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ORIGINAL ARTICLE

Post COVID-19 pneumonia lung fibrosis: A worrisome sequelae in surviving patients.

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ABSTRACT… Objective: To assess the frequency of pulmonary fibrosis after coronavirus infection through computed tomography (CT) severity score analysis. **Study Design:** Cross-sectional Prospective study. **Setting:** Tertiary Care Hospital Kharian. **Period:** 12 November 2021 to 11 May 2022. **Methods:** It included 100 patients with age range of 20 to 70 years. The demographics, clinical history and severity level of patients was noted at admission. The CT was conducted at follow up of 6 weeks. The eminent CT findings and severity score were recorded for each patient. The occurrence of fibrosis was recorded at 12 weeks follow-up. The data was assessed by statistical software for social sciences (SPSS) v.23 through means and standard deviations or frequencies and percentages. The association of CT severity score and occurrence of fibrosis was checked through correlation analysis with p value of 0.05 as significant. **Results:** The findings of CT at week 12 was significant correlated with CT severity score at week 6. **Conclusion:** The CT findings and scoring can help in assessing the probability of occurrence of pulmonary fibrosis. This can be helpful for timely treatment of the disease.

Key words: Coronavirus, Computed Tomography, Lung Fibrosis.

INTRODUCTION

The destruction caused by coronavirus pandemic is no more a secret. This disruption was enormous in terms of health. The pandemic of coronavirus started at the end of 2019, and was spread widely all over the word. The common symptoms of coronavirus infection ranges from mild upper respiratory tract symptoms to severe acute respiratory distress syndrome (ARDS). The risk factors of coronavirus infection have been reported as old age, male gender and co-morbidities such as diabetes and heart problems.[1] Till date, the infection of coronavirus has infected more than 531 million individuals with death of more than 6 million patients.

After the coronavirus pandemic, the number of survivors have increased all over the world. Although these survivors have successfully battled against the infection, they still have to face the negative impact imparted by the infection. Despite being tested negative for laboratory test, the survivors may still show symptoms after disease.[2] These symptoms may vary from being mild form of fatigue to serious form needing long-term oxygen therapy or lung transplantation due to pulmonary fibrosis. Literature indicates that coronavirus infection is followed by post-viral fibrosis, physical disabilities, and respiratory diseases including acute respiratory distress syndrome.[3] This is evident through frequent follow-up of patients after coronavirus infection. At least 70% to 80% of survivors show 1 symptom of disease post-infection. Thus, the overall burden of fibrotic pulmonary disease may increase at significant level.[4]

Fibrosis is a common finding after severe and continuous damage to lungs from causes such as connective tissue disorders, medications, chronic granulomatous diseases and respiratory infections.[5] However, it is not apparent usually after other viral pneumonias. But it has prevalence of 8% among patients of coronavirus

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infection.[6] According to an estimate, at least 4.8 million individuals are supposed to suffer from pulmonary fibrosis after coronavirus infection.[7] Although majority of them may survive without lung damage, many individuals may suffer from residual outcomes. In this regard, anti-fibrotics has been used successfully to reduce fibrosis.[8]

Fibrosis usually effect adults with more prevalence in men as compared to women. Its presentation includes chronic and progressive dyspnea along with dry cough.[9] The management of disease comprises of long term oxygen therapy, smoking cessation, lung transplant or anti-fibrotic medications.[10] However, it is required to forecast the probability of developing fibrosis at early stage. This approach can be useful in selecting appropriate treatment. The present research work is aimed to assess patients that may develop such serious complications, which may help in introduction of anti-fibrotic drugs.

METHODS

The present cross-sectional prospective study was conducted from 12 November 2021 to 11 May 2022 at Tertiary Care Hospital Kharian. The study was approved by institutional ethical committee (No.2347-25/6/2022). It comprised of 100 patients with 50 (50%) males and 50 (50%) females with age range of 20 to 70 years. After receiving informed consent from the patients, complete clinical data including, age, gender, and clinical history (fever, diarrhea, dyspnea or dry cough) was collected.

The inclusion criteria comprised of patients with positive computed tomography (CT) findings of coronavirus infection and confirmed polymerase chain reaction test (PCR). The follow-up of 6 weeks was performed to assess the extent of recovery and residual fibrotic change among the patients with negative PCR. Further follow-up was conducted of 12 weeks for patients with residual symptoms and lung fibrotic changes. The exclusion criteria comprised of pregnant females, history of chronic interstitial lung disease, severe respiratory motion artifacts on CT images and any chronic medical co-morbidity including hypertension, autoimmune diseases and diabetes.

The participants went under chest CT and the images were acquired from both lungs in supine position at full inspiration, foot first and without contrast medium. The CT chest findings including consolidation, ground glass opacities (GGO), vascular thickening and bronchial thickening were evaluated along with location and distribution. The pulmonary fibrosis is depicted through features of fibrotic strips, bronchovascular bundle distortion, architectural distortion, traction bronchiectasis and interlobar septal thickening. CT was repeated at initial diagnosis, 6 week and 12 week intervals. Severe ARDS case was defined as respiratory distress more than 30 breaths/minute, SpO_2 less than 93% at rest state, PaO_2/FIO_2 ratio less than 300, more than 50% progression within 24-48 hours in pulmonary imaging.

CT severity score was assessed for each CT image, which depicts degree of lung impact on the basis of 5 lung lobes. The score comprises of 0 to 5 level with 0 shows no involvement, 1 shows less than 5% involvement, 2 shows 5% to 25% involvement, 3 shows 26% to 49% involvement, 4 shows 50% to 75% involvement and 5 show more than 75% involvement. The total CT score was obtained by adding score of 5 lobes and ranged from 0 to 25. The occurrence of fibrosis was recorded at follow-up of 12 weeks.

The statistical software for social sciences (SPSS) v.23 was used to depict findings. The quantitative variables such as age and time to CT were presented as means and standard deviations, whereas, qualitative variables such as gender, clinical history, ARDS level, CT characteristics, occurrence of fibrosis on CT and association of CT severity score with fibrosis were presented as frequencies and percentages. The association of CT severity score and occurrence of fibrosis was checked through correlation analysis with p value of 0.05 considered as significant.

RESULTS

The Table-I shows patient characteristics at the time of admission. The mean age was 47.08 ± 13.5 years with 50 (50%) male individuals and 50

(50%) female individuals. In clinical presentation, fever (n = 32; 32%) was the most common. Majority of the patients were declared as severe (n = 41; 41%) on the basis of ARDS at the time of admission. This was followed by 30 (30%) moderate and 29 (29%) mild cases.

Characteristics of the Patients	Frequency n (Percentage %)
Age (years) (mean ± SD)	47.08 ± 13.5
Gender	
Male	50 (50%)
Female	50 (50%)
Clinical history	
Fever	32 (32%)
Diarrhea	21 (21%)
Dyspnea	25 (25%)
Dry cough	22 (22%)
ARDS level	
Mild	29 (29%)
Moderate	30 (30%)
Severe	41 (41%)

Table-I. Patient characteristics at the time of admission

The Table-II shows characteristics of CT at 6 weeks of follow-up. The mean time to CT was 56.1 ± 1.5 days. Only 20% of patients showed GGO on CT, with majority (40%) being depicted as central. Fibrous stripes were shown in 29% of patients with majority (37.93%) being depicted as both central and peripheral. Subpleural line was apparent in 5% patients, interlobular septal thickening in 38% patients, consolidation in 5% patients, traction bronchiectasis in 6% patients, small nodules in 2% patients, lymph node enlargement in 5% patients, and pericardial effusion in 1% patients. These peculiar manifestations were more prominent in patients marked as severe cases. Main CT presentation was depicted as reticulation predominance in 57% of patients. Lung segments involvement was more than 174/126 in 25% patients with dominance in severe cases. Again the severity score of more than 17/25 was evident in 41% of cases with dominance in severe cases.

The Table-III shows occurrence of fibrosis on CT at 12 weeks of follow-up. Only 33% of patients showed presence of pulmonary fibrosis, whereas, 67% of patients showed absence of it.

Computed Tomography (CT) Characteristics of Patients	Frequency n (Percentage %)
Time to CT (days) (mean ± SD)	56.1 ± 1.5
Ground glass opacities (GGO)	20 (20%)
Central	8 (40%)
Peripheral	6 (30%)
Both	6 (30%)
Subpleural line	5 (5%)
Interlobula septal thickening	38 (38%)
Fibrous stripes	29 (29%)
Central	9 (31.03%)
Peripheral	9 (31.03%)
Both	11 (37.93%)
Consolidation	5 (5%)
Traction bronchiectasis	6 (6%)
Small nodules	2 (2%)
Lymph node enlargement	5 (5%)
Pericardial effusion	1 (1%)
Main computed tomography (CT) manifestations	
Ground glass opacities (GGO) predominance	43 (43%)
Reticulation predominance	57 (57%)
Lung segments involved (174/126)	25 (25%)
CT severity score more than 17/25	41 (41%)

Table-II. Computed tomography (CT) characteristics of patients at 6 weeks follow-up

Occurrence of Fibrosis on Computed Tomography (CT)	Frequency n (Percentage %)
Presence	33 (33%)
Absence	67 (67%)

Table-III. Occurrence of fibrosis on computed tomography (CT) at 12 weeks follow-up

The Table-IV shows association of CT severity score with presence of fibrosis. It is evident that fibrosis was present in 33% of patients with CT score of more than 17. On the other hand, it was absent in 59% patients not showing CT more than 17. However, 8% patients showing more than 17 score on CT did not develop fibrosis.

Severity Score More Than 10	Fibrosis Presence		Total n (%)
	Yes n (%)	No n (%)	
Yes n (%)	33 (33%)	8 (8%)	41 (41%)
No n (%)	0	59 (59%)	59 (59%)
Total n (%)	33 (33%)	67 (67%)	100

Table-IV. Association of computed tomography (CT) severity score with presence of fibrosis

The Table-V shows correlation between CT severity score and occurrence of fibrosis through

correlation analysis. The value of 0.842 (0.1 to 0.3 for low association; 0.3 to 0.5 for moderate association; 0.5 to 1 for high association) shows high association between the two with high significance value of $p < 0.001$. Thus, CT severity score is a predictor of occurrence of fibrosis.

Pearson Correlation	0.842
p value	< 0.001*

Table-V. Correlation between computed tomography (CT) severity score and occurrence of fibrosis *significant with $p < 0.05$

DISCUSSION

The occurrence of pulmonary fibrosis has appeared as a common finding after the recovery of coronavirus infection.[11] Literature indicates that the patients with mild and moderate forms of acute respiratory distress syndrome (ARDS) usually recovers completely. However, some of the cases in severe category may remain hypoxemic despite receiving appropriate medical treatment.[12] The development of permanent pulmonary architectural distortion and irreversible pulmonary dysfunction can be worrisome as majority of the world population has already passed through the coronavirus tragedy. Yet the occurrence of another tragic consequence for the survivors can be a threat to world's population.[14]

Although many theories have been suggested to depict the mechanism of occurrence of pulmonary fibrosis after coronavirus infection, still it is not clear that why some people recover completely from the infection, whereas, others develop pulmonary fibrosis.[15] However, the use of CT findings and scoring can help in assessing the occurrence of fibrosis in suspected patients.[16] This study was aimed at assessing likability of occurrence of pulmonary fibrosis after coronavirus infection through computed tomography (CT) severity score analysis.

Literature has emphasized that occurrence of fibrosis is highly related to the age, gender, cigarette smoking, prolonged ICU admission and CT severity score.[17] The relation of age and pulmonary fibrosis was eminent in present study also as fibrosis was mostly evident for individuals with age range 60 to 70 years. This can be explained on the basis of growing suppression of immune system with age.[18] On the other hand, male population showed higher incidence of the disease. Previous research works have indicated 1.3 times more occurrence of pulmonary fibrosis in male individuals.[19] The effect of androgen has been regarded as responsible for this fact. This hormone impairs antibody response and help in fusion of virus with host cells.[20]

The present study clearly related the CT severity score with occurrence of pulmonary fibrosis in later stages. This is evident through the fact that CT severity score of more than 17/25 is mostly present in patients marked as severe cases. Literature indicates that increased disease severity marks the lung tissue disruption and high mortality rate.[21] Thus, the use of CT findings can be helpful in utilizing prevention and treatment of pulmonary fibrosis timely.[22] The early diagnosis can be aid in adopting appropriate medication timely. This will not only overcome the associated morbidity but also reduce mortality of the patients.[23-25] The previous research works highly advocates the use of CT for predictability of pulmonary fibrosis. This has been justified by the present study also.

CONCLUSION

The CT findings and scoring is a good means of assessing the likability of future occurrence of pulmonary fibrosis following coronavirus infection. This approach can be useful in timely treatment of the patients by anti-fibrotic drugs and reduction of associated mortality and morbidity. Thus the use of CT should be enhanced among coronavirus infected patients to avoid any upcoming health issues.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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