Short Communication

An updated awareness on Covid-19 and Respiratory System Disorders

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Learning Objectives: Effects of Covid-19 on the respiratory system, in terms of pathophysiology, symptomatology, risk factors outcome and management options.

Introduction:

COVID-19 (SARS-CoV-2), has been a severe multifocal disease. The burden of **acute infection** has resulted in the form of acute hypoxemic respiratory failure, involving parenchymal and vascular lung disease. A piece of growing evidence has shown **a chronic form** of lung disease which has resulted in chronic fibrotic lung disease. Different treatment modalities and management protocols have been tried with debatable evidence and outcome.

Pathophysiology:

The ACE2 receptor is expressed in type 2 alveolar epithelial cells in the lungs, heart, kidney, and gut. However, the lungs are particularly the prime viral target, because of their large surface area and because alveolar epithelial type 2 cells act as a reservoir for virus replication. It induces an inflammatory response which is one of the mechanisms of lung injury. **(**1,2**)**

Usually, a tight connection exists between the alveolar epithelium (type-1 cells) and the capillary. COVID-19 involves AT2 cells, causes apoptosis and load the alveolus. Also, there is evidence for vascular microthrombi, which may cause vascular occlusion.

Cytokine storm syndrome (CSS), is a hyperimmune response, secondary to a heavy viral load. Macrophage activation syndrome (MAS) and secondary Hemophagocytic Lymphohistiocytosis (sHLH) are two clinically similar CSSs mechanisms. These result from excess proinflammatory and inadequate inflammatory stimuli. **(**1,2,3**)**

A major issue with COVID-19 is with gas exchange in the alveolus. Physiological mechanisms vary, depending on the severity of the lung involvement. In mild to moderate forms, there is only V/Q mismatch resulting in hypoxemic respiratory failure, responsive to oxygen therapy. As the disease progresses, the V/Q mismatch gets worse and develops shunt physiology, which does not respond to high oxygen therapy. It results in severe respiratory failure with PaO2/FiO2 reaching less than 100. At this point, the ARDS picture prevails and is managed as such.

These may develop and progress into a variety of clinical conditions:

- Severe pneumonia
- Acute respiratory distress syndrome (ARDS)
- Secondary bacterial infections with or without sepsis
- Vaso occlusive disease.

Effect of Covid-19 on chronic lung conditions:

Patients with chronic lung diseases are at an increased risk of severe respiratory illness.

- The CDC has identified patients with moderate-to-severe asthma, who are at a higher risk for severe respiratory illness when infected with SARS-CoV-2. Patients with chronic obstructive pulmonary disease (COPD) have high levels of ACE2, which increases the risk of severe lung disease. A meta-analysis of seven studies with 1,592 patients, showed up to five times increased severity with COPD.
- The prevalence of chronic respiratory diseases and diabetes were studied in COVID-19 patients in China and was compared with data available for SARS from China, Canada, and Hong Kong. Chronic respiratory diseases are surprisingly underrepresented. However, there might be a higher number of patients with undiagnosed respiratory illnesses.
- A meta-analysis of eight studies, with approximately 46,000 patients, showed the most common comorbidities in severe COVID-19 disease were diabetes and hypertension, followed by cardiac disease and chronic respiratory disease. Further studies are needed to investigate the actual risk

of disease acquisition, severity, and management in these vulnerable populations.

- Currently, there is no evidence to suggest that the utilization of inhaled corticosteroids worsens the risk of COVID-19 acquisition. Hence, the recommendation is to continue the utilization of long-term inhaler therapy for patients with asthma or COPD.

Post Covid-19 Lung fibrosis: "Covid Lung"

Risk factors: **(**4**)**

- Older age
- Severity: It is the critical category as mentioned above, that has the worst prognosis and the highest chance of developing lung fibrosis.
- ICU Length of stay and need for mechanical ventilation- ICU care is required in 5-12%.
  The risk of VALI-induced lung injury should be minimized by using Lung protective strategy.
- Smokers. **(**5**)**
- Chronic Alcoholism

Management of Acute form

- Although no randomized control trial exists, the target is to support hypoxemia up to a level of 88-92%. Several options for oxygen delivery exist. These can include:
- A simple nasal cannula, which can provide up to 6 L or approximately 44% FiO2.
- Further oxygen demand can be met by a nonrebreather mask, which can increase flow to 6-15 L while providing 100% FiO2.
- Currently, the utilization of noninvasive ventilation in COVID-19 patients is under intense debate. A high-flow nasal cannula (HFNC) and noninvasive positive-pressure ventilation (NIPPV) have become standards of care in the ICU for patients with hypoxemic respiratory failure, and have been shown to help prevent endotracheal intubation.
- All intubations should be performed, in negative-pressure rooms.
- Minimize bag-mask ventilation

- All intubations should be performed by an experienced practitioner using rapid sequence intubation to maximize first-pass intubation.
  The balloon should be inflated immediately after intubation to stop further viral spread.

- All severe forms of ventilated covid pneumonia, with ARDS, should be managed by ARDS protocol which includes low tidal volume and higher ventilator rate strategy to minimize the risk of volutrauma.

ECMO: The most important series of 1035 patients from the Extracorporeal Life Support Organization (ELSO) registry, has shown that patients undergoing ECMO support had an in-hospital 90-day death rate of 37.4%.

ECMO is indicated for patients with a PaO2/FiO2 ratio of less than 60 mm Hg for more than 6 hours or less than 50 mm Hg for more than 3 hours. ECMO support should be started, within 7 days of severe ARDS.

Management of Chronic form – Lung fibrosis in Covid-19

Antifibrotic agents like pirfenidone and Nintedanib and azithromycin are currently being used for post covid pulmonary fibrosis, in addition to antivirals. **(**6,7,8,9**)** High-dose steroids are continually being used to treat CSS which may benefit long-term pulmonary complications.
Recently, Ivermectin has been used, prophylactically or therapeutically, in many regions to explore its benefits. However, apart from some anecdotal reports, no real evidence exists for its use.
Pulmonary rehabilitation has been considered to be beneficial. **(**10**)**
Further research is needed, to develop evidence-based guidelines, for further management.

Conclusion

With the growing number of Covid-19 patients, even rare complications like post covid pulmonary fibrosis will have major health implications. Elderly patients, who require ICU care and the need for mechanical ventilation are the highest risk factors, to develop pulmonary fibrosis. Currently, no fully proven options are available for the treatment of post-inflammatory COVID 19 pulmonary fibrosis. Further research is required to find the best evidence-based treatment.

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