

Faculty of Health Sciences

Hypertension in Africa Research Team

Covid-19 HART Information Sheet

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Figure 1: SARS-CoV-2 (2019-nCoV) spike protein, which belongs to class I virus fusion protein, contains two subunits, S1 and S2. S1 mainly contains a receptor binding domain (RBD), which is responsible for identifying cell receptors. S2 contains the basic elements needed for the membrane fusion process. It has been reported that SARS-CoV-2 (2019-nCoV) spike protein interacts with human ACE2 to infect human respiratory epithelial cells. (Creative Diagnostics, 2020)

Transmission (spreading) and infection





Figure 3: Zoonotic Transmission (Biotek Webinar 2020)

Screening for SARS-Cov-2 virus (COVID-19)

Screening tests are done in South Africa when it is established that a person has travelled to high risk countries/areas, had contact with anyone with confirmed covid-19 in the last 14 days, and when a person has symptoms such as fever, cough and difficulty in breathing. Your forehead is scanned to take your temperature.

Testing for SARS-Cov-2 virus (COVID-19)

There are two types of Covid-19 tests

 A viral test tells you if you have a current infection: Testing for COVID-19 involves inserting a 6-inch long swab (like a long Q-tip) into the cavity between the nose and mouth (nasopharyngeal swab) for 15 seconds and rotating the swab several times. The swabbing is then repeated on the other side of the nose to make sure enough material is collected. The swab is then inserted into a cooler box and sent to a lab for testing.

Sample preparation includes SARS-CoV-2 RNA extraction that entails

the process of breaking cell membranes through centrifugation buffers to release the RNA and to separate this RNA from other cell components without damaging the fragile RNA. RNA extraction can be performed manually or with automated platforms. Guanadinium thiocyanate is generally used for its strong RNase inhibitor and protein denaturant properties. At this stage the genetic material is not enough to be detected and is amplified through reverse transcriptase-Polymerase Chain Reaction (PCR). The first complementary DNA (cDNA) strand is synthesised from the RNA sample using a reverse transcriptase enzyme. DNA sequences known as primers and another enzyme, usually Taq polymerase are added to create more DNA copies. This process is repeated for 20-30 cycles that exponentially amplify the DNA. Primers used in the amplification process separate from their respective probes, releasing a dye which generates a fluorescence signal that can be detected known as real time-PCR.



Figure 4: SARS-CoV-2 testing procedure (Dheda et al., 2020)

- a. Having the complete virus sequenced was a scientific breakthrough to design primers that will only detect SARS-CoV-2 and no other closely related coronaviruses that would give false positive results.
- b. Testing can take a matter of hours to complete and is safe and robust. The technology lends itself to high-end automation, allowing the processing of large numbers of samples with minimal handling by a technician.
- c. Virus testing can only identify patients with active infection. Individuals within the recovery period of COVID-19 illness might not have detectable virus and may test negative.
- d. If a swab is done in the incubation window after a person is exposed, but before the infection has developed, the test can come back negative.
- e. Studies found that saliva samples taken from just inside the mouth provide greater detection sensitivity and consistency throughout the course of an

infection than the broadly recommended nasopharyngeal (NP) approach. Once tests and laboratories are validated for using saliva, this could be rapidly implemented and immediately resolve many of the resource and safety issues with SARS-CoV-2 testing.

The real-time reverse transcription polymerase chain reaction (rRT -PCR) test is the current gold standard diagnostic test but is not considered to be optimal in every aspect. Austell Pharmaceuticals (Pty) Ltd, a local South African pharmaceutical company already developed a new diagnostic test under the leadership of Professor Anne Grobler, a former director of the NWU's Preclinical Drug Development Platform. This test can deliver results faster, is less expensive, detect the genetic material of the SARS CoV-2 virus very specifically and provide results with the same accuracy as the currently used kits supported by the Centers for Disease Control and Prevention and the World Health Organization. For approval, test validation and evaluation in clinical samples is necessary. The NWU's Faculty of Health Sciences has been requested to perform these tests.



Figure 5: Testing and Detection (Biotek Webinar 2020)

- 2. An antibody test tells you if you had a previous infection:
- a. This tests for the body's immune response to the virus and can tell an individual if they have been previously exposed to infection with SARS-CoV-2. A blood sample is taken and tested for the presence of antibodies such as IgM or IgG developed by the immune system. It can take 1-3 weeks after infection to make antibodies. We do not know yet if having antibodies to the virus can protect someone from getting infected with the virus again, or how long that protection might last.
- b. Antibody tests can be performed in specific laboratories but also can be adapted into a testing format for community use. A number of rapid tests for use in community pharmacies or at home has been approved for use internationally.
- c. According to the developer of one such antibody test, Swiss pharma giant Roche, the rapid test has a specificity greater than 99.8% and sensitivity of 100%, pinpointing antibodies to COVID-19 present in blood samples.

SARS-CoV-2 and the Host **BioTek** The Host Immune Response to SARS-CoV-2 A part of Agilent **Clinical Data CT: Ground Glass Opacities** ↑ Neutrophils ↓WBC, Lymphocytes ↑D-dimer, Urea, Creatinine ↑ IL-2, IL-6, IL-7, IL-10, Gines (e.g. IFN-CSF, IP-10, MCP-1, MIP-1a, TNFa Luna Tissue Inflammation ThICTHE ed from Rokni, M. et al 2020 Imm is of SARS-CoV-2 ng an outbreak in Iran: Con on with SARS and ME v Med Virol 2020:1-6

SARS-CoV-2 and the immune response

Figure 6: The host immune response to SARS-CoV-2 (Biotek Webinar 2020)



Figure 7: Interfering with Interferon (Biotek Webinar 2020)

COVID-19, age and comorbidities

Current clinical data suggest that older people and people with other comorbidities, including cardiovascular disease, diabetes, chronic respiratory disease and hypertension, appear to develop serious COVID-19 illness compared with others.

COVID-19 and age

Breakdown of the number of COVID-19 deaths in the Western Cape according to age confirm the age aspect.



Figure 8: Breakdown of COVID-19 deaths in the Western Cape according to age (Winde 2020)

COVID-19 and Hypertension

Hypertension remains one of the most common comorbidities linked to an increased risk for COVID-19 infection and worse outcomes.



IMPORTANT! This does not necessarily imply there is a causal relationship between hypertension and COVID-19 as well as the severity of its effects.

 Hypertension is highly common in the elderly, and older people seem to be the ones mostly infected with COVID-19 and experience severe effects.

Therefore: It is not yet clear if uncontrolled blood pressure is a risk factor for COVID-19 or if controlled blood pressure (with medication) is or is not less of a risk factor.

What about treatment of hypertension with angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)?

This is known:

- 1. SARS-CoV-2, the virus that causes COVID-19 enters the lungs via a member of the renin-angiotensin-system (RAS), known as angiotensin-converting enzyme 2 (ACE2). Binding of the virus to ACE-2 receptors allows entry into the lungs.
- 2. ACE inhibitors and ARBs increase ACE2 levels.

Theoretical assumptions:

By increasing ACE2, more SARS-CoV-2 will bind to the lungs, followed by pathophysiological process leading to greater lung injury.

Experimental evidence:

ACE-2 protects from lung injury by antagonising the inflammatory effects of angiotensin II.

Therefore:

By reducing the formation of angiotensin II with ACE inhibitors or blocking the effects of angiotensin II with ARBs, there will be a reduction in inflammation at system level and in target organs such as the heart, lung and kidney.

So far, there is no evidence to show that hypertension has a causal effect on COVID-19 outcomes.

There is also no concrete proof that ACE inhibitors or ARBs are harmful in COVID-19 patients.

Based on current evidence, use of antihypertensive medication targeting the renin-angiotensin-aldosterone system should be maintained for the control of blood pressure.

COVID-19 and HIV

Does HIV increase the risk to get COVID-19?

People living with HIV (approximately 7,97 million in 2019) who are on effective treatment do not seem to have an increased risk of getting COVID-19 or developing severe symptoms at present, also not in the Western Cape, South Africa.

COVID-19 deaths with HIV as comorbidity is indicated as 13% (Table 1) versus diabetes as 34% and hypertension as 32%.

Analysis of deaths in the Western Cape:

The breakdown of deaths to date in the Western Cape is as follows:

| HIV | 13% |
|---------------------------------------|-----|
| Diabetes | 34% |
| Obesity | 6% |
| Hypertension | 31% |
| Previous TB | 1% |
| Cardiac | 8% |
| Chronic Kidney Disease | 3% |
| Chronic Obstructive Pulmonary Disease | 4% |
| >1 comorbidity | 32% |
| No comorbidities | 41% |

Table 1: Breakdown of COVID-19 deaths in the Western Cape 6 May 2020 (Winde 2020)

- Important to be virally suppressed and have high CD4 count and low viral load
- People living with HIV and TB may be more susceptible to COVID-19 and may develop serious illness.

What about treating COVID-19 with ART?

Insufficient data to assess the effectiveness of any type of antiretrovirals.

A recent study published in the New England Journal of Medicine showed that a combination of lopinavir and ritonavir – both antiretrovirals used to treat and prevent HIV – was not associated with clinical improvement or mortality in seriously ill patients with COVID-19 compared to standard of care alone.

COVID-19 and TB vaccination

- Besides being a vaccine for TB, BCG (Bacille Calmette-Guèrin) vaccine has beneficial non- specific effects on the immune system and the question arose whether vaccination with the BCG vaccine could have a measurable and favourable impact on COVID-19.
- Although early results seem promising, research is ongoing, mostly in countries where BCG vaccination is not given to children anymore. Thus insufficient data is available to come to a clear conclusion.

References

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