

Covid-19 induced severe hyperglycemia in previously non-diabetic patients

Awe OO.

Department of Surgery, Irrua Specialist Teaching Hospital, Irrua Edo State, Nigeria
Department of Surgery, Faculty of Clinical Sciences, College of Medicine, Ambrose Alli University, Ekpoma Edo State, Nigeria

Abstract

Severe acute respiratory syndrome causing coronavirus 2(SARS COV2) first discovered at the Wuhan, China in the last quarter of 2019, also called COVID-19 (Coronavirus disease 2019). It was a novel infection causing mainly severe respiratory disease. It has been implicated to lead to organ(s) failure which include lungs, liver, kidney and adrenals. This may be due to direct viral infection of the organs leading to inflammation or an autoimmune response to the viral proteins produced and binding to specific receptors on these organs. In a few cases, there have been reports of recent onset diabetes in patients who were previously non-diabetic. I present a health worker who presented with severe hyperglycemia 4 days after he was diagnosed of mild form of COVID-19 during the second wave (last quarter of 2021) of the pandemics in Nigeria. He was not a known diabetic.

Keywords: Severe hyperglycemia, new-onset diabetes, COVID-19 induced, non-diabetic

Introduction

A COVID-19 pandemic was a novel infection from the new type of coronavirus resulting in severe acute respiratory syndrome that rapidly progressed to multiple organ failure especially in the elderly and those with systemic co-morbidities. There were so many asymptomatic carriers which made the control of the spread of the disease and contact tracing very difficult. Most symptomatic patients usually present with respiratory symptoms and low or high-grade fever. There are patients who presented with generalized body weakness, malaise, loss of appetite and severe headache like malaria fever until the polymerase chain reaction test revealed coronavirus. Many patients have presented with cardiopulmonary failure, liver failure and adrenal failure as complications of the COVID-19. Few cases of new-onset diabetes mellitus presenting severe hyperglycemia or diabetic ketoacidosis (DKA) have been reported in the literature. There are several hypotheses in trying to explain the pathogenesis of diabetes.

Cases

A 48-year-old male health worker presented to the emergency room (ER) of the Irrua Specialist Teaching Hospital, Irrua Edo State, Nigeria with a week history of high grade, intermittent fever associated with chills and rigor, headache, loss of appetite and generalized body weakness transiently relieved with the use of Paracetamol (PCM). There was no diarrhea, vomiting or nausea. There was neither cough, difficulty with breathing nor hemoptysis. There was no dysuria, hematuria, loin pain. There were no bleeding dyscrasias.

At the onset of the illness, the patient had blood tested for malaria parasite, Lassa fever antigen and antibody, and COVID-19. The COVID 19 infection was confirmed positive and was commenced immediately on COVID 19 medications i.e. hydroxyl-chloroquine, zinc sulphate and vitamin C tablets.

Three (3) days after the onset of the illness, he noticed a progressive worsening of the generalized body weakness with associated polyuria and polydipsia but no polyphagia. He was not a known diabetic but has a positive history in a first-degree relation (his late father). There was no history of recurrent upper respiratory tract

Corresponding author Dr. Awe O.O
Department of Surgery, Irrua Specialist Teaching Hospital,
Irrua Edo State, Nigeria
Email:olasupoawe06@yahoo.com
Phone Number: +2348033924824

infection, urinary tract infection, blurring of vision, poor wound healing, intermittent claudication or foot ulcer. He is married in a monogamous setting with 3 children. His wife is a chartered accountant working with the hospital.

At presentation, he is a middle-aged man, calm, not in any obvious distress, not pale, anicteric, a-cyanosed but dehydrated. He has no pedal edema. His vital signs were pulse rate of 88 beats per minute, respiratory rate of 20 cycles per minutes, and blood pressure of 120/75mmHg. The chest was clinically clear, and the abdomen was essentially normal. The admitting random blood sugar (RBS) was un-recordable with strip-glucometer.

A diagnosis of hyperglycemic emergency 2° COVID 19 was made. He was immediately admitted and commenced on intravenous fluid resuscitation. He had 10 IU of soluble insulin intramuscularly and another 10 IU intravenously stat dose then was placed on 8 IU hourly until the RBG was \leq 250mg/dl.

After 8 hours, the RBG was 211mg/dl and pre-meal 8 IU soluble insulin was commenced. However, over the next 24 hours, the RBG was fluctuating 211mg/dl and 320mg/dl. So, the soluble insulin was increased to 10 IU pre-meal.

2 days after admission, the RBG was still 267mg/dl (pre-meal) and 294mg/dl (2HPP), so the insulin was increased to 16 IU pre-meal with subcutaneous (SC) Glargine 14iu at 7 pm. Results of electrolytes, and urea was as follows:

HCO₃⁻ 27mmol/L,
K⁺ 5.0mmol/L,
Na⁺ 137mmol/L,
Cl⁻ 96mmol/L,
Urea 44mg/dl.
HbA1C 11.2%

On the third day on admission, his FBG was 282mg/dl and the RBG was 302mg/dl. SC Novomix 18 IU pre-meal was prescribed with SC Glargine 14 IU at 7 pm. He was then discharged home to have thrice daily monitoring of the glucose level.

Two weeks after discharge, he was in the clinic with FBG 104mg/dl and 2HPP of 178mg/dl. The SC Novomix 18 IU with breakfast and dinner was

maintained, while SC Glargine was increased to 26 IU at 7pm.

Six weeks after discharge, the FBG was 94mg/dl, HbA1C was 8%. The SC Novomix was reduced to 8 IU pre-breakfast and pre-dinner. The SC Glargine was withheld.

Six months after discharge, FBG range from 75 – 128mg/dl within the period and the repeat HbA1C has reduced to 5.4%. SC Novomix was discontinued and then was replaced with metformin SR (slow releasing) tablets 500mg twice daily.

12 months after discharge, the FBG ranges between 75 – 115mg/dl with HbA1C of 4%. The metformin tablets were reduced to 250mg twice daily

18 months after discharge, the FBG ranges between 68 – 95mg/dl. The metformin tablet was discontinued.

24 months after the discharge, the FBG between 65 – 98mg/dl. He was discharged from the clinic.

Discussion

A COVID-19 pandemic has been a catastrophic disease worldwide with significant health, economic, social and political consequences. The disease mainly starts with mild respiratory symptoms that may progressively worsen to a respiratory failure. It has been found out that presentation and progression of the disease is worse with comorbidities like diabetes mellitus, hypertension and obesity¹. There have been other associated organs failure that noticed including liver, kidney, heart, adrenals and pancreas.

There is a novel presentation that called COVID-19 induced diabetes or new-onset diabetes following COVID-19. This entity is said to be a different entity from the patients who have underlying diabetes before the COVID -19 infections. It has been found that the morbidity and the mortality is higher in these patients and therefore possibly has a different pathology².

There are different postulations trying to explain the basis for the new-onset diabetes

1. COVID-19 patients with new-onset diabetes in the absence of autoantibodies present with high

incidence of diabetic ketoacidosis which is suggestive of acute viral induced pancreatic damage. These patients also showed remarkably poorer glycaemic control and increased interleukin-6 levels. There has been increased incidence in new-onset T1DM and T2DM with the onset of COVID-19 pandemics³. Omotosho et al reported the case of 45yr-old female who developed latent auto-immune diabetes of adulthood (LADA) on background of COVID infection⁴.

- The pathogenesis of the COVID-19 induced DM in acute-onset DM is not well understood but angiotensin converting enzyme (ACE) 2 has been identified as functional receptor for severe acute respiratory syndrome coronavirus. ACE2 receptors are present on many organs and tissues including pancreatic β cells and lead to acute damage of the β cells of the pancreas leading to insulin deficiency and subsequent DKA and hyperosmolar hyperglycemic state (HHS). Down-regulation of the ACE2 receptors after binding with SARS coronavirus causes elevation in angiotensin 2 level resulting in vasoconstriction and reduced blood flow to the islet cells accompanied by delayed insulin release¹⁻³.

The case presentation was of a young adult with a normal BMI, who was presenting with acute-onset diabetes. Similar case reports have been presented with acute-onset DM in lean COVID-19 patients with normal HbA1C results presenting with signs of insulin resistance (Ghesh et al⁸ and Chee et al⁹). 37-year-old COVID-19 positive male who presented with DKA had BMI of 22.6kg/m² and evidence of insulin resistance and 41-year-old non-obese man also respectively.

Our index case, the hyperglycemia gradually resolved with soluble insulin and then oral hypoglycemic agent. He was eventually weaned off medication with subsequent normal fasting and 2-hour post-prandial (2HPP) blood sugar after about 18 months following diagnosis. This may indicate pancreatic β cell recovery, which has been mentioned in some literature. Gupta et al followed up 19 patients of new-onset diabetes following COVID-19 and found about 79% were able to discontinue completely insulin and oral hypoglycemic

drugs after 6 months suggesting β cells recovery and regeneration. Kuchay et al also found that the need for insulin in these patients decrease significantly 4-6 weeks after discharge¹⁰⁻¹².

Conclusion

Acute-onset diabetes induced by COVID-19 is an established entity which must be considered a possibility in any COVID-19 patient presenting with symptoms whether mild or in severe form. This is very important because of the rapid progression to severe hyperglycemia or diabetic ketoacidosis.

References

- Dominguez-Rojas JA, Severe diabetic ketoacidosis precipitated by COVID-19
- Alsadham I, Albuhrashid S, Alhamed M, Alajmi S, Alshehri S, Alfadhli A, Ekhzaimy M. Diabetic Ketoacidosis precipitated by COVID -19 Infection: Case Series. *Current Therapeutic Research*; vol 93 2020, 102609
- Joshi SC, Pazzilli P. COVID-19 induced diabetes: A novel presentation. *Diabetic Research & Clinical Practice* vol 191, Sept 2022, 110034. Doi.org/10.1016/j.diabetes.2022.110034
- Omotosho YB, Ying GW, Stellar M, Mallari AJP. COVID-19 induced diabetic Ketoacidosis in an adult with latent Autoimmune Diabetes. *Cureus*: 13 (1)2021 p.e12690.
- Heaney AI, Griffin GD, Simmon EL. Newly diagnosed diabetes and Diabetic Ketoacidosis precipitated by COVID-19 infection. *Am J Emerg Med*; 38(11): 2020 pg 2491
- Lance A, Rodriguez C, Diamantina C, Fitas AL. COVID-19 in two children with new-onset diabetes: Case Reports: *BMJ Case Report*; 15(1):2022.
- Motarrea KR, Abbas KS, AbdelQuadri YH, Monib FA. New-onset diabetes mellitus in a COVID-19 patient: a case report. *Metabolism*, 128 (2022) article 155105.
- Ghesh A, Misra A. Marked hyperglycemia and Ketosis in a non-obese patient with a new-onset diabetes and very mild COVID-19 symptoms: case report. *Diabetes Metab. Syndr.* 15(1): 2021; 213-214
- Chee YJ, Ng SJH, Yeoh E. Diabetic Ketoacidosis precipitated by COVID-19 in a patient with newly diagnosed diabetes mellitus. *Diabetes Res Clin. Pract.* 164(2020) p. 108166.
- Gupta RD, Atri A, Mondel S, Bhattacharjee A, Garaj R, Haerak AK. Characterizing progressive β cell recovery after new-onset Diabetic Ketoacidosis in COVID-19 provoked ketosis prone diabetes: A prospective study from Eastern India. *J Diabetes Complications*: 36(2); 2022
- Kuchay MS, Reddy PK, Gagneja S, Matthew A, Mishra SK, Short-term follow-up of patients with acute onset diabetes and Diabetic Ketoacidosis during episodes of COVID-19 Diabetic Metabolic Syndrome: *Clin Res Rev* 14(6)2020; 2039-2041.
- Anca PS, Ioana-Christina B. (CAPISCO) New-onset Diabetes Mellitus in COVID-19: A scoping Review: *Diabetic Therapy* 15(1): 2024 p 33-60.