Correlation of Chest Radiographic Findings and Coagulation Abnormality with Disease Severity in COVID-19 Positive Patients

Yogender Aggarwal, Ankur Malhotra, Deepti Arora[1], Shruti Chandak, Ashutosh Kumar[1], Vivek Bhandari

Departments of Radiodiagnosis and [1]Pathology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India

Abstract

Introduction: The pandemic of coronavirus disease 19 (COVID-19) has engulfed most of the world and has constrained already overburdened health care systems, especially in developing countries. There is an urgent need of a rapid investigation to assess disease severity in suspected patients and the baseline chest radiograph may serve as a triage tool. The aim is to correlate chest radiographic findings and coagulation abnormality with disease severity in COVID-19 positive patients. **Materials and Methods:** This was a retrospective observational study which comprised 100 reverse transcription-polymerase chain reaction positive COVID-19 cases which were clinically stratified into three groups based on clinical parameters. Baseline chest radiograph and serum D-dimer levels at the time of admission for all the patients were reviewed. A radiographic severity score (Radiographic Assessment of Lung Edema [RALE]) was determined for all four quadrants of both lungs. The scores of each quadrant were added to yield the final severity score. **Results:** Baseline chest radiograph was abnormal in 75% of patients, whereas 25% of patients had normal chest radiograph. Most frequent radiographic abnormality was ground-glass opacity (GGO) ($n = 31$, 41.3%) followed by lung consolidation ($n = 19$, 25.3%), while 7 patients (9.3%) had both GGO and consolidation. The most common pattern of disease distribution was bilateral 34 (57.7%) and peripheral in 58 (69%). The optimal cut-off RALE score for identifying symptomatic patients was ≥3 (area under the curve [AUC] 0.760) and for identifying severe cases was ≥7 (AUC 0.870). Similarly, the optimal cut-off D-Dimer value for identifying symptomatic patients was ≥567 ng/ml (AUC 0.836) and for diagnosing severe disease was ≥1200 ng/ml (AUC 0.99). **Conclusions:** Radiographic RALE score and elevated serum D-Dimer levels correlate strongly with disease severity in COVID-19 patients and can be utilized for early identification of high-risk cases which can ultimately reduce mortality and morbidity.

Keywords: Chest radiograph, COVID-19, D-dimer, Radiographic Assessment of Lung Edema score, severe disease

Introduction

Toward the end of the year 2019 a virus, called as severe acute respiratory syndrome coronavirus 2, spread worldwide from China (Wuhan city) with the first positive case in India reported on January 30, 2020.[1] The pandemic disease caused by this new virus was labeled as coronavirus disease 19 (COVID-19) by the World Health Organization on February 11, 2020. The disease caused by this novel virus is highly contagious and can progress from mild pneumonia to severe Acute respiratory distress syndrome (ARDS).[2,3] The only gold standard diagnostic test available worldwide is the real-time reverse transcription-polymerase chain reaction (RT-PCR) of viral nucleic acid.[2] However, the long turnaround time and the significant number of false-negative results, limit the clinical utility of this test. Thus, imaging evaluation of suspected COVID-19 patients awaiting RT-PCR report is of prime importance for early assessment of pulmonary involvement and appropriate management.

Most of the developed countries adopted computed tomography (CT) thorax as the initial first-line investigation

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Address for correspondence: Dr. Shruti Chandak, Department of Radiodiagnosis, Teerthanker Mahaveer Medical College and Research Centre, Moradabad - 244 001, Uttar Pradesh, India.
E-mail: chandakshruti@yahoo.com

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in the diagnosis of COVID-19 owing to its better sensitivity and specificity in comparison to chest radiography.[4,5] However, performing CT scans in each and every case is not possible during this pandemic, especially in country like India where resources are limited and health care system is already overburdened. In addition, there is inherent risk of radiation exposure to the younger population and scanner decontamination after each CT scan may disrupt radiological services and limit throughput. Considering these limitations, portable chest radiography seems more appropriate in our clinical setting. The added advantages of using chest radiography are faster results and reduced patient movement which help in preventing the spread of the virus.[6,7]

There are reports of coagulopathy with D-dimer elevation in 3.75%–68.0% of the patients infected with COVID-19. The exact pathophysiology of this mechanism is still unclear. However, it increasingly believed that SARS-CoV 2 induces cytokine storm which triggers coagulation pathway resulting in disseminated intravascular coagulation (DIC). The circulating D-dimer levels in the blood are a sensitive indicator of underlying thrombotic events and DIC. Thus, elevated D-dimer levels in COVID-19 patients may help in severity stratification and early identification of the patients who are at increased risk of thromboembolic complications.[2,5,6]

With this background, the present study was undertaken to evaluate the role of chest radiography in the early detection of COVID-19 disease and to identify various chest radiographic manifestations in RT-PCR confirmed COVID-19 patients stratified by clinical severities. In addition, the authors also sought to correlate serum D-Dimer levels with disease severity. There is only limited literature available on this novel disease, especially in the context of the Indian population so, we believe that our study will fill the required knowledge gaps and will better equip our fellow clinicians in combating this global pandemic.

Materials and Methods

This retrospective observational study with a sample size of 100 patients was conducted in the department of Radiodiagnosis, in a designated COVID hospital (level-3 COVID Care facility) in northern India. Prior approval from Institutional Review Board (letter no. IRB/02/2021 dated 29/01/2021) was taken and written informed consent was waived.

All the Patients with positive RT-PCR test (Thermo Fisher QuantStudio 5 Real-time PCR system) on nasopharyngeal and throat swab in August 2020 were enrolled in the study. Only patients who had undergone Chest radiograph and D-dimer levels at the time of admission were included in the study. Demographic data, clinical details, and relevant laboratory parameters were collected from the clinical records of all the patients. Exclusion criteria included age <18 years, pregnancy, malignancy, and chronic liver disease.

Severity stratification was done in all the patients based on clinical parameters as per Clinical Management Protocol: COVID-19 (ver 3, 13.06.20) issued by MoHFW and DGHS.[8] The patients were grouped into mild, moderate, and severe disease as per the guidelines.

The D-dimer level was tested using immunoturbidimetric assay (normal range 0–500 ng/ml). All chest radiographs were acquired on portable digital X-ray unit (Allengers Medical systems) with either anteroposterior or posteroanterior projection and images were achieved on picture archiving and communication system. Two radiologists independently reviewed the chest radiographs of all the COVID-19 patients and recorded findings in predesigned proforma. In case of any discrepancy, the consensual agreement was reached.

The chest radiographic findings (ground-glass opacities, consolidation) were interpreted and diagnosed in accordance with Fleischner society terminology.[9] The radiographs were further assessed for laterality (unilateral/bilateral), symmetry, disease distribution (peripheral/parahilar predominance), and pleural effusion (present/absent). Other associated cardiopulmonary abnormalities like vascular congestion, pneumothorax, and cardiomegaly were also evaluated.

To further quantify the extent of pulmonary involvement, a severity score was calculated using simplified version of the Radiographic Assessment of Lung Edema score (RALE).[10] Each lung was assigned a score of 0-4 depending on the degree of involvement by ground-glass opacities or consolidation (nil involvement - 0; ¼th involvement - 1; ¼–½ involvement - 2; ½——th involvement - 3; —th or > involvement - 4). The final severity score was obtained by adding individual scores for each lung.[11]

Statistical analysis

SPSS program for Windows, version 22.0 (SPSS program, IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) was employed for statistical analysis. All the variables which were continuous in nature were represented as mean ± standard deviation (SD), and all categorical variables were represented as absolute numbers and percentage. Normality of data before statistical analysis was checked using Shaipro–Wilk test. Comparison of normally distributed continuous variables was done by using ANOVA. In cases with significant F value and homogeneous variance, Tukey multiple comparison test was used to determine the difference between individual categories; otherwise, Tamhane's T2 test was used. Variables which were not distributed normally were tested using Kruskal–Wallis test and further comparisons were done using Mann–Whitney U-test. Chi-square test was used to analyze categorical variables.

To determine the optimal cut-off value of RALE score and serum D-dimer a receiver operating characteristics (ROC) analysis was done. The diagnostic values of these markers were calculated using the area under the curve and its SD (AUC_SD), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. The $P < 0.05$ was considered statistically significant for all statistical tests.

Results

This retrospective study comprised 100 RT-PCR confirmed COVID-19 cases which were divided into four clinical categories according to COVID-19 symptoms. Twenty-four patients were asymptomatic, 48 had mild symptoms, 22 had moderate symptoms and 6 were severely symptomatic. The clinical category-wise demographic and radiographic data are presented in [Table 1].

The mean age of the patient in the asymptomatic group was 34.54 ± 15.06 years, in mildly symptomatic was 45.38 ± 16.37 years, in moderately symptomatic was 44.50 ± 15.77 years and in patients with severe symptoms was found to be 47.67 ± 12.69 years. The statistically significant (P = 0.03) difference (−10.833 ± 3.966) was found between the mean age of asymptomatic patients and patients with mild symptoms whereas for other categories this difference was insignificant [Table 2].

Out of 100 patients, 31 were female (9 asymptomatic, 17 mildly symptomatic, 5 moderately symptomatic, and none with severe symptoms) and 69 were males (15 asymptomatic, 31 mildly symptomatic, 17 moderately symptomatic, and 6 with severe symptoms).

Twenty-five patients (14 asymptomatic, 9 mildly symptomatic, 2 moderately symptomatic, and none with severe symptoms) had normal chest radiograph and 75 patients (10 asymptomatic, 39 mildly symptomatic, 20 moderately symptomatic, and 6 with severe symptoms) showed radiographic abnormalities [Figure 1].

Out of these 75 cases with positive chest radiographic finding, 31 patients (6 asymptomatic, 19 mildly symptomatic, 5 moderately symptomatic, and 1 with severe symptoms) showed ground-glass opacities, 23 patients (1 asymptomatic, 8 mildly symptomatic, 11 moderately symptomatic, and 3 with severe symptoms) showed consolidation, and 7 patients had both consolidation and ground-glass opacities on chest radiographs. Fourteen patients showed increased reticular markings and 9 had associated mild pleural effusion. Twenty-five patients had unilateral lung involvement and 36 had bilateral involvement. Peripheral (58 patients) and asymmetric (32 patients) distribution of the radiographic findings was seen in the majority of patients [Figures 2-4].

According to RALE scoring criteria right lower quadrant left upper quadrant, and left lower quadrant showed

Table 1: Clinical category-wise distribution of demographic details, various chest radiographic, and biochemical findings in coronavirus disease 19 patients

Characteristic	Asymptomatic patients (%)	Mildly symptomatic patients (%)	Moderately symptomatic cases (%)	Severely symptomatic patients (%)	*P*
Age	34.54±15.06	45.38±16.57	44.50±15.77	47.67±12.69	0.041
Sex					
Female	9 (37.5)	17 (35.4)	5 (22.7)	0	0.23
Male	15 (62.5)	31 (64.6)	17 (77.3)	6 (100)	
Total	24 (100)	48 (100)	22 (100)	6 (100)	
Chest radiography findings					
Normal	14 (58.3)	9 (18.8)	2 (9.1)	0	<0.001
Abnormal	10 (41.7)	39 (81.3)	20 (90.9)	6 (100)	
Type of parenchymal opacity on chest radiography					
Ground glass opacities	6 (25)	19 (39.6)	5 (22.7)	1 (16.7)	0.342
Consolidation	1 (4.2)	4 (16.7)	11 (50)	3 (50)	0.001
Both GGO's and consolidation	0	3 (6.3)	2 (9.1)	2 (33.3)	0.039
Prominent reticular markings	7 (29.2)	7 (14.6)	0	0	0.635
Associated pleural effusion	1 (4.2)	3 (6.3)	3 (13.6)	2 (33.3)	0.110
Laterality					
Unilateral	6 (25.0)	15 (31.3)	3 (13.6)	1 (16.7)	0.001
Bilateral	1 (4.2)	17 (35.4)	14 (63.6)	4 (66.7)	
Symmetry					
Asymmetrical	1 (100)	15 (100)	13 (92.9)	3 (75.0)	0.298
Symmetrical	0	0	1 (7.1)	1 (25.0)	
Distribution					
Peripheral	7 (29.2)	29 (60.4)	17 (77.3)	5 (83.3)	0.004
Parahilar	0	1 (2.1)	2 (9.1)	0	0.142
RALE score (mean)	1.00±1.77	3.98±5.54	8.32±7.80	13.33±8.55	<0.001
Serum D-Dimer (mean, ng/ml)	287.5±289.8	673.8±601.26	1935.3±2269.9	4685.5±1802.8	<0.001

GGO: Ground glass opacity, RALE: Radiographic assessment of lung edema

Table 2: Comparison of mean difference in the age of coronavirus disease-19 patients (asymptomatic/symptomatic) with various clinical categories (mild/moderate/severe)

COVID severity	Mean difference (I-J)	SE	*P*	95% CI (lower bound-upper bound)
Asymptomatic				
Mild	−10.833*	3.966	0.037	−21.2-−0.47
Moderate	−9.958	4.682	0.152	−22.2-2.28
Severe	−13.125	7.24	0.274	−32.05-5.8
Symptomatic				
Mild				
Moderate	0.875	4.084	0.997	−9.8-11.55
Severe	−2.292	6.868	0.987	−20.25-15.67
Moderate				
Severe	−3.167	7.306	0.973	−22.27-15.93

SE: Standard error, CI: Confidence interval, COVID: Coronavirus disease, *statistically significant $P<0.05$

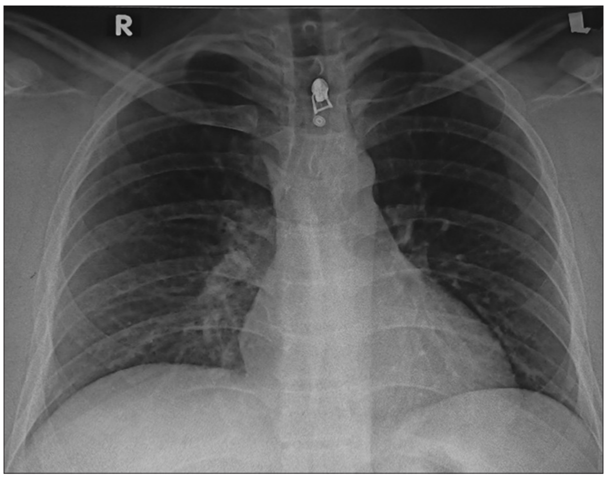

Figure 1: A 47-year-old asymptomatic COVID-19-positive male patient with normal chest radiograph (Radiographic Assessment of Lung Edema Score 0, serum D-dimer 39 ng/ml)

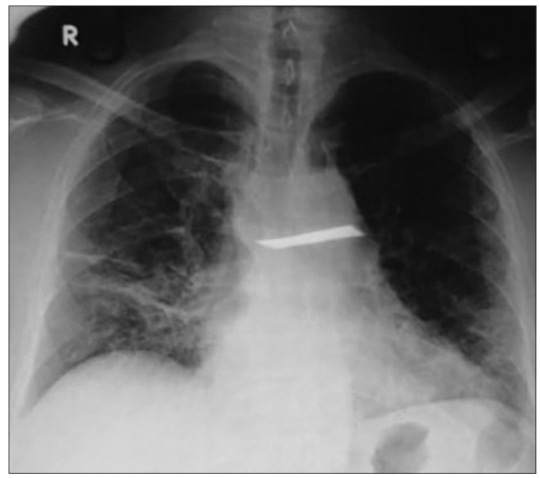

Figure 2: Chest radiograph in a 60-year-old female patient with mild COVID-19 symptoms shows bilateral peripheral asymmetrical lower quadrant consolidation (mainly in right paracardiac region) with few reticular opacities and right paracardiac atelectatic bands (Radiographic Assessment of Lung Edema score 4, serum D-dimer 667 ng/ml)

significant involvement ($P < 0.001$). The mean RALE score in asymptomatic patients was 1.00 ± 1.77, in mild cases was 3.98 ± 5.54, in moderate cases was 8.32 ± 7.80, and in severe cases was 13.33 ± 8.55 ($P < 0.001$). The difference between the mean RALE score of the asymptomatic vs mild group (−2.979 ± 1.434, $P = 0.168$) and moderate vs severe (−5.015 ± 2.642, $P = 0.236$) group showed no significant difference while for all other categories statistically significant difference was found [Table 3].

Mean serum D-dimer values for the asymptomatic group was found to be 287 ± 289 ng/ml, for mild cases were 675.83 ± 601.26 ng/ml, for moderate cases was 1935.39 ± 2269.96 ng/ml, and for severe cases was 4685.50 ± 1802.85 ng/ml ($P < 0.001$). The difference between the mean serum D-Dimer values of the asymptomatic vs mild group (−386.354 ± 305.527 ng/ml, $P = 0.588$) was insignificant while for all other categories this difference was found to be statistically significant [Table 4].

A ROC analysis was done to determine optimal cut-off values for RALE score and D-dimer in differentiating asymptomatic from symptomatic cases and mild from severely diseased cases. The optimal cut off RALE score for identifying symptomatic patients was found to be ≥3 (AUC 0.760, 95% confidence interval [CI], 0.664–0.856) with resulting sensitivity of 59.2%, specificity of 83.3%, PPV of 91.8%, the accuracy of 65%, and NPV of 39.2% [Figure 5]. Similarly, the optimal cut off D-dimer value for correctly identifying symptomatic patients was found to be ≥567 ng/ml (AUC 0.836, 95% CI, 0.741–0.93) with the sensitivity of 71.1%, specificity of 87.5%, PPV of 94%, the accuracy of 75%, and NPV of 48.8% [Figure 6].

To differentiate mild COVID-19 cases from severe cases the optimal RALE score cut off value came out to be ≥7 (AUC 0.870, 95% CI, 0.756–0.984) with the sensitivity of 83.3%, specificity of 81.3%, PPV of 35.7%, accuracy of 81.5%, and NPV of 97.5% [Figure 7]. The optimal cut off D-dimer value for differentiating mild from severe cases was found to be ≥1200 ng/ml (AUC 0.99, 95% CI, 0–1) with resulting sensitivity of 83.3%, specificity of 81.3%, PPV of 35.7%, accuracy of 81.5%, and NPV of 97.5% [Figure 8].

Table 3: Comparison of mean difference in the radiographic radiographic assessment of lung edema score of coronavirus disease -19 patients (asymptomatic/symptomatic) with various clinical categories (mild/moderate/severe)

COVID severity	Mean difference (I-J)	SE	*P*	95% CI (lower bound-upper bound)
Asymptomatic				
Mild	−2.979	1.434	0.168	−6.73-0.77
Moderate	−7.318*	1.693	<0.001	−11.75-−2.89
Severe	−12.333*	2.618	<0.001	−19.18-−5.49
Symptomatic				
Mild				
Moderate	−4.339*	1.477	0.021	−8.2-−0.48
Severe	−9.354*	2.484	0.002	−15.85-−2.86
Moderate				
Severe	−5.015	2.642	0.236	−11.92-1.89

SE: Standard error, CI: Confidence interval, COVID: Coronavirus disease, *statistically significant *P*<0.05

Table 4: Comparison of mean difference in the D-dimer values (ng/ml) of coronavirus disease-19 patients (asymptomatic/symptomatic) with various clinical categories (mild/moderate/severe)

COVID severity	Mean difference (I-J)	SE	*P*	95% CI (lower bound-upper bound)
Asymptomatic				
Mild	−386.354	305.527	0.588	−1185.19-412.48
Moderate	−1647.864*	360.721	<0.001	−2591.01-−704.72
Severe	−4398.000*	557.814	<0.001	−5856.46-−2939.54
Symptomatic				
Mild				
Moderate	−1261.509*	314.649	0.001	−2084.19-−438.82
Severe	−4011.646*	529.189	<0.001	−5395.27-−2628.03
Moderate				
Severe	−2750.136*	562.862	<0.001	−4221.8-−1278.47

SE: Standard error, CI: Confidence interval, COVID: Coronavirus disease, *statistically significant *P*<0.05

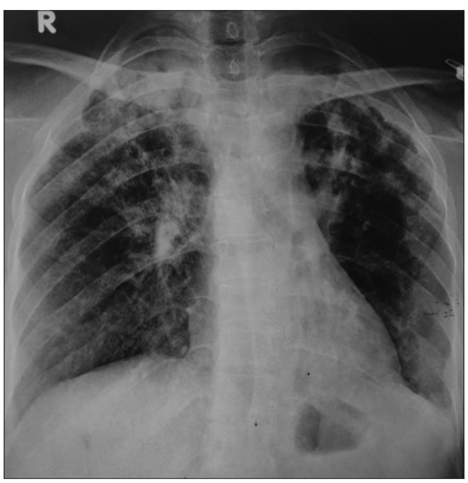

Figure 3: Chest radiograph in a 23-year-old female patient with moderate COVID-19 symptoms shows bilateral asymmetrical both peripheral and parahilar consolidation (Radiographic Assessment of Lung Edema score 16, serum D-dimer 756 ng/ml)

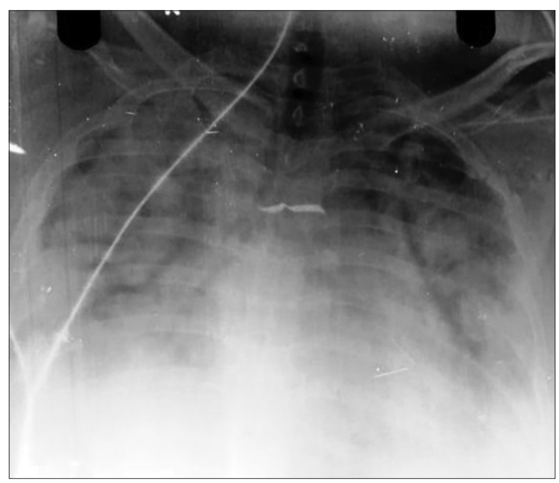

Figure 4: Chest radiograph in a 40-year-old male patient with severe COVID-19 symptoms shows bilateral nearly symmetrical extensive consolidation (white out lungs) in all four quadrants (Radiographic Assessment of Lung Edema score 24, serum D-dimer level 6578 ng/ml)

Discussion

As this COVID-19 pandemic continues to advance globally without any respite in the near sight, we need rapid radiological investigations for early identification and categorization of these patients as per disease severity for initiation of appropriate treatment and better prognosis. Although CT is more sensitive and specific in diagnosing COVID-19 disease,[7] we believe that in developing country like ours, CT cannot replace chest radiography as first-line investigation in COVID-19 patients. Not only the cost of the procedure, the operational complexities

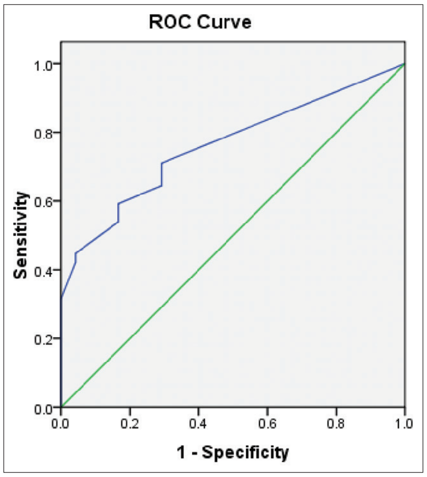

Figure 5: Receiver operating characteristics analysis of optimal Radiographic Assessment of Lung Edema cut-off score to differentiate symptomatic and asymptomatic COVID-19 patients

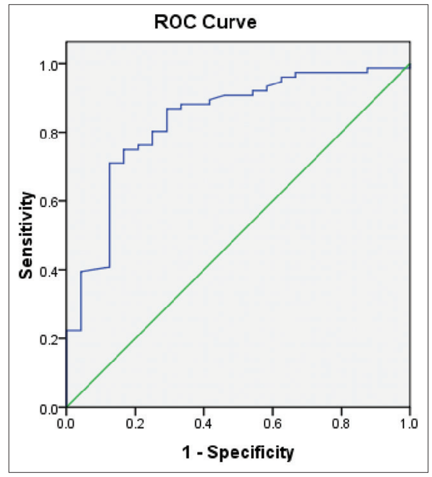

Figure 6: Receiver operating characteristics curve of optimal serum D-dimer levels cut-off to differentiate between symptomatic and asymptomatic COVID-19 patient

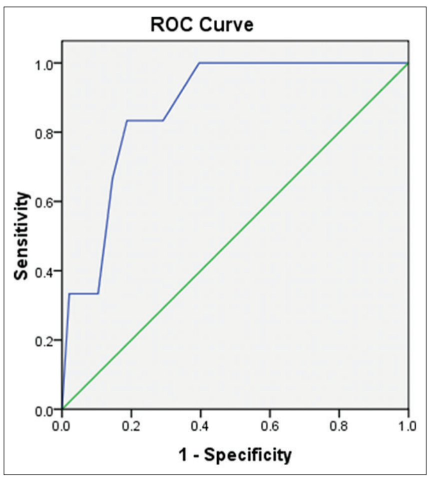

Figure 7: Receiver operating characteristics curve of optimal Radiographic Assessment of Lung Edema cut-off score to distinguish mild and severe COVID-19 patients

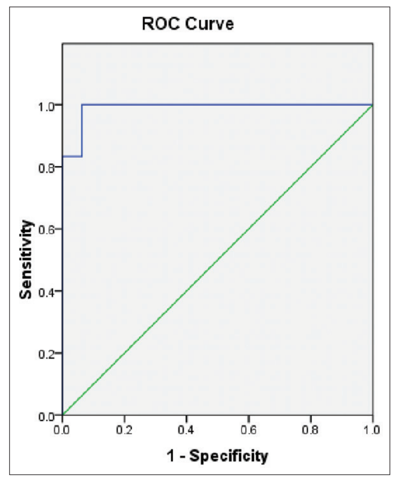

Figure 8: Receiver operating characteristics curve of optimal serum D-Dimer level cut-off to differentiate mild and severe COVID-19 patients

involved in performing CT chest like scanner contamination, sick patient mobility, cross-infection, etc., precludes its widespread use as an initial screening test in COVID patients. For such reasons, portable chest radiography continues to play an important role in the management of COVID-19 disease. The ease of performing the procedure at the patient's bedside, that too with lower radiation exposure and lower risk of cross-infection makes it a preferred early triage tool.[11]

The sensitivity of baseline chest radiography in recently reported data shows a wide variability ranging from 60% to 75%.[10] Baseline chest radiograph was abnormal in 75% of our patients whereas 25% of patients had normal chest radiograph at the time of admission. The sensitivity of chest radiography in the studies by Gatti *et al*.,[12] and Cozzi *et al*.,[10] were 61% and 68%, respectively, which matches with our study.

The older patients in this study (mean age of 45.38 ± 16.57) were more likely to have symptomatic COVID-19 disease at the time of presentation in contrast to younger patients (mean age 34.54 ± 15.06) who were mostly asymptomatic and the difference (−10.833 ± 3.966) between the mean age of asymptomatic and mildly symptomatic patients was found to be statistically significant ($P = 0.03$). The weaker immune system coupled with frequent association of comorbidities probably makes the older population more vulnerable for symptomatic and severe disease.[13] The symptoms such as fever, cough, and shortness of breath were common in older patients (especially the elderly) in the study of Guo *et al*.,[13] when compared with the younger age group. Jin *et al*.,[14] also found a strong association between disease severity and mortality with older age and comorbidities in patients with COVID-19 and SARS. Lui *et al*.,[15] stated that the low lymphocytes level may be an indicator of severity in COVID-19 disease and significantly lower levels of lymphocytes in older patients as compared to younger patients make them prone for severe disease.

Although 69% of our study patients were males and the remaining were females, this difference was not found to be statistically significant ($P = 0.230$). Thus, we cannot comment on the gender predisposition of this disease. Jin *et al*.[14] reported a similar prevalence of COVID-19 in men and women without any gender predisposition of this disease.

Bilateral asymmetric lung involvement was more common than unilateral lung involvement (36 vs 25 patients). Our study revealed typical peripheral subpleural ($n = 58$) disease predominance. The pattern of parenchymal involvement in this study closely matched the previous literature. The most common pattern of disease involvement was bilateral (57.7%) and peripheral (69%) in the study by Cozzi *et al*.[10] Jacobi *et al*.[16] also reported similar findings in their study.

In this study, the most commonly detected chest radiographic abnormality in COVID-19 patients was ground-glass opacity (GGO) which was seen in 31 (41.3%) patients. However, the distribution of GGO in asymptomatic and symptomatic categories was statistically insignificant ($P = 0.342$). Consolidation was the second-most common radiographic abnormality seen in 23 (30.6%) patients with statistically significant distribution among various disease categories ($P = 0.001$). Seven patients (9.3%) had both GGO and consolidation and all were moderate to severely symptomatic at the time of presentation. Consolidation was the most common finding (30 of 64; 47%) followed by GGO (21 of 64; 33%) in the study by Wong H and *et al*.[11] A systematic review and meta-analysis by RodriguezMorales *et al*.[17] also stated that the main thoracic manifestations of the COVID-19 disease include bilateral pneumonia (72.9%) and GGOs (68.5%). The Cleverley *et al*.[18] reported ground glass appearance as a common earlier presentation in COVID patients which may precede the appearance of consolidation. The ground-glass opacities can be very subtle and are characterized by an area of parenchymal opacification with only partial obscuration of underlying lung markings.[18] Although GGO was the most common radiographic finding in our patients at the time of admission, it was a poor predictor of symptomatic disease. Pleural effusion is not a common manifestation of this disease,[12] a finding which is well depicted in this study, as only 9 cases had associated mild pleural effusion at the time of presentation**.**

For objective assessment of parenchymal involvement and for better quantification of parenchymal changes various scoring systems have been proposed and validated in the past.[10,11,19] One such scoring system is RALE (Radiographic Assessment of Lung Edema) which is commonly used in patients of ARDS to quantify involvement of lung parenchyma to standardize and objectively quantify the radiographic report and to calculate a prognostic score at the patient's admission.[11] The present study also utilized RALE scoring which was done in all the patients using all four quadrants of both lungs to assess the severity of disease for quantification of lung involvement. The distribution of radiological findings was found to be insignificant in the right upper quadrant ($P = 0.146$) whereas was statistically significant in the rest three quadrants ($P \leq 0.001$). The mean cut-off value of the RALE score in the present study was found to be $\geq 3.98 \pm 5.54$ in mildly symptomatic patients and $\geq 13.33 \pm 8.55$ in severely symptomatic patients. The ROC curve analysis was also done to determine optimal cut-off values for RALE score in differentiating asymptomatic from symptomatic cases and mild from severely diseased cases. The optimal cut-off RALE score for identifying symptomatic patients was found to be ≥3 (AUC 0.760) and for identifying severe cases was ≥7 (AUC 0.870). We observed strong positive correlation between the RALE score and disease severity, i.e. as the severity of symptoms increased RALE score also increased. Cozzi *et al*.[10] found statistically significant correlation between RALE score and patients' outcome and higher risk of ICU admission in patients with RALE score >15. Ciceri *et al*.[20] also reported positive correlation between the severity of disease and RALE score and the median RALE score in their study was 9 (interquartile range 4–16).

Induction of cytokine storm by SARS CoV-2 triggers the coagulation cascade, resulting in thrombotic complications which leads to DIC and adverse clinical outcomes in COVID-19 patients. Postautopsy reports of patients who succumbed to COVID 19, showed fibrinous thrombi, the tumefaction of endothelium, and megakaryocytes in the small pulmonary vasculature.[21] A fibrin degradation product known as D-dimer rises in the blood of these COVID patients due to the process of fibrinolysis. Thus, to diagnose thrombotic states in COVID 19 patients, the determination of serum D-dimer levels constitutes a sensitive test. The elevated levels of serum D-dimer help in the rapid identification of severely diseased and complicated cases who are at risk of landing into DIC and pulmonary thromboembolic state. This would enable appropriate risk stratification and the early administration of therapeutic measures which might reduce COVID-19-related morbidity and mortality.[21] Our study confirms the statistically significant positive correlation between disease severity and serum D-Dimer levels ($P < 0.001$). The mean cut-off serum D-dimer value was found to be 673.8 ± 601.26 ng/ml in mildly symptomatic patients and 4685.5 ± 1802.8 in severely symptomatic patients which was significantly higher than the upper normal limit (0–500 ng/dl). The optimal cut-off D-Dimer values for correctly diagnosing symptomatic and severe disease were found to be ≥567 ng/ml (AUC 0.836) and ≥1200 ng/ml (AUC 0.99), respectively. Paliogiannis *et al*.[21] also found significantly higher D-dimer concentrations in patients with more severe COVID-19 disease (serum D-Dimer: 910 ng/dl; $P < 0.0001$). Fu *et al*.[22] stated that D-dimer level can distinguish severe COVID-19 (serum D-Dimer value 1220) cases from the mild/moderate (serum D-Dimer value 70–1180 ng/dl) and the AUC of D-dimer in their study was 0.74.

Our study has few limitations

The small sample size of this study may limit statistical relevance. The retrospective study design without the inclusion of control patients may limit the evaluation of the accuracy of chest radiography. No consideration was given to associated comorbidities in patients due to the lack of such data in the majority of cases. The reproducibility of some subtle radiographic findings may be challenging in suboptimal viewing conditions, especially for nonradiologists.

Conclusion

The most common chest radiographic features of COVID-19 include GGO and consolidation with typical bilateral asymmetric peripheral predominance. The consolidation on the chest radiograph at the time of admission is a better predictor of symptomatic disease than GGO. Radiographic RALE score can be utilized at the time of admission for objective quantification of lung parenchymal involvement and assessment of disease severity in COVID-19 patients which may help in appropriate triaging of patients. The elevated serum D-dimer levels correlate strongly with severe COVID-19 disease and can be utilized for the early identification of patients at risk of thromboembolic events. The timely administration of blood anticoagulants in these patients can ultimately help in the reduction of mortality and morbidity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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