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# Clinical profile and outcome of critically ill NCOVID-19 patients with special reference to diabetes mellitus

**Minal Shastri[1], Suketu Dave[2], Darshankumar Manubhai Raval[2], Keshav Shah[3], Ummayhany Bharmal[4*]**
[1] Professor, Department of Medicine, Government Medical College Baroda, Gujarat, India
[2] Senior Resident, Department of Medicine, Government Medical College Baroda, Gujarat, India
[3] Intern Doctor, SSG Hospital, Government Medical College Baroda, Gujarat, India
[4] Government Medical College Baroda, Gujarat, India

**Abstract**
**Objectives:** To study the clinical profile and outcome of critically ill nCOVID-19 Patients with special reference to Diabetes Mellitus and to compare and contrast the clinical course, Inflammatory markers, and outcome of critically ill Covid 19 patients with and without Diabetes Mellitus.
**Study Design:** Prospective Observational Study.
**Study Setting:** This study was conducted at SSG Hospital, a tertiary care hospital in Vadodara.
**Participants:** 150 patients in the age group between 18 -80 years and having SpO2 < 90% on room air or respiratory rate of more than e >24 were included in the study.
**Results:** The presence of underlying diabetes in patients with COVID-19 is associated with an increased risk of mortality as well as the severity of COVID-19. This study also suggests that there is an increase in mortality in diabetic patients aged more than 45. In patients who had uncontrolled diabetes COVID-19, the disease severity was greater than in patients who had controlled diabetics. Amongst patients having severe COVID-19 uncontrolled diabetics had significantly higher mortality than controlled diabetes. No such significant difference was found in mortality amongst moderate COVID-19 patients having either controlled or uncontrolled diabetics. Higher mean scores (≥3) of inflammatory markers on admission were associated with diabetics.

**Keywords:** NCOVID-19, critically ill, diabetes mellitus

## Introduction

In early December 2019, the first case of the Novel Coronavirus was identified in Wuhan, the capital city of Hubei province. The novel pathogen was named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), with phylogenetic similarity to SARS-CoV [1]. On March 11, 2020, the WHO (World Health Organization) declared the pandemic status [2]. As of 19 November 2021, India has reported 34,489,623 cases and 4,65,082 Deaths [3]. Globally, up to February 3, 2021, there have been 103.201.340 confirmed cases of COVID-19, including 2.237.636 deaths have been reported [4].

The clinical spectrum of SARS-CoV-2 infection ranges from mild to critically ill cases, manifesting as asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death [5]. Although most infected people have a favourable prognosis, chronic diseases are commonly seen in elderly people, and with comorbidities such as hypertension, diabetes mellitus, and cerebral vascular disease [6].

A meta-analysis showed that the most prevalent comorbidities in people with COVID-19 were hypertension and diabetes, followed by cardiovascular diseases and respiratory system disease [7]. Moreover, comorbid diabetes mellitus is thought to increase the risk of COVID-19 infection [8]. The overall prevalence of diabetes is estimated to be 9.3% (463 million people) [9]. According to various studies, the prevalence of diabetes in COVID-19 patients ranged from 5% to 36%. COVID-19 and diabetes are both associated with acute and chronic inflammation, respectively. Both disease conditions can impact each other in terms of clinical progression and outcome. Considering that diabetes is one of the most important comorbidities in COVID-19 patients, it is necessary to clarify all the aspects concerning the links between the two conditions to offer the scientific and clinical community those elements useful to face this pandemic in the best possible way.

## Methodology

After obtaining consent from Institutional Ethics Committee Human Research-PG Research the study was conducted in SSG Hospital a tertiary care Hospital in Vadodara, Gujarat. From the period of April 2020 to December 2021. 150 patients in the age group between 18 -80 years and having SpO2 < 90% on room air or respiratory rate more >24 were included in the study. Patients were divided into 2 groups depending on whether they have Diabetes or not. For the patients in both these groups, the Inflammatory score [10] was calculated as

given in table 1. The total inflammatory score ranged from a minimum of 0 to a maximum of 4. A higher score indicated greater disease severity [10]. Chest X-ray for all the patients was done upon admission.

**Table 1:** Inflammatory score

| Markers | Score 0 (Normal) | Score 1 |
|---|---|---|
| CRP | <5 mg/L | >5 mg/L |
| Ferritin | <300 ng/ml | >300 ng/ml |
| LDH | <460 U/L | >460 U/L |
| d- Dimer | <500 ng/ml | >500 ng/ml |

For the study, patients in both categories were classified into 2 subgroups at the time of admission: those having the moderate disease - requiring nasal 02 and hemodynamically stable with those SpO2-90% or RR >24 and those having the severe disease- requiring invasive/noninvasive ventilator support or hemodynamically unstable. FiO2 for all the patients was calculated using the formula 20% + (4×oxygen liter flow). Patients with nasal cannula were placed on 1-6 liters, simple oxygen masks were placed on 5-12 liters, nonrebreather masks were placed on 8-15 liters and those on BiPAP and invasive ventilation were placed on 15 liters on the oxygen flow meter.

Diabetic patients who had HbA1C > 8% were regarded to have uncontrolled diabetes and those diabetic patients having HbA1c < 8% were regarded to have controlled diabetes.

Patients having a pulse rate > 100 beats per minute on admission were considered to have higher pulsates and those having a pulse rate between 60-100 beats per minute on admission were considered to have e normal pulse rate. Patients having a respiratory rate ≥31 were considered to have higher respiratory rate.

We have compared differences in clinical profile, inflammatory markers, radiological profile, progression, and, the outcome of patients with and without diabetes The data was analyzed using the T-test and Chi-square test (www.socscistatistics.com) at appropriate places using and the p-value < 0.05 was considered significant.

**Result**

Here we have studied the clinical profile and outcome of critically ill nCOVID-19 patients with Diabetes Mellitus.

The association Of Diabetes Mellitus to the outcome is analyzed as described below (Table 2) using the square area are test at a confidence interval of 95% and value <0.05.

**Table 2**

| Outcome | Diabetic | Non-Diabetic | Total |
|---|---|---|---|
| Death | 47 (67.2%) | 28 (35%) | 75 (50.0%) |
| Discharge | 23 (32.8%) | 52 (65%) | 75 (50.0%) |
| Total | 70 | 80 | 150 00%) |

**Age and Gender**

The mean age of the patients was 45.5 ±13.3 years. Of the total 150 patients 68 patients were below the age of 45 (45.3%) and 82(54.7%) patients were above the age of 45. Of the 68 patients below 45 years of age, 24 (35.3%) patients died and 44(64.7%) patients were discharged. Out of the 82 patients that belonged to the age group above 45 years, 51 (62.2%) died and 31(37.8%) were discharged. (p-value: 0.001).

More than half of the patients were male (67.3%) and the rest 32.7% of patients were female of the total patients enrolled in the study. Of the total 101 male participants 48 (47.5%) died and 53 (52.5%) were discharged. The total no. of female participants was 49 and of them, 27 (55.1%) died and 22 (44.9%) were discharged (p-value: 0.384).

**Comorbidities**

The distribution of all the patients enrolled in the study according to the comorbidity is done in Table 3

**Table 3:** Distribution of patients according to comorbidities.

| Comorbid condition | Number | Percentage |
|---|---|---|
| Diabetes Mellitus only | 64 | 42.7 |
| Hypertension + Diabetes | 1 | 0.6 |
| Hypertension only | 7 | 4.7 |
| Diabetes + IHD | 1 | 0.6 |
| Diabetes + CKD | 1 | 0.6 |
| Diabetes + COPD + Smoking | 1 | 0.6 |
| Diabetes + Hypertension + IHD + CKD + Smoking | 1 | 0.6 |
| Diabetes + Hypertension + IHD + CKD + COPD + Smoking | 1 | 0.6 |
| Hypothyroidism | 2 | 1.3 |
| PLHA | 2 | 1.3 |

| | | |
|---|---|---|
| Others | 4 | 2.6 |
| No Comorbidity | 65 | 43.4 |
| Total | 150 | 100.0 |

Of the total patients, 81 (54%) patients had only 1 comorbidity, 2 (1.3%) patients had 2 comorbidities and, 3 (2%) patients had more than 2 comorbidities. Of the patients having only one comorbidity 47 patients died and 31 patients were discharged. All the patients having 2 or more 2 comorbidities died.

**Diabetes**

In total 70 patients had Diabetes. Among patients with diabetes, 82.9% patients had a severe form of COVID-19 disease, use and 17.1% of patients had a moderate disease form of COVID-19 as per the criteria stated in the methodology. While among 80 patients without diabetes, 63% of patients had severe COVID-19 disease, and 37%of patients had moderate COVID-19 disease-valuable 0.0056). Mortality was more among patients with diabetes (68.1%) compared to patients without diabetes (34.6%) in the case of both moderate and severe forms of COVID-19 patients, suggesting significantly poor output among patients with diabetes ($p<0.05$).

Mortality was 100% among patients with diabetes combined with other comorbidities. While mortality was 65.4% among patients with diabetes only. The difference was statistically significant ($p<0.05$). The limitation of this analysis was the very few sample size of people having diabetes combined with other comorbidities. Amongst Diabetics, 20 patients were regarded to have controlled diabetes mellitus and 50 patients were regarded to have uncontrolled diabetes. Amongst the patients having controlled diabetes 7 (35%) had moderate disease and 13 (65%) had severe disease. Amongst the patients having uncontrolled diabetes 5 (10%) had moderate disease and 45 (90%) had severe disease (p-value: 0.012). Of the patients having controlled diabetes 6 (30%) died and 14 (70%) were discharged of the patients having uncontrolled diabetes 36 (72%) died and 14 (28%) were discharged (p-value. 0011). There was no significant difference in mortality of moderate COVID-19 patients with controlled and uncontrolled diabetes (p-value: 0.7353). Amongst severe COVID -19 patients having controlled diabetes 4(31%) died and 9(69%) patients were discharged and of the severe COVID-19 patients having uncontrolled diabetes 35 (78%) died and 10 (22%) patients were discharged (p-value: 0.0014). Amongst 70 diabetics 15 patients were below the age of 45 and 55 patients were above the age of 45. Amongst the patients below the of 45, 4 (27%) died and 11 (73%) patients sits were discharged. Of the diabetic patients above the age of 45, 43 (78%) died 12 (22%) patients were discharged. These results were statistically significant (p-value: 0.0001).

**Symptoms**

Of all the patients involved in the study, the most common symptoms were Dyspnea (85.5%) and cough (73.9%) in patients with diabetes. While most common symptoms were Dyspnea (93.8%) and fever (60.5%) in patients without diabetes.

**General Examination and Vitals**

On admission, 7u General Examination of all the patients revealed that Pulse Rate and Respiratory Rate were significantly higher (mean pulse rate and respiratory rate in patients with DM were wwere121.0±16.8 and 31.8±8.7 respectively and the mean pulse rate and respiratory rate in non-diabetic patients was 110.8±15.0 and 28.4±6.7) among patients with DM ($p<0.05$). SpO2 was significantly lower (mean SpO2 amongst diabetics was 89.2±8.8 and the mean SpO2 amongst nondiabetics was 92.2±7.4) among patients with DM ($p<0.05$). There was no significant difference in Systolic and diastolic blood pressure among patients with and without DM ($p>0.05$).

On admission, of all the 150 patients, 123 (82%) patients had a higher pulse rate and the rest 27 (18%) patients had a normal pulse rate. Of the patients having higher pulse rates, 62(41.4%) patients were diabetics and 61 (40.7%) patients were nondiabetics. Among the diabetics having high pulse rates 45 (30%) patients died and 17 (11.3%) patients were discharged. Of the non-diabetic patients having high pulse rates 17(11.3%) patients died and 44 (29.3%) patients were discharged. (p-value < 0.05). On admission of all the patients, 89 patients had a respiratory rate below 31 and the rest 61 patients had a respiratory rate above 31. Of the patients having a respiratory rate of more than 31, 31 (20.7%) patients were diabetics, of which 30(20%) patients died and 1(0.6%) patient was discharged, and 20 (13.3%) patients were nondiabetics, amongst them 13(8.6%) patients died and 7 (4.6%) patients were discharged (p-value: 0.002317)

**Radiological investigation**

On Chest X-ray 40.6 % of patients with DM had more than 4 zones of lung involved while only 22.2% of patients without DM had more than 4 zones of lung involved. The difference was statistically significant ($p<0.05$). The mortality in diabetic and nondiabetic patients showing involvement of more than 4 lung zones showed a statistically significant difference-values < 0.05).

**Inflammatory score**

The mean inflammatory score amongst diabetics who had moderate COVID-19 disease was 3.63±0.48 and was 3.40±0.49 amongst nondiabetics who had moderate COVID-19 disease (p-value: 0.0066).

The mean inflammatory score amongst diabetics who had severe COVID-19 disease was 3.50±052 and was 2.30±0.46 amongst nondiabetics who had moderate COVID-19 disease (p-value < 0.05).

**Mode of Ventilation**

Among patients with diabetes, on admission majority of patients were on IPPV (30%) of them all the patients died and NRBM (27%), the 55% of patients died and 45% of patients were discharged. While among patients without diabetes, on admission majority of patients were on NRBM (49.4%), 20% died and the rest 80% were discharged, and on BIPAP (22.2%), of the 29.4% patients died and the rest 70.6% patients were discharged. The difference in mortality was statistically significant in patients who were on NRBM on admission (p-value < 0.05). The difference in SpO2/FiO2 ratio between diabetics and nondiabetics was statistically significant (p<0.05).

**Discussion**

In our study, the majority of patients were in the age group of 31 to 45 years (39.3%) and 46 to 60 years (34.7%) with the mean age of the patients being 45.5 ± 13.3 years. The age group was most affected in Ahsan ASMA et al. [11], were 61–70 years (37.2 %) and the mean age was 63.6 ± 12.8 years. Shah P et al [11]. shows the median age was 63 years.

In our study, there was a significant difference in the proportion of male (67.3%) and female (32.7%) patients, which was consistent with the results of a study performed by Ahsan ASMA et al [11]. (61.6% male and 38.4% female). Guang et al [12]. in their results showed that males (58.1%) were more likely to be infected than females (41.9%).

Regarding clinical symptoms, Dyspnea (90%), fever (64.7%), and cough (64.7%) were most commonly present in our study. In Ahsan ASMA et al [10]. 96.5% of patients presented with respiratory distress, 93.02% with cough, and 84.9% with fever. In a study by Ahmed NU et al [13]. showed fever was the dominant symptom (77%) and 35.5% of the patient presented with cough. In another study Xie J et al [14]. also showed the most common presenting symptoms were fever (85.9%), dry cough (75%), and dyspnoea (60.7%). A systematic review by Rodriguez-Morales et al [15]. of data on 656 cases reported fever in 88.7%, cough in 57.6%, dyspnoea in 45.6%, and diarrhea in 6.1%.

In the present study, the most common comorbidities were Type 2 Diabetes Mellitus (45.3%) followed by Hypertension (5.3%), Smoking (4%), Ischemic Heart Disease(2.7%), and Chronic Renal Disease present (2.7%).In Ahsan ASMA et al [11]. 91.9% had DM, 77.9% had HTN, 14.0% had Asthma, 17.4% had COPD, 19.8% had IHD and 18.6% had CKD. Shah P et al [11] showed in their study, that the most common comorbidities were HTN (79.7%), obesity (66.5%), and DM (42.3%). In another study by Xie J et al [14]. showed hypertension (42%) as the most common comorbidity, followed by diabetes (18.8%) and coronary heart disease (12.7%).

Our results on prevalence are in contrast to a large Chinese nationwide study of 1590 patients which had shown the prevalence of diabetes in COVID-19 patients to be 8.2% [12]. Fadini et al [16]. also reported the prevalence of diabetes in COVID-19 patients as 10.3%. Thus, the susceptibility of the diabetic population to COVID-19 infection was increased compared to the non-diabetic population.

Serum levels of inflammatory biomarkers such as CRP, LDH, Ferritin, and D dimer levels were higher among patients with diabetes. Also, the reduction in their levels after thirteen days of follow-up was found more among non-diabetic patients compared to diabetic patients. Guo et al [17]. also found that C-reactive protein, D-dimer, IL-6, serum ferritin, and coagulation index, were significantly higher in diabetic patients compared to those without, suggesting that patients with diabetes are more susceptible to an inflammatory storm that leads to worsening of COVID-19.

In the present study, half of the patients (50%) were discharged and half of the patients (50%) died. Similar findings were observed by Ahsan ASMA et al [1]. in which 51.16% of patients were transferred to the isolation ward or discharged at home who were considered to survive and 48.8% of patients died. Xie J et al [13]. showed 53.8% mortality in 733 critically ill patients with COVID 19 in their study.

For improvement of oxygenation of COVID patients in the present study, the majority of patients were on NRBM (40%), BIPAP (22%), and IPPV (20%). Mechanical Ventilation is required more among patients with diabetes compared to patients without diabetes (p<0.05). Similarly, Ahsan ASMA et al [11]. treated the majority of patients by Non-Rebreather Mask (20.9%), High Flow Nasal Cannula (22.1%), and Mechanical Ventilation (25.6%).

In the present study, the severe disease was significantly higher among patients with diabetes (82.6%) compared to patients without diabetes (63%) (p<0.05). Involvement of more than four-zone in the lung was also observed significantly higher in patients with diabetes (40.6%) compared to patients without diabetes (22.2%) (p<0.05). Mortality was significantly higher among patients with diabetes (68.1%) compared to patients without diabetes (34.6%). Thus, the outcome was poor among patients with diabetes.

A. Kumar et al [18]. also found that diabetic patients with COVID-19 are twice more likely to develop severe COVID-19 disease and twice more likely to die due to it. de Almeida-Pititto et al [18]. identified a 2.3-fold increase in the risk of severity and a 2.5-fold increase in mortality associated with COVID-19 in patients with DM. Thus, patients with COVID-19 and diabetes are more likely to develop ARDS, need ICU care, need invasive ventilation, and are more vulnerable to succumbing to it. A meta-analysis, by Fadini et al [15]. (6 studies, 1687 patients) and Wang et al [20]. (6 studies, 1558 patients), which gave an odds ratio of 2.26 and 2.47, respectively, for diabetic patients developing more adverse diseases due to SARS-CoV-2 infection. Another study by Singh et al [20]. also suggested that diabetes is a determinant of severity and mortality of COVID-19 patients.

The question of whether diabetes is an independent determinant of severity was investigated by Guo et al. in their case-control study in China [17], in which they compared COVID-19 patients with and without diabetes and found

that even in the absence of other comorbidities, diabetics were at increased risk of severe pneumonia, uncontrolled inflammatory response, greater levels of enzymes related to tissue damage and the highest state of hypercoagulability.

**Conclusion**

In conclusion, the presence of underlying diabetes in patients with COVID-19 is associated with an increased risk of mortality as well as the severity of COVID-19. This study also suggests that there is an increase in mortality in diabetic patients aged more than 45. On admission pulse rate, and respiratory rate was significantly higher in diabetics and SpO2 was significantly lower in diabetics. In diabetics, higher pulse rate and respiratory rate on admission were associated with significantly higher mortality as compared to nondiabetics having similar pulse and respiratory rates.

The most common symptoms in diabetics were dyspnoea and cough while the most common symptoms in nondiabetics were dyspnoea and cough. Thus, despite COVID 19 being an infectious disease, diabetic patients did not commonly present with fever.

The prognosis of patients was poor who had more than one comorbidity when compared to patients who had only one comorbidity.

In patients who had uncontrolled diabetes COVID-19, the disease severity was greater than in patients who had controlled diabetes. Amongst patients having severe COVID-19 uncontrolled diabetics had significantly higher mortality than controlled diabetics. No such significant difference was found in mortality amongst moderate COVID-19 patients having either controlled or uncontrolled diabetics.

Higher mean scores (≥3) of inflammatory markers on admission were associated with diabetics.

Chest X-ray on admission in diabetics revealed the involvement of more than 4 lung zones as compared to nondiabetics who revealed the involvement of less than 4 lung zones. Mortality was higher in diabetics who showed radiological involvement of more than 4 lung zones compared to diabetics showing similar radiological involvement.

No significant difference in mortality was found between males and females irrespective of their diabetic status. This necessitates enhanced prevention of COVID-19 in diabetics, increased vigilance in patients with diabetes for COVID-19, and a lower threshold for monitoring, hospitalization, and ICU care if diabetics develop this infection.

The results of our study emphasize the need for further investigation on the pathogenic mechanism of the relationship between diabetes and COVID-19, and to explore its therapeutic implications

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