Clinicoradiological Evaluation and Correlation of High-Resolution Computed Tomography Findings with Type 2 Diabetes Mellitus in Coronavirus Disease-19 Patients

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ABSTRACT

BACKGROUND

Type 2 diabetes mellitus (T2DM) has emerged as the leading comorbidity in patients with coronavirus disease 2019 (COVID-19). However, data obtained on the correlation between the incidences of T2DM with COVID-19 are limited. We wanted to assess the severity of patients with T2DM and COVID-19, and study the correlation between the high-resolution computed tomography (HRCT) findings and hyperglycaemia with disease severity.

METHODS

This cross-sectional study included 100 patients with a history of diabetes and diagnosed COVID-19 positive. Data were collected using a semi-structured questionnaire. $P < 0.05$ was considered statistically significant.

RESULTS

The mean age was 58.81 ± 11.43 years with male preponderance (71 %). The difference was statistically significant in mean glycated haemoglobin (HbA1c) (7.32 ± 1.39 %, $P < 0.001$), mean high - density lipoprotein (HDL ; 39.78 ± 6.76 mmol / L), low - density lipoprotein (LDL; 63.23 ± 13.36 mmol / L), and triglyceride (TG; 140.70 ± 43.57 mg / dL) levels ($P < 0.05$) in different CT severity score. Mean HbA1c ($P < 0.001$), LDL, and CT severity scores ($P = 0.034$ and $P < 0.001$) were highly significant in patients who died than the discharged patients. A significant positive correlation was seen between CT severity score with HbA1c, LDL, and TG levels and chances of death ($P < 0.001$) rates, and also between the patients who died and HbA1c ($P < 0.001$) and LDL ($P = 0.034$) levels and CT severity score ($P < 0.001$).

CONCLUSIONS

Ideal management of the metabolic equilibrium of glucose was crucial in assuring an improved clinical outcome. Increased surveillance was warranted for diabetic COVID-19 patients.

KEY WORDS

COVID-19, Glycated Haemoglobin A, Hyperglycaemia, Severe Acute Respiratory Syndrome Coronavirus 2

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BACKGROUND

The rapid outbreak of coronavirus disease 2019 (COVID-19), which resulted from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has resulted in a public health emergency of international concern.[1] COVID-19 has contributed to a huge adverse impact globally. COVID-19 infections can lead to diverse clinical outcomes from asymptomatic to severe life-threatening course or even death.[2] Based on the evidence of rapidly increasing incidence of infections and the probability of asymptomatic carriers transmission, SARS-CoV-2 can be transmitted effectively among humans and exhibits a high potential for a pandemic.[3-6] COVID-19 is distinguished by quick onset of symptoms which may include fever, fatigue, cough, dyspnoea, and chest tightness.[4] A notable impact of comorbidities of chronic diseases on the clinical consequences in patients with COVID-19 infection has been suggested by evidence. According to COVID-19 reports from the Centres for Disease Control and Prevention of the US Department of Health and Human Services, type 2 diabetes mellitus (T2DM) and metabolic syndrome patients may have up to 10 times higher risk of death when infected with COVID-19.[7] T2DM is a common chronic metabolic disease. In India, there are about 69.2 million people with diabetes and are expected to cross 123.5 million by 2040.[8]

T2DM and the associated microvascular and macrovascular complications are the leading causes of mortality and morbidity all over the world. The incidence of contracting infections is more in T2DM patients as it has a clear cut compromised immune dysfunction, which might be accounted for multiple complications.[9] Respiratory infections like pneumonia, tuberculosis and influenza are more common and more serious in older people with T2DM.[10] Diabetes mellitus is a chronic inflammatory state having multiple metabolic and vascular abnormalities which may alter host response to pathogens. Increased synthesis of cytokines, oxidative stress and adhesion molecules promoted by hyperglycaemia and insulin resistance may lead to a higher predisposition to infections in T2DM patients.[11] The clinical and imaging manifestations are particularly important in the preliminary stages of COVID-19. Chest computed tomography (CT) scans, particularly the high-resolution computed tomography (HRCT) scans help in diagnosing patients with COVID-19 infections in an early stage when clinical symptoms may be non-specific.[12,13] They also have significant prognostic importance, especially in co-morbid patients. These can be employed to confirm the diagnosis, adjust the treatment plan, and predict clinical recovery or progression of disease in patients with COVID-19 infection, particularly those with T2DM.

The prevalence of diabetes in India is high, and there is a paucity of literature on its association with COVID-19. This warrants identification of factors responsible for the severe outcome in such patients. Hence, the present study intended to assess the severity of patients with diabetes and COVID-19 and correlate HRCT findings and hyperglycaemia with disease severity.

METHODS

A cross-sectional study was carried out on 100 COVID-19 patients who were admitted to the hospital for 6 months from May 2020 to October 2020 at the Department of Medicine in a tertiary care hospital and teaching institute in a metropolitan city in Western Maharashtra. Patients of both genders aged more than 18 years with a history of diabetes diagnosed as COVID-19 positive were included in the study. Patients with other critical illnesses, type 1 diabetes mellitus, and patients who were unwilling to participate in the study were excluded. The sample size was based on the assumption of a moderate positive correlation of 0.3 between CT severity score and hyperglycaemia with a 5 % level of significance and 85 % power to attain a minimum sample size of 96 patients. Ethical clearance was taken from the institutional ethics committee.

Statistical Analysis

Data on CT severity grades were collected using a semi-structured pre-tested questionnaire. The data collected were entered in Microsoft Excel and were represented in frequencies and percentages, charts, and graphs. Mean and standard deviation (SD) of quantitative variables were recorded. Appropriate statistical tests were applied using SPSS software version 21 for data analysis. The student's t-test was used for comparison wherever applicable. Pearson's correlation was used for correlation analysis and $P < 0.05$ was considered statistically significant.

RESULTS

A total of 100 COVID-19 patients admitted to the hospital were recruited for this study. The mean age of the study participants was 58.81 ± 11.43 years. There were 71 males (71 %) and 29 females (29 %) in this study. Mean glycated haemoglobin (HbA1c) of the study participants was 7.32 ± 1.39 %, mean high-density lipoprotein (HDL) was 39.78 ± 6.76 mmol/L, mean low-density lipoprotein (LDL) was 63.23 ± 13.36 mmol/L, and mean triglycerides (TG) was 140.70 ± 43.57 mg/dL, respectively. Based on the CT severity and age, mean age in patients with mild CT was 57.06 ± 13.96, moderate CT was 58.26 ± 10.53, and severe CT was 59.67 ± 12.83 years, respectively.

Based on the CT severity grading, out of all participants, 46 cases had mild (46 %), 42 cases had moderate (42 %), and 12 cases had severe (12 %) lung involvement on HRCT (figure 1). A significant difference was observed in the mean HbA1c levels of the patients with different CT severity grades ($P < 0.001$). Table 1 shows that mean HbA1c was found higher in severe and moderate patients as compared to mild grade patients.

A significant difference was observed in mean HDL, LDL, and TG levels in different CT severity score patients ($P < 0.05$). Mean HDL in mild severity cases was higher as compared to the moderate and severe CT severity grades. In terms of LDL levels, mean LDL in mild severity cases was lower than moderate and severe cases. Similarly, mean TG levels in mild severity cases were lower than moderate and

severe cases. The overall results showed that in the severe group, mean HDL was lowest and mean LDL and TG levels were highest in comparison to mild and moderate groups (table 2).

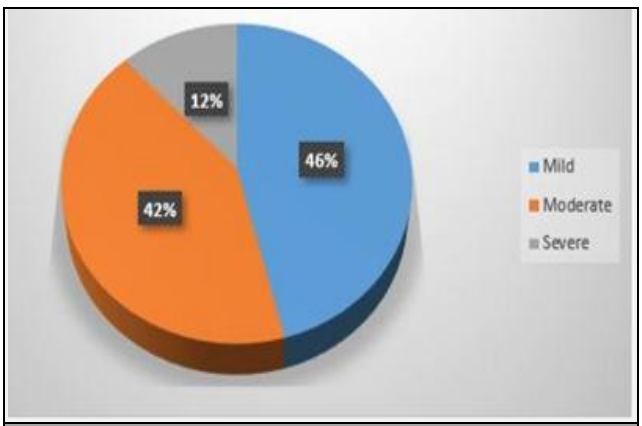

Figure 1. CT Severity Grades, CT Computed Tomography

CT Severity Grade	HbA1c (%) Mean ± SD
Mild	6.55 ± 0.61
Moderate	7.36 ± 1.39
Severe	8.43 ± 1.58
p < 0.001* [t test between mild and severe & moderate and severe]	

Table 1. CT Severity and HbA1c

CT, Computed tomography; HbA1c, Hemoglobin A1c
*p < 0.05 was considered statistically significant

CT Severity Grade	HDL (mmol/L) (mean ± SD)	LDL (mmol/L) (mean ± SD)	TG (mg/dL) (mean ± SD)
Mild	41.29 ± 6.08	52.24 ± 7.84	132.29 ± 32.12
Moderate	39.85 ± 7.01	64.97 ± 13.29	141.35 ± 46.46
Severe	36.33 ± 4.19	69.67 ± 10.94	151.22 ± 33.95
p-value [t test between mild and severe & moderate and severe]	0.010*	< 0.001*	< 0.001*

Table 2. CT Severity and Lipids

CT, Computed tomography; HDL, High - density lipoprotein; LDL, Low - density lipoprotein; TG, Triglycerides
*P < 0.05 was considered statistically significant

The difference observed in mean HbA1c levels, mean LDL levels, and mean CT severity score of patients who had died with respect to the prognosis of patients was statistically significant as compared to those patients who were discharged.

The mean HbA1c levels were highly significant (P < 0.001) in patients who died in comparison to those patients who were discharged. Similarly, the mean LDL levels and mean CT severity scores were also observed to be statistically significant (P = 0.034 and P < 0.001) in patients who died than those patients who survived. Table 3 shows that the difference was statistically insignificant in terms of HDL and TG levels and age.

Variables	Death / Discharge	N	Mean	Std. Deviation	P - Value
HbA1c (%)	Death	5	10.16	2.03	<0.001*
	Discharged	95	7.20	1.27	
HDL (mmol/L)	Death	5	36.20	4.02	0.228
	Discharged	95	39.97	6.87	
LDL (mmol/L)	Death	5	75.60	7.89	0.034*
	Discharged	95	62.58	13.37	
TG (mg/dL)	Death	5	162.60	35.73	0.253
	Discharged	95	139.55	44.03	
CT severity score	Death	5	17.40	1.82	<0.001*
	Discharged	95	8.55	4.66	
Age (years)	Death	5	64.60	11.72	0.250
	Discharged	95	58.51	11.46	

Table 3. Prognosis of the Patient

HbA1c, Haemoglobin A1c; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; TG, Triglycerides
*P < 0.05 was considered statistically significant

Pearson correlation between CT severity scores and different variables are presented in Table 4. A statistically significant positive correlation was noted between the CT severity score and HbA1c, LDL, and TG levels, and chances of death (P < 0.001). Similarly, regarding death, a statistically significant positive correlation was observed between the patients who died and HbA1c (P < 0.001) and LDL (P = 0.034) levels and CT severity score (P < 0.001). These results demonstrated that patients with higher CT severity scores had higher HbA1c, LDL, and TG levels and higher chances of death and patients with high HbA1c and LDL levels and CT severity scores had higher chances of death due to COVID-19 (table 4).

Correlations		Age	HbA1c	HDL	LDL	TG	CT Severity Score	Death
CT severity score	Pearson Correlation	0.088	0.537	- 0.137	0.506	0.197	1	0.391*
	p - value	0.383	< 0.001*	0.175	<0.001*	0.049		<0.001*
	N	100	100	100	100	100	100	100
Death	Pearson Correlation	0.116	0.445	- 0.122	0.212	0.115	0.391	1
	p - value	0.250	< 0.001*	0.228	0.034*	0.253	<0.001*	
	N	100	100	100	100	100	100	100

Table 4. Pearson's Correlation

*Correlation is significant at the 0.05 level (2 - tailed).
CT, Computed tomography; HbA1c, Haemoglobin A1c; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; TG, Triglycerides
*p < 0.05 was considered statistically significant

DISCUSSION

COVID - 19 is characterized by high morbidity and mortality particularly in patients with severe comorbidities like diabetes. Epidemiological data has revealed that diabetic patients are at higher risk of severe clinical outcomes of COVID-19. The presence of diabetes mellitus was observed to be independently associated with COVID-19 severity and increased mortality.[14-17] Also, diabetes mellitus patients generally fall into higher categories of SARS-CoV-2 infection severity in comparison to those without diabetes mellitus.[18,19] As a result, understanding the interactions between diabetes and COVID-19 will be crucial to help, protect, and manage people with diabetes or at high risk of metabolic dysfunction. Combining imaging assessments with clinical and laboratory findings could help identify SARS-CoV-2 infections early.

In the current study, mean HbA1c levels were highly significant (P < 0.001) with different CT severity grades. Wu et al. reported mean HbA1c levels as 9.2 % which was higher than the current study levels. Higher HbA1c levels could be associated with inflammation, hypercoagulability, and low arterial oxygen saturation (SaO_2) in COVID-19 patients.[20] The mean HDL levels were lower in the severe group and mean LDL and TG levels were higher as compared to mild and moderate groups in the present study. Hu et al. reported reduced HDL levels and increased LDL levels in patients with COVID-19.[21] The higher LDL and TG levels and lower HDL levels could be attributed to the fact that patients with such comorbidities are at higher risk for COVID-19.

In the present study with reference to the Pearson correlation, a significant positive correlation was observed between the CT severity score and HbA1c, LDL, and TG levels and chances of death. These results indicated that patients with higher CT severity scores have higher HbA1c, LDL, TG

levels and higher chances of death. According to Wang et al. COVID-19 disease severity as assessed on CT severity score showed a positive correlation with hyperglycaemia and dyslipidemia, which is in line with the current study.[22]

The present study provides the first direct evidence supporting the frequency of the coexistence of T2DM in patients with COVID-19. Another novel finding in the present study is the potentiated severity in COVID-19 patients with metabolic comorbidities. Although previous studies have reported diabetes as one of the most common comorbidities in patients with SARS-CoV-2 infections, the pathophysiological consequence of the close association between diabetes and COVID-19 progressions remains elusive.[23-25] Thus, the current study demonstrated that diabetes and its associated metabolic complications play a significant role in enhanced morbidity and mortality in COVID-19 patients.

CONCLUSIONS

As many countries continue to struggle with the COVID-19 pandemic while others begin to relax the norms with strict measures of social distancing, recognizing high-risk populations is crucial to successfully control this disease. Being vigilant on patients with diabetes and a raised HbA1c level, while permitting a more humane method to patients with the well-managed disease may manifest favourable outcomes in decreasing the social and economic burdens related to an unsystematic method. The authors found a strong correlation between COVID-19 severity and glycemic control. Strict sugar control is needed to prevent complications in COVID-19 patients. Moreover, once a vaccine is available, concentrating on those who are at the highest risk for severe COVID-19 will be crucial to efficiently control this disease.

Limitations

However, the current study has few limitations. Firstly, the study included data collection using a questionnaire, which could result in inaccurate and incomplete information and the rate of non - response could be high. Secondly, the sample size was relatively small. Therefore, the findings observed in this study warrant further validation through future studies with large sample size.

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