

COVID-19 and Newly Diagnosed Diabetes: A Report of Two Cases from Mthatha, South Africa

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ABSTRACT There are increasing reports of diabetes mellitus diagnosed during coronavirus disease-2019 (COVID-19) pandemic. Indeed, the relationship between diabetes and COVID-19 is bi-directional. COVID-19 worsens hyperglycaemia in persons already known with diabetes with often marked requirements of insulin to achieve euglycaemia. Diabetes is also associated with adverse outcomes following COVID-19 illness. COVID-19 is associated with new-onset hyperglycaemia and diabetes by mechanisms which include the stress of severe acute disease, use of steroids and cytopathic effect of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) on pancreatic beta cells. The proposed mechanism of SARS-CoV-2 infection of pancreatic beta cells is by binding to the angiotensin converting enzyme-2 receptors which are expressed on pancreatic beta cells. We report an adolescent girl and middle-aged woman with clinical and laboratory profiles consistent with Type 2 diabetes.

Keywords: Coronavirus disease-2019; SARS-CoV-2; diabetes; Mthatha; South Africa

A bi-directional relationship between coronavirus disease-2019 (COVID-19) and diabetes has been observed.^{1,2} COVID-19 causes deterioration of blood sugar in persons with diabetes and often with markedly increased requirements for insulin to achieve euglycaemia in those with severe disease.³ Furthermore, diabetes mellitus has been shown to be a marker of increased mortality in COVID-19.⁴ In one study, the mortality was higher with COVID-19 in patients with new-onset diabetes when compared with those who are known with diabetes.⁵

There are increasing reports of new-onset diabetes in patients with COVID-19 illness.⁶⁻⁹ The type of diabetes may be ascertained by clinical features (family history of diabetes, obesity, presence of acanthosis nigricans) and laboratory parameters (markers of islet cell immunity and islet beta cell reserve). While some reports showed negative islet-associated antibodies in their patients, the other reports did not indicate patients' islet antibody status.⁶⁻⁹ Nei-

ther of these studies reported any measure of beta cell reserve.⁶⁻⁹

We hereby report two patients (an adolescent and middle aged) with diabetes diagnosed during COVID-19 illness with negative islet antibodies and preserved beta cell function.

CASE REPORTS

CASE 1

A 14-year-old female was diagnosed with diabetes when she was admitted in June 2020 with diabetic ketoacidosis (DKA) and COVID-19. She was discharged on subcutaneous (SC) basal and bolus insulin; 20 units of insulin glargine at bedtime and 20 units of insulin aspart before meals with a presumed diagnosis of Type 1 diabetes.

At a clinic consultation in August 2020, she weighed 123 kg with a height of 162 cm and body

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mass index (BMI) of 46.6 kg/m². She had acanthosis nigricans in her neck. Because of family history of diabetes, the morbid obesity and acanthosis nigricans, the diagnosis of Type 2 diabetes was entertained. Three-times daily doses of insulin aspart was discontinued and insulin glargine was reduced to 10 units daily. Oral metformin at the dose of 850 mg twice daily was commenced and she was advised on lifestyle modification with a referral to a dietician. Results of laboratory tests done in August 2020 were consistent with Type 2 diabetes with a negative serum anti-GAD antibody <5 IU/mL, anti-IA2 antibody (Normal <10 IU/mL). Serum C-peptide level was 886 pmol/L (260-1720). Glycosylated haemoglobin (HbA1c) was 10.2% (88 mmol/mol). Results of liver, renal and thyroid functions were normal.

CASE 2

A 52-year-old female with diabetes detected in July 2020 after a 3-day history of generalised fatigability, polyuria, and polydipsia. This was preceded by a sore throat and dry cough. She was, however, not breathless. She has a background history of hypertension treated with indapamide, 2.5 mg daily. She also has a positive family history of diabetes. COVID-19 test results came back positive with an elevated serum C-reactive protein (CRP) of 24 mg/L (0-7.4). Results of renal, liver, and thyroid functions were normal. She was managed as an outpatient with SC insulin aspart/insulin aspart protamine at 25 units and 15 units before breakfast and supper, respectively. She also received 7 days oral course of doxycycline 100 mg twice daily, Zinc 20 mg daily, vitamin C 1,000 mg daily, and a single dose of vitamin D₃ 50,000 IU.

She was seen again in September 2020 for review and optimization of her glycaemic control. She weighed 90.1 kg with a height of 150 cm and BMI of 40 kg/m². Random blood glucose was 29.7 mmol/L with no ketonuria and negative serum beta-hydroxybutyrate. The doses of Novomix 30 were escalated to 30 units twice daily and metformin 1 gm twice daily was added. Laboratory test results were consistent with Type 2 diabetes with serum Anti-GAD <5 IU/mL (normal <10 IU/mL), and serum C-peptide of

729 pmol/L (260-1720). HbA1c was 12.3% (111 mmol/mol).

DISCUSSION

We have reported two patients who are newly diagnosed with diabetes in the course of COVID-19 infection. The first case was initially wrongly labelled as Type 1 diabetes probably because of her young age and presentation with ketoacidosis. Her morbidly obese status, acanthosis nigricans, preserved beta cell function based on normal C-peptide levels and negative antibodies (anti-GAD and anti-IA) ruled out the possibility of Type 1 diabetes. Age below 30 years, presentation with DKA at diagnosis of diabetes and absence of islet auto-immune antibodies argues against a diagnosis of Latent Autoimmune Diabetes of Adults in our 14-year-old patient. The second case fits the typical age and anthropometric profiles of Type 2 diabetes which was further confirmed by preserved C-peptide levels and absent auto-immune antibodies. Although subacute thyroiditis has been reported in COVID-19 illness and may present with a sore throat, our patients' thyroid function tests were normal. The raised CRP is likely related to immune mediated inflammatory response to severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection.

It is possible that these patients had asymptomatic undiagnosed Type 2 diabetes that became unmasked following the COVID-19 illness. We do not have the HbA1c levels at initial diagnosis of diabetes as a normal HbA1c level then will argue for a new rather than pre-existing diabetes. To the extent that not all patients with COVID-19 become diabetic will suggest that those who manifest diabetes are either predisposed to it or already have pre-existing glucose intolerance which is worsened by COVID-19.

The suggested mechanism of new-onset diabetes with COVID-19 illness is direct cytopathic effect of SARS-CoV-2 by attaching to the angiotensin converting enzyme-2 receptor which is abundantly expressed on beta cells.^{10,11}

A phenotype resembling antibody-negative Type 1 diabetes (Type 1B) with low C-peptide levels would be expected with direct cytopathic effect

of the virus on beta cells as is reported with other viral infections.¹² This is, however, not the case in both patients.

We have reported two cases of newly diagnosed diabetes mellitus (DM) with clinical and laboratory profiles in keeping with Type 2 diabetes associated with COVID-19 disease. While DM particularly with poor glycaemic control is associated with adverse COVID-19 outcomes, COVID-19 may trigger a new diagnosis of diabetes by mechanisms that are still incompletely elucidated.

Informed Consent

Consent was obtained from both patients to publish this report without revealing any information that may identify them.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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