Original Research Paper

Radio-Diagnosis

HRCT CHEST EVALUATION OF SEQUELAE OF COVID-19 PNEUMONIA

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ABSTRACT Since December 2019, many unexplained cases of pneumonia have been reported, as a result of exposure in Wuhan city, Hubei province, China. The pathogen identified was coronavirus and the disease was named COVID-19 by World Health Organization (WHO). Based on the epidemiological surveys done, dry cough, fever and fatigue were the main clinical manifestations reported.(Huang et al., 2020; X. Liu et al., 2020) Few patients had symptoms such as runny nose, nasal obstruction, myalgia, sore throat, and diarrhoea. Seriously ill patients rapidly progressed to ARDS. The COVID-19 outbreak has been declared public health emergency of international concern by the WHO. A specific viral nucleic acid assay, real time reverse transcription-polymerase chain reaction (RT-PCR) was developed to diagnose COVID-19. However, published literature on COVID-19 pneumonia showed some patients with initial negative RT-PCR results. According to current literature, HRCT thorax may show abnormalities earlier than even RT-PCR(Zhou et al., 2020). Therefore, high resolution CT had been included as one of the main tools particularly for screening and in the evaluation of the severity of disease (Salameh et al., 2020) Although most of the patients showed complete resolution from illness, some of the them were likely to have some kind of long-term lung damage. Radiological findings have proven to be helpful in estimating the course of the disease and they can be used to evaluate long-term consequences of the disease. CT had been recommended as an important tool for screening and also for evaluation of severity of the illness.(Dai et al., 2020; Shah et al., 2021)

AIM:
• Aim of the study was to determine the sequelae of COVID-19 pneumonia in positive patients 4 – 8 weeks after RT-PCR negative report.

OBJECTIVE:
• To describe the HRCT chest findings of sequelae of COVID-19 pneumonia- GGO, fibrosis, bronchovascular bundle distortion and small pleural effusion.
• To explore the relevant factors affecting the sequelae - initial clinical symptoms of onset, risk factors, age, and gender and laboratory examinations.
• To determine the cumulative percentage of complete radiological resolution - using CT severity score.

KEYWORDS :

COVID-19 shows characteristic CT features during its course, so serial CT examinations prove to be helpful in monitoring disease course and to assure a timely treatment. The hallmark of COVID-19 is the bilateral presence of the patchy ground glass opacities (GGOs) that may coalesce into dense and consolidative lesions with a predominantly peripheral distribution under the pleura and along the bronchovascular bundles. With the progression of disease, the number of lesions rapidly increases and extends to central areas with the left lower lobe being more often involved. During recovery, the lesions are gradually absorbed over a period of two weeks, eventually leading to the formation of fibrotic stripes. In addition to GGOs and consolidations, COVID-19 pneumonia shows other CT findings or patterns which include reticular opacities, crazy-paving, Halo sign and reversed halo or atoll sign, pulmonary embolism, airway changes, pleural effusion, Pulmonary vascular enlargement, lung nodules, lymphadenopathy , pericardial effusions and Acute Respiratory Distress Syndrome.

HRCT CHEST SEVERITY SCORE
CT-SS is used to calculate the severity of pulmonary involvement objectively and rapidly in patients with COVID-19 pneumonia.(Yang et al., 2020) It is now an integral part of everyday practice in thoracic radiology. The severity score is defined as a semi-quantitative scoring system which is used to estimate the pulmonary involvement of COVID-19 related abnormalities on the basis of the particular area involved. Thus, each of the 5 lung lobes is visually scored on a scale of zero to five.
✓ 0: None (no involvement in lobe)
✓ 1: < 5% of lobe
✓ 2: 5%- 25% of lobe
✓ 3: 26%- 49% of lobe
✓ 4: 50%- 75% of lobe
✓ 5: >75% of lobe

Total CT score is the addition of the individual lobar scores and ranges from zero (no involvement) to twenty-five (maximum involvement). It has been observed that a higher CT score (equal to or more than eighteen) on the initial CT is an independent prognostic factor for presence of fibrotic-like changes on the six months follow up exam.(Han et al., 2021; Yasin et al., 2021) The CTSS has been found to be higher in critical cases when compared to mild cases. High CTSS corresponds to poorly aerated compromised lung areas and thus the severe disease.(Zayed et al., 2021).CT severity score also shows co-relation with the laboratory markers of severe disease.(D. Liu et al., 2020; Sun et al., 2020)

Figure 20 CT scan stages in patients with COVID-19(Source Fatima S, Ratnani I, Husain M, et al. (April 12, 2020) Radiological Findings in Patients with COVID-19. 12(4): e7651.

SEQUELAE OF COVID-19 PNEUMONIA ON HRCT

If time between the initial clinical symptom and HRCT is two days or less (thirty-six of ninety- four patients), the patient is known to have been imaged in the early phase of illness. Patients are classified according to the time after the onset of the initial symptoms, namely stage-one (0–4 days); stage-two (5–9 days); stage-three (10–14 days); stage-four (15–21 days); stage-five (22–28 days); and stage-six (⬜28 days).(Ding et al., 2020; Pan et al., 2020).In stage one (early stage, zero to four days after the onset of initial symptoms), GGO is seen to be the main and major radiologic demonstration and is seen distributed sub-pleurally in lower lobes bilaterally.

In stage two (progressive stage, five to eight days after the onset of initial symptoms), the infection quickly/rapidly aggravates to a bilateral multilobar distribution with crazy-paving pattern, diffuse GGO and consolidation.(Ding et al., 2020; Pan et al., 2020). In stage three, (peak stage, nine to thirteen days after the onset of the initial symptoms), the involved areas of the lungs slowly increase to peak involvement and dense consolidations become more and more prevalent.(Ding et al., 2020; Pan et al., 2020) In stage four (absorption stage, fourteen days after the onset of initial symptoms), the consolidation is gradually absorbed. Though, in this process, extensive GGOs can be found as the demonstration of consolidation absorption.(Ding et al., 2020; Pan et al., 2020) On the basis of total CT score, the absorption stage extends beyond twenty-six days from the onset of initial symptoms. Predominant pattern of abnormality changes over time.

MATERIAL & METHODS

STUDY AREA: Patients referred from casualty, triage and OPD to Department of Radiodiagnosis, Lilavati hospital and Research centre.

STUDY EQUIPMENT : HRCT scans are conducted on 128-slice dual source CT scanner. (Somatom Definition FLASH)

STUDY POPULATION: All patients (after application of the exclusion criteria) who are referred to the Department of Radiodiagnosis for HRCT chest.

INCLUSION CRITERIA

All patients diagnosed of COVID-19, age >18 years with either HRCT or RT-PCR positive at admission.

EXCLUSION CRITERIA

✓ Incomplete clinical or laboratory information.
✓ Images with excessive motion artifacts.
✓ Patients with coexistent lung conditions.
✓ Paediatric patients
✓ Attrition due to death
✓ Patients not willing to consent.

SAMPLE SIZE AND TECHNIQUE: Sample size of the study (84) was determined using SAS 9.2 package.

HRCT CHEST PROTOCOL

✓ Slice thickness: 0.625-1.25 mm
✓ Kv: 120
✓ Mas: 100-200
✓ Scan time: 0.5-1 second
✓ Collimation: 1.5-3 mm
✓ FOV: 35 cm
✓ Reconstruction algorithm: high spatial frequency
✓ Window: lung window
✓ Level of inspiration: full inspiration.
✓ Patient position: supine.

STUDY DESIGN: A prospective observational, analytical study.

STUDY DURATION: From July 2020 to May 2021

METHOD OF MEASUREMENT OF OUTCOME OF INTEREST: Interpretation of HRCT chest images as per the departmental protocol was followed.

DATA COLLECTION METHODS:

Data was collected prospectively from the department as and when the scans were done after the ethics committee approval.

✓ Patients satisfying the inclusion criteria were taken for the study.
✓ Informed consent was obtained .
✓ Two experienced radiologists who have had specific training of COVID-19 presentation on chest CT by online courses and real-life cases reviewed the CT images on a PACS workstation.
✓ The final decision was reached by the consensus of the two radiologists
✓ Two sequential CT scans were compared.

FIRST SCAN -at the time of admission and SECOND SCAN - 4 - 8 weeks after RT-PCR negative report.

OBSERVATIONS AND RESULT

Table 1 : Correlative Factors With Resolution.

Characteristic	Complete Radiological Resolution		P value
	No (n=32)	Yes (n=52)	
Gender			
Male	24 (42.9%)	32(57.1%)	F=0.24,DF=1,NS,P
Female	8(28.6%)	20(71.4%)	=0.24
Age	No (n=32)	Yes (n=52)	
≤40	7(21.9%)	25(78.1%)	F=0.021,DF=1,S,P=
>40	25(48.1%)	27(51.9%)	0.021
CT score			
≤8	14 (22.9%)	47 (77%)	F=0.001,DF=1,S,P=
>8	18 (78.2%)	5 (21.7%)	0.001

Table 2 :correlative Factors With Fibrosis

Characteristic	Correlative Factors With Fibrosis.		P value
	No (n=77)	Yes(n=7)	
Gender			
Male	51(91.1%)	5(8.9%)	F=1.0,DF=1,NS,
Female	26(92.9%)	2(7.1%)	P=1.0
Age			
≤40	31(96.9%)	1(3.1%)	F=0.24,DF=1,NS
>40	46(88.5%)	6(11.5%)	, P=0.24
CT score	No (n=77)	Yes(n=7)	
≤8	60(98.4%)	1(1.6%)	F=0.001,DF=1,S,
>8	17(73.98%)	6(26.1%)	P=0.001

Table 3: Hrct Features On First Scan And Second Scan Respectively

HRCT FEATURE	Ct features on first scan (Percentage of study subjects) (%)	CT features on second scan. (Percentage of study subjects) (%)
LUNG CHANGE		
GGO	92.9	33.3
Consolidation	59.5	23.8
Crazy paving	21.4	16.7
Vascular distortion	44.0	21.4
Fibrosis	01.3	08.3
BRONCHIAL CHANGE		
Bronchus distortion	14.5	16.7
Bronchiectasis.	13.7	16.7
PLEURAL CHANGE		
Pleural effusion.	06.0	01.2

Table No 4 : Correlation Of Complete Radiological Resolution With Hrct Findings.

Features On First Scan	Resolution On Second Scan
Ground Glass Opacities	74/78= 94.8 %

Consolidation	39/50=78.0%
Crazy Paving	11/18=61.1%
Vascular Distortion	72/78= 92.3 %

Table No 5: Correlation Of Fibrosis With Hrct Findings.

Features On First Scan	Fibrosis On Second Scan
Ggo	Percentage Of People Who Developed Fibrosis On Second Scan With Ggo On First Scan 2/78= 2.56 %
Consolidation	Percentage Of People Who Developed Fibrosis On Second Scan With Consolidation On First Scan 6/50=12.0%
Crazy Paving	Percentage Of People Who Developed Fibrosis On Second Scan With Crazy Paving On First Scan 4/18=22.2%

Table No 6 : Agewise Distribution Of Hrct Features

	First Scan		Second Scan	
Age Categories	<40YRS (n=32)	>40YRS (n=52)	<40YRS (n=32)	>40YRS (n=52)
Ggo	0=3(50.0%) 1=29(37.2%)	0=3(50.0%) 1=49(62.8%)	0=26(46.4%) 1=6(21.4%)	0=30(53.6%) 1=22(78.6%)
Consolidation	0=14(41.4%) 1=18(36.0%)	0=20(58.8%) 1=32(64.0%)	0=28(43.8%) 1=4(20.0%)	0=36(56.3%) 1=16(80.0%)
Crazy Paving	0=29(43.9%) 1=3(16.7%)	0=37(56.1%) 1=15(83.3%)	0=31(44.3%) 1=1(7.1%)	0=39(55.7%) 1=13(92.9%)
Bronchial Distortion	0=28(39.4%) 1=4(30.8%)	0=43(60.6%) 1=9(69.2%)	0=31(44.3%) 1=1(7.1%)	0=49(55.7%) 1=13(92.9%)
Bronchiect-Asis	0=29(41.4%) 1=3(21.4%)	0=41(58.6%) 1=11(78.6%)	0=31(44.3%) 1=1(7.1%)	0=39(55.7%) 1=13(92.9%)
Vascular Distortion	0=24(51.1%) 1=8(21.6%)	0=23(48.9%) 1=29(78.4%)	0=30(45.5%) 1=2(11.1%)	0=36(54.5%) 1=16(88.9%)
Pleural Effusion	0=30(38.0%) 1=2(40.0%)	0=49(62.0%) 1=3(60.0%)	0=30(37.5%) 1=1(25.0%)	0=50(62.5%) 1=3(75.0%)
Ctss (>8)	0=4(50.0%) 1=28(36.8%)	0=4(50.0%) 1=48(63.2%)	0=30(49.2%) 1=2(8.7%)	0=31(50.8%) 1=21(91.3%)

Table No 6: Correlation Of Ggo On First Scan With Subsequent Hrct Features.

	Hrct Features On Second Scan
Ggo On First Scan	PERSISTENT GGO 3/78=3.84 %
	RESOLUTION. 74/78=94.8%
	CONSOLIDATION 2/78 = 2.56%

	CRAZY PAVING 1/78=1.28%
	FIBROSIS 2/78=2.56%

DISCUSSION

Table 1 Correlative Factors With Resolution.

According to study conducted by Liu Det al, significant difference was observed in complete radiological resolution at 3-week follow-up between males and females and between <1 and ≥ 1 CT scores at discharge, while a significant difference was observed between groups with different ages. (D. Liu et al., 2020) Patients ≤44 years old showed a significantly higher cumulative percentage of complete radiological resolution than patients > 44 years old at the 3-week follow-up. Thus, in the study conducted by Liu Det al, younger age was associated with a better outcome in the study.(D. Liu et al., 2020) In this study, there was no significant difference in complete radiological resolution at 4-8 week follow-up between males and females. A significant difference was observed between groups with different ages, with age < 40 years showed a significantly higher cumulative percentage of complete radiological resolution than patients > 40 years. Significant difference in complete radiological resolution was also observed between CT scores ≤ 8 and > 8 with CT score ≤ 8 showing significantly higher rate of complete radiological resolution.

Table 2 Correlative Factors With Fibrosis.

In line with our study, Yu et al. found that SARS patients who developed fibrosis on follow- up were older than patients without fibrosis.(Yu et al., 2020). According to study conducted by Han X et al., age > 50 years on initial CT scans was recognised as an independent predictor of lung fibrosis.(Han et al., 2021) In this study, no significant difference in post-covid fibrosis was observed at 4-8 week follow-up between males and females. A marginal difference was observed between groups with different ages, with age > 40 years showed higher rate of fibrosis development than patients < 40 years. Significant difference in development of fibrosis was observed between CT scores ≤ 8 and > 8 with CT score ≤ 8 showing significantly less rate of fibrosis development.

Table 3 Hrct Features On First Scan And At Second Scan.

According to study conducted by Xun Ding et al, in the early stage (Stage-1), GGO was the most important imaging manifestation and in certain patients, crazy-paving pattern, consolidation and or even linear opacities were observed.(Ding et al., 2020) As per the study conducted by Xiaoyu Han et al, evidence of fibrosis was observed in 40/114 (35%) patients on follow-up CT scans. The remaining patients showed either complete radiological resolution or residual GGO or interstitial thickening.(Han et al., 2021) According to study conducted by Liu D et al, the predominant patterns of abnormalities observed at discharge were ground-glass opacity (GGO) and fibrosis. GGO and fibrosis showed resolution during the first and the third week after discharge, respectively.(D. Liu et al., 2020). Bronchial distortion and "tinted" sign were two features observed during the follow-up scans. The "tinted" sign was described as decrease in density of GGO and extension of the GGO area. This pattern implies resolution of inflammation with re-expansion of alveoli and hence recovery. (D. Liu et al., 2020).According to study conducted by Yasin R et al, regarding the peak CT manifestations of COVID-19 pneumonia, it showed GGO and crazy-paving appearance as the predominant pattern followed by consolidation and air bronchogram. Fibrosis was seen in comparatively less patients while pleural effusion was seen in only 1.0 percentage of the study subjects.(Yasin et al., 2021) According to this study, GGO was the most common finding in the lung parenchyma in first scan (92.9 %), followed by consolidation (59.5 %) and crazy paving pattern (21.4 %).

Vascular distortion was observed in (44.0 %) and fibrosis in (01.3 %) cases. On second scan , 33.3 % study subjects had GGO and 23.8 % study subjects had consolidation. Fibrosis was observed in 08.3 % cases. Bronchial changes were more evident in second scan.   The percentage of pleural effusion was significantly less.

Table No 4.correlation Of Complete Radiological Resolution With Hrct Findings.

According to study conducted by Zhang S et al, bilateral ground-glass opacities mainly in the subpleural lung and a combination of consolidation and ground-glass opacities is a noteworthy HRCT feature of COVID-19 pneumonia, which may help in the early diagnosis of the disease (Zhang et al., 2020). According to Saeed et al, Studies showed that round GGOs show evolution into patchy GGOs and consolidation as the disease progresses and the crazy-paving pattern decreases with disease regression. Similarly, the linear opacities are more frequently observed with higher CT severity scores.(Saeed et al., 2021). In the present study, the percentage of resolution was higher in subjects with GGO followed by vascular distortion, consolidation and crazy paving.

Table No 5. Correlation Of Fibrosis With Hrct Findings.

According to study conducted by Yasin R et al, pure GGO was more prevalent in the non- fibrotic group, while pure consolidation or GGO with consolidation, crazy paving, air bronchogram and fibrotic changes were significantly higher in fibrotic groups. As regards CT severity score calculated from the initial CT during admission , there was a statistically significant difference between the two groups with higher values among the fibrotic group compared to the non-fibrotic group.(Yasin et al., 2021). In the present study, fibrosis on second scan was observed in approximately 22.2 % subjects with crazy paving on first scan, 12.0 % with consolidation on first scan and 2.56 % study subjects with GGO on first scan. The percentage of fibrosis was less in study subjects with GGO on first scan as compared to consolidation and crazy paving.

Table No 6 Correlation Of Ggo On First Scan With Subsequent Hrct Features On Second Scan.

Study conducted by Bernheim et al. and Pan et al. showed disease evolution from GGOs in the early stage to "crazy paving pattern" and consolidation in later stages.(Bernheim et al., 2020; Pan et al., 2020). In the present study, 94.8 % study subjects who had GGO on first scan showed complete resolution on second scan. Fibrosis was observed in 2.56 % study subjects with GGO on first scan. 3.84 %, 2.56% and 1.28 % study subjects showed residual changes in the form of persistent GGO, consolidation and crazy paving appearance, respectively.

CONCLUSION

1. In this study of 84 patients, there was no significant difference in complete radiological resolution and post-covid fibrosis at 4-8 week follow-up between males and females.
2. Patients with age < 40 years showed a significantly higher cumulative percentage of complete radiological resolution than patients > 40 years. Marginally higher rate of fibrosis was observed in patients with age > 40 years
3. Significantly higher rate of complete radiological resolution and less rate of fibrosis development was noted amongst patients with CT score ≤ 8.
4. GGO was the most common finding in the lung parenchyma in first scan followed by consolidation, crazy paving pattern, vascular distortion and fibrosis. Fibrosis and bronchial changes were more evident in second scan.
5. Presence of clinical symptoms like dry cough, fatigue had no statistical correlation with complete resolution of lung changes on second scan.
6. The percentage of resolution was higher in subjects with GGO and vascular distortion in first scan as compared to consolidation and crazy paving.
7. Changes of fibrosis on second scan was more commonly observed in patients who demonstrated crazy paving and consolidation on first scan as compared to those who presented with only GGO on first scan.
8. Lung parenchymal abnormalities (GGO, consolidation, crazy paving appearance) ; bronchial changes (bronchial distortion , bronchiectasis) , vascular distortion and pleural effusion were significantly higher in study subjects > 40 years on both the first and second scan in the present study.

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