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REVIEW ARTICLE

A Simplified Approach to Covid-19 Disease in Adult Patients for General Practitioners

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Abstract

The pandemic of coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents a challenge to all doctors worldwide for detection of disease, differentiating it from those with similar presenting symptoms.

The initial evaluation of the patient with suspected Covid-19 disease is usually performed by general practitioners; who, unfortunately; as their knowledge about the on growing changing faces of this pandemic disease presenting symptoms and evolving new information are not continually updated, miss the diagnosis of some cases, with fatal consequences to these cases.

This simplified review is intended to provide those doctors basic, quick but essential information that will enable them to better at detecting and diagnosing cases. The current medical literature that is applicable to this simplified review was identified by a computerized search in WHO and the CDC, websites and in most of the reputed English language printed medical journals and was evaluated using standardized methods till the time of publication.

Keywords

COVID-19, SARS-CoV-2, Coronavirus, pandemic, PCR, CT, Vaccine

Q1: How does the virus infect cells?

SARS-CoV-2, a single-stranded RNA-enveloped virus having structural spike (S) protein that binds to the viral proteins angiotensin-converting enzyme 2 (ACE2) receptor present on cells. Following receptor binding, the virus these enter cells. Once inside the cell, viral polyproteins are synthesized [1].

Q2: What are the various presenting symptoms?

- Incubation period: 2-14 days [2,3].
- Symptoms and signs vary: [2,3].

*__General:__ Fever, fatigue, muscle or body aches, headache, chills.

*__Respiratory:__ Cough, sputum production, shortness of breath, sore throat, congestion or runny nose, rarely hemoptysis.

*__Gastrointestinal:__ Anorexia, nausea, vomiting, new loss of taste or smell (anosmia or ageusia), diarrhea, abdominal pain.

*__Ocular:__ Conjunctival hyperemia, chemosis, epiphora or increased secretions.

*__Asymptomatic.__

What is silent hypoxemia and what is/are its explanation?

Some patients with COVID-19 described as exhibiting oxygen levels incompatible with life without dyspnea. The pairing-dubbed happy hypoxia, but more precisely termed silent hypoxemia [4].

Some proposed explanations:

- The ventilatory response to hypoxia is decreased by 50% in people older than 65 years and in diabetics. Given that dyspnea response to hypoxia parallels the ventilatory response, it is likely that older or diabetic COVID-19 patients are more prone to silent hypoxemia [5-7].
- Chemical drive to breathe (in response to hypercapnia and hypoxia) exhibits as much as 300% to 600% variation between one subject and the next [8].
- Pulse oximetry is less reliable in critically ill pa-

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tients than in healthy volunteers [9].

- Fever, prominent with COVID-19, causes the curve to shift to the right; any given PaO_2 will be associated with a lower SaO_2. These shifts produce substantial desaturations without change in chemoreceptor stimulation (because carotid bodies respond only to PaO_2, and not SaO_2)-another factor contributing to silent hypoxemia [10-12].

Q4: What is the Covid-19 Type L and H pneumonia?

Gattinoni, et al. [13], have mentioned that the COVID-19 pneumonia are two types, L and H.

The Type L is characterized by [13]:

*__Low__ elastance with normal compliance. Combination not seen in other acute respiratory distress syndrome (ARDS).

*__Low__ ventilation to perfusion ratio.

*__Low__ lung weight detected by computerized tomography of chest (CT chest).

*__Low__ lung recruit ability with very low non-aerated lung tissue.

The Type H is characterized by [13]:

*__High__ elastance due to increase oedema.

*__High__ right to left shunt.

*__High__ lung weight detected by computerized tomography of chest (CT chest).

*__High__ lung recruit ability with increased amount of non-aerated lung tissue.

N.B: Those patients have severer ARDS criteria [13].

Q5: What is meant by cytokine storm?

Secondary haemophagocytic lymphohistiocytosis (sHLH) is an underecognised, hyperinflammatory syndrome characterized by a fulminant and fatal hypercytokinaemia with multiorgan failure [14].

- In adults, sHLH is most commonly triggered by viral infections [14].
- Cardinal features of sHLH include [15].

*unremitting fever,

*cytopenias,

*hyperferritinaemia,

*pulmonary involvement (including ARDS)

Q6: Is chest X-ray beneficial in diagnosis?

The chest film is insensitive early in the disease; however, it can be useful in the follow-up of the disease [16].

Q7: What are the CT findings in COVID-19 infection?

Initially: Bilateral, multilobar, ground glass opacities (GGO), with a peripheral or posterior distribution, mainly in lower lobes less commonly in middle lobe [17].

Box 1: GGO: Is a radiological finding in computed tomography (CT) consisting of a hazy opacity that does not obscure the underlying bronchial structures or pulmonary vessels [18].

- **Other CT findings:** Consolidation, crazy paving, vascular dilation, traction bronchiectasis, pleural thickening, subpleural bands and architectural distortion [17,19].
- **Uncommon findings include:** Pleural effusion, pericardial effusion, lymphadenopathy, cavitation, reversed CT halo sign and pneumothorax [17].

Box 2: Crazy paving: Is a radiological finding in computed tomography (CT) consisting of a thickened inter and intralobular lines with GGO [20].

Box 3: Reversed CT halo sign: Is a radiological finding in computed tomography (CT) of a rounded area of GGO surrounded by a complete or almost complete ring of consolidation [18].

How is CT used to detect severity of lung affection?

- The severity of lung involvement on CT correlated with the disease severity [19].
- The severity of CT is evaluated by visual assessment and this is the easiest method [19].
- Another method is by scoring percentage involvement of each of the five lobes with a total score calculated by the sum of individual lobar score divided by the number of lobes [19].

Q9: CT chest findings during the follow-up of clinically recovered patients?

Serial chest CT scans could be used as a monitoring modality to help clinician better understanding the course of the disease. There are few reports about post discharge follow- up chest CT findings. However, one study evidenced peak of pulmonary involvement 3-4 weeks after onset of disease with predominant GGO and consolidation. Pulmonary lesions still existed on discharge and the pulmonary lesions continued decreasing. Around 2 months after symptom onset, subpleural parenchymal bands were the predominant feature, and complete radiological resolution started in this period [21].

Author's comment: *As the GGO increases during the first 3-4 weeks it might be misinterpreted as deterioration of the case , thus if clinically the patient is improving the radiological findings should not affect decision making of discharge or stoppage of medications.*

Q10: Type of tests in COVID-19?

There are two types of tests:

- **Diagnostic:** To show active infection, it is either molecular test (RT-PCR) that detects the virus's genetic material [22], or antigen tests that detect specific proteins on the surface of the virus [23].
- **Antibody test:** Detect antibodies made by immune system in response to the virus [24].

Q11: Can we consider patient COVID if the PCR Test negative and patient has symptoms suggestive of COVID-19?

If patient has strong symptoms of COVID-19, it is safest to self-isolate, even if the swab test is negative [25].

Q12: Do we consider COVID patient still with active infection, if the PCR test is positive after total subsidence of symptoms?

A positive result of PCR or IgM assay in patients who displayed no clinical manifestation should not be considered indicative of being infectious [26].

Q13: Is there a definitive treatment for COVID-19?

Currently there is neither established treatment regimen for COVID-19 nor established prevention for SARS-CoV-2 [27].

Q14: Has azithromycin a role in COVID-19 treatment?

Azithromycin given alone early in the course of COVID-19 infection showed encouraging effects [28].

Q15: What is the role of hydroxychloroquine/chloroquine in COVID treatment?

The use of such medication in treating COVID-19 cases appeared in international guidelines alone or in combination with azithromycin. However, although it is a well tolerated medication it can cause corrected QT interval and cardiac arrhythmias which is greater if combined with azithromycin. Thus close monitoring by clinicians is recommended [29].

Q16: Is dexamethasone beneficial in treating COVID cases?

Dexamethasone 6 mg per day for up to 10 days reduces 28-day mortality in COVID-19 patients receiving invasive mechanical ventilation by one third, and by one fifth in patients receiving oxygen without invasive mechanical ventilation. Similarly, benefit was clearer in patients treated more than 7 days after treatment onset, when inflammatory lung damage is likely to have been more common [30].

Q17: What is the role of remdesivir in COVID treatment?

An intravenous drug that is metabolized intracellularly inhibiting the virus RNA polymerase thus inhibits virus replication [31].

- To be used in hospitalized patients with COVID-19 who require supplemental oxygen but who are not on high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) [31,32].
- The current dose under investigation is a single 200-mg loading dose, followed by 100-mg daily infusion for 9 days [31,32].

Q18: What is the role of favipiravir in COVID treatment?

- This intravenous drug that is metabolized intracellularly inhibiting the virus RNA polymerase thus inhibit virus replication [33].
- A loading dose is recommended (2400 mg to 3000 mg every 12 hours for 2 doses) followed by a maintenance dose (1200 mg to 1800 mg every 12 hours). Limited clinical experience has been reported supporting the use of favipiravir for COVID-19 [34].

Q19: What is the role of lopinavir/ritonavir in COVID-19 treatment?

Lopinavir/Ritonavir (Kaletra), an oral combination agent for treating HIV [35], that inhibits the "3-chymotrypsin like protease" which is responsible for breaking the synthesized viral polypeptides to non-structural proteins in host cell [32].

The most commonly used and studied lopinavir/ritonavir dosing regimen for COVID-19 treatment is 400 mg/100 mg twice daily for up to 14 days [36]. They can be used in pregnancy [37].

Q20: What is the role of toculizumab in COVID treatment?

- Tocilizumab, a monoclonal antibody IL-6 receptor antagonist, is used to treat RA [38]. A report in Covid-19 cases at a dose of 400 mg IV or 8 mg/kg for 1-2 doses., and a second dose 8-12 hours after first dose if inadequate response, was associated with clinical improvement [39].

Q21: What is the role of zinc in COVID-19?

- Zinc has the ability to enhance innate and adaptive immunity in the course of viral infection [40].
- Reported to inhibit SARS-CoV-2 RNA-dependent RNA polymerase (RdRp) thus stopping the virus replication in infected cells [40].
- Chloroquine enhances zinc uptake by lysosomes [40].
- Daily dosage: 15-30 mg [40].

Q22: What is the role Vitamin D in COVID-19?

- Vitamin D has a protective effect against respiratory tract infection [41].
- Some studies showed correlation between vitamin D level and COVID-19 cases and outcome; however, other studies lacked this conclusion [41].

Q23: What is the role of lactoferrin in COVID treatment?

- Lactoferin is a common nutritional support with laboratory evidence as an antiviral and immune-modulator [42].
- Studies showed possible reduced severity and duration of infection with preventive effect in contacts [42].

Q24: What is convalescent plasma? Who can donate the plasma? How could it help patient with COVID-19?

- Plasma collected from recovered asymptomatic proved COVID-19 cases, whose test turned negative and their blood contains antibodies and is compatible with the recipient and is negative for HIV [43].
- Used in deteriorating cases. Proved to improve clinical symptoms, increase survival rate, decrease hospital stay, reduce lung lesions in CT chest, and ameliorate routine laboratory criteria and pulmonary function and increase neutralizing antibody titers and cause disappearance of SARS-Cov-2 RNA [44].

Q25: What is the role of awake prone positioning in COVID treatment?

- In the absence of effective targeted therapies for COVID-19, optimization of supportive care is essential [45].
- Awake prone positioning appears to be safe and may slow the respiratory deterioration in select patients with COVID-19, who require oxygen supplementation or NIV/CPAP. This in turn may reduce demand for invasive mechanical ventilation [45].
- However, further studies are required to assess the degree to which awake prone positioning may be beneficial [45].

Q26: What is the role of HFNO (High-Flow Nasal Oxygen) in COVID treatment?

- HFNO is a commonly used therapy for patients with acute hypoxaemic respiratory failure [46].
- For patients considered unsuitable for tracheal intubation but who are deteriorating despite standard nasal oxygen or facemask oxygen, HFNO and CPAP are the only remaining options in active management and should be considered [46].
- Unfortunately, as the potential for aerosolisation of virus particles with increased risk that healthcare workers could become infected with coronavirus, this had limited the use of HFNO in many guidelines [46].

Q27: What is the role of ECMO in COVID-19 treatment?

- As several therapeutic strategies in managing COVD-19 have proven to be partially ineffective, even show many side effects. Thus the idea of adopting any adjuvant therapies that may contribute to a better outcome has pushed some physicians to recommend ECMO for those with severe ARDS from COVID-19 infection. ECMO therapy and COVID-19 itself are associated with synergistic changes in hematological and inflammatory status of the patients, thus the efficacy of ECMO is largely dependent on centers' experience with such therapies [47].

Q28: What is the role of vaccine in prophylaxis against COVID-19?

There is no vaccine against COVID-19 at this time. Over 100 candidate vaccines are in clinical trials or preclinical evaluation [48].

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