (2020)	3 patients, age 26-54	known case of diabetes	General weakness, fever, dyspnoea, polyuria, polydipsia	None	Yes
Current study	3 patients, age 18-65	2 patients-new onset diabetes 1-known case of diabetes	fatigue, polyuria, polydipsia	None	Yes: 2 cases No: 1 case

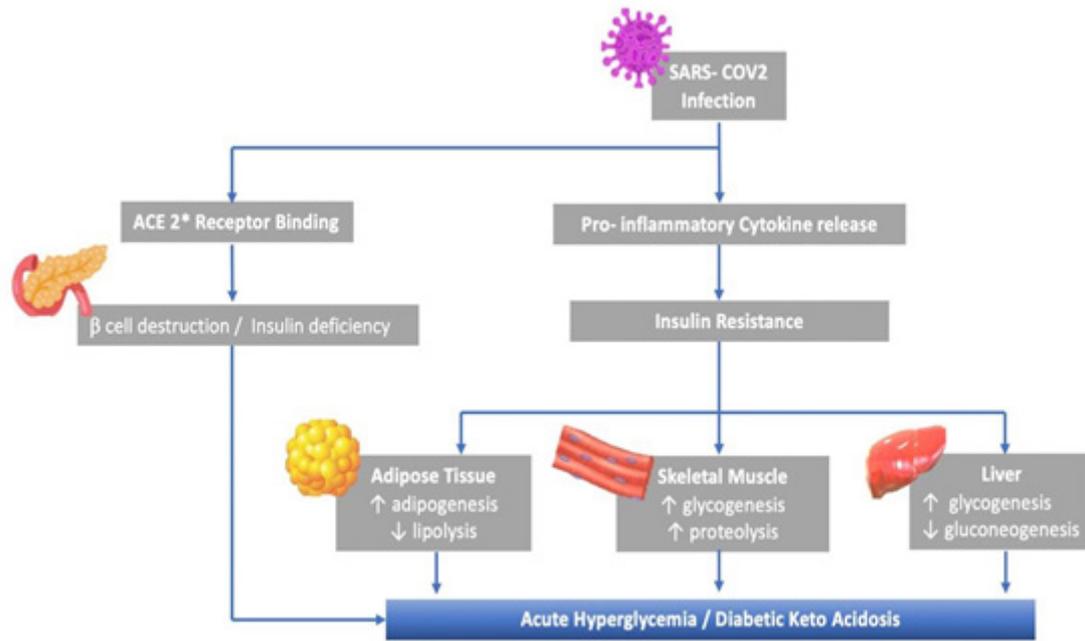


Figure 1: Illustration of the proposed mechanism of hyperglycemia in response to SARS-COV2 infection.

flu like or pulmonary symptoms or being entirely asymptomatic. This review article aims to create awareness among physicians across the globe that treat various types of patients with DM and DKA. Screening a patient with acute hyperglycemia for COVID-19 is uncommon, however with emerging evidence seems to be the need of the hour. COVID-19 seems to have tilted the balance in diabetes management.

Conclusion

A strong connection of acute hyperglycemia as a risk factor as well as its co-occurrence with COVID-19 has been demonstrated in the three patients. The asymptomatic nature of coronavirus infection with acute hyperglycemia or ketoacidosis may pose a major health risk that needs to be explored further so that a management protocol can be defined. We recommend a more vigilant screening of all the patients with clinical presentation of diabetic ketoacidosis or acute hyperglycemia for COVID-19 in addition to other parameters.

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