



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Newly diagnosed diabetes in patients with mild to moderate COVID-19

Thirunavukkarasu Sathish ^{a,*}, Mary Chandrika Anton ^b^a Population Health Research Institute (PHRI), McMaster University, Hamilton, ON L8L 2X2, Canada^b Department of Biochemistry, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India

ARTICLE INFO

Article history:

Received 20 January 2021

Received in revised form

22 February 2021

Accepted 25 February 2021

Keywords:

COVID-19

Newly diagnosed diabetes

New-onset diabetes

Diabetes

Hyperglycemia

ABSTRACT

Background and aims: We aimed to study newly diagnosed diabetes in patients with mild to moderate COVID-19.**Methods:** This was a retrospective cohort study of COVID-19 patients who were admitted to a tertiary care hospital in India from May to October 2020.**Results:** Of 102 patients, 21 (20.6%) had newly diagnosed diabetes on admission. Of which, four (19.0%) had marked hyperglycemia with no ketosis or ketoacidosis.**Conclusion:** In this study of patients with mild to moderate COVID-19, newly diagnosed diabetes and marked hyperglycemia in those with newly diagnosed diabetes were common.

© 2021 Diabetes India. Published by Elsevier Ltd. All rights reserved.

Funding

None.

1. Introduction

Coronavirus disease 2019 (COVID-19) infection in people with pre-existing diabetes can worsen glycemia, cause acute metabolic complications such as ketosis and ketoacidosis, and lead to worse outcomes [1,2]. Intriguingly, emerging evidence shows that newly diagnosed diabetes is frequently observed in COVID-19 patients and is a risk factor for poor prognosis, particularly in those with severe to critical COVID-19 [3–5]. However, there is a dearth of evidence regarding newly diagnosed diabetes in patients with mild to moderate COVID-19 who constitute about 80% of COVID-19 infections [6]. We aimed to study the proportion of newly diagnosed diabetes in COVID-19 patients with mild to moderate illness. We also aimed to examine the glycemic characteristics and clinical outcomes of patients with newly diagnosed diabetes.

2. Methods

2.1. Study design and participants

This was a retrospective cohort study of 102 patients who were admitted with mild to moderate COVID-19 to the designated wards at a tertiary care hospital in Chennai, India. These patients were hospitalized between May and October 2020. COVID-19 was diagnosed based on a positive reverse transcription polymerase chain reaction (RT-PCR) test.

2.2. Data collection

Patients' data on demographics, clinical signs and symptoms, laboratory investigations, treatment measures, and clinical outcomes were retrieved from the case report forms. Blood samples were taken within 24 h of admission and before the administration of steroids. Plasma glucose and HbA1c were measured using standard assays and protocols [7].

2.3. Definitions

Newly diagnosed diabetes was defined as fasting plasma glucose ≥ 126 mg/dl or 2-hr post prandial blood glucose ≥ 200 mg/dl or

* Corresponding author.

E-mail address: speaktosat@gmail.com (T. Sathish).

Table 1
Studies on newly diagnosed diabetes with marked hyperglycemia in patients with mild to moderate COVID-19.

Study and country	Study design	Age (years)	Sex	FPG (mg/dl)	PPBG (mg/dl)	RBG (mg/dl)	HbA1c (%)	Acute metabolic complications
Current study, India	Retrospective cohort	57	Male	–	–	148	6.8	None
		66	Male	–	–	170	7.6	None
		39	Male	–	–	185	6.6	None
		65	Male	–	–	321	8.2	None
Gosh et al. [12], India	Case report	41	Male	246	505	–	14.9	Ketosis
Chee et al. [13], Singapore	Case report	37	Male	–	–	715	14.2	Ketoacidosis
Heaney et al. [14], USA	Case report	54	Male	–	–	463	–	Ketoacidosis
Alsadhan et al. [15], Saudi Arabia	Case series	47	Male	–	–	432	15.1	Ketoacidosis
Kuchay et al. [16], India	Case series	60	Male	–	–	582	12.6	Ketoacidosis
		34	Male	–	–	940	12.0	Ketoacidosis
Suwanwongse et al. [17], USA	Case series	51	Male	–	–	795	12.4	Ketoacidosis
		64	Female	–	–	353	–	Ketosis

FPG, fasting plasma glucose; PPBG, post prandial blood glucose; RBG, random blood glucose. **Note:** Blood glucose was measured before the initiation of steroid therapy.

HbA1c \geq 6.5% in those without a prior history of diabetes [7]. Marked hyperglycemia was defined as random blood glucose (RBG) $>$ 140 mg/dl [7].

3. Results

Of 102 patients, 21 (20.6%) had newly diagnosed diabetes on admission. Among these 21 patients, the HbA1c of 19 (90.4%) was \geq 6.5% (range: 6.5%–8.5%), while the remaining two did not have an HbA1c value. The mean age of those with newly diagnosed diabetes was 50.2 (SD: 13.1) years, and the majority (76.2%) were male. The most common symptoms of these patients were fever, cough, and myalgia or fatigue. SpO₂ was more than 90% at all times during hospitalization.

Of 21 patients with newly diagnosed diabetes, 4 (19.1%) had marked hyperglycemia with RBG values ranging from 148 to 321 mg/dl (Table 1). All these four patients were tested negative for urinary ketones. None of them showed signs and symptoms of ketoacidosis during hospitalization, and all were discharged alive. Patients were treated with dexamethasone, low molecular weight heparin, and non-invasive supplemental oxygen. No anti-virals, oral anti-hyperglycemic medications, or insulin therapy were given. At the time of discharge, patients were given lifestyle change advice and were asked to follow-up with their routine healthcare providers for a repeat blood glucose test and further management.

4. Discussion

In this study of 102 mild to moderate cases of COVID-19, 20.6% were newly diagnosed with diabetes on admission. Nearly all of those with newly diagnosed diabetes had an HbA1c value of \geq 6.5%. This suggests that they likely had previously undiagnosed diabetes. About 19.1% of those with newly diagnosed diabetes had presented with marked hyperglycemia with no acute metabolic complications.

Studies have reported a widely varying proportion of newly diagnosed diabetes (from 0.6% to 46.2%) in COVID-19 patients, the majority of whom had severe or critical illness [5]. COVID-19 infection in people with diabetes (including newly diagnosed diabetes) can cause marked hyperglycemia through several complex but inter-related factors. These include, but are not limited to, the inflammatory response triggered by the virus and subsequent release of counterregulatory hormones, activation of the renin-angiotensinogen system, and destruction of pancreatic β cells by the virus itself or by the cytokines triggered by the virus [8,9].

In the literature, there are a few case reports and case series of marked hyperglycemia in patients with mild to moderate COVID-19 who were newly diagnosed with diabetes (Table 1). The RBG values

of these cases ranged between 353 and 940 mg/dl, which were much higher than those of our patients with newly diagnosed diabetes. Further, they had developed ketosis or ketoacidosis, whereas none of our patients had any of these complications. Of note, the HbA1c of these cases was very high (12.0%–15.1%). This indicates that they had poor glycemic control before admission and their underlying chronic inflammatory state was severe, such that even a mild COVID-19 infection was enough to precipitate acute metabolic complications.

Studies have shown that newly diagnosed diabetes is a risk factor for poor prognosis in COVID-19 patients, mainly in those with severe to critical illness [4,10]. However, none of our patients with newly diagnosed diabetes progressed to severe illness or died, probably because of the mild infection. Nevertheless, COVID-19 patients with newly diagnosed diabetes, particularly those with marked hyperglycemia, should be followed-up for the emergence of full-blown diabetes and other cardiometabolic disorders [5,11].

In conclusion, in this study of patients with mild to moderate COVID-19, newly diagnosed diabetes and marked hyperglycemia in those with newly diagnosed diabetes were common.

Ethics approval

The study was approved by the ethics committee of Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India. The requirement for written informed consent from the patients was waived by the ethics committee, given the retrospective nature of the study.

Declaration of competing interest

Nothing to declare.

Acknowledgment

We thank the nurses who retrieved patients' data from the case report forms.

References

- [1] Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: prevalence, pathophysiology, prognosis and practical considerations. *Diabetes Metab Syndr* 2020;14:303–10.
- [2] Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, Del Prato S. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. *Lancet Diabetes Endocrinol* 2020;8:782–92.
- [3] Sathish T, Cao Y. Is newly diagnosed diabetes as frequent as preexisting diabetes in COVID-19 patients? *Diabetes Metab Syndr* 2020;15:147–8.
- [4] Sathish T, Cao Y, Kapoor N. Newly diagnosed diabetes in COVID-19 patients. *Prim Care Diabetes* 2021;15:194.
- [5] Sathish T, Kapoor N, Cao Y, Tapp RJ, Zimmet P. Proportion of newly diagnosed

- diabetes in COVID-19 patients: a systematic review and meta-analysis. *Diabetes Obes Metab* 2021;23:870–4.
- [6] Centres for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19). Atlanta, USA: Centres for Disease Control and Prevention.
- [7] American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2020. *Diabetes Care* 2020;43:S14–s31.
- [8] Sathish T, Tapp RJ, Cooper ME, Zimmet P. Potential metabolic and inflammatory pathways between COVID-19 and new-onset diabetes. *Diabetes Metab* 2020. <https://doi.org/10.1016/j.diabet.2020.10.002>.
- [9] Ghosh A, Anjana RM, Shanthi Rani CS, Jeba Rani S, Gupta R, Jha A, et al. Glycemic parameters in patients with new-onset diabetes during COVID-19 pandemic are more severe than in patients with new-onset diabetes before the pandemic: NOD COVID India Study. *Diabetes Metab Syndr* 2020;15: 215–20.
- [10] Sathish T, de Mello GT, Cao Y. Is newly diagnosed diabetes a stronger risk factor than pre-existing diabetes for COVID-19 severity? *J Diabetes* 2021;13: 177–8.
- [11] Sathish T, Cao Y. What is the role of admission HbA1c in managing COVID-19 patients? *J Diabetes* 2021;13:273–5.
- [12] Ghosh A, Misra A. Marked hyperglycemia and ketosis in a non-obese patient with new onset diabetes and very mild COVID-19 symptoms: a case report. *Diabetes Metab Syndr* 2020;15:213–4.
- [13] Chee YJ, Ng SJH, Yeoh E. Diabetic ketoacidosis precipitated by Covid-19 in a patient with newly diagnosed diabetes mellitus. *Diabetes Res Clin Pract* 2020;164:108166.
- [14] Heaney AI, Griffin GD, Simon EL. Newly diagnosed diabetes and diabetic ketoacidosis precipitated by COVID-19 infection. *Am J Emerg Med* 2020;38: e3–4. 2491.
- [15] Alsadhan I, Alruwashid S, Alhamad M, Alajmi S, Alshehri S, Alfadhli E, et al. Diabetic ketoacidosis precipitated by Coronavirus disease 2019 infection: case series. *Curr Ther Res Clin Exp* 2020;93:100609.
- [16] Kuchay MS, Reddy PK, Gagneja S, Mathew A, Mishra SK. Short term follow-up of patients presenting with acute onset diabetes and diabetic ketoacidosis during an episode of COVID-19. *Diabetes Metab Syndr* 2020;14:2039–41.
- [17] Suwanwongse K, Shabarek N. Newly diagnosed diabetes mellitus, DKA, and COVID-19: causality or coincidence? A report of three cases. *J Med Virol* 2021;93:1150–3.