

# SA Heart® Statement on COVID-19 and cardiovascular disease

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Cardiovascular disease (CVD) is the leading cause of death worldwide and globally claims up to 17.9 million lives every year. It is responsible for a third of all deaths,<sup>(1)</sup> most of which are occurring in the developing world, including South Africa which is experiencing a rapid rise in CVD-related morbidity and mortality. For example, in 2019, more South Africans died of CVD than of all cancers combined.<sup>(2)</sup>

The South African Heart Association (SA Heart®) is an association of cardiologists, paediatric cardiologists, cardiac surgeons, as well as allied cardiac professionals, whose vision is to advance cardiovascular care for each of our country's citizens and to be the scientific leaders in South African cardiac healthcare

delivery, education and research. As such, we are ideally placed to advise the National Department of Health (NDoH) about the cardiac implications of the COVID-19 pandemic, as well as how we tackle non-communicable cardiovascular disease (NCD) going forward.

## CVD IN SOUTH AFRICA & COVID-19

Approximately 215 people die daily from heart disease or strokes<sup>(3)</sup> and COVID-19 which has diverse clinical manifestations that can involve the heart and circulatory system, is likely to increase these numbers. Patients with underlying CVD, diabetes, hypertension and obesity are also at greater risk for complications and an adverse outcome, if they contract the virus.<sup>(4)</sup> There is therefore more to consider than the issue of oxygenation and respiratory distress.

## CVD HEALTHCARE RISKS DURING THE EPIDEMIC

Patients with underlying CVD, diabetes and hypertension are at increased risk of not receiving the required level of care during the pandemic. Because of a fear of contracting the virus, many patients with CVD are cancelling follow-up appointments or not seeking medical attention in the first place. In the public sector, access to care for patients with chronic conditions has been seriously compromised because of closed clinics and outpatient departments.

SA Heart® is therefore increasingly concerned and we fear a possible second public health emergency with respect to CVD and other NCD. It is a world-wide phenomenon that patients ignore symptoms and acute cases present at emergency facilities too late and very ill or they die at home. Out of hospital cardiac arrests have recently soared; patients are also less likely to receive cardiopulmonary resuscitation from bystanders and are more likely to die before reaching hospital.

Face-to-face visits are certainly required, and patients should not cancel a clinic appointment without first consulting their physician. Where there are signs that COVID spread is diminishing, many patients will benefit from increased access to care and opening up of health facilities. We wish to emphasise

that, even during the pandemic, the public (particularly if symptomatic with chest pain, shortness of breath or dizziness) should not delay in seeking urgent healthcare services.

Every minute counts with acute myocardial infarction and “time is muscle”. Hospitals and cardiologists are certainly doing their utmost to treat patients in a safe environment. The unprecedented burden of COVID-19 on health systems threatens to exceed hospital capacity, making it a challenge to care for other emergencies requiring hospitalisation, such as acute coronary syndromes.<sup>(5)</sup> As healthcare facilities divert resources to manage the COVID onslaught, we call on the system to maintain some mechanisms for patients with cardiac and other non-COVID emergencies to receive appropriate care. Importantly, aside from events related to the pandemic, the management of STEMI (ST Elevation MI), which is the most devastating manifestation of acute coronary syndromes, is of concern. We urge that facilities that are the first point of medical contact, be equipped with functioning ECG machines, that essential therapy such as fibrinolytic agents (Streptokinase or Tenecteplase) be made available at such facilities, and that access to a catheterisation laboratory for coronary angiography within 24 hours (the recommended standard of care worldwide) be considered. SA Heart®, through its members both in the public and private sectors, hopes to be involved in facilitating such a pathway of care, especially with the envisaged implementation of National Health Insurance.

COVID-19 is not only a respiratory disease. Attending clinicians must be vigilant for cardiovascular complications, such as thrombotic events, arrhythmias and myocarditis. Potential mechanisms include virus-induced inflammation, increased risk of thrombosis, ischaemia due to increased oxygen demand, microvascular ischaemic injury and an accelerated immunologic response (cytological storm) mediated injury. There have been reports of cardiac complications including myocardial injury, acute coronary events, and heart failure. Such patients with these complications (including troponin elevation) are at a higher risk of mortality.<sup>(6)</sup>

It is a major concern that a proportion of patients on chronic medications are presently not collecting medication from hospitals and without treatment their condition may well deteriorate. For chronic patients that are stable, we applaud the NDoH's decision to allow patients to receive year-long medication rather than the usual 6-month prescription and we believe this will be of great benefit. However, for many patients, such as those on Warfarin (who need frequent INR monitoring) or those with poor sugar and blood pressure control or advanced chronic heart failure, this is not an ideal approach, and we recommend strategies to provide access for these patients be explored.

In a recent editorial in the Cardiovascular Journal of Africa, Lukhna et al. provide the following salient practical advice:

“The vast majority of patients presenting with symptoms and signs of acute cardiac disease will indeed have acute cardiac disease and should be treated as such. Although the finding that the prevalence of hypertension, diabetes, obesity and cardiovascular disease among those presenting with symptomatic COVID-19 is high, this does not mean that the corollary is also true (that among those presenting with cardiovascular syndromes, COVID-19 is high). In fact, the opposite is true: most patients presenting with acute cardiac disorders as their primary presentation will be COVID-19 free, and the vast majority of patients with COVID-19 do not have cardiovascular complications. This is important because the temptation to delay the diagnostic work-up and treatment of acute cardiac syndromes until patients have been tested and the disease has been excluded, has major consequences and should be avoided. The outcomes of most acute cardiac disorders such as acute MI are time-sensitive and time-dependent. So, if you need to test patients for COVID-19, do so, but don't ignore the obvious in front of you.”<sup>(6)</sup>

### CHILDREN & COVID-19

Children are not as susceptible as adults to contracting COVID-19. However, the full extent of COVID in children is wide ranging and includes the socio-economic effects of poor nutrition, interpersonal violence and absence of usual childhood interactions on well-being. Five percent of patients that have been admitted to hospital are children and fortunately less than 1% have died from the infection.

Multisystem Inflammatory Syndrome (MIS-C), also called PIMS-TS (Paediatric Inflammatory Multisystem Syndrome-Temporality associated with SARS-CO-V-2) is a new “hyperinflammatory syndrome” in children and adolescents associated with SARS-Cov-2, bearing some similarities with Kawasaki Disease. There are slight differences in the case definitions between the UK, WHO and USA, but the principles of diagnosis are similar. These children may present extremely ill. The condition is amenable to treatment if diagnosed early. Current literature indicates that MIS-C occurs about a month after the peak of the pandemic. These children require intensive care management and thus early diagnosis is important for improved outcomes.

- A case definition was rapidly produced by the Royal College of Paediatrics in the UK and is helpful to define MIS-C / PIMS-TS further: A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP, and lymphopaenia) with evidence of single or multi-organ dys-

function (shock, cardiac, respiratory, renal, gastrointestinal, or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki Disease.

- Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, and infections associated with myocarditis such as enterovirus.
- SARS-Cov-2 may be positive or negative.

Risk communication is important in order to raise awareness in the medical community about PIMS-TS and inform parents and caregivers about the possible signs and symptoms. Timely contact with a healthcare worker should also be stressed. According to our European colleagues, risk communication should emphasise that PIMS-TS is a rare condition and that its potential link with COVID-19 is neither established nor well understood. However, it is well documented that presentation of these cases lagged by about 4 weeks from the initial peak of the pandemic in countries like the UK and many cases were of African or Asian descent. Therefore, we recommended that:

- PIMS be notifiable.
- Research be carried out to understand the disease more.
- A national registry should be established with the cases.
- There be longitudinal follow-up of cases with specific standardised research questions.

Although children infected with SARS-COV-2 are asymptomatic or mildly symptomatic, children with underlying conditions appear to be among those at higher risk of severe disease. The numbers of those becoming seriously ill and requiring hospitalisation are still far less than adults with cardiovascular disease and the specific risk for congenital heart disease (CHD) remains unclear. In the face of the pandemic, the greatest threat to child health is likely from the disruption of current healthcare systems.<sup>(7)</sup>

Disruption already seen within the paediatric cardiac services includes:

- Postponement of elective clinic visits, surgery and cardiac catheterisations to reduce hospital and clinic volumes.
- Reduced access to healthcare services: Poor availability and increased cost of transport coupled with reduced household incomes, as well as confusion regarding safety and legality of movement, which has increased the number of patients missing essential visits and the filling of their prescriptions. Limited internet and cellphone access reduces the utility of remotely filling prescriptions and

“teleconsultations”. CHD patients are at increased risk of severe disease from vaccine-preventable disease outbreaks due to reduced immunisations.

- The reluctance of patients requiring urgent interventions to be admitted for fear of contracting COVID-19 infection in hospital, has been exacerbated by reduced bed availability for boarder mothers in some hospitals, as well as the prohibition or severe restriction of visitors in most institutions.

Should the pandemic progress as anticipated and services be overwhelmed or strained, surgical and catheter interventional services are likely to be further reduced or suspended. This will compound the existing burden of undetected and untreated CHD contributing to the significant mortality and morbidity of these patients. We wish to strongly emphasise that cardiac intervention for paediatric patients is extremely time sensitive. Timeous surgery is essential for children with CHD detected soon after birth; this also includes older children, especially with intra-cardiac shunts.

Early detection of critical congenital heart disease (CCHD) through new-born pulse-oximetry (POx) screening is an effective strategy for reducing paediatric morbidity and mortality rates and has been adopted by much of the developed world. Evidence now confirms that it is also cost-effective and does not over-burden the health system, while identifying CHD early in the neonatal period. Local data show that implementation of a POx programme is feasible with a high success rate of screening along with sufficiently low barriers and resource drain. We have shown that the anticipated barriers of increased cardiology service workload and cardiac care costs, high equipment expenses and a lack of parent and nursing acceptability, were not encountered.<sup>(8)</sup> This is currently ideal for a community-level project as pulse oximeters now clearly have a role in all health centres post-COVID. The Paediatric Cardiac Society of South Africa (a special interest group of SA Heart®) calls for and are very keen to assist with:

- Ensuring that there are pulse oximeters in all birthing institutions in the country.
- Recognition of the unique elements of measuring POx in neonates in order to diagnose CCHD.
- Recognition of the importance of heart disease in children in the Road to Health book by introducing POx screening for all new-borns and recording this in the book.

### CARDIAC SURGERY & COVID-19

With respect to the state of cardiac surgery during the pandemic, operations are currently reduced to emergencies only.

**TABLE I: General advice: Paediatrics and COVID-19.**

General community	General practitioners and referring paediatricians	Patients and parents
<p>All children should receive their routine vaccinations during this time.</p> <p>All children should be protected, and good food, exercise and regular activity should be encouraged.</p> <p>Children should not be separated from their parents if at all possible, with special emphasis on the breastfeeding infant.</p> <p>We support the role of schools (and the workplace) beyond just education: activity, social interaction, but also food provision and protection from household violence. However, in the case of high-risk cardiac patients, the benefit of return to the school should be carefully balanced against the risk of severe infection.</p>	<p>Cardiology services are still open albeit curtailed – speak to your local cardiologist if concerned.</p> <p>Shortness of breath in children must be considered as a cardiac symptom, not only of COVID.</p> <p>Conduct POx screening at 24 hours of age to rule out CCHD.</p> <p>Consider vaccination against the influenza virus and Palivizumab for respiratory syncytial virus in infants if available</p> <p>Discuss COVID status of patient PRIOR to referral to a tertiary centre.</p>	<p>We stress the importance of continuing with current medication.</p> <p>Contact your cardiologist if you are have an upcoming appointment – some of these appointments can be done remotely.</p> <p>Contact your cardiologist prior to coming to hospital if possible; each hospital has new protocols regarding admission and screening upon arrival.</p> <p>High-risk cardiac children (complex defects, single ventricle), severe cyanosis, reduced cardiac function or heart failure, arrhythmias, pulmonary hypertension, heart surgery within the last three months, or heart transplant patients should continue to be seen regularly.</p>

Adult patients with valvular heart disease can wait for a period of time before surgery. Patients with ischaemic heart disease are dealt with on an emergency level with operative numbers presently reduced to about 30% of previous figures.

**STAFFING & COVID-19**

Staffing of ICU units has been problematic in the Free State. Universitas Hospital has addressed this with an ambulatory care unit with high flow oxygen and continuous positive airway pressure (CPAP) to prevent lung injury. The cardiothoracic surgery department in the Free State has allocated 50% of staff to respiratory care for COVID patients.

In an article entitled “Supplemental Oxygen Therapy in COVID-19”, Smit, et al.<sup>(9)</sup> report:

“South Africa faces a significant shortage of ventilator supported intensive care (ICU) beds during the peak phase of the COVID-19 pandemic, further exacerbated by severe ICU-staff shortages. It is also recognised that the mortality rate for ventilated patients might be as high as 88%. In the absence of a vaccine and proven effective pharmaco-therapy, it is important to understand the pathophysiology processes causing progression. Early type-L COVID-19, associated with pulmonary thrombo-embolism may be amenable to treatment with careful anticoagulation and supplementary oxygenation strategies. This could attenuate the severe hyperventilation phase causing patient self-inflicted lung injury (P-SILI) that contributes to the development of type-H COVID-19 pneumonia. Type-H is an acute respiratory distress syndrome (ARDS) variant requiring intubation and ventilation and is associated with a very high

mortality rate. Stepwise non-invasive positive pressure ventilation strategies (NIPPV) providing supplementary oxygen have shown benefit and, in the South African context, may be the only realistic strategy to deal with high numbers of patients during the early type-L phase of the disease. To address this, a mobile wall unit has been created that allows for stepwise supplementary oxygen therapy according to protocol, including non-invasive positive pressure ventilation (NIPPV) as well as standard ventilation. The unit can support modified wards, field hospitals or high care areas in existing facilities. It allows for NIPPV support within a hood system linked to scavenger lines addressing aerolisation. Standard humidification, flow regulators, vacuum systems, high flow nasal canula (HFNC) and continuous positive airway pressure (CPAP) systems as well as monitoring equipment that are readily available in South Africa can be linked to the system addressing availability issues.”

**ACE- INHIBITORS & ANGIOTENSIN RECEPTOR BLOCKERS AND COVID**

SA Heart® was specifically asked about the risks of ACE-inhibitors (ACE-Is) and angiotensin receptor blockers (ARBs) in patients with COVID-19 disease:

- Given that there is a significant proportion (30% - 40%) of hypertensive patient among critically ill COVID-19 patients, concerns have been raised about the potential risk associated with Renin-Angiotensin-Aldosterone (RAAS) Inhibitors.
- In a step-by-step article, Manga<sup>(10)</sup> explains that the SARS-CoV-2 virus through its spike protein, binds to the ACE2 receptor and thereby gains entry into host cells. Early

reports suggested that because ACE-Is and ARBs upregulate ACE2 expression these agents may facilitate COVID-19 infection or contribute to increased severity of the disease.

- However, the scientific evidence thus far is different and currently there is no compelling evidence that withdrawal of ACE-Is or ARBs prevents infection or impacts clinical outcomes. Importantly, peer-reviewed studies published to date have not found higher rates of COVID-19 infection, greater severity of COVID-19 disease, ICU admissions or increased mortality among patients treated with RAAS inhibitors. There are some studies even suggesting a lower mortality risk in those on these agents.

Based on current evidence all major medical societies including SA Heart®, we have recommended continuation of RAAS inhibitors in those patients already on RAAS inhibitors. There are at least 7 randomised trials currently ongoing to evaluate clinical outcomes for COVID-19 patients treated with ACE-Is or ARBs. Until more evidence becomes available, it is important for clinicians to treat all hypertensive patients to target based on current practice guidelines.<sup>(10)</sup>

**Conflict of interest: none declared.**

#### In summary, our final recommendations:

- More central points for collecting medication away from clinics and hospitals. Resourcing clinics to see more patients. Improving ease of decentralised access to medication. Systems need to be enabled so that patients can collect their medications from primary healthcare centres, thus allaying the fear of attending tertiary facilities where COVID patients are being treated.
- Broad-based information dissemination to the public around the importance of seeking urgent medical care with the onset of new possible cardiac symptoms.
- Patients with CVD and NCDs are still able to attend their follow-up appointments; they must be encouraged to adhere to medication and treatment plans.
- Information dissemination (public, referring hospitals) about MIS-C in children and the importance of early treatment thereof.
- Utilise the opportunity to improve integrative services: i) Pulse Oximetry for Critical Congenital Heart Disease, while the use of oximeters have gained importance; ii) Create hypertension outreach clinics to screen for and therefore manage, recognising its role as a risk factor for mortality in COVID-19. SA Heart® is prepared to help with both these projects.
- Information and education of other healthcare providers/emergency rooms that cardiac patients might present with symptoms similar to COVID-19, and care must be taken to make an accurate diagnosis.
- Screening for especially paediatric patients in safe areas away from the hospitals to address both parental fear and to reduce hospital staff infection.

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