

COVID-19: The virus, vaccine and paediatric heart

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The coronavirus disease 2019 (COVID-19) pandemic has resulted in much morbidity and mortality around the world. The development of vaccines has cushioned the effect of the virus and thus, provided hope in the fight against the disease.¹ Yet, there are still small battles with COVID-19, at the bench and bedside. Medical professionals in Singapore and beyond have all had a long battle against COVID-19. Many of us would have some degree of pandemic fatigue. However, given the endemic nature of COVID-19 now and with a real possibility of another emerging infectious disease, it is important and timely to reflect on our corporate experience and consolidate the current science.

In this issue of the *Annals*, Broberg et al. presents a well-written, well-researched and comprehensive review on the cardiovascular effects of the SARS-CoV-2 virus and the COVID-19 vaccine on the paediatric heart.³ There have been unique aspects of the pandemic in Singapore² and around the world from a paediatric perspective.⁴ In their paper, Broberg et al. consider direct viral effects on cardiac function and rhythm, the immunology of the virus, as well as the effects of mRNA vaccines on the paediatric heart. This paper provides scientific rigour to issues such as differentiating viral myocarditis from multisystem inflammatory syndrome in children (MIS-C), addresses concerns regarding surveillance for adverse vaccine events, and considers the current follow-up requirements for long-term cardiovascular sequelae.

The authors have done well to put together a much-needed paper that is a consolidated review of current science. This paper is expected to be a good guide for patient care. The perspectives, opinions and conclusions are relevant and applicable to Singapore. For further contextualisation to paediatric practice in Singapore, I would like to refer readers to 2 papers in particular: Nadua et al.⁵ describe a case series of 12 paediatric patients with MIS-C presenting to KK Women's and Children's Hospital, while Yap et al.⁶ is a paper on the epidemiology of COVID-19 vaccine-associated myocarditis in the Singapore context. Having had the privilege to read the article, *Cardiovascular effects of COVID-19 in children* in this journal, I would like to highlight a few points for further consideration.

Building the evidence base. In paediatrics, the care of the child remains our foremost priority. Academic clinicians have the responsibility of building the evidence base. The paper by Broberg et al. calls for more research on the cardiovascular sequelae of COVID-19. There remains much to be understood about genetics, immunological mechanisms, management options and long-term sequelae of COVID-19 myocarditis, MIS-C and mRNA vaccine-associated myopericarditis. There are a number of questions yet to be answered. Are there human genetic variants associated with increased susceptibility to COVID-19 infection and severe COVID? Is there a genetic predisposition for MIS-C? Which groups of children are at the greatest risk of being infected with COVID-19 and which are at risk of myocardial disease? What are the management options for inflammation and immunologic dysfunction associated with MIS-C? What is the long-term arrhythmogenic risk of vaccine-associated myocarditis? We should continue to establish data and scientific evidence on the biological and social determinants of COVID-19 infection and its influence on the cardiovascular system.

Multidisciplinary clinical guidelines. We have learnt that the management of COVID-19 requires collaboration across medical specialties. Honing in on the Singapore context, the paediatric academic community here is encouraged to continue working together as multidisciplinary teams on key aspects of COVID-19 management—to evaluate the strength of evidence and the applicability of this evidence in the population of children in Singapore. For example, the multidisciplinary team comprising paediatric intensivists, infectious disease specialists, immunologists, cardiologists and haematologists from 2 major paediatric centres had developed guidelines for the acute and convalescent management of MIS-C in the Singaporean population.⁵ It also remains important to encourage collaboration across institutions and beyond national borders to develop long-term follow-up recommendations for the viral and vaccine sequelae as clinical practice guidelines. The broad combined experience will benefit our patients.

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Need for national and international clinical registries. Pooled data from major centres will provide an important resource for clinical care⁷ and policy development. There is a need to synthesise the current knowledge following COVID-19 infection, based on current scientific literature and real-world experience. One way to pool data and track long-term outcomes is to establish registries for paediatric COVID-19 survivors, for those who had MIS-C, as well as for those with myopericarditis after COVID-19 vaccine. The weight of the evidence would be stronger with combined data.

Registries and long-term cohort studies are expensive, but there is a need to continue funding these initiatives. Given that the paediatric case numbers are small, there may be a need for the paediatric cohorts to be nested within adult cohort populations. Drawing from my experience of being funded for COVID-19 cardiovascular research during the pandemic—because severe COVID-19 numbers are lower in the paediatric age group compared with that in the adult population, the funding structure is such that paediatric studies may need to be nested within a larger cross population cohort. Singapore, having a small geographical area and a highly connected population, is particularly favourable for such follow-up cohort studies.

Guiding policy and healthcare leadership decision-making. The pandemic has taught us the need for the medical community to act proportionately on accurate, reliable and real-time information. During the pandemic, there was much debate surrounding the need to vaccinate children against COVID-19 in Singapore and around the world.⁸ A strong evidence-base with good registry data will help guide healthcare policy, as the ground shifts from pandemic to endemic COVID-19.

Good long-term vaccine safety data will help medical practitioners and parents make value judgements on vaccine and booster requirements. For example, with respect to COVID-19 vaccination, based on available safety data, individual medical practitioners could reasonably advocate for vaccines in a proportionate manner, with strength of recommendation commensurate with evidence of vaccine efficacy, incidence of vaccine adverse events and virus prevalence within the context of the local situation. Furthermore, from a policy perspective, based on the prevailing COVID-19 situation in Singapore, a responsive vaccine strategy may be developed, articulated and operationalised.

Long-term sequelae and exercise recommendations. The long-term consequences of COVID-19 pertaining to cardiovascular risk remain unknown. Harmonised longitudinal studies

assessing cardiovascular aspects of COVID-19 infection sequelae in children are much needed. As mentioned by the authors, there is also a need for paediatric guidelines on sports competition and exercise after recovery from COVID-19 and mRNA vaccine-associated myopericarditis. The recommendations are currently, primarily for adult athletes and are based on expert opinion.⁹ These guidelines are not aligned internationally. Such international consensus guidelines are particularly important for safe and fair competition at national, regional and international sporting events in a post-COVID world.

As COVID-19 becomes endemic, children may remain vulnerable to COVID-19 and its complications. At the time of writing, a new variant is emerging—the BA.2.86, also known as the Pirola variant.¹⁰ With the emergence of each new variant, there are still many unknowns. Clearly, we have learnt that we cannot act with complete knowledge in this pandemic and indeed, we will need to act as the evidence continues to evolve. The article by Broberg et al. is a good consolidation of current evidence, and is useful to those interested in the cardiac complications of COVID-19.

Keywords: cardiology, COVID-19, myocarditis, paediatrics, vaccine

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