

Association of HbA1c with HRCT Thorax among Diabetic and Non-Diabetic COVID Patients

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Abstract

Introduction and objectives: Diabetes mellitus is a multiorgan disease which is slowly growing as a major disease burden on world health. COVID-19 is an active deadly pandemic that is still threatening human lives. It has been observed that the interaction of these two slow and rapid pandemics together leads to severe mortality and morbidity. The study was done to assess the severity of COVID disease in diabetic and non-diabetic patients according to HRCT severity score and duration of hospital stay.

Methods: This retrospective single centred case control study was conducted in SVBP hospital and LLRM Medical College, Meerut in admitted patients during September 2020 to May 2021 of COVID-19 disease. The calculated sample size came out to be 81. So, 81 COVID positive diabetic patients were enrolled and an equal number of non-diabetic Covid patients were taken as control. In our study, association of HbA1c with CT severity score and their duration of hospital stay was studied.

Results: It was observed that the HRCT severity score was more in the uncontrolled than in controlled diabetic group of Covid patients. The association of HRCT severity score with various HbA1c levels among diabetic and non-diabetic patients was significant with p value of 0.029. Similarly, the duration of hospital stay was associated with HRCT severity score significantly. HRCT severity score was raised in both the groups diabetic and non-diabetic with significant p value of 0.001 and 0.008 respectively.

Conclusion: COVID-19 disease with diabetes is a lethal combination. Association of HRCT severity score is significantly associated with increasing HbA1c levels rather than diabetes status. Poor glycaemic control can lead to severe disease related complications. Duration of hospital stay was significantly associated with HRCT severity score among both diabetic and non-diabetic Covid patients. Thus, in known diabetic patients with strict glycaemic control, early CT-imaging of the disease severity can have better outcomes in COVID pandemics.

Key words: COVID-19 disease, diabetes mellitus (DM), HRCT severity score.

Introduction

COVID-19 disease was a pandemic caused by the novel SARs-COV-2 discovered in December 2019 in Wuhan, China. COVID-19 infection was highly contagious and communicable which had spread around the world, within weeks. Amongst COVID-19 infected patients, majority of the patients had milder symptoms, but few patients had severe illness including respiratory distress as major killer. COVID-19 disease caused huge death tolls¹ in elderly and co-morbid patients. In India, from 3 January 2020 to 6:07 pm CEST, 31 May 2023, there have been 44,990,278 confirmed cases of COVID-19 with 5,31,867 deaths, reported to WHO². Diabetes mellitus is a chronic multi-system disease, which is caused by inadequate or inappropriate insulin synthesis and metabolism in the body. The resultant hyperglycaemia causes serious damage to various organ systems of the body and results in dysfunction of the immune system. This leads to failure of protection from pathogenic invasions and infections³. Diabetes mellitus forms a major portion

of non-communicable disease and causes large mortality and morbidity worldwide. Diabetic people are more likely to develop serious complications with COVID-19 infection⁴. Therefore, this study was done to see the association of HRCT severity score in COVID-19 patients with HbA1c. HRCT thorax is one of the main diagnostic tools for COVID-19 severity grading as well as prognosis. On HRCT thorax scan, infected individuals generally showed a multifocal or mono-focal involvement of ground-glass opacity (GGO)⁵. HRCT thorax had been widely accepted for prognostication of COVID-19 pneumonia⁶. Several remarkable chest CT findings had been reported in more than 70% of RT-PCR test-proven COVID-19 cases, including ground-glass opacities, vascular enlargement, bilateral abnormalities, lower lobe involvement, and posterior predilection⁷. The severity of the lung involvement on the CT correlates with the severity of the disease. HRCT thorax imaging severity scores of >18 have been linked to higher risks of death and have been found to be better predictor of death among diabetic COVID-19

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patients⁸. HRCT thorax is sensitive in identifying the lung involvement in the early stages of Corona virus disease. It is used for the screening and diagnosis of clinically suspicious COVID-19 patients^{9,10}. Though, chest CT scans have been found normal sometimes¹¹. This pictorial essay aims to overview the various spectrums of HRCT patterns in COVID-19 pneumonia. Therefore, an important diagnostic tool like HRCT thorax was undertaken to study the correlation of such ongoing long COVID disease symptoms with its severity at initial and acute phase along with various parameters. HRCT severity score was classified as mild with CT severity score (CTSS) < 8, moderate (CTSS 9 - 16) and severe (CTSS 16 - 25) grading on the basis of the scale 0 - 25.

Aims and objectives

1. To evaluate the correlation of HbA1c with HRCT thorax severity score among diabetic and non-diabetic COVID patients.
2. To study the correlation of HRCT severity score with duration of hospital stay of COVID patients with or without diabetes.

Material and Methods

This retrospective case and control single-centered study was done with 162 admitted COVID patients in the tertiary COVID care SVBP hospital during March 2020 to June 2021. The ethical clearance was taken from Ethical committee of the institution LLRM Medical College, Meerut with no./sc-1/2022/7830. The Sample size was calculated as per the formula $\text{sample size} = z^2 p(1-p)/d^2$, where z is the level of confidence taken as 95%. According to a published study, Prevalence (p) of positive HRCT findings in COVID positive patients was taken as 70% and respectively (1-p) as 30%. Considering absolute precision (d) as 10%, sample size was calculated to 80.67^{12,13}.

After considering the exclusion criteria, 81 COVID positive diabetic patients were taken as the cases and 81 COVID positive non-diabetic patients as the control. Patients admitted in this hospital during this COVID phase were selected and taken as cases and control. Their demographic, clinical details, laboratory investigations were recorded and radiological imaging was done. Patients were divided into four groups based on HbA1c values. Various blood investigations including ESR, CRP, LFT, KFT, HbA1c and radiological investigations HRCT severity score, CXR PA views were done. The data was collected with the help of questionnaire and was entered in Microsoft Excel Spreadsheets. Statistical tests were applied using SPSS software and chi square value (with confidence interval of

95% and p value < 0.05) was calculated to assess the associations of this study.

Inclusion criteria:

CASE

- Patients who are known cases of diabetes mellitus who had COVID-19 infection
- Age more than >18 yrs

CONTROL

- Patients who are not a known case of diabetes mellitus and had COVID-19 infection
- Age more than >18 yrs

Exclusion criteria:

- Non COVID-19 patients
- ARDS cause other than COVID-19 infection
- Pregnant female
- Active immunological disease
- Evidence of clinical cardiovascular disease (cardiac, cerebral or peripheral vascular disease).
- Immuno-compromised group.
- People with known malignancies.
- Age less than < 18 years and more than > 65 years.

Results

A total of 162 laboratory confirmed COVID-19 patients were enrolled in this study, out of which 81 were diabetic (cases) and 81 were non diabetic (control).

In the cases, i.e., diabetic COVID group 4 cases (4.9%) of the total 81 cases belonged to the age group of (18 - 25 years), 41 cases (50.6%) belonged to the age group of (26 - 50 years) and the remaining 36 cases (44.4%) belonged to the age group of (51 - 65 years).

In the controls, i.e., non diabetic COVID group, 18 cases (22.2%) of total 81 controls belonged to the age group of (18 - 25 years), 35 cases (43.2%) belonged to the age group (26 - 50 years) and 28 cases (34.6%) belonged to the age group (51 - 65 years).

This difference between age groups was significant (with p value of 0.006), i.e., our study had more people of the age above 26 years.

There are 31 (38.3%) females and 50 (61.7%) males in the diabetic group. Non-diabetic group comprised 28 (34.6%) females and 53 (65.4%) males. Males are more than females

but this difference between genders was non-significant (with p value of 0.624).

Table I: HRCT severity score according to HbA1c of the diabetic COVID patients and non-diabetic COVID patients.

COVID patients	HRCT SEVERITY GRADING								p-value
	Mild score		Moderate score		Severe score		Total		
	No.	%	No.	%	No.	%	No.	%	
Non-diabetic (HbA1c < 5.4%)	25	49.02%	22	43.14%	4	7.84%	51	100%	0.029
Pre-diabetic (HbA1c 5.4 - 6.7%)	20	66.67%	8	26.67%	2	6.67%	30	100%	
Controlled diabetic (HbA1c 6.7 - 8%)	7	35.00%	12	60.00%	1	5.00%	20	100%	
Uncontrolled diabetic (HbA1c > 8%)	23	37.70%	25	40.98%	13	21.31%	61	100%	
Total	75		67		20		162		

Table I shows that, out of 81 diabetic COVID cases 20 patients, i.e., 24.69% patients had controlled diabetes that is HbA1c between 6.7 - 8% and 61 patients (75.31%) had uncontrolled diabetes with HbA1c more than 8%.

Out of 20 controlled diabetic COVID patients, 7 patients (35%) had mild HRCT score, 12 patients (60%) had moderate HRCT score and 1 patient (5%) had severe HRCT score.

Out of 61 uncontrolled diabetic COVID patients, 23 (37.7%) patients had mild HRCT severity score, 25 (40.98%) patients had moderate severity score and 13 (21.31%) patients had severe severity score.

It also shows out of 81 non-diabetic COVID control patients 51 (62.96%) patients were non-diabetic that is HbA1c < 5.4% and 30 patients (37.04%) were pre-diabetic with HbA1c 5.4 - 6.7%.

Out of 51 non-diabetic COVID patients, 25 (49.02%) patients had mild HRCT score, 22 (43.14%) patients had moderate HRCT score and 4 (7.84%) patients had severe HRCT score.

Out of 30 pre-diabetic COVID patients, 20 (66.67%) patients had mild HRCT severity score, 8 (26.67%) patients had moderate severity score and 2 (6.67%) patients had severe severity score.

The association of the HRCT severity score with various HbA1c level patient groups came out as statistically significant with p value of 0.029.

Table II shows that, out of 81 diabetic COVID cases, 30 (37.04%) patients had a Mild HRCT severity score that is less than 8/25, 37 patients (45.67%) had moderate HRCT severity score with score 9 - 16/25, 14 (17.28%) patients

had severe HRCT severity scores.

Table II: Shows association of duration of hospital stay with HRCT severity score in diabetic and non-diabetic COVID patients.

Duration of hospital stay in COVID patients	HRCT Severity grading								p-value
	Mild		Moderate		Severe		Total		
	No	%	No	%	No	%	No	%	
Diabetics 1 week	21	80.77%	3	11.54%	2	7.69%	26	100%	0.001
2 weeks	8	23.53%	23	67.65%	3	8.82%	34	100%	
>3 weeks	1	4.76%	11	52.38%	9	42.86%	21	100%	
Total	30		37		14		81		
Non-diabetics 1 week	17	80.95%	4	19.05%	0	0.00%	21	100%	0.008
2 weeks	26	54.17%	19	39.58%	3	6.25%	48	100%	
>3 weeks	2	16.67%	7	58.33%	3	25.00%	12	100%	
Total	45		30		20		162		

Out of 26 diabetic COVID patients, who had 1 week hospital stay, 21 (80.77%) patients had mild HRCT score, 3 (11.54%) patients had moderate HRCT score, 2 (7.69%) patients had severe HRCT score.

Out of 34 diabetic COVID patients, who had 2 weeks hospital stay, 8 (23.53%) patients had mild HRCT score, 23 (67.65%) patients had moderate HRCT score and 3 (8.82%) patients had severe HRCT score.

Out of 21 diabetic COVID patients, who had more than 3 weeks hospital stay, 1 (4.76%) patient had mild HRCT score, 11 (52.38%) patients had moderate HRCT score and 9 (42.86%) patients had severe HRCT score. There is an increase in duration of hospital stay as per increasing grade of HRCT severity scores in diabetic COVID patients. The association of this HRCT severity score with duration of hospital stay in diabetic COVID group is highly significant with p value of 0.001.

It also shows that out of 81 non-diabetic COVID control patients, 45 (55.56%) patients had a Mild HRCT severity score that is less than 8/25, 30 patients (37.04%) had moderate HRCT severity score with score 9 - 16/25, 6 (7.40%) patients had severe HRCT severity scores.

Out of 21 non-diabetic COVID patients, who had 1 week hospital stay, 17 (80.95%) patients had mild HRCT score, 4 (19.05%) patients had moderate HRCT score, 0 (0.0%) patients had severe HRCT score.

Out of 48 non-diabetic COVID patients who had 2 weeks hospital stay, 26 (54.17%) patients had mild HRCT score, 19 (39.58%) patients had moderate HRCT score and 3 (6.25%) patients had severe HRCT score.

Out of 12 non-diabetic COVID patients, who had more than

3 weeks hospital stay, 2(16.67%) patients had mild HRCT score, 7 (58.33%) patients had moderate HRCT score and 3 (25.0%) patients had severe HRCT score. There is an increase in duration of hospital stay as per increasing grade of HRCT severity scores in non-diabetic COVID patients. The association of this HRCT severity score with duration of hospital stay in non-diabetic COVID group is highly significant with p value of 0.008.

Discussion

Compared with the non-diabetic patients with COVID-19, the diabetic patients with COVID-19 had poorer prognosis and higher mortality. The Study of clinical and imaging characteristics of these patients is helpful to deepen our understanding of the mechanism of critical conditions of the COVID patients with diabetes. It also helps to promote, its early clinical diagnosis and better treatment.

The objective of this case control study was to assess the severity of COVID-19 disease in diabetic patients based on HRCT severity score and HbA1c levels. Most of the patients in diabetic group belonged to the age group of (26 - 50 years), i.e., 41 cases (50.6%) and in non-diabetic group most of the patients also belonged to the age group (26 - 50 years) 35 (43.2%) cases. This difference between age groups in this study was significant (with p value of 0.006), i.e., our study had more people of the age above 26 years. Statsenko *et al* stated with univariate analysis, that the risk of the non-mild COVID-19 was significantly higher ($p < 0.05$) in midlife adults and older adults compared to young adults¹⁴.

In our study, males are more than females in both diabetic and non-diabetic group.

This difference between genders was non-significant (with p value of 0.624). Similar study by Tabassum *et al* 2022 had an increased number of males (85.8%) and lesser number of females (14.2%)¹³. Further studies are needed involving an equal number of females and explore the outcomes in females. Statsenko *et al* showed increased severity in male¹⁴. Similar findings were seen in our study however more studies needed to be done before coming to any conclusion.

Among 81 patients of the diabetic group, (24.7%) 20 patients were controlled diabetic, i.e., with hbA1c level 6.7 - 8% and (75.3%) 61 cases were uncontrolled diabetic with hbA1c level > 8%.

Among 61 uncontrolled diabetic COVID patients, 13 (21.31%) patients were found to be having severe HRCT findings (i.e., score 16 - 25). Whereas 1 (5%) patient out of 20 controlled COVID diabetic patients had severe HRCT finding.

Among the control group, 2 (6.67%) patients out of 30 pre-diabetic COVID patients and 4 (7.84%) patients out of 51 non-diabetic COVID patients. This shows that poor glycaemic control status increases the risk and severity of COVID disease as compared to well controlled diabetics. Thus, it is an imperative to have strict glycaemic control during COVID pandemics.

A similar finding was seen by Rangankar *et al*, who had HRCT severity score of 220 patients, 41 patients had diabetes and 179 patients were non-diabetics. Out of 41 diabetics, severe form of COVID disease on HRCT severity score was found in 12 patients (29.3%), moderate disease in 16 patients (39%) and milder disease in 13 patients (31.7%). COVID disease was severe in 12 diabetic patients (29.3%) as compared to 20 non-diabetic patients (11.7%)¹⁵.

SARS COV-2 has shown to down regulate the ACE2 protein in diabetics and this might be the cause of poor clinical outcome in diabetes patients¹⁶.

In our study, out of 14 diabetic COVID patients, 9 patients having severe HRCT score stayed for more than 3 weeks, 3 (50%) patients with moderate HRCT score stayed for up to 2 weeks, 2 patients with mild CT score stayed for up to 1 week. Whereas out of 6 non-diabetic COVID patients 3 patients having severe HRCT score stayed for more than 3 weeks, 3 (50%) patients having moderate CT score stayed for up to 2 weeks. This difference was significant with p value 0.001 and 0.008 respectively.

A similar study by Saeed *et al*, which showed 3.9% and 4.7% COVID patients with severe and moderate HRCT score respectively, had a hospital stay of more than 16 days¹⁷.

Conclusion

COVID-19 is a lethal viral disease that infects and damages the lung parenchyma. The HRCT severity score of COVID-19 patient increases with poor diabetic control, i.e., HbA1c more than 8%. The association of HRCT severity scores with HbA1c level was very significant. It was found that the poor glycaemic control was significantly associated with the disease severity as well as hospital stay. So, strict glycaemic control should be observed during such COVID pandemics. The duration of hospital stay of diabetic COVID-19 patient increases with rising HRCT scores and this association was statistically significant. Thus, early HRCT imaging and scoring can prove useful in prognosticating, triaging and determining duration of hospital stay.

Limitations of this study: Small sample size is the limitation of this study. It should be done on larger sample size too.

Conflict of interest: The author has no conflict of interest

to disclose with respect to this study.

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