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Research Article

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Patients having Lung Fibrosis after Covid-19: A Problematic Sequelae in Surviving Patients

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ABSTRACT

Introduction: COVID-19 has infected people all over the world. By the end of November 2020, it was confirmed that about 67M people were suffering from COVID-19 and almost 1.7 million people had died due to it. The symptoms of COVID-19 had a wide range from mild upper respiratory indications to severe acute respiratory distress syndrome. Certain factors of COVID-19 include old age, males, hypertension, and diabetes.

Aim: To detect and predict those patients who would develop lung fibrosis after Covid-19 infection as early introduction of anti-fibrotic drugs can be started.

Methodology: Overall, 85 individuals were involved in this study. Patients who were having COVID-19, confirmed by PCR, were examined by follow-up MDCT. CT scan was performed and similar research was involved with some follow-up data that include residual fibrotic changes and different radiological signs. Some risk factors were predicted that were said to be the source of lung fibrosis after COVID-19. These factors include cigarette smoking, old age, CT severity score being high and mechanical ventilation in the long term.

Results: The analysis of 85 patients, from which males were 43 and females were 42. Their age varied from 24 to 76 years old. A total of 30 (37.5%) individuals had a history of cigarette smoking of more than 25 cigarettes per day for more than ten years. People in the age group 60 to 76 years old had the highest commonness of getting post-COVID-19 pulmonary fibrosis. About 15 out of thirty-two patients, which is 46.2 percent, had pulmonary fibrosis. Patients of the age group 45 to 60 years had mild prevalence which is 7 out of 27 patients (25.9 percent).

Conclusion: If post-COVID-19 pulmonary fibrosis is detected early in individuals, there may be some changes to prevent such long-term complications.

Key Words: Covid-19, Complications, CT scan chest, Lung fibrosis, PCR, MDCT

INTRODUCTION

COVID-19 has infected people all over the world. By the end of November 2020, it was confirmed that about 67M people were suffering from COVID-19 and almost 1.7 million people had died due to it. The symptoms of COVID-19 had a wide range from mild upper respiratory indications to severe acute respiratory distress syndrome.[1] Certain factors of COVID-19 include old age, males, hypertension, and diabetes.[2]

Some patients tested negative for COVID-19 in the laboratory after surviving COVID-19 but they still had symptoms. The number of these individuals was increasing which increases the importance of COVID-19 and actions to manage it. Due to pulmonary fibrosis, consequences can range from minor forms of fatigue to significant ones. They need oxygen therapy in long term or even need a transplant of lungs.[3]

There has been significant post-COVID-19 fibrosis and physical abnormalities associated with previous coronavirus epidemics. Following COVID-19, patients must have regular follow-ups.[4] Due to COVID-19, a large variety of respiratory diseases are caused that have a high chance of development of acute respiratory distress syndrome.[5]

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The global burden of fibrotic pulmonary disease will be dramatically rising as a result of the expected large load of fibrotic pulmonary alterations caused by SARS-CoV-2 infection.[6] As compared to other viral pneumonia, fibrosis is not a common one. It has never been reported after H1N1 pneumonia. However, fibrotic changes have been seen in about 9.01 percent of patients affected with severe acute respiratory syndrome and 19.9 percent of individuals affected with H7N9 influenza.[7]

In this pandemic, almost 92 million people have been infected by a coronavirus. A greater number of patients were having mild COVID-19, 15 percent of people suffered from severe COVID-19 pneumonia, and five percent were affected with ARDS. This means that 4.8 million people will be affected by severe pulmonary pneumonia. Most of the patients will be cured without having their lungs damaged while a significant number of people will be affected by residual sequelae.[8] Proper treatment for post-COVID-19 pulmonary fibrosis is yet to be discovered. However, using anti-fibrotic in the initial stage of severe disease with ARDS might decrease the severity of fibrosis.[9] This research focuses on detecting and predicting those patients who would develop such serious changes which involve the use of anti-fibrotic drugs at an early stage.

Study design: A cross-sectional study

Place and Duration: This study was conducted at Jhalwan Medical College Khuzdar, Pakistan from February 2021 to February 2022.

Methodology

This research is a cross-sectional analysis of 85 patients, from whom males were 43, which is 50.5 percent, and females were 42, which is 49.5 percent. Their age varies from 24 to 76 years old. The average age calculated was 43.2 years. The ratio of males to females was 1.02:0.98. Patients who were aged from 24 to 45 years old were 26 in number. Those extending from 45 to 60 years old were 27 in number. Lastly, patients from the age group of 60 to 76 years were 32 in number. Proper clinical data of patients were taken, which included their sex, age, complaint, and history. Permission was taken from the ethical review committee of the institute.

Patients who were having CT scans of the chest that verified COVID-19 by PCR test were involved. A follow-up CT was done which led to negative PCR results. These patients were assessed on their level of recovery and fibrotic changes. Follow-ups were done at 4 to 6 weeks and 9 to 12 weeks for patients who were having residual lung fibrotic changes or symptoms.

Females that were having severe respiratory motion artifacts seen on CT scans were excluded. Moreover, pregnant women were also excluded. Patients who had a history of interstitial lung disease or hypertension, DM, or autoimmune disease were also excluded.

Patients underwent a chest CT using an MDCT (Multi-detector CT) scanner that had sixty-four channels. Table No. 1 shows the parameters for CT acquisition. Without using a contrast agent, the patient was placed in the supine position at full inspiration while having CT pictures taken. For a more accurate assessment of the disease distribution, all images were reformatted into 2D coronal and sagittal images after acquisition in the lung windows of 999 WW and -599 WL and the mediastinal windows of 399 WW and 59 WL. Data findings such as consolidation, vascular thickening, and ground glass were assessed through CT chest. They were tested whether they were single or two-sided, central and occipital performance. Architectural deformation, fibrotic strips, tension bronchiectasis, Broncho vascular bundle deformation, and interlobular septal thickening are all characteristics of pulmonary fibrosis that can be seen on a CT scan. CT was performed in the early stage with a negative PCR at 4 to 5 weeks and 9 to 12 weeks intervals. 2 radiologists, who had an experience of 15 years, separately assessed the CT scan without having the clinical data.

CT severity score is to identify the degree of lung affection. The lung is divided into five lung lobes. Each lobe of affection had a scale of 0-5. 0 shows no participation, 1 show<6 percent participation, 2 shows 5 to 25 percent participation, 3 shows 26 to 50 percent participation, 4 shows 50 to 80 percent participation, and 5 shows >80 percent participation. The total CT score would be achieved by adding all the lobar scores. The score would vary from 0 to 25, where 0 shows no participation and 2 shows the highest participation.[10,11]

All individuals involved in this study gave their consent in written form. The findings of this research were used for scientific purposes only, keeping the confidentiality of data. Due to the limited sample size, results are shown as medians and interquartile ranges, while variables are represented in the form of whole numbers as well as percentages.

RESULTS

This research is a cross-sectional analysis of 85 patients, from whom males were 43 and females were 42. Their age varies from 24 to 76 years old. The average age calculated was 43.2 years. They all were confirmed COVID-19 positive and tested by PCR. As a diagnostic and follow-up procedure, MSCT of the chest was recommended for them. CT was conducted at an early stage. Later, a follow-up CT chest was done which led to negative PCR results. These patients were assessed on their degree of recovery and fibrotic changes. Follow-ups were done at 4 to 6 weeks and 9 to 12 weeks for patients who were having residual lung fibrotic changes or symptoms. (Fig. 1 (a, b, c, d) and Fig. 2 (a, b,c,d)) Table 2

shows a clinical history of patients that were included in our research.

Table 1: Total voltage

Tube Voltage	120 kVp
Current in tube	Standard level - 61 to 120 Low-dose level - 32
Thickness of slice	1.01 millimeter
Reconstruction interval	1.01-3 millimeter

Table 2: Clinical history of patients

Patients n (%)	Disease
63 (74.1)	Dry cough
42 (49.4)	Dyspnea
43 (50.5)	Fever
27 (31.7)	Diarrhea

Figure 1 A male smoker of 50 years who had a dry cough, dyspnea, and fever presented with a positive PCR result for COVID-19. CT severity score was 16/25 at admission. Axial and coronal follow-up. After six weeks after the onset of symptoms, an MSCT chest scan revealed two-sided lung fibrotic complications.

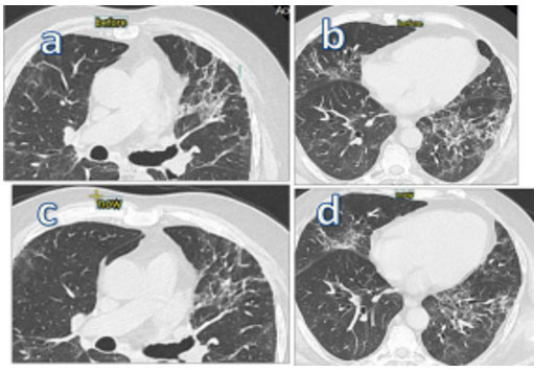

Figure 1: Lung fibrotic changes.

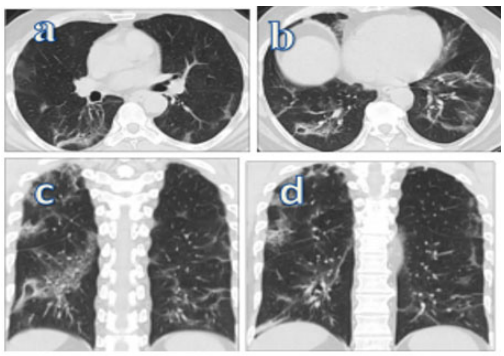

Figure 2: Axial slices MSCT showing persisting fibrotic alterations and ground-glass opacities.

Figure 2: A male of 60 years who had been experiencing fever, severe dyspnea, and cough underwent a first MSCT on the twelfth day of symptoms, which revealed the classic COVID-19, CT severity score was 18/25. Individual presented in the twelfth week with ongoing dyspnea, and an axial slices MSCT revealed persisting fibrotic alterations and ground-glass opacities that had previously regressed.

A total of 30 individuals had a history of cigarette smoking of more than 25 cigarettes per day for more than ten years. They were 37.5 percent. People in the age group 60 to 76 years old had the highest commonness of getting post-COVID-19 pulmonary fibrosis. 15 out of thirty-two patients, which is 46.2 percent, had pulmonary fibrosis. Patients of the age group 45 to 60 years had mild prevalence which is 7 out of 27 patients (25.9 percent). The age group 24 to 45 years had the lowest prevalence, which is 5 out of 25 patients (19.2 percent). Patients who were cigarette smokers had a higher prevalence of post-pulmonary fibrosis than the ones who did not smoke. Out of thirty smoking patients, post-pulmonary fibrosis had occurred in 18 of them. (Fig. 3)

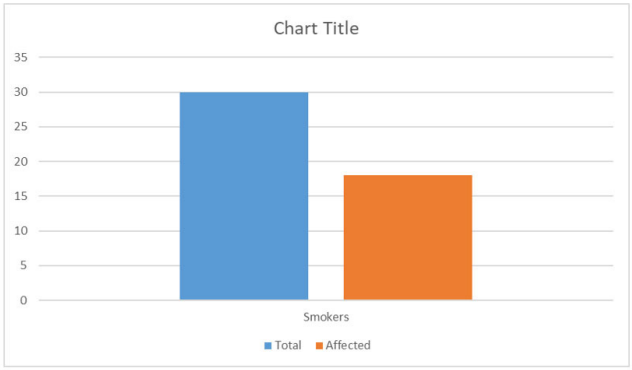

Figure 3: smoking status of study participants having post-pulmonary fibrosis.

When compared to the moderate group of 38 patients, the severe group had 42 patients and showed a greater occurrence of post-COVID-19 pulmonary fibrosis, which was seen in 18 patients (42.8 percent), whereas the mild group had just 7 patients (18.4 percent). (Fig. 4)

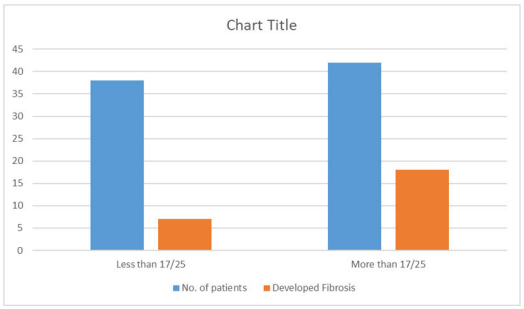

Figure 4: comparison between moderate and severe group of patients regarding post-COVID 19 pulmonary fibrosis.

According to this study, men are around 1.5 times more likely than women to experience post-COVID-19 lung fibrosis. Only 10 of 42 females (23.8 percent) developed post-COVID-19 pulmonary fibrosis, compared to 16 of 43 males (37.2 percent) who underwent the procedure. Further CT imaging findings that showed fibrosis included Broncho vascular bundle distortion, fibrotic strips, tension bronchiectasis, architectural distortion, subpleural curvilinear atelectasis, and interlobular septal thickening.

DISCUSSION

The symptoms of COVID-19 had a wide range from mild upper respiratory indications to severe acute respiratory distress syndrome that leads to lung damage permanently or even mortality.[12] Many cases that were mild and moderate were able to recover completely. Acute respiratory distress syndrome (ARDS) severe cases were rare, and only a tiny percentage of them persisted in being hypoxemic despite receiving effective medical care.[12] Post-COVID-19 pulmonary fibrosis has been declared as a worrisome sequela in surviving patients.[13]

Many theories declared several causes of post-COVID-19 pulmonary fibrosis. However, it is still unknown why some patients get completely recovered from such disease while others develop pulmonary fibrosis.[14]

In the following research, CT chest abnormalities were examined at an early stage, 3 to 4 weeks after clinical manifestations. It was also recorded 10 to 12 weeks after to monitor the progress of post-COVID-19 pulmonary fibrosis. There were many possibilities associated with the occurrence of post-COVID-19 pulmonary fibrosis. Those possibilities include older age, cigarette smoking, male gender, ICU admission, and CT-SS.

It was concluded that age has a higher correlation with post-COVID-19 pulmonary fibrosis. They were 37.5 percent. People in the age group 60 to 76 years old had the highest prevalence of getting post-COVID-19 pulmonary fibrosis. 15 out of 32 patients, which is 46.2 percent, had pulmonary fibrosis. This finding is similar to one of the researchers, Wong et al.[15] He concluded that older people are more likely to get infected with pulmonary fibrosis following MERS. Patients of the age group 45 to 60 years had mild prevalence which is 7 out of 27 patients (25.9 percent). The age group 24 to 45 years had the lowest prevalence, which is 5 out of 25 patients (19.2 percent). According to Das K.M, et al., age and SARS-CoV 2 are correlated with the development of pulmonary fibrosis.[16]

According to this study, men are around 1.5 times more likely than women to experience post-COVID-19 lung fibrosis. Only 10 of 42 females (23.8 percent) developed post-COVID-19 pulmonary fibrosis, compared to 16 of 43 males (37.2 percent) who underwent the procedure. This might be explained by how testosterone affects the transcription of the transmembrane protease, and serine 2 genes. The SARS-Cov-2 spike protein is primed by that encoded protein, which lowers antibody response and encourages the fusion of the virus and host cells.[17]

One more risk factor for pulmonary fibrosis was cigarette smoking. Patients who were cigarette smokers had a higher prevalence of post-pulmonary fibrosis than the ones who did not smoke. Out of 30 smoking patients, post-pulmonary fibrosis had occurred in 18 of them (60 percent). According to Vardavas C.I. et al. people who smoke are 1.4 times more likely to develop symptoms of post-COVID-19 pulmonary fibrosis.[18]

CT severity score is also one of the important risk factors that contribute to the development of post-COVID-19 pulmonary disease. When compared to the moderate group of 38 patients, the severe group had 42 patients and showed a greater incidence of post-COVID-19 pulmonary fibrosis, which was seen in 18 patients (42.8 percent), whereas the mild group had just 7 patients (18.4 percent). This is similar to one of the researchers, Zhou F. et al. He concluded that when a disease's severity increases, it reliably predicts the loss of lung tissue and is linked with high mortality risk.[19] The World Health Organization states that eighty percent of SARS-CoV2 infections are mild, fourteen percent of patients are affected by severe symptoms while six percent of patients will become critically ill.

At this moment, it is unclear how antifibrotic drugs will help prevent and treat post-COVID-19 lung fibrosis. Nevertheless, these drugs are useful for patients who have acute exacerbations of ILD which decreases the damage to pulmonary tissues. It also regresses mortality and morbidity rates in patients who have a high incidence of fibrosis.[20]

There were certain limitations of this research that included a limited number of patients, excluding patients who had a significant history of interstitial lung disease or any significant health situation like hypertension, DM, or autoimmune disease, and a short-term follow-up.

CONCLUSION

Post-COVID-19 pulmonary fibrosis is considered to be the worrisome sequel because it has severe consequences. It causes lung damage permanently. Patients who have a high risk of pulmonary fibrosis should go for early treatment which includes taking antifibrotic drugs. This will decrease the mortality and morbidity rate of the disease.

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Permission

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