Updates on COVID-19
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The use of dexamethasone was found to be most striking in critically ill COVID-19 patients, particularly in those who were on oxygen therapy or mechanical ventilation. Emerging evidence in the form of DEXA-ARDS, a randomized controlled trial, showed more ventilator free days and decreased mortality in critically ill patients with acute respiratory distress syndrome who were given dexamethasone versus usual care. In June 2020, the UK RECOVERY trial, a large open label multi-arm randomized clinical trial of hospitalized patients with COVID-19 found a decrease in 28 days mortality from 25.7% in the control group to 22.9% among patients treated with a low dose of 6 mg per day of dexamethasone. It also reduced the need for mechanical ventilation by 2.1% and shortened hospital length of stay by 1 day. In mechanically ventilated COVID-19 patients, it reduced 28 days mortality from 41.4% to 29.3%, signifying a number needed to treat of 8. This study found the benefit of dexamethasone use in mechanically ventilated COVID-19 patients but found increased mortality in COVID-19 patients who were not on supplemental oxygen. Initially, there were 3 multicenter randomized controlled trials assessing corticosteroid therapy in critically ill patients with COVID-19 which were stopped after the RECOVERY trial. The REMAP-CAP trial showed low likelihood of organ failure and CODEX found a reduction in mechanical ventilation use by 2.2 days.

COVID-19: An alert for emergency physicians and neurologists
During the COVID-19 pandemic as cases were growing, studies reported neurologic manifestations in patients with COVID-19. One published study reported the neurologic manifestations of COVID-19 patients in 78 of 214 patients with laboratory confirmed diagnosis of COVID-19 in Wuhan. The patients showed neurologic manifestations, especially acute cerebrovascular disease, conscious disturbance, and skeletal muscle injury. It was postulated that severe infections had high D-dimer and elevated creatine kinase levels and were more likely to develop the cerebrovascular disease. Significantly elevated pro-inflammatory cytokines in serum may cause skeletal muscle damage. Observational case series of 58 patients in France showed neurologic manifestations in patients admitted to the ICU with COVID-19 pneumonia, mainly agitation, corticospinal tract signs, dysexecutive syndrome, inattention, disorientation, or poorly organized movements in response to command. Neurological manifestations developing after ICU admission point towards encephalopathy. A case report from Italy showed neurologic deficits as typical features of COVID-19-associated Guillain-Barre syndrome or from a critical illness neuropathy or myopathy and suggests a possible association of SARS-CoV-2 and Guillain-Barre syndrome. Anosmia was reported in a COVID-19 patient hence this symptom could be used as a triage tool. Stroke is a time sensitive condition hence any concerning symptoms should be addressed and avoidance of ‘stay at home’ should be practiced at that time. This letter may generate information and awareness about extra-respiratory symptoms on COVID-19 patients and should prompt clinicians to consider SARS-CoV-2 infection as a differential diagnosis to avoid delayed diagnosis or misdiagnosis and prevention of transmission.

Mathematical models in predicting...
disease burden in COVID-19 pandemic: How accurate are they: Numerous mathematical models have been reported for predictions on the COVID-19 pandemic. Models are taken into account to calculate how frequently individuals are acquiring an infection while working in health care, hence models can be very complex and require huge input data and assumptions for those variables that are not fully understood. This led us to have a wide range of assumptions. While we think of modeling a hurricane with less certain estimation, the same modeling can be applied for planning in this pandemic.\(^{(3)}\)

Studies from Oxford University suggest that complexity and even detailed mathematical models are not capable of prediction, however, it can be an important tool for predicting the time course of pandemic and evaluation of public health interventions. It shows that complex models may not be reliable due to the larger numbers of parameters estimated.\(^{(3)}\) Their results could be useful for public health officials, about strict quarantine and their findings suggest a theoretical validation of effectiveness. In addition, this may provide warnings to public health officials. For such an unprecedented global health issue, we need to share information, experience, and knowledge.

COVID-19 and Immunity

SARS-CoV-2 belongs to the beta-coronavirus genus which includes the SARS-CoV-1 coronavirus, Middle Eastern respiratory syndrome (MERS) coronavirus, and two other human coronaviruses, HCoV-OC43 and HCoV-HKU1.\(^{(4)}\) In 1977, one strain of coronavirus was inoculated in 18 volunteers who developed symptoms. Six of them were given the same strain and none developed symptoms. Another 12 volunteers were given mildly different strain a year later who developed partial immunity.\(^{(4)}\) In 1990, in a study by Callow et al,\(^{(4)}\) 15 volunteers were inoculated with one strain of coronavirus with ten developing asymptomatic infection. Changes in circulating antibodies were followed in the volunteers inoculated with coronavirus 229E. Infected volunteers showed mild lymphocytopenia. Uninfected volunteers were rechallenged. 14 of these subjects were re-inoculated with the same strain a year later. Eight of them became re-infected. However, the period of virus shedding was shorter than before and none of the subjects developed symptoms. The results were correlated with natural infections such as rhinovirus infections.\(^{(4)}\) These studies suggest that most who recover will develop full or partial immunity for a year and could help scientists to develop vaccines.

Hydroxychloroquine: A controversy in the COVID-19 treatment

In the COVID-19 pandemic, new treatment options are being widely discussed in the literature. One of the commonly debated agents was an antimalarial agent, hydroxychloroquine (HCQ). It was postulated that HCQ lowers endosomal pH, interferes with glycosylation of cell receptors, and ultimately inhibits COVID from binding to ACE 2 and decreasing viral intensity.\(^{(5)}\) Brazilian randomized controlled trial (RCT) for COVID-19 (CloroCovid-19 trial) is a double-blinded RCT of HCQ therapy for COVID-19 which was stopped in Brazil after 6 days of launch due to high risk of cardiac arrhythmias. This trial investigated the safety and efficacy of dosages of HCQ in 2 forms in severe COVID-19 patients. Patients randomized to 600mg HCQ twice daily for 10 days (Total dose 12g) versus HCQ 450mg twice daily for 5 days (Total Dose 2.7g). All patients also received ceftriaxone 1g twice daily for 7 days, azithromycin 500mg four times daily for 5 days, and oseltamivir 75mg twice daily for 5 days when influenza was suspected (89.6% of the study population). 81 patients were enrolled. Due to a higher lethality rate of 13.5%, patient recruitment to this arm was stopped. This trial suggested 2 things: Firstly, a higher dose of HCQ (12 g) for 10 days resulted in QTc prolongation in 25% of the patients, therefore, high dose HCQ should not be used. Secondly, low dose HCQ 450mg twice daily loading dose and for 5 days daily does not work for patients with severe acute respiratory distress syndrome.

CONFLICT OF INTEREST: Authors declared no conflict of interest.

Funding: None to declare

REFERENCES


