



## To Predict the COVID-19 Severity in Patients with Diabetes Using Hemoglobin A1C

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### Abstract

To correlate the level of Hemoglobin A1c (HbA1c) to severity of COVID-19 infection in patients with diabetes. Based on demographic characteristics, at greater risk of complications and death caused by COVID-19 in old age people. We have collected the data and analysed using electronic medical records system based on the conditions such as Demographic and Clinical characteristics like Age, Gender, HbA1c level and comorbid conditions such as Heart problems, Hypertension, Dyslipidemia, Transplant and Tuberculosis disease etc. To overcome this situation, we have described here the correlation of Hemoglobin A1c (HbA1c) levels and COVID-19 severity as determined by group of patients with diabetes tested and hospitalized. Totally, we have investigated 120 COVID-19 patients for the study and 102 were hospitalized. In a Multivariate regression analysis, we have found that No. of male patients were hospitalized higher when compared with female from baseline characteristics of HbA1c levels and also comorbid conditions such as hypertension, heart problems, Thyroid and Dyslipidemia showed higher risk of hospitalization associated with diabetes were statistically significant ( $p < 0.05$ ), but not for Transplant and Tuberculosis conditions. Primary outcome of the study suggested that prognosis of COVID-19 severity in diabetic patients showed that increased risk based on the level of HbA1c  $\geq 9\%$ . Pre-comorbid risk factors useful for management of this disease associated with diabetes patients and minimize the socioeconomic burden with sensitivity approach.

### Keywords

Coronavirus Infectious Disease 2019 (COVID-19); Comorbid Conditions; Haemoglobin A1C (HBA1C).

### Introduction

The novel corona virus disease (COVID-19) Outcomes is worsen, it's caused severe acute respiratory syndrome that appeared from Wuhan in China, spread most of the countries worldwide promptly. A COVID-19 patient has been each symptomatic and well state related to respiratory organ failure, severe respiratory disorder. At higher risk resulting in death largely in adulthood cluster those that have comorbid conditions like Diabetes Mellitus (DM) and cardiovascular disorder (CVD) square measure gift in additional variety of patients

[1]. At multiplied risk for disorder and mortality with or while not DM raised the HbA1c levels. The outcome of genetic disorder is worsened; Based on the HbA1c levels predicts covid severity. In our study, we have taken 120 covid patients with diabetes upon hospitalization; hyperglycemia is identified as associated with severity of disease and cause death in some cases. In a retrospective study of 201 patients with covid-19 and Pneumonia increased glucose levels were identified as a risk factor of acute respiratory distress syndrome [2].

Some of the evidence showed that the socioeconomic status and those lacks of access to routine health care leading to cause morbidity and mortality. The increase risk from COVID-19 and therefore subject to increased preventive measures. Though risk is clearly increased risk from COVID-19. To identify patterns of dyslipidaemia among newly diagnosed type II DM patients with and without hypertension and to identify correlations between HbA1c levels and lipid profiles [3]. Moreover, our study is important because of the enormous numbers of people afflicted with diabetes and those likely to become diabetic. The primary endpoint of the study was in hospital mortality and respiratory distress syndrome and categorical variables as number and percentage. Association of hyperglycaemia and diabetes with all-cause mortality survival distributions. Biomarkers significantly associated with morality in multivariate analysis. Univariate analysis showed that age, hypertension, cerebrovascular disease, cognitive impairment, chronic kidney disease and sepsis. However, a bidirectional relationship between COVID-19 and hyperglycaemic may be postulated. Irrespective of the underlying mechanisms, poor prognosis associated with hyperglycemia [4].

This study showed a reduction of HbA1c 0.37% ( $P < 0.001$ ) compared to checks in telemedicine category. In a recently published review of 46 studies, which including patients with diabetes mellitus type 2 have been studied. Diabetes is the second co-morbidity after hypertension in patients with COVID-19 disease. Insulin is the standard therapy to control hyperglycemia in hospitalized patients. 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 type 2 diabetes [5].

Studies that provided detailed glycemic parameters consistent with the severity of COVID-19 were quite limited. It is necessary to update the metaanalysis in the future when more researches were performed to focus on this topic. Third, interpretation of our findings could be limited by the sample size. However, studies included during this meta-analysis were administered during a mixed population with and without diabetes and no separated data were provided supported diabetes status. Future studies are required to confirm the association of COVID-19 with glycemic parameters in patients with and without diabetes [6]. In conclusion, this meta-analysis suggests that severe COVID-19 is associated with increased blood glucose. Attention should be paid to watch blood sugar status in patients with COVID-19 and better glycemic control could also be a crucial supportive treatment. We included all research articles in adult patients diagnosed with COVID-19; with direct or indirect information on the result of disease severity or mortality grouped by

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comorbid diabetes. The COVID-19 severity or mortality with positive association of diabetes was observed. It is indicated that patients with preexisting diabetes were at higher risk of having worse outcome including severe COVID-19 infection or death, compared to those without diabetes [7-12]. The study is aimed to determine the risk and predictors of in-hospital mortality from COVID-19 in patients with DM, Hypertension, Dyslipidemia and CVD.

## Materials and Methods

### Study design and Participants

In this study, we have included 120 post COVID-19 patients who were hospitalized and Non- Hospitalized category from the period of March 2020 to October 2020 in Chennai, India.

### Data Collection

We have collected the data from electronic medical record system, pharmaceutical and laboratory information updated. In our study, we took totally 120 post covid patients with diabetes and without diabetes as control [13-18]. Based on the demographic characteristics including age, gender, HbA1c, pre-existing conditions like Hypertension, Cardiovascular disease, Dyslipidemia, Thyroid and Tuberculosis. From the selected population, we identified that those who have minimal risk of COVID-19 and who were hospitalized due to COVID-19. This was done after patients hospitalization collected the demographic characteristics and HbA1c levels, pre-existing conditions developed before.

### Comorbidity

The admitted patients were asked if they had a history of pre-existing disease or medication use for the comorbidities listed below: DM, Hypertension, Cardiovascular disease, Thyroid, TB. In the first part we divided all patients consistent with whether or not they had DM/CVD. In the second part to explore the pure effect of DM/CVD part we excluded patients with comorbidities aside from DM/CVD. These two aims we classified comorbidities into six groups: DM (having with DM or without other comorbidities), only DM (having DM without other comorbidities), CVD (having with CVD or without other comorbidities), only CVD (having CVD without other comorbidities).

### Statistical analysis

The analysis was conducted using STATA 12 software. Assumptions were two sided with a p- value of 0.05. Initial analysis compared demographic characteristics between the patients with positive or negative covid-19 tests, using Student's test and Fischer's exact test for continuous and categorical variables respectively. Based on normal distribution and variable characteristics. Data on continuous variables with normal distribution and variable characteristics. Multivariate regression was used to estimates the odds ratios (OR) and 95% CI for the independent association between the following clinical characteristics age, HbA1c  $\geq$  9%, Hypertension, Dyslipidemia and COVID-19 disease severity has assessed by the need for hospitalization. The controlling for multiple prior clinical conditions, the sole parameter related to a significantly increased risk for hospitalization was HbA1c  $\geq$  9% (adjusted OR 4.95; 95% CI, P < 0.05) using statistical analysis. The multivariate analysis with an HbA1c cutoff of >7% or with HbA1c as a continuous variable was observed. From this analysis, we have identified the pre-infection glycaemic control as a risk factor for COVID-19 severity.

### Results

We identified total of 120 patients with diabetes who were tested for COVID-19 positive were diagnosed with the pre-existing disease [19-22]. In a Multivariate analysis, patients with COVID-19 more likely to be male had a higher HbA1c and had fewer pre-existing medical conditions (Table 1). Furthermore, among COVID-19 patients, more patients had an HbA1c  $\geq$  9% (p < 0.05; crude OR of 1.76; 95% CI; Table 2).

We have conducted a statistical analysis among patients who were COVID-19 negative used as control. Patients who were found negative to COVID-19 but with an HbA1c  $\geq$  9% it showed that No differences were observed in prevalence of pre-existing medical conditions (Thyroid, HTN, CVA, Dyslipidemia and TB) in these patients (Table 3 & 4).

Other factors significantly associated with hospitalization were older age, female sex, CVA. In our study we have included group of individuals based on the comorbid conditions like obesity and Thyroid were not associated with an increased risk for hospitalization. In a multivariate analysis, controlling for multiple prior clinical

Table 1: Clinical characteristics of patients with diabetes and COVID-19.

Variable	COVID-19 n=120	Control n=1200	p-value
Mean age, years (CI)	54.65 (52.9-53.8)	59.45 (58.7-60.5)	P<0.001
Age (Years) n (%)			
0-20	0(0.0)	2(0.2)	P<0.001
20-40	8(8.0)	108(9.0)	P<0.001
40-60	39(39.0)	435(36.3)	P<0.001
60-80	42(42.0)	614(51.1)	P<0.05
Male n (%)	30(30.0)	835(69.5)	P<0.05
Female n (%)	12(12.0)	365(30.4)	P<0.05
Mean HbA1c% (CI)	7.0(6.92-7.25)	6.43(6.35-6.58)	P<0.05
Hypertension	42(42.0)	757(63.08)	P<0.05
Heart Problems	7 (7.0)	186(7.16)	0.034
Dyslipidemia	38(38.0)	105(8.75)	0.056
Transplant	0(0.0)	6(0.5)	0.047
Thyroid	10(10.0)	567(47.25)	P<0.05
TB	0(0.0)	5(41.56)	0.042

**Table 2:** HbA1c and OR for COVID-19 in patients with diabetes.

Variable	COVID-19, n=120	Control, n=1200	Crude OR (95% CI) for COVID-19	P-value
(HbA1c)				
<7%	8 (4.3%)	832(69.3%)	1	-
7%-7.9%	7(3.82%)	467(38.9%)	1.045	0.431
8.0%-8.9%	12(6.5%)	85(7.08%)	1.43	0.03
≥9%	14(7.6%)	34(2.83%)	1.76	P<0.05

**Table 3:** Clinical characteristics of patients with diabetes hospitalized due to COVID-19.

Variable N (%)	Hospitalized n=102	Not Hospitalized n=18	P-value
Mean age, years (CI)	57.9	65	P<0.001
Age (Years) n (%)			P<0.001
0-20	0(0.0)	0(0.0)	-
20-40	7(8.53)	5(27.7)	P<0.001
40-60	36(43.9)	8(44.4)	0.132
60-80	39(47.5)	4(22.2)	P<0.05
Male n (%)	27(32.9)	7(38.8)	0.051
Female n (%)	12(14.6)	11(61.1)	0.032
Mean HbA1c % (CI)	8.21(7.65)	8.0 (7.23)	P<0.005
Hypertension	35(42.6)	6(33.3)	P<0.001
Heart Problems	7(8.54)	3(16.6)	P<0.05
Dyslipidemia	38(46.3)	4(22.2)	0.05
Transplant	0(0.0)	0(0.0)	-
Thyroid	10(12.1)	5(27.7)	0.043
TB	0(0.0)	0(0.0)	-

**Table 4:** HbA1c and OR for hospitalization in patients with diabetes and COVID-19.

Variable (HbA1c)	Hospitalized, n=82	Not Hospitalized, n=18	Crude OR (95% CI) for COVID-19	P-value
<7%	24 (29.3)	7(22.2)	1	-
7%-7.9%	16 (19.5)	5(11.1)	3.25	0.046
8.0%-8.9%	21 (25.6)	2(27.7)	4.32	p<0.05
≥9%	18 (21.9)	4(38.8)	6.21	P<0.01

**Table 5:** 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	0.5	0.52
Female	0.36	0.48
Hypertension	0.78	0.03
Heart Problems	0.42	0.07
Dyslipidemia	0.25	0.14
Transplant	0	0
Thyroid	1.87	0.32
TB	0.19	0

conditions, the only parameter associated with a significantly increased risk for hospitalization was HbA1c  $\geq$  9% (adjusted OR 6.21; 95% CI; P < 0.05). Other variables had no significant impact on the risk for hospitalization due to COVID-19. The OR for hospitalization in patients with an HbA1c > 7% was 3.25 (95%CI P< 0.005). Furthermore, an increased risk for hospitalization was observed in patients with prior (Table 5) congestive heart failure and a reduced risk for hospitalization. In the latter analysis, any increase in HbA1c by 1% above a 5% baseline was associated with an OR for hospitalization of (95% CI; P < 0.05).

## Discussion

Using pre-infection glycaemic control data, we found HbA1c as a clear predictor of COVID-19 severity. Other clinical characteristics which were significantly linked to hospitalization included female gender, age, pre-existing conditions like Obesity, HTN, Thyroid and CVA. Unexpectedly obesity and male were not associated with hospitalization despite being suggested as risk factors in previous publications.<sup>8</sup> In a multivariate regression analysis adjusting for multiple potential risk factors and comorbid conditions which

may have a effect on disease outcomes (including age, gender, hypertension, CVA, obesity, Thyroid and TB), only HbA1c  $\geq$  9% remained a significant predictor for hospitalization.<sup>13</sup> In the fact, 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.<sup>15</sup> Association between the glucose levels in hospital and disease severity suggested linked glycaemic control studied in previous publications. Although, rather than COVID-19 severity outcomes in hospitalized patients lead to glycemic control improvement failed.<sup>15</sup> Based on our study report, It showed that HbA1c level is a predictor to find the COVID-19 severity in patients with diabetes. Other strengths of our study is to find the more severity patients based on HbA1c  $\geq$  9 and those patients 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.

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