ORIGINAL ARTICLE

HRCT FEATURES OF COVID-19 IN RELATION TO DURATION OF DISEASE

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Background: Despite the fact that much has been written on various aspects of COVID-19, literature lacks a detailed and accurate description of HRCT findings in relation to the duration of the disease. The aim of this study was to investigate the difference in HRCT scan findings depending on the time after onset of the disease. The objective of the study is to identify and compare findings of HRCT scan at different time points after onset of the disease. **Methods:** A total of 224 patients, scanned over a period of 2 months, were placed in one of the four groups at the time of their scan depending on the days lapsed after their symptoms appeared. All scans were carried out on the same machine. Findings in each group were recorded and compared. A finding showing significant difference between groups indicates its importance in describing the course of the disease. Analysis was done on SPSS 23. **Results:** Ground glass opacities in posterior segments of one or more lobes was the most common feature and had a significant association with first 5 days of the disease (p=.027). Interlobular thickening and subpleural reticulation, are found between 3–5 days or later in the course of the disease (p=.000). **Conclusion:** Ground glass opacities located in posterior segments are the predominant feature in patients who are scanned up to 5 days after their symptoms appear. This feature is the most common in scans done in asymptomatic cases too. Interlobular septal thickening and subpleural reticulation start appearing at 3 days of disease process.

Keywords: Duration; HRCT; COVID-19; Segments

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INTRODUCTION

The pandemic of COVID-19 continues to be a matter of global concern. Although this disease may manifest with extra-pulmonary features, the strain of coronavirus that causes it is called severe acute respiratory syndrome coronavirus 2 (SARS CoV-2). The disease was first identified in Wuhan, China, in late December 2019 before it spread throughout the world.[1,2] This epidemic was declared by World Health Organization as a pandemic on 11 March 2020.[2]

Most symptoms associated with COVID-19 patients are nonspecific. Patients of COVID-19 have been typically described to present with fever (98%), may or may not have cough (76%), and develop dyspnoea over a period of a week to 10 days (55%).[1,2] These symptoms are not only non-specific, but inconsistent, and cannot be relied upon to make a diagnosis of COVID-19.[3] Nucleic acid testing has been widely used for diagnosing and screening COVID-19 but a large number of false negative reports reduce its diagnostic accuracy.[4] High resolution CT (HRCT) scan of chest was reported to have great value in screening and detecting patients with COVID-19 especially in suspected cases who were asymptomatic and were negative on nucleic acid testing.[5] HRCT chest has been reported to have a better diagnostic yield with only 3.9% of missed diagnosis.[6–8] Depending on the resources available, it may be employed as a reliable, quick method for diagnosis. In fact, before widespread availability of laboratory testing facility in Pakistan at the start of the outbreak, many hospitals across the country used HRCT for both diagnosis and evaluation of COVID-19.

In Pakistan, the number of cases was on the rise during the period of this study. The diagnostic workup being used for COVID-19 included nucleic acid test and HRCT scan of chest. The diagnostic features on HRCT scan were described by studies conducted in China and elsewhere[6,7] but studies on imaging features of chest CT in COVID-19 have been reported to suffer from quality concerns regarding methodology[9]. Much has been written about COVID-19 including its clinical manifestations[3], laboratory findings[10], and radiological features[3,7]. Nevertheless, literature lacks a description of HRCT findings in relation to the duration of the disease. A need was found to elaborately and accurately describe HRCT scan features at various stages of the disease in relation to the day after onset. This would help in improving the diagnostic guidelines. Aim of the study was to

investigate and compare HRCT scan changes in patients of COVID-19 depending on the day of their presentation, before as well as after onset of clinical features.

The objective of the study is to identify and compare findings of HRCT scan at different time points after onset of the disease.

MATERIAL AND METHODS

This cross-sectional, observational study was a descriptive review of patients who underwent HRCT scan for screening or evaluation of COVID-19 in two months duration from April 1, to May 30, 2020. Sample size comprised 224 patients. Details of the patients who had undergone HRCT scan were retrieved from radiology database, irrespective of age and sex. All patients who underwent HRCT scan for COVID-19 in the study period were included in the study. Patients who were PCR-negative or had pre-existing pulmonary disease were excluded. Patients were placed in different groups on the day of their scan, based on the day after onset of their symptoms: Group 1 included asymptomatic patients and scans done for screening purpose; Group 2 included scans 0–2 days; Group 3 included scans 3–5 days; and Group 4 included scans done on day 6 or later, after onset of symptoms. HRCT imaging findings and distribution of findings in the pulmonary lobes and segments was recorded. Distribution of radiological findings in the pulmonary field included laterality, number of lobes involved, areas of lobes involved, and involved segments. Findings were compared between all groups. Features of COVID-19 as seen on their HRCT[11] including ground glass opacities (GGOs) (Figure-1), interlobular thickening, subpleural reticulation, consolidation, crazy paving (Figure-2), and pleural effusion, were also compared between groups. The data was analysed on SPSS 23 and comparison across these four groups was done using chi-square test, considering *p*-value of 0.05 as statistically significant.

RESULTS

A total of 224 cases were included in the study spanning over a period of two months. 40.2% (n=90) of them were female and 59.8% (n=134) were male. 21.4% (n=48) of the total subjects were in Group 1 (asymptomatic) at the time of their HRCT, which was done for screening before surgery or some other aerosol-generating procedure; 16.1% (n=36) were in Group 2; 39.3% (n=88) in Group 3; and 23.2% (n=52) in Group 4. Age distribution of study population is shown in Figure-3. Respiratory signs and symptoms were found in 66.5% (n=149), whereas non-pulmonary clinical features were present in 41.9% (n=94) subjects. Fever with or without myalgias was found in 57.1% (n=128) subjects.

Pulmonary distribution of COVID-19 findings on HRCT was compared between all groups. The details of the compared parameters are shown in Table-1. A total of 76.8% (n=172) cases were bilateral, most of them in groups 3 and 4. Difference in bilaterality among the groups was statistically significant (p=0.000). Multi-lobar involvement was more in Group 3 (37.1%) and 4 (21.4%) out of a total of 83.9% of multi-lobar cases. This difference between groups was statistically significant (p=0.000). A total of 89.3% (n=200) cases had only peripherally located findings while 5.4% (n=12) had both peripheral and centrally located findings. Only 12 cases were found to have centrally located findings only, and 8 of them were from asymptomatic group. Difference between groups regarding the location of HRCT findings was statistically insignificant (p=0.061). Table-2 shows the comparison between all groups in relation to presence of various features of COVID-19 as seen on HRCT scan. Frequency of involvement of various pulmonary lobes and segments is shown in Table-3. Association of involved segments with the day of presentation, as shown in Figure 4, was statistically significant (p=0.027).

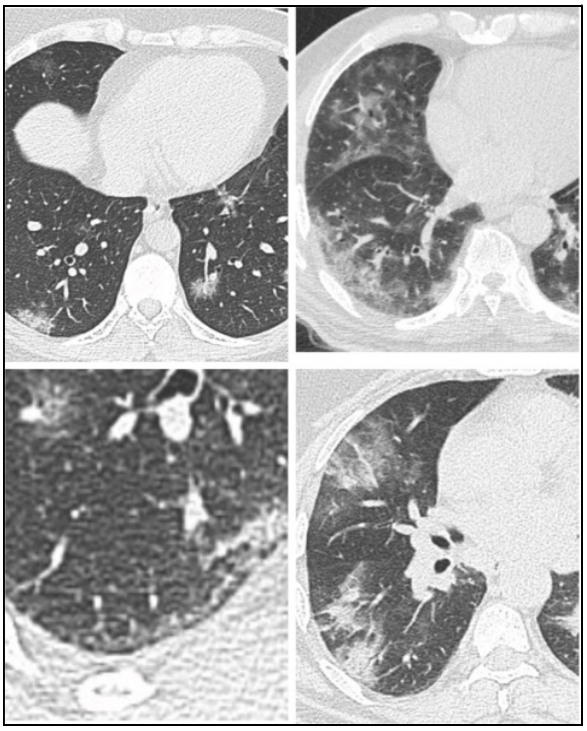

Figure-1: (From upper left clockwise) Central and peripheral rounded ground glass opacities; Interlobular septal thickening; Subpleural reticulations; Subsegmental consolidations.

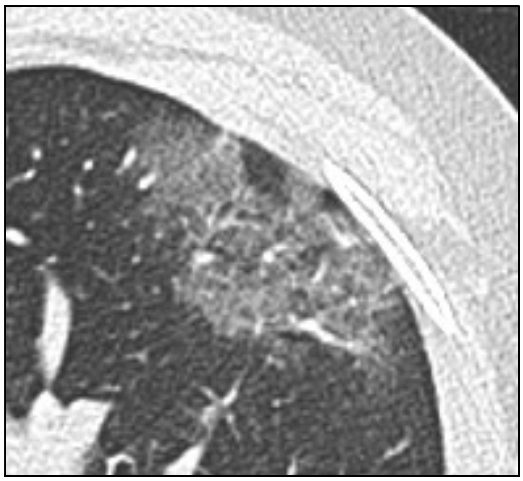

Figure-2: **GGO with crazy paving.**

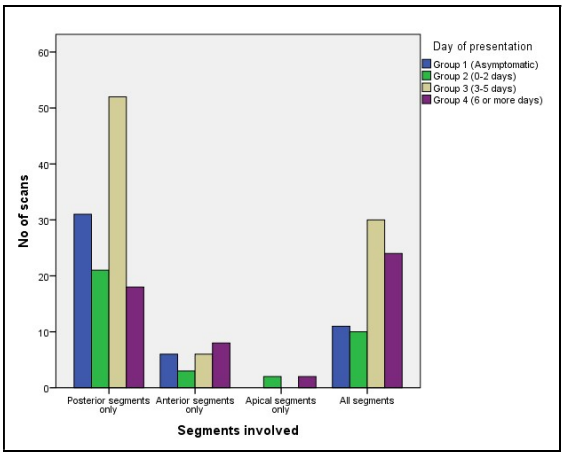

Figure-4: **Association of involved segments with day of presentation (*p*= .027)**

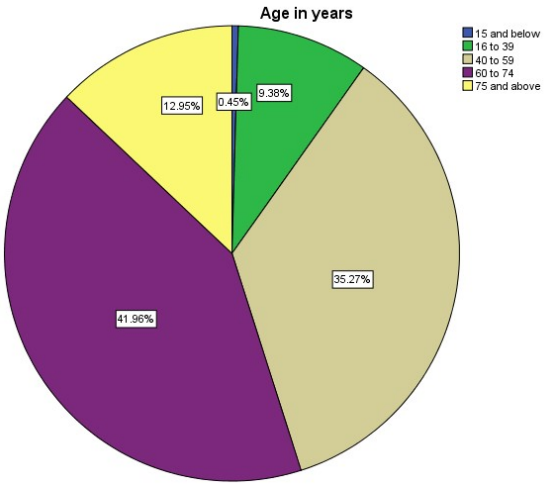

Figure-3: Age distribution

Table-1: Comparison of pulmonary distribution of COVID-19 between groups

Pulmonary distribution of features			Day of presentation				Total	*p*-value
			Group 1 (Asymptomatic)	Group 2 (0-2 days)	Group 3 (3-5 days)	Group 4 (6 or more days)		
Laterality	Unilateral	Count	21	15	8	8	52	.000
		% of Total	9.4%	6.7%	3.6%	3.6%	23.2%	
	Bilateral	Count	27	21	80	44	172	
		% of Total	12.1%	9.4%	35.7%	19.6%	76.8%	
Total		Count	48	36	88	52	224	
		% of Total	21.4%	16.1%	39.3%	23.2%	100.0%	
Lobes involved	Uni-lobar	Count	16	11	5	4	36	.000
		% of Total	7.1%	4.9%	2.2%	1.8%	16.1%	
	Multi-lobar	Count	32	25	83	48	188	
		% of Total	14.3%	11.2%	37.1%	21.4%	83.9%	
Total		Count	48	36	88	52	224	
		% of Total	21.4%	16.1%	39.3%	23.2%	100.0%	
Location in the lung	Centrally located	Count	8	3	1	0	12	.061
		% of Total	3.6%	1.3%	0.4%	0.0%	5.4%	
	Peripherally located	Count	39	29	84	48	200	
		% of Total	17.4%	12.9%	37.5%	21.4%	89.3%	
	Central and peripheral	Count	1	4	3	4	12	
		% of Total	0.4%	1.8%	1.3%	1.8%	5.4%	
Total		Count	48	36	88	52	224	
		% of Total	21.4%	16.1%	39.3%	23.2%	100.0%	

Table-2: Comparison of HRCT features between Groups

HRCT Features			Day of presentation				Total	*p*-Value
			Group 1 (Asymptomatic)	Group 2 (0-2 days)	Group 3 (3-5 days)	Group 4 (6 or more days)		
Ground glass opacities	No GGOs	Count	1	2	1	2	6	
		% of Total	0.4%	0.9%	0.4%	0.9%	2.7%	.530
	Patchy GGOs	Count	35	25	56	38	154	
		% of Total	15.6%	11.2%	25.0%	17.0%	68.8%	
	Rounded GGOs	Count	12	9	31	12	64	
		% of Total	5.4%	4.0%	13.8%	5.4%	28.6%	
Total		Count	48	36	88	52	224	
		% of Total	21.4%	16.1%	39.3%	23.2%	100%	
Lung consolidation	No	Count	33	31	63	31	158	.063
		% of Total	14.7%	13.8%	28.1%	13.8%	70.5%	
	Yes	Count	15	5	25	21	66	
		% of Total	6.7%	2.2%	11.2%	9.4%	29.5%	
Total		Count	48	36	88	52	224	
		% of Total	21.4%	16.1%	39.3%	23.2%	100%	
Interlobular septal thickening, band formation	No	Count	35	29	42	18	124	
		% of Total	15.6%	12.9%	18.8%	8.0%	55.4%	.000
	Yes	Count	2	7	67	24	100	
		% of Total	0.9%	3.1%	29.9%	10.7%	44.6%	
Total		Count	37	36	109	42	224	
		% of Total	16.5%	16.1%	48.7%	18.7%	100%	
Crazy paving	No	Count	48	33	84	47	212	
		% of Total	21.4%	14.7%	37.5%	21.0%	94.6%	
	Yes	Count	0	3	4	5	12	.150
		% of Total	0.0%	1.3%	1.8%	2.2%	5.4%	
Total		Count	48	36	88	52	224	
		% of Total	21.4%	16.1%	39.3%	23.2%	100%	
Pleural effusion	No	Count	38	33	83	52	206	
		% of Total	17.0%	14.7%	37.1%	23.2%	92.0%	
	Unilateral	Count	5	1	3	0	9	
		% of Total	2.2%	0.4%	1.3%	0.0%	4.0%	.012
	Bilateral	Count	5	2	2	0	9	
		% of Total	2.2%	0.9%	0.9%	0.0%	4.0%	
Total		Count	48	36	88	52	224	
		% of Total	21.4%	16.1%	39.3%	23.2%	100%	

Table-3: Frequency of lobes and segments involved

Lobe Involved	No of Patients	Percent
Left upper lobe	7	3.1
Left lower lobe	14	6.3
Multiple lobes unilateral	10	4.5
Multiple lobes bilateral	168	75.0
Right upper lobe	6	2.7
Right middle lobe	3	1.3
Right lower lobe	16	7.1
Total	224	100.0
Segments Involved		
Posterior segments only	122	54.5
Anterior segments only	23	10.3
Apical segment only	4	1.8
All segments	75	33.5
Total	224	100.0

DISCUSSION

This study included patients who presented with pulmonary as well as extra-pulmonary clinical features of COVID-19. According to age, 45.1% (n=101) were below or at the age of 59 years while 54.9% (n=123) were of 60 years or older. This corresponds to the global statistics of a mean age of 50.8 years.[12] Common clinical features were found to be respiratory (66.5%) which is similar to previous reports.[13] Comparison was done between groups of patients depending on the day after their presentation of symptoms as well as those who were scanned at a subclinical stage.

Analysis of pulmonary distribution of HRCT features of COVID-19 revealed 76.8% (n=172) to be bilateral, majority of them being in

Group 3 and Group 4 (35.7% and 19.6% respectively) (p=0.000). This is less than previously reported bilaterality at 84%.[14] Whereas 83.9% cases were multi-lobar, most of them belonged in Group 3 and 4 (p=.000). This is in conformity to the previous studies.[14] In our study, difference between groups regarding the location of HRCT findings was statistically insignificant (p=.061) and peripherally located findings are a common feature in all groups. This compares favourably with previous studies.[14,15] Results of our study reveal that 75% (n=168) of the scans showed involvement of multiple lobes bilaterally (Table-3). This is in conformity to a recent study by Salehi *et al* that reported involvement of multiple lobes.[15] Regarding segmental distribution, 54.5% (n=122) of the scans show the disease to be involving only the posterior segments in one or more lobes (Table-3). Difference of segmental involvement between the study groups was statistically significant (p= .027). Majority of the asymptomatic cases and early cases, up to 5 days after appearance of symptoms, showed involvement of posterior segments only. This corroborates the findings in literature although, unlike our study, previous studies have not analysed it in terms of number of days.[16]

Features of COVID-19 as seen on HRCT include ground glass opacities, consolidation, interstitial thickening, crazy paving and pleural effusion (Figure 1–5). Results of our study show that ground glass opacities (GGOs) were not found in 2.7% (n=6) patients, whereas 68.8% (n=154) showed patchy GGOs and 28.6% (n=64) showed rounded GGOs. Difference between groups was statistically not significant (p=.530), meaning that presence of GGOs is a common feature irrespective of the duration of disease. This is consistent with previous studies.[15,16] A common feature of COVID-19 on CT scan was interstitial thickening, present in 44.6% (n=100). Majority (29.9%) of these cases (n=67) were in Group 3 (3–5 days) and the difference between groups was statistically significant (p=.000). This is consistent with previously reported figures.[14]

Lung consolidation was found in 29.5% (n=66); crazy paving in 5.4% (n=12); pleural effusion in 8% (n=18) cases only. None of them provided a significant difference across the groups statistically although they were predominantly found in scans done on third or later day after onset of symptoms (Table-2).

Despite a relatively smaller sample size, this study provides empirical evidence in the difference of various HRCT features in relation to the days after onset of COVID-19 symptoms. Whereas it corroborates most of the already known findings regarding distribution and features found on HRCT, it adds to the available literature on COVID-19 in two important aspects. Firstly, this study provides empirical evidence (p= .027) that HRCT findings are mostly distributed in posterior lung segments in patients up to 5 days after onset, as well as in those who are asymptomatic (Figure-7). Secondly, this study reveals that interlobular thickening and subpleural reticulation, in the absence of previous pulmonary disease, can differentiate between the stages of COVID-19 as they are overwhelmingly found between 3 to 5 days or later in the course of the disease (p=.000).

CONCLUSION

In asymptomatic cases, as well as in patients up to five days after their symptoms appear, the most common findings are patchy or rounded ground glass opacities located in posterior segments. Interlobular septal thickening and subpleural reticulation, is another feature that commonly starts appearing at three to five days of disease process.

AUTHORS' CONTRIBUTION

SS: Conceived the research question and study design. Approved the final draft. ZM: Collected data and wrote the first draft. Approved the final draft. IS: Analysed the data, revised the first draft of manuscript and approved the final draft. SB: Performed literature search and approved the final draft. FA: Collected and analysed data. Approved the final draft of manuscript. AN**:** Corrected the first draft of manuscript and approved the final draft.

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