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### **Original Research Article**

## A retrospective study on the clinical picture of COVID-19 patients associated with type 2 diabetes mellitus in India

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#### ABSTRACT

**Background**: The clinical characterization of COVID varies from mild to severe. In the initial phases of the disease, symptoms like fever, cough, and dyspnea can occur. The severity and outcome of COVID vary with preexisting conditions, particularly type 2 diabetes mellitus (T2DM). Objective of current study was to assess the clinical presentation and laboratory derangements of COVID-19 patients associated with T2DM.

**Methods:** The present retrospective study was started after the approval of the Institutional Ethics Committee. Various clinical (Sp02, final diagnosis, co-morbidity, and outcome) and biochemical parameters (CBC, LFT, RFT, LDH, Trop I, CK-MB D-dimer, CRP, ferritin levels, RBS, HbA1c) of Covid-19 patients were collected from Central Laboratory and & Medical Record Department of our institution. Patient names were anonymized and data were analyzed. The results are expressed in percentages.

**Results:** A total of 24 COVID-19 patients (with T2DM) details were collected from the medical record department and central laboratory. Out of 24 patients, 16 (66.6%) were male, and the remaining 08 (33.3%) were female. Out of 24, 05 patients had mild covid, 02 were moderate and the remaining 17 suffered from severe COVID. The mean values of oxygen saturation, LDH, D-dimer, Troponin-I, CRP, Ferritin, Procalcitonin, and CK-MB were 76%, 797.3 U/l, 1614.2 ng/ml, 6.93 ng/ml, 72.6 mg/dl, 521.2  $\mu$ g/l, 2.33  $\mu$ g/l and 40.59 ng/ml respectively. The average random blood sugar level and glycosylated hemoglobin were 308.8 mg/dl and HbA1c 10.22%. Mean values of 42.5 mg/dl and 1.54 mg/dl were recorded for blood urea and S. creatinine. Regarding liver function test, mean values of 0.87 mg/dl, 0.37 mg/dl, 0.49mg/dl, 344.8U/l, 115.6U/l,108U/l respectively noted for total bilirubin, direct, indirect, SGOT, SGPT and ALP. Regarding patient outcome, 09 (37.5%) patients recovered and 15 (62.5%) died due to COVID. The values of glycosylated Hb and random blood sugar among the 15 patients who died due to septic shock.

**Conclusions:** Though the laboratory mean values of the liver function test and renal function test shows moderate variations the mean values of CRP, LDH, Procalcitonin, and Ferritin which are the acute inflammatory markers are highly disrupted when compared to normal ranges.

Keywords: COVID-19, Diabetes mellitus, Retrospective studies

#### **INTRODUCTION**

The world faced a newer problem in the year 2019 when China reported a cluster of pneumonia cases of unknown etiology originating from "Wuhan, Hubei Province, China". The etiology of the illness was attributed to a novel virus belonging to the Corona Virus (CoV) family. The virus spreading around the world and emergency care services are of top need right now. On 11th March 2020, WHO declared COVID-19 as a pandemic. India confirmed its first case on 30th January 2020 in Kerala. The clinical characterization of COVID-19 has been broadly defined by WHO with most of the confirmed COVID-19 cases having mild to moderate clinical presentation.<sup>1</sup>In the initial phases of the disease, symptoms like fever, cough, and dyspnea can occur.<sup>2</sup> Some of the patients rapidly develop acute respiratory distress syndrome (ARDS) and additional severe complications, which are ultimately ending in multiple organ failure.<sup>3</sup> Hence, timely diagnosis of patients is very crucial. Recent studies confirmed that an independent predictor of mortality and morbidity is having a diabetic history in patients with SARS and diabetes is associated with increased mortality in COVID-19 patients.<sup>4-6</sup> High blood concentrations of inflammatory markers i.e ferritin, procalcitonin, C-reactive protein, and high neutrophil-tolymphocyte ratio with increased concentrations of inflammatory cytokines and chemokines have been predominantly associated with both COVID-19 severity and death.<sup>7</sup> Elderly patients with chronic kidney disease, diabetes, obesity, heart disease, and chronic obstructive pulmonary disease are at high risk of severe COVID-19 and require hospital admissions and a long incubation time of up to 24 days.8 So there is a need to understand the pathophysiology of the disease in diabetic patients admitted to the hospital with COVID-19 for better treatment and disease control. The present study was carried out aiming to describe the clinical presentation and laboratory derangements of COVID-19 patients associated with T2DM.

#### **METHODS**

This retrospective study included various clinical (Sp02, final diagnosis, co-morbidities, and outcome) and biochemical parameters (Complete Blood Count, Liver Function Test, Renal Function Test, Lactate De-Hydrogenase, Troponin I, Creatine Kinase-MB D-dimer, C-Reactive Protein, Serum ferritin, Random Blood Sugar and Glycosylated hemoglobin-HbA1c) of Covid-19 patients were collected from central laboratory and medical record department of our institution. Patient details were anonymized and data were collected and analyzed.

#### Study population

Covid-19 patients who are admitted in our institution during 22 June 2020 to 22 July 2020 of any age and gender having all the required details like laboratory parameters in their case file and central laboratory data base are included in this study. A total of 24 COVID patients with T2DM details were collected.

#### Statistical analysis

To analyze the data, descriptive statistical methods were used. Descriptive methods such as frequency and

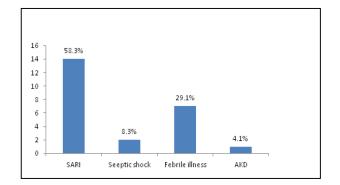
percentage were calculated for categorical data. Mean values were calculated to summarize all laboratory parameters. Analysis was performed using SPSS version 23 was used.

#### RESULTS

The demographic details of COVID patients with T2DM patients are shown in (Table 1).

# Table 1: Demographic details of COVID patients with<br/>T2DM.

Details	Description N (%)	
Gender	Male: 16 (66.6)	
	Female: 8 (33.3)	
Age	34-75 years (57.5)	
Severity of COVID	Mild: 05 (20.8)	
	Moderate: 02 (8.3)	
	Severe: 17 (70.8)	
Co-morbidities	Hypertension: 07	
	Peripheral Vascular Disease: 02	
	Hypothyroidism: 01	
	Only T2DM: 14	



# Figure 1: Clinical presentation of COVID patients with T2DM.

Out of 24 patients, 16 (66.6%) were male, and the remaining 08 (33.3%) were female. Out of 24, five patients had mild, 02 were moderate and the remaining 17 suffered from severe COVID. Moreover, 07 patients had hypertension, 02 patients had hypothyroidism and one patient had the peripheral vascular disease in addition to T2DM. The clinical presentation of COVID patients with T2DM is represented in (Figure 1). 14 (58.3%) presented with SARI (severe acute respiratory illness), one with acute kidney disease (4.1%), 02 (8.3%) patients with septic shock, and the remaining 07 (29.1%) presented with febrile illness. The mean values of various biochemical parameters are mentioned in (Table 2). The mean values of oxygen saturation, LDH, D-dimer, Troponin-I, CRP, Ferritin, Procalcitonin, and CK-MB

were 76%, 797.3 U/l, 1614.2 ng/ml, 6.93 ng/ml, 72.6

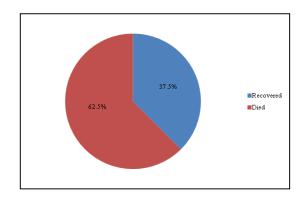
mg/dl, 521.2  $\mu$ g/l, 2.33  $\mu$ g/l and 40.59 ng/ml respectively.

#### Table 2: Variations in the biochemical parameters of COVID patients with T2DM.

Parameters	Mean value	
		Normal range
Oxygen saturation (SpO2) (%)	76	98-100
Random Blood Sugar (RBS) (mg/dl)	308.8	70-140
Glycosylated hemoglobin (HbA1c) (%)	10.22	4.2 to 6.2
Procalcitonin (µg/l)	2.33	<0.5: Sepsis is unlikely /local bacterial infection possible, >0.5 and <2.0: Possible Sepsis, >2.0 and <10: Sepsis is likely and High Risk for progression to severe sepsis. >10.0: Likelihood of severe sepsis or septic shock.
C-Reactive Protein (CRP)	72.6 mg/dl	0 to 5 mg/l
D-dimer (ng/ml)	1614.2	<500
Troponin-I (ng/ml)	6.93	0-0.03
Creatine Kinase-MB (ng/ml)	40.59	0-2.37
Ferritin (µg/l)	521.2	6.24 - 137
Lactate De-Hydrogenase (LDH) (U/l)	797.3	120-246
Hemoglobin (Hb%)	13.3	12 to 15
Total Leucocyte count	10.7 x 10 <sup>3</sup> /µl	$4-11 \times 10^3 / \mu l$
Differential lymphocyte count (%)	14.3	25 to 40
Differential monocyte count (%)	4.9	1 to 10
Differential eosinophil count (%)	0.9	1 to 6
Differential neutrophil count (%)	79	40 to 75
Differential basophil count (%)	0.3	0 to 1
Total platelets	278.27 x 10 <sup>3</sup> /µl	150 to 450 x $10^3/\mu l$
Erythrocyte Sedimentation rate (ESR)	38.3	0 to 20 mm/1hr
Blood urea (mg/dl)	42.5	19-43
Serum creatinine (mg/dl)	1.54	0.62-1.1
Total bilirubin (mg/dl)	0.87	0-2
Direct bilirubin (mg/dl)	0.37	0-0.2
Indirect bilirubin (mg/dl)	0.49	0-1.1
SGOT (U/I)	344.8	0-31
SGPT (U/I)	115.6	0-34
Alkaline phosphatase (U/l)	108	60-170
Total serum protein (gm/dl)	7.5	6.3-8.2
Serum albumin	3.95	3.2-4.4
Serum globulin:	3.58	2.5-3.5
Albumin/Globulin ratio	1.12	1.2-1.5

With respect to complete blood count, average values of 13.3G,  $10.7x10^{3}/\mu$ l, 14.3%, 4.9%, 0.9%, 79%, 0.3%,  $278.27 x 10^3 / \mu l,$  and 38.3 respectively noted for hemoglobin, total count, differential counts of lymphocyte, monocyte, eosinophil, neutrophil, basophil, total platelets and ESR. The average random blood sugar level and glycosylated hemoglobin were 308.8 mg/dl and 10.22%. Mean values of 42.5 mg/dl and 1.54 mg/dl were recorded for blood urea and S. creatinine. Regarding liver function test, mean values of 0.87 mg/dl, 0.37 mg/dl, 0.49 mg/dl, 344.8U/l, 115.6 U/l, 108U/l respectively noted for total bilirubin, direct, indirect, SGOT, SGPT and ALP. The mean value of total protein, albumin, globulin, and A/G ratio was found to be 7.5 gm/dl, 3.95 gm/dl, 3.58 gm/dl, and 1.12 respectively. The clinical outcomes of COVID patients admitted to our institution is depicted in (Figure 2). 09 (37.5%) patients recovered and 15 (62.5%)

died due to COVID.





The values of glycosylated hemoglobin and random blood sugar of 15 patients who died due to COVID infection suggested uncontrolled diabetes Mellitus and 7 of them had associated hypertension and died due to septic shock.

#### DISCUSSION

SARS-CoV-2 is an airborne disease spread through the droplets generated during coughing and sneezing of symptomatic patients and asymptomatic patients during the incubation period. The heterogeneous pattern of the disease may vary from the asymptomatic stage to the need for intensive care unit admission (ICU) for acute respiratory distress syndrome (ARDS), pneumonia, respiratory failure, and sepsis with multi-organ failure. The severity of the COVID infection is caused by a defective immune response with hyperstimulation, rapid multiplication of macrophages, natural killer cells, and T cells, and high production of more than 150 chemical mediators including pro-inflammatory cytokines like IL-6, IL-1 $\beta$ , TNF- $\alpha$  and chemokines leading to the cytokine storm which leads to increased vascular permeability and multiple-organ failure. The negative impact on the cardiovascular system may be due to high levels of IL-6, which promotes cardiomyopathy. The cytokine storm leads to the impairment in endothelial function leading to capillary leakage, coagulopathy, and hypotension with a more severe course of COVID-19.9 Various biochemical parameters like serum ferritin, C-reactive protein, Procalcitonin, D-dimer, Lactate dehydrogenase enzyme, interleukins-6, cardiac markers like Troponin-I and CK-MB are found to be elevated during the course of the infection. These parameters can be used as a predictor of the disease prognosis and response of the patient towards the treatment. This parameter can be used as a reference for weaning off the patient from antibiotic and steroid treatment and assessing the prognosis of the infection. In a study by Miriam et al it is mentioned that cardiovascular diseases and type 2 diabetes have been identified as the most common co-morbidities for SARS-CoV-2 infection and are associated with worse outcomes and more severe course of the infection. In a retrospective study, patients with diabetes had higher concentrations of lactate dehydrogenase,  $\alpha$ -hydroxybutyrate dehydrogenase, y-glutamyl transferase, and alanine aminotransferase. These findings are similar to our study results.<sup>7-9</sup> In another study by Celestino Sardu, Giuseppe Gargiulo et. al. mentioned that type 2 diabetes mellitus (T2DM) appears as a most frequent co-morbidity in COVID-19, and secondly, T2DM is one of the major causes of death in COVID-19 infection.<sup>10</sup> In our study, it is observed that D-dimer, a marker of coagulopathy is highly elevated along with the inflammatory markers like serum ferritin, Pro-calcitonin, C-reactive protein, Lactate dehydrogenase, and ESR when compared to normal levels which show the immense reaction of the body against the infection. In our study, the death of 15 (62.5%) COVID-19 patients with T2DM was due to exaggerated immune response leading to cytokine storm.

#### CONCLUSION

Our study observed that T2DM patients with associated co-morbidities like hypertension could not cope with the infection due to existing metabolic and immunological derangements in the body. COVID-19 is an infection that alters the immune response of the body and is more severe in patients with existing T2DM. Though the laboratory mean values of liver function and renal function tests show moderate variations but the mean values of CRP, LDH, Procalcitonin, and serum ferritin which are the acute inflammatory markers and D-dimer, a marker of coagulopathy are highly disrupted when compared to normal ranges.

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