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Original Article

Radiology Section

Predictive Value of Chest CT Score in Assessing Disease Severity and Short-term Mortality in COVID-19 Pneumonia at a Tertiary Care Centre in Northern India: A Prospective Observational Study

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ABSTRACT

Introduction: Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) infection, also known as Coronavirus Disease-2019 (COVID-19) is the global pandemic, first described in Wuhan city of China in December 2019. Its diagnosis depends upon real time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). On chest Computerised Tomography (CT), it is almost similar to other viral pneumonia with extensive parenchymal involvement. Semiquantitative scores depicting this extensiveness of involvement could correlate with disease severity, laboratory parameters, mortality like Intensive Care Unit (ICU) admission, requirements of ventilatory support and longer hospital stay.

Aim: To define the role of chest CT score in determining disease severity, predicting poor prognosis and mortality of COVID-19 pneumonia in short-term follow-up.

Materials and Methods: This prospective study enrolled 547 admitted real time RT-PCR positive patients for COVID-19 at All India Institute of Medical Sciences, Rishikesh, India from 15th April 2021 to 31st May 2021. All patients were assigned semi-quantitative CT scores based on the extent of lung parenchymal involvement of 20 lung regions in chest CT. Finally, 205 patients were enrolled for the final analysis. Clinical severity was matched with chest CT scoring and laboratory findings. Survival curves along with univariate and multivariate analysis was applied to define the role of CT scoring in predicting short-term prognosis.

Results: Total 205 subjects were included in the study, of which the chest CT score showed a significant association with clinical severities (p-value <0.001). CT score was correlating significantly with increased serum C-Reactive Protein (CRP) (p-value=0.001) and D-dimer (p-value=0.01), and decreased lymphocyte count (p-value <0.001). A CT score ≥31 was found to be associated with an increased risk of mortality in both univariate and multivariate analysis {Odd Ratio (OR)=276.8; 95% Confidence Interval (CI)=45.21-1695.43; p-value <0.001}.

Conclusion: Chest CT score can be imaging measure of disease severity and predict a higher probability of mortality in score ≥31. It can also predict other defined variables of short-term prognosis. So, it has an advantage in speedy diagnostic workflow of symptomatic cases, timely referral of patients to higher centre, and better management of critical care resources.

Keywords: Coronavirus disease-19, Computed tomography severity score, Ground glass opacity

INTRODUCTION

The COVID-19 infection has resulted in 190,860,860 confirmed cases and 4,101,414 deaths as of 21st July 2020 [1]. The concern regarding high infectivity, morbidity and mortality with COVID-19 infection has resulted in worldwide lockdown to contain the spread of disease [2]. Currently, different parts of the world are preparing for the third and subsequent wave of infection including community transmission [1]. Fever, fatigue, cough and dyspnoea are the common clinically presenting complaints and quite similar to other respiratory virus infections, more specifically other coronavirus infections like Middle East Respiratory Syndrome (MERS) Coronavirus and SARS-CoV-2 [3,4].

On non contrast chest CT imaging, it resembles viral pneumonia as symmetrical involvement of lung parenchyma with Ground Glass Opacity (GGO), with or without associated consolidation, predominately in peripheral and posterior distribution [5,6]. Authors hypothesise that extent of lung parenchymal involvement, depicting as chest CT score could correlate with the clinical severity of COVID-19 infection and predicts disease outcome.

There is growing evidence of insensitivity of single RT-PCR testing for diagnosis of COVID-19 infection [7,8]. The sensitivity of RT-PCR testing depends upon sample collection technique and test's technical characteristics. Inadequate sampling is also an add-on to this cumbersome test when a quick diagnosis is sought. In symptomatic patients with the first RT-PCR negative test, chest CT imaging can be a supplement [9]. The relatively lower sensitivity of a single RT-PCR testing with a long turnaround time insinuates that a large bulk of COVID-19 patients could not be isolated quickly to contain the disease. Management of these patients based on the clinical severity.

The primary objective of the present research was to examine the role of CT score in assessing the disease severity and predicting short-term mortality. Secondary objective was to bring out a cut-off of CT score beyond which they had experienced a higher mortality in the present study population. Thirdly, its role in predicting other variables of prognosis like ICU admission, ventilatory support, and long hospital stay was also investigated.

MATERIALS AND METHODS

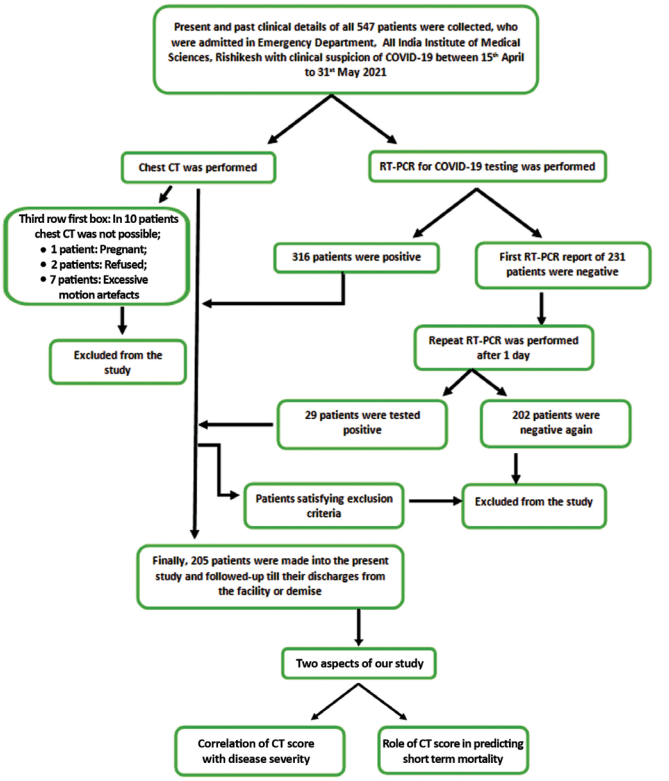
This prospective observational study was conducted in the Department of Radiodiagnosis and Imaging and Department of General Medicine at All India Institute of Medical Sciences, Rishikesh, India, from 15th April 2021 to 31st May 2021 after getting ethical clearance from Institutional Ethics Committee (letter No- AIIMS/IEC/20/441, Reg No: ECR/736/Inst/UK/2015/RR-18), following the principles of the Declaration of Helsinki.

Authors initially enrolled all patients who were admitted to the Emergency Department of the institute with clinical suspicion of COVID-19 infection during the study period (n=547). The criteria for clinical suspicion of COVID-19 infections were based upon guidelines laid by World Health Organisation (WHO) [10]. Informed consent was obtained from all patients before enrolment into the study.

Inclusion criteria: Patient admitted in the institute with clinical suspicion of COVID-19 infection.

Exclusion criteria: Two serial RT-PCR reports coming out to be negative with a gap of one day within them (As per our institutional protocol to say someone negative for COVID-19 infection), patients with primary and metastatic lung neoplasms, active pulmonary tuberculosis, any acute medical and surgical conditions that had independent risk of mortality were excluded from the study. Previously diagnosed with Interstitial Lung Disease (ILD) cases or patients with contraindication of CT scan, patients who refused for consent or had poor chest CT imaging due to excessive motion artifacts etc., were also excluded from the study.

Finally, 205 patients were enrolled for the study. During this study, all patients were managed with standard guidelines for clinical management and they were not enrolled in any other studies [Table/Fig-1].



[Table/Fig-1]: Flow diagram showing the present study design.

Clinical Workflow and Disease Staging

Detailed present and past clinical history, and vital parameters such as respiratory rate, pulse rate, oxygen saturation was maintained in predefined clinical sheets. Chest CT and laboratory investigation like complete haemogram, Arterial Blood Gas (ABG), serum level of acute phase reactants like C-Reactive Protein (CRP), D-dimer, Procalcitonin (PCT) and Lactate Dehydrogenase (LDH) was carried out routinely within one day of hospital admission. Whenever a first RT-PCR came negative, a repeat RT-PCR was done after a gap of one day.

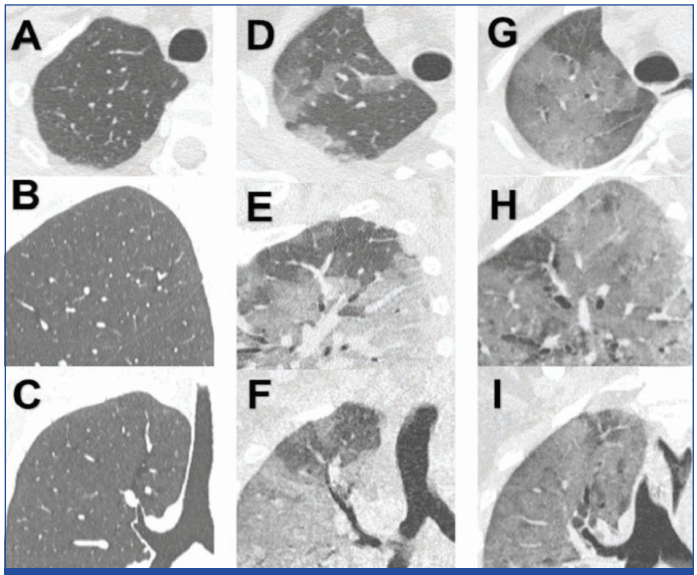
Disease severity classification was done using the Chinese Centers for Disease Control and Prevention (CDC) guidelines as mild, severe and critical [11]. To know the evolution of disease in chest CT, the course of the disease was divided into early (<7 days) and late (≥7 days) phase based on the days of symptoms [12]. All patients were followed for clinical progression throughout their hospital stay. Hospital stay was divided as short (<20 days) and long (≥20 days) [13].

In all stages blinding was maintained, neither the clinician nor the radiologist knew about each other's findings to prevent selection bias, only conventional CT reports were provided.

CT Protocol

Maintaining appropriate infection prevention and control measures, image acquisition was done using a single source Multidetector Computed Tomography (MDCT) scanner Ingenuity core 64 slice (Philips, Netherlands), in a supine position during a single inspiratory breath-hold, from the apex of the lung to the costophrenic angle. The scanning parameters were KVp=120; mAs=40; rotation time-0.5 second; pitch-1.0; section thickness-5 mm; intersection space-5 mm. Images were reconstructed at 1 mm slice thickness in all three planes and viewed in the mediastinal (C=60, W=400 and Matrix=512) and lung (C=-600, W=1600 and Matrix=768) windows.

Image analysis: Three radiologists with 5-10 years of experience in chest radiological reporting reviewed all the provided reconstructed images independently and had been completely blinded to the clinical and laboratory findings. In case of any discrepancies in the interpretation, the final result was reached by blinded voting among them. The standard radiological terms were used as described in the standard glossary for thoracic imaging reported by the Fleischner Society [14]. CT scoring was done as proposed by Yang R et al., which was an adaptation of previously clinically and laboratory parameters correlating scoring technique to describe lung involvement in patients of SARS [15,16]. The 18 anatomical segments of both lobes of the lung were divided into twenty lung regions, each lung region was scored as 0 (no involvement) 1 (<50% lung involvement), and 2 (>50% lung involvement) [Table/Fig-2].



[Table/Fig-2]: CT severity scoring pattern in apical region of right upper lobe in different RT-PCR positive COVID-19 patients; A, B, C) No lung involvement in 54-year-old male, implies CT score zero; D, E, F) Less than 50% involvement of apical segment of right upper lobe in 48-year-old female, implies CT score one; G, H, I) More than 50% involvement of apical segment of right upper lobe in 45 years, implies CT score two.

STATISTICAL ANALYSIS

Statistical analysis was applied using Statistical Package for the Social Sciences (SPSS) software version 23.0. For a single and multiple comparisons, Mann-Whitney and Kruskal-Wallis tests were performed respectively. The association with CT Severity Score (CT SS) was done using the 2-tailed Chi-square test or Fisher's-exact test. The Receiver Operating Characteristic (ROC) curve was drawn to determine the optimal cut-off point for CT score as an all-cause mortality. Pearson Chi-square, continuity correction, likelihood ratio, Fisher's-exact test and linear by linear association tests were applied to define association of CT score with variables. Kaplan-Meier test which was used to evaluate the relationship between CT score and all-cause mortality, which was compared with the logrank test. Cox proportional hazards regression modelling was performed

to determine the Hazard Ratio (HR) for CT score as an all-cause mortality predictor.

Univariate analysis was applied between mortality and other variables including CT SS, sex, age, co-morbidities and laboratory parameters. Multivariate analysis was also performed using all statistically significant variables in univariate analysis as independent variables to identifying predictors of death in COVID-19. In all statistical tests, a p-value <0.05 was considered to be significant.

RESULTS

The mean turn around time was 14.3±2 hours for RT-PCR and 22±10 minutes for chest CT. Another 30 minutes were required for sanitation of the CT machine before it was ready for the next patient. Out of 205 cases, 71.7% were males and 28.3% were females. Maximum cases were seen in the age range of >45 to 65 years. Diabetes mellitus was the most common co-morbidity, seen in 40.5% of patients; followed by hypertension (37.1%). A 20% of patients had both diabetes mellitus and hypertension. In clinical presentation; fever was seen in 77.1% of patients; followed by cough (63.4%) and shortness of breath (53.6%) [Table/Fig-3].

Variables	No. of patients (%)	
Sex		
Male	147 (71.7%)	
Female	58 (28.3%)	
Age distribution		
10 to 25 years	9 (4.4%)	
>25 to 45 years	51 (24.9%)	
>45 to 65 years	104 (50.7%)	
>65 years	41 (20%)	
Co-morbidities		
Diabetes Mellitus (DM)	83 (40.5%)	
Hypertension (HTN)	76 (37.1%)	
Both DM and HTN	41 (20%)	
Chronic kidney disease	10 (4.8%)	
Chronic obstructive pulmonary disease	11 (5.4%)	
Neoplasm	8 (3.9%)	
Immunocompromised status	9 (4.4%)	
Morbid obesity	6 (2.9%)	
Symptoms		
Fever	158 (77.1%)	
Cough	130 (63.4%)	
Shortness of breath	110 (53.6%)	
Expectoration	51 (24.8%)	
Dyspnoea	48 (23.4%)	
Gastrointestinal symptoms	32 (15.6%)	
Asymptomatic	11 (5.36%)	
Clinical findings		
Decreased O_2 saturation (<93%)	160 (78.1%)	
Decreased PaO_2/FiO_2 ratio (<300 mm Hg)	119 (58.0%)	
Laboratory findings	**No. of patients (%)**	**Mean±SD**
Increased CRP level (>6 mg/L)	167 (81.5%)	81.0±78.2 mg/L
Decreased lymphocyte count (20%)	150 (73.1%)	14.7±12.2%
Increased D-dimer level (>500 ng/mL)	127 (61.9%)	1062±127.9 ng/mL
Increased LDH level (>480 U/L)	85 (41.5%)	464.4±248.6 U/L
Leukocytosis (>10x103/cumm)	72 (35.1%)	14,400±11,200/cumm
Increased PCT level (>0.5 ng/mL)	41 (20%)	0.486±1.07 ng/mL

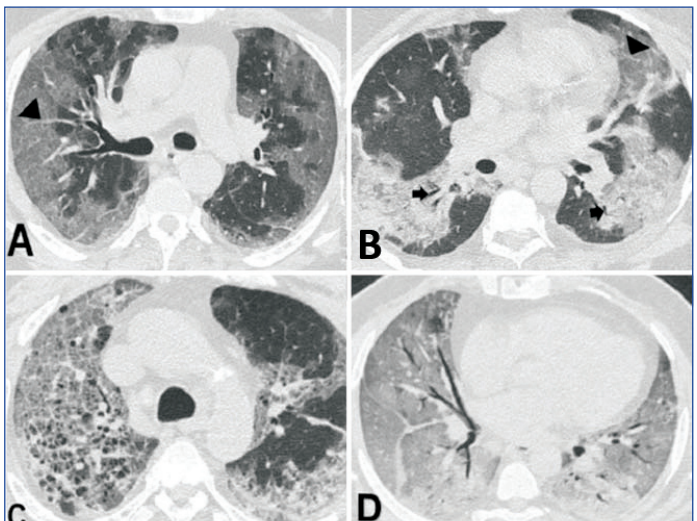
[Table/Fig-3]: Demographic and clinical characteristics of the study population. (N=205). SD: Standard deviation; CRP: C-reactive protein; LDH: Lactate dehydrogenase; PCT: Procalcitonin

Chest CT finding regarding imaging features, complications, lobar involvement, disease localisation are presented in [Table/Fig-4].

The most common chest CT finding [Table/Fig-5] was Ground Glass Opacities (GGO) seen in 156 patients (76.1%), followed by parenchymal consolidation (n=143; 69.7%) and crazy paving pattern (n=101; 49.3%).

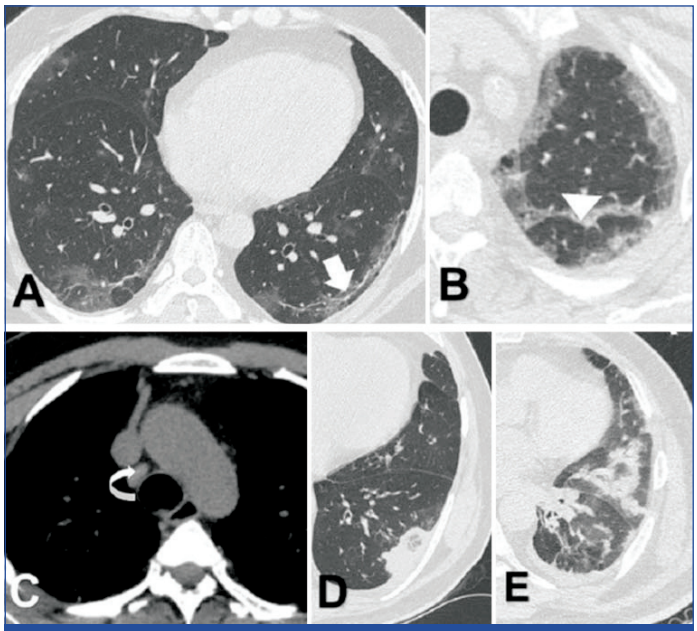
Variables	No. of patients (%)		
Main features			
Ground Glass Opacities (GGO)	156 (76.1%)		
Consolidation	143 (69.7%)		
Crazy paving	101 (49.3%)		
No pattern	9 (4.4%)		
Related features			
Fibrosis	98 (47.8%)		
Subpleural lines	82 (40%)		
Mediastinal lymphadenopathy	46 (22.4%)		
Reverse Halo sign	3 (1.5%)		
Complications			
Pleural effusion	25 (12.2%)		
Systemic thrombosis	20 (9.8%)		
Pulmonary thromboembolism	14 (6.8%)		
Pneumomediastinum and pneumothorax	9 (4.4%)		
Anterio-posterior distribution			
Anterior	5 (2.4%)		
Posterior	45 (22%)		
Both anterior and posterior	146 (71.2%)		
None	9 (4.4%)		
Axial distribution			
Peripheral	66 (32.2%)		
Peripheral and central	130 (63.4%)		
None	9 (4.4%)		
Lobar involvement	**No. of patients (%)**	**Mean CT SS±SD**	**p-value‡**
Right upper lobe	188 (91.7%)	3.3±1.5	0.0001*
Left upper lobe	194 (94.6%)	5.6±2.4	0.0001*
Right middle lobe	186 (90.7%)	2.4±1.1	0.0001*
Right lower lobe	196 (95.6%)	7.2±2.6	0.0002*
Left lower lobe	194 (94.6%)	7.0±2.6	0.0001*

[Table/Fig-4]: COVID-19 chest CT finding: Features, complications, lobar involvement, disease localisation (n=205).
‡p-value was estimated using Kruskal-Wallis test; *p-value <0.05 was considered statistically significant



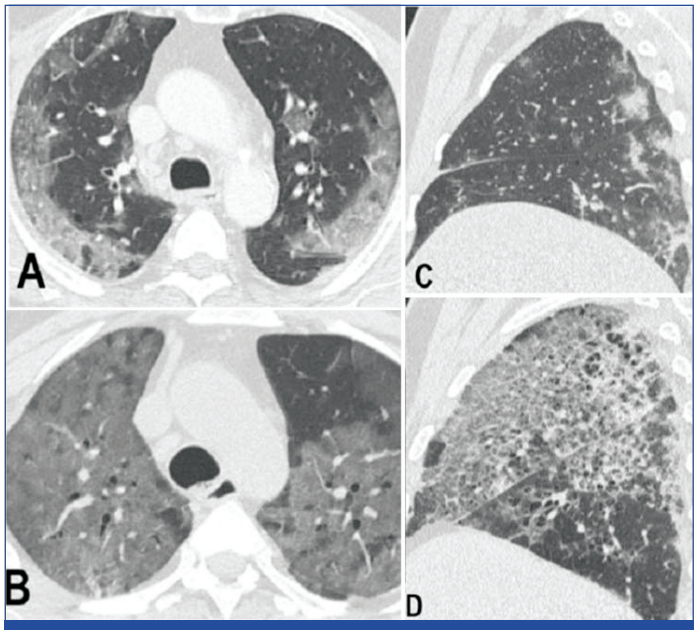
[Table/Fig-5]: Axial non contrast chest CT showing main CT features in COVID-19 (RT-PCR positive) patients as ground glass opacity (arrow head in image A and B), consolidation (arrow in image B), crazy paving pattern (image C) and completely white out lung likely ARDS (image D).

Auxillary findings [Table/Fig-6] like fibrosis (n=98; 47.8%), subpleural lines (n=82; 40%), mediastinal lymphadenopathy (n=46; 22.4%), and reversed halo sign (n=3; 1.5%) was also seen. Significant lower lobe involvement was seen with right sided preference.



[Table/Fig-6]: Axial non contrast chest CT showing related CT features in COVID-19 (RT-PCR positive) patients as subpleural line (arrow in image A), fibrosis (arrow head in image B), mediastinal lymph node at 4R station (curved arrow in image C) and reverse halo sign (image D and E).

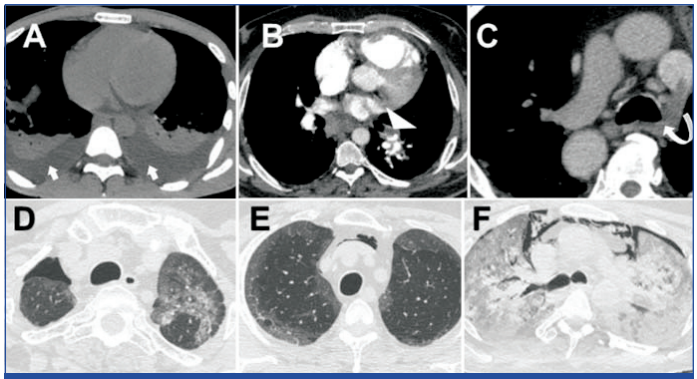
On the anterio-posterior dimension, there is more involvement of the posterior location with peripheral predominance [Table/Fig-7]. Nine patients showed normal chest CT.



[Table/Fig-7]: Non contrast axial chest CT in COVID-19 (RT-PCR positive) patients showing peripheral (image A) and both central and peripheral distribution (image B). Sagittal chest CT showing posterior (image C) and both posterior and anterior distribution of disease (image D).

Authors also noticed various complications like pleural effusion, systemic venous thrombosis and spontaneous pneumothorax [Table/Fig-8]. CT score in early versus late phase disease [Table/Fig-9] [12]. GGO was more seen in the early phase whereas consolidation, crazy paving, fibrosis, subpleural lines and mediastinal lymphadenopathy were more seen in the late phase with a significant p-value (p-value <0.05).

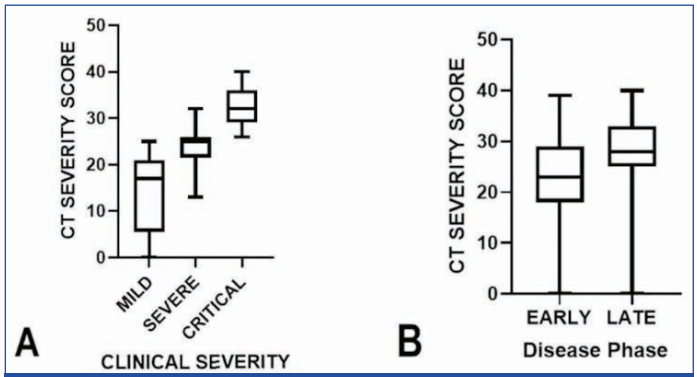
CT score versus clinical severity: The chest CT score showed significant association with clinical severity; higher the score, more the severity clinically. The mean CT scores in mild, severe, and critical groups of patients were 13.73±8.51, 23.49±3.75 and 32.42±4.01, respectively (p-value <0.0001). It is described in [Table/Fig-10,11].



[Table/Fig-8]: Chest CT showing different complications in COVID-19 (RT-PCR positive) patients as bilateral pleural effusion (arrow in image A), pulmonary thromboembolism (arrow head in image B), azygous vein thrombosis (curved arrow in image C), spontaneous pneumothorax (image D), pneumomediastinum (image E) and both pneumothorax and pneumomediastinum (image F).

Variables	Early phase (n=94)	Late phase (n=111)	p-value‡
Main features			
Ground glass opacities (GGO)	86/94 (91.5%)	70/111 (63.1%)	0.0001*
Consolidation	47/94 (50%)	96/111 (86.5%)	0.0001*
Crazy paving	12/94 (12.7%)	89/111 (80.2%)	0.0001*
No pattern	8/94 (8.5%)	1/111 (0.9%)	0.0132*
Related features			
Fibrosis	9/94 (9.6%)	89/111 (80.2%)	0.0001*
Subpleural lines	20/94 (21.3%)	62/111 (55.9%)	0.0001*
Mediastinal lymphadenopathy	14/94 (14.9%)	31/111(27.9%)	0.0001*
Pleural effusion	13/94 (13.8%)	12/111 (10.8%)	0.5103
Reverse halo sign	1/94 (~1.0%)	2/111 (1.8%)	1
CT score (Mean±SD)	22±10.08	28±6.79	0.0001*

[Table/Fig-9]: Difference between chest CT findings in early verses late phase.
*Marked results means statistically significant.
‡p-value was estimated using Mann-Whitney test. *p-value <0.05 was considered statistically significant



[Table/Fig-10]: Box and Whisker plots showing comparisons between CT severity score versus clinical severity as per the Chinese CDC guidelines (A) and disease phases (B) in RT-PCR positive COVID-19 patients. The line in the box represents mean value of the continuous variables. p-values were <0.0001 for both the graphs. 2-tailed Chi-square test or Fisher's-exact tests were used for p-value estimation.

Clinical severity in age, sex and co-morbidities adjusted cohort: The milder form of the disease was more common in the younger population; however, there were no statistically significant patterns in the cases of severe and critical patients. There was no sex predilection while comparing different clinical severity groups. More severe forms of disease, predominantly critical forms were seen in patients having any known co-morbidities. CT score has no significant association with age, sex and co-morbidities [Table/Fig-12-14].

Short term prognosis in age, sex and co-morbidities adjusted cohort: Although parameters of short-term prognosis were more prevalent in the older age group; however, statistical significance was seen in ICU admission, ventilator support and death. On crosstab statistics, a significant association of CT score was seen with ICU

Lung region	Mild (n=45) (Mean CT SS±SD)	Severe (n=65) (Mean CT SS±SD)	Critical (n=95) (Mean CT SS±SD)	p-value‡
Right upper lobe	1.55±1.34	3.15±1.04	4.30±1.16	0.0001*
Apical	0.31±0.51	0.85±0.53	1.18±0.48	0.0001*
Anterior	0.56±0.50	0.98±0.41	1.47±0.56	0.0001*
Posterior	0.69±0.59	1.29±0.52	1.64±0.50	0.0001*
Left upper lobe	3.00±2.18	4.84±1.34	7.28±1.50	0.0001*
Apical	0.36±0.48	0.68±0.58	1.13±0.41	0.0001*
Anterior	0.60±0.53	0.95±0.44	1.36±0.41	0.0001*
Posterior	0.64±0.64	1.06±0.49	1.66±0.47	0.0001*
Superior lingular	0.69±0.66	1.03±0.52	1.62±0.48	0.0001*
Inferior lingular	0.71±0.58	1.11±0.47	1.52±0.50	0.0001*
Right middle lobe	1.35±1.15	2.16±0.83	3.07±0.81	0.0001*
Lateral	0.82±0.74	1.14±0.60	1.67±0.49	0.0001*
Medial	0.53±0.50	1.05±0.41	1.39±0.53	0.0001*
Right lower lobe	4.00±2.61	6.98±1.63	8.92±1.09	0.0001*
Superior	0.67±0.56	1.45±0.50	1.88±0.32	0.0002*
Anterior basal	0.73±.058	1.15±0.40	1.56±0.49	0.0003*
Posterior basal	1.00±0.67	1.60±0.58	1.91±0.29	0.0001*
Medial basal	0.80±0.66	1.34±0.53	1.73±0.44	0.0001*
Lateral basal	0.80±0.66	1.45±0.63	1.85±0.35	0.0001*
Left lower lobe	3.84±2.66	6.36±1.57	8.84±1.27	0.0001*
Superior	0.60±0.53	1.34±0.50	1.74±0.46	0.0002*
Anterior basal	0.69±0.59	0.94±0.39	1.59±0.53	0.0001*
Posterior basal	0.98±0.72	1.54±0.53	1.95±0.53	0.0001*
Medial basal	0.78±0.63	1.23±0.52	1.73±0.47	0.0001*
Lateral basal	0.78±0.63	1.34±0.56	1.84±0.36	0.0001*
Total mean CT SS	13.73±8.51	23.49±3.75	32.42±4.01	0.0001*

[Table/Fig-11]: Comparison of CT score of each lung regions between clinical severity groups.
*p-value <0.05 was considered statistically significant; ‡p-value was estimated using 2-tailed Chi-square test

admission, ventilator support and death. However, no significant association with long hospital stays was seen [Table/Fig-12-14].

A statistically significant higher number of ICU admission and deaths were noticed in patients with any known co-morbidities in comparison to previously healthy individuals. In case of diabetes and hypertension, the same prognostic parameters were seen at lower CT score than previously healthy individuals. On crosstab statistics, CT score had no significant association with co-morbidities.

Variables	Age <60 years⁺	Age ≥60 years⁺	p-value‡
No. of patients			
Mild	38/143 (26.5%)	7/62 (11.2%)	0.0163*
Severe	44/143 (30.7%)	21/62 (33.8%)	0.7442
Critical	61/143 (42.6%)	34/62 (54.8%)	0.1273
ICU admission	97/143 (67.8%)	52/62 (83.8%)	0.0251*
Ventilatory support	74/143 (51.7%)	41/62 (66.2%)	0.0495*
Long hospital stays	34/143 (23.7%)	21/62 (33.8%)	0.1692
Death	26/143 (18.2%)	20/62 (32.2%)	0.0303*
CT score (Mean±SD)			
Mild	13.61±8.4	14.4±9.77	0.6494
Severe	23.7±3.70	22.9±3.90	0.6302
Critical	32.4±4.02	32.4±4.05	0.9493
ICU admission	29.48±5.38	29.23±5.87	0.9102
Ventilator support	31.35±4.44	31.24±4.57	0.8943
Long hospital stays	24.21±4.17	24.33±4.39	0.8293
Death	35.85±3.00	34.85±3.42	0.3492

[Table/Fig-12]: No of patients and their mean CT scores in clinical severity and short-term prognosis aspect in age adjusted group.
*p-value <0.05 was considered statistically significant
‡p-value was estimated using 2-tailed Chi-square test; ⁺Due to lower sample size, authors made two age groups to have larger comparing sample. National Centre for Disease Control, India considers people with age more than equal to 60 years with any co-morbidity are at high risk

Variables	Male n (%)	Female n (%)	p-value‡
No. of patients			
Mild	32 (21.7%)	13 (22.4%)	0.9991
Severe	46 (31.3%)	19 (32.7%)	0.8683
Critical	69 (46.9%)	26 (44.8%)	0.8764
ICU admission	108 (73.4%)	41 (70.7%)	0.7293
Ventilatory support	86 (58.5%)	29 (50%)	0.2782
Long hospital stays	45 (30.6%)	10 (17.2%)	0.0491*
Death	32 (21.7%)	14 (24.1%)	0.8523
CT score (Mean±SD)			
Mild	20.7±10.76	11.4±10.2	0.5292
Severe	23.5±4.11	23.3±2.81	0.6201
Critical	32.2±3.76	33.0±4.63	0.4982
ICU admission	29.33±5.30	29.56±6.16	0.9467
Ventilator support	30.99±4.28	32.28±4.94	0.2885
Long hospital stays	28.51±2.90	29.20±4.94	0.8838
Death	35.22±2.93	35.86±3.80	0.3085

[Table/Fig-13]: No of patients and their mean CT scores in clinical severity and short-term prognosis aspect in sex adjusted group.
No. of males=147, No. of females=58; ICU: Intensive care unit; CT: Computed tomography; SD: Standard deviation
*p-value <0.05 was considered statistically significant
‡p-value was estimated using 2-tailed Chi-square test

Kaplan-Meier survival curves and univariate and multivariate analyses: Out of the 205 cases in the present study cohort, 46 patients (22.4%) died during hospital stay out of which 42 had known co-morbidities. Diabetes mellitus was reported in 27 (58.7%) of 46 deaths, followed by hypertension in 23 (50%) patients and other co-morbidities in 7/46 (15.2%). Four (6.1%) patients who had no known co-morbidities also died during hospital stay. In the present study death was only seen in critical group patients [Table/Fig-14].

As per Kaplan-Meier analysis and ROC curve, the mortality risk was significantly higher with the increase in CT Score, using an estimated cut-off of ≥30.5 {logrank p-value <0.0001; HR-46.30 (CI:14.35-149.34); p-value <0.001} on a follow-up period of 30 days. Area under ROC Curve [Table/Fig-15] was reported to be 0.97 (p-value <0.0001). Bivariate analysis showed a significant association of CT SS with phase of disease (p-value <0.001), clinical severity (p-value <0.001), lymphocytopenia (p-value <0.001), raised CRP level (p-value <0.001), raised LDH level (p-value <0.001), raised D-dimer level (p-value <0.001), raised PCT level (p-value <0.001) and mortality (p-value <0.001).

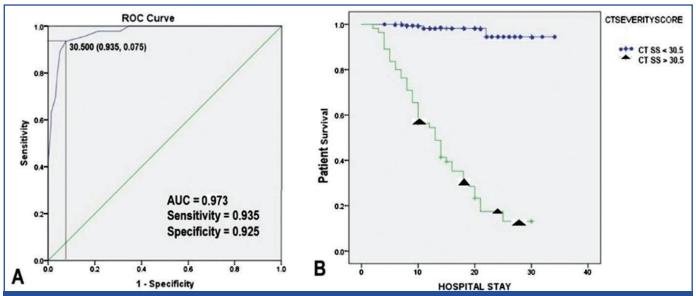
Univariate analysis demonstrated a higher risk of mortality with an increase in age, associated co-morbidities, higher CT SS, and raised CRP and D-dimer levels. Multivariate analysis applied on significant statistical variables proven by univariate analysis confirmed the role of CT score as an independent predictor of death (OR=276.8; 95% CI=45.21-1695.43; p-value <0.001) together with co-morbidities (OR=19.36; 95% CI=3.50-107.09; p-value=0.001) and raised D-dimer (OR=25.02; 95% CI=1.90–328.43; p-value=0.014). The Nagelkerke R Square is estimated at 0.820 indicating that 82.0% of the variance in mortality can be predicted from the linear combination of high CT severity score, presence of co-morbidity and high D-dimer levels supposed to be the predictors of mortality.

DISCUSSION

The most common imaging findings of COVID-19, in the present study were bilateral GGOs with or without consolidation, with

Variables	DM only (n=42) n (%)	HTN only (n=35) n (%)	Both (n=41) n (%)	Others (n=22) n (%)	None (n=65) n (%)	p-value‡
No. of patients						
Mild	9 (21.4%)	4 (11.4%)	5 (12.2%)	2 (9.1%)	25 (38.4%)	0.0021*
Severe	14 (33.3%)	11 (31.4%)	13 (31.7%)	7 (31.8%)	20 (30.7%)	0.9994
Critical	19 (45.2%)	20 (57.1%)	23 (56.1%)	13 (59.1%)	20 (30.7%)	0.0275*
ICU admission	32 (76.2%)	29 (82.8%)	34 (82.9%)	19 (86.3%)	35 (53.8%)	0.0013*
Requirement of ventilator support	24 (57.1%)	22 (62.8%)	28 (68.3%)	14 (63.6%)	27 (41.5%)	0.0491*
Long hospital stays	8 (19.0%)	14 (40%)	11 (26.8%)	6 (27.3%)	16 (24.6%)	0.3383
Death	12 (28.5%)	8 (22.8%)	15 (36.5%)	7 (31.8%)	4 (6.1%)	0.0022*
CT score (Mean±SD)						
Mild	19.11±5.66	10.0±10.67	15.2±9.03	11.0±7.87	12.43±8.73	0.1243
Severe	22.71±2.86	22.81±4.68	24.69±4.34	22.83±3.18	23.81±3.62	0.3627
Critical	32.94±3.55	31.25±4.45	33.43±4.05	32.91±4.60	31.66±3.48	0.2728
ICU admission	28.78±6.03	28.83±5.74	30.97±5.13	30.16±6.03	28.49±4.89	0.4075
Requirement of ventilator support	31.13±4.82	30.91±4.40	32.25±4.62	32.64±4.71	30.15±3.81	0.3799
Long hospital stays	28.75±3.99	28.71±2.26	29.64±4.17	29.00±3.57	27.69±3.17	0.6354
Death	34.75±2.95	35.50±3.54	35.20±3.50	36.14±2.96	36.75±3.30	0.7966

[Table/Fig-14]: No of patients and their mean CT scores in clinical severity and short-term prognosis aspect in co-morbidity adjusted group.
DM: Diabetes mellitus; HTN: Hypertension; CT: Computed tomography; SD: Standard deviation
*p-value <0.05 was considered statistically significant
†marked: Sample size in co-morbidities other than Diabetes mellites and hypertension were less, so not evaluated individually. This group of patients not have co-morbidities other than diabetes mellites and hypertension
‡p-value was estimated using Fisher's-exact test



[Table/Fig-15]: ROC curve (image A) and Kaplan-Meier survival analysis curve (image B) for CT SS=30.5 (for practical purpose taken as ≥31) showing area under the curve for mortality is 0.973. Patient survival is expressed on the y-axis, while hospital stay (duration of followed-up) in days is expressed on the x-axis.

a predominant peripheral, lower lobe and posterior anatomic distribution. It is quite consistent with previous studies [12,15,17]. The reason for the more common imaging occurrence of GGO in the early phase of disease can be attributed to the acute phase alveolar injury leading to air space oedema, bronchiolar fibrin depositions and interstitial thickening [18]. As the disease progress, there is activation of humoral as well as cell-mediated immune system by virus specific B and T-cells; causing intense production of proinflammatory markers leading to uncontrolled autoimmune reaction. A combination of alveolar oedema, bacterial superinfection, and interstitial inflammatory changes are seen in the late phase, which may explain the higher prevalence of consolidations and crazy-paving pattern in the late phase [19].

Raised leukocyte count, decreased lymphocyte count, raised serum CRP, LDH, PCT and D-dimer levels were commonly observed in COVID-19 patients. These correlated strongly with higher CT scores. Raised serum CRP and D-dimer levels may be explained as a result of the pronounced inflammatory activation and disseminated coagulopathy, characteristics of severe disease [20,21]. Raised serum PCT can be seen in the setting of secondary bacterial infection, suggesting a bad prognosis [22]. CT score, co-morbidities and serum level of D-dimer has a significant predictor of mortality on multivariate analysis. Age and serum level of CRP shows significant risk of mortality on univariate analysis; however, no significant association was defined on multivariate analysis.

A Kaplan-Meier survival analysis was performed between CT score and days of hospital stay, to confirm chest CT findings' prognostic significance for an observational period of 30 days. By using this method, the present study was able to demonstrate that a cut-off CT score of 30.5 is predictive of mortality. But a score of 30.5 is not possible in this study scoring system, so authors took it as ≥31. Similar observations were previously published by Colombi D et al., and Francone M et al., [23,24]. CT severity score more than 31 out of 40 was associated with poor prognosis in the present study population which is comparable to observation made by Francone M et al., [24]. They have found score equal or more than 18 out of 25 had poor outcome.

There was a significantly higher mortality in a population of more than 60 years of age in comparison to younger ones. The univariate analysis also proved increased risk of mortality with an increase in age. No significant gender preponderance was seen with the severe form of disease and bad prognosis.

A chest CT score, the objective value of the radiologist's observation, depicting the extent of lung involvement can correlate well with disease severity and active phase inflammatory marker findings. It can also predict the outcome or clinical course of the disease, as it represents the disease burden. This prospective study explored all the clinical utility of chest CT score in predicting disease severity and short-term prognosis of the disease. Apart from this, a CT score can come in handy in the management of patients in a few more ways.

Due to the short turnaround time of chest CT in comparison to RT-PCR, it can be very useful in the early isolation of patients to contain the disease in the hospital. There is a statistically significant difference between the turnaround time of chest CT and RT-PCR. In 29 patients with first RT-PCR negative, authors had to repeat RT-PCR for diagnosis. This further increases the time for diagnosis. Sometimes sampling is also poor; causing more delay in diagnosis. Although, the diagnostic role of CT remains controversial and a hot debate topic in the current pandemic situation. A group of researchers believe chest CT has higher sensitivity [25,26] in comparison to RT-PCR while others believe vice-versa [27]. Several authors and radiological fraternities do not believe in the use of CT as a first-line investigation due to radiation exposures [28]. In the present study, CT also did not appear much sensitive; nine patients were RT-PCR positive despite their chest CT imaging were normal. Due to less turnaround time and significant association with laboratory parameters, CT score can be helpful speedy diagnostic

workflow of symptomatic patients. In COVID-19 infection, there is more extensive involvement of lung parenchyma in comparison to other viral pneumonia [5,6,29]. A higher CT score has a more probability of the COVID-19 infection. So, authors recommend the use of chest CT routinely in all symptomatic severe patients.

Limitation(s)

The present study had some limitations as recall bias regarding the previous diagnosis of ILD or any co-morbidities and authors experienced a higher number of critical patients and mortality in this study group in comparison to our national data as we were a referral center. The survival analysis study lacks longer follow-up data. Due to the smaller sample size, authors could not define the role of individual co-morbidity in disease mortality. Authors suggest a future prospective study with a larger sample size, co-morbidity adjusted individual cohort and a study to look predictive value of CT score for delayed complications.

CONCLUSION(S)

Chest CT findings are quite evident and correlating well with the novel acute phase reactants. So, CT score can be used as an imaging tool to predict the future course of disease and plan management accordingly in areas lacking with the modern laboratories. In a developing country, this can guide timely referral of patients to higher centers with better intensive care facilities. Whereas in the developed country, it can help hospital administration for better preparedness for critical events and management of hospital resources. Due to its objectiveness, it can make communication easier between the caregivers and the caregiver, and the patient's caretaker. The higher chest CT score with higher probability of COVID-19 infection can be helpful in containing the disease by early isolation.

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