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Original Article

Predicting the Coronavirus Disease 2019 Severity in Patients with Diabetes using Hemoglobin A1c

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Abstract

Aim: The current study aimed to evaluate the association between the levels of HbA1c with the severity of COVID-19 among T2DM patients.

Materials and Methods: This is a retrospective, observational study included post COVID-19 T2DM patient's aged ≥18 years with preexisting comorbid conditions in India, from March 2020 to October 2020. The demographic and clinical characteristics were recorded accordingly.

Results: A total of 120 Post COVID T2DM patients were included in the study, of which 102 were hospitalized and the 18 were home quarantined based on the severity of COVID-19. Among hospitalized patients majority of them were males with various preexisting comorbid conditions such as HTN, Heart problem etc., The current study finding highlighted that the levels of HbA1c and comorbid conditions such as hypertension, heart problems, Thyroid and Dyslipidemia showed higher risk of hospitalization which is significantly associated with diabetes.

Conclusion: Thus the study suggested that the prognosis of COVID-19 severity in diabetic patients showed higher risk based on the level of HbA1c ≥ 9%. Uncontrolled T2DM might be responsible for an overall higher hospitalization for COVID-19 infection. Thus focusing on the preexisting comorbid risk factors among diabetic patients can be used in the management of COVID-19 severity and can minimize socio-economic burden.

Key words: Comorbid conditions, Coronavirus infectious disease 2019, Hemoglobin A1c

INTRODUCTION

The novel coronavirus disease 2019 (COVID 19) is caused by a severe acute respiratory syndrome, which mainly affects the lungs and the immune system. It was first recognized in the city of Wuhan in China and spreads worldwide. The current pandemic situation has caused a large number of deaths in many parts of the world. The COVID-19 confirmed cases were increasing worldwide. India, is a nation already been the diabetes capital of the world, further the dual burden of COVID worsens the current situation.[1] Some of the evidence showed that the socioeconomic status and those who lacks the access to routine health care leading to cause morbidity and mortality. A recent study showed that there is a bidirectional relationship between COVID-19 and hyperglycemic which might be postulated, irrespective of the underlying mechanisms, poor prognosis associated with hyperglycemia.[2]

People with diabetes and COVID-19 may need special attention and clinical care.[3] Recent studies highlighted that the severity and the mortality associated with COVID-19 was related to age and comorbid conditions such as diabetes mellitus (T2DM), Hypertension (HTN), cardiovascular disease (CVD) and cerebrovascular disease.[4,5] Diabetes and CVD are the major underlying comorbidities condition which might increase the risk of mortality in COVID patients.[6-10]

Diabetes is the second comorbidity after HTN in patients with COVID-19 disease. Insulin is the standard therapy to control hyperglycemia in hospitalized patients.

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Metformin could also be continued in mild cases of COVID-19 in absence of contraindications. The anti-diabetic effect of hydroxyl chloroquine can be virtually beneficial in COVID-19 patients with T2DM.[11] Recent study highlighted that Hyperglycemia is an independent factor which is associated with severe prognosis in people hospitalized for COVID-19.[12] Further the impact of HbA1c control on the management of COVID-19 infection[13] also played a major role. Since diabetes has been reported to be associated with poor prognosis of COVID-19, the management of HbA1c for patients with both T2DM and COVID-19 has gained considerable attention.[14,15] There are evidences that better glycemic control is closely associated with improvement in clinical outcomes in COVID-19 patients.[16,17] Perhaps, still there is no clear understanding, whether COVID-19 contributes to hyperglycemia. In India the prevalence of T2DM is high and there is a paucity of literature on the association of T2DM with COVID-19, thus there is a need to identity the possible responsible factor for severe outcome among T2DM patients. Thus the current study was designed to evaluate the association between the levels of HbA1c with the severity of COVID-19 among T2DM hospitalized COVID affected patients.

MATERIALS AND METHODS

The present retrospective, observational study was conducted among post COVID-19 patients with diabetes in Chennai. A consecutive 120 post COVID T2DM individuals (hospitalized due to COVID/ home quarantined due to mild COVID-19 infection), were recruited during the period of March to October 2020. The study subjects were recruited base on inclusion and exclusion criteria, Diabetic patients who were mentally oriented, aged between 18 and 80 years and took treatment for COVID-19, T2DM patients with preexisting comorbid conditions were included in the study. Those individuals who were on alternative treatment for COVID-19 and other serious illness pregnant women were excluded from the study. Demographic and clinical characteristics including age, gender, HbA1c, pre-existing conditions such as Hypertension, Cardiovascular disease, Dyslipidemia and Thyroid were recorded accordingly.

Means and proportions of the given data for each variable were calculated. For the comparison between groups t test was used for continuous variables and Chi-square tests were used for categorical variables. Multivariate regression was used to estimates the odds ratios (OR) and 95% CI for the independent association between the following clinical characteristics age, HbA1c ≥ 9%, Hypertension, Dyslipidemia and COVID-19 disease severity has assessed by the need for hospitalization. Multivariate regression was used to identify the factors associated with COVID -19 hospitalization among T2DM patients. The multivariate analysis with an HbA1c cutoff of >7% or with HbA1c as a continuous variable was observed. Statistical significant was determined at p value less than 0.05 <0.05. STATA 12 software was used to assess the data.

RESULTS

Of 120 T2DM patients who were tested for COVID-19 positive were diagnosed with the pre-existing disease and recovered from COVID. Of 120 patients enrolled in the study, 93 were male and 27 were females. The study participants had a mean age of 54.65 (±14.33) years and ranged from 21 to 80 years. About 53.79 % of the patients were greater than 50 years of age. Among preexisting comorbid conditions majority of the patients had Hypertension (35.0%), followed by Dyslipidemia (31.6%), heart problem (5.83%) and Thyroid (8.33%). The demographic characteristics of the study patients were presented in Table 1. With reference to HbA1C level, Majority of the patients had HbA1C level > 9%, followed by 8-8.9%, 7-7.9% and <7% respectively. Among 120 post covid- 19 patients with diabetes, 102 were hospitalized and 18 were home quarantined. Table 2 shows the clinical characteristics of post COVID hospitalized and non-hospitalized patients with diabetes. The Multivariate analysis, controlling for multiple prior clinical conditions showed the significant higher risk of hospitalization, among the patients with HbA1c ≥ 9% with adjusted Odds ratio of 6.21 (P < 0.01) (Table 3). Furthermore, an

Table 1: Demographic characteristics of Post COVID 19 T2DM patients

Variable	COVID-19 n=120
Mean age, years (CI)	54.65 (52.9-53.8)
20-40	23(19.1)
40-60	51(42.5)
60-80	46(38.3)
Gender	
Male n (%)	93(77.5)
Female n (%)	27(22.5)
Mean HbA1c% (CI)	9.0(8.52.-9.35)
HbA1c	
≤ 7%	36 (30.0%)
7% -7.9%	27(22.5%)
8.0% -8.9%	29(24.1%)
≥9%	28(23.3%)
Comorbid conditions	
Hypertension	42(35.0)
Heart Problems	7 (5.83)
Dyslipidemia	38(31.6)
Thyroid	10(8.33)

increased risk for hospitalization was observed in patients with prior congestive heart failure and a reduced risk for hospitalization. In the later analysis, any increase in HbA1c by 1% above a 5% baseline was associated with an OR for hospitalization of (95% CI; P < 0.05) (Table 4).

DISCUSSION

Using pre-infection glycemic control data, we found HbA1c as a clear predictor of COVID-19 severity.[18] Other clinical characteristics which were significantly linked to hospitalization included female gender, age, pre-existing conditions like Obesity, HTN, Thyroid and CVA.[14] Unexpectedly obesity and male were not associated with hospitalization despite being suggested as risk factors in earlier studies.[19] In a multivariate regression analysis adjusting for multiple potential risk factors and comorbid conditions which may have an effect on disease outcomes (including age, gender, hypertension, CVA, obesity, Thyroid and TB), only HbA1c ≥ 9% remained a significant predictor for hospitalization.[20] HbA1c remained a strong predictor of hospitalization due to COVID-19 when the model was repeated with an HbA1c cutoff of >7% as a continuous variable.[21] Association between the glucose levels in hospital and disease severity suggested linked glycemic control studied in previous studies. The improvement in glycemic control failed in hospitalized patients rather than COVID-19 severity outcome.[22.23] The current study finding suggested that the HbA1c level is a predictor to find the COVID-19 severity in patients with T2DM. Patients with long term uncontrolled HbA1c level (greater than 9%) needs more attention. However, who are at greater risk of COVID-19 severity will be critical to determine till the vaccine is available to overcome this disease.

Table 2: Clinical characteristics of T2DM patients hospitalized due to COVID-19

Variable N (%)	Hospitalized n=102	Not Hospitalized n=18	P-value
Mean age, yrs	25.5	4.50	P<0.001
20-40	19(18.6)	6(33.3)	P<0.001
40-60	47(46.0)	8(44.4)	0.132
60-80	36(35.2)	4(22.2)	P<0.05
Gender			
Male n (%)	89(87.2)	7(38.8)	0.051
Female n (%)	13(12.7)	11(61.1)	0.032
Mean HbA1c % (CI)	8.21(7.65)	8.0 (7.23)	P<0.005
co-morbid condition			
Hypertension	35(34.3)	6(33.3)	P<0.001
Heart Problems	7(6.86)	3(16.6)	P<0.05
Dyslipedemia	38(37.2)	4(22.2)	0.05
Thyroid	10(9.80)	5(27.7)	0.043

Table 3: HbA1c of T2DM patients hospitalized due to COVID-19

Variable (HbA1c)	Hospitalized, n=102	Not Hospitalized, n=18	Crude OR (95% CI) for COVID-19	P-value
<7%	24 (29.3)	7(22.2)	1.00	-
7%-7.9%	17 (20.7)	5(11.1)	3.25	0.046
8.0%-8.9%	23 (28.0)	2(27.7)	4.32	p<0.05
≥9%	38 (37.2)	4(38.8)	6.21	P<0.01

Abbreviations: CI, confidence interval; odds ratio.

Table 4: Multivariate logistic regression analysis, controlling for comorbid conditions accessing the OR for hospitalization in patients with diabetes and COVID-19

Variable	Adjusted OR (95% CI)*	P-value
HbA1c≥9	4.32	<0.01
Age	1.07	0.06
Male	0.50	0.52
Female	0.36	0.48
Hypertension	0.78	0.03
Heart Problems	0.42	0.07
Dyslipedemia	0.25	0.14
Thyroid	1.87	0.32

Abbreviations: CI, Confidence interval; OR, odds ratio
*Adjusted for age, gender and co-morbidities.

CONCLUSION

In the current retrospective study, we have considered 120 post COVID-19-infected patients with T2DM and characterized with biochemical and other clinical parameters. From the various observations, it can be concluded that uncontrolled diabetes mellitus might be responsible for hospitalization of T2DM patients and severity of COVID-19 infection.

The timely intervention to control HbA1c is required for patients along with the treatment regimen of COVID 19 during the pandemic. There is a need for more research data from other vulnerable population. As the COVID-19 pandemic situation continues, the present study finding helps in planning a comprehensive support strategies for individuals with diabetes in the health care sector. To conclude, the study findings highlighted that regular monitoring of HbA1c should be encouraged along with the specific screening strategies for COVID patients with diabetes.

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