

Newly diagnosed diabetes in patients with COVID- 19: In a tertiary care center in central India

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Abstract

Background: Diabetes mellitus (DM) is associated with adverse clinical outcomes and high mortality in patients with corona virus disease 2019 (COVID-19). The relationship between diabetes and COVID-19 is known to be bidirectional.

Aim: To analyze the rate of new-onset diabetes in COVID-19 patients and assess the clinical outcomes of new-onset diabetes and hyperglycemia among COVID-19 patients

Methods: This cross sectional study has enrolled those individuals admitted with COVID-19 and has newly diagnosed diabetes mellitus. (DM; based on laboratory diagnoses).

Results: Analysis showed that 13.7% (84/610) of COVID-19 patients had newly diagnosed DM. Majority of the newly diagnosed diabetic patient was male (58.3%), most of them (33.3%) were 51-60 year age group. Higher incidence of DM was reported in urban population (54.8%). The significant risk factors of diabetes were found family history of diabetes, (53.6%) and obesity (72.6%). Hypertension was the most common (61.7%) comorbidity associated with the DM.

Conclusions: Diabetes diagnosed at COVID-19 presentation is associated with lower glucose but higher inflammatory markers and ICU admission, suggesting stress hyperglycemia as a major physiologic mechanism.

Keywords: COVID-19, newly diagnosed diabetes, incidence, hyperglycemia

Introduction

Diabetes is a common chronic metabolic disease, and one of the major causes of morbidity and mortality, which leads to huge health and financial burden worldwide. Patients with diabetes have an increased risk of severe complications, including severe acute respiratory syndrome (SARS) and multi-organ failure ^[1].

The human pancreas is a target of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). Following SARS-CoV-2 infections, reduced numbers of insulin secretory granules in

beta cells and impaired glucose-stimulated insulin secretion have been observed [2]. SARS-CoV-2 may damage beta cells by triggering proinflammatory cytokines leading to chronic low-grade inflammation in adipose tissue play an important role in the pathogenesis of insulin resistance and type 2 diabetes [3].

Many reports suggest that newly diagnosed diabetes mellitus (NDDM), or hyperglycemia without known prior diagnosis of diabetes mellitus (DM) is common at the time of admission for COVID-19, as well as in the months following COVID-19 [4-7]. 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 [8-9].

Aims and Objectives

Aim of the study to evaluate proportion of newly diagnosed diabetes in COVID-19 patients. We also aimed to examine the glycemic characteristics and clinical outcomes of patients with newly diagnosed diabetes.

Methods

This cross-sectional observational study was conducted in the department of medicine in a tertiary care hospital in central India. Patients those attended medicine OPD or admitted in wards/ICU with COVID-19 were enrolled in our study. COVID-19 was diagnosed based on a positive reverse transcription polymerase chain reaction (RT-PCR) test. A diagnosis of COVID-19 illness was based on a positive SARS-CoV-2 laboratory result under World Health Organization (WHO) interim guidance [10].

Inclusion criteria: Age > 18 years old, confirmed cases of COVID-19, and newly diagnosed cases of DM

Exclusion criteria

Age <18 years old, pregnancy, unconfirmed cases of COVID-19, and previously diagnosed cases of DM

All patients underwent thorough clinical and laboratory assessment and chest computerized tomography (CT). Biochemical blood tests included FPG, HbA1c; C-reactive protein (CRP), serum total bilirubin, albumin, Transaminases (ALT, AST), LDH, creatinine, and urea nitrogen was measured.

According to the American Diabetes Association, newly diagnosed DM was defined as either new-onset DM (no preceding history of DM with fasting plasma glucose [FPG] >126 mg/dL or random blood glucose [RBG] >200 mg/dL and HbA1c > 6.5%) [11].

Statistical analysis

Data was entered into Microsoft Excel and analyzed using SPSS software version 20. Pearson's Chi Square test was applied. P value < 0.05 was considered significant.

Results

A total of 610 diagnosed cases COVID-19 was enrolled in current study, out of them 84 (13.7%) was newly diagnosed as type 2 diabetes mellitus [figure: 1]

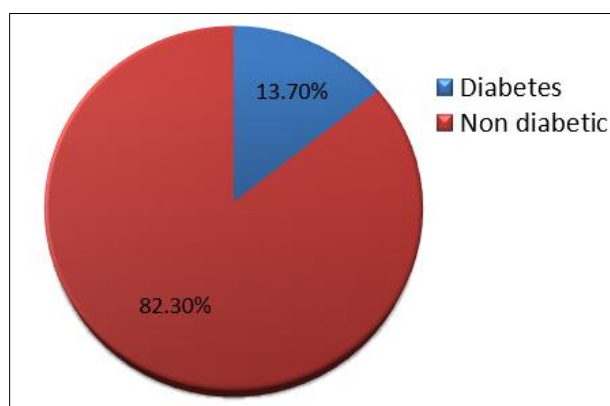


Fig 1: Incidence on newly diagnosed diabetes mellitus in COVID 19

Incidence of newly onset diabetes mellitus in COVID- 19 patients was higher (58.3%) in male participant as compared to female. Mainly (33.3%) seen in the age group between 51-60 years, followed by (28.6%) among 41-50 years of age. Majority of the diabetic patients (54.8%) residing at urban areas. Most of them (53.6%) were associated with the family history of diabetes mellitus. Incidence of diabetes was higher among the subjects with obesity (72.6%),

Table 1: Baseline characteristics of newly diagnosed diabetes cases

Baseline characteristics	Number (N=84)	Percentage	
Age (in years)	19-30	7	8.3%
	31-40	13	15.5%
	41-50	24	28.6%
	51-60	28	33.3%
	>60 years	12	14.3%
Gender	Male	49	58.3%
	Female	35	41.7%
Place of residence	Urban	46	54.8%
	Rural	38	45.2%
Family history of diabetes	Absent	39	46.4%
	Present	45	53.6%
Obesity	Obese	61	72.6%
	Non-obese	23	27.4%

Chronic diseases associated with the newly onset diabetes mellitus were hypertension (63.1%), coronary artery diseases (50%) and chronic pulmonary disease (42.9%). Details shown in table:2

Table 2: History of chronic diseases present in the DM patients

Chronic disease	Number	Percentage
Diabetes	0	0%
Hypertension	53	63.1%
Coronary heart disease	42	50%
Stroke	24	28.6%
Chronic pulmonary disease	36	42.9%
Chronic liver disease	20	23.8%
Chronic kidney disease	14	16.7%
Peripheral vascular disease	29	34.5%

Discussion

This study found an increased incidence of type 2 diabetes in individuals with Covid-19 after recovery.

Incidence of newly onset type 2 diabetes mellitus in COVID 19 patients was found 13.7%, our finding was similar with the many other studies likes: Rathmann *et al* [12], S.J. Cromer *et al.*, [13] reported incidence of newly diagnosed DM was 15%, and 13% respectively, in contrast to that Li H *et al.*, [14] and Sathish T *et al.*, [15] reported quite higher incidence of diabetes in their study.

Incidence on newly diagnosed DM was higher in males (58.3%) than males in our study, similar result was shown by Zhou *et al.*, [16], Smith *et al.*, [17] and Fadini *et al.*, [18] reported male predominance in their study, whereas Qeadan *et al.*, [19] reported female predominance in their study.

Present study found most of the newly diagnosed diabetic participant were 51-60 years age group, concordance to the Suwanwongse *et al.*, [20]. Kuchay *et al.*, [21] and Heaney *et al.*, [22] In the present study, the newly diagnosed diabetic patients had significantly obese and positive family history of diabetes, this was in agreement with Farag, A.A *et al.*, [23] and Khunti K *et al.*, [24].

Significant association of newly diagnosed diabetes mellitus with the other chronic diseases like: hypertension (61.7%), coronary artery disease (50%) and chronic pulmonary disease was found in 42.9% cases, accordance with the Zheng J *et al.*, [25] and Shrestha DB *et al.*, [26]

The reason of newly diagnosed diabetes in COVID-19 patients could be due to the stress response associated with severe illness or treatment with Glucocorticoids, the diabetogenic effect of COVID-19 should also be considered.

Conclusion

The incidence of newly diagnosed diabetes mellitus in COVID-19 patients was 13.7%, The newly diagnosed diabetes may confer a greater risk for poor prognosis of COVID-19 than no diabetes or pre-existing diabetes. Therefore, COVID-19 patients with newly diagnosed diabetes should be managed early and appropriately and closely monitored for the emergence of full-blown diabetes and other cardio metabolic disorders.

Conflict of interest: None

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References

1. Pearson-Stuttard, J.; Blundell, S.; Harris, T.; Cook, D.G.; Critchley, J. Diabetes and infection: Assessing the association with glycaemic control in population-based studies. *Lancet Diabetes Endocrinol.* 2016, 4, 148–158. [Cross Ref].
2. Muller JA, Grob R, Conzelmann C *et al* (2021) SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas. *Nat Metab* 3(2):149–165. <https://doi.org/10.1038/s42255-021-00347-1>.
3. Sathish T, Tapp RJ, Cooper ME, Zimmet P (2021) Potential metabolic and inflammatory pathways between COVID-19 and new onset diabetes. *Diabetes Metab* 47(2):101204. <https://doi.org/10.1016/j.diabet.2020.10.002>.
4. Vargas-Vazquez A, Bello-Chavolla OY, Ortiz-Brizuela E, *et al.* Impact of undiagnosed type 2 diabetes and pre-diabetes on severity and mortality for SARS-CoV-2 infection. *BMJ Open Diabetes Res Care.* 2021; 9. <https://doi.org/10.1136/bmjdr-2020-002026>.
5. Yuan S, Li H, Chen C, Wang F, Wang DW. Association of glycosylated haemoglobin HbA1c levels with outcome in patients with COVID-19: a retrospective study. *J Cell Mol Med.* 2021; 25:3484–3497. <https://doi.org/10.1111/jcmm.16431>.

6. Mamtani M, Athavale AM, Abraham M. Association of hyperglycemia with hospital mortality in nondiabetic COVID-19 patients: a cohort study. *Diabetes Metab.* 2021; 101254. <https://doi.org/10.1016/j.diabet.2021.101254>. Published online March 26.
7. Ayoubkhani D, Khunti K, Nafilyan V, *et al.* Post-COVID syndrome in individuals admitted to hospital with COVID-19: retrospective cohort study. *BMJ.* 2021; 372, n693. <https://doi.org/10.1136/bmj.n693>.
8. Sathish T, Cao Y. Is newly diagnosed diabetes as frequent as preexisting diabetes in COVID-19 patients? *Diabetes Metab Syndr* 2020; 15:147e8.
9. 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; 23:870e4.
10. World Health Organization. Clinical management of severe acute respiratory infection when novel corona virus (2019-nCoV) infection is suspected: interim guidance. 2020. <https://apps.who.int/iris/handle/10665/330893>. Accessed January 28, 2020.
11. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of medical Care in diabetes-2020. *Diabetes Care* 2020, 43 (Suppl. 1), S14–S31.
12. Wolfgang Rathmann & Oliver Kuss & Karel Kostev, Incidence of newly diagnosed diabetes after Covid-19, *Diabetologia* (2022) 65:949–954, <https://doi.org/10.1007/s00125-022-05670-0>.
13. Sara J. Cromer a,b,*, Caitlin Colling a,b, Daria Schatoff a,b, Michael Leary c, Maria I. Stamou a,b, Daryl J. Selen a,b, Melissa S. Putman a,b,d, Deborah J. Wexler, Newly diagnosed diabetes vs. pre-existing diabetes upon admission for COVID-19: Associated factors, short-term outcomes, and long-term glycemic phenotypes, *Journal of Diabetes and Its Complications* 36 (2022) 108145
14. Li H, Tian S, Chen T, *et al.* Newly diagnosed diabetes is associated with a higher risk of mortality than known diabetes in hospitalized patients with COVID-19. *Diabetes Obes Metab.* 2020; 22:1897–1906. <https://doi.org/10.1111/dom.14099>.
15. 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; 23:870–874. <https://doi.org/10.1111/dom.14269>.
16. Zhou W, Ye S, Wang W, Li S, Hu Q. Clinical features of COVID-19 patients with diabetes and secondary hyperglycemia. *J Diabetes Res.* 2020; 2020:1-9.
17. Smith SM, Boppana A, Traupman JA, *et al.* Impaired glucose metabolism in patients with diabetes, prediabetes, and obesity is associated with severe COVID-19. *J Med Virol.* 2020. <https://doi.org/10.1002/jmv.26227>.
18. Fadini GP, Morieri ML, Boscari F, *et al.* Newly-diagnosed diabetes and admission hyperglycemia predict COVID-19 severity by aggravating respiratory deterioration. *Diabetes Res Clin Pract.* 2020; 168:108374.
19. Qeadan F, Tingey B, Egbert J, Pezzolesi MG, Burge MR, Peterson KA, *et al.* (2022) The associations between COVID-19 diagnosis, type 1 diabetes, and the risk of diabetic ketoacidosis: A nationwide cohort from the US using the Cerner Real-World Data. *PLoS ONE* 17(4): e0266809.
20. Suwanwongse K, Shabarek N. Newly diagnosed diabetes mellitus, DKA, and COVID-19: causality or coincidence? A report of three cases. *J Med Virol* 2021; 93:1150e3.
21. 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; 14:2039e41.
22. Heaney AI, Griffin GD, Simon EL. Newly diagnosed diabetes and diabetic ketoacidosis precipitated by COVID-19 infection. *Am J Emerg Med* 2020; 38: e3e4. 2491.
23. Farag, A.A.; Hassanin, H.M.; Soliman, H.H.; Sallam, A.; Sediq, A.M.; Abd elbaser, E.S.; Elbanna, K. Newly Diagnosed Diabetes in Patients with COVID-19: Different Types and Short-Term Outcomes. *Trop. Med. Infect. Dis.* 2021, 6, 142. <https://doi.org/10.3390/tropicalmed6030142>.
24. Kamlesh Khunti,¹ Stefano Del Prato,² Chantal Mathieu,³ Steven E. Kahn,⁴ Robert A.

- Gabbay,5,6 and John B. Buse7, COVID-19, Hyperglycemia, and New-Onset Diabetes, *Diabetes Care* 2021;44:2645–2655 | <https://doi.org/10.2337/dc21-1318>.
25. Li H, Tian S, Chen T, *et al.* Newly diagnosed diabetes is associated with a higher risk of mortality than known diabetes in hospitalized patients with COVID-19. *Diabetes Obes Metab.* 2020; 22:1897–1906.
 26. Shrestha DB, Budhathoki P, Raut S, Adhikari S, Ghimire P, Thapaliya S, Rabaan AA, Karki BJ. New-onset diabetes in COVID-19 and clinical outcomes: A systematic review and meta-analysis. *World J Virol* 2021; 10(5): 275-287.