ORIGINAL RESEARCH

Evaluation of findings on initial and follow up chest ct imaging in COVID-19 Pneumonia

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ABSTRACT

Aim: To study the dynamic changes of COVID-19 pneumonia on chest CT imaging. To demonstrate mild/moderate/severe progression or regression of COVID-19 pneumonia, as manifested by increasing/decreasing extent and density of lung opacities on chest CT imaging. **Materials and methods:** This is a prospective and retrospective review of patients with RT-PCR confirmed COVID-19 pneumonia presenting to our hospital for treatment or isolation between time period of 1st July 2020 to 30th June 2021. RTPCR confirmed COVID-19 patients who had undergone chest CT during the initial or active phase of illness and at least one follow-up CT with a gap of at least 3 months between the two scans were enrolled in the study. If the patient had undergone more than one CT scan during the initial illness, then the CT with highest percentage of total lung involvement (highest CT severity score) was selected. Repeat Chest CT were followed up after minimum period of 3months and more. A scoring system was used in this study to quantitatively estimate the pulmonary involvement of all these abnormalities on the basis of the area involved. Each of the 5 lung lobes was visually scored from 1 to 5. The percentage of lung involvement was calculated from AI algorithm based CT Pneumonia Analysis prototype. The data was divided into three groups: Group 1 included the participants with complete resolution of GGO or consolidations on the follow up study, Group 2 included participants with residual GGO/Consolidation in COVID19 pneumonia on follow up study, Group 3 cases includes the follow up with residual lesions in form of either interlobular septal thickening, curvilinear or linear parenchymal bands and bronchiectasis irrespective of GGO and consolidations.

Results:

- In this study, age of patients was ranging from 23.00 – 87.00 years with average being 58.36 among Group 1, 70.55 years among Group 2 and 65.57 years among Group 3 respectively.
- On follow up, mean No. of lung lobes involved showed a significant fall of 100.0% among Group 1, 29.0% among Group 2 and 77.3% among Group 3 from initial.
- Mean percentage of lung involvement was 50.80 among Group 2 which was significantly more as compared to 32.77 among Group 3 and was more as compared to 21.33 among Group 1 but the difference was not statistically significant on initial study. After follow up, mean percentage of lung involvement showed a significant fall of 100.0% among Group 1, 79.5% among Group 2 and 89.4% among Group 3 from initial.
- At initial, mean CT Severity Score was 18.18 among Group 2 which was significantly more as compared to 9.90 among Group 1 and comparable to 13.42 among Group 3 and the difference was statistically significant. After follow up, mean CT Severity Score showed a significant fall of 100.0% among Group 1, 64.5% among Group 2 and 84.1% among Group 3 from initial.
- 97.1% of cases from Group 1, 100% from Group 2 and 96.8% from Group 3 had Pure GGO at Initial. On follow up % of cases with Pure GGO had significant reduction in Group 1 and Group 3 and no change in Group2.
- 50.0% of cases from Group 1, 54.5% from Group 2 and 61.3% from Group 3 had Linear/curvilinear parenchymal bands at baseline. During follow up there was significant reduction among Linear/curvilinear parenchymal bands in Group 1 and significant increase among Group 2 and insignificant change in Group3 from baseline.
- 38.2% of cases from Group 1 had Interlobular septal thickening which was significantly less as compared to , 81.8% from Group 2 and 58.1% from Group 3 at baseline. During follow up there was significant reduction among Interlobular septal thickening in Group 1 and insignificant reduction in Group 2 and 3 from baseline.
- 7.4% of cases from Group 1 & 9.7% in Group 3 had bronchiectasis which was significantly less as compared to 81.8% from Group 2 at baseline. During follow up there was insignificant reduction among bronchiectasis in Group 2 and insignificant increase among Group 1 and 3 from baseline.

Conclusion: Follow up CT scan obtained with minimal interval period of 3 months of disease onset shows there is near total resolution of ground-glass densities and consolidations in more than 2/3rd of patients in RT-PCR proven COVID-19 infection. Significant residual findings after mid term follow up were seen in older patients and had more CT severity score during the acute phase. Patients with more involvement of lungs with high severity score are prone to significant residual lesions on follow up study. Mixed pattern was predominant pattern associated with persistent lung findings on follow up, thus speculated as more advanced stage of disease.

Keywords- COVID-19, Pneumonia, Pulmonary

INTRODUCTION

On 31th December 2019 many pneumonia cases were reported to WHO from Wuhan, China. On January 7th 2020 novel corona virus was confirmed for these cases. Analysis of bronchoalveolar lavage fluid samples and electron microscopy revealed the culprit to be a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a virus with a characteristic crown morphology at scanning electron microscopy, which is due to the presence of viral spike peplomers emanating from the viral envelope. It is an enveloped RNA virus about 60–140 nm in diameter that genetically belongs to lineage B of genus Betacoronavirus. [12] WHO declared it to be pandemic on 10th January 2020. The diagnosis of infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents major challenges. Reverse transcriptase polymerase chain reaction (RT-PCR) testing is used to diagnose a current infection, but its utility as a reference standard is constrained by sampling errors, limited sensitivity (71% to 98%) and dependence on the timing of specimen collection. People with suspected COVID-19 need to know quickly whether they are infected, so that they can self-isolate, receive treatment, and inform close contacts. Currently, formal diagnosis of COVID-19 infection requires laboratory analysis of blood or nose and throat samples. The laboratory test, called RT-PCR, requires specialist equipment and takes at least 24 hours to produce a result. Further, RT-PCR is not completely accurate and a second RT-PCR or a different test may be required to confirm the diagnosis. Chest imaging tests are being used in the diagnosis of COVID-19 disease, or when RT-PCR testing is unavailable or in high suspicion cases with immediate intervention needed. Apart from use as diagnostic purpose, it can also be used for prognostication, response to therapy and to evaluate disease progression [21] The consensus guidelines from various radiological societies across the world have discouraged the routine use of chest computed tomography (CT) for establishing the diagnosis of COVID-19. . However, performance of CT is essential in a subset of patients with severe disease and those showing respiratory deterioration during the course of illness. CT is also needed to monitor the course of disease or response to therapy.

MATERIALS AND METHODS

The definite diagnosis of COVID19 pneumonia included RT-PCR positive status with swab samples from anterior nasal cavity and throat. HRCT chest were performed on SOMATOM definition and Biograph Horizon (Siemens healthineers, Germany) at the end of full inspiration. Pulmonary B70F kernel and a mediastinal B30F kernel (Siemens healthineers, Germany) without intravenous contrast medium injection were assessed, in particular for the presence and distribution of parenchymal abnormalities including ground-glass attenuation, airspace consolidation, nodules and interlobular septal thickening. CT scan were acquired holding single breath with head first supine position of the patient into the gantry. All CT data were reconstructed using a high spatial frequency algorithm. Tube voltage 120–140 kVp, tube current of 90–130 mAs, and a beam pitch of 1.5. The tube current was regulated by an automatic exposure control system. Images were reconstructed using reconstruction increment of 0.7 mm into a slice thickness of 1 mm. The images were viewed in lung window settings (width of 1200HU and centering of – 600 HU) and mediastinal window (width of 300–400 HU and centering of 40 HU). We reviewed prospectively and retrospectively HRCT images of all patients came to breach candy hospital with suspected/diagnosed/isolation of COVID19 pneumonia. Ground-glass attenuation was defined as a hazy increase in lung attenuation with no obscuration of underlying vessels. Airspace consolidation was defined as an area of opacification that obscured the underlying vessels. The anatomic distribution of parenchymal abnormalities was classified as subpleural, central or peripheral; lobular or lobar in the axial plane; upper or lower in the longitudinal plane; peribronchovascular. Any other associated findings were also evaluated including the presence of pleural effusion and mediastinal or hilar lymphadenopathy.

The following CT imaging characteristics were studied: (1) presence or absence of lung opacities; (2) distribution of **lung opacities:** unilateral vs bilateral lung involvement; (3) number of lobes affected; (5) dominant type of lung **opacity:** ground glass opacity (GGO), consolidation, mixed pattern of GGO, and consolidation and linear/curvilinear opacities.

The data was divided into three groups: Group 1 included the participants with complete resolution of GGO or consolidations on the follow up study, Group

2 included participants with residual GGO/Consolidation in COVID19 pneumonia on follow up study, Group 3 cases includes the follow up with residual lesions in form of either interlobular septal thickening, curvilinear or linear parenchymal bands and bronchiectasis irrespective of GGO and consolidations.

AI based CT Pneumonia Analysis software was used, which automatically identifies and quantifies hyperdense areas of the lung.

The CT Pneumonia Analysis prototype performs automated lung opacity analysis on axial CT data with slice thicknesses up to 5 mm. Will get MPR series containing segmentations of the high opacity abnormalities and of the lungs as well as a table with various measurements, e.g. the relative ("percentage of opacities") and absolute volume of the lungs affected by opacities.

The mean and standard deviation of HU values between lung parenchyma and the detected opacities can be compared. All quantitative results are also presented separately for the left and right lung as well as per lung lobe.

An AI algorithm automatically detects and quantifies abnormal tomographic patterns commonly present in lung infections, namely ground glass opacities (GGO) and consolidations.

Based on 3D segmentations of lesions, lungs, and lobes, the algorithm quantifies the extent of overall abnormalities and the presence of high opacity abnormalities, both globally and lobe-wise.

The algorithm can roughly be outlined as follows:

1. Automatic computation of the lung and lobe segmentation mask
2. Abnormality segmentation

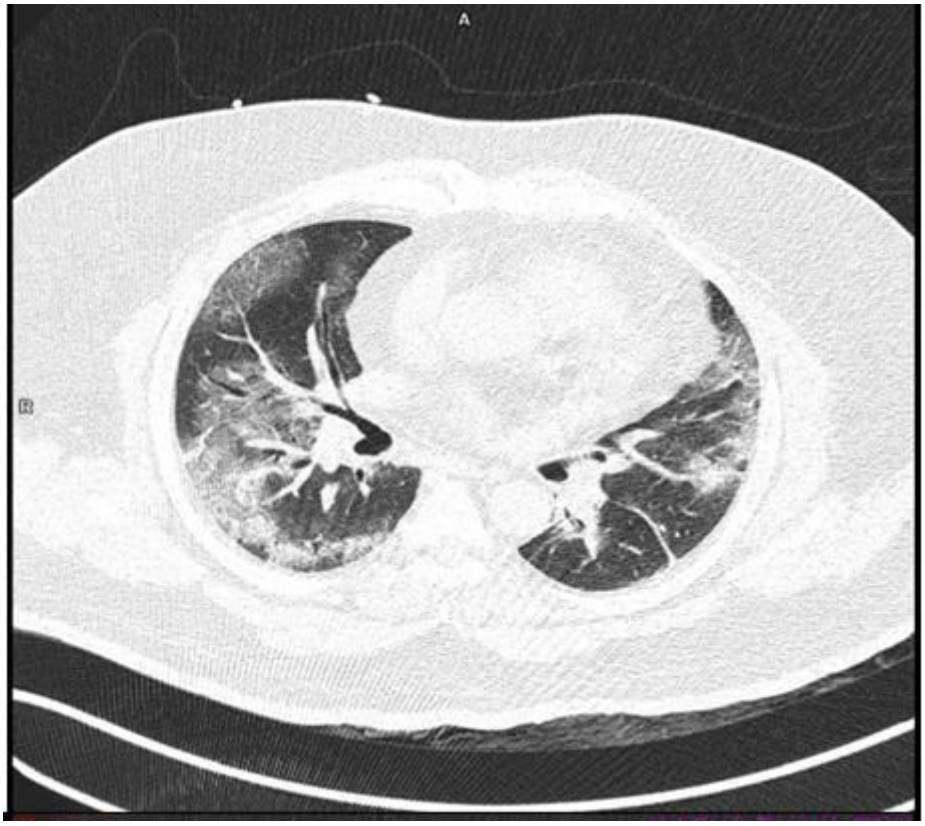
Total opacity score: Range between 0 and 20. To obtain this score, the opacity scores of the five lung lobes are summed up.

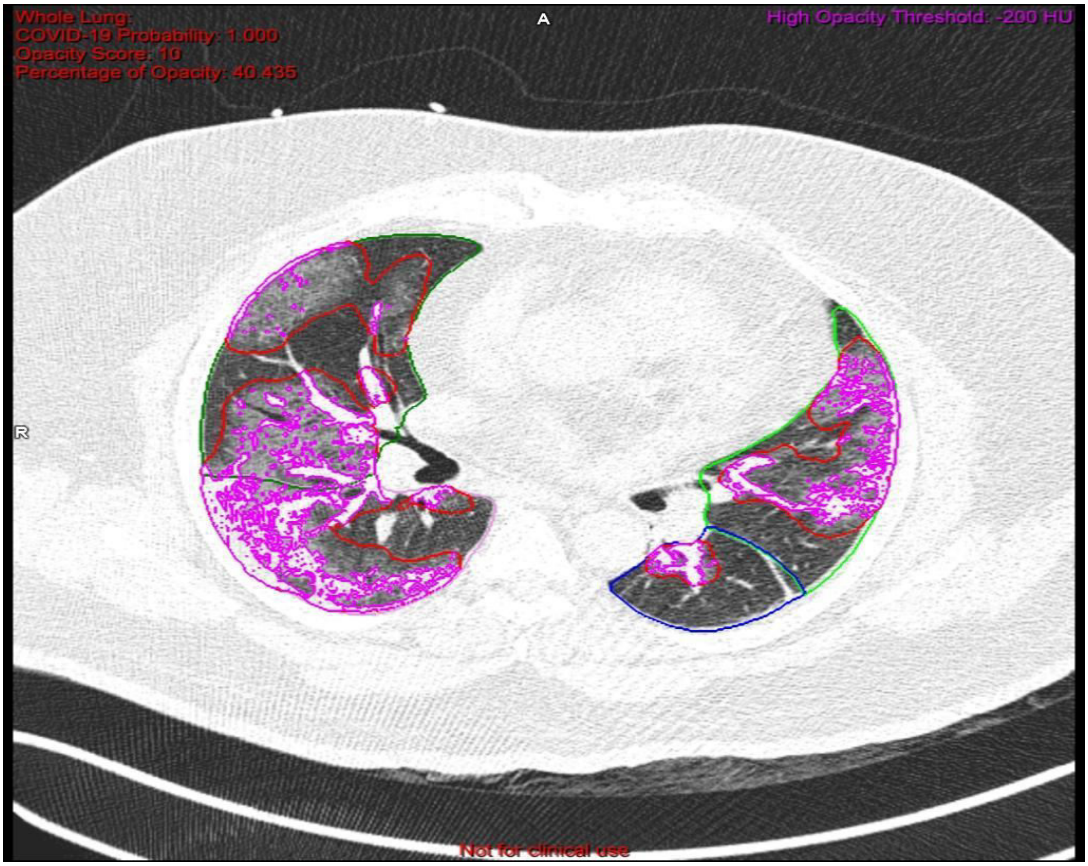
Percentage of opacity: This value represents the percentage of opacity for the whole lung.

Opacity score

% of opacity within a given region <=1: Score = 0
% of opacity within a given region <= 25: Score = 1
% of opacity within a given region <= 50: Score = 2
% of opacity within a given region <= 75: Score = 3
% of opacity within a given region > 75: Score = 4

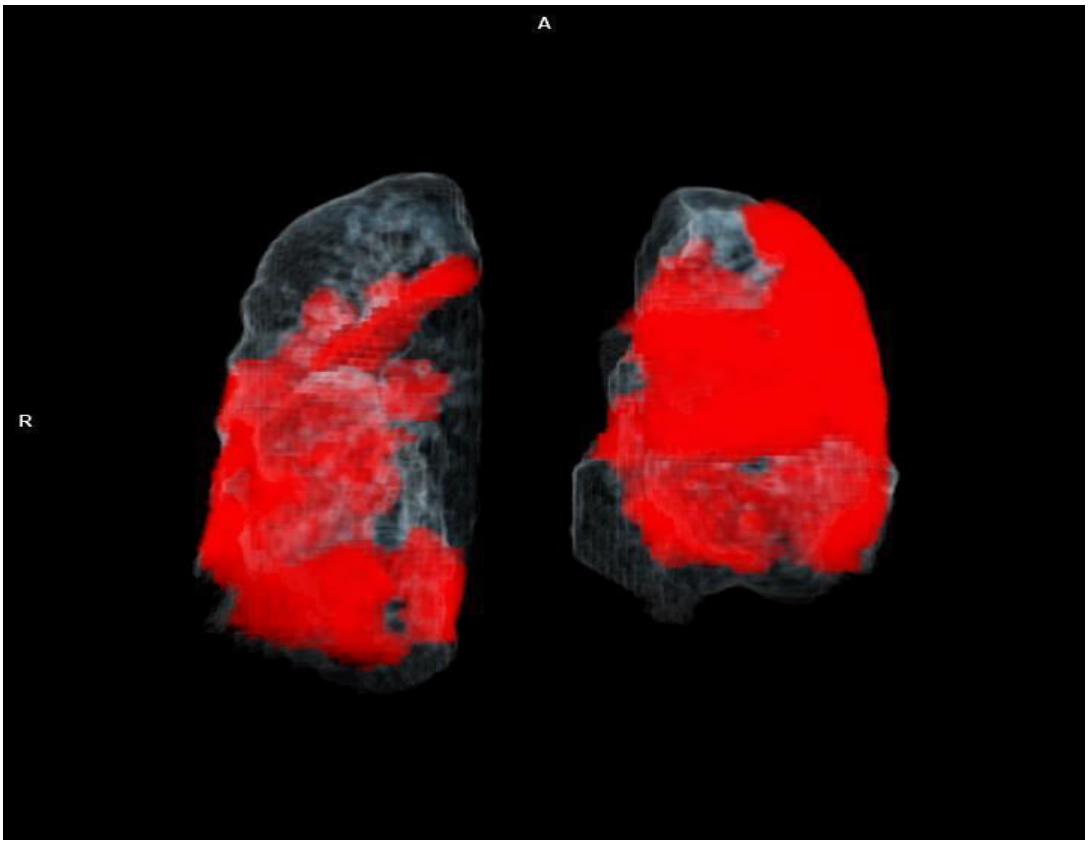
This score will be calculated for each lobe. For the left/right lung, the opacity score is the sum of the respective lobes and for the total opacity score all lobe values are summed up.Percentage of opacity within a given lung region (%)





	Both lungs	Left lung	Right lung
Affected	Yes	Yes	Yes
Opacity Score	10	3	7
Lung volume (ml)	1977.38	887.58	1089.80
Volume of opacity (ml)	799.55	250.71	548.84
Percentage of opacity	40.43	28.25	50.36
Volume of high opacity (ml)	190.23	51.28	138.95
Percentage of high opacity	9.62	5.78	12.75
Mean HU total	-602.46	-638.23	-573.33
Mean HU of opacity	-435.17	-470.16	-419.18
Standard deviation total	301.57	291.38	306.54
Standard deviation of opacity	292.32	294.05	290.12

	Both lungs	Left upper lobe	Left lower lobe	Right upper lobe	Right middle lobe	Right lower lobe
Affected	Yes	Yes	Yes	Yes	Yes	Yes
Opacity Score	10	1	2	3	2	2
Lung volume (ml)	1977.38	521.50	366.08	364.50	259.54	465.76
Volume of opacity (ml)	799.55	119.07	131.65	198.63	117.83	232.38
Percentage of opacity	40.43	22.83	35.96	54.49	45.40	49.89
Volume of high opacity (ml)	190.23	19.57	31.71	53.48	13.73	71.74
Percentage of high opacity	9.62	3.75	8.66	14.67	5.29	15.40
Mean HU total	-602.46	-665.83	-598.91	-546.39	-655.62	-548.55
Mean HU of opacity	-435.17	-498.98	-444.10	-398.31	-517.37	-387.23
Standard deviation total	301.57	279.20	303.60	302.16	256.75	326.70
Standard deviation of opacity	292.32	278.81	304.84	282.15	246.43	306.07



A scoring system was used in this study to quantitatively estimate the pulmonary involvement of all these abnormalities on the basis of the area involved. Each of the 5 lung lobes was visually scored from 1 to 5. The percentage of lung involvement was calculated from AI algorithm based CT Pneumonia Analysis prototype:
0, no involvement;

1, <5% involvement;
2, 25% involvement;
3, 26%-49% involvement;
4, 50%-75% involvement;
5, >75% involvement.

RTPCR confirmed COVID-19 patients who had undergone chest CT during the initial or active phase of illness and at least one follow-up CT with a gap of at least 3 months between the two scans were enrolled in the study. If the patient had undergone more than one CT scan during the initial illness, then the CT with highest percentage of total lung involvement (highest CT severity score) was selected.

Study setting

The study will be conducted in the Department of Radiology, Breach Candy Hospital, Mumbai.

Study population

Inclusion criteria

1. Study must include patients with or suspected of COVID-19 or RT-PCR proven.
2. Patients admitted for treatment or isolation

There were no age or gender restrictions.

Exclusion criteria

1. Patients who refuse to give an informed consent for the study.
2. Pregnant patients.

Sample size

All the patients reporting to hospital for a one year period from 1st June 2020 to 31st May 2021 satisfying the eligibility criteria will be included by consecutive sampling in the study, that is complete enumeration method will be used.
Minimal sample size of 100.

Study design: Hospital-based prospective longitudinal study.

Study duration: 12 months from 1st July, 2020 to 30th June, 2021.

Data collection methods

Patients who fulfil the inclusion criteria with clinically suspected and confirmed RT-PCR COVID19 test are included in study and further follow up CT scan are monitored.

RESULT

DEMOGRAPHICAL DATA

Parameters	Group 1 (N=68)	Group 2 (N=11)	Group 3 (N=31)	P Value
@Age (years)	N=67		N=30	
Mean	58.36	70.55	65.57	*0.001
SD	12.20	08.88	12.04	
Range	23.00 – 87.00 yrs	52.00 – 81.00 yrs	38.00 – 87.00 yrs	
#Sex (%)				
Male	52 (76.5)	04 (36.4)	18 (58.1)	*0.013
Female	16 (23.5)	07 (63.6)	13 (41.9)	

@ By ANOVA * Significant
# By Chi Square Test

- In this study, age of patients was ranging from **23.00 – 87.00 years** with average being **58.36** among Group 1, **70.55 years** among Group 2 and **65.57years** among Group 3 respectively.
- If compared mean age was significantly less among Group 1 than Group 2. Mean age was comparable between Group 2 and Group 3 and difference was significant.
- **76.5%** of total cases were male in Group 1, which was significantly more as compared to **34.4%** in Group 2 and **58.1%** in Group 3.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH LATERALITY OF LUNG INVOLVEMENT BETWEEN THE GROUPS

Laterality of lung involvement	Proportion of cases with Laterality of lung involvement											
	Group 1 (N=68)				Group 2 (N=11)				Group 3 (N=31)			
	Initial (N=68)		Follow up (N=68)		Initial (N=11)		Follow up (N=10)		Initial (N=31)		Follow up (N=08)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Bilateral	64	94.1	*00	00.0	11	100.0	07	70.0	31	100.0	*06	75.0
Unilateral	04	05.9	00	00.0	00	00.0	03	30.0	00	00.0	02	25.0

By Chi Square Test * Significant (P<0.05), NS = Not Significant

This result reveals that at Initial, 94.1% of study cases had Bilateral Lung involvement in Group 1, 100.0% among Group 2 and Group 3 which were comparable, and difference was not significant.

During follow up, % of bilateral involvement significantly reduced among Group1 & Group 3 and insignificant fall in Group 2.

COMPARISON OF CHANGES IN MEAN NO. OF LUNG LOBES INVOLVED BETWEEN THE GROUPS

Duration	Mean No. of lung lobes involved ($\bar{x}$ ± SD)			P Value
	Group 1 (N=68)	Group 2(N=11)	Group 3(N=31)	
Initial	4.41 ± 1.19	5.00 ± 0.00	4.97 ± 0.18	P>0.05 (NS)
Follow up	0.00 ± 0.00	3.55 ± 1.75	1.13 ± 2.00	-
Mean Change(Initial – Follow up)(p value)	*-4.41 ± 1.19 (0.001)	*-1.45 ± 1.75 (0.021)	*-3.84 ± 1.98 (0.001)	*0.001

@ By ANOVA * Significant
#By Student t test

- As per this analysis at initial, mean No. of lung lobes involvedwas **4.41** among Group 1which was comparableto **5.00** among Group 2 and **4.97** among Group 3 and the difference was not statistically significant.
- After follow up, mean No. of lung lobes involvedshowed a significant fall of **100.0%** among Group 1, **29.0%** among Group 2 and **77.3%** among Group 3 from initial. If compared Group 2 showed significantly less change than Group 1 and Group 3. If compared Group 1 showed more change than Group 3 but the difference was not significant.

COMPARISON OF CHANGES IN MEAN PERCENTAGE OF LUNG INVOLVEMENT BETWEEN THE GROUPS

Duration	Mean Percentage of lung involvement ($\bar{X}$ ± SD)			P Value
	Group 1 (N=68)	Group 2 (N=11)	Group 3 (N=31)	
Initial	21.33 ± 19.39	50.80 ± 20.67	32.77 ± 22.30	*0.001
Follow up	00.00 ± 00.00	10.43 ± 06.62	03.48 ± 06.42	-
Mean Change (Initial – Follow up) (p value)	*-21.33 ± 19.39 (0.001)	*-40.37 ± 21.46 (0.001)	*-29.29 ±20.12 (0.001)	0.007 (NS)

@ By ANOVA NS= Not Significant * Significant
#By Student t test

- As per this analysis at initial, mean percentage of lung involvementwas **50.80** among Group 2which was significantly more as comparedto **32.77** among Group 3 and was more as compared to **21.33** among Group 1 but the difference was not statistically significant.
- After follow up, mean percentage of lung involvementshowed a significant fall of **100.0%** among Group 1, **79.5%** among Group 2 and **89.4%** among Group 3 from initial. If compared Group 2 showed a significantly more change than Group 1 and insignificantly more than Group3. If compared Group 1 showed comparable change with Group 3 and the difference was not significant.

COMPARISON OF CHANGES IN MEAN CT SEVERITY SCORE BETWEEN THE GROUPS

Duration	Mean CT Severity Score ($\bar{x}$ ± SD)			P Value
	Group 1 (N=68)	Group 2 (N=11)	Group 3 (N=31)	
Initial	09.90 ± 05.36	18.18 ± 04.00	13.42 ± 05.12	*0.001
Follow up	00.00 ± 00.00	06.45 ± 03.93	02.13 ± 03.90	-
Mean Change (Initial – Follow up) (p value)	*-09.90 ± 05.36 (0.001)	*-11.73 ± 5.08 (0.001)	*-11.29 ± 04.22 (0.001)	0.308 (NS)

@ By ANOVA NS= Not Significant * Significant
#By Student t test

- As per this analysis at initial, mean CT Severity Score was **18.18** among Group 2 which was significantly more as compared to **9.90** among Group 1 and comparable to **13.42** among Group 3 and the difference was statistically significant.
- After follow up, mean CT Severity Score showed a significant fall of **100.0%** among Group 1, **64.5%** among Group 2 and **84.1%** among Group 3 from initial. If compared Group 2 showed an insignificantly more change than Group1 and Group3.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH CT PATTERNS BETWEEN THE GROUPS

CT pattern	Proportion of cases with CT pattern											
	Group 1 (N=68)				Group 2 (N=11)				Group 3 (N=31)			
	Initial		Follow up		Initial		Follow up		Initial		Follow up	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Pure GGO	66	97.1	00	*00.0	11	100.0	11	100.0	30	96.8	09	*29.0
Consolidation	36	52.9	00	*00.0	09	81.8	00	00.0	24	77.4	00	*0.0
Mixed	34	50.0	00	*00.0	09	81.8	00	00.0	23	74.2	00	*0.0

By Chi Square Test

Above results reveals that, **97.1%** of cases from Group 1, **100%** from Group 2 and **96.8%** from Group 3 had Pure GGO at Initial. After treatment, % of cases with Pure GGO had significant reduction in Group 1 and Group 3 and no change in Group2. If compared reduction were significantly more in Group I than Group 2 and Group3.

Proportion of cases with consolidation & mixed had a significant fall in all three groups from Initial. If compared change were same in all three groups and difference was not significant.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH LINEAR/CURVILINEAR PARENCHYMAL BANDS PATTERNS BETWEEN THE GROUPS

No of cases with Linear/curvilinear parenchymal bands					
Groups	Initial		Follow up		P value
	No	%	No	%	
Group 1 (N=68)	34	50.0	19	27.9	*0.008
Group 2 (N=11)	06	54.5	08	72.7	0.659 (NS)
Group 3 (N=31)	19	61.3	26	83.9	*0.046
Between Groups (P value)	0.578 (NS)				

By Chi - Square Test NS= Not Significant * Significant

Above results reveals that, **50.0%** of cases from Group 1, **54.5%** from Group 2 and **61.3%** from Group 3 had Linear/curvilinear parenchymal bands at baseline which were comparable, and difference was not statistically significant.

After treatment, during follow up there was significant reduction among Linear/curvilinear parenchymal bands in Group 1 and significant increase among Group 2 and insignificant change in Group3 from baseline.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH INTERLOBULAR SEPTAL THICKENING PATTERNS BETWEEN THE GROUPS

No of cases with Interlobular septal thickening					
Groups	Initial		Follow up		P value
	No	%	No	%	
Group 1 (N=68)	26	38.2	08	11.8	*0.001
Group 2 (N=11)	09	81.8	08	72.7	0.610 (NS)
Group 3 (N=31)	18	58.1	14	45.2	0.915 (NS)
Between Groups (P value)	*0.011				

By Chi - Square Test NS= Not Significant * Significant

Above results reveals that, **38.2%** of cases from Group 1 had Interlobular septal thickening which was significantly less as compared to , **81.8%** from Group 2 and **58.1%** from Group 3 at baseline.

After treatment, during follow up there was significant reduction among Interlobular septal thickening in Group 1 and insignificant reduction in Group 2 and 3 from baseline.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH BRONCHIECTASIS PATTERNS BETWEEN THE GROUPS

No of cases with Bronchiectasis					
Groups	**Initial**		**Follow up**		**P value**
	No	**%**	**No**	**%**	
Group 1 (N=68)	05	07.4	06	08.8	0.753 (NS)
Group 2 (N=11)	09	81.8	06	54.5	0.361 (NS)
Group 3 (N=31)	03	09.7	09	29.0	0.053 (NS)
Between Groups (P value)	*0.001				

By Chi - Square Test NS= Not Significant

Above results reveals that, **7.4%** of cases from Group 1 & 9.7% in Group 3 had bronchiectasis which was significantly less as compared to **81.8%** from Group 2 at baseline.

After treatment, during follow up there was insignificant reduction among bronchiectasis in Group 2 and insignificant increase among Group 1 and 3 from baseline.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH PLEURAL EFFUSION PATTERNS BETWEEN THE GROUPS

No of cases with Pleural effusion					
Groups	**Initial**		**Follow up**		**P value**
	No	**%**	**No**	**%**	
Group 1 (N=68)	06	08.8	00	00.0	*0.012
Group 2 (N=11)	01	09.1	00	00.0	1.000 (NS)
Group 3 (N=31)	03	09.7	00	00.0	0.075 (NS)
Between Groups (P value)	0.990 (NS)				

By Chi - Square Test NS= Not Significant * Significant

Above results reveals that, 8.8% of cases from Group 1, 9.1% from Group 2 and 9.7% from Group 3 had pleural effusion at baseline which were comparable, and difference was not statistically significant.

After treatment, during follow up there was significant reduction among pleural effusion in Group 1 but insignificant reduction among Group 2 and 3 from baseline.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH MOSAIC ATTENUATION PATTERNS BETWEEN THE GROUPS

No of cases with Mosaic attenuation on follow up					
Groups	**Initial**		**Follow up**		**P value**
	No	**%**	**No**	**%**	
Group 1 (N=68)	01	01.5	11	16.2	*0.002
Group 2 (N=11)	00	00.0	02	18.2	0.476 (NS)
Group 3 (N=31)	00	00.0	09	29.0	*0.001
Between Groups (P value)	0.732 (NS)				

By Chi - Square Test NS= Not Significant * Significant

Above results reveals that, **1.5%** of cases from Group 1, **0.0%** from Group 2 and **0.0%** from Group 3 had mosaic attenuation at baseline which were comparable, and difference was not statistically significant.

After treatment, during follow up there was significant increase among mosaic attenuation in Group 1 and Group 3 but insignificant increase among Group 2 from baseline.

COMPARISON OF CHANGES IN PROPORTION OF CASES WITH CT PATTERNS BETWEEN THE GROUPS

No of cases with Pneumomediastinum/Pneumothorax					
Groups	**Initial**		**Follow up**		**P value**
	No	**%**	**No**	**%**	
Group 1(N=68)	02	02.9	00	00.0	0.154(NS)
Group 2(N=11)	02	18.2	00	00.0	0.476(NS)
Group 3(N=31)	01	03.2	00	00.0	0.313(NS)
Between Groups (P value)	0.072 (NS)				

By Chi - Square Test NS= Not Significant * Significant

Above results reveals that, **2.9%** of cases from Group 1had pneumomediastinum/pneumothorax which was insignificantly less as compared to, **18.2%** from Group 2, and **3.2%** from Group 3 were comparable at baseline, and difference was not statistically significant.

After treatment, during follow up there was insignificant reduction among pneumomediastinum/pneumothorax in Group 1, Group 2 and 3 from baseline.

COMPARISON OF MEAN TIME LAPSE BETWEEN INITITAL AND FOLLOW UP BETWEEN THE GROUPS

Groups	**Mean Time lapse between initial and follow up ($\bar{X}$ ± SD)**
Group 1 (N=68)	85.34 ± 61.51
Group 2 (N=11)	149.09 ± 43.75
Group 3 (N=31)	112.16 ± 70.63
p value	*0.004

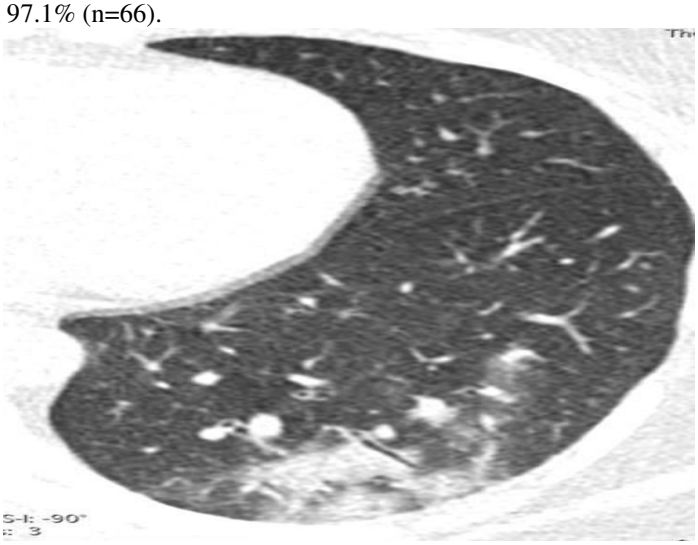
By ANOVA *Significant

As per this analysis, mean time lapsewas **85.34** among Group 1 which was significantly less as compared to **149.09** among Group 2 and was less than **112.16** among Group 3 but the difference was not significant.

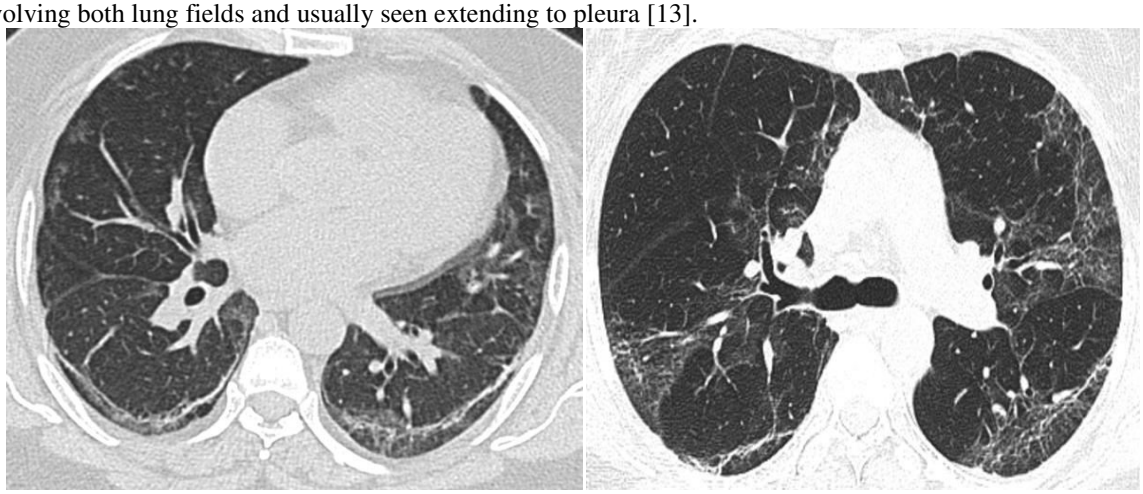
DISCUSSION

Patterns of COVID19 pneumonia on HRCT chest, found in our study includes:

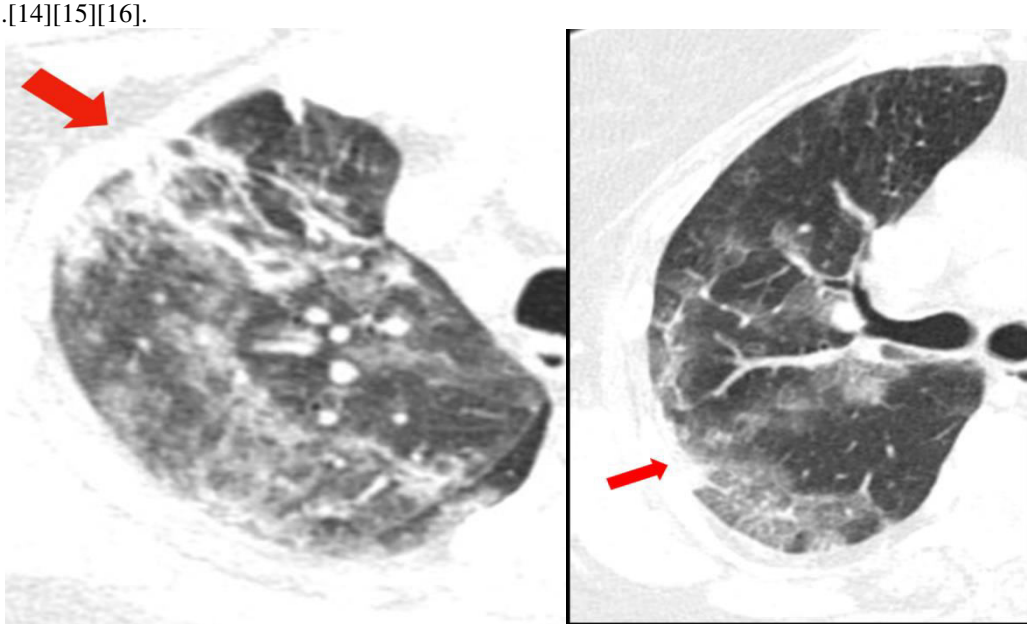
MIXED PATTERN is subgroup involving the features of both GGO and consolidation. Although GGO being the predominant pattern 97.1% (n=66).



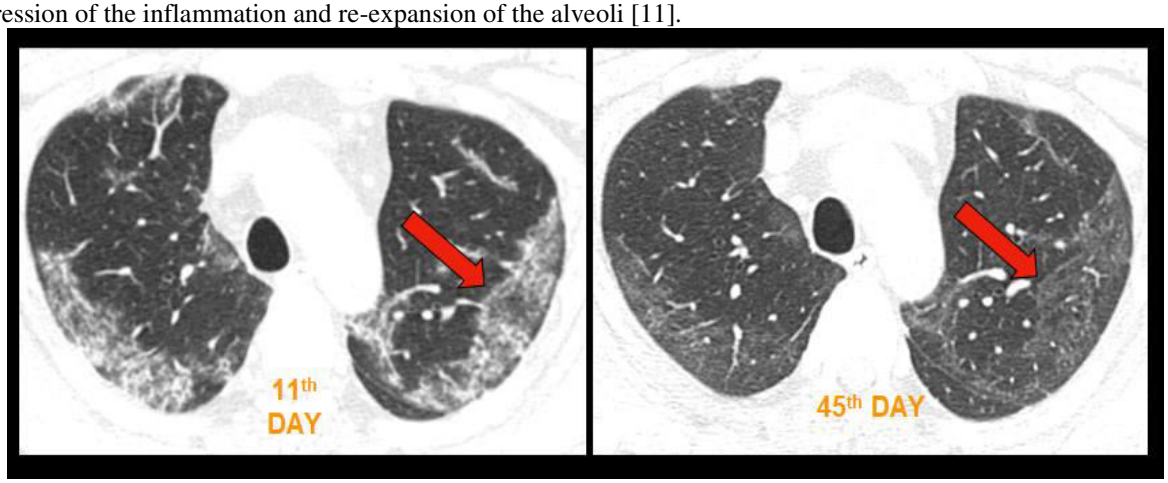
PARENCHYMAL BAND represents subpleural curvilinear opacities or peribronchovascular linear opacities involving both lung fields and usually seen extending to pleura [13].



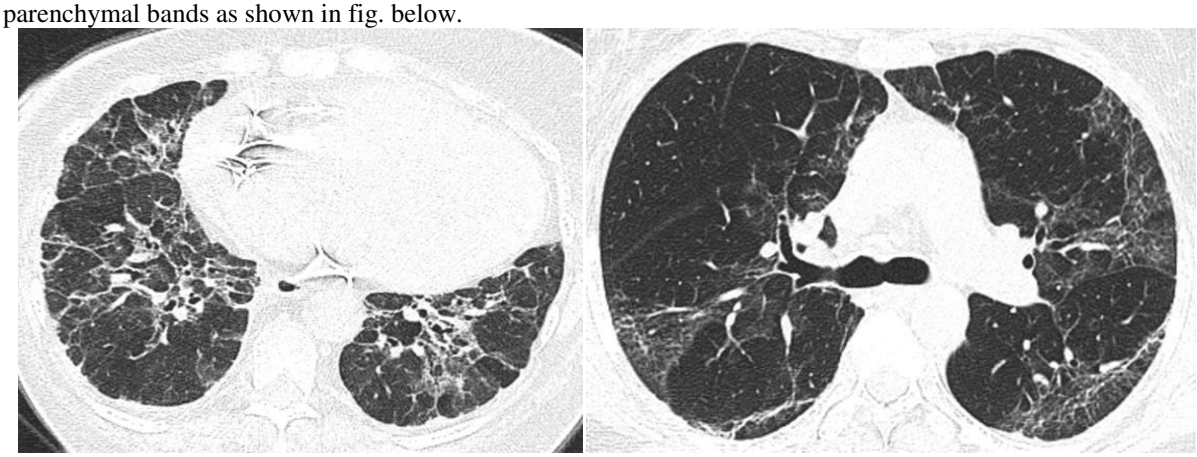
PLEUROPARENCHYMAL INTERFACE IRREGULARITIES or 'PLEURAL RETRACTION' are subpleural opacities causing pulling of visceral pleura resulting to fine irregularities and thickening of pleural surfaces.[14][15][16].



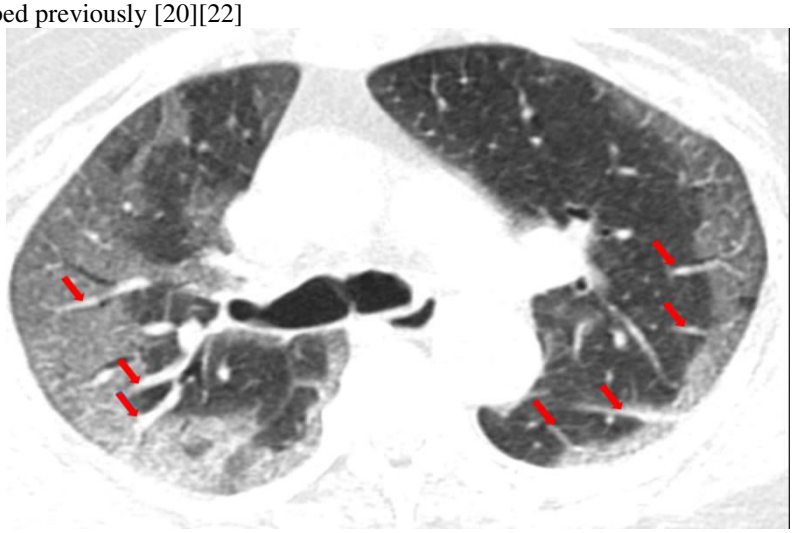
TINTED SIGN OR MELTING SUGAR SIGN are defined as an imaging appearance of increased extension of the GGO/Consolidation with decreased attenuation on follow up study, which may indicate the gradual regression of the inflammation and re-expansion of the alveoli [11].



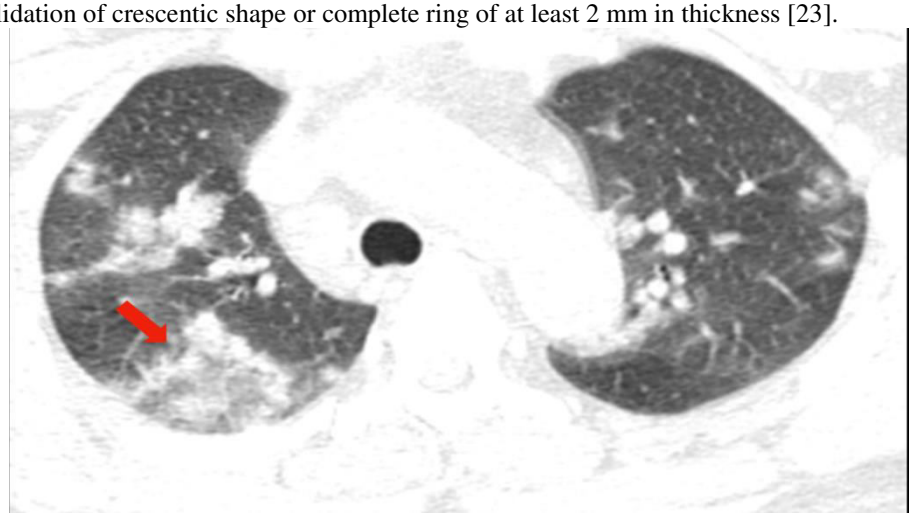
INTERSTITIAL THICKENING is thickening of interlobular and intralobular septa. These findings were predominantly seen in subpleural distribution. In majority of cases, these findings are overlapped with parenchymal bands as shown in fig. below.



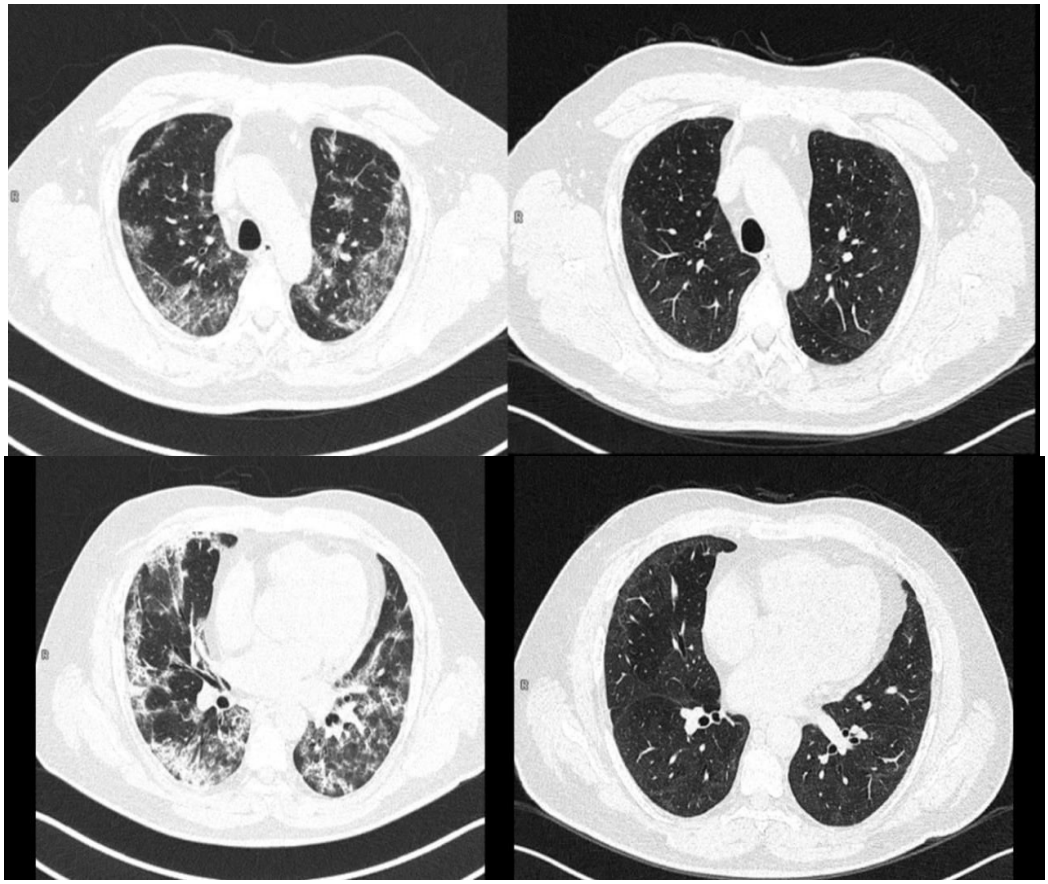
VESSEL ENLARGEMENT in the region of GGO or consolidation, were common findings seen in our study which were described previously [20][22]



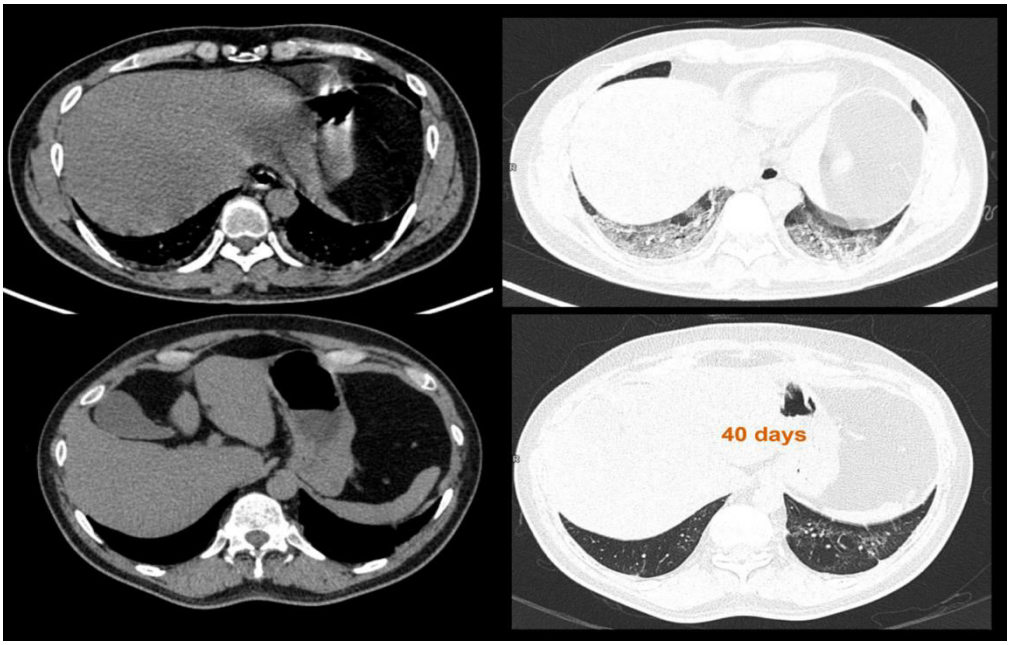
REVERSED HALO SIGN OR ATOLL SIGN is defined as central ground-glass opacity surrounded by denser consolidation of crescentic shape or complete ring of at least 2 mm in thickness [23].



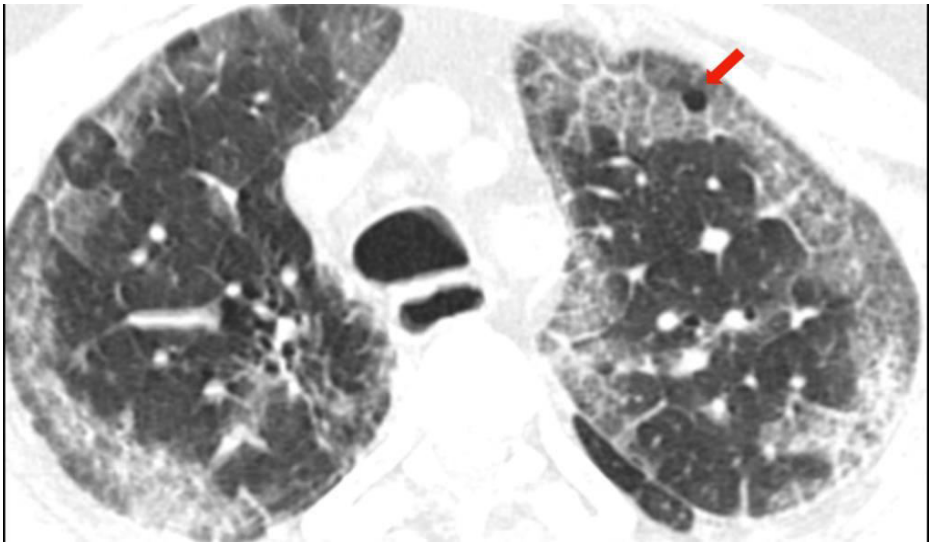
MOSAIC PATTERN is differing attenuation of the lung parenchyma. Many of the follow up study 16.2% in group 1 and 18.2% in group 2 shows presence of mosaic pattern attenuation.



43/M COVID19 positive patient showing maximum severity score of 13/25 with involvement of 36.96% lungs associated with minimal rim of pleural effusion in lung bases. Follow up study at the interval 40days shows near total resolution of GGO. There is resolution of previously visualized minimal rim of pleural effusion.



AIR BUBBLE SIGN (VACUOLAR SIGN) refers to a small air-containing space < 5 mm in length within the lung lesion [25].



In our study 11 out of 79 (13.9%) who recovered from COVID19 pneumonia developed residual lesions in form of ground glass opacity or consolidation in the lungs on follow up period (minimum 3months).

Using ANOVA and Chi Square Test

Variables found significant in Group 2	
Mean Age	70.55
Bilateral involvement	100%
No. of lobes involved on initial study	5
Mean Percentage of lung involvement ($\bar{x}$ ± SD)	50.80 ± 20.67
Mean CT Severity Score ($\bar{X}$ ± SD)	18.18 ± 04.00
Pattern	Pure GGO(100%) > Consolidation (81.8%)

Variables found significant in Group 1	
Mean Age	58.36
Bilateral involvement	94.1
No. of lobes involved on initial study ($\bar{X}$ ± SD)	4.41 ± 1.19
Mean Percentage of lung involvement ($\bar{X}$ ± SD)	21.33 ± 19.39
Mean CT Severity Score ($\bar{X}$ ± SD)	09.90 ± 05.36
Pattern	Pure GGO(97.1%) > Consolidation (52.9%)

	Group 1 (N=68)		**Group 2 (N=11)**	
	Initial	**Follow up**	**Initial**	**Follow up**
Linear/Curvilinear Parenchymal Bands	34* (50.0%)	19* (27.9%)	06 (54.5%)	08 (72.7%)
Interlobular Septal thickening	26 (38.2%)	08 (11.8%)	09 (81.8%)	08 (72.7%)
Bronchiectasis	05 (07.4%)	06 (08.8%)	09 (81.8%)	06 (54.5%)
Pleural Effusion (Bilateral Minimal To Moderate)	06* (08.8%)	00	01 (09.1%)	00
Mosaic Attenuationon Follow Up	01* (01.5%)	11* (16.2%)	00	02 (18.2%)
Pneumomediastinum/Neumothorax	02 (02.9%)	00	02 (18.2%)	00
Time Lapse Between Initital And Follow Up ($\bar{x}$ ± SD)	85.34 ± 61.51		149.09 ± 43.75	

*significant P value.

Group 1 with pure GGO pattern (97.1%) shows complete resolution compared to mixed pattern (50.0%). Thus it could be speculated that Pure GGO pattern may represent initial or mild form of disease process compared to mixed pattern.

Group 3 included participants showing residual follow lesions other than ground glass opacity and consolidations and includes viz. linear/curvilinear parenchymal bands, interlobular septal thickening and bronchiectasis.

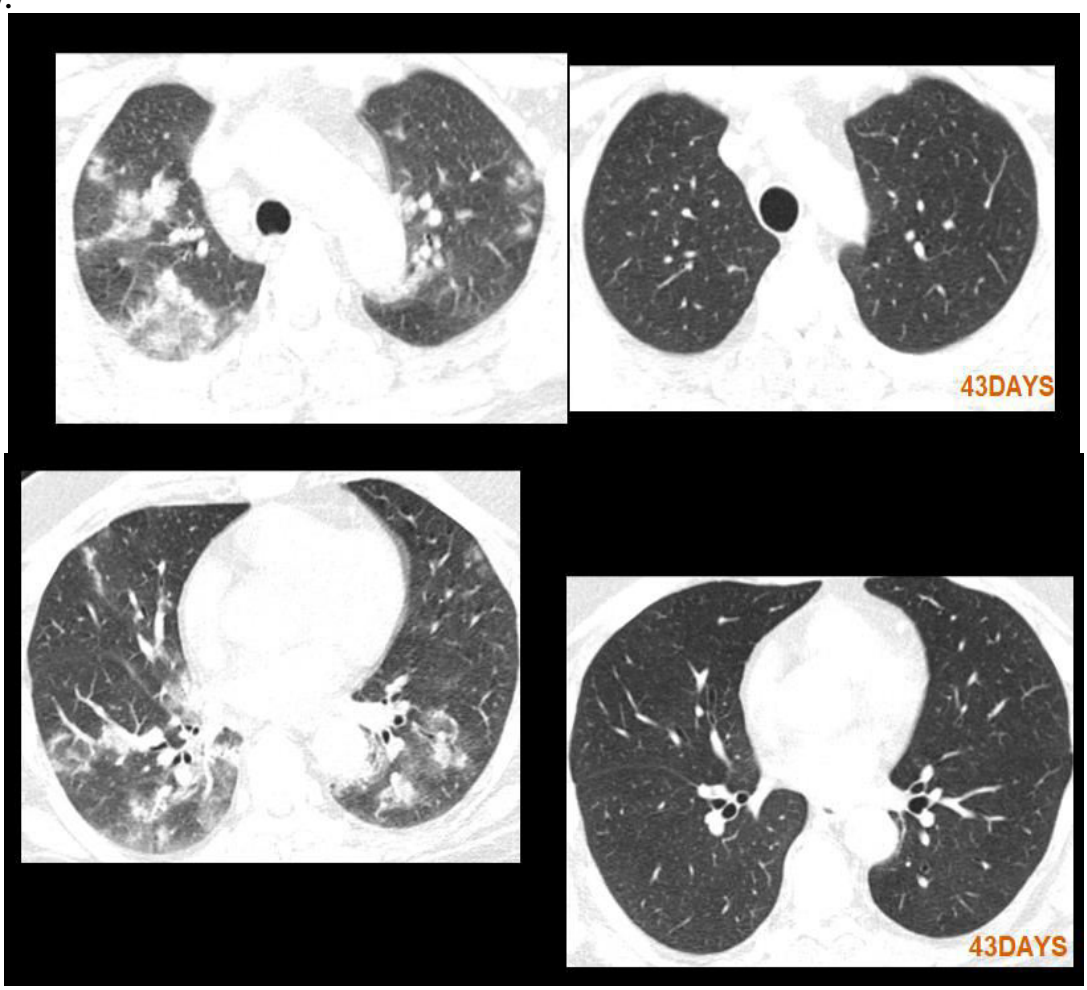
	Group 3	
	Initial	**Follow up**
Linear/Curvilinear Parenchymal Bands	19 (61.3%)	26 (83.9%)
Interlobular Septal Thickening	18 (58.1%)	14 (45.2%)
Bronchiectasis	03 (09.7%)	09 (29.0%)
Pleural Effusion (Bilateral Minimal To Moderate)	03 (09.7%)	00
Mosaic Attenuation On Follow Up	00	09 (29.0%)
Pneumomediastinum/Pneumothorax	01 (03.2%)	00
Time Lapse Between Initital And Follow Up ($\overline{X}$ ± Sd)	112.16 ± 70.63	

The residual lung lesions in this study are uncertain if represents true fibrotic changes like pathological condition and needs more long term study. Whether or not these residual lung lesions, after 3 months, reflect permanent change in the lung needs further investigation. Association of consolidation/mixed pattern was found to have more residual lesions on follow up study with mean time lapse period of 149.09±43.75 days. Thus it could be speculated that mixed pattern may represent more advanced stage of disease and more severe clinical form compared to pure GGO.

Significant decrease in CT scores for total lesions, GGO, and consolidation were observed at follow-up CT compared with the initial CT.

GGO in the acute phase of COVID-19 pneumonia may represent the inflammatory infiltrates, edema, or hemorrhaging [11]. The pathophysiology behind GGO and its corelation with fibrosis is worthy further investigation.

Group 1 included the participants with complete resolution of GGO or consolidations on the follow up study:



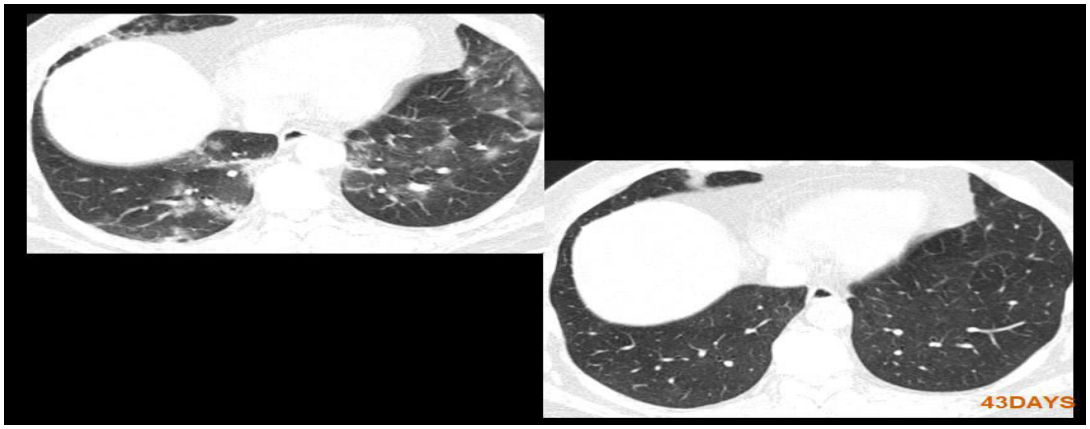


Fig1a: shows patchy peribronchovascular and subpleural mixed ground glass opacity and consolidation on initial presentation. Follow up study after time lapse of 43 days shows complete resolution on GGO and consolidation with CT severity score of 0. Residual lesions like linear/curvilinear bands, interlobular septal thickening, bronchiectasis may or may not be present on follow up study.

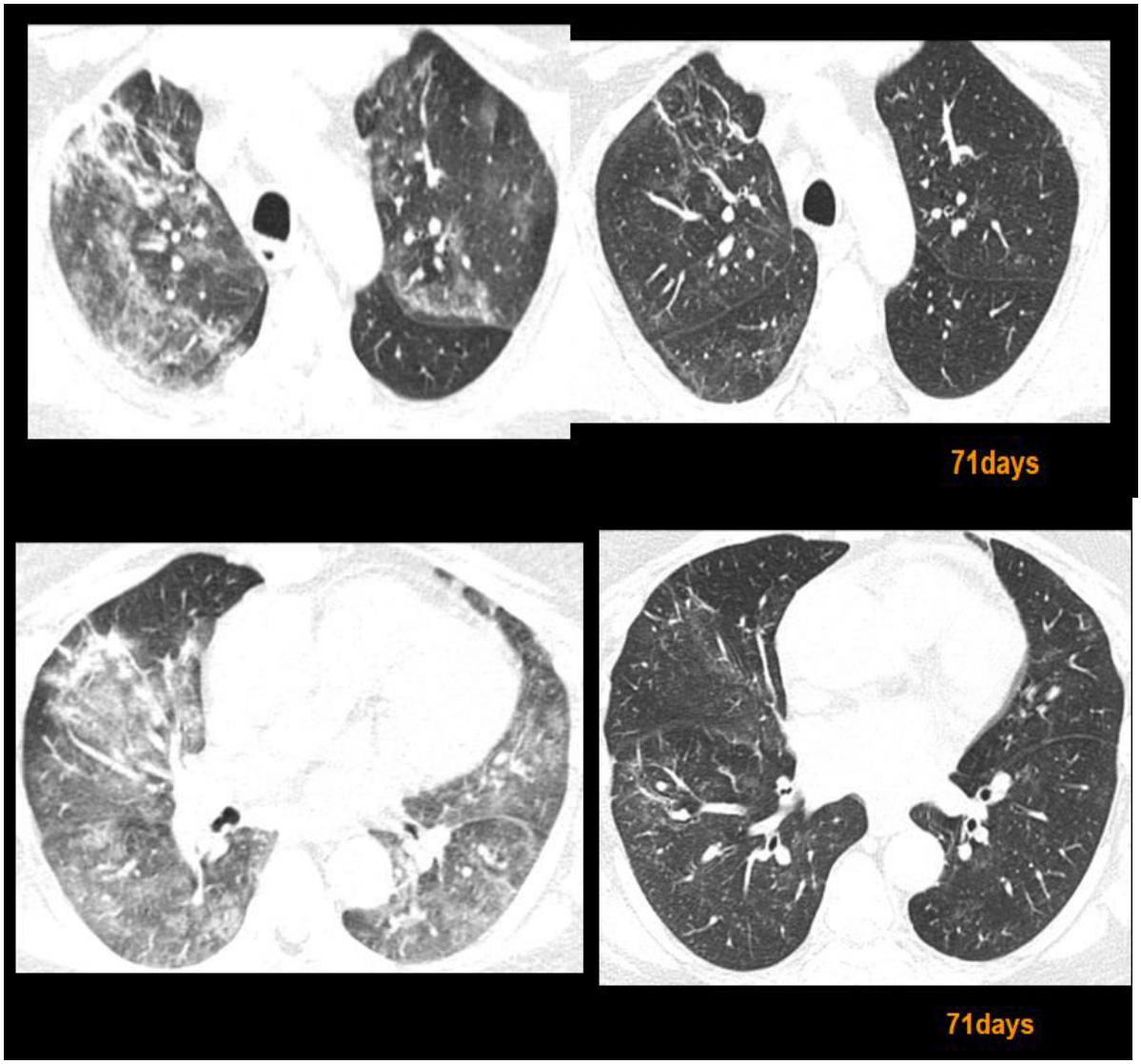
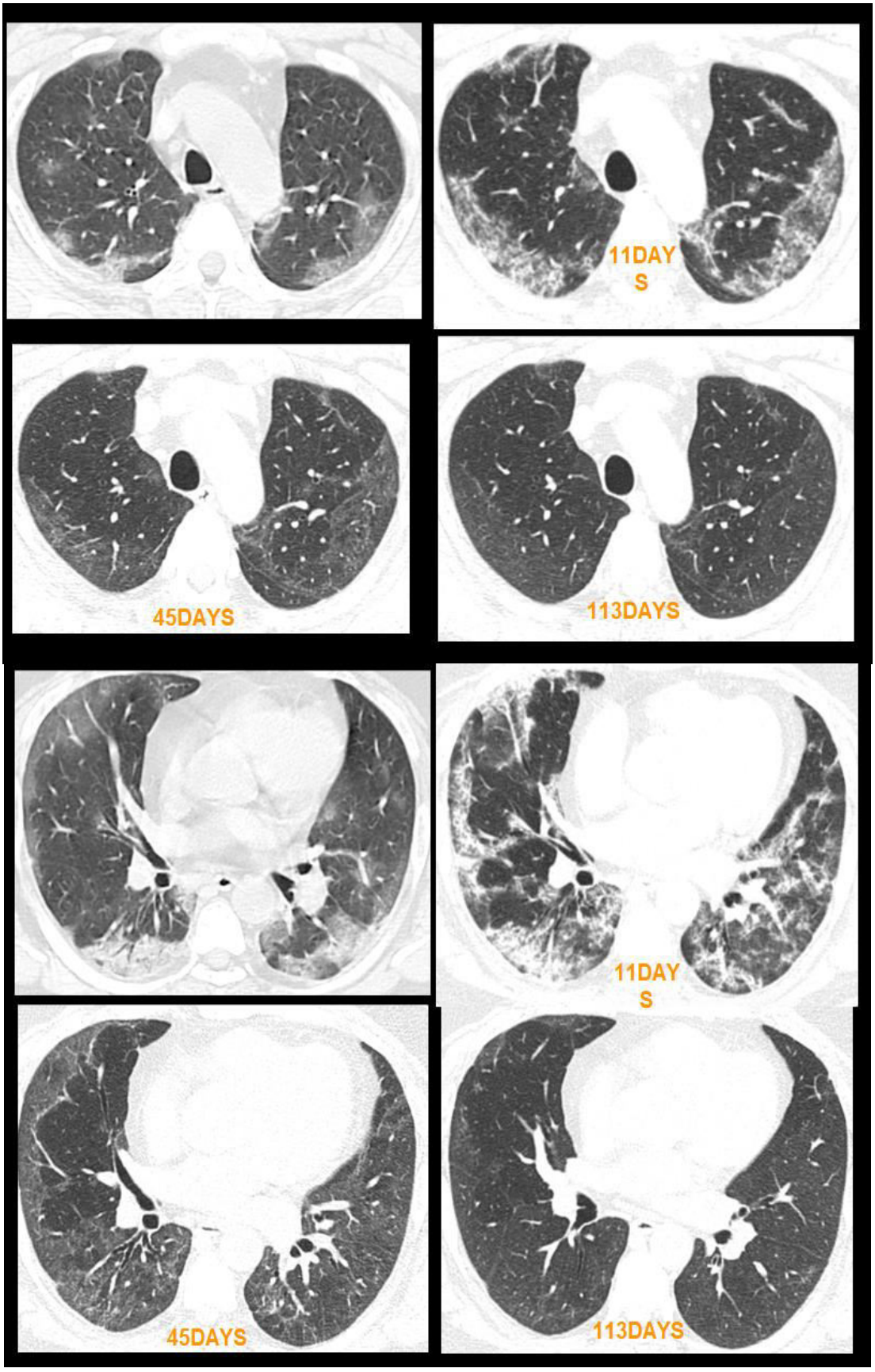


Fig1b: Peribronchovascular mixed GGO and consolidation on initial presentation and follow up study after 71days shows resolution of GGO and consolidation. There are few peribronchovascular linear parenchymal bands.



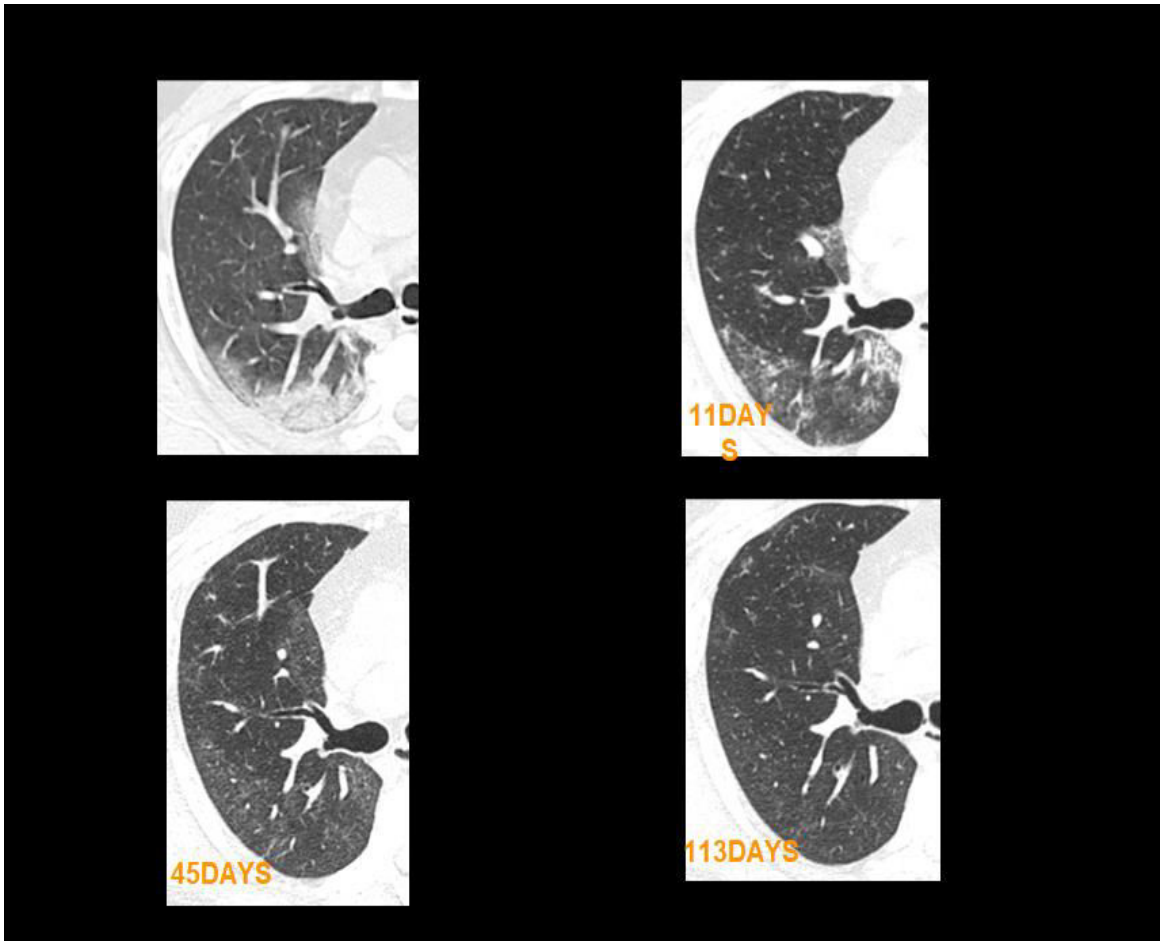


Fig1c: Temporal evolution of the COVID19 pneumonia. Initial GGO shows 'Tinted sign' in form of extension of GGO and reduced attenuation on follow study after 45 days. Follow up at 113days shows complete resolution of the GGO.

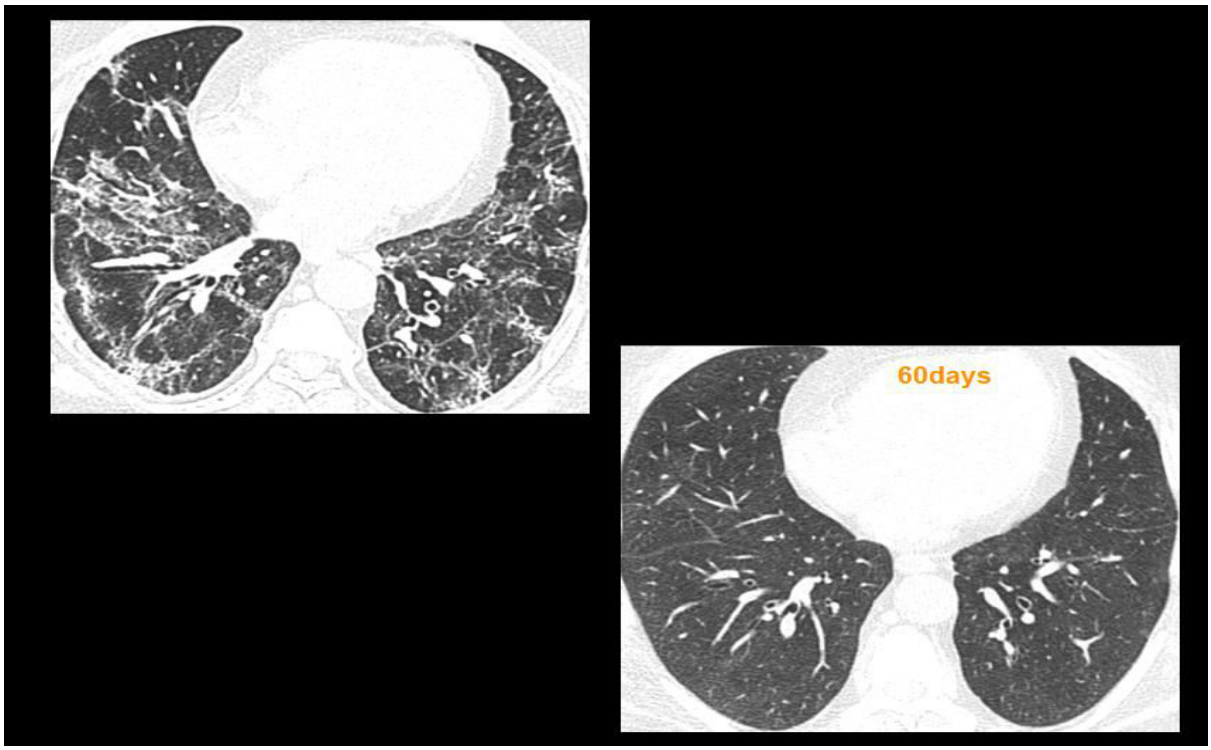


Fig1d: RT-PCR proven COVID19 pneumonia, after 6days of fever onset shows GGO, consolidations associated with parenchymal bands and interlobular septal thickening on initial CT. Follow up study

after 60days shows complete resolution of the disease process. There are subtle areas of mosaic attenuation on follow up study.

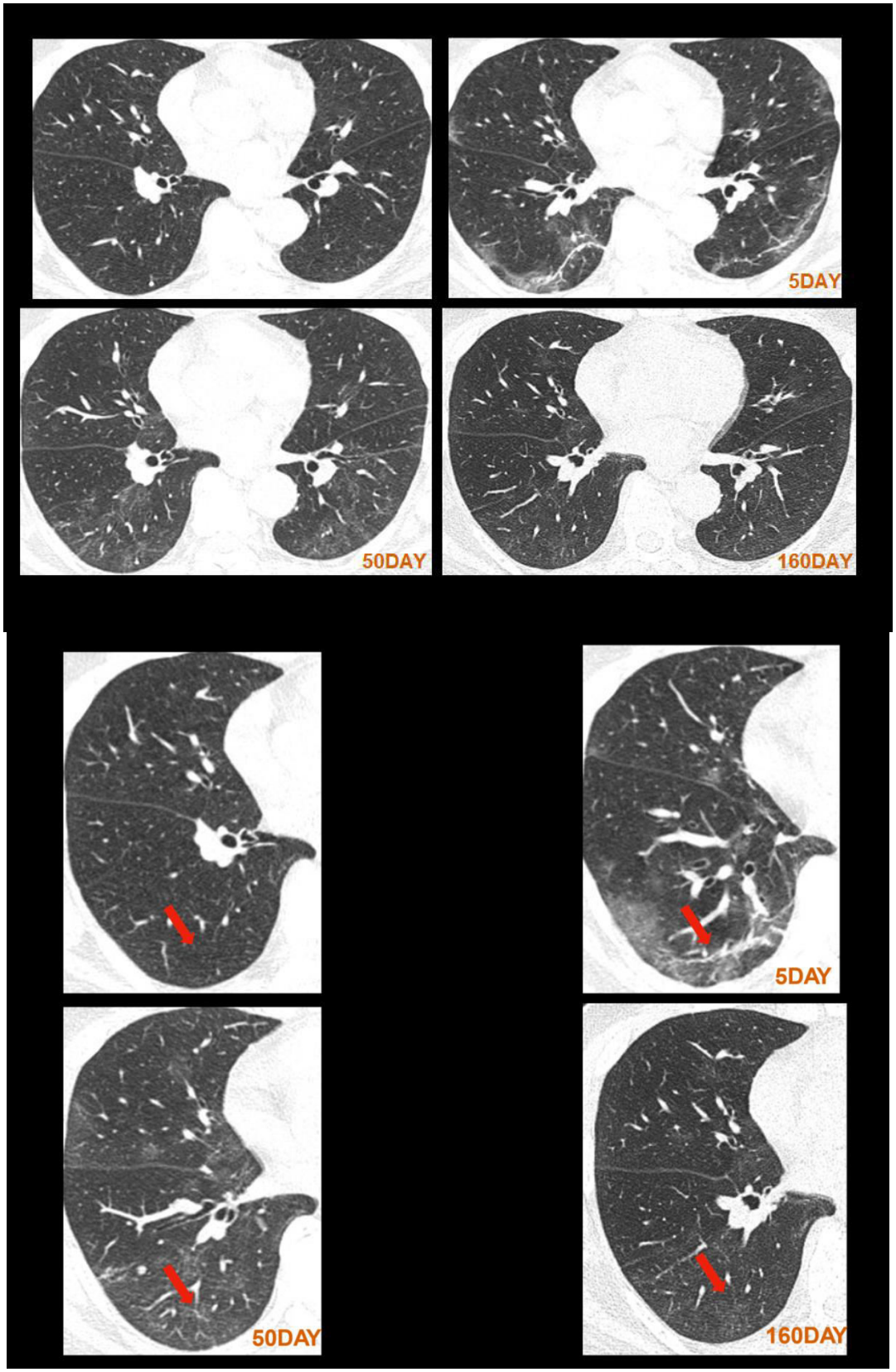


Fig1e: RT-PCR positive case shows normal CT on initial study. Follow up study after 5days shows GGO with subpleural curvilinear parenchymal bands. 50days follow shows 'Tinted sign' likely representing expansion of alveolus. Complete resolution with no residual on follow up 160th day.

Group 2 included case with residual GGO/Consolidation in COVID19 pneumonia for follow up period of minimum 90days.

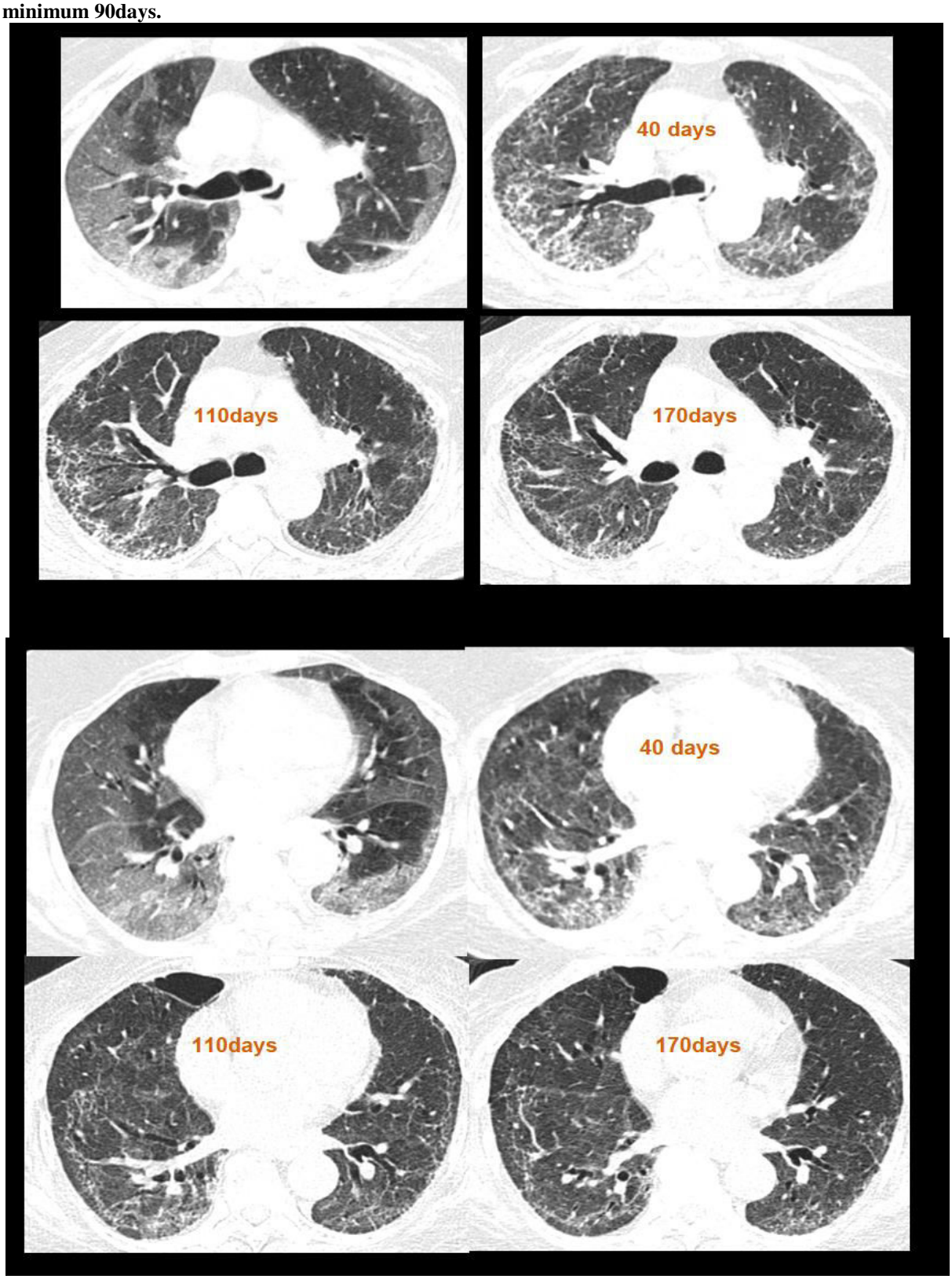


Fig 2a: Initial presentation of GGO with crazy paving pattern. 40days interval period shows GGO with extensive interlobular septal thickening and architectural distortion. No significant change was seen on follow up 110days and 170days respectively. Architectural distortion resulting to subpleural emphysematous bulla formation in right middle lobe on follow up study.

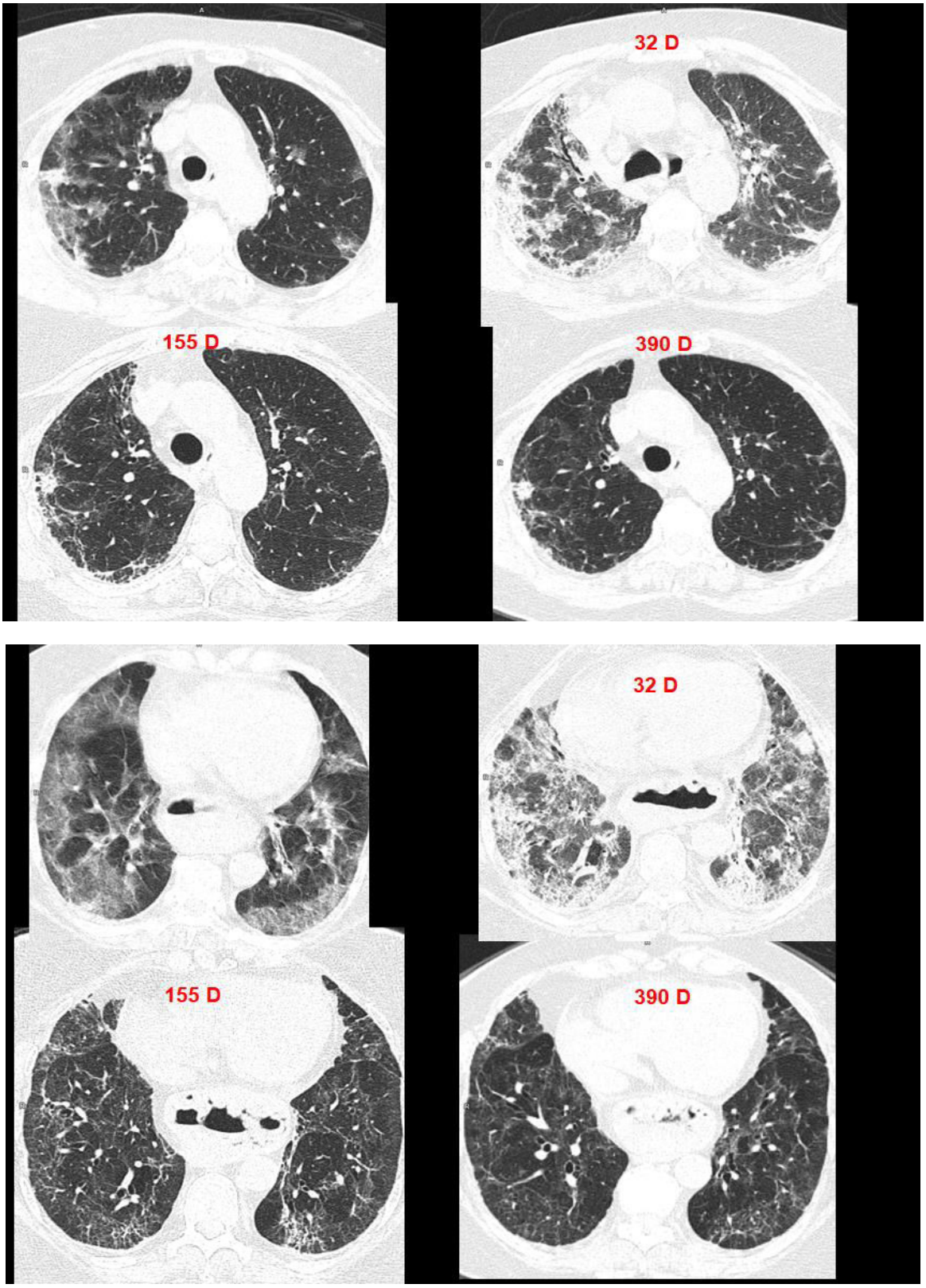


Fig2b: Initial CT chest shows patchy areas of peribronchovascular and subpleural ground glass opacity with focal superimposed consolidations diffusely involving both lung fields. Follow up study 30days shows progression of disease process in form of predominant consolidation pattern and beginning of interlobular septal thickening. Further follow up at 155 and 390 days shows regression in GGO and consolidation with mild regression of interlobular septal thickening.

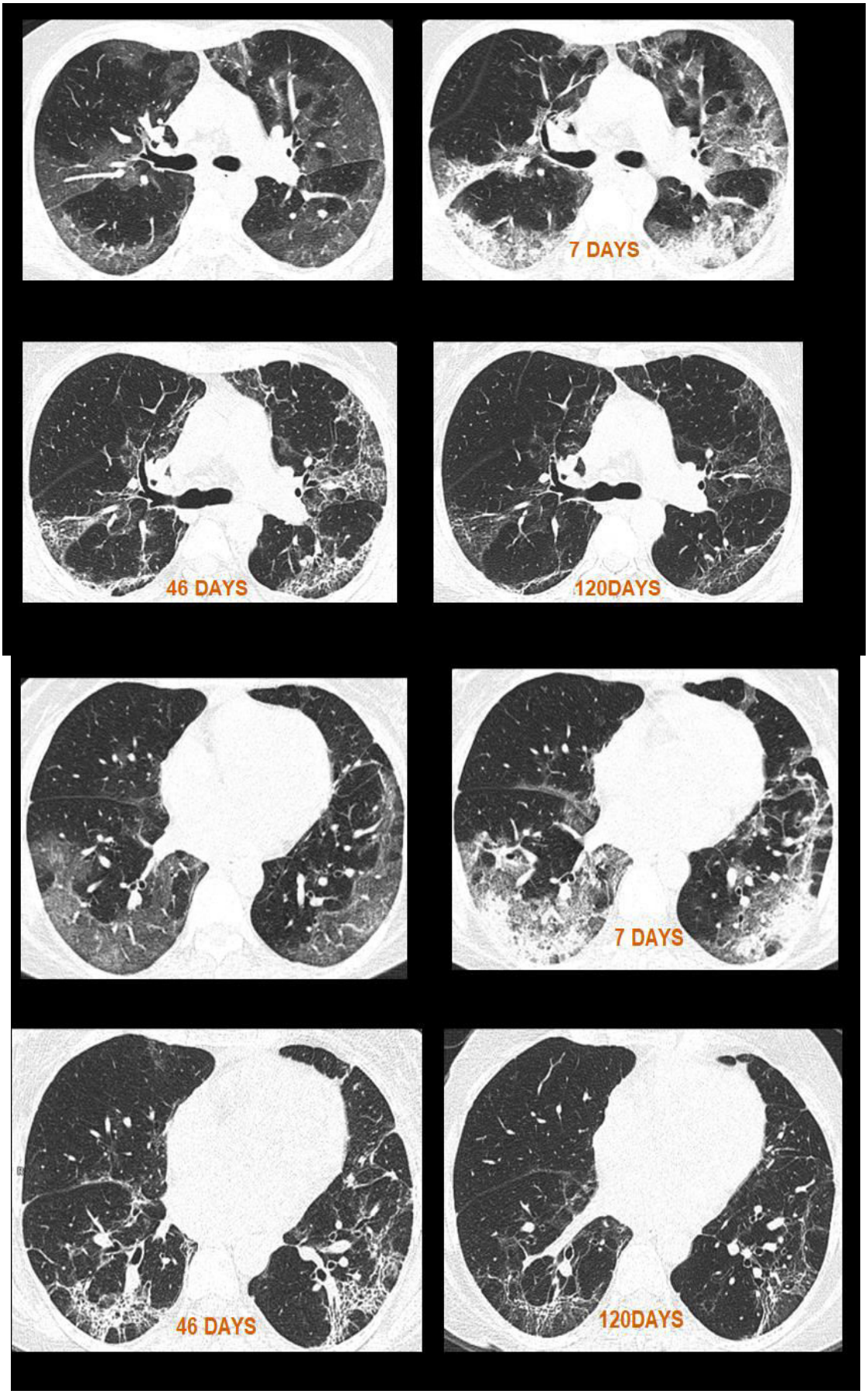


Fig2c: Initial CT shows pure GGO lesions diffusely involving both lung fields.Follow up study after one week shows focal superimposed consolidation. 46days follow up study shows resolving GGo with

interlobular thickening. 120 days follow shows resolved GGO with resolving interlobular septal thickening associated with parenchymal bands.

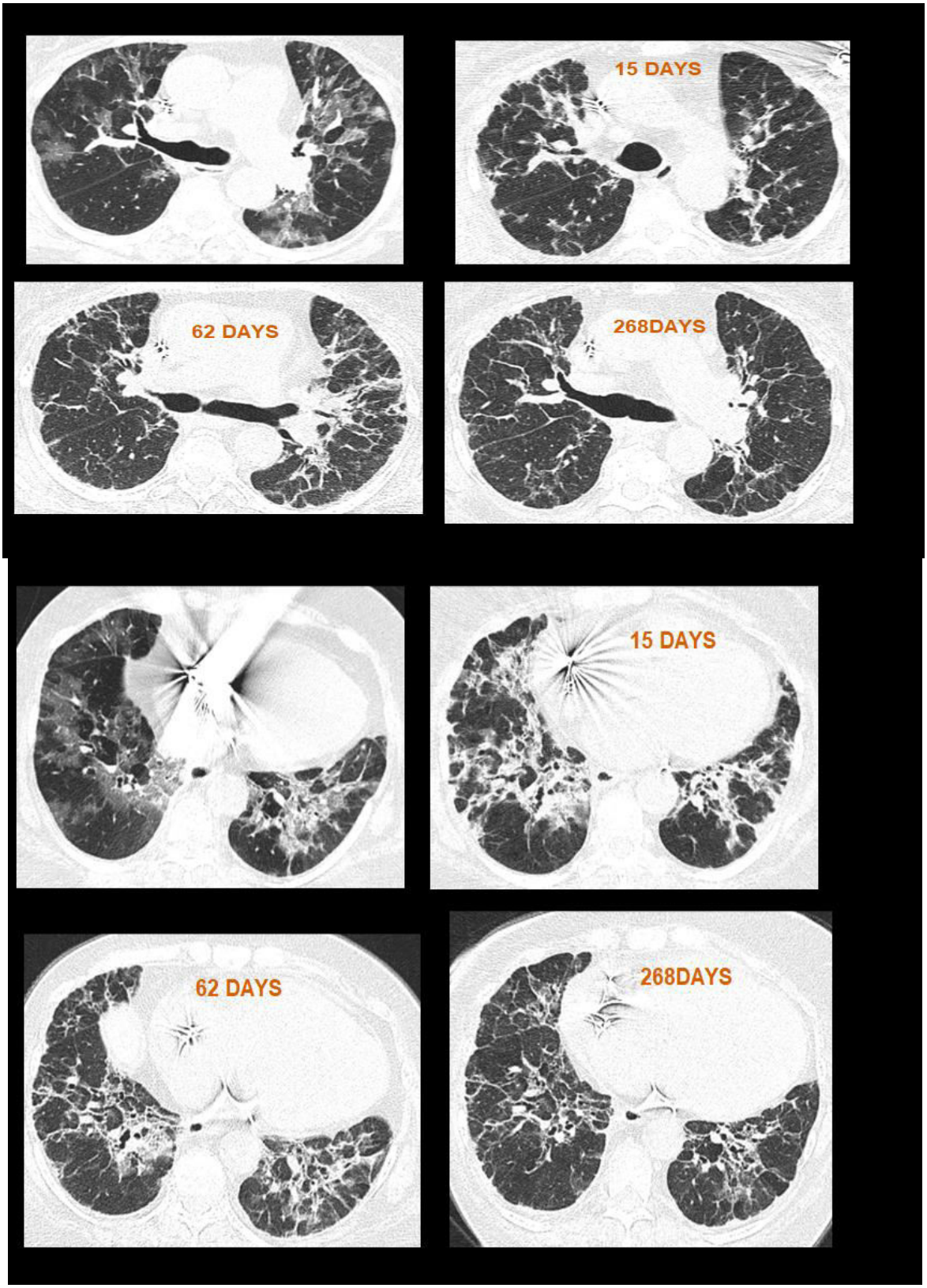


Fig 2d: Another example with follow CT on 268th day shows gradual evolution of GGO to consolidation followed by interstitial thickening and parenchymal bands.

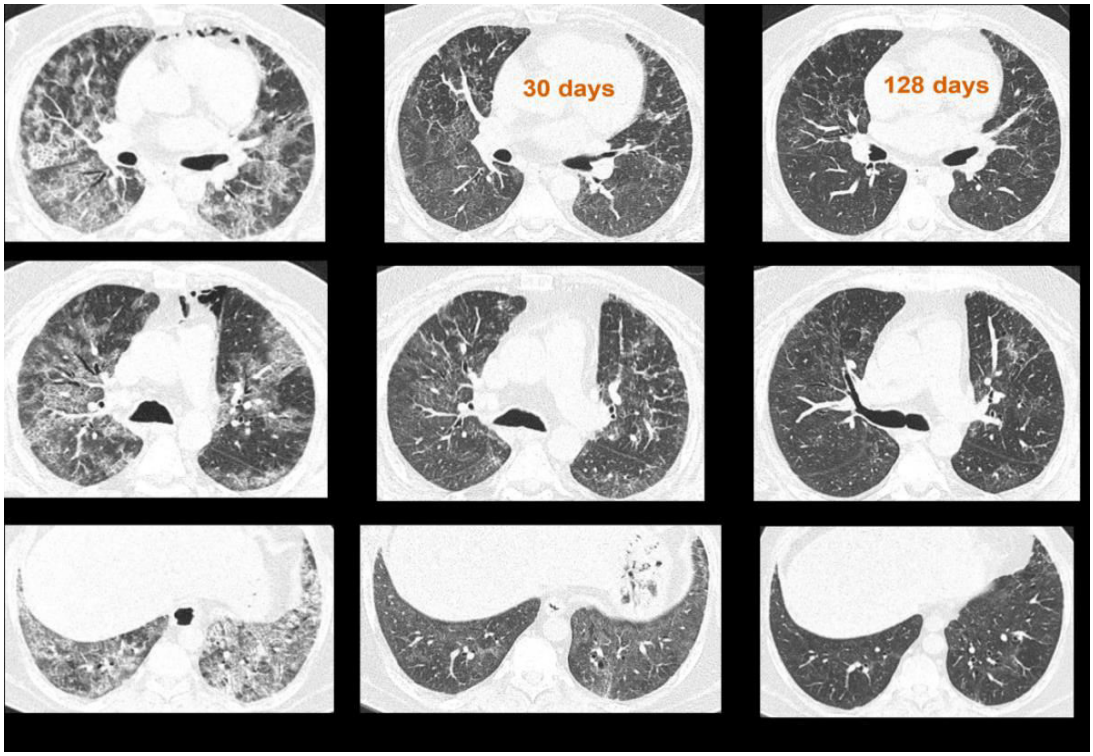
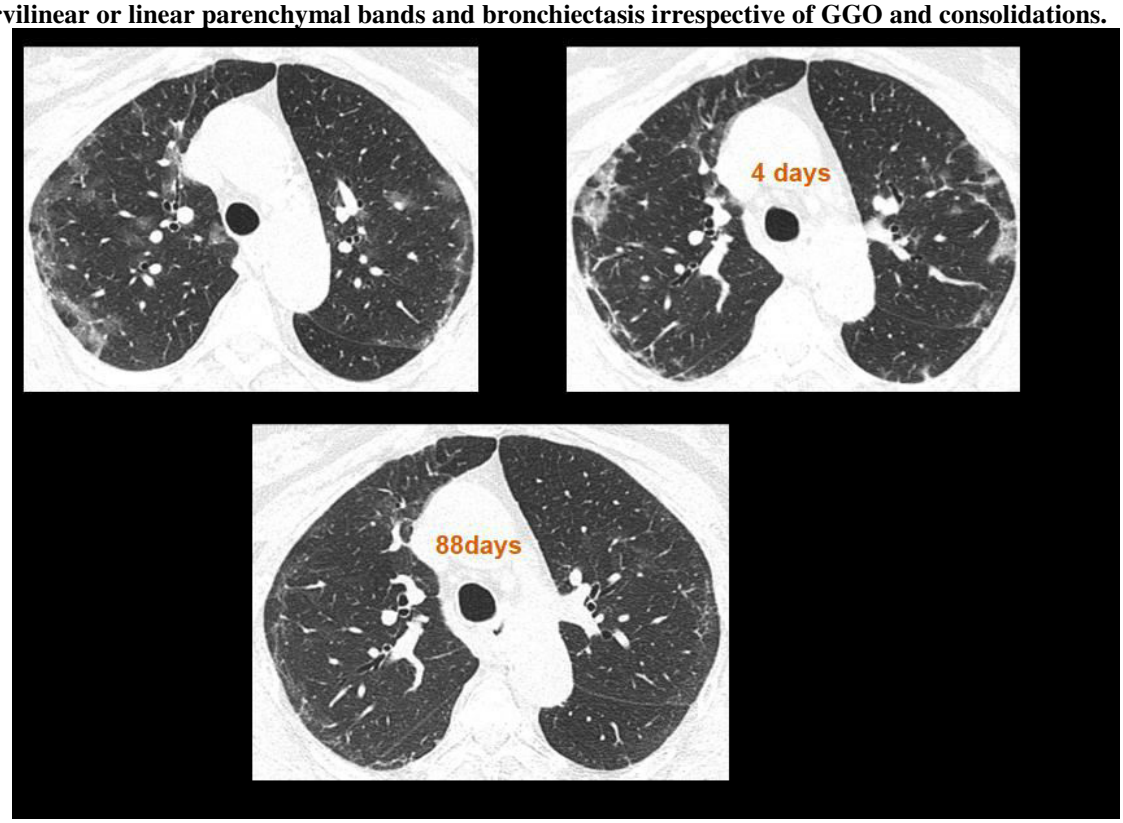


Fig 2e: 52/M with RT-PCR positive status performed HRCT chest on day6 of fever, significant drop in oxygen saturation and on oxygen supply shows peribronchovascular ground glass opacity with interstitial thickening, dark bronchus and mild pneumothorax. 30 days interval period shows regression of peribronchovascular ground glass opacity associated with interstitial thickening and complete resolution of pneumothorax. On further follow up interval period of 128days shows near total resolution of GGO with significant regression in interstitial thickening.

Group 3 cases includes the follow up with residual lesions in form of either interlobular septal thickening, curvilinear or linear parenchymal bands and bronchiectasis irrespective of GGO and consolidations.



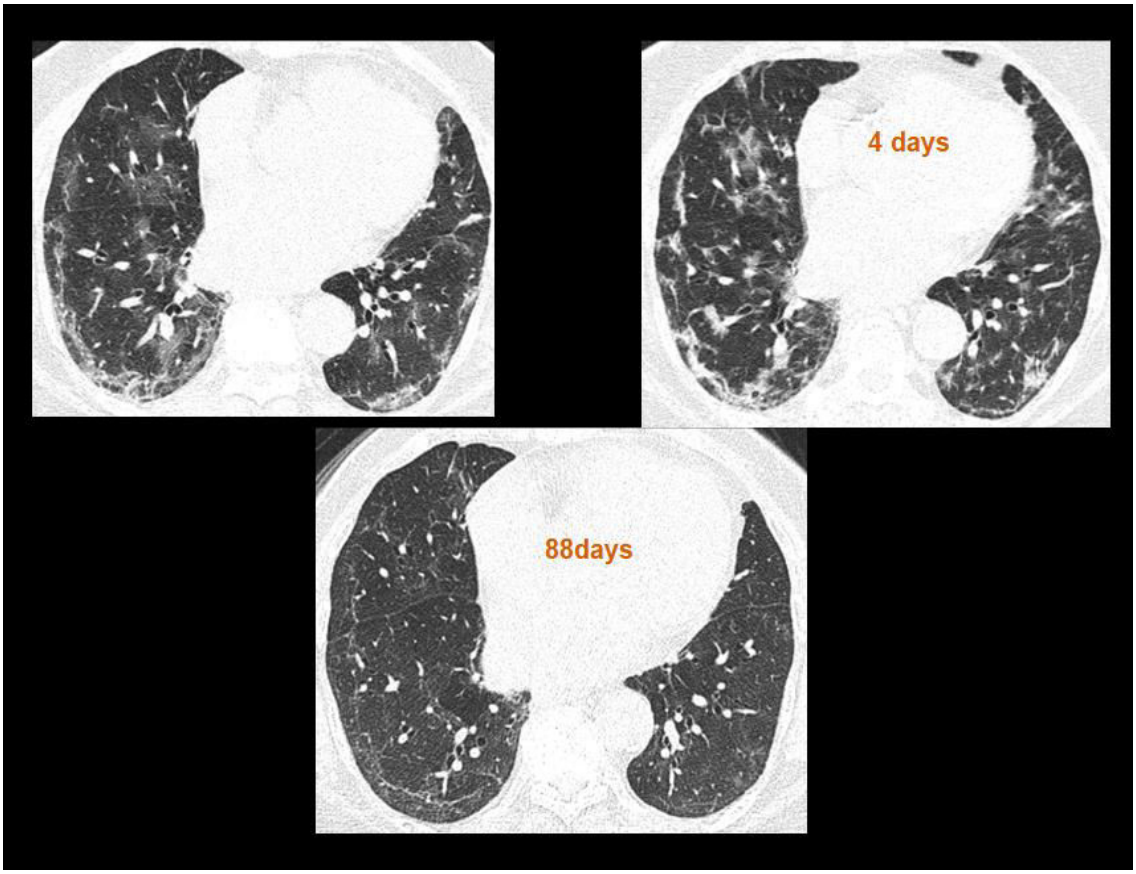


Fig3: Evolution of GGO to consolidation with residual parenchymal bands and near total resolution of GGO and consolidation on follow up 88th day.

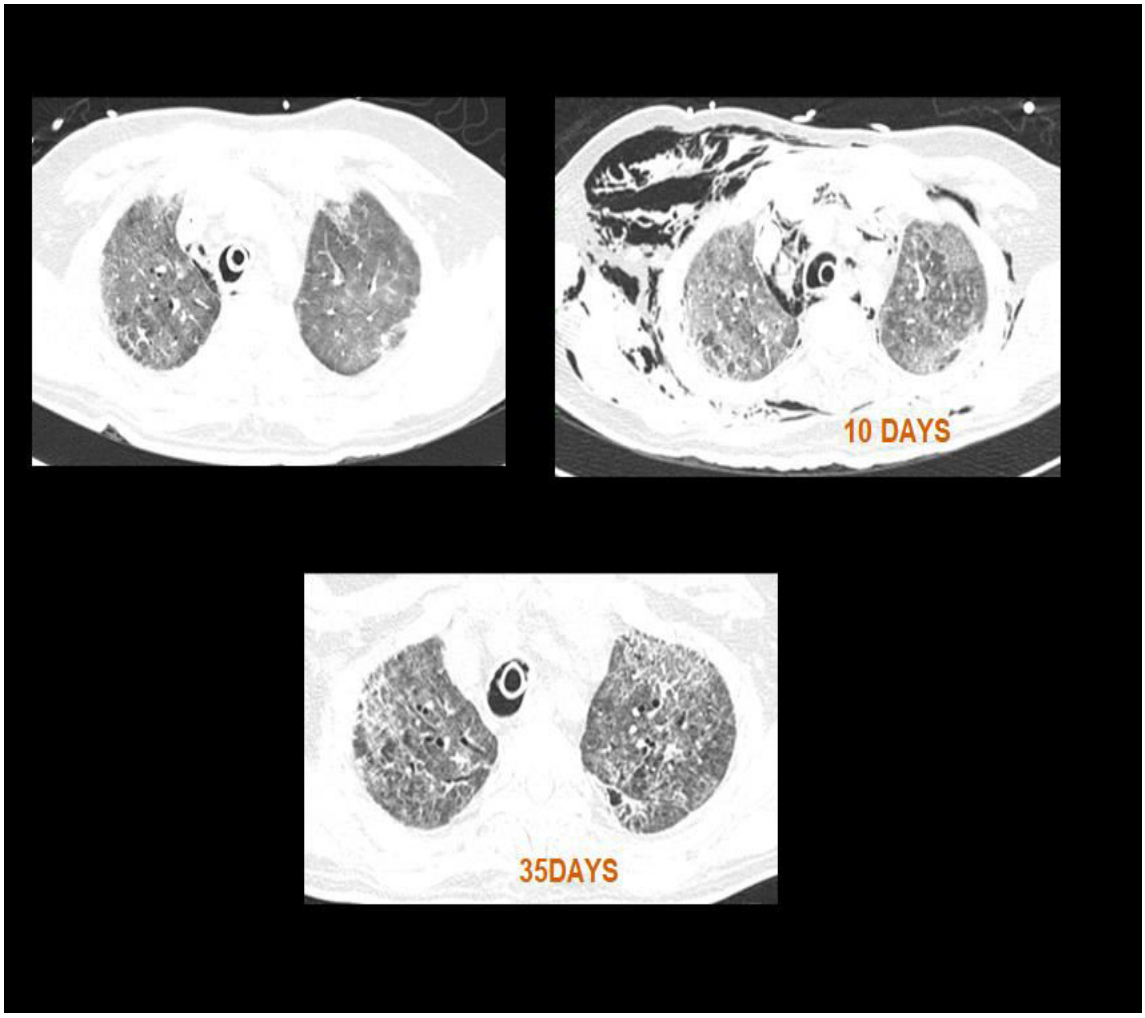
Pleural effusion was uncommon was seen in 8.8% of cases from Group 1, 9.1% from Group 2 (was not statistically significant) manifesting mainly in patients with moderate to severe disease, which may indicate parapneumonic effusion or fluid overload.

Group 2 includes more older age group compared to Group1, thus extensive lung involvement with residual lung disease on follow up study were more prone in older age group with mean age of 70.55yr, while lesser lung involvement with complete resolution of lung lesion on follow up i.e Group 1 were in much younger group with mean age of 58.36yrs. This finding were consistent with previous studies [7] [20].

Pulmonary complications related to COVID19 pneumonia found in our study includes pneumomediastinum and pneumothorax. The presence of air in the mediastinum is explained by air dissecting that extends centripetally through the Broncho vascular sheaths, serous structures and adipose tissue due to an increase of the intrathoracic pressure that determines alveolar rupture [26][27]. Barotrauma due to mechanical ventilation, central venous catheter insertion, causing alveoli rupture due to pulmonary overexpansion finally forming pneumomediastinum, pneumothorax and emphysema [19].

We found few pneumothorax and pneumomediastinum cases in out study showing complete resolution on follow up study. Literature mentions the association between COVID19 and spontaneous pneumothorax, however the correlation and prognostic importance remains uncertain [28].

Few of our study cases reveals patients with barotrauma presenting with pneumothorax and pneumomediastinum extending to subcutaneous emphysema most likely due to barotrauma secondary to ventilation.



In our study pneumomediastinum/pneumothorax as pulmonary complication related to COVID19 pneumonia were seen more commonly in GROUP2 (18.2%) compared to GROUP1 (2.9%), although statistically the data was insignificant. Our study has some limitations. Sample size was small and follow up study was conducted only for the period of 3 to 12 months. Sample size is restricted to patients only presenting to our hospital for treatment or isolation. Fibrotic lung changes needs pathological correlation for confirmation. This study includes residual lesions without any quantification, which can be done by a computer based analysis. This study includes a semi quantitative scores for ground-glass densities and consolidations. Semi quantitative scores for residual findings other than ground-glass densities and consolidations were not included in this study. Other clinical history like that of smoking, asthma,, interstitial lung disease was not evaluated in this study. There is a lack of histological correlation for lung findings of COVID-19 infection in our study. Further studies are needed to examine whether the residual lesions in the form of interlobular septal thickening/parenchymal planned on the CT scan whether represents true pathological fibrosis. Our study do not include the findings in children, as these might be different from seen in adults. Our study does not include many of pulmonary and extrapulmonary complications related COVID19 infection, predominant thromboembolic events.

SUMMARY

Follow up CT scan obtained with minimal interval period of 3 months of disease onset shows there is near total resolution of ground-glass densities and consolidations in more than 2/3rd of patients in RT-PCR proven COVID-19 infection. Significant residual findings after mid term follow up were seen in older patients and had more CT severity score during the acute phase, this may represent the underlying immune response [17].

Patients with the severe form and persistent residual lesions (Group 2) on follow up (median age, 70 years; interquartile range [IQR]: 52.00 – 81.00 yrs) (P = 0.001) were older than those with complete resolution of disease (Group 1) (median age, 58.36 years; IQR: 23–87 years) (P = 0.013).

Extensive involvement of lungs and with consolidations were significantly more predominant in patients who were older than 50 years (mean 70.55yrs) than in those who were 50 years or younger

(mean 58.36yrs), consistent with previous studies [7] [20].

Patients with Group 2 shows more lung involvement (mean percentage of lung involvement 50.80%±20.67% Vs 21.33%±19.39%) (P= 0.001) and CT severity score (18.18±04.00 /25 Vs 09.90±05.36 /25) on initial CT findings compared to Group 1.

Consolidation alone was rare finding only 2 cases among 68 in Group 1. Mixed was common finding in Group 1 (52.9%) and Group 2 (81.8%). It is speculated that mixed pattern may represent more advanced stage of disease and more severe clinical form compared to pure GGO, consistent with previous studies [12] [7].

Pleural effusion was uncommonly seen in 8.8% of cases from Group 1, 9.1% from Group 2 (was not statistically significant) manifesting mainly in patients with moderate to severe disease, similar to previous study. [12]

REFERENCES

1. Novel Coronavirus (2019-nCoV). World Health Organization. https://www.who.int/emergencies/diseases/novel-Coronavirus-2019. Published January 7, 2020.
2. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. World Health Organization. https://www.who.int/csr/sars/country/table2004_04_21/en/. Published April 21, 2004.
3. Middle East respiratory syndrome Coronavirus (MERS-CoV). World Health Organization. https://www.who.int/emergencies/mers-cov/en.
4. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients Read More: https://www.ajronline.org/doi/full/10.2214/AJR.20.23034AJR 2020; 215:1–7.
5. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, Cui J, Xu W, Yang Y, Fayad ZA, Jacobi A. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV) Radiology. 2020 Apr; 295 (1): 202–207. doi: 10.1148/radiol. 2020200230.
6. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, Zheng D, Wang J, Hesketh RL, Yang L, Zheng C. Time course of lung changes at chest CT during recovery from coronavirus disease 2019 (COVID-19). Radiology. 2020 Jun;295(3):715-21.
7. Wang H, Wei R, Rao G, Zhu J, Song B. Characteristic CT findings distinguishing 2019 novel coronavirus disease (COVID-19) from influenza pneumonia. European radiology. 2020 Sep;30(9):4910-7.
8. Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raoof S, Schluger NW, Volpi A, Yim JJ, Martin IB, Anderson DJ. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. Radiology. 2020 Jul;296(1):172-80.
9. Liu N, He G, Yang X, Chen J, Wu J, Ma M, Lu W, Li Q, Cheng T, Huang X. Dynamic changes of chest CT follow-up in coronavirus disease-19 (COVID-19) pneumonia: relationship to clinical typing. BMC Medical Imaging. 2020 Dec;20(1):1-8.
10. Wang Y, Dong C, Hu Y, Li C, Ren Q, Zhang X, Shi H, Zhou M. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. Radiology. 2020 Aug;296(2):E55-64.
11. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, Li Y, Cao Y, Gu J, Wu H, Shi H. Six-month follow-up chest CT findings after severe COVID-19 pneumonia. Radiology. 2021 Apr;299(1):E177-86.
12. Yu M, Xu D, Lan L, Tu M, Liao R, Cai S, Cao Y, Xu L, Liao M, Zhang X, Xiao SY. Thin-section chest CT imaging of COVID-19 pneumonia: a comparison between patients with mild and severe disease. Radiology: Cardiothoracic Imaging. 2020 Apr 23;2(2):e200126.
13. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008 Mar;246(3):697-722.
14. Zerhouni EA, Naidich DP, Stitik FP, Khouri NF, Siegelman SS. Computed tomography of the pulmonary parenchyma. Part 2: Interstitial disease. Journal of thoracic imaging. 1985 Dec 1;1(1):54-64.
15. Zhou Z, Guo D, Li C, Fang Z, Chen L, Yang R, Li X, Zeng W. Coronavirus disease 2019: initial chest CT findings. European radiology. 2020 Aug 1:1.
16. Li X, Zeng W, Li X, Chen H, Shi L, Li X, Xiang H, Cao Y, Chen H, Liu C, Wang J. CT imaging changes of corona virus disease 2019 (COVID-19): a multi-center study in Southwest China. Journal of translational medicine. 2020 Dec;18(1):1-8.
17. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. International Journal of Infectious Diseases. 2016 Aug 1;49:129-33.
18. Yuan Y, Tao XF, Shi YX, Liu SY, Chen JQ. Initial HRCT findings of novel influenza A (H1N1) infection. Influenza and other respiratory viruses. 2012 Nov;6(6):e114-9.
19. Wang Q, Zhang Z, Shi Y, Jiang Y. Emerging H7N9 influenza A (novel reassortant avian-origin) pneumonia: radiologic findings. Radiology. 2013 Sep;268(3):882-9.
20. Ojha V, Mani A, Pandey NN, Sharma S, Kumar S. CT in coronavirus disease 2019 (COVID-19): a systematic review of chest CT findings in 4410 adult patients. European radiology. 2020 Nov;30:6129-38.
21. Tabatabaei SMH, Talari H, Moghaddas F, Rajebi H (2020) Computed tomographic features and short-term prognosis of coronavirus disease 2019 (COVID-19) pneumonia: a single-center study from Kashan, Iran. Radiology: Cardiothoracic Imaging 2(2):e200130.
22. Bianco A, Valente T, Perrotta F, Stellato E, Brunese L, Wood BJ, Carrafiello G, Parrella R, Aronne L, Boccia M, Lassandro F. Remarkable vessel enlargement within lung consolidation in COVID-19 compared to AH1N1 pneumonia: A retrospective study in Italy. Heliyon. 2021 May 1;7(5):e07112.
23. Chiarenza A, Ultimo LE, Falsaperla D, Travali M, Foti PV, Torrisi SE, Schisano M, Mauro LA, Sambataro G, Basile A, Vancheri C. Chest imaging using signs, symbols, and naturalistic images: a practical guide for radiologists and non-radiologists. Insights into imaging. 2019 Dec;10(1):1-20.
24. Lin L, Li TS (2020) Interpretation of “Guidelines for the diagnosis and treatment of novel coronavirus (2019-nCoV) infection by the National HealthCommission(Trial Version5)”. ZhonghuaYiXue Za Zhi 100:E001

25. Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. American Journal of Roentgenology. 2020 Jun;214(6):1287-94.
26. Meireles J, Neves S, Castro A, França M. Spontaneous pneumomediastinum revisited. Respiratory Medicine CME. 2011 enero 1; 4(4): 181-183. 9.
27. Murayama S, Gibo S. Spontaneous pneumomediastinum and Macklin effect: Overview and appearance on computed tomography. World J Radiol. 2014 noviembre 28; 6(11): 850-854.
28. Rohailla S, Ahmed N, Gough K. SARS-CoV-2 infection associated with spontaneous pneumothorax. CMAJ. 2020 abril 21; 192(19): E510.