Newer onset of diabetes mellitus and thyroid dysfunction in COVID-19: Study from rural India

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ABSTRACT

Background: Cytokine and bardykine storm plays important role in then pathogenesis of COVID-19 diseses, as result there are raised inflammatory markers and blood sugar. Patients and Method: Patient with RTPCR positive with signs and symptoms of COVID-19 were investigated for fasting and postprandial blood sugar and glycated hemoglobin percentage, inflammatory markers TSH and Covid antibodies. Result: All the 17 cases detected newly onset of diabetes with normal HBA1c and raised thyroid stimulating hormones in five cases. Significant raised levels of inflammatory markers and D-diamer. All cases showed bilateral pneumonias in the lungs. Conclusion: Newer onset of diabetes mellitus due to COVID-19 disease should be mangled with insulin therapy.

Keywords: ACE receptors, beta cells of pancreas, COVID-19, diabetes mellitus

Introduction

In COVID-19, diabetes mellitus (DM) is a two-edged sword; already existing DM patients are more prone to being infected with SARS-CoV-2 virus, resulting in severe acute respiratory syndrome. A non-diabetic person if suffered from severe COVID-19 will manifest with hyperglycaemias and their subsequent complications. SARS-CoV-2 virus has great affinity for angiotensin-converting enzyme 2 (ACE-2) receptors. ACE-2 receptors are present in beta cells of pancreas and follicular cells of thyroid gland. Inhibition and dysfunctions of ACE-2 receptors over the insulin secretion of beta cells of pancreas and inhibition of thyroid secretion by blocking the follicular cells of thyroid gland by SARS-CoV-2 virus result in hyperglycaemia and rise in thyroid-stimulating hormone (TSH). In the present study, we found that 17 patients who suffered from COVID-19, with raised inflammatory markers, had significant hyperglycaemia with normal HbA1c, confirming the newer onset of diabetes mellitus.

Patients

Seventeen (M8) patients of the age group 32–73 (mean 45.23) suffered from fever, dry non-productive cough, transient loose motion, body ache, breathlessness and oxygen saturation <90% at ambient air with bilateral patchy pneumonic shadows in both lungs seen in high-resolution chest tomography (HRCT) scan and raised inflammatory biomarkers [Table 1]. All the patients were detected positive for reverse transcriptase polymerase chain reaction (RT-PCR) SARS-CoV-2 RNA virus. None of them had diabetes or a family history of diabetes mellitus (DM) and hypothyroidism. These 17 cases were investigated for DM. Their fasting blood sugar was 120–198 (mean 150.52) (normal <110) Mg/dl, postprandial was 167–320 (mean 207.23) (normal <140) mg/dl, and glycosylated haemoglobin (HbA1c) was 5.25–6.6 (mean 5.96) (normal <6.4). Five female patients’ thyroid-stimulating hormone was 9.4, 6.02, 8.5, 6.65 and 8.9 uTU ml (normal <4), suggestive of subclinical hypothyroidism [Table 1].
All 17 patients recovered with short acting insulin, favipiravir, aspirin, doxycycline, low molecular weight heparin, metformin, statin, ivermectin, vitamin D, C and zinc and nasal oxygen. All the 17 cases totally recovered from COVID-19, except hyperglycaemia for which they were advised to use oral hypoglycaemic agents. For the last 3.5 months, we have been following these cases in the outpatient department. All of them had raised immunoglobulin against SARS-CoV-2 virus [Table 1].

**Discussion**

Diabetes mellitus is a two-edged sword; already existing DM is more prone to severe acute respiratory syndrome due to coronavirus (SARS-CoV-2) infection [Figure 1]. Newer onset of DM with persistent hyperglycaemias occurred due to SARS-CoV-2 virus infection.[6] SARS-CoV-2 viruses get attached to the angiotensin-converting enzyme 2 (ACE-2) receptors.

Figure 1: HRCT of patient no. 4 [see Table 1]—a 54-year-old female who developed newer diabetes soon after the COVID-19 symptoms

![HRCT scan](image)

High-concentration ACE-2 receptors are located in insulin-secreting beta cells of pancreas, fatty tissue, small intestine, nasal mucosa, stomach, colon, skin, lymph anodes, thymus, bone marrow, spleen, liver, kidney and brain.[8] Recently, it has been reported that the mRNA encoding for ACE-2 receptor is expressed in thyroid follicular cells.[9] SARS-CoV-2 virus may be responsible for pleiotropic alternation of carbohydrate metabolism, responsible for susceptible and severity of SARS-CoV-2 viral infection in an already existing diabetic victim. In a non-diabetic patient, newer onset of hyperglycaemia occurred due to infection by SARS-CoV-2 virus [Table 1]. During infection with SARS-CoV-2 virus, the persistent newer hyperglycaemia results in severe clinical manifestations with poor outcomes. Hypertension, diabetes, obesity, sedentary life, old people and immuno-suppression such as HIV, and cancer cases are more susceptible to SARS-CoV-2 virus infection with poor outcomes.[6] In the present study, the fasting and postprandial blood sugar significantly raised with normal HbA1c value, confirming the newer onset of diabetes mellitus. Further, it is confirmed that SARS-CoV-2 virus is responsible for newer onset of diabetes and its persistence with the presence of SARS-CoV-2 antibody explored the possibility of immune damage of beta cells of pancreas. GAD-65 antibody detection facilities are not available in this part of India.

Thyroid follicular cells are rich in ACE-2 receptors; the possibility of SARS-CoV-2 virus could also infect the thyroid cells. It is observed that different virus-like particles are seen in the follicular epithelium of patients with sub-acute thyroiditis.[5] Moreover, thyroid gland is anatomically continuous with upper respiratory tract, a major entrance of SARS-CoV-2 virus.[8] It is important to note that ACE-2 receptors coexist with type II serine protease trans-membranes (TAMPRSS2) and thyroid tissues exhibit a high expression of the TAMPRSS2 mRNA.[7] Autopsies of fatal cases of SARS-CoV-2 have confirmed the primary injury of thyroid cells with apoptosis of follicular cells.[7]

| No/name | Age/sex | Blood sugar mg/dl | HBA1c | TSH U/l | HRCT mg/dl | CRP n-0-6 mg/dl | Ferritin <500/ng/ml | D-Diamer u/ml | Covrd IGG |
|---------|---------|--------------------|-------|---------|-------------|-----------------|-------------------|-----------------|----------|
| 1 AHA   | 67/m    | 141.4              | 173.7 | 6.2     | -           | 25%             | 56.3              | ND              | 287.82   | 674      |
| 2 IK    | 44/m    | 198                | 220   | 5.8     | -           | 50%             | 66.2              | 983.21          | 1198.23  | 1899     |
| 3 PPJ   | 52/f    | 168                | 192   | 5.7     | 9.4         | 50%             | 89.2              | 389.57          | 203      | 1503     |
| 4 RJK   | 54/f    | 153                | 266.27| 6.2     | -           | 75%             | 77                | 753.18          | 1732     | 1644     |
| 5 SSP   | 57/f    | 121                | 168.7 | 6       | 6.02        | 50%             | 137.8             | 1200            | 66.34    | 474      |
| 6 mYT   | 43/f    | 120.2              | 187.2 | 6       | 50%         | 80               | 465.65            | 334             | 383      | 393      |
| 7 MDS   | 55/f    | 161.7              | 252.4 | 7       | -           | 25%             | 29.5              | 500.38          | 2353.11  | 1478     |
| 8 ASS   | 46/m    | 112.2              | 159.4 | 5.7     | 50%         | 142.9            | 1150.4            | 1154.32         | 2749     | 2749     |
| 9 BPA   | 47/m    | 123                | 186.7 | 6.6     | -           | 25%             | 89                | 214.63          | 942      | 524      |
| 10 ASA  | 73/m    | 137                | 206.9 | 5.5     | 50%         | 43               | 257               | 893             | 2732     | 2732     |
| 11 AAN  | 36/f    | 134.9              | 167.7 | 6.2     | 8.5         | 50%             | 68.23             | 1250.8          | 1007.4   | 1325     |
| 12 CSS  | 32/m    | 168.2              | 184.8 | 5.8     | 25%         | 39.1             | 150.58            | 362.13          | 3723     | 3723     |
| 13 MMK  | 53/m    | 180                | 320   | 5.7     | -           | 50%             | 57.5              | 118.23          | 2997.8   | 1676     |
| 14 PAG  | 43/f    | 148                | 192   | 5.2     | 6.65        | 25%             | 58.4              | 128.3           | 430.96   | 1443     |
| 15 SSS  | 42/f    | 154.1              | 167.3 | 5.5     | -           | 25%             | 4.2               | 38.2            | 321      | 723      |
| 16 khs  | 34/f    | 168.4              | 230   | 6.1     | 8.9         | 50%             | 53.6              | 823.98          | 1870.9   | 2367     |
| 17 PHK  | 48/m    | 169.8              | 248   | 6.2     | -           | 50%             | 42.9              | 1021.8          | 2143.4   | 1857     |

HBA1c —glycosalated haemoglobin; TSH —Thyroid stimulating hormone; HRCT —High resolution chest scan; CRP —C-reactive protein; IGG —immunoglobulin
In a short history of human infection with SARS-CoV-2 virus, and understanding of how COVID-related diabetes and hypothyroidism develop, the natural history of these two endocrinological diseases and their appropriate management will be helpful. Thus, the ACE-2 receptor plays an important role in the pathogenesis of endocrine disorders.[7] ACE-2 receptor agonists will be a universal antidote for the management of endocrine disorders. Irrespective of the vaccination, these COVID-19 cases need a long-term follow-up.[8]

**Authors’ contributions**

HSB examined the cases and collected the data. PHB investigated the cases for laboratory and HRCT scans. Both authors followed the cases. HSB wrote the draft, and PHB searched the references. Final draft is written by both and approved.

H.S. Bawaskar is the guarantor of this work and as such had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Conflicts of interest**

There are no conflicts of interest.

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