# Editorial :The SARS-COV2 (COVID-19) Pandemic: What Clinicians should Know

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Up to 1st of June 2020 COVID 19 pandemic affected more than 6 million people worldwide with more than 350,000 case fatalities , putting healthcare systems under severe strain .

At this issue of Afro-Egyptian Journal of Infectious and Endemic Diseases ; a review article titled "The SARS-COV2 (COVID-19) Pandemic: What clinicians should knew"(page:65-92) discussing virology, pathogenesis, clinical picture, investigations and treatment of covid19 which is a novel coronavirus, now designated SARS-CoV-2, emerged and was identified as the cause of an outbreak of acute respiratory illness in Wuhan, a city in China in late 2019. COVID-19 is one of the Beta corona viruses. They include; Middle-East Respiratory Syndrome (MERS-CoV), Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV2) the causative agent of COVID-19 pandemic .

There are 2 types of proteins characterizing HCoVs; structural [Nucleocapsid (N), Spike (S), Matrix (M) and Envelope (E)], and non-structural proteins [nsp12 and RNA dependent RNA polymerase] . Cell entry of SARS-CoV-2 is facilitated by the spike protein which is priming by serine 2 (transmembrane protease ;TMPRSS2) [1,2].

The pathogenesis of COVID-19, cannot be caught on, many mechanisms were adopted, The main site of viral replication is the mucosa of the upper respiratory tract followed by affection of the lower respiratory tract and gastrointestinal tract. This may be explained by the presence of ACE2 receptors at these sites. After cell entry by the virus, presentation of its antigens (Ags) to the antigen presenting cells occurs. Major histocompatibility complex is responsible for presentation of viral antigenic peptide followed by viral recognition by specific T lymphocytes. MHC I molecules and to lesser extent MHC II are responsible for antigen presentation of SARS-CoV [3].

Cytokine storm and subsequent ARDS is the most danger and potentially life-threatening event related to covid 19 , the chemokine system is involved in inflammatory response characterized by the release of excessive amounts of pro-inflammatory cytokines (IL-6, IL-12, IL-18, ,IFN-α, IFN-γ, TNF-α, , etc.) .The final consequence is ARDS and multiorgan failure, and death in severe cases. among stable COVID-19 patients would be explained by this diffuse thrombotic state besides the dissociation of hemoglobin noticed among those patients.

Large droplet during sneezing or coughing is the main method of transmission of COVID-19 [4]. Transmission between healthcare workers was reported in 3.8% of COVID-19 . Infection is acquired through inhalation of the infected droplet or by touching a contaminated surface and then touching the nose, mouth or eyes. The virus was also discovered in stool with the potential contamination of water resources and feco- oral transmission .The infected droplet can spread within 1-2 meters to settle on surfaces where the virus can stay viable in convenient atmospheric conditions but can be destroyed within a minute by the usual disinfectants .

The incubation period of the disease ranges from 2- 14 days with average of 5 days. Asymptomatic infections have also been described . There are no specific clinical features that can distinguish COVID-19 from other viral respiratory infections. The top 7 COVID19 symptoms, ranked by prevalence are Fever in(83- 99 percent), Fatigue(44- 70 percent) , Dry cough ( 59-82 percent), Anorexia ( 40-84 percent), Myalgias (11- 35 percent), Dyspnea ( 31-40 percent) and Sputum production(28-33 percent).

Less common 7 symptoms include headache ,confusion, runny nose,sore throat ,hemoptysis ,chills that causing prolonged shaking and loss of smell and taste disorders (e.g., anosmia and dysgeusia) , gastrointestinal symptoms (e.g., nausea and diarrhea) have been reported; and in some patients, they may be the presenting

complaint [5].Severe acute respiratory illness requiring hospitalization without any other cause explaining the clinical presentation can be considered as a suspected case also .

Laboratory findings are usually nonspecific. There is normal leucocytic count or mild leucopenia. Lymphopenia is common; a decrease in the lymphocytes below one thousand commonly occur in severe disease. There is normal platelet count or mild thrombocytopenia. The ESR and CRP usually increase, on the other hand procalcitonin level is within the normal range. Procalcitonin increase indicates a bacterial co-infection and need for ICU. Other lab markers like liver enzyme, coagulation profile, kidney function, LDH, CPK and D-dimer, serum ferritin may increase and high levels of previous laboratory marker commonly occur in severe disease [6]. US CDC states that collecting the upper respiratory nasopharyngeal swab have more yielding results than oropharyngeal (OP). Regarding SARS-CoV-2, Real-time reverse transcription polymerase chain reaction (RT-PCR) of viral nucleic acid is considered the diagnostic reference standard [7]. Regarding serologic tests, using lateral flow immuno-chromatography technique, qualitative rapid test detects IgG and IgM antibodies to COVID-19 in blood, serum and plasma samples has been approved by the Food and Drug Administration . The IgM-IgG combo assay is more sensitive than single IgM or IgG test. It could be considered for rapid screening of COVID-19. A period of 3-5 days after exposure to the virus needs to be lapsed .

Chest CT is suggested as an important tool for SARSCoV-2 infection diagnosis especially in patients with false negative RT-PCR results, with sensitivity up to 98% [8]. Typical X-ray and CT imaging findings, including, bilateral ground glass opacities, which are multiple, patchy, sub-segmental or segmental.

Until now, the therapeutic strategies to deal with COVID-19 are only supportive. There are some anti-viral therapies created based on observational studies and case reports and no strong recommendation to hold up to date. REMDESIVIR (compassionate use only) [9] is investigational antiviral drug, which initially developed for treatment of Ebola. It has been shown to inhibit SARS-CoV-2 in vitro. Lopinavir/Ritonavir [10] reduces viral replication by 50% in MERS –COV in vitro.

Dose: Adult: one tablet contains (Lopinavir200mg/ritonavir 50mg), give 2 tablets PO Q12h for 6-10 days. Favipiravir[11]:It is a novel antiviral drug active against a broad range of RNA viruses used by Japan and China to treat uncomplicated influenza.

Tocilizumab is FDA-approved for the treatment of several disorders, including cytokine release syndrome [12]. The interest in using tocilizumab to treat persons with COVID-19 is based on the observations that some persons with COVID-19 develop a massive inflammatory response that can result in acute respiratory distress syndrome (ARDS), multi-organ failure, and potentially death [13]. This massive systemic inflammatory response has been characterized as a cytokine storm and very high levels of IL-6, thereby suggesting IL-6 may play a central role in the acute clinical decompensation [14]. Tocilizumab is a humanized monoclonal antibody that binds to interleukin (IL)-6 receptors, thereby could potentially diminish this massive systemic inflammatory response [15].

High clinical suspicion for cytokine release syndrome supported by Serum IL-6 ≥3x upper normal limit,Ferritin >300 ug/L (or surrogate) with doubling within 24 hours.CRP > 100 mg/L with doubling within 24 hours,Elevated D-dimer (>1 mg/L).Ferritin > 600 ug/L at presentation and LDH >250.

Anticoagulation [16]: All patients should receive standard prophylactic anticoagulation with low molecular weight heparin (LMWH) in the absence of any contraindications (Contraindications include platelet count less than 25,000 or active bleeding); monitoring advised in severe renal impairment; abnormal PT or APTT is not a contraindication. If LMWH contraindicated due to renal failure (Creatinine Clearance < 30mL/min), Unfractionated Heparin 5000 units SC q12 (UFH) can be used as an alternative. Fondaparinux is preferred in those with heparin-induced thrombocytopenia.

Corticosteroids: Clinicians need to carefully weigh the risks and benefits of corticosteroids on the individual patient level. This need for a risk benefit assessment in individual. glucocorticoid that is equivalent to methylprednisolone 1-2 mg/kg/day for 3-5 days or less.

Treatment according to severity of covid19:

- Mild uncomplicated illness without risk factor /co-morbidities: Supportive &Symptomatic treatment.

-Mild uncomplicated illness with Co-morbidities/Risk Factors: Supportive &Symptomatic treatment. Enoxaparin 40-60mg day (if not contraindicated; dose adjust with CrCl < 30ml/min) &Observe closely.

- Moderate Illness(Dyspnea,Respiratory rate > 22 - 24/minm,SPo2 <94 - 92% on room air.<50% lung involvement on imaging ): the above + N/C O2, 2L /min if needed (max 4 L/min; consider early transfer to ICU for escalation of care). Start empirical antibiotics as per local institutional protocol for treatment of community acquired pneumonia.

-Severe Illness(Respiratory rate > 24/min,SPo2 <92% on room air,>50% lung involvement on imaging,High risk factors for severe illness) : High flow O2 support (HFNC/NIV) taking adequate precautions to reduce aerosolization,Awake proning can be tried as a rescue measure,Anti-viral (Lopinavir/Ritonavir, Remdesivir, Favipravir) can be initiated on a compassionate basis. No proven benefit (Better to start before clinical deterioration).

-Critical Illness (Respiratory failure, Shock, Multi organ dysfunction): Anticoagulation: Therapeutic dose of LMWH (if not at high risk of bleeding).Tocilizumab ,Convalescent plasma and Steps of escalation of respiratory support.

From point of view this article covers most of topics regarding covid 19 and we add some points:

1-There is no evidence to date that respiratory viruses being transmitted via food or food packing.

2-Severity of covid 19 is also determined by PaO2/FiO2 which is normally 400-500 mmHg and if decreased less than 300 mmHg the case is considered severe.

3-Debates of role of hydroxychloroquine in managing covid 19 especially if taken with azithromycin with abnormal ECG.

4.Role of lactoferrin in prophylaxis & early treatment of covid 19 as it prevents binding of the virus to ACE2 receptors .

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