

IMPACT OF COVID-19 PATIENTS WITH DIABETES MELLITUS AND ITS ASSOCIATION WITH CLINICAL OUTCOMES

Manoj Karki,¹ Shatdal Chaudhary,¹ Niraj Kumar Jaiswal,¹ Bidhata Rayamajhi,¹ Narayan Gautam,² Jharana Shrestha,² Mahmud Alam Khan,¹ Pradip Chettri³

ABSTRACT

INTRODUCTION

COVID-19 is a debilitating disorder affecting lungs with multiple organs. Diabetes mellitus is considered as a common co-morbidity whose impact has not been fully understood. There is a hypothesis that patients with diabetes are at increased risk of severe disease or death due to COVID-19. The main objective of the present study was to find the the association of COVID-19 diabetes mellitus (DM) and non-diabetes mellitus patients with the clinical outcomes.

MATERIAL AND METHODS

This cross-sectional study was conducted in hospitalized patients with COVID-19 at Universal College of Medical Sciences (UCMS), Bhairahawa. Total of 200 patients were enrolled in the study period from July 2021 to January 2022 whose clinical profile, socio-demographic and biochemical variables were assessed. The study variables taken were symptoms, random blood glucose (RBG), glycosylated hemoglobin (HbA1c) and their outcomes like High Dependency Unit/Intensive Care Unit (HDU/ICU) or COVID ward admission, hospital stay and mortality.

RESULTS

A total of 40% of the patients require HDU/ICU hospitalization with 20% requiring ventilator support. The findings revealed a strong link between diabetes mellitus and fatigue ($p=0.012$) as well as mortality ($p=0.032$). The difference in hospital stay between ventilator and non-ventilator groups was substantial ($p=0.001$). The hospital stay in the mortality group was significantly shorter ($p=0.026$). Likewise, RBG and HbA1c are higher than in the non-mortality group (189 vs 167; 5.7 vs 5.6 %).

CONCLUSION

Hypertension and diabetes are the most common morbidities associated with COVID-19 individuals. Diabetes mellitus was found to have a substantial link to fatigue, but there was no link between HbA1c and the length of hospital stay or the method of ventilation.

KEYWORDS

COVID-19, Clinical profile, Diabetes, Hospital stay, Mortality.

1. Department of Internal Medicine, Universal College of Medical Sciences, Bhairahawa, Nepal
2. Department of Biochemistry, Universal College of Medical Sciences, Bhairahawa, Nepal
3. Department of Community Medicine, Universal College of Medical Sciences, Bhairahawa, Nepal

<https://doi.org/10.3126/jucms.v10i02.51249>

For Correspondence

Dr. Manoj Karki
Department of Internal Medicine
Universal College of Medical Sciences,
Bhairahawa, Nepal
Email: manojkarki7777@gmail.com

INTRODUCTION

Since the start of the corona virus disease-2019 (COVID-19) in Wuhan, China, the disease has spread rapidly and affected more than 528 million cases.¹ Studies have shown that patients at high risk of severe COVID-19 infection or death have several characteristics including advanced age, male sex, and have underlying health conditions such as diabetes mellitus, obesity and cardiovascular disease.² Diabetes mellitus, particularly type 2 diabetes mellitus (T2DM), has been reported as the second most common comorbidity of COVID-19 after hypertension.³ Due to increasing prevalence of diabetes mellitus, it is considered a public health concern worldwide and involvement in the development of several diseases including stroke, kidney failure, and heart disease. As diabetes has been associated with poor prognosis of COVID-19, glycemic management for patients with diabetes and COVID-19 has gained much more attention.⁴⁻⁶ To accurately estimate the relationships of diabetes, obesity and hypertension with the risk of severe illnesses/conditions in patients with COVID-19, high-quality studies are needed. This study will be the first of its kind in the south western region of Nepal where COVID-19 patients with or without underlying co-morbidity like diabetes or hypertension who got admitted to UCMS-TH were studied regarding hospital stay and mortality. If these co-morbid conditions are handled timely, it can help us to prevent form the extra burden. The objective of this study was to explore whether glycemic control is a relevant prognostic factor for acute COVID-19 infection or not.

MATERIAL AND METHODS

A cross-sectional study was conducted in confirmed COVID-19 cases admitted to Universal College of Medical Sciences (UCMS) COVID-19 unit from July 2021 to January 2022 after receiving ethical clearance from the Institutional Review Committee at UCMS (IRC No:040/21).

This study included 200 COVID-19 patients with comorbid conditions like diabetes, high blood pressure and obesity. Convenience sampling was used, and a following formula was used to calculate sample size.

$P=0.355$ % (Situation Update #26 – Coronavirus Disease 2019 (COVID-19) WHO Country Office for Nepal= $355/100000$)³

$q=0.645$ (Non-occurrence, $1-p$)

$E=0.08$ (allowable margin of error, 8%)

$n = (1.96)^2 \times \frac{P \times Q}{E^2} = 3.84 \times \frac{0.355 \times 0.645}{0.08^2} = 138$ patients

Hence, the sample size of 200 was taken for the period of six months.

RESULTS

The figure 1 shows the age wise distribution of the study population. The median interquartile range (IQR) of the

patient's age was 48 (39-55.75) years with majorities in age group 41-50 years. The predominant gender in overall age group were 55% males.

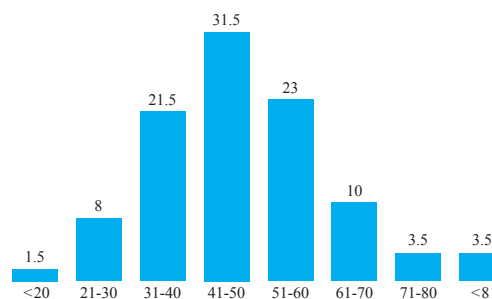


Figure 1. Frequency (%) of descriptive statistics of age wise distribution of study population

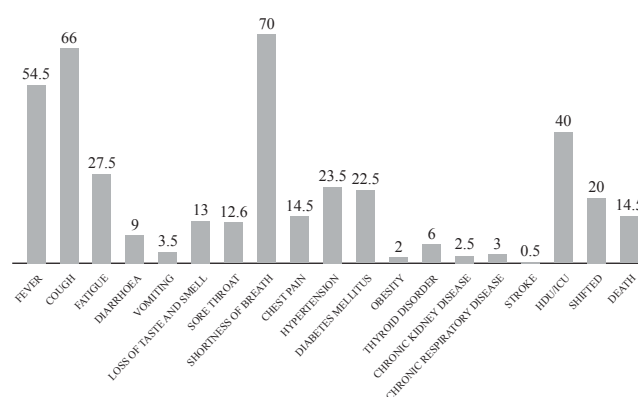


Figure 2. Frequency (%) of descriptive statistics of clinical and outcome variables

Figure 2 shows that shortness of breath (SOB), cough and fever were the predominant complaints. Hypertension and diabetes were the main chronic diseases. Among the total patients, 40% of them needed for HDU/ICU admission and around 20% needed ventilator support. The case fatality rate was 14.5%.

Table 1. Association between socio-demographic and clinical profile variables and diabetes mellitus

Variables	Diabetics (%)	Non-Diabetic (%)	P Value
Gender			
Male	19 (17.3)	91 (82.7)	0.061
Female	26 (28.9)	64 (71.1)	
Fatigue			
Yes	19 (34.50)	36 (65.5)	0.022
No	26 (17.9)	119 (82.1)	
Chest Pain			
Yes	3 (10.3)	26 (89.7)	0.066
No	42 (21.5)	129 (75.4)	
Chronic Kidney disease			
Yes	3 (60)	2 (40)	0.076
No	42 (21.5)	153 (78.5)	
Mortality			
Yes	11 (37.9)	18 (62.1)	0.032
No	34 (19.9)	137 (80.1)	

The result in table 1 shows a significant association between diabetes mellitus with fatigue ($p=0.012$) and mortality ($p=0.032$). The result shows that 34.5% diabetes mellitus

patients had complaint of fatigue whereas there was no significant association between diabetes mellitus and other variables like fever, cough, diarrhea, vomiting, loss of taste/smell, shortness of breath, hypertension, obesity, thyroid disorder, stroke, chronic respiratory diseases, HDU/ICU admission and ventilator support.

Table 2. Median and interquartile range (IQR) differences of parameters between diabetics and non-diabetics patients

Variables	Diabetics (n=45)	Non-Diabetics (n=155)	Total (n=200)	P Value
Age	49 (42.5-54)	47 (36-58)	48 (39-55.7)	0.719
SPO ₂	90 (87-93)	90 (88-92)	90 (87.25-92)	0.793
RBG	231 (189.5-289.5)	167 (134-189)	172 (145-198)	<0.001
HbA _{1c}	8 (7-9.3)	5.3 (5-5.7)	5.6 (5.02-6.40)	<0.001
Number of Hospital stay (Days)	8 (5-13.5)	7 (5-12)	8 (5-12)	0.867

The table 2 shows that the median hospital stay of patients with diabetics and non-diabetics were 8 (5-13.5) and 7 (5-12) days respectively. There was significant difference in median RBG and HbA_{1c} between diabetics and non-diabetic patients ($p < 0.001$).

Table 3. Median and interquartile range (IQR) of parameters between ventilator and non-ventilator

Variables	Age	SpO ₂	RBG	HbA _{1c}	Hospital stay
Ventilator	48.5 (40-52.15)	89 (87-91.7)	181 (146.25-227.5)	5.65 (5.12-6.1)	12.5 (7.16)
Non Ventilator	48 (38-56.75)	90 (88-92)	168.5 (141.25-197)	5.65 (4.90-6.65)	7 (4-11)
P value	0.819	0.440	0.133	0.88	0.001

The table 3 shows the average SpO₂ of ventilator group (89%) was less than non-ventilator group (90%) at the time of presentation. RBG was higher in ventilator group in comparison to non-ventilator group (181 vs 168.5) mg/dl. There was significant difference in hospital stay between ventilator groups than non-ventilator group ($p < 0.001$).

Table 4. Median and interquartile range (IQR) of parameters between ICU/HDU and ward patients

Variables	Age	SpO ₂	RBG	HbA _{1c}	Hospital stay
ICU/HDU	46.5 (35.25-55)	90 (87.25-91)	168.5 (145-195.25)	5.55 (5-6.4)	12 (6.25-17)
Ward	49 (39.25-56)	90 (87.25-92)	176 (145-198)	5.7 (5.2-6.37)	6.5 (4-9)
P value	0.335	0.152	0.001	0.521	0.510

The table 4 shows that the average RBG in ICU patient was less than the ward patients which is statistically significant ($p < 0.001$).

Table 5. Median and interquartile range (IQR) of parameters between mortality and non-mortality patients.

Variables	Age	SpO ₂	RBG	HbA _{1c}	Hospital stay
Mortality					
Yes	48 (41-54)	89 (87-91)	189 (150.5-224)	5.7 (5.2-7.15)	5 (3.5-9)
No	48 (36-56)	90 (88-92)	167 (145-197)	5.6 (5-6.1)	9 (5-13)
P value	0.864	0.132	0.169	0.187	0.026

The table 5 shows the average RBG, and HbA_{1c} in mortality group are more than in non-mortality group (189 vs 167, 5.7 vs 5.6%). Hospital stay in mortality case was less than in non-mortality case which is statistically significant ($p = 0.026$).

DISCUSSION

In our study, which included 200 hospitalized patients, 45 of them were diabetics. One hundred ten (55%) of the patients were male which was similar to the study done in Italy which shows male predominance in COVID-19 [six hundred thirty three (63.3%) males and three hundred sixty seven (36.7%) females].⁷ The median age of the patients was 47.66 ± 13.01 years and majorities were between age group 41-50 years which is not similar to another study where mean age at the time of hospital admission was $63.8 + 16.9$ years.⁷

Most common symptom which patients reported was shortness of breath (70%), followed by cough (66%) and fever (54.5%). A systematic review done by Viner et al showed similar result with fever and cough as most common symptoms.⁸ Symptoms like sore throat and anosmia were less common (12.6% and 13% respectively) in hospitalized patients at our center which is contradictory to a large study (REACT 1) done on one million people demonstrating loss or change of taste and smell as predominant symptoms.⁹ This discrepancy could be due to inclusion of asymptomatic cases in this study.

Previous observational and retrospective studies conducted near Wuhan area have reported that hypertension is the most common co-morbidity observed in patients affected by COVID-19, ranging from 15 to 30% which is same as our study where 23.5% were hypertensive.¹⁰ The prevalence of diabetes in our study was 22.5%, which is comparable to study done by Zhou Y et al in which the prevalence of diabetes in COVID-19 patients was 19%.¹¹ The overall prevalence of diabetes among COVID-19 patients was 5.3 to 20%.¹² The median (IQR) age of patients with diabetes in our study was 49 (42.5-54 years) and that of non-diabetic patients with COVID 19 infection was 47 (36-58 years). A systemic review done by Abate SM et al showed rate of ICU admission was 32% whereas in our study the ICU admission rate was 40% which is slightly higher.¹³ In one Chinese study, mechanical ventilation among patients admitted was 29.1% whereas in our study 20% of admitted patient required mechanical ventilation.¹⁴

Mortality among diabetic patients with COVID 19 was 24.4% compared to mortality among non-diabetic patients which was only 11.61% which is similar to study by

Alguwaihes et al in Saudi Arabia (20.5% vs 12.3%).¹⁵ The median (IQR) RBG among patients with mortality was 189 (150.5-224) compared to 167 (145-197) among survivors. Study done by Permana H et al, however, showed contrast in RBG among survivors and non-survivors {112 (97-129) vs 144 (105-213)}.¹⁶ The same study showed significant rate of mortality among patients with RBG >140 which was comparable with our study.¹⁶

Study by Ye Liu et al showed increased mortality in patients with HbA1c >5.7%. Additionally, patients having HbA1c >7% had mortality up to 28.1% and having HbA1c <5.5 had mortality only 2.3%.¹⁷ However, in our study average HbA1c in mortality group was 5.7% than non-mortality group 5.6 %.

CONCLUSION

The prevalent morbidity linked with COVID 19 patients is a high prevalence of hypertension and diabetes. Therefore, intensive monitoring should be considered. Shortness of breath, cough and fever were the predominant symptoms. There was significant association between diabetes mellitus with fatigue. Similarly, there was significant mean difference in RBG and HbA1C between diabetics and non-diabetics patients. On the other hand, there is no significant association of HbA1c with number of hospital stay and mode of ventilation. Henceforth, the COVID-19 vaccination program should target such patients in order to prevent the disease severity and its poor outcome as well as to lower the mortality.

REFERENCES

1. COVID-19 Coronavirus – update. Available from: <https://virusncov.com/>. Accessed October 29, 2021
2. Lim S, Bae JH, Kwon HS, Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to clinical management. *Nat Rev Endocrinol*. 2021;17:11–30.
3. Gerganova A, Assyov Y, Kamenov Z. Stress Hyperglycemia, Diabetes Mellitus and COVID-19 Infection: Risk Factors, Clinical Outcomes and Post-Discharge Implications. *Frontiers in Clinical Diabetes and Healthcare*.:18.
4. Laiteerapong N, Cifu AS. Screening for prediabetes and type 2 diabetes mellitus. *JAMA*. (2016) 315:697–8.
5. Katulanda P, Dissanayake HA, Ranathunga I, Ratnasamy V, Wijewickrama P, Yogendranathan N, et al. Prevention and management of COVID-19 among patients with diabetes: an appraisal of the literature. *Diabetologia*. (2020) 63:1440–52.
6. Shehav-Zaltzman G, Segal G, Konvalina N, Tirosh A. Remote glucose monitoring of hospitalized, quarantined patients with diabetes and COVID-19. *Diabetes Care*. (2020) 43:e75–6.
7. Quaresima V, Scarpazza C, Sottini A, Fiorini C, Signorini S, Delmonte OM, Signorini L, Quiros-Roldan E, Imberti L. Sex differences in a cohort of COVID-19 Italian patients hospitalized during the first and second pandemic waves. *Biology of sex Differences*. 2021 Dec;12(1):1-1.
8. Viner RM, Ward JL, Hudson LD, Ashe M, Patel SV, Hargreaves D, Whittaker E. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. *Archives of disease in childhood*. 2021 Aug 1;106(8):802-7.
9. Elliott J, Whitaker M, Bodinier B, Eales O, Riley S, Ward H, Cooke G, Darzi A, Chadeau-Hyam M, Elliott P. Predictive symptoms for COVID-19 in the community: REACT-1 study of over 1 million people. *PLoS medicine*. 2021 Sep 28;18(9):e1003777.
10. Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, Wang M. Presumed asymptomatic carrier transmission of COVID-19. *Jama*. 2020 Apr 14;323(14):1406-7.
11. Zhou Y, Chi J, Lv W, Wang Y. Obesity and diabetes as high-risk factors for severe coronavirus disease 2019 (Covid-19). *Diabetes/Metabolism Research and Reviews*. 2021 Feb;37(2):e3377.
12. Abu-Farha M, Al-Mulla F, Thanaraj TA, Kavalakatt S, Ali H, Abdul Ghani M, Abubaker J. Impact of diabetes in patients diagnosed with COVID-19. *Frontiers in immunology*. 2020:3112.
13. Abate SM, Ahmed Ali S, Mantfardo B, Basu B. Rate of Intensive Care Unit admission and outcomes among patients with coronavirus: A systematic review and Meta-analysis. *PloS one*. 2020 Jul 10;15(7):e0235653.
14. Wang Y, Lu X, Li Y, Chen H, Chen T, Su N, Huang F, Zhou J, Zhang B, Yan F, Wang J. Clinical course and outcomes of 344 intensive care patients with COVID-19. *American journal of respiratory and critical care medicine*. 2020 Jun 1;201(11):1430-4.
15. Alguwaihes AM, Al-Sofiani ME, Megdad M, Albader SS, Alsari MH, Alelayan A, Alzahrani SH, Sabico S, Al-Daghri NM, Jammah AA. Diabetes and Covid-19 among hospitalized patients in Saudi Arabia: a single-centre retrospective study. *Cardiovascular diabetology*. 2020 Dec;19(1):1-2.
16. Permana H, Huang I, Susandi E, Wisaksana R. The association of admission random blood glucose concentration and body-mass index with mortality in COVID-19 patients. *European review for medical and pharmacological sciences*. 2021 Nov 1;25(22):7144-50.
17. Liu Y, Lu R, Wang J, Cheng Q, Zhang R, Zhang S, Le Y, Wang H, Xiao W, Gao H, Zeng L. Diabetes, even newly defined by HbA1c testing, is associated with an increased risk of in-hospital death in adults with COVID-19. *BMC Endocrine Disorders*. 2021 Dec;21(1):1-0.