SPECTRUM OF CHEST X-RAY FINDINGS IN COVID-19 POSITIVE PATIENTS UTILIZING MODIFIED RALE SCORE FOR SEVERITY ASSESSMENT

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ABSTRACT

Objective: To assess chest x-ray appearance of patients with positive RT-PCR test for SARS-Cov-2 and utilize modified RALE score for severity assessment of chest x-ray findings for correlation with clinical spectrum of disease.

Study Design: Prospective observational study.

Place and Duration of Study: Armed Forces Institute of Radiology & Imaging, Pak Emirates Military Hospital, Rawalpindi, from Apr 2020 to May 2020.

Methodology: First 1000 consecutive chest x-rays of COVID-19 patients with RT-PCR confirmation at our setup were analyzed. Positive chest x-rays were assessed for consolidation, ground glass opacities and location of involvement. A severity index using modified RALE score was calculated for each & both lungs.

Results: Nine hundred and thirty two patients were males and 68 were females with an average age of 40.77 years ± 13.58. Out of 1000 patients, 759 (75.9%) had normal chest x-rays. Two hundred and forty one patients had positive findings, ground glass opacities being the most frequent feature 211 (87.6%) showing peripheral 219 (90.9%), bilateral 182 (75.5%) and lower zone predominance 221 (91.7%). The optimal modified RALE score threshold for recognizing severe disease was 4.5 (area under curve, 0.943), with 79.2% sensitivity and 96.3% specificity.

Conclusion: COVID-19 patients with positive chest x-ray findings frequently showed ground glass opacities with bilateral lower zone involvement in peripheral distribution. Modified RALE score can be used for objective evaluation of clinically severe patients.

Keywords: Chest x-ray, COVID-19, Modified RALE score.

INTRODUCTION

Corona virus disease 2019 (COVID-19) is an infectious disease first seen as an outbreak in December 2019 in Wuhan City, Hubei Province, People's Republic of China. The disease indicated proof of human to human transmission with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) recognized as the primary causative agent[1].

The disease demonstrated rapid transmission rates spreading worldwide and on 11 March 2020, World health Organization (WHO) declared it a global pandemic. By 31st March 2020, over 750,000 COVID-19 positive cases had been confirmed globally with significant number of deaths amounting to over 35,000[2]. Patients suffering from COVID-19 show clinical evidence of flu like disease with fever and respiratory symptoms the most common features. However, few cases do not provide evidence of significant clinical or radiological findings but can still serve as asymptomatic carriers[3].

The COVID-19 literature published has been predominantly focused on Computed Tomography (CT) findings as CT has been shown to be more sensitive than chest X-ray (CXR)[4,5]. Mainland China also primarily employed CT as the primary imaging modality during the outbreak. However, CXR still remains the first line imaging investigation for evaluating acute respiratory illness in immunocompetent patients[6]. The utilization of CT as first line modality can lead to huge

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burden on radiology departments as well as posing challenges pertaining to infection control and sterilization of the CT suite.

The American College of Radiology identified that decontamination of CT machines needed after scanning of COVID-19 patients may lead to disruption of radiological services, and further suggested that portable CXR may be used as a method to curtail risk of cross-infection[7]. Hospitals across UK and Italy also utilized CXR as a first-line diagnostic tool due to prolonged turn around times of reverse transcription polymerase chain reaction (RT-PCR) test for viral detection[8,9].

Hence, in countries exhibiting relative excess of COVID-19 cases, employment of CT over CXR cannot be taken as a plausible option considering dearth of available resources. As prevalence of COVID-19 keeps on increasing, it also seems essential that clinicians of all specialties are able to recognize CXR features of COVID-19 for identification of the disease in CXRs that are done for other possibilities. At the same time ability to differentiate severity of disease on CXR can help in segregation of cases for provision of appropriate patient care.

The aim of our study was: (I) to assess CXR appearances of COVID-19 patients showing positive results on real time RT-PCR testing for SARS-Cov-2 nucleic acid, (II) to utilize modified RALE score as criteria for assessment of severity of CXR findings and (III) correlate CXR severity score with clinical severity of disease in COVID-19 positive patients.

METHODOLOGY

It was a prospective observational study performed over 2 months, starting from 1st April 2020 till 31st May 2020. The first 1000 consecutive CXRs performed at our setup during this duration of clinically suspected COVID-19 patients with RT-PCR confirmation on nasopharyngeal swabs were evaluated using universal sampling method.

The study was approved by the Ethical review board committee, AFIRI (IERB approval certificate no: 009). Patients with clinical symptoms but without RT-PCR confirmation were excluded from the study. Patients with clinical symptoms but negative on RT-PCR were also excluded from the study. CXRs with inadequate technical parameters were omitted.

"Diagnosis and Treatment Program of Pneumonia of New Coronavirus Infection (Trial Fifth Edition)"[10]. Recommended by China's National Health Commission on February 5, 2020, was used to classify COVID-19 patients into minimal, common, severe and critical categories. Patients following minimal criteria have subtle symptoms and no significant lung changes on imaging (CXR and CT scan chest). Symptoms like respiratory tract infection and fever were encountered in common criteria with chest imaging demonstrating lung opacities. Severe cases were identified to follow any of three criteria:

(1) Dyspnea, RR ≥30 beats/min;

(2) Reduced blood oxygen saturation ≤93%; or

(3) Decreased arterial blood oxygen partial pressure (PaO2)/oxygen concentration (FiO2) (≤300 mmHg).

Critical criteria should be meeting following scenarios

(1) Respiratory failure and needs ventilator support;

(2) Shock;

(3) ICU monitoring treatment secondary to other organ failure.

For this study, severe and critical criteria were grouped together as severe/critical group.

All CXRs of COVID-19 positive patients referred to Armed Forces Institute of Radiology & Imaging, Rawalpindi were acquired in standard AP/PA projections as per departmental protocols. All CXRs in quarantine/isolation/inpatient wards were performed in AP projection with portable X-ray units as per local protocols.

Two consultant radiologists with 15 and 12 years of working experience respectively reported all CXRs independently. Further opinion was

taken from a senior consultant radiologist with 20 years of experience in case of any disagreement. Radiographic characteristics comprising ground glass opacities (GGOs), consolidation, and pulmonary nodules were assessed as per Fleischner Society glossary of terms[11].

Distribution of lung parenchymal findings was classified as (I) peripheral or perihilar involvement (delineation described as midpoint between outer most margin of lung and ipsilateral lung hilum); (II) unilateral (right/left), or bilateral lung involvement; and (III) zonal involvement (interpreted as upper, mid or lower zones). Appearance of other associated chest findings like pleural effusion or old infective changes was also recorded.

To measure the degree of infection, a severity score was created by modifying the Radiographic Assessment of Lung Edema (RALE) score which was proposed by Warren *et al*[12], and further initially employed by Wong *et al*[13]. Each lung considering range of involvement by GGO or consolidation was given a score of 0-4 (0= no involvement; 1=up to 25%; 2=25 to 50%; 3=50 to 75%; 4=75% to 100%). Each lung scores were aggregated for a final severity score (Range=0-8). To correlate modified RALE score with the clinical criteria, we further devised a CXR criteria applied on the severity score (0=Normal, 1-2=Mild, 3-4=Moderate, 5-6=Severe, 7-8=Critical).

The IBM SPSS 25 program was used for statistical analysis. Descriptive statistics were analyzed as mean ± standard deviation or median values for continuous variables and as percentages for nominal variables. Student's t-test was used to assess significance of variation of means and medians and pearson's chi-squa-red test was utilized for assessment of nominal variables.

Inter-rater reliability between observers was evaluated by intra-class correlation coefficient (ICC) for CXR severity scores in each individual lung as well total score of both lungs (ICC was classified as follows: acceptable = 0.70-0.80, good = 0.80-0.90, excellent = 0.90-1.0). A *p*-value ≤0.05 was defined as statistically significant.

The degree of association between CXR criteria and clinical criteria in abnormal CXRs was estimated by Spearman's rank correlation analysis. A Wilcoxon rank sum test was used to compare the difference of left lung, right lung and total score between the mild group and the severe group, and the Wilcoxon matched-pairs signed-rank test was used to compare the difference of scores between left lung and right lung. ROC curve analysis was used to assess Area under the Curve (AUC) and identify sensitivity, specificity and threshold for discrimination of Mild/Moderate from Severe/Critical group.

RESULTS

There were 932 (93.2%) males and 68 (6.8%) females, with a mean age of 40.77 years ± 13.58 (range 6 to 89 years). Majority of the cases 570 (57%) were in 21-40 age group (table-I). The ICC for modified RALE score was found to be excellent (n=1000, ICC median=0.946, ICC mean=

Table-I: Demographics in COVID-19 cases with normal and positive chest x-ray findings.

Variable	Normal chest x-ray (n: 759)	Positive chest x-ray (n: 241)	*p*-value
Age	36.42 ± 10.54	54.48 ± 12.98	<0.001
Gender			
Male	729 (96%)	203 (84.2%)	<0.001
Female	30 (4%)	38 (15.8%)	
Age Group			
1 (1-20 years)	20 (2.6%)	-	<0.001
2 (21-40 years)	528 (69.6%)	42 (17.4%)	
3 (41-60 years)	196 (25.8%)	106 (44%)	
4 (61-80 years)	13 (1.7%)	93 (38.6%)	
5 (81 years & above)	2 (0.3%)	-	

0.972). For further analyses, CXR reporting and severity scores calculated by one of the consultants were randomly chosen.

Seven hundred and fifty nine patients (75.9%) had normal CXRs showing no evidence of any lung parenchymal changes. Two hundred and forty one out of 1000 CXRs demonstrated abnormalities on reporting, highlighting suspicion of COVID-19. GGO was the commonest finding 211 (87.6%), followed by consolidation 170 (70.5%). Peripheral 219 (90.9%) and lower zone distribution 221 (91.7%) were the commonest locations, with majority of cases having bilateral involvement 182 (75.5%). Associated CXR findings like pulmonary nodules 37 (15.4%) and pleural effusion 31 (12.9%) were also seen in few of the positive CXRs (table-II).

Table-II: Chest x-ray findings in 1000 COVID-19 patients.

Characteristics	n (%)
Number of normal chest x-rays	759 (75.9%)
Number of abnormal Chest x-rays	241 (24.1%)
Type of parenchymal opacity in abnormal chest x-rays (n=241)	
Ground glass opacities	211 (87.6%)
Consolidation	170 (70.5%)
Distribution in abnormal chest x-rays (n=241)	
Peripheral predominance	219 (90.9%)
Perihilar predominance	162 (67.2%)
Right lung	19 (7.8%)
Left lung	40 (16.6%)
Bilateral lungs	182 (75.5%)
Upper zone involvement	89 (36.9%)
Middle zone involvement	190 (78.8%)
Lower zone involvement	221 (91.7%)
Other features in abnormal chest x-rays (n=241)	
Pleural effusion	31 (12.9%)
Pulmonary nodules	37 (15.4%)

Of the total cases, all cases with normal findings were given severity score of zero. Out of the 241 abnormal CXRs, 76 (31.5%) had total severity score of 1-2 falling into the mild criteria. More severe involvement was noted in 76 (31.5%) and 67 (27.8%) cases, who had severity scores of 3-4 and 5-6 and labeled as moderate and severe respectively. Twenty two (9.1%) patients had severity score greater than 6 on CXR and were classified as critical (table-III).

On the basis of clinical criteria, 747 patients were categorized as minimal, 147 as common or moderate and 106 patients as severe/critical (10.6%). Spearman's rank correlation analysis demonstrated significant association between clinical and CXR severity (0.791, p=0.01). CXR criteria showed 85.53% positive predictive value for common cases on clinical criteria and significantly higher positive predictive value of 94.38% for severe/critical cases. The average total lung score was 2.36 (1.00-6.00) in common patients and 5.31 (3.00-8.00) in severe/critical patients (table IV).

ROC analysis showed area under the curve (AUC) for discriminating patients in the common and severe/critical group to be 0.943 (S.E: 0.014; 95%CI, 0.916-0.969) (figure). The optimal modified RALE score threshold for classifying severe cases was 4.5, with 79.2% sensitivity and 96.3% specificity.

Table-III: Comparison of chest x-ray criteria and clinical criteria in positive chest x-rays.

		Clinical Criteria = n(%)		Total	*p*-value
		Common	Severe to Critical		
CXR Criteria	Mild (1-2)	76 (31.5%)	-	76 (31.5%)	<0.001
	Moderate(3-4)	54 (22.4%)	22 (9.1%)	76 (31.5%)	
	Severe (5-6)	5 (2.07%)	62 (25.7%)	67 (27.8%)	
	Critical (7-8)	-	22 (9.1%)	22 (9.1%)	

DISCUSSION

COVID-19 was announced as a public health emergency of international concern by the World Health Organization on January 30th, 2020. COVID-19 is a highly infectious disease and spread worldwide. Approach for stifling disease and patient care predominantly depend on disease confirmation[14-15]. However, COVID-19

detection has been confronted by slender laboratory facilities and reduced availability of nucleic acid kits[16]. Radiology emerged to have a forefront role in identification of COVID-19 cases with CT scan and CXRs as the modalities of choice. While CT scan is more sensitive[17-18], CXR has the advantages of being easily available, economical and portable as compared to CT imaging.

Table-IV: Comparison of scores of both lungs between clinical severity groups.

Variable	n	Common (n=135)	Severe/Critical (n=106)	*p*-value	ICC*
Right Lung					
0	40	40 (29.6%)	-	<0.001	
1	47	43 (31.9%)	4 (3.8%)		
2	77	47 (34.8%)	30 (28.3%)		
3	62	5 (3.7%)	57 (53.8%)		
4	15	-	15 (14.2%)		
Total Right Lung	241	1.12 (1.00, 3.00)	2.78 (2.00, 4.00)	<0.001	0.963
Left Lung					
0	19	19 (14.1%)	-	<0.001	
1	79	70 (51.9%)	9 (8.5%)		
2	82	40 (29.6%)	42 (39.6%)		
3	50	6 (4.4%)	44 (41.5%)		
4	11	-	11 (10.4%)		
Total Left Lung	241	1.24 (1.00, 3.00)	2.53 (1.00, 4.00)	<0.001	0.957
Total Both Lungs	241	2.36 (1.00, 6.00)	5.31 (3.00, 8.00)	<0.001	0.972

**ICC = Intraclass Correlation Coefficient*

In our study, 24.1% COVID-19 positive patients had abnormal chest radiographic findings. In a study published by Wong *et al*[13], to study the CXR features of 58 COVID-19 positive patients, 38 (38/64, 59%) showed changes on baseline CXR. The number of patients demonstrating CXR changes in our study is also lower than that seen in the case series of 9 patients by Yoon *et al*[19], (5/9, 56%). This difference may be ascribed to the dis-similarity in sample size of these studies, the point at disease course where CXR was taken, the difference in disease spectrum in ethnically different populations or variability in CXR reporting.

Majority CXRs in our study were normal (n=759) showing no evidence of lung parenchymal changes. The same patients predominantly remained asymptomatic or showed minimal symptoms clinically. The commonest feature of COVID-19 disease on CXRs in our study was GGOs, present in 87.6% of the abnormal CXRs. This was followed by consolidation which was present in 70.5% abnormal CXRs. These features are consistent with previously published case series[18-19]. The lower zones were involved in 91.7% cases followed by involvement of the middle zones in 78.8% abnormal CXRs. The study by Wong *et al*[13], had similar radiological distribution of disease. This pattern of disease distribution was also present in a study by Yang *et al*[20], using HRCT to study COVID-19 cases. Among uncommon findings, pulmonary nodules were seen in 15% cases and pleural effusions found in 12.9% cases. Pleural effusion was also found to be uncommon in the study by Wong *et al*.

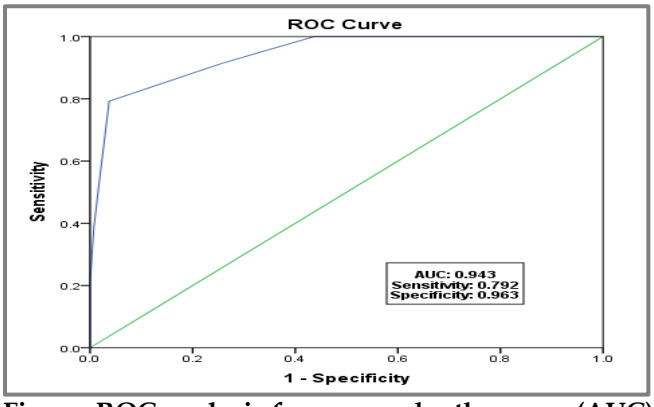

Figure: ROC analysis for area under the curve (AUC) for modified RALE score.

In our study, we utilized a semi-quantitative scoring system for zonal assessment of each lung involved by disease process. We established that modified RALE score was more in severe cases in contrast to mild ones. Similarly, identifying modified RALE score thre shold of 4.5 to ascertain severe COVID-19 was of paramount importance (79.2% sensitivity and 96.3% specificity).

CXR criteria showed 85.53% positive predictive value for common cases on clinical criteria and significantly higher positive predictive value of 94.38% for severe/critical cases. Moreover, inter reader agreement between our radiologists was excellent with an average ICC of 0.972 for modified RALE score. We propose that this reasonably simple method could impart objectivity to hasten the recognition of severe patients, especially in circumstances of meager healthcare resources. Hence, indoor patients can be followed up on CXR for disease severity instead of CT scan to avoid unnecessary radiation exposure to patients as well as COVID-19 exposure of health care workers at the radiology department.

There are several limitations linked to our study. Not all cases were assessed till final conclusion, hence correlation with disease course is diminished for few patients. Time duration between CXRs and RT-PCR testing was controlled by clinical course and inconstant, thus potentially influencing precision of our analysis. Lastly, few CXR features were subtle, which may limit reliability in suboptimal viewing conditions or by non-specialists. We suggest further studies for correlation of CXR findings with HRCT findings and chronological comparison of CXRs to assess radiological course of the disease.

In summary we report spectrum of CXR findings in COVID-19 positive patients. Modified RALE score correlates better with clinical disease at higher scores.

CONCLUSION

Majority of COVID-19 patients undergoing CXR remain asymptomatic with no significant CXR findings in our population. Therefore, limiting baseline CXR in asymptomatic carriers can decrease unnecessary COVID-19 exposure in health care workers of radiology department. COVID-19 patients with positive CXRs showed GGOs as the commonest finding with bilateral lower zone involvement in peripheral distribution. Modified RALE score can be used for objective evaluation of clinically severe patients with a higher positive predictive value. Hence, indoor patients can be followed up on CXR for disease severity instead of CT scan to avoid unnecessary radiation exposure of patients and COVID-19 exposure of health care workers.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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