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Opinion

COVID 19 — Practical Considerations Related to Diagnosis & Current Treatment Options - @

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OPINION

A novel corona virus SAR-CoV-2 which causes COVID-19 is a very insidious and lethal single stranded RNA (Ribonucleic Acid) Virus which has caused devastation around the world by killing millions of people around the globe including frontline healthcare workers [1]. Unlike the seasonal flu, COVID-19 is a systemic illness with a higher mortality. World Health Organization (WHO) has called it a Pandemic which spreads mainly by droplet route of infection but can remain aerosolized in poorly ventilated or confined spaces and also through fomites (various objects touched by the infected patient) it could stay on stainless steel and Plastic for upto 48 and 72 hrs respectively or so and on cardboard for around 24 hours [2].

An advice to maintain a two meter social distancing has been given to prevent its spread by the droplet route [3]. Cleaning hands for 20 seconds with soap water or a sanitizer containing more than 60% alcohol and disinfecting common objects held by the patients should be appropriately disinfected with disinfectant solution, which causes the cell wall lysis and so the virus is killed. Signs and symptoms of COVID-19 are varied include anosmia or a loss of taste and a loss of appetite. Fever seen in about 80%, normally dry cough but could be productive, with myalgia, arthralgia, shortness of breath diarrhea, sometimes abdominal pains. Presentations could vary with Arterial thrombi and an (MI) Myocardial Infarction [4] or a full- blown Cerebra Vascular Disease (CVA) and a stroke noted even in less than 50 years of age [5,6]. About 80.9% cases of COVID-19 are mild and are managed at home. Among the remaining cases, 13.8% require hospitalization because of low oxygen saturations (hypoxia), chest pains and occasionally altered mentation, and only 4.7% require ITU admissions with intubation and ventilation [7].

Most patients show signs and symptoms of an acute respiratory distress syndrome from the 2nd week onwards and this is thought to be secondary to the cytokine storm: a response that is initiated by the body's defense mechanism after the virus replicating in the RNA of type 2 Pneumocyte cells in the alveoli before release of mediators like Interleukin-1 (IL-1) and Interleukin-6 (IL-6) and TNF alfa causing increased permeability from the capillaries around the alveoli leading to alveolar oedema and reduced surfactant secreted from these type 2 Pneumocytes. It is also due to the elevated cytokine response that the thrombotic complications are more pronounced in these patients as opposed to other types of pneumonia. The disease process then proceeds to involve multiple systems as reported by other authors wherein involvement of the respiratory, nervous, cardiac, gastrointestinal and renal systems takes place [8]. Older age and male sex were independent risk factors for poor outcome of the illness [9].

The difficulty in diagnosis and treatment can partly be attributed to the relatively high false negative rates of RT-PCR throat and nasopharyngeal swabs as evidenced by several studies done in China with some authors reporting a detection rate as low as 60% in some exclusive swab based diagnosis [10-12]. There is currently work going on in bringing the results time shorter on nasopharyngeal swab testing but new test using saliva can bring the results of COVID 19 within few seconds or so and we impatiently wait for progress on that front. The limitation of swab RT-PCR testing creeps in due to several factors including but not limited to swab technique, viral load, respiratory symptoms at the time of diagnosis and other logistic factors [12].

As the author at this passage of time we would recommend a full biochemical, radiological testing along with RT-PCR testing to aid in obtaining a correct diagnosis. The blood tests are expected to show lymphopenia, occasionally eosinopenia, high CRP, fibrinogen count, LDH, D-dimer, troponin and occasionally deranged liver function tests. The radiological findings are those of unilateral or bilateral peripheral infiltrates on a chest x-ray and the author recommends CT Scans being important especially in swab negative grey cases the sensitivity is reported to be greater than 95% [10].

Management of COVID19 in most patients remains initially supportive with a focus on maintaining the oxygen concentration greater than 92% in only hypoxic patients the first instance [13], along with symptomatic therapy with paracetamol and fluids intake to maintain hydration. In the hospital setting hypoxic patients were usually started on supplemental oxygen once the saturations dropped down to less than 92% and interestingly these patients were not overtly distressed even with saturations much lower than 88%. In most centers the oxygen was usually started with a venture mask set at 24% FiO_2 and progressively increased to 40% depending on the patients need. Once the inspired fraction of oxygen increases to 40%, the patients were then trialed on Continuous Positive Airway Pressure Ventilation (CPAP) with a starting pressure of 5cm and building up to 10cm.

The CPAP is to be used for the entire length of the day in these patients and oral intake can be supplemented by means of nasogastric tube feeding to ensure adequate nutrition is maintained. Intensive care involvement is usually sought early but specifically when the FiO_2 increases to 60% and certainly when commencing CPAP therapy. Further therapy like invasive ventilation or Extracorporeal Membrane Oxygenation (ECMO) can also be used especially in those needing prolonged oxygenation.

Further treatment strategies include starting low dose Dexamethasone which has been shown to reduce deaths in one-third of the ventilated hospitalized COVID 19 patients and one-fifth in other patients receiving Oxygen only. However, there was no benefit in patients not requiring any Oxygen or respiratory support from one treatment arm of the Recovery Trial, UK. The author welcomes the use of Dexamethasone 6 mg once a day for 10 days [14].

In case patients hospitalized with COVID 19, the use of dexamethasone resulted in lower 28-day mortality on patients receiving invasive mechanical ventilation or Oxygen alone.

The second medication being used is Remdesivir, an antiviral drug which shortens the time of recovery by about 4 days in adults hospitalized with COVID19 and evidence of lower respiratory tract infection in a study in New England Journal of Medicine [15]. Early medicine usage scheme Remdesivir is indicated for the treatment of adults and adolescent patients aged ≥ 12 years and weighing at least 40 kg hospitalized with suspected or laboratory confirmed SARS-CoV-2 infection and severe disease.

Newer agents like Tocilizumab (TCZ) an IL-6 blocker used in Cytokine Release Syndrome (CRS) has problems with late onset infections seen in 23% patients with other complications including abnormal LFT s in 51% hence careful considerations should be made before its usage and its efficacy has still to be proven [16]. Transfusion of convalescent plasma does not seem to have benefit due to both when antibodies develop in infected patients and the variability of the levels of antibodies in plasma [17,18].

Further considerations are COVID-19 antibody test could tell us that a patient had recovered from the viral illness and have developed

immunity against COVID-19 [19]. The IgG appears around 14 days whereas the IgM appears much earlier. The Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Serologic Testing suggests using serologic testing to diagnose SARS-CoV-2 infection three to four weeks following symptom onset [20].

Respiratory teams were the specialty overseeing ward based, COVID-19 patients with profound respiratory complications generating high SARS-CoV-2viral load. Moreover, the treatment of these patients entails CPAP (Continuous Positive Airway Pressure) machines that is recognized as an aerosolizing procedure running a much higher risk of exposure of staff to very high viral loads.

The use of CPAP treatment for COVID-19 patients is not a short procedure but CPAP is running 24 hours a day when the COVID-19 patients are awake and asleep thus aerosolizing SARS-CoV-19 and at even higher titers than all other aerosolizing procedures. The vast majority of these wards are not equipped to deal with a highly contagious pandemic; only few wards have negative pressure ventilation.

All staff including the nursing staff of all grades and doctors indeed any other staff that enter the respiratory wards are thus exposed to extremely high viral loads and are at a very high risk of repeated exposure and contracting the virus themselves and developing COVID-19. Guidance from Public Health England (PHE) dated 2nd April 2020is that COVID-19 patients on CPAP are recognized as patients undergoing a continuous aerosolizing procedure that is at high risk of infecting all Health Care Workers (HCW) and PHE recommend the following:

- 1-A Filtering Face Piece Respirator (FFP3) face mask
- 2-Single use disposable fluid resistant long-sleeved gown
- 3-single use disposable gloves
- 4-single use face protection

Despite these PHE guidelines, NHS trusts nationwide in the UK, were finding it quite challenging to provide the PHE approved PPE to protect health care workers on the respiratory wards with CPAP patients.

The most significant piece of evidence regarding the importance of PPE has come from Cotugno Hospital, Infectious Diseases Centre in Naples, Italy where none of the healthcare workers have developed COVID-19. There they are wearing full protective wear including fullface ventilators and equivalent of hazmat suits. This is in comparison to north Italy where over 140 doctors have died from COVID-19 contracting the virus wearing inadequate PPE, whilst treating COVID-19 patients. The American College of Chest Physicians however have published clear guidelines American College of Chest Physicians March 2020

All suspected and confirmed cases in the A&E, ward requires Personal Protective Clothing (PPE) which includes:

a)- isolation gown

- b)- 2 pairs of gloves
- c)- a face shield

d)-FFP3 or N95 respiratory facemask

e)- instead of c & d - use of a Powered Air Purifying Respirator (PAPR)

More than 150 healthcare workers have died in England after contracting COVID19 infection reported in the national news so data suggesting these recommendations of PPE may or may not be adequate to protect 100% the frontline staff. In case of a second wave of COVID-19 we would need to consider stepping up the standard PPE or use more of battery-operated hoods with filters which were noted to be very successful in protecting healthcare workers, equally also the use of Hazmat Suits in aerosolized environment could provide a very good level of protection i.e., about 100% protection to our frontline staff and HCWs.

We are all waiting impatiently the development of safe and effective COVID-19 vaccine and work is in stage 3 of development of vaccine around the world including USA, UK, China and the Russia, the vaccines now used slightly ahead is the Russian and the Chinese vaccine and its efficacy is yet to be reviewed. Unless an efficacious vaccine is discovered quickly there is very high likelihood of a second wave of COVID 19 pandemic especially at the start of the winter-time and we should have contingency plans ahead of that time.

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