ORIGINAL ARTICLE

THE ESSENTIAL ROLE OF CONVENTIONAL RADIOGRAPHY IN COVID-19; PERSPECTIVE OF A DEVELOPING COUNTRY

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Background: The Coronavirus disease (COVID-19) pandemic has shaken the world. So far, CT has emerged as main stay of imaging whereas the local data on radiographic features of COVID-19 is sparse. **Methods:** Prospective study includes 402 chest X rays (CXRs) of 105 patients presenting with symptoms of COVID-19. The nature of abnormality, distribution and lung zone involvement was documented. Following British Society of Thoracic Imaging (BSTI) guidelines, CXRs were grouped into classic/ probable COVID-19, indeterminate, non-COVID-19 and normal categories. The lung involvement was scored according to modified Radiographic Assessment of Lung Edema (RALE) scoring. The follow up radiographs were assessed for disease progression and improvement. **Results:** Seventy-six males and 29 females with mean age of 50 years were included in our study. 47 out of 105 baseline radiographs were categorized as classic/ probable COVID-19, 26 as indeterminate, 7 as Non-COVID-19 and 25 as normal. 75 patients were positive and 30 were negative on RT-PCR testing. The sensitivity of CXR in diagnosing COVID-19 is 84%. The worsening radiographic features and higher RALE score correlates with longer hospital stay, ICU admissions and mortality. The ground glass opacities and consolidations in peripheral distribution involving bilateral mid and lower zones are the predominant findings of COVID-19 in Pakistani population. **Conclusion:** Combination of bilateral peripheral ground glass opacities and consolidations are the cardinal feature of COVID-19 on CXRs. The diagnostic categories described by BSTI correlates with PCR results in Pakistani population. The worsening radiographic findings correspond to poor prognosis; hence serial radiographs can be used for assessing disease course.

Keywords: COVID-19; Chest X ray; RALE scoring

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INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) came to light with the first reported case in December 2019 in Wuhan, China resulting from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1] The outbreak was declared a Public Health Emergency of international concern on January 30, 2020 and later, declared a pandemic on March 11, 2020 by World Health Organization (WHO).[2]

In Pakistan, the first case of COVID-19 was reported on February 26, 2020. As of now (August 10, 2020) 2,84,000 confirmed cases have been reported in Pakistan with a death toll of 6097.[3] The number is continuously rising. Reverse Transcriptase- Polymerase Chain Reaction (RT-PCR) is used as a primary diagnostic tool, worldwide. The imperative role of imaging in COVID-19 cannot be denied. Chest radiograph being part of baseline investigation provides beneficial information for assessing the lung status.[4] The investigation is readily available, non-invasive and inexpensive. Portable radiography as recommended by American College of Radiology (ACR) guidelines is ideal in the current scenario, as it prevents the spread of infection.[5] In low to middle socio-economic countries (LMIC) like Pakistan, HRCT is costly investigation. Moreover, it is not widely available; hence majority of the imaging is relied on CXRs. This consideration led to the need of acquiring data comprising of chest radiographic findings of COVID-19 in our population.

Studies on Chinese and Korean population have documented ground glass opacities and consolidations as predominant pattern on radiographs of COVID-19 patients. There is usually multi-lobar involvement of bilateral lungs, more pronounced at the peripheries and lower zones.[6–8] Similar features were also reported by British Society of Thoracic Imaging.[9] Worsening of radiographic findings on serial images suggests poor prognosis.[6]

There is no proven treatment of COVID-19, likewise no vaccine is commercially available for disease prevention till date (August, 2020).[10]

Isolation remains the mainstay of management along with supportive measures usually required for respiratory symptoms. CXR findings correlate well with worsening respiratory symptoms; therefore, it can be adopted as a tool for assessing disease course.

MATERIAL AND METHODS

The prospective study was approved by Institutional ethical review board of Shaheed Zulfiqar Ali Bhutto Medical University/ Pakistan Institute of Medical Sciences, Islamabad.

Both male and female patients aged between 12–90 years, presenting with suspicion of COVID-19 and undergoing chest radiographs as part of investigation work up were included in our study.

Patients with unknown PCR status and with known co-morbid having evident findings on chest radiographs related to illness other than COVID-19 like congestive heart failure and metastatic pulmonary disease were excluded from the study.

RT-PCR test is an established diagnostic tool for COVID-19 in our population. RT-PCR test results are taken as reference for correlation with CXR diagnosis.

The RT-PCR tests were performed after RNA extraction (Qiagen Viral Mini Kit) on ABI 7500 Real Time RT-PCR detection system with internal and external positive controls using the SARS-CoV-2 protocols by National Institute of Health Sciences (WHO International Centre for Influenza Surveillance). The RT-PCR test results were followed, and brief histories were obtained.

All chest radiographs were performed in the isolation and COVID-19 ICU ward using Shimadzu portable digital X-ray unit. The radiographs were performed in frontal projection (AP or PA views depending upon patient's clinical condition). The technicians performing the radiographs were provided with personal protective equipment. The departmental Standard Operating Procedures (SOPs) for radiation protection, staff safety and disinfection were followed.

All radiographs performed during 21st March 2020 to 15th May 2020 were reported on X-ray reporting station of radiology department by two radiologists having 5 and 20 years of experience. The abnormalities seen on chest X ray were categorized as ground glass opacities, consolidation and reticular opacities (ground glass opacities refer to faint area of air space opacification that do not obscure broncho-vascular markings, consolidation refers to dense area of air space opacification obscuring the broncho-vascular markings and reticulations refer to linear opacities). The predominant pattern of distribution was classified into central/ perihilar, peripheral, both central and peripheral and random/no specific distribution (The 1/3 area of lung from medial margin is taken as central/ perihilar whereas 1/3 lung from lateral margin is regarded as peripheral). The lung is divided into three zones in vertical aspect, each upper, mid and lower zone comprising 1/3 height of lung. The chest x ray findings were grouped into one of the four following diagnostic categories; normal (no lung abnormality detected), classic/ probable COVID-19 (Bilateral multiple opacities in peripheral distribution in lower lobe, less commonly unilateral), indeterminate for COVID-19 (The findings do not match with classic and non COVID-19 descriptors) and non- COVID -19 (Features that are not diagnostic of COVID-19 like lobar pneumonia, pleural effusion, pneumothorax and pulmonary edema). The extent of lung involvement was assessed on RALE scoring (Score 0; Normal, Score 1; <25% lung involvement, score 2; 25–50% lung involvement, score 3; when 50–75% lung is involved and score 4; >75% lung involvement). The cumulative score was acquired by summing up individual score of both lungs. The additional findings including pleural effusions, pneumothorax, cavitation and nodules were also reported.

Patients with follow up radiographs were reviewed and compared with prior radiographs to assess for disease progression/ improvement. The RALE scores for subsequent radiographs were also compared with initial radiographs.

Qualitative variables are expressed as frequency and percentage while quantitative variables are measured as Mean ± Standard Deviation. Statistical analysis was performed using Graphpad Prism 5 (GraphPad Software, Inc. CA, USA). Chi square or Fisher exact test was used to compare the qualitative parameters with p-value <0.05, taken as significant.

RESULTS

A total of 402 radiographs from 105 (n) patients fulfilling the inclusion criteria were included in the study. Among these, 105 were baseline radiographs and 297 were subsequent follow up radiographs. Sixty patients out of 105 (57.1%) had follow up imaging. The number of follow up radiographs ranged from 1 to 28. Majority of the patients 76 (72.4 %) were males and rest 29 (27.6 %) were females. 59 out of 76 (77.6%) males and 16 out of 29 (55%) females have positive results on RT-PCR. No significant difference was found based on gender on CXR classification.

On RT-PCR testing, 75 (71.4 %) patients were positive and 30 (28.6%) were negative. The study participants aged between 12 to 90 years with mean age of 50±17 years. Fifty-three out of 105 (50.5%) were aged above 50 years. The mean age of RT-PCR positive patients is 54±16 which correlates well with the mean age of 55±15 of patients having classic COVID-19 on CXR. The mean age of patients in Indeterminate, Non-COVID-19 and Normal categories is 54±18, 51±19 and 36±12 respectively.

Out of total 105 baseline CXRs, 81 (78.1%) were abnormal whereas 25 (23.8 %) were normal. Sixty-six out of 75 (88 %) RT-PCR positive patients had abnormal baseline CXRs. None of the Classic, Indeterminate and Non-COVID-19 categories had normal radiographs. Significant correlation was found in the percentage of normal CXRs and negative RT-PCR results. Forty-seven out of 105 (44.7 %) baseline radiographs were categorized as classic/ probable COVID-19, 26 (24.8%) as indeterminate, 7 (6.67%) as non-COVID-19 and 25 (23.8%) as normal. Among the 47 patients characterized as classic COVID-19 on baseline radiographs, 45 (95.7%) were positive on RT-PCR. Out of 26 patients in the indeterminate category, 18 (69.23%) were positive and 8 were negative on RT-PCR.

Among the 7 patients in Non-COVID-19 category, 6 were also negative on RT-PCR. 11 out of 25 patients in the normal category based on baseline radiographs had positive results on RT-PCR, 7 of which were asymptomatic. Majority of the patients in the Non COVID-19 and normal category were also RT-PCR negative (figure-1) Bilateral lung involvement was noted in 56 out of 75 (74.67%) RT-PCR positive patients. Forty-two out of 47 (89.3%) patients in Classic COVID-19 category had bilateral lung involvement. Among 75 RT-PCR positive patients, 56 (74.6%) showed lower zone, 49 (65.3%) mid zone and 18 (24%) upper zone involvement. The most common features detected in our population in COVID-19 confirmed patients include consolidation (58.6%) followed by ground glass opacities (42.6%). Other features less frequently noticed include pleural effusion (0.05%), calcification (0.04%) and cavity formation (0.012%). None of the patients in our study population presented with nodules and pneumothorax. The predominant pattern of distribution documented in COVID-19 patients was peripheral (54.67%) followed by random (17.3%).

On baseline radiograph, the highest and lowest RALE score were 7 (0.026%) and 0 respectively. Majority patients, 79 out of 105 (75.23%) on presentation had RALE score ≤3. Patients having RALE score ≥4 on baseline radiographs were 26 (24.7%).

On follow up radiographs, all of 16 positive patients (31.3%) showing significant radiographic improvement recovered and were discharged. 20 out of 51 positive patients, on follow up imaging showed worsening of features. 9 (45%) of these had ICU admission, 3 (15%) patients died and 1 (2%) was shifted to other hospital. Sixteen (31.3%) positive patients showed no change on follow up imaging. All of these had baseline RALE score ranging from 0 to 2 and were discharged. Two patients showed waxing and waning pattern of radiographic features on follow up imaging during hospital stay, later both were discharged on improvement. Forty-nine (65.33%), 20 (26.66%) and 4 (0.053%) PCR positive patients had mild, moderate and severe disease on baseline radiographs. These results correlated with the severity of disease in classic group having 28 (59.57%), 16 (34%) and 3 (0.06%) patients in mild, moderate and severe classes.

Sixty-eight out of 75 (90.67%) RT-PCR positive patients were admitted to hospital, the remaining asymptomatic patients were home quarantined. Out of the admitted patients 14 (18.67%) died.

Among the Classic category, 45 (95.7%) were admitted to hospital, out of these 45, 9 (20%) patients lost the battle. Significant correlation was found in the results of these parameters between RT-PCR test and BSTI diagnostic categories (figure-2)

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of CXR in diagnosis of COVID-19 is 84% (95% CI 73.72 to 91.45%), 66.67 % (95% CI 47.2 to 82.7%), 86.3% (95% CI 79 to 91.34%), 62.5% (95% CI 48.35 to 74.8%) and 79.05% (95% CI 70 to 86.4%) respectively.

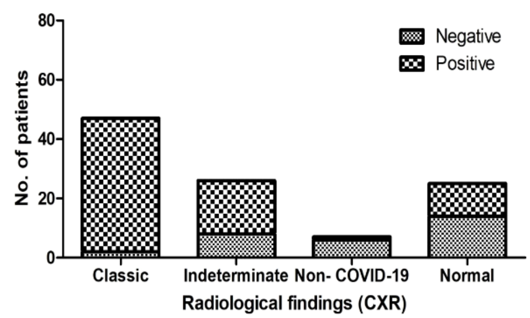

Figure-1: Ratio Bar graph correlating CXR diagnosis with RT-PCR results

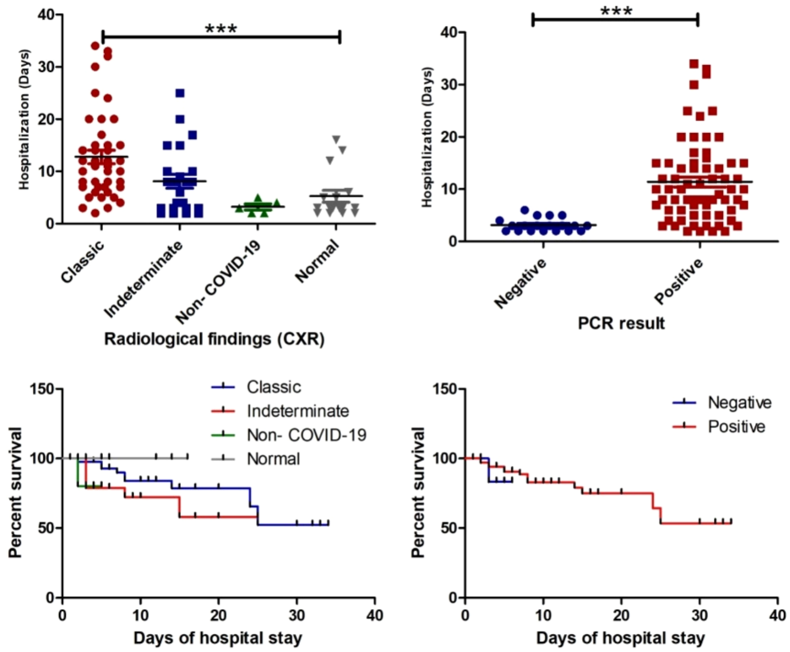

Figure-2: Relationship of CXR features and PCR result with duration of hospital stay and patient outcome

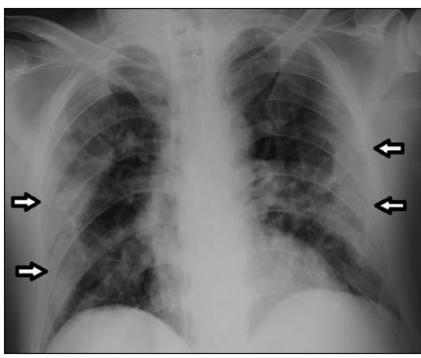

Figure-3: Bilateral peripheral patches of consolidations in mid and lower zones corresponding to Classic COVID-19

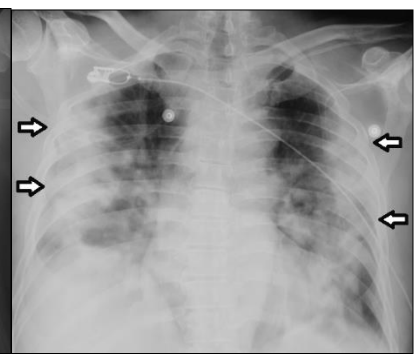

Figure-4: Peripheral patches of consolidation involving right upper zone, bilateral mid and lower zones representing Classic COVID-19

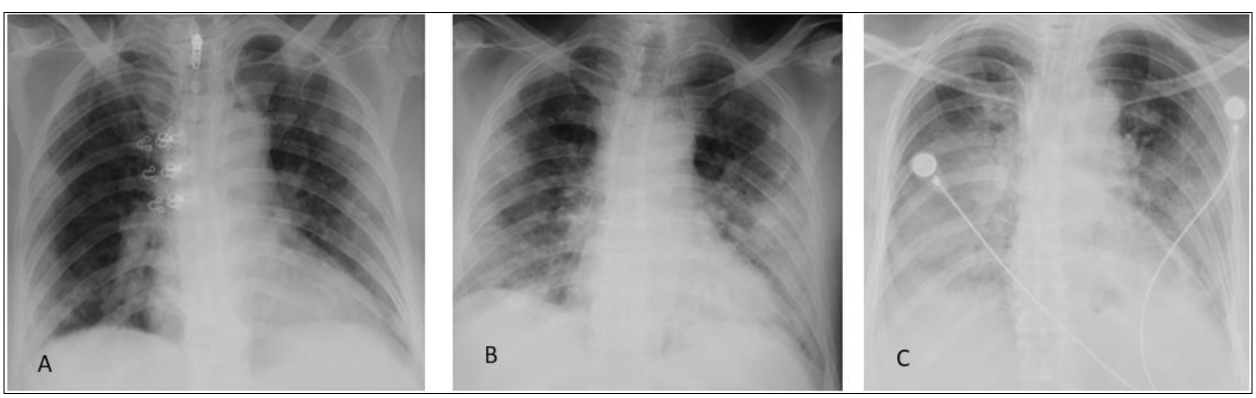

Figure-5: (A) represents small peripheral patches of consolidation in bilateral mid and lower zones corresponding to mild Classic COVID-19. (B): shows larger patches of consolidation in bilateral mid and lower zones affecting half of the lung parenchyma corresponding to moderate Classic COVID-19. (C) shows large consolidations involving more than half of the lungs corresponding to severe Classic COVID-19.

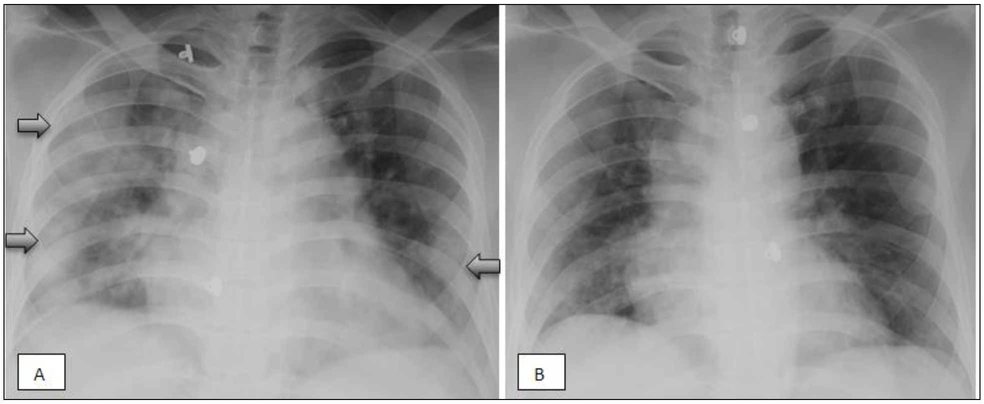

Figure-6: (A) shows Peripheral patches of ground glass opacification and consolidation marked by arrows involving right mid zone and bilateral lower zones. (B); Follow up CXR, 11 days apart shows significant resolution of these patches representing improvement.

Table-1: Comparison of demographic features, disease progression and clinical outcome with diagnosis of patients using CXR and PCR

Row Labels	**Grand Total**	**Positive**	**Negative**	***p*-value**	**Classic**	**Indeterminate**	**Non-COVID-19**	**Normal**	***p*-value**
Grand Total	105	75	30		47	26	7	25	
Age (mean±SD)	50±17	54±16	40±16	<0.0001	55±15	54±18	51±19	36±12	< 0.0001
Hospital stay in days (mean±SD)	9.6±7.7	11.4±7.8	3.2±1.3	<0.0001	13±8.4	8±6.4	3.2±1.3	5.2±4.5	< 0.0001
Mean age									
<50	52	28	24	<0.0001	16	10	4	22	0.0001
≥50	53	47	6		31	16	3	3	
Gender									
Female	29	16	13	0.0303	10	5	4	10	0.0775
Male	76	59	17		37	21	3	15	
Baseline CXR									
Abnormal	80	64	16	0.0009	47	26	7	0	< 0.0001
Normal	25	11	14		0	0	0	25	
Lung involvement									
Bilateral	68	56	12	0.0013	42	22	4	0	< 0.0001
Unilateral	12	8	4		5	4	3	0	
N.A	25	11	14		0	0	0	25	
GGO									
Absent	60	43	17	1	26	8	3	23	0.0001
Present	45	32	13		21	18	4	2	
Consolidation									
Absent	57	31	26	<0.0001	12	14	6	25	< 0.0001
Present	48	44	4		35	12	1	0	
Pleural effusion									
Absent	92	71	21	0.0014	46	19	2	25	< 0.0001
Present	13	4	9		1	7	5	0	
Cavity									
Absent	104	74	30	1	47	25	7	25	0.3813
Present	1	1	0		0	1	0	0	
Follow up radiographs									
Available	60	51	9	0.0005	34	17	0	9	0. .0003
Not available	45	24	21		13	9	7	16	0
Radiographic changes on follow up									
Improvement	17	16	1	0.0099	9	6	0	0	0.0006
Progression	22	19	3		16	6	0	0	
Static	19	14	6		6	4	0	10	
Waxing and waning pattern	2	2	0		2	0	0	0	
N.A	43	23	20		12	9	7	15	
Symptomatic									
Yes	96	69	27		46	26	6	18	
No	9	6	3	0.7127	1	0	1	7	0.0006
Hospital admission									
Yes	87	68	19		45	23	5	14	
No	18	7	11	0.0028	2	3	2	11	0.0002
Outcome									
Died	16	14	2	0.0046	9	6	1	0	0.001
Discharged	70	54	16		34	16	4	16	
Home Quarantine	16	6	10		2	3	1	10	
Shifted to other hospital	3	1	2		2	1	0	0	

DISCUSSION

The COVID-19 pandemic has mobilized all health departments to engage resources in utilizing best way for diagnosis and management of disease. Due to its human-to-human transmission, preventive measures and early diagnosis remains the mainstay of management. The recommendations of Italian Society of Radiology (SIRM) suggest use of CXR as first line investigation in diagnosis of COVID-19.[11] The use of CXR in early detection of COVID-19 is of paramount importance, particularly in regions having limited access to RT-PCR testing.[12] Moreover, the use of CXR in follow up imaging obviates the need of CT scanning reducing the radiation dose and decreasing the risk of disease spread via CT suite.

In Pakistani population, majority of the patients (78.1%) presenting with symptoms of COVID-19 had abnormal baseline radiographs. Similar observation was made by Fleischner Society.[13] The main features of COVID-19 on CXR in our population include consolidation followed by ground glass opacification that correlates with researches conducted by Ng M-Y *et al* and Yoon *et al*[14,15]. Wong HY et al. documented lower zone as the commonest site of lung involvement in peripheral distribution whereas our results show both mid and lower zone involvement in our population.[16] A research conducted in China by Bernheim A *et al.* also showed similar pattern of distribution[17].Pleural effusions, calcification and cavitation are found in only 0.05%, 0.04% and 0.012% of Pakistani COVID-19 patients respectively. These features are uncommonly reported in COVID-19 pneumonia and suggest alternate diagnosis.[18] Our results show that higher RALE score ($\geq$4) on baseline radiograph is associated with ICU admissions, longer hospital stay and poor outcome in comparison to those having low RALE score on admission. This finding can be utilized in triaging patients based on severity of disease. Our results show that serial imaging has a significant role in predicting disease outcome. Other studies have also documented the use of chest radiography in assessing disease severity and its role in predicting disease progression.[19]

The use of BSTI classification for COVID-19 CXR reporting correlates well with RT-PCR results. The CXR has sensitivity of 84 % in our population in comparison to 69% reported by Wong HY.[16]The higher sensitivity, lower cost and wide availability makes CXR a feasible tool for first line imaging investigation in diagnosing COVID-19.

CONCLUSION

Peripheral consolidations and areas of ground glass opacification involving bilateral mid and lower zones are the common features of COVID-19 in our population. CXR hold prime importance in resource poor, low to middle income countries (LMIC) in diagnosing COVID-19 where RT-PCR testing is expensive and time consuming. Serial CXRs have a role in predicting disease progression and outcome as well; hence establishing its beneficial role in disease management.

AUTHORS' CONTRIBUTION

AIM: Conceptualization. AIM & FR: Literature search, data interpretation, write-up, proof reading. SKR: Literature search, data analysis, data interpretation, proof reading. JK: Data collection, data interpretation, proof reading.

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