Original Research Article

STUDY TO IDENTIFY THE PREVALENCE AND PREDICTIVE FACTORS OF POST COVID LUNG FIBROSIS IN COVID -19

ABSTRACT

BACKGROUND

SARS CoV-2 has affected more than 494 millions of people all over across the globe till date. Most lethal infection of SARS-CoV-2 is highly representative of patients suffering with idiopathic pulmonary fibrosis (IPF)[1]. Interstitial thickening, irregular interface, coarse reticular pattern, and parenchymal bands manifesting in the course of the disease might be predictors of pulmonary fibrosis in these patients[2].

OBJECTIVES AND METHODS

Objective of the study is to identify the prevalence and predictive factors of post covid lung fibrosis in covid-19 patients. The study was conducted in a retrospective manner and included 100 patients in our tertiary care center. HRCT thorax conducted in all patients were evaluated on admission, one month , 3 month and 6 months whereever indicated.

RESULTS

The prevalence of post covid lung fibrosis was 2 % at 6 months , with CT severity score more for elderly male population. In our study we found a significant corelation between clinical severity and post covid fibrosis.

CONCLUSION

From our study, the post COVID lung changes are reversible, with only 2 % developing the post covid lung fibrosis.

KEY WORDS : CLINICAL SEVERITY, POST COVID FIBROSIS, CT SEVERITY SCORE, ARDS

INTRODUCTION

SARS CoV-2 has affected more than 494 millions of people all over across the globe till date. Most lethal infection of SARS-CoV-2 is highly representative of patients suffering with idiopathic pulmonary fibrosis (IPF)[1]. Previous studies inferred that substantial proportion (about 25%) of patients who developed ARDS in the pre-COVID era, irrespective of aetiology, experienced residual and long-term impairment of their pulmonary function, with radiographic evidence of pulmonary fibrosis on computed tomography (CT). Interstitial thickening, irregular interface, coarse reticular pattern, and parenchymal bands manifesting in the course of the disease might be predictors of pulmonary fibrosis in these patients[2]. A

study by Chang et al. in patients with SARS showed that when a second CT scan was repeated 4–6 months after the initial scan in patients with these two viral pneumonias, the parenchymal bands,traction bronchiectasis, and even honeycombing had regressed in significant numbers[3].

The severity of the lung injury and the inflammatory response are known to correlate with the extent of fibroblastic response required to repair the injury[4]. Higher levels of inflammatory markers like CRP, IL-6, LDH etc. during illness might lead to the formation of fibrosis during recovery and were also found to significantly correlate with the risk of pulmonary fibrosis following other coronavirus infections like MERS-CoV infection [5,6] and SARS.

COVID - 19 is a disease caused by SARS CoV – 2, a virus of the coronavirus family. The strain originated in Wuhan, China in November of 2019 and spread across the globe causing the worst pandemic known to mankind and claiming 6,152,898 lives [7]. The transmission of the virus is from human-to-human via respiratory route but alternative routes have been suggested - zoonotic spread [8,9,10].

Symptoms of COVID – 19 show a great diversity, that range from a mild illness to respiratory failure and death [11,12]. Common symptoms are headache, loss of smell and taste, nasal congestion and runny nose, cough, muscle pain, sore throat, fever, diarrhoea and breathlessness [13]. People with the same infection may have different symptoms, and their symptoms may change over time. Three common clusters of symptoms have been identified: one respiratory symptom cluster with cough, sputum, shortness of breath, and fever; a musculoskeletal symptom cluster with muscle and joint pain, headache, and fatigue; a cluster of digestive symptoms with abdominal pain, vomiting, and diarrhoea[17]. In people without prior ear, nose, and throat disorders, loss of taste, combined with loss of smell is associated with COVID-19 and is reported in as many as 88% of cases [14,15,16]

COVID – 19 is a systemic disease and has many sequelae. Of these, one is post-COVID lung fibrosis. Following an initial phase of lung injury causing acute inflammation, repair mechanisms can elicit the restoration of normal pulmonary architecture or they may lead to pulmonary fibrosis with architectural distortion and irreversible lung dysfunction. The nature of the inflammatory response may influence the resident tissue cells and the ensuing inflammatory cells, since the latter additionally exacerbate inflammation by secreting chemokines, cytokines, and growth factors. [18] Many cytokines are involved throughout the wound-healing response, with specific groups of genes activated in different conditions. Interleukin (IL)-4 (IL-4), IL-13, and transforming growth factor-beta (TGF-β) are cytokines that have received attention with regard to various pulmonary fibrotic conditions since each can exhibit pro-fibrotic activity by promoting the recruitment, activation and proliferation of fibroblasts, macrophages, and myofibroblasts.[19] Various biological and radiological markers have been postulated to predict the sequalae of COVID – 19. The biomarkers for acute phase of COVID-19 that predict fibrosis are – CRP, Lymphocyte count, LDH, IFN- gamma, MMP-9, sST2[20,21,22,23]. Those of the follow-up period are – TNF–alpha, IL-17A, IL-17D, VCAM-1, ICAM-1, PIGF, KL-6. [24,25,26]

Chest CT plays a vital role in the diagnosis and follow-up of patients with COVID-19 pneumonia. Xiaoyu Han et.al. in their study concluded that follow-up CT scans within 6 months of disease onset showed fibrotic-like changes in the lung in more than one-third of patients who survived severe COVID-19 pneumonia and also found that patients were older and had more severe disease during the acute phase[27]. MehrdadNabahati et.al. in their study revealed that patients with severe COVID-19 pneumonia, consolidation, older age, acute respiratory distress syndrome, longer hospital stays, tachycardia, non-invasive mechanical ventilation, and higher initial chest CT score in the initial chest CT scan, was associated with increased risk of post-COVID-19 lung fibrosis[28].

Determining the predictive factors for the post-COVID-19 lung fibrosis can possibly help in management of morbid complication through controlling of the risk factors and/or administrating the anti-fibrotic drugs in high-risk cases. In the current study, we aimed to prospectively assess the prevalence, clinical, radiological characteristics like lung fibrotic-like changes as well as to explore their predictive factors, in the patients who survived COVID-19 infection.

METHODOLOGY

Retrospective evaluation of 100 patientsRT- PCR positive for SARS CoV – 2, from the time period of April 2021 to June 2021 and collected their data on development of post-COVID fibrosis, and post-COVID sequelae. The study has been conducted after ethics committee approval. The study centre is Ruby Hall Clinic, Pune, India.

INCLUSION CRITERIA

a. Age between – 20-80 years
b. Male and Female patients.
c. RT-PCR positive disease
d. Rapid antigen positive disease

EXCLUSION CRITERIA

a. Pre-existing ILD
b. Pre-existing lung metastasis.
c. Age greater than 80 years
d. Pre-existing Interstitial Lung abnormalities

METHOD

HRCT thorax of all patients were done in MDCT scanner with 64 channels.The tube voltage used was 120 Kvp, low dose CT-scan of Thorax was taken, and slice thickness were 1.0 mm with a reconstruction interval of 1-3mm. CT images were taken in supine position with full inspiration without a contrast medium. The different CT patterns like ground glass opacities, reticulations, consolidation, cavitation, septal thickening, architectural distortion, traction bronchiectasis, honeycombing were evaluated.Other parameters studied were -

peripheral or central shadows, unilateral or bilateral distribution. The HRCT thorax were done initially at the time of admission, or when patients developed breathlessness and desaturation, at one month, 3 months and 6 months.All the above-mentioned patterns were evaluated on HRCT Thorax.

CT severity score

It is a score for degree of lung affection based on dividing the lung into five lung lobes; each lobe affection was visually scored on a scale of 0–5, with 0 indicating no involvement, 1 indicating less than 5% involvement, 2 indicating 5–25% involvement, 3 indicating 26–49% involvement, 4 indicating 50–75% involvement, and 5 indicating more than 75% involvement. The total CT score was the sum of the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement) [29]

Clinical severity [30]

- Asymptomatic or Presymptomatic Infection: Individuals who test positive for SARS-CoV-2 using a virologic test (a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms that are consistent with COVID-19.
- Mild Illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- Moderate Illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO_2) ≥94% on room air at sea level.
- Severe Illness: Individuals who have SpO_2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%.
- Critical Illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

ETHICAL CONSIDERATIONS

Ethical committee approval has been taken from IEC. The informed consent had been waived off by the ethical committee considering the retrospective case registry based evaluation.

RESULTS

Table 1: Demographic result

Mean age Male Female	44.26 48
GENDER Male Female	26 74
CT severity index Male Female	5.46 7.97
Need of ICU admission	20
Discharged from ICU	9
Prevalence of post COVID fibrosis 3 months	2%

6months	2%

the table shows that means age of males in study is 44.26 and females is 48. Females are more affected. The CT severity index was more in females. 20 patients required ICU admission, and 9 patients among them got discharged from ICU. The prevalence of post covid fibrosis at 3 and 6 months are 2% each.

Table 2 : HRCT features at admission, one month, 3 month, 6 months

CT FEATURES	INITIAL CT	1 MONTH	3 MONTHS CT	6 MONTHS CT
GGO	100	10	4	1
Consolidation	4	3	1	1
Reticulations	3	3	1	2
Septal thickening	3	6	2	2
Traction Bronchiectasis	0	2	2	2
Honey combing	0	0	2	2
Cavity	0	2	2	1

Table 2 : Table 2 shows the HRCT thorax features at admission, one month, 3 month and 6 month where GGO, consolidation, reticulations, septal thickening, traction bronchiectasis, honeycombing and cavity evaluated.

Table 3:Association of clinical severity and death

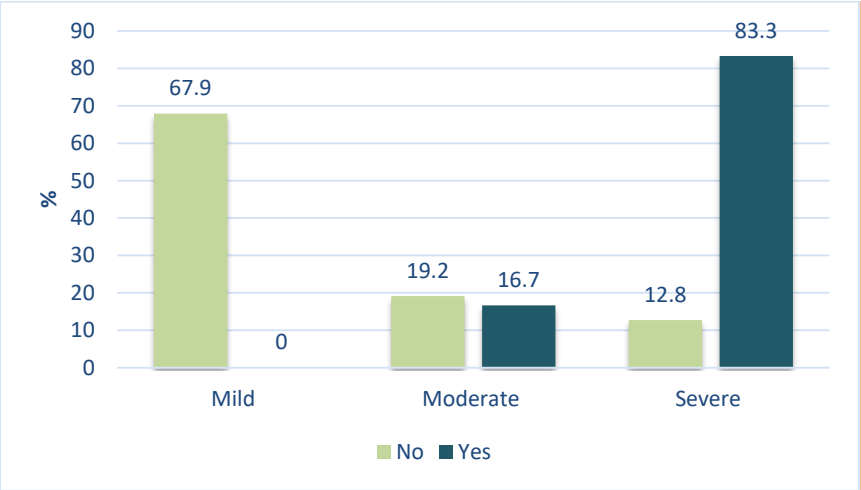
	Mean	**SD**	**t value**	**P value**
Died	12.45	4.03	13.71	<0.001**
Discharged	6.68	4.96		

Table 4: Prevalence of post COVID lung fibrosis

	n	**%**
1 month	6	6
3 month	2	2
6 month	2	2

Table 5: Association of clinical severity and fibrosis at one month

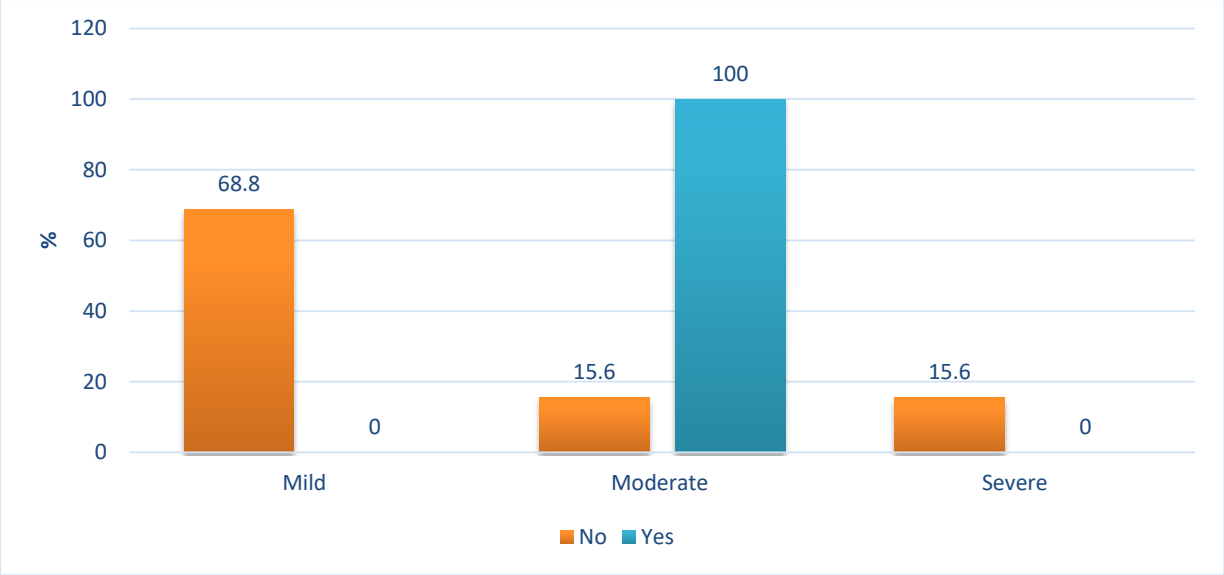
1month	No	Yes	X^2 value	P value
Mild	53(67.9)	0	21.62	<0.001**
Moderate	15(19.2)	1(16.7)		
Severe	10(12.8)	5(83.3)		



Graph 1 : Association of clinical severity and fibrosis at one month

Table 6 : Association of clinical severity and fibrosis at 3 month

3 month	No	Yes	X^2 value	P value
Mild	53(68.8)	0	23.62	<0.001**
Moderate	12(15.6)	2(100)		
Severe	12(15.6)	0		



Graph 2: **Association of clinical severity and fibrosis at 3 month**

Table 7 : Association of clinical severity and fibrosis at 6 month

6 month	**No**	**X^2 value**	**P value**
Mild	53(73.6)	-	-
Moderate	12(16.7)		
Severe	7(9.7)		

Table 8 : Association of CT severity index and Post covid lung fibrosis at one month

1month	**Mean**	**SD**	**P value**
No	5.82	4.09	
Yes	15.83	5.67	<0.001**

Table 9 : Association of CT severity index and Post covid lung fibrosis at 3 month

3 month	Mean	SD	P value
No	6.05	4.58	
Yes	11.0	9.89	<0.001**

DISCUSSION

The mean age of the patients enrolled in our study is 44.(36 for females and 48.27 for males). There were 26 % females and 74% males in our study. 30 % of the patients were from 31-40 years followed by 23 % patients who were 51-60 years.

53 % of the patients in our study were having mild clinical severity where as 20 % were moderate and 27 % belongs to severe clinical severity class.

CT severity index was maximum for 61-70 years followed by 51-60 years and 41-50 years. CT severity index was more for male patients.This is in correlation with study done byAmmarMosa Al-Mosawe et al[31] which showed strong positive correlation between higher CT severity score and male gender. In this study, there was significant correlation of CT severity score and increasing age. Zhichao Feng et al [32] in 2020 also identified positive correlation of CT severity score with increasing age.

CT severity index is maximum for age > 60 years in a study conducted by Ammarmosa Al-mosawe et al[31], Liu et al[33]which is correlating with our study.This relation can be mostly attributed to the aging of lung in older age group and presence of co-morbidities. [31]

The initial CT scan was done within 10 days of onset of symptoms or when patient developed breathlessness. All patients had ground glass opacities in their first scan, where as 4 % patients had consolidation. This study enrolled patients during the second wave of COVID-19 in India where hospitalisation was more for patients with co-morbidities, and HRCT showing pneumonia.In the study by Ammar Mosa Al-Mosawe et al [(31)]ground glass opacities were the most common encountered pattern of pulmonary changes and were seen in (79%). Zhichao Feng et al [(34)]reported that initial CT severity score is an independent predictor of short term disease progression. The study conducted by Omar et al[(35)] and Adnan et al[(36)] also predicts that ground glass opacities were the most common radiological pattern in COVID-19 pneumonia.

The CT scan done at one month was showing ground glass opacities in 10 % patients, septal thickening in 6 % patients , consolidation and reticulations in 3 % patients each. The CT scan after 3 months showed ground glass opacities in 4 % patients, where as 2 % patients had septal thickening and traction bronchiectasis (figure 1) and 1 % patients had either reticulations or consolidation. 2 % patients at 6 months had septal thickening, reticulations, traction bronchiectasis and honeycombing. Most of the patients showed significant resolution at 3 months post covid (figure 2).

The prevalence of post COVID fibrosis after 3 and 6 months is 2 % each. 20 % of the patients were requiring intensive care, and 11 % patients died due to COVID or post COVID sequelae. The mean duration of stay in hospital were 10.22 days. This is similar to many studies that reported mean duration of hospital stay between 8 to 14 days.

There was significant correlation between clinical severity and death, fibrosis at 3 and 6 months. GhufranAref Saeed et al [(37)] in their study concluded that the oxygen requirements and length of hospital stay were increasing with the increase in scan severity. Mehrdad Nabahati et al [(38)]observed Post-COVID19 lung fibrosis in about half of the survivors in their study. They also found that patients with severe COVID-19 pneumonia were at a higher risk of pulmonary fibrosis. Moreover, consolidation, as well as a higher CSS, in the initial chest CT scan, was associated with increased risk of post-COVID-19 lung fibrosis.

There was significant correlation between CT severity and fibrosis Jia-Ni Zou et al [(39)] reported that ground-glass opacities, linear opacities, interlobular septal thickening, reticulation, honeycombing, bronchiectasis and the extent of the affected area were significantly improved 30, 60 and 90 days after discharge compared with at discharge. The more severe the clinical severity of COVID-19, the more severe the residual pulmonary fibrosis was; however, in most patients, pulmonary fibrosis improved or even resolved within 90 days after discharge.

Rasha Mostafa Mohamed Ali et al [(40)] noted that although there was no specific cause for post-COVID19 lung fibrosis, there were some predicting factors such as old age, cigarette smoking, high CT severity score, and long-term mechanical ventilation.

Mehrdad Nabahati et.al. [(38)] observed Post-COVID-19 lung fibrosis in about half of the survivors. Also, patients with severe COVID-19 pneumonia were at a higher risk of

pulmonary fibrosis. Moreover, consolidation, as well as a higher CSS, in the initial chest CT scan, was associated with increased risk of post-COVID-19 lung fibrosis. In their study, repeat CT was done after 6 months and in 61% people fibrotic changes remained unchanged. This is in contrast to our study.

CONCLUSION

From our study, the post COVID lung changes are reversible, with only 2 % developing the post covid lung fibrosis.

LIMITATIONS

The main limitations are the study being retrospective, there is bias in timing of HRCT thorax (in some patients HRCT was done at the time of admission vs HRCT thorax done at first episode of desaturation or breathlessness)

The study being conducted in a single tertiary centre which includes patients with more of moderate to severe lung involvement.

DECLARATIONS

1) ETHICS APPROVAL AND CONSENT OF PARTICIPATION

Ethical committe approval is taken before conducting the study.

2) CONSENT FOR PARTICIPATION

The need for consent for participation in the study has been waived off by the ethical committe as the study is retrospective.

3) DATA AND MATERIAL AVAILABILITY

The data and material for the case report has been obtained from hospital records.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFERENCES

1. Brompton R, Foundation HN, Md G, Phd J, Jenkins G, George PM, et al. Pulmonary fibrosis and COVID-19: the potential role for antifibrotic therapy [Internet]. Thelancet.com. 2019 [cited 2022 Apr 6]. Available from: https://www.thelancet.com/pdfs/journals/lanres/PIIS2213-2600(20)30225-3.pdf
2. Udwadia ZF, Koul PA, Richeldi L. Post-COVID lung fibrosis: The tsunami that will follow the earthquake. Lung India [Internet]. 2021 [cited 2022 Apr 6];38(Supplement):S41–7. Available from: https://journals.lww.com/lungindia/Fulltext/2021/00001/Post_COVID_lung_fibrosis__The_tsunami_that_will.8.aspx?WT.mc_id=HPxADx20100319xMP
3. Chang Y-C, Yu C-J, Chang S-C, Galvin JR, Liu H-M, Hsiao C-H, et al. Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome: evaluation with thin-section CT. Radiology [Internet]. 2005;236(3):1067–75. Available from: http://dx.doi.org/10.1148/radiol.2363040958
4. Wallace WA, Fitch PM, Simpson AJ, Howie SE. Inflammation-associated remodelling and fibrosis in the lung A process and an end point. Int J ExpPathol 2007;88:103-10
5. Yu M, Liu Y, Xu D, Zhang R, Lan L, Xu H. Prediction of the development of pulmonary fibrosis using serial thin-section CT and clinical features in patients discharged after treatment for COVID-19 pneumonia. Korean J Radiol 2020;21:746-55
6. Das K, Lee E, Singh R, Enani M, Al Dossari K, van Gorkom K, et al. Follow-up chest radiographic findings in patients with MERS-CoV after recovery. Indian J RadiolImag 2017;27:342
7. Ritchie, Hannah; Mathieu, Edouard; Rodés-Guirao, Lucas; Appel, Cameron; Giattino, Charlie; Ortiz-Ospina, Esteban; Hasell, Joe; Macdonald, Bobbie; Beltekian, Diana; Dattani, Saloni; Roser, Max (2020–2021). "Coronavirus Pandemic (COVID-19)". Our World in Data.
8. Hu B, Guo H, Zhou P, Shi ZL (March 2021). "Characteristics of SARS-CoV-2 and COVID-19". Nature Reviews. Microbiology. 19 (3): 141–154. doi:10.1038/s41579-020-00459-7
9. Multiple sources:
   "The COVID-19 coronavirus epidemic has a natural origin, scientists say – Scripps Research's analysis of public genome sequence data from SARS-CoV-2 and related viruses found no evidence that the virus was made in a laboratory or otherwise engineered". EurekAlert!. Scripps Research Institute. 17 March 2020. Retrieved 15 April 2020.
   Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF (April 2020). "The proximal origin of SARS-CoV-2". Nature Medicine. 26 (4): 450–452. doi:10.1038/s41591-020-0820-9. PMC 7095063. PMID 32284615.
   Latinne A, Hu B, Olival KJ, Zhu G, Zhang L, Li H, et al. (August 2020). "Origin and cross-species transmission of bat coronaviruses in China". Nature

Communications. 11 (1): 4235. Bibcode:2020NatCo..11.4235L. doi:10.1038/s41467-020-17687-3. PMC 7447761. PMID 32843626.
Fox M (7 July 2021). "Coronavirus almost certainly came from an animal, not a lab leak, top scientists argue". CNN.Retrieved 9 July 2021.
"Market in China's Wuhan likely origin of COVID-19 outbreak - study". Reuters. 19 November 2021. Retrieved 19 November 2021
10. To KK, Sridhar S, Chiu KH, Hung DL, Li X, Hung IF, et al. (March 2021). "Lessons learned 1 year after SARS-CoV-2 emergence leading to COVID-19 pandemic". Emerging Microbes & Infections. 10 (1): 507–535
11. "Symptoms of Coronavirus". U.S. Centers for Disease Control and Prevention (CDC). 22 February 2021. Archived from the original on 4 March 2021.Retrieved 4 March 2021.

12. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, Wade RG (23 June 2020). "The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries"

13. "Coronavirus Disease 2019 (COVID-19) – Symptoms". Centers for Disease Control and Prevention. 22 February 2021. Retrieved 19 January 2022.

14. Paderno A, Mattavelli D, Rampinelli V, Grammatica A, Raffetti E, Tomasoni M, et al. (December 2020). "Olfactory and Gustatory Outcomes in COVID-19: A Prospective Evaluation in Nonhospitalized Subjects"

15. Chabot AB, Huntwork MP (September 2021). "Turmeric as a Possible Treatment for COVID-19-Induced Anosmia and Ageusia"

16. Niazkar HR, Zibaee B, Nasimi A, Bahri N (July 2020). "The neurological manifestations of COVID-19: a review article".

17. "COVID-19/csse_COVID_19_data/csse_COVID_19_time_series at master · CSSEGISandData/COVID-19"

18.Chambers RC. Role of coagulation cascade proteases in lung repair and fibrosis.European Respiratory Journal. 2003 Sep 20;22(44 suppl):33s-5s.

19. Wilson MS, Wynn TA. Pulmonary fibrosis: pathogenesis, etiology and regulation. Mucosal Immunol 2: 103–121. Lung toxicity of PHMG-P. 2009.

20. Ragusa R, Basta G, Del Turco S, Caselli C. A possible role for ST2 as prognostic biomarker for COVID-19.Vascular Pharmacology. 2021 Jun 1;138:106857.

21. Hu ZJ, Xu J, Yin JM, Li L, Hou W, Zhang LL, Zhou Z, Yu YZ, Li HJ, Feng YM, Jin RH. Lower circulating interferon-gamma is a risk factor for lung fibrosis in COVID-19 patients. Frontiers in immunology. 2020 Sep 29;11:2348.

22. Huang W, Wu Q, Chen Z, Xiong Z, Wang K, Tian J, Zhang S. The potential indicators for pulmonary fibrosis in survivors of severe COVID-19.Journal of Infection. 2021 Feb 1;82(2):e5-7

23. Yu M, Liu Y, Xu D, Zhang R, Lan L, Xu H. Prediction of the development of pulmonary fibrosis using serial thin-section CT and clinical features in patients discharged after treatment for COVID-19 pneumonia. Korean journal of radiology. 2020 Jun;21(6):746.

24. Zhou M, Yin Z, Xu J, Wang S, Liao T, Wang K, Li Y, Yang F, Wang Z, Yang G, Zhang J. Inflammatory profiles and clinical features of COVID-19 survivors three months after discharge in Wuhan, China. The Journal of Infectious Diseases.2021 Apr 4.

25. Ishikawa N, Hattori N, Yokoyama A, Kohno N. Utility of KL-6/MUC1 in the clinical management of interstitial lung diseases. Respiratory investigation. 2012 Mar 1;50(1):3-13.

26. Kuwana M, Shirai Y, Takeuchi T. Elevated serum Krebs von den Lungen-6 in early disease predicts subsequent deterioration of pulmonary function in patients with systemic sclerosis and interstitial lung disease. The Journal of Rheumatology. 2016 Oct 1;43(10):1825-31.

27. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, et al. Six-month follow-up chest CT findings after severe COVID-19 pneumonia. Radiology [Internet]. 2021;299(1):E177–86. Available from: http://dx.doi.org/10.1148/radiol.2021203153

28. Nabahati M, Ebrahimpour S, KhaleghnejadTabari R, Mehraeen R. Post-COVID-19 pulmonary fibrosis and its predictive factors: a prospective study. Egypt J RadiolNucl Med [Internet]. 2021;52(1). Available from: http://dx.doi.org/10.1186/s43055-021-00632-9

29. Mansour MG, Abdelrahman AS, Abdeldayem EH. Correlation between CT chest severity score (CT-SS) and ABO blood group system in Egyptian patients with COVID-19. Egypt J Radiol Nucl Med [Internet]. 2021;52(1). Available from: http://dx.doi.org/10.1186/s43055-021-00571-5

30.) Information on COVID-19 treatment, prevention and research [Internet]. COVID-19 Treatment Guidelines. [cited 2022 Apr 30]. Available from: https://www.covid19treatmentguidelines.nih.gov/

31. Al-Mosawe, A. M., Abdulwahid, H. M., & Fayadh, N. A. H. (2021). Spectrum of CT appearance and CT severity index of COVID-19 pulmonary infection in correlation with age, sex, and PCR test: an Iraqi experience. The Egyptian Journal of Radiology and Nuclear Medicine, 52(1). https://doi.org/10.1186/s43055-021-00422-3

32. Feng Z, Yu Q, Yao S, Luo L, Zhou W, Mao X, et al. Early prediction of disease progression in COVID-19 pneumonia patients with chest CT and clinical characteristics. Nat Commun [Internet]. 2020;11(1):4968. Available from: http://dx.doi.org/10.1038/s41467-020-18786-x

33. Liu, K., Chen, Y., Lin, R., & Han, K. (2020). Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *The Journal of Infection, 80*(6), e14–e18. https://doi.org/10.1016/j.jinf.2020.03.005

34. Feng Z, Yu Q, Yao S, Luo L, Zhou W, Mao X, et al. Early prediction of disease progression in COVID-19 pneumonia patients with chest CT and clinical characteristics. Nat Commun [Internet]. 2020;11(1):4968. Available from: http://dx.doi.org/10.1038/s41467-020-18786-x

35. Omar, S., Motawea, A. M., & Yasin, R. (2020). High-resolution CT features of COVID-19 pneumonia in confirmed cases. *The Egyptian Journal of Radiology and Nuclear Medicine*, *51*(1). https://doi.org/10.1186/s43055-020-00236-9

36. Adnan, A., Baghdad Teaching Hospital - Medical City Complex - Baghdad - Iraq., Joori, S., H. Hammoodi, Z., A.Ghayad, H., Ibrahim, A., Institue, X.-R., Ghazi Alhariri hospital for specialised surgeries, Institue, X.-R., & Iraqi center for heart diseases. (2020). Spectrum of Chest Computed Tomography findings of Novel Coronavirus disease 2019 in Medical City in Baghdad, a case series. *Journal of the Faculty of Medicine, Baghdad*, *62*(1,2), 6–12. https://doi.org/10.32007/jfacmedbagdad.621.21744

37. Saeed GA, Helali AAA, Shah A, Almazrouei S, Ahmed LA. Chest CT performance and features of COVID-19 in the region of Abu Dhabi, UAE: a single institute study. Chin J Acad Radiol [Internet]. 2021;4(4):248–56. Available from: http://dx.doi.org/10.1007/s42058-021-00075-1

38. Nabahati M, Ebrahimpour S, Khaleghnejad Tabari R, Mehraeen R. Post-COVID-19 pulmonary fibrosis and its predictive factors: a prospective study. Egypt J Radiol Nucl Med [Internet]. 2021;52(1). Available from: http://dx.doi.org/10.1186/s43055-021-00632-9

39. Zou J-N, Sun L, Wang B-R, Zou Y, Xu S, Ding Y-J, et al. The characteristics and evolution of pulmonary fibrosis in COVID-19 patients as assessed by AI-assisted chest HRCT. PLoS One [Internet]. 2021;16(3):e0248957. Available from: http://dx.doi.org/10.1371/journal.pone.0248957

40. Ali RMM, Ghonimy MBI. Post-COVID-19 pneumonia lung fibrosis: a worrisome sequelae in surviving patients. Egypt J Radiol Nucl Med [Internet]. 2021;52(1). Available from: http://dx.doi.org/10.1186/s43055-021-00484-3

Chart 1 : Association of CT severity index and Post covid lung fibrosis at 3 month

3 month	**Mean**	**SD**	**P value**
NO	6.05	4.58	<0.001
YES	11.0	9.89	

Chart 1 : chart shows the significant association of CT severity index and post covid lung fibrosis at 3 months with a p value of < 0.001.

FIGURE LEGENDS

FIGURE 1) The CT thorax of patient showing predominant ground glass opacities at the admision, predominant seotal thickening and reticulations at one month post covid, with septal thickening and traction bronchiectasis at 3 months post covid.

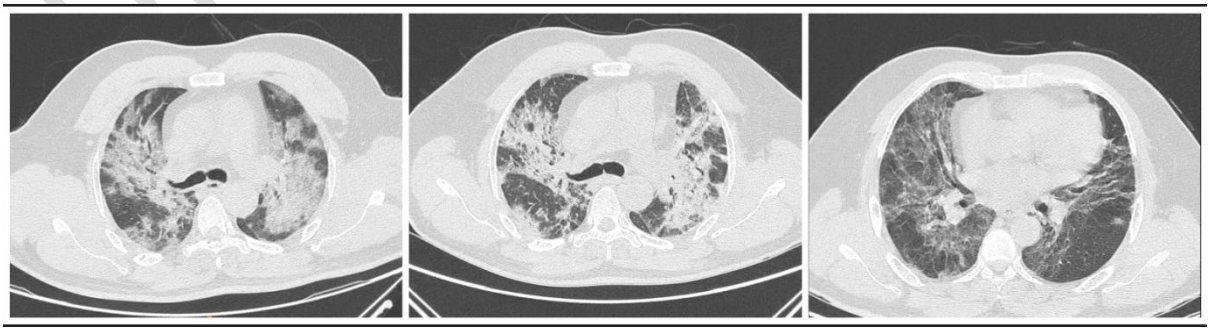


FIGURE 2) The CT thorax of the patient showing predominant ground glass opacities at the admision, with total resolution at 3 months post covid.