Editorial

SARS-Cov-2 pandemic; what we know; effect on Orthopaedic services and academics

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Corona viruses (CoVs) commonly cause relatively mild respiratory illness in humans and animals. However, within two decades, mankind experienced three highly pathogenic and deadly human corona virus infections, SARS-CoV (2002), MERS-CoV (2012) and SARS-CoV-2 (2019). Compared to mortality rate of SARS-CoV (> 10%) and MERS-CoV (35%), SARS-Cov-2 has a lower mortality rate but is more contagious. Current pandemicity of SARS-CoV-2, later named as COVID-19 by WHO in February 2020, has infected about 50 million and caused more than 1.2 million deaths in more than 200 countries, and about 200 thousands are infected and about one thousands died till date in Nepal, and the number is exponentially increasing, challenging health systems. Second wave of the infection in China, America and Europe has become a great challenge and the same in Nepal during winter may create an overwhelmingly unmanageable condition.

SARS-CoV-2 virus particle phylogenetically belongs to genera Betacoronavirus (capsulated RNA virus with core nucleocapsid). The spike (S) protein in the capsule binds to ACE2 (angiotensin converting enzyme-2) receptor (abundant in lung and cardiac tissue) of the host cell allows it to enter and infect cells where it replicates and affect new cells. L strain of COVID-19 virus is aggressive and spreads rapidly; while the S type might remain milder. Based on the clinical observation of last 8 months, its clinical spectrum can be: asymptomatic (1.2%); mild to medium cases (80.9%); severe cases (13.8%); critical case (4.7%); and death (2.3%). Under 10 children have more asymptomatic infection (15.8%).

COVID-19 patients are the *source of infection*, and the virus is *transmitted* mostly through respiratory droplets and direct contact. At this stage of community transmission, theoretically, all individuals are at *risk of infection*. However, major risk factors are old age, male and co-morbidities. The *diagnosis* is based on sign and symptoms with high index of suspicion. The chest x-ray or chest CT can show features of pneumonia. However, all COVID-19 cases do not develop pneumonia and all pneumonia is not caused by it. Laboratory blood tests and Potential biomarkers level, Serological tests (Serum IgM and IgG antibody), antigen test and nucleic acid test (RT-PCR and CRISPR) are helpful for diagnosis and monitoring of the disease. Unfortunately, none of the test has 100% sensitivity, thus Diagnosis can be more accurate on adjunct of the serological tests to nucleic acid test.

According to WHO interim guidance, *clinically* Covid -19 cases can be 1. Moderate (mild symptoms including fever, cough, headache, or soreness from cough but no pain), 2. Severe (inflammation of lungs, extreme breathlessness, pain in the chest, fast heartbeat, or unwell appearance and low blood pressure), and 3. Critical cases (features of acute respiratory distress syndrome (ARDS). Cardiovascular, renal, and neurological complications may occur in COVID. Disseminated intravascular coagulation (DIC) is a grave complication causing multi-system failure. Leaked blood through endothelial lesion in lungs vessels triggers generalized inflammation and fuels cytokine storm. Children may develop paediatric inflammatory multisystem syndrome (PIMS). Though too early to comment on long term effect of COVID-19 infection fatigue, dyspnoea and decreased quality of life are the most common persistent symptoms (long COVID).

There is no *treatment* approved for COVID-19 till date. Therefore, the treatment strategy is supportive care only. However, several virus-based and host-based treatments have been introduced to manage severe ARDS. Asymptomatic or mild cases can be treated at home provided the infrastructure and clinical monitoring facilities are adequate. If not they should be treated in isolation to break the chain of transmission. Moderately sick cases need hospital treatment with Oxygen therapy (low to high flow) in prone and Antiviral treatment. Chloroquine competes for the ACE receptors of host cells and inactivates virus by decreasing acidity in cell endosomes. However, risk of dysrhythmias has limited its use. Treatment of Severe and critically ill cases need intensive care and the aim is to provide supportive treatment, active prevention and treatment of complications, management of chronic medical diseases, and prevention of secondary infections and to support multiple organ functions. Convalescent plasma transfusion reduces the viral load. Plasmapheresis, IL6 inhibitor and immunomodulator (tocilizumab) is used in case of cytokine storm. Corticosteroid use should be limited to specific co-morbidities and during respiratory distress. Antibiotics are given to treat existing infection or to prevent secondary infection; however unnecessary or inappropriate use should be avoided. Psychotherapy for patients who develop high level of anxiety is very useful.

A *vaccine* which is safe and effective should be made available globally to return to the pre-pandemic normalcy. Transmission-mitigation strategies (physical/ social distancing, frequent hand wash and use of proper mask) implemented in most countries has prevented most citizens from being infected during current pandemic time. However, epidemiologically this will paradoxically leave a large un-immune population susceptible to additional waves of SARS-CoV-2 infection. Development of corona virus vaccines is historically not easy. Further, there is a concern that vaccination, as with natural corona viral infection, may not induce long lived immunity. In corona virus, S protein elicits neutralizing antibody and is a major target antigen for vaccine development. Laboratories in different countries have come up with various types of vaccines at different stages of trials; hopefully it will be globally available by 2021.

Socioeconomic impact of current COVID-19 pandemic is extremely dreadful. Unavailability of specific medical treatment and the fast spread of information /misinformation about the ongoing pandemic have created an annoying infodemic and that causes unnecessary worldwide panic. Unprecedented physical and social distancing, quarantine and border closing measures has caused sudden and profound economic hardship, with marked decreases in global trade and local small business activity. If the same situation persists, full ramifications may be more painful.

Orthopaedic academics and services are badly affected by COVID-19 pandemic. It has changed the clinical discourse of patients in every medical discipline. Fear of transmission has limited hospital visits of sick people; patient's care is compromised by social distancing. Persistent use of protective measures like PPE by health personnel has make them early tired and fatigue. Unprecedented use of resources in COVID patient care and increasing trend of health personnel being infected has created severe depletion in hospital resources and manpower. In such situation many non-COVID and elective cases have been compelled not to seek medical services. Thus, they present in advanced stage of the disease. During this pandemic, orthopaedic departments have to calibrate and recalibrate operative services. Trauma, tumors and infections are put in top priority. Spinal conditions with neurology are considered as semi-urgent cases for operation. Avoidance of aerosol-generation procedures and involvement of less number of surgeons and proper use of protective measures might reduce the chances of disease transmission. Less number of patients and operation has limited clinical exposure and thesis work of residents. Bed side teaching and class room group teaching is being replaced by virtual classes. This might be an opportunity, in long run, to improve academic activities by hybridizing the web-based and live learning process.

With increasing understanding on the virus, epidemiology of infection and mitigation strategies spread of the disease can be slowed to flatten the curve. Global effort to explore preventive measures, possible therapies and proper management of socio-economic issues will eventually return the world to a "new normal."

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