



## Frequency and presentation of pulmonary fibrosis in covid19

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### ABSTRACT

**Introduction:** COVID19 Is a viral infection that appear in Wuhan city, China in December 2019 as severe pneumonia, that soon became a global and declared by WHO as pandemic in March 2020, COVID caused by a new strain of corona virus therefore it took the name( novel ) nCOVID19. The disease mainly spread by droplet but other mode of transmission are reported. COVID19 usually presented as upper respiratory tract infection that usually resolve spontaneously, but severe disease that involve the lower respiratory tract and other extrapulmonary tissues and systems may occur and this result in many complications that increase mortality. Pulmonary complications are more common and pulmonary fibrosis is the most disabling complication that occur.

Later the term post COVID syndrome or long term COVID appear and it indicate long term COVID sequences such as fatigability, depression, breathlessness on exertion or even at rest that may long term oxygen support. All theses post COVID symptoms and problems most likely secondary to pulmonary fibrosis, so this study discuss the underline causes of pulmonary fibrosis in COVID19 patients, its frequency and clinical, laboratories and radiological presentation.

**Objectives:** This study aim to know the frequency and presentation of pulmonary fibrosis in COVID9. **Methodology:** This is prospective, descriptive, hospital based study, done in Port Sudan COVID isolation centre, Port Sudan, Sudan, from June 2021 to September 2021.

**Result:** 138 COVID19 PCR positive patients were enrolled in this study, 26 (18.8%) of them developed pulmonary fibrosis, from those who developed pulmonary fibrosis 53.8% were male and 46.2% female, 46.2% had comorbidity, inflammatory markers that detected ( C-reactive protein, serum ferritin, lactate dehydrogenase and d. dimer polymerase) were elevated in all patients who developed pulmonary fibrosis, all those patient also has leucocytosis and lymphopenia. Staph aureus, pseudomonas, mychoplasma and citrobacter ferundii were isolated from patients or equipments.

Ground- glass appearance was seen in HRCT chest of all 26 patients (100%) and this was diagnostic criteria, 5 patient(19.2%) showed consolidation, 1 patient (3.8%) had radiological feature of traction bronchiectasis, 1 patient (3.8%) showed reticulonodular infiltration and other 1 patient (3.8%) showed interlobular thickening.

**Conclusion:** Pulmonary fibrosis occur in about one fifth of COVID19 patients and it result in all COVID19 sequences that appear as post COVID syndrome. Pulmonary fibrosis most probably occur due to cytokine storm that cause idiopathic pulmonary pneumonitis, but other causes such as cryptogenic organizing pneumonia, ARDS, and hypersensitivity pneumonitis may precipitate pulmonary fibrosis in COVID19.

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### INTRODUCTION

Corona viruses are single- stranded, enveloped RNA viruses that have spike which form crown like cap that give it the name corona, this virus don't grow well in cell culture therefore it is difficult to be studied. Corona virus mainly affect the upper respiratory tract but it may affect the lower respiratory tract, gastrointestinal tract and other system and tissue.

In 2002 corona virus cause severe acute respiratory syndrome (SARS), that declared by WHO in March 2003 as epidemic

which extend up to 2004. Again in 2012 corona virus caused middle east respiratory syndrome (MERS). In December 2019 in Wuhan city, China a new strain of corona virus cause severe pneumonia like disease that soon affect many countries and in March 2020 WHO declared the disease as pandemic and take the name n COVID19 (1).

COVID19 mainly spread by droplet but other mode of transmission are reported and it presented early as upper respiratory tract infection showed symptoms like fever, headache, sore throat, cough, shortness of breath and chest pain, but soon its presentation showed different picture and it presented with extrapulmonary manifestation such GIT symptoms and neurological symptoms. In most cases COVID19 has begun course usually mild to moderate that resolve spontaneously or with minimum supportive drugs such

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as paracetamol and vitamins, but severe disease may occur mainly in elder and those with comorbidities and lead to many complication such as interstitial lung disease, ARDS, liver impairment, and kidney injury. Some COVID sequences and complication remain for long time and this known as post COVID syndrome or long COVID(2), the most serious post COVID problem is pulmonary fibrosis which is may cause all post COVID problems such as exertional dyspnea, progressive dyspnea, fatigability, depression and arrhythmia and its and cardiac vascular complication.

Since it appear in December 2019 till August 2021 COVID affect about 206 million and it kill more than two million throughout the world (2), in Sudan first case was registered in March 2020(3) and by August 2021 total of 37564 cases was registered in Sudan 1893 of these cases was registered in Red Sea state, eastern Sudan – area of study-(4). In June 2021-period of study- 154 COVID PCR positive cases was admitted to Port Sudan COVID isolation center in Red Sea state, from them 16 patient died(5). In this center diagnosis of COVID depend on PCR sample but pulmonary complications detected radiologically by high resolution computed tomography (HRCT) or chest ultrasound. Although many management protocol are established but still COVID19 patients should be manage individually.

**Objectives**

This study aim to detect the frequency of pulmonary fibrosis among COVID19 patients and to know its clinical, laboratories, and radiological presentation in Port Sudan, Red Sea state, eastern Sudan.

**METHODOLOGY**

This is a prospective, descriptive, hospital based study, that done in Port Sudan COVID isolation center. From June 2021 to September 2021, in which 138 COVID PCR positive patients who was admitted to Port Sudan COVID isolation center. Those patients were followed from June 2021 to September 2021 for clinical and/ or radiological features of pulmonary fibrosis. Questionnaire that contain age, sex, symptoms of cough, breathlessness, chest pain, fever, headache and fatigability and comorbidity was submitted. Clinical examination and chest high resolution computed tomography was done for all patient. Then laboratory investigation of complete blood picture, D. dimer polymerase and inflammatory markers (C- reactive protein, lactate dehydrogenase and serum ferritin). Blood and sputum culture was taken for those who need mechanical ventilation beside samples from ventilator accessories and water. Then all data analysed.

**RESULT**

138 patient were enrolled in this study, 26 (18.8%) developed pulmonary fibrosis, 14 (53.8%) male and 12 (46.2%) female, their age between 22 years to 76 years, from those 6 (32.1%) was need mechanical ventilation support. 12 patients (46.2%) have comorbidities, 6 (23.1) have both diabetes and hypertension, 4 patients (15.4%) are diabetic but not hypertensive, one patient (3.8%) had ischemic heart disease and heart block and other one patient(3.8%) with morbid obesity.

22 patients (84.6%) presented with dry cough, 18 patients (69%) with exertional dyspnea and 3 patient (11.5%) had

breathlessness at rest, 5 (19.2%) patient with chest pain, and 7 patients (26.9%) showed other different non respiratory symptoms as palpitation, fatigue, dizziness and headache. LDH and D. dimer were elevated in all patients (100%), serum ferritin elevated in 22 patients (84.6%), all patient showed leucocytosis with neutrophilia and lymphopenia. Culture isolate pseudomonas from one patient (3.8%), and mycoplasma from one patient(3.8%), s.aureus isolated from ventilator circuit and citrobacterferundii was isolated from ventilator humidified water of one patient.

In HRCT chest ground glass appearance appear in all patient (100%) mainly pleural based in both lower lobe, but 3 patient showed bilateral diffuse ground glass appearance, 5 patients (19.2%) have consolidation, one patient (3.8%) showed interlobular thickening, other one (3.8%) showed bronchiectatic changes and one patient (3.8%) showed bilateral reticulonodular infiltration.

No	Sample	Organism Isolated	H <sub>2</sub> O <sub>2</sub>	Alcohol+H <sub>2</sub> O <sub>2</sub>
1	Blood Culture and sensitivity	No. growth after 7 days		
2	Hand strap Water from respiratory instrument	S. aureus	Conc.	70:30
3		Citrobacterferundii	Conc.	40:60

No	Sample	Organism Isolated	Solution
1	Water from respiratory instrument	S. aureus	Conc.
2	Cartridge	Pseudomonas spp	Conc.

Figure 1 Different culture

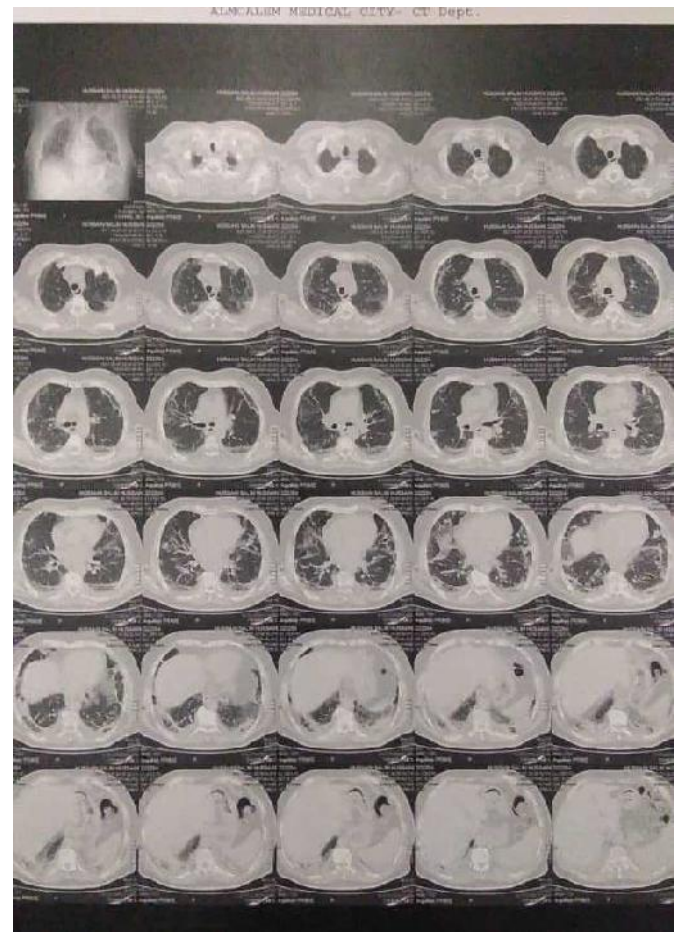


Figure 2 CT

## DISCUSSION

Pulmonary fibrosis which is the end result of multiplicity of pathological process, from infection to autoimmune (6) may occur as pulmonary complication in COVID19 and when it happened it explain most of COVID complication even that known as post COVID syndrome or long term COVID disease as hypoxia that occur secondary to pulmonary fibrosis result in fatigability, muscle cramps, breathlessness, anxiety and depression, hypoxia also may cause arrhythmia that may lead to heart failure and thromboembolic diseases, the later may occur directly from hypoxia and in long term pulmonary may cause hypoxic pulmonary hypertension, so most probably post COVID syndrome is not a separate disorder but these are consequences of pulmonary fibrosis.

In this study pulmonary fibrosis occur in 18.8% of patients of COVID19, less than 50% of them have comorbidity which is mean that pulmonary fibrosis in COVID occur in previously healthy individual as it occur in those with comorbidity, and elevation of inflammatory markers (CPR, LDH, serum ferritin and neutrophil) in all patient who developed pulmonary fibrosis support the probability that cytokine storm is the main cause of pulmonary fibrosis in COVID19(7) and this give the possibility of idiopathic pulmonary fibrosis as common cause of pulmonary fibrosis in COVID19 as despite that the cause of idiopathic pulmonary fibrosis is unknown, it may be defensive reaction to deal with microorganism that initiate uncontrolled inflammatory reaction(6), in addition prescience of lymphopenia and neutrophilia which are feature of early phase of pulmonary fibrosis in IPF also support the probability of IPF as cause of pulmonary fibrosis(6), in same time the distribution of ground – glass appearance in the lower lobe as pleural based also support the possibility of IPF as cause of pulmonary fibrosis(8). Although usual interstitial pneumonitis (UIP), lymphoid interstitial pneumonitis (LIP) and desquamated interstitial pneumonitis may occur in COVID19, cryptogenic organizing pneumonia (COP) being the most common as it occur as complication of virus itself in addition to cytokine storm.

ARDS is known complication of COVID 19(9) and it may occur early due to increase vascular permeability or late secondary to cytokine storm which plays role in all stage of ARDS as interleukin has role in vascular remodeling, fibroblast chemotaxis, and fibroblast proliferation, and through the latter ARDS may cause pulmonary fibrosis(6). Presence of neutrophilia beside the radiological features of consolidation and reticulonodular shadows raise the possibility of pneumonia and this beside isolation of mycoplasma make mycoplasma pneumonia other cause of fibrosis in COVID19 as pulmonary fibrosis is known complication of mycoplasma pneumonia(6), in addition bronchiolitis proliferation may complicate mycoplasma pneumonia and cause fibrosis that partially or completely resolve. *Citrobacter ferundii* that isolated from ventilator may trigger hypersensitivity pneumonitis which may cause pulmonary fibrosis(10).

## CONCLUSION

Pulmonary fibrosis occur in significant percentage in COVID19 patient and it result in hypoxia and its consequences of fatigability, disabling dyspnea, arrhythmia and its cardiac and vascular complications. These post fibrotic problem explain all features that known as post COVID syndrome or long term COVID disease.

Although cytokine storm is the corner stone of pulmonary fibrosis in COVID18, many other conditions may cause pulmonary fibrosis in COVID19, these are cryptogenic organizing pneumonia (COP), ARDS, mycoplasma pneumonia and hypersensitivity pneumonitis. Pulmonary fibrosis in COVID19 occur in both those of comorbidity and previously healthy lung.

Hence all features of post COVID19 syndrome may be sequences of hypoxia that occur due to pulmonary fibrosis so suitable intervention to treat all risk factors for pulmonary fibrosis should be taken to decrease these post COVID 19 sequences

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