Original Article

Chest radiographic findings and their correlation with disease progression in COVID-19 patients in northern India

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Abstract

Introduction: The present study was undertaken to describe and quantify the spectrum of radiographic findings on coronavirus disease 2019 (COVID-19) patients. The study also aimed to analyse the changes in chest X-ray (CXR) with disease progression. **Methods:** COVID-19 patients admitted between the period of 15 March 2020 and 1 July 2020 were retrospectively enrolled. CXR images were assessed and reported as 'Normal' or 'Abnormal'. A severity score was calculated using Warren *et al.*'s Radiographic Assessment of Lung Edema scoring. Correlations of the severity score thus calculated were sought with age, sex, clinical manifestations and presence of comorbidities. **Results:** Five hundred patients (342 males, 158 females) were enrolled, median age being 35 years. Fever and cough were the most common symptoms but significant correlation of an abnormal CXR was found with dyspnoea. CXRs were normal in 67% and abnormal in 33% patients. The commonest comorbidities were diabetes mellitus and cardiovascular disease including hypertension, coronary artery disease and congestive heart failure. Predominant pattern was ground glass opacities, reticular alteration and consolidation peaking in the second week from symptom onset. The most frequent distribution was bilateral, peripheral with middle/lower predominance. Increasing age, male sex, presence of dyspnoea and comorbidities correlated with abnormal findings on CXR. Critical illness and mortality correlated strongly with increasing age, male sex and presence of dyspnoea, less so with presence of comorbidities. **Conclusion:** In the current scenario with clinicians and radiologists working in tandem, CXR seems to be a promising tool in providing relevant information in a simplified way.

Keywords: Chest X-ray, COVID-19, radiography, severity

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a beta-coronavirus that was first identified in Wuhan, China, in the end of 2019 and is known to cause the acute respiratory syndrome called coronavirus disease 2019 (COVID-19).[1] The virus subsequently spread to 188 countries with more than 17 million cases reported all over the world as on 30 July 2020, with 1581,963 cases reported in India so far.[2]

As the physicians are trying their best to combat this ongoing pandemic, imaging is critical in assessing the severity and disease progression.

A lot of recent COVID-19 radiological literature is focused on computed tomography (CT) findings.[3-6] In the developed countries all around the world, CT chest has been often a first-line investigation for COVID-19.[7] However, the increasing

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number of hospitalized patients and need for repeated evaluation places a huge burden on the radiology resources; this poses a big challenge for infection control in the CT suite and results in significant radiation exposure to the patients. Need for subsequent decontamination also disrupts the imaging services and often becomes a capacity constraint for patient management.

The British Society of Thoracic Imaging has proposed a diagnostic algorithm for COVID-19 pandemic in March 2020 where it recommended chest X-ray (CXR) as the initial diagnostic imaging tool.[8] Around the same time, the American College of Radiology recommended use of CT only in specific clinical indications and not for screening COVID-19 patients.[9]

In a developing country like ours, CT scanners are not ubiquitous, and chest radiographs are usually the first modality to investigate respiratory illnesses. Even in primary healthcare centres, establishing a clinical correlation with chest radiography would assist the primary care physicians in the management and decision making of COVID-19 patients.

Since we are a tertiary care government-run hospital of the National Capital Region of India and acting as the Nodal centre for the disease, we are amongst the first few hospitals to encounter cases of COVID-19.

COVID-19 shows a close relationship between pulmonary involvement and adverse clinical outcome.[10] The purpose of this study was to retrospectively study the extent, distribution and spectrum of radiographic findings in COVID-19 patients admitted to our hospital and to analyse the changes in CXR with disease progression.

Materials and Methods

The study commenced after the approval of the Scientific Research Committee and Ethics Committee of our institute.

The COVID-19 patients admitted to our hospital between the period of 15 March 2020 and 1 July 2020, who had a positive Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) for SARS-CoV-2 from nasopharyngeal swab samples, were retrospectively enrolled. The pregnant patients were however excluded from our study. DICOM (Digital Imaging and Communications in Medicine) images of the CXR were assessed. It is worth mentioning here that at the time of writing this article, in India, as per our national guidelines all patients who tested positive for COVID-19 were to be hospitalized.

All the CXRs were acquired as computed radiographs on a portable X-ray unit in the isolation wards. Posteroanterior projection was preferred for image acquisition, anteroposterior projection being used only when patient was too sick to be upright. Two radiologists scored each radiograph in consensus as 'Normal' or 'Abnormal'. The CXRs were assessed for abnormalities like consolidation, ground glass opacity (GGO), pleural fluid, cardiomegaly, lymphadenopathy and so on.

A severity index was calculated by adapting and simplifying the Radiographic Assessment of Lung Edema score proposed by Warren *et al.*[11] A score of 0–4 was assigned to each lung depending on the extent of involvement by consolidation or GGO (0 = no involvement; 1 = <25%; 2 = 25–50%; 3 = 50–75%; 4 = >75% involvement). The scores for each lung were summed to produce the final 'Severity score'. Thus, the lowest score was '0' which represented a normal CXR and the highest score given was 8.

The distribution of parenchymal involvement was categorized into (i) peripheral predominance, perihilar predominance (peripheral and perihilar demarcation was defined as halfway between lateral edge of the lung and hilum), or neither; (ii) right, left or bilateral lung involvement; and (iii) upper zone, mid zone, lower zone or no zonal predominance.

Correlations of patient characteristics like age, sex, clinical features and comorbidities were sought with normal or abnormal CXR.

When correlating the severity score with above-mentioned patient characteristics, in patients who underwent more than one CXR, the highest severity score was considered for analysis (maximum ever during hospital stay as per the serial CXRs).

The common pattern of evolution of findings on CXR over time was also described.

Statistical analysis

The data are presented as the number (%) or the median because the age of the patients and the CXR score were not normally distributed.

The Mann–Whitney *U* test and multiple correlation coefficient were used to find relation between abnormal CXRs, their severity index in relation to age of the patient, underlying comorbidities and common symptoms.

Results

In our study, 500 patients were included with positive RT-PCR for COVID-19 between 15 March 2020 and 1 July 2020, who underwent CXR for evaluation. Of the total 500 patients, 342 were males (68.4%) and 158 (31.6%) females. The median age in our study subjects was 35 years ranging between 3 and 82 years [Table 1].

Forty-one patients were asymptomatic while remaining 459 patients who were symptomatic had fever and cough as the most common symptoms presenting in 280 (56%) and 270 (54%) patients, respectively. Other symptoms recorded were dyspnoea, sore throat, myalgia, diarrhoea, headache, anosmia,

Table 1: Age, sex, symptoms and comorbid illness details of patients enrolled in the study (*n*=500)

Characteristic	Number (% of 500 patients)
Sex	Males=342 (68.4%)
	Females=158 (31.6%)
Median age	35 years
Symptom	
Asymptomatic	41 (8.2%)
Symptomatic	459 (91.8%)
Fever	280 (56%)
Cough	270 (54%)
Dyspnoea	133 (26.6%)
Sore throat	105 (21%)
Myalgia	74 (14.8%)
Diarrhoea	18 (3.6%)
Headache	17 (3.4%)
Anosmia	11 (2.2%)
Nausea	7 (1.4%)
Dizziness	5 (1%)
Loss of taste/appetite	4 (0.8%)
Comorbidities	
DM	74 (14.8%)
CVD	72 (14.4%)
HTN	61 (12.2%)
CAD	5 (1%)
CHF	6 (1.2%)
Thyroid disorder	20 (4%)
Chronic respiratory illness	7 (1.4%)
Chronic kidney disease	6 (1.2%)
Chronic liver disease	5 (1%)
Epilepsy	1 (0.2%)
Idiopathic thrombocytopenic purpura	1 (0.2%)
Total patients with comorbidities	129 (25.8%)

DM: Diabetes mellitus; CVD: cardiovascular disease; HTN: hypertension; CAD: coronary artery disease; CHF: congestive heart failure

nausea, dizziness and loss of appetite in decreasing order of frequency. The commonest comorbidity in our study was found to be diabetes mellitus (DM) followed by cardiovascular diseases (CVD) comprising hypertension (HTN), coronary artery disease (CAD) and congestive heart failure [Table 1].

In our study, the CXRs of 335 (67%) out of 500 patients were found to be normal. Of the remaining 165 (33%) patients whose CXRs were abnormal, predominant parenchymal abnormality encountered was GGOs followed by reticular alteration and consolidation, patchy or lobar. Bilateral involvement, peripheral and mid or lower zonal predominance were seen commonly [Images 4 and 5]. Other findings though less frequent were pleural effusion and lymphadenopathy [Table 2].

The percentage of abnormal CXR was higher in males as compared to females [Table 3]. On using the Mann–Whitney *U* test, there was found to be a no significant difference in severity between CXR of males and females (*P*-value is 0.968).

It was also observed that the percentage of abnormal CXR increased significantly in patients above 40 years of age

Table 2: CXR characteristics of 500 COVID-19 patients

	Number (% of 500 patients)
CXR finding	
Normal	335 (67%)
Abnormal	165 (33%)
	Number (% of 165 patients)
Parenchymal abnormality	
Ground glass opacity	116 (70%)
Reticular alteration	85 (51%)
Consolidation	52 (31%)
Fibrosis	11 (6%)
	Number (% of 165 patients)
Parenchymal distribution	
Unilateral	66 (40%)
Bilateral	99 (60%)
Peripheral	83 (50%)
Perihilar	6 (3%)
Neither	76 (46%)
Lower zonal predominance	129 (78%)
Mid-zonal predominance	21 (13%)
Upper zonal predominance	7 (4%)
Mid- and lower zonal predominance	46 (28%)
No zonal predominance/diffuse	8 (25%)
Other findings	
Pleural effusion	4 (2%)
Lymphnodes	2 (1%)
Cardiomegaly	35 (21%)

[Table 4 and Image 1]. The average age of patients having abnormal CXRs was 46.9 years and median age to be 46 years.

One or more comorbidities were present in 126 (25.2%) of our sample population of COVID-19 patients, comprising 78 males and 48 females. The most prevalent comorbidity observed was DM (14.8%), followed by HTN (12.2%). Multiple correlation coefficient test was used to establish correlation of abnormal CXRs with presence of comorbidities, which revealed a high positive correlation with the coefficient of correlation being 0.99. CVD showed maximum correlation with abnormal CXR (coefficient of correlation 0.98 with *P* value as 0), followed by chronic obstructive pulmonary disease and DM. Likewise, there was found to be a positive correlation between presence of comorbidities and increased severity score of CXRs, with the coefficient of correlation being 0.63 (P-value < 0.05).

When seeking a relation between presence of symptoms and an abnormal CXR, a moderate positive correlation was observed with the coefficient of correlation being 0.53. Though fever was the commonest recorded symptom, maximum correlation of an abnormal CXR was found to be with dyspnoea where the coefficient of correlation was 0.478 which is a moderately strong correlation.

In our data set, there were 77 patients who had subnormal arterial oxygen saturation (<90% on room air) and required supplemental oxygen. In this subset of 77 patients, 69 had abnormal

CXRs (89.6%) which is much higher vis-à-vis in the overall data set (33%). The average as well as mean age of this subset of patients was 48 years as opposed to 35 years in the overall data set [Table 5].

Amongst symptoms in this data set, the coefficient of correlation between CXR being abnormal is highest (0.56) with dyspnoea followed by anosmia and cough. The same holds good when correlations are sought with severity indices.

In our overall data set, the correlation between abnormal CXR and presence of comorbidities is very high; however, the same did not hold good for this critical subset of patients. At the same time, this subset showed a weak positive correlation of severity score of CXR with presence of comorbidities.

Total of 852 CXRs were evaluated of the 500 patients included in the study. The evolution of CXR findings were studied from the day of symptom onset (considered as day 1 of illness). It was observed that in 1–7 days after symptom onset, there is rapid progression of findings. In this phase though GGO was the commonest abnormality, reticular alteration was also commonly encountered, frank consolidation being relatively rare.

From 8–14 days, the lung involvement showed maximum severity scores [Table 6 and Image 6]. Though GGO and reticular pattern was still common, consolidation increased. During this period, asynchronous and mixed pattern of involvement was commonly observed.

After 14 days, the severity scores started to decline with decrease in the reticular opacities and consolidation. However, GGO was again observed as the most common finding.

Table 3: Number and percentages of normal and abnormal CXRs in males and females

	Number	Percentage
CXR in males	342	(*n*=342)
Normal	220	64%
Abnormal among males	122	36%
CXR in females	158	(*n*=158)
Normal	115	73%
Abnormal among females	43	27%

In severe cases, this decline was more prominent during the third week of illness.

Even on discharge in few patients, the most common residual abnormality observed was GGO.

It was also observed that the average severity scores were higher in the critical subset of 77 patients as compared to the total sample of 500 patients [Table 6, Images 2 and 3].

Discussion

We hereby report a study of 500 patients admitted to our hospital with RT-PCR confirmed SARS-CoV-2 infection. This is one of the first few studies to explore the CXR findings in SARS-CoV-2 positive cases in the Indian population to give a peek into the radiographic distribution, frequency and severity.

Out of 500 patients, 335 (67%) had normal CXR while 165 (33%) were abnormal. We had a total of 459 symptomatic patients, out of which 161 had abnormal findings on CXR. Forty-one patients in our study were asymptomatic throughout their hospital stay, out of which only four had abnormal CXR. Similar results were reported in a study done by Weinstock *et al.*[12] where they found 58.3% CXR to be normal in 636 symptomatic patients. Another study by Vancheri *et al.*[13] comprising 240 symptomatic patients also described 25% CXRs to be normal.

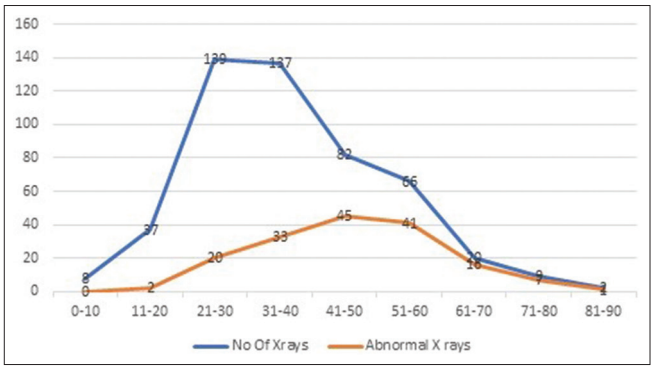

Image 1: Graphical representation of total CXRs versus number of abnormal CXRs with increasing age groups. The blue curve represents total number of CXRs done in different age groups and orange curve represents the number of abnormal CXRs out of the total done

Table 4: Percentage of abnormal CXRs in different age groups

Age group	Number of CXR done	Number of abnormal CXR	Abnormal Cases as % of CXR taken in particular age range %	Remarks
0-10	8	0	0.0	Percentage of abnormal cases with respect to number of CXRs is higher in patients >40 years of age
11-20	37	2	5.4	
21-30	139	20	14.4	
31-40	137	33	24.1	
41-50	82	45	54.9	
51-60	66	41	62.1	
61-70	20	16	80.0	
71-80	9	7	77.8	
81-90	2	1	50.0	

In our study, distribution of findings on abnormal CXR was predominantly bilateral, peripheral and lower zonal. This corroborates with other similar studies done worldwide.[13,14]

We found GGOs to be by far the most common parenchymal abnormality seen in 116 patients (70%) followed by reticular opacities in 85 (51%) and consolidation in 52 (31%), while pleural effusion (4%) and lymphadenopathy (2%) were found in only a few patients. Weinstock *et al.*[12] reported interstitial and GGOs to be the prominent descriptive findings in CXR. Vancheri *et al.*,[13] Shi *et al.*[14] and Zhao *et al.*[15] also described GGOs as the most common abnormality on chest imaging. In the Indian context, a recent study also echoed our findings.[16] However, in a study done by Wong *et al.*,[17] the most common finding reported was consolidation followed by GGO.

Our study comprised 342 male and 158 female confirmed COVID-19 patients, thus showing a male preponderance. Most of the studies conducted worldwide have shown similar trends of males being more prone for infection.[18]

Out of the 165 patients with abnormal CXRs, 74% were males and 26% females. However, no statistically significant difference was found in severity indices between males and females. The percentage of abnormal CXRs increased significantly in patients above 40 years of age.

We also found a strong correlation between presence of comorbidities and an abnormal CXR. The severity on CXRs was also seen to correlate positively with presence of comorbidities. Out of the major comorbidities in our study, CVD (comprising HTN, CAD and CHD) showed maximum correlation with abnormal CXR. Similar findings were also reported in other international and national studies.[19-21]

Out of the total symptomatic patients, fever (56%) and cough (54%) were the most common presenting manifestations, followed by dyspnoea, sore throat and myalgia. The clinical presentation of COVID-19 as reported by various studies conducted document similar symptoms in patients.[19,20,22]

Another important observation was that presence of symptoms correlated well with CXR. Though fever and cough were the most common recorded symptoms, maximum correlation of an abnormal CXR was found to be with dyspnoea which was recorded in 133 patients (26.6%). We could not find sufficient literature on the correlation of abnormal CXR with dyspnoea in COVID-19.

In our study, there were 76 patients who had a fall in arterial oxygen saturation and required admission or transfer to intensive care unit (ICU). The mean age of these sick patients was higher, that is 48 years as opposed to 35 years in the overall sample. Out of the patients who were managed in ICU, eight patients succumbed to COVID-19-related illness, out of which seven were males and their mean age was 56.5 years. Multiple recent studies document older age and male sex to be associated with increased disease severity and mortality.[19,20,22]

Table 5: Characteristics and outcome of the 77 patients of COVID-19 who developed hypoxemia and required ICU admission

	Females	Males	Total
No of patients	19	58	77
Abnormal CXR	17	52	69
% of abnormal CXR	89.4	89.6	89.6
Average age	52.63 years	47.89 years	49.06 years
Median age	55 years	48 years	48 years
Deaths	01	07	

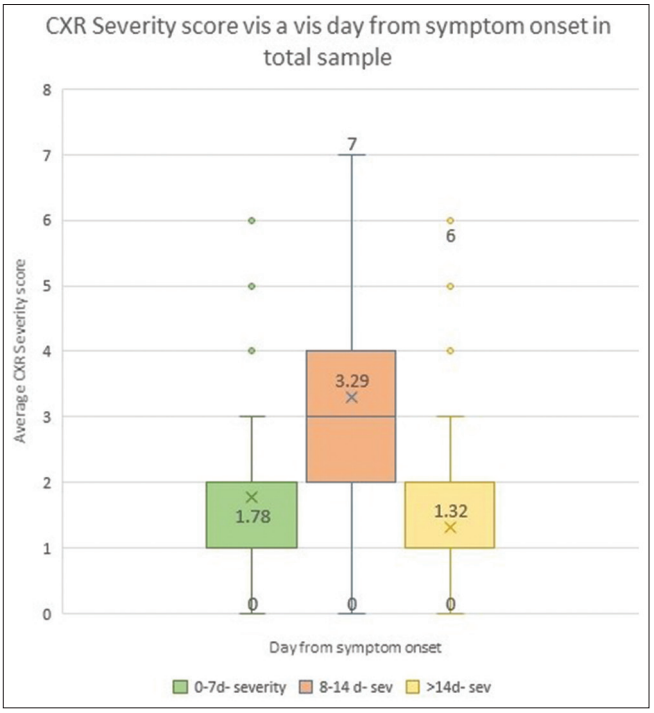

Image 2: Graphical representation of average CXR severity scores (*y*-axis) and days from symptom onset (*x*-axis) in total sample of 500 COVID-19 patients

Table 6: Average CXR severity scores with days of symptom onset in total sample of 500 COVID-19 patients and the critical subset of 77 patients

	0-7 days (from symptom onset)	8-14 days (from symptom onset)	>14 days (from symptom onset)
Average CXR severity score in total sample of 500	1.77	3.29	1.31
Average CXR severity score in 76 patients who had a fall in oxygen saturation	2.13	3.79	1.56

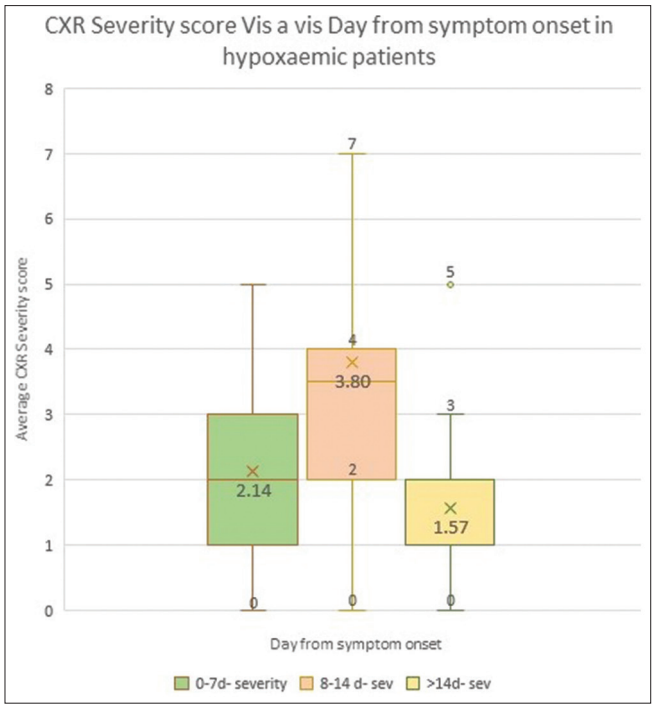

Image 3: Graphical representation of average CXR severity scores (*y*-axis) and days from symptom onset (*x*-axis) in 77 critically ill COVID-19 patients

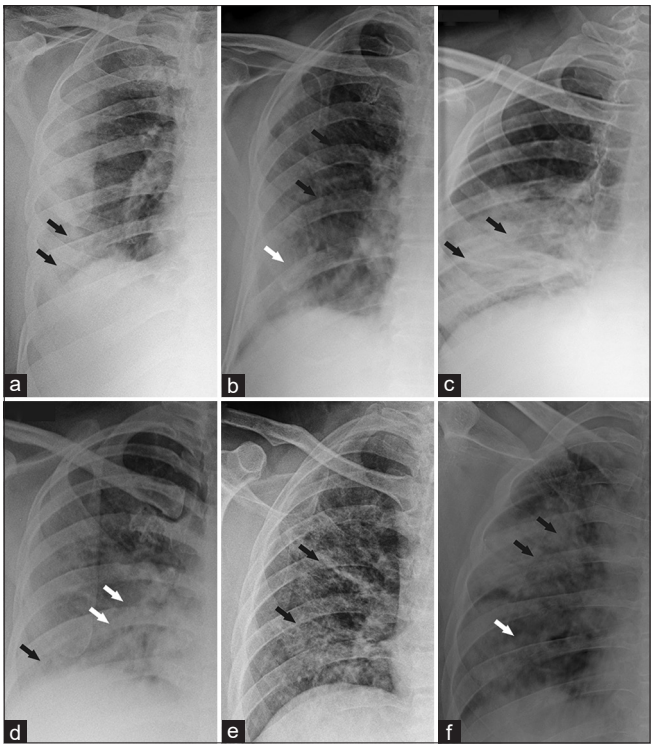

Image 4: The common findings on chest radiography in COVID-19 patients. (a) Peripheral ground glass opacities (black arrows), (b) ground glass opacities (black arrows) with reticular alteration (white arrows), (c) consolidation (black arrows), (d) ground glass opacities (black arrow) with consolidation (white arrows), (e) reticular opacities (black arrows) and (f) reticular opacities (white arrow) with consolidation (black arrows)

The average CXR severity score of these 76 patients was higher than that of the overall sample, thus establishing an association of CXR severity with the severity of disease in our study.

In this subset of patients, the percentage of abnormal CXRs was much higher (89.6%) as compared to that found in the total sample (33%). The seven patients in this subset had normal CXRs that could not be explained by plain radiography alone and CT was not available. Thus, the possibility of false-negative CXR cannot be ruled out in these seven patients. The most recent literature documents sensitivity of CXR to vary between 69% and 90%.[23]

Forty-two patients out of 76 who required ICU admissions had one or more baseline comorbidities like DM, HTN, thyroid disorders and so on. Five out of the eight who died also had underlying comorbid illnesses. However, presence of comorbidities was not found to be strongly associated with critical illness. Most of the recent literature in this context suggest association of underlying comorbidities with critical illness and mortality.[19-23] However, a large study from New York concluded comorbidities to be strong predictors of hospital admission and to a lesser extent of critical illness and mortality in people with COVID-19.[24]

From the evolution of CXR findings with the course of the disease, we inferred that COVID-19 initially involved both lung parenchyma and lung interstitium, manifesting as GGO, GGO plus consolidation or GGO plus reticular pattern, causing single or multiple abnormalities simultaneously. As the disease progressed, both the parenchymal and interstitial abnormalities progressed, GGO turned into GGO plus reticular pattern and GGO plus reticular pattern turned into consolidation. Meanwhile, some lesions began to absorb. Thereafter, the intensity of the previous abnormalities decreased. Thus, our study highlights the role of chest radiograph and its severity scoring in determining the disease severity. This becomes even more relevant in areas with limited resources.[25] These findings also correlated well with the recent studies carried out worldwide.[13,26-28]

A recent European study which compared chest radiography and CT chest in triage setting of COVID-19 patients also concluded that clinical triage is safely assisted by CXR.[29]

Our study had few limitations. First, review CXRs were decided by the clinical need and was not uniform, thus may have affected the precision of our analysis. Second, CT was not available, thus limiting evaluation of the sensitivity and specificity of CXR, and the possibility of the normal CXRs having subtle abnormalities cannot be completely ruled out. Third, as no confirmation of the findings was done by lung biopsy, other potential causes of GGO, such as pulmonary haemorrhage, could not be investigated. Fourth, although radiologists were instructed not to let the diagnosis of COVID-19 influence their interpretation, yet some possibility remains.

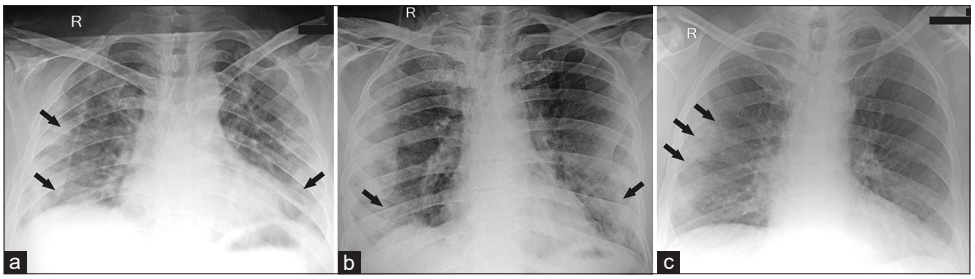

Image 5: Usual distribution of chest radiographic findings in COVID-19 patients. (a) CXR showing bilateral ground glass opacities involving lower zones and peripheral patchy consolidation (arrows), (b) another CXR of a COVID-19 patient showing bilateral ground glass opacities with lower zonal predominance (arrows), (c) CXR showing patchy peripheral consolidation involving right mid lung zone (arrows)

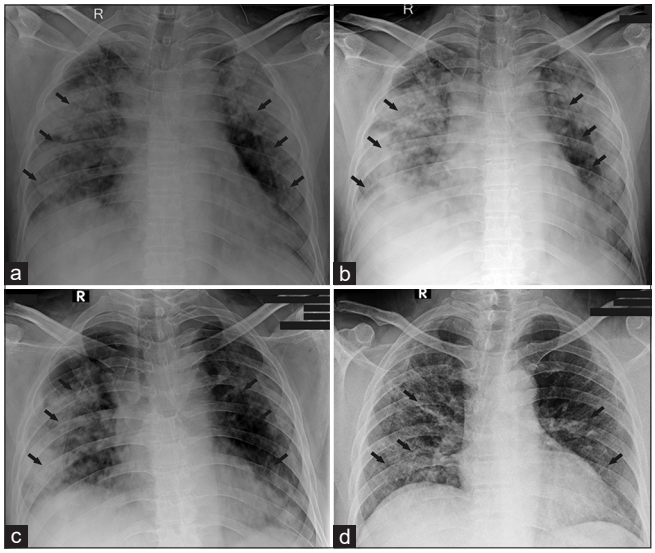

Image 6: Pattern of evolution of chest radiographic findings in COVID-19 patients. (a) CXR of a 38-year-old man, acquired on the fifth day since the onset of symptoms, showing bilateral peripheral ground glass opacities and consolidation involving predominantly the mid- and lower lung zones; (b) CXR of the same patient acquired on the tenth day since the onset of symptoms, showing increase in the radio-opacities bilaterally; (c) CXR of the same patient acquired on the 10th day since the onset of symptoms, showing the bilateral radio-opacities starting to decrease; (d) CXR done on 15th day from the day of symptom onset showing significant resolution of patchy consolidation, however persistence of reticular and peripheral ground glass opacities

Conclusion

COVID-19 pneumonia manifested on CXRs as GGOs, reticular alteration and consolidation causing single or multiple abnormalities simultaneously, which peaked in the second week from symptom onset. The most frequent distribution was bilateral, peripheral with middle/lower predominance.

Increasing age, male sex, presence of dyspnoea and presence of comorbidities correlated well with increasing abnormal findings on CXR in COVID-19 patients.

Elderly males having dyspnoea and hypoxemia were more likely to be admitted in ICU.

Critical illness and mortality correlated strongly with increasing age, male sex and presence of dyspnoea, less so with presence of comorbid conditions.

Chest radiography is a useful, ubiquitously available tool in a hospital setting that can assess the severity of the COVID-19 pneumonia in a simplified way correlating well with an increased risk of ICU admission or progression to critical illness. This also goes a long way in aiding the primary care physicians who are the first level of medical care for majority of Indian population.

Thus, it is imperative for every radiologist and clinician to be familiar with the radiographic features and act in tandem to fight this tiring battle of the ongoing pandemic.

Key points

CXR has emerged as the initial imaging tool to assess the severity of the COVID-19 pneumonia in a simplified way. It is ubiquitously available even in the settings where there is a dearth of resources and at the same time correlates well with progression to critical illness.

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Institutional scientific and ethical research committees approvals

The authors certify that above-mentioned approvals were duly taken before commencement of the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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