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Original Article

IMPACT OF DIABETES MELLITUS ON CLINICAL PROFILE AND OUTCOME OF COVID-19 PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: A novel coronavirus infection (SARS-CoV-2) pneumonia (COVID-19) has been quickly spreading throughout China and the rest of the world since December 2019. Respiratory tract infections are frequently linked to diabetes mellitus (DM), a different risk factor. This study has reported the clinical presentation and therapeutic outcomes of COVID-19 with diabetes.

Methods: From medical records and histories provided by 72 Covid-19-infected patients with diabetes admitted to the KMCH institute of health sciences and research, Coimbatore, data on demographics, clinical, laboratory, and radiological characteristics as well as treatment outcomes were collected using data collection forms. Real-time reverse transcription polymerase chain reaction (RT-PCR) assay of 2019-CoV RNA was used to screen patients with Covid-19.

Results: 72 diabetes patients who tested positive for Covid-19 were admitted for this study. SPSS software version 26 was used to evaluate the data that had been collected. Clinical profiles and outcomes of patients with and without diabetes underwent descriptive analysis. Controlled diabetics had a mean plasma glucose of 112.22±11.41, while uncontrolled diabetics had a mean plasma glucose of 154.2±23.22. Fever was the most prevalent symptom in both managed and uncontrolled diabetes patients (94% and 100%), followed by sore throat (84% and 88%). In patients with uncontrolled diabetes compared to those with controlled diabetes, breathlessness is considerably higher ($p<0.05$). In the CORADS scoring, 11 of the 34 diabetics with uncontrolled blood sugar levels had CORADS 6 (32.35%), compared to just 2 of the 38 diabetics with regulated blood sugar levels (5.26%), which is considerably higher ($p<0.01$). In uncontrolled diabetics, the length of hospital stay is much longer ($p<0.001$). Compared to diabetics with controlled blood sugar, uncontrolled patients SPO2 dramatically dropped ($p<0.001$). Those with uncontrolled diabetes are more likely to be admitted to the ICU than patients with controlled diabetes ($p<0.05$). In uncontrolled diabetes compared to controlled patients, the severity was considerably higher ($p<0.05$). One person who had uncontrolled diabetes died, although no one who had controlled diabetes died.

Conclusion: Covid 19, persons with uncontrolled diabetes appear to be more likely to sustain lung damage, necessitating admission to the ICU, an extended stay in the hospital, and oxygen assistance throughout the duration of the illness.

Keywords*:* COVID-19, Diabetes, Clinical profile, Treatment outcome

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INTRODUCTION

A novel coronavirus infection (SARS-CoV-2) infected pneumonia (COVID-19) has been quickly spreading throughout China and the rest of the world since December 2019. The International Committee on Virus Taxonomy refers to this virus as SARS-CoV-2 and the illness as COVID-19 (ICTV). The high infectivity of COVID-19 caused a large increase in new cases. Over 85,000 people are infected as it aggressively spreads throughout China. Invading Europe in March 2020, it wreaked havoc on Italy, Spain, France, Germany, the United Kingdom, and finally, the United States, causing a terrible loss of life and property [1, 2]. India, the second-most populous nation in the world, has already surpassed the United States as the COVID-19-infected nation. As of September 10, 2020, 76,348 fatalities had been reported in India out of a total infection rate of about 4,568,770. The WHO proclaimed COVID-19 a global pandemic on March 11, 2020 [3]. The main means of transmission of the virus appear to be human-to-human droplet transmission and contact with fomites. Even though 80% of the infected population is asymptomatic or just mildly ill, people continue to go to work and even travel abroad [4, 5]. The virus may produce modest illness in many people, but in the elderly or those with coexisting conditions, the illness can be severe and lead to hospitalization or even death. Respiratory tract infections are frequently linked to diabetes mellitus (DM), which is a distinct risk factor. Several articles have provided descriptions of the epidemiological information, clinical manifestations, and clinical outcomes of people with confirmed COVID-19. There are, however, very few investigations, notably on COVID-19-positive diabetes patients. Studies [6, 7] have shown a correlation between blood glucose levels and the clinical progression of the severe acute respiratory syndrome. Little is known about the clinical traits of individuals with diabetes who have developed the 2019 novel SARS-COV-2 pneumonia. This study aims to investigate any differences between diabetic and non-diabetic patients in terms of clinical symptoms and results.

The coronavirus has received greater attention than other pneumonia-causing agents since the epidemics of Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) (MERS). A kind of beta coronavirus called 2019-n CoV has been related to human cases of SARS and MERS, according to full-genome sequencing and phylogenetic analysis. In terms of risk factors, clinical symptoms, and clinical outcomes, COVID-19 is similar to SARS and MERS. Diabetes is a reliable, independent predictor of morbidity and mortality in SARS patients. HbA1c and the chance of being admitted to the hospital for infections in general, and respiratory infections in particular, have been linked by prior studies in a J-curve fashion. An increased risk of infection was noted during prior outbreaks of the H1N1 influenza virus, Middle East respiratory syndrome, and severe acute respiratory syndrome;

however, this does not seem to be the case with COVID-19. According to a prospective cohort analysis of COVID-19 patients from New York City, hospital admissions were associated with higher rates of diabetes and obesity (35% vs. 308% for obesity and 347% vs. 97% for diabetes, respectively) [8].

In one study, 11 COVID-19 pneumonia patients with diabetes died, compared to 7 COVID-19 pneumonia patients without diabetes, who perished at a rate of 5.7%. In research published on January 29, 2020, Guan *et al.* examined 1099 patients with lab-confirmed Covid-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China. The most prevalent symptoms were fever (43.8 percent upon admission and 88.7% while in the hospital), cough (67.8%), and didiarrhea3.8 percent). There has been evidence of a severe version of the disease in the elderly and people with comorbidities. In all, 15 deaths (1.4%) were reported in this study. The patient who was reported from the United States had the virus in his respiratory and faecal samples; he had respiratory failure and required oxygen assistance.

From asymptomatic to severe, the sickness can range in severity; a significant portion of those with a clinically obvious infection go on to develop a serious illness. Due to the unknown total number of cases, which includes undiagnosed individuals with milder illnesses, the case fatality rate (mortality rate among diagnosed patients) has a broad range [9, 10]. A study done in England (UK) found that type 2 diabetes was present in 32% and type 1 diabetes was present in 15% of COVID-19 patients dying in hospitals, with odds of death being 203 and 35 times higher than for those without diabetes, respectively [11, 12]. French patients in the CORONADO trial had type 1 diabetes in 23.3%, type 2 diabetes in 88.5%, other types of diabetes in 5.4%, and type 2 diabetes in 3.1%. Diabetes was connected to an increased mortality risk. A lower risk of death has been associated with anti-diabetic medications [13]. Acute diabetes is caused by SARS-CoV-2 virus infection, which, according to multiple studies, damages pancreatic islet cells [14]. Diabetes and COVID-19 pneumonia patients' clinical characteristics and prognoses were uncommon till recently in India.

MATERIALS AND METHODS

This study was conducted after getting approval from the Institutional human ethics committee (Approval No. 56/IHEC/2020). From October 2020 to April 2021, this cross-sectional study was conducted at the KMCH Institute of Health Sciences and Research in Coimbatore after participant consent. This study comprised 72 COVID-19 patients of both genders who had diabetes and were taking antidiabetic medications (oral or/and insulin) for their disease, with or without other concomitant conditions. Under no circumstances has any patient information been released. Patients with COVID-19 who were under the age of 18 were not included in the study.

Methods

Anonymized data from the medical records of all COVID-19 patients with diabetic infections were entered and analyzed using a data collecting tool after receiving consent from the institution's human ethical council. Based on plasma blood glucose levels upon admission, the cases were split into managed and uncontrolled diabetic groups, and the differences between the groups were compared.

The following data were entered

- Clinical profile (Symptoms, Signs, comorbidities, O2 saturation, plasma blood glucose, HbA1c, duration of hospital stay, systolic and diastolic blood pressure, CORADS score)
- Treatment outcome (i.e. ICU admissions, severity, death) (i.e. ICU admissions, severity, mortality)

Statistical analysis

SPSS software version 26 was used to evaluate the data that had been collected. Clinical profiles and outcomes of patients with and without diabetes underwent descriptive analysis.

Table 1: Distribution of the study population according to various clinical profiles and treatment outcome parameters

Parameter	Controlled diabetics (38)		Uncontrolled diabetics (34)		CSV	P value
	Number	%	Number	%		
Symptoms and signs						
Fever	36	94.74	34	100.00	1.841	0.175
Sore throat	32	84.21	30	88.24	0.243	0.622
Cough	18	47.37	16	47.06	0.001	0.98
Headache	16	42.11	19	55.88	1.363	0.24
Loose stools	4	10.53	5	14.71	0.287	0.59
Loss of taste and smell	21	55.26	19	55.88	0.003	0.96
Fatigue	30	78.95	31	91.18	2.073	0.15
Breathlessness	11	28.95	19	55.88	5.356	0.02*
CORADS						
1	12	31.58	2	5.88	21.026	0.0008***
2	10	26.32	3	8.82		
3	6	15.79	5	14.71		
4	5	13.16	4	11.76		
5	3	7.89	10	29.41		
6	2	5.26	11	32.35		
ICU						
Needed	9	23.68	18	52.94	6.554	0.01*
Not needed	29	76.32	16	47.06		
Severity						
Mild	18	47.36	7	20.58	6.534	0.038*
Moderate	11	28.94	9	26.47		
Severe	9	23.68	16	47.05		
Mortality						
Yes	0	0	1	2.94		
NO	38	100	33	97.06		
Comorbidities						
Hypertension	8	21.05	7	20.59	0.002	0.96
Bronchial asthma	2	5.26	3	8.82	0.352	0.55
Coronary artery disease	3	7.89	1	2.94	0.839	0.36
Chronic kidney disease	1	2.63	0	0.00	0.907	0.34

Values are expressed as number and percentage, p value is indicated as *p<0.05, ** p<0.01, ***p<0.001

RESULTS

Controlled diabetics had a mean plasma glucose of 112.22±11.41, while uncontrolled diabetics had a mean plasma glucose of 154.2±23.22. Fever was the most prevalent symptom in the managed diabetes patients (94%) and was followed by sore throat (84%), fatigue (78%), loss of taste and smell (55%), cough (47%), headache (42%), breathlessness (28%), and loose stools (10.5%). Even in diabetes patients with uncontrolled blood sugar levels, fever (100%) was the most prevalent symptom, followed by sore throat (88%), dyspnea (55%), headache (55%), loss of taste and smell (55%), cough (47%), and loose stools (14.7%). In patients with uncontrolled diabetes compared to those with controlled diabetes, breathlessness is considerably higher ($p<0.05$).

When 34 uncontrolled diabetics are scored using CORADS, 11 of them have CORADS 6 (32.35%), compared to just 2 of the 38 controlled diabetics (5.26%), which is considerably higher ($p<0.01$). While only 11 patients in the uncontrolled diabetic group had co-morbidities such as hypertension (20.59%), bronchial asthma (8.82%), coronary artery disease (2.94%), and no chronic kidney disease, 14 patients (14.28%) in the controlled diabetic group had underlying comorbidity in the form of hypertension (21.05%), bronchial asthma (5.26%), chronic kidney disease (2.63%), or coronary artery disease (7.89%) (table 1).

In patients with controlled diabetes, the average length of stay is 10.43 d; in patients with uncontrolled diabetes, it is 7.22 d; and so on. In uncontrolled diabetics, the length of hospital stay is much longer ($p<0.001$). In controlled diabetes, the mean SPO2 was 99.24±0.81, but in uncontrolled diabetics, it was 96.11 2.32. Compared to diabetics with controlled blood sugar, uncontrolled patients' SPO2 dramatically dropped ($p<0.001$) (table 2).

Only 8 of the controlled diabetic patients (23.68%) required ICU admission, compared to 18 of the uncontrolled diabetic patients (52.94%). Those with uncontrolled diabetes are more likely to be admitted to the ICU than patients with controlled diabetes ($p<0.05$). As opposed to uncontrolled diabetics, who had mild (20.58%), moderate (26.47%), and severe (47.05%) severity, controlled diabetics had mild (47.30%), moderate (28.94%), and severe (23.68%) severity. In uncontrolled diabetes compared to controlled patients, the severity was considerably higher ($p<0.05$). One person who had uncontrolled diabetes died, although no one who had controlled diabetes did (table 1).

Table 2: Distribution of study population according to other socio-demographic parameters

Parameter	Controlled diabetics		Uncontrolled diabetics		Mean difference	T value	P value
	Mean	SD	Mean	SD			
Age	42.4	17.42	44.7	15.71	2.3	-0.586	0.560
Plasma glucose	112.22	11.41	154.2	23.22	42.01	-9.902	0.001*
SBP	127.22	11.21	129.81	14.23	2.59	-0.862	0.391
DBP	82.41	8.42	84.22	9.83	1.81	-0.841	0.403
SPo2 at the time of presentation to the ER	99.24	0.81	96.11	2.32	3.13	7.81	<0.001**
Duration of hospital stay	10.43	1.82	7.22	1.04	3.21	9.044	<0.001****

Values are expressed as mean and standard deviation, p-value is indicated as *p<0.05, ** p<0.01,***p<0.001

DISCUSSION

The results of our investigation showed that diabetes affects how COVID patients respond to treatment. Fever was the most frequently reported symptom in both people with managed and uncontrolled diabetes, and all of the patients were symptomatic. Breathlessness and the requirement for ICU care were more common in patients with uncontrolled diabetes. The group of uncontrolled diabetics reported more than one death, indicating a severe illness. According to research conducted on a retrospective cohort of hospitalized patients in the UK (30), long-term anti-diabetic medications reduced COVID-19 mortality in diabetic patients, particularly because diabetic patients are more susceptible to cumulative organ injury from SARS-CoV-2 due to already compromised pulmonary, cardiac, and renal systems. In both groups, metformin was the most frequently used anti-diabetic drug, followed by sulfonylureas and insulin.

To fully comprehend the pathogenesis of both Covid-19 pneumonia and T2DM, we must carefully explore the pathogenic pathways of lung disease in T2DM patients. The lung's alveolar-capillary network may be a target of T2DM. T2DM in patients with lung illness causes micro-vascular damage. T2DM sufferers, however, frequently struggle with their breathing and have a higher risk of developing a range of pulmonary problems. When examining the molecular mechanisms behind microvascular injury in T2DM patients, we must take into account Systemic inflammation. Contrary to popular belief, insulin resistance and disordered glucose homeostasis in T2DM patients are the real causes of alveolar capillary microangiopathy and interstitial fibrosis [15].

Several molecular pathways have been postulated to explain the microvascular disease, endothelial dysfunction, and damage that follow in the lungs of T2DM patients. These pathways are all brought on by excessive inflammation. One of these pro-inflammatory endothelial pathways in the small capillaries is Interleukin 6 (IL-6). IL-6, a well-known biomarker of inflammation and metabolic inefficiency, has been suggested as a predictor of lung disease severity. Particularly, compared to non-T2DM people, T2DM patients show significantly higher plasma levels of IL-6. Currently, abnormal clot development in T2DM patients is connected to chronic, systemic inflammation. The coagulation profiles of T2DM samples are indeed noticeably more hyper-coagulable than healthy samples. Thus, uncontrolled inflammatory circulating molecules may contribute to a hypercoagulable state and vascular dysfunction in T2DM patients. It's interesting to note that higher interleukin and MMP-12 levels have separately been linked to several morphological and functional markers of organ damage to the cardiovascular system in T2DM patients. Additionally, targeting IL-6, a key member of the inflammatory cytokine network, may be a possible treatment strategy for the COVID-19-induced cytokine release syndrome [16, 17]. IL-6 expression may vary between patients in the ICU and those who are not in the ICU, and IL-6-blocking biological medicines may be utilized to measure IL-6 for risk assessment and therapy impact monitoring [18].

Notably, thromboembolic events and lowered lung function may arise with the development of Covid-19 pneumonia. Most frequently, T2DM patients exhibit these signs of microvascular endothelial dysfunction and damage. As of right now, these effects can reduce forced vital capacity, forced expiratory volume, lung diffusing capacity, and lung elastic recoil in T2DM patients in both a restrictive and an obstructive way.

The increasing trend in cases, hospitalizations, and mortality for T2DM patients following Covid-19 infection would seem to be logically explained by this pathogenic scenario. Furthermore, it suggests that lung disease in T2DM patients shares a relationship with IL-6 and hyperglycemia. These theories are supported by an ongoing and promising experimental therapy in Italy employing a monoclonal antibody against the IL-6 receptor, which appears to improve the severity of lung disease and prognosis in patients with Covid-19 infection. Since it can reduce IL-6 levels, tocilizumab, a monoclonal antibody against IL-6, is a helpful therapeutic option for Covid-19 patients who are at risk for cytokine storms. Tocilizumab, a monoclonal antibody against IL-6, has been suggested for repeated doses in critically sick patients with elevated levels of this cytokine [19].

Therefore, a more accurate and exact risk assessment is needed for patients with T2DM with Covid-19 infection. It is feasible to hypothesize that if people with T2DM were identified as a high-risk group during a Covid-19 infection, we may start a more aggressive course of treatment immediately away to lessen and control pulmonary and systemic inflammation. This might prevent people with T2DM from having a worse prognosis and decrease the course of lung disease. Most of the patients with controlled diabetics were on Metformin, Sulfonylureas and insulin.

It may be necessary to provide insulin intravenously for a longer amount of time in patients with T2DM with Covid-19 infection to enhance glucose homeostasis and clinical outcomes. Additionally, better glycemic control may lead to better insulin sensitivity and a better reaction from the patient to Covid-19. Not to mention, it's possible that this could improve the therapeutic outcome of the anti-IL-6 medication. These views, however, are speculative and need to be clarified in more ongoing trials on T2DM and Covid-19. Due to its single centre and smaller sample size, this study has some limitations. Additional research with a bigger sample size and at many centres is necessary.

CONCLUSION

According to Covid 19, persons with uncontrolled diabetes appear to be more likely to sustain lung damage, necessitating admission to the ICU, an extended stay in the hospital, and oxygen assistance throughout the duration of the illness. To dramatically improve outcomes in this vulnerable demographic that is disproportionately affected by COVID-19, enhancing our knowledge of anti-diabetic medications can be a beneficial and effective method.

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AUTHORS CONTRIBUTIONS

All the authors contributed equally to experimental work and manuscript preparation.

CONFLICTS OF INTERESTS

The authors declared there are no conflicts of interest.

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