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Case management in the context of a South African COVID-19 surge

The case management of COVID-19 has come into the spotlight as the numbers of active cases rises, putting our health care system to the test.

Novel Coronavirus (SARS-CoV-2) was initially reported to the World Health Organisation (WHO) on December 31, 2019. On January 30, 2020, WHO declared the COVID-19 outbreak a global health emergency. On March 11, 2020, the WHO declared COVID-19 a global pandemic, its first such designation since the H1N1 influenza pandemic in 2009.

The world has experienced six months of COVID-19, and in our case, we are beginning the fourth month. Clinical and epidemiological knowledge around this disease has developed at an unprecedented rate and a vaccine has already ascended to human trial phase. This is how determined we are, collectively, to beat this virus and minimise its impact on us as humanity.

As the numbers of admissions increase, so too must our clinical acumen. We are constantly learning more about the behaviour of the virus when it enters the body. Our ability to refine our clinical management will have a significant impact on the overall burden of the disease on our health care system.

The virus was initially isolated from the bronchoalveolar lavage (a washout of the lung airways) of three patients who were admitted to a hospital in Wuhan.

We have since learnt that the virus is shed through the airways and spreads by infected droplets passing from one individual to another

The virus has also been detected in saliva, lacrimal (tear) fluid, in stool, and in the semen of men with acute infection, as well as semen of some male patients who have recovered. Having said that, sexual transmission of the virus has not been recorded.

There have been intense studies into the duration of viral shedding (expulsion and release of the virus) as well as ascertaining how long Coronavirus survives on surfaces.

The duration of viral shedding varies significantly between different studies and may depend on severity of disease or the nature of the study itself.

PCR detection has been used a proxy for viral shedding in some studies: one found PCR positivity from 8-37 days, with a median of 20 days. A different study found no viral shedding in 90% of patients with mild illness, whereas results were positive for longer durations in patients with severe COVID-19. Another study found a median shedding duration of 31 days (range, 18-48 days).

Although the PCR may remain positive for prolonged duration, a better marker of viral shedding may come from studies that culture the virus. A small study from Germany early in the pandemic, showed that virus could be cultured from specimens taken during the first week of symptoms (17% from swabs, 83% from sputum), but no positive cultures were obtained from samples taken after 8 days from symptom onset, despite the PCR remaining positive. A more recent Canadian study of 90 patients that were PCR positive showed that culture of virus was possible in 29% but

no growth of virus was detected in samples taken after 7 days from symptom onset. In summary, shedding of live virus may be of shorter duration than PCR positivity.

There is also variability with regard to Coronavirus persistence on various surfaces. A study found that SARS-CoV-2 remained detectable for up to 72 hours on some surfaces despite decreasing infectivity over time. Notably, the study reported that no viable Coronavirus was measured after 4 hours on copper or after 24 hours on cardboard.

COVID-19 is defined as illness caused by SARS-CoV-2.

Presentations of COVID-19 have ranged from asymptomatic/mild symptoms to severe illness and death. Symptoms may develop between two days and two weeks following exposure to the virus.

Clinical characteristics of COVID-19 include fever and symptoms typical of a viral respiratory tract infection: cough, sore throat, loss of taste and loss of smell, nasal congestion, and even conjunctivitis, have been reported.

Further, gastrointestinal symptoms of nausea, vomiting, and diarrhea are also common with COVID-19.

The virus can progress to cause lower respiratory tract infection resulting in, pneumonia and its complications.

Acute Respiratory Distress Syndrome (ARDS) is a serious complication of COVID-19. The lungs may become stiff and difficult to ventilate. It is for this reason that ARDS is associated with a high mortality rate. Added to this, some reports from Italy seem to suggest there is an atypical form of ARDS in patients with COVID-19, leading to much higher oxygen requirements.

There have been two major advancements in the case management of severely ill patients who require ventilatory support. First is the advent of dexamethasone which

has shown that deaths can be reduced by a third for patients on ventilators and can also help patients who only need supplemental oxygen.

It is easy to appreciate why that is, if one understands the pathology.

The spikes that have become a branding trademark of COVID-19 are made up of proteins that like to interact with a certain receptor, called the angiotensin-converting enzyme 2 receptor (or ACE-2), that is found in large amounts in the alveoli.

This causes direct injury to the lung tissue due to a local inflammatory response. This response is mediated by a hyperactive immune response system that is meant to deal with the virus. Unfortunately, in ARDS, this response is exaggerated, resulting in significant and sustained inflammatory damage to lung tissue itself. Oedema (water in the lungs) also forms a part of this pathology.

With pneumonia, the pathology is slightly different in that the spaces in the lung alveoli fill up with inflammatory sediment causing a consolidation (all the air filled up) of a particular part of the lung. The body can, to some extent, redirect its blood flow to healthier parts of the lung during pneumonia. We call this shunting. And so, pneumonia is generally a little bit easier to manage than ARDS, which causes widespread lung damage.

In both these instances, the process mediating the inflammatory response is an important part of the damage caused. And so, dexamethasone and other corticosteroids exert their effect by attenuating the inflammatory response, thus reducing damage to lung tissue which means less stiff lungs that are more compliant to the work of breathing or ventilating.

It is for this reason that we now recommend early administration of dexamethasone to critically ill patients who require oxygen support.

Apart from dexamethasone, we are also learning a great deal about ventilating patients. Evidence increasingly supports the avoidance of invasive ventilation strategies as far as possible.

This is because when one is very ill, they generate a fight or flight response. These hormones drive your body to work harder to breathe; your heart to beat faster to circulate oxygen and nutrients to a body that is demanding more; and for you to be able to pay attention to warning signs such as pain or heat. When we intubate a patient and ventilate them artificially, this has to be facilitated by sedation and a limited period of muscle relaxation. These processes remove, or significantly dampen, the fight or flight response and therefore remove the ability for the patient to physiologically cooperate with the interventions you are making as a doctor. Therefore, it is always better to have a patient who can optimally mount these responses that lead to improved outcomes.

We soon expect the Ministerial Advisory Committee on COVID-19 to issue advisories on the use of high flow oxygen for patients who are very ill but can be managed without intubation and ventilation.

We were very pleased to receive the National Institute of Communicable Diseases' sentinel report completed on June 21. This report brings all these issues home and gives us a sense of the burden we have faced, how the system has coped and marries these lessons to the projections that have been modelled of the coming surge.

The NICD reported 10 700 COVID-19 admissions from 269 facilities (71 public-sector and 198 private-sector) in all nine provinces of South Africa between March 5 and June 21, 2020.

These were the key findings:

- The median age of COVID-19 admissions was 50 years; 338 (3%) admissions in patients ≤ 18 years and 1386 (13%) in > 70 years. Fifty-four percent (5 778/10 700) were female.

- Among 8 245 (77%) patients with data on co-morbid conditions, 2 810 (34%) had one co-morbid condition and 3126 (37%) had two or more co-morbid conditions.
- Of the 5 836 patients who had a co-morbid condition, the most commonly reported were hypertension 3419 (59%) and diabetes 2813 (48%); and there were 1 116 (19%) patients admitted with HIV, 240 (4%) with active tuberculosis (TB) and 579 (10%) patients with previous history of tuberculosis.
- Obesity, while not consistently recorded for all reported COVID-19 admissions, was noted by clinicians as a risk factor in 297 (3%) patients.
- Of the 10700 admissions, 3 260 (31%) patients were in hospital at the time of the report, 5 925 (55%) patients were discharged alive or transferred out, and 1 515 (14%) patients had died.
- Of the 7 324 COVID-19 patients who had recorded in-hospital outcomes (died and discharged), 1 515 died, equating to an in-hospital case fatality ratio (CFR) of 21%.
- Some of the factors associated with in-hospital mortality were older age groups; male sex; and having co-morbid hypertension, diabetes, chronic cardiac disease, chronic renal disease, malignancy, HIV and obesity.

We are a government that values science and we remain guided by scientific literature as higher levels of evidence emerge from more robust studies.

Although we have previously highlighted the key issues covered in the scope of this statement, we wish to detail them for the public to demonstrate the connection between science and the recommendations that we make.

We have recommended frequent hand-washing, avoidance of touching the face and cleaning of surfaces - this is to protect one from acquiring the virus as one interacts with surfaces.

We have recommended social distancing based on the fact that droplets traverse a certain distance from person to person.

We have recommended the wearing of face masks based on clear evidence that masks reduce the amount of exhaled Coronavirus. The various studies on viral shedding show too much variability in the time one sheds the virus. We also now know that one can shed the virus days before showing symptoms and for days after they recover from their symptoms – and so by wearing face-masks, one can literally save someone else from acquiring the virus. If that person is elderly or living with a co-morbidity, you can save that life.

We have recommended that the elderly and those with co-morbidities should take extra care, avoid leaving home, and ensure that their chronic conditions are well under control. The NICD report confirms that indeed these population groups are particularly vulnerable.

These recommendations are easy enough to follow for a few weeks, but they now need to become a new normal. We need to establish and keep new habits and inculcate them into our traditions, our customs and our working lives forever.

This is proving to be particularly difficult for South Africans to sustain and we appreciate that it is not easy to become accustomed to a new way of life.

As such, we are engaging the process of behavioral change through a multi-sectoral approach and we will do our best as government to reach out to our people and appeal to their sense of survival because these interventions are recommended for the sake of saving lives.

These are the things that will prevent one from being admitted into hospital in the first place.

But for those unfortunate ones who do become ill and need hospitalisation, we should be assured our doctors and nurses in facilities are doing a terrific job.

They have hitherto kept the morbidity and mortality rates lower than the average that is seen globally. We must salute each and every health care worker in this country for putting South Africa in the leadership of global COVID-19 combat.

For each and every patient on advanced levels of respiratory support that is pulled through, this is a result of the highest quality care that anyone could attain.

For every patient that is discharged and recovered, this is a celebration of South African medicine which is world famous for its excellence and leadership in many areas, particularly infectious diseases.

We once again appeal to the public to partner with government in the face of COVID-19.

We are riding into the storm, but, together, we will prevail.

Dr. Zwelini Mkhize

Minister of Health

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