

COVID-19 and heart disease in children: What have we learned?

The world has nearly recovered from the effects of the COVID-19 pandemic. Children initially were thought to have only milder forms of the illness, but later realized to have a less common but severe form of disease named multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19. Cardiac involvement is the most serious manifestation of MIS-C.^[1] The COVID-19 pandemic resulted in widespread disruption of clinical care of all non-COVID illnesses. Children with congenital heart disease (CHD) also suffered collateral damage due to a lack of surgical facilities during the pandemic's peak. However, the COVID-19 pandemic brought out some of humanity's best facets, including the ability to come together to fight off a crisis, resilience, adaptability, and versatility. The COVID-19 pandemic has taught us a few lessons for the future and in this editorial, we discuss some of the learnings concerning children with heart disease.

COVID-19 AND HEALTH-CARE CHALLENGES

The initial phase of the pandemic posed serious challenges to the health-care infrastructure across the world, more so in low-and middle-income countries (LMICs). It exposed the under-penetrated, under-funded, and under-staffed public health sector and unregulated private health sector in India. India's response to the pandemic was commendable. However, COVID-19 provided a much-needed wake-up call for the health-care system in our country. We effectively managed the four essential components of surge capacity including staff, supplies, space, and structure. The way we were able to source increased capacity in oxygen generation and manufacture ventilators, personal protective equipment kits, masks, face shields, sanitizers, and intensive care unit beds is commendable. The major achievements included the development, mass production, and free-of-cost administration of the indigenous COVID-19 vaccine-Covaxin, and the mass production of Covishield vaccine. India also demonstrated its ability in delivering care to the 140-crore population with effective use of technology (CoWIN and Aarogya Setu applications) on a massive scale that has never been seen in our country.

MANAGING CHILDREN WITH HEART DISEASE

The COVID-19 pandemic has brought even the developed nation to its knees and overwhelmed the health

infrastructure globally.^[2] The COVID-19 pandemic created a crisis in the care of children with heart disease arising from both demand and supply side issues. Some possible reasons are summarized in Table 1. The challenges were unforeseen, and especially pronounced in LMICs like India, where the centers caring for children with heart disease are limited. A large, multicentric, retrospective study by Choubey *et al.*^[3] reported outpatient footfalls, admission statistics, and procedural numbers during the first wave from 24 pediatric cardiac centers across the country and compared it with the corresponding period in 2019. The study documented 68%–75% reductions in outpatient visits (from 54,213 to 13,878), hospitalizations, cardiac surgeries, and catheterization procedures. This is despite the maternal and neonatal care services being functional during most of the lockdown in India.

Across the globe, hospitalization rates and rates of health system utilization decreased significantly during the pandemic. Pediatric cardiac admissions and procedures were reduced by 20%–40% in North America,^[4] Europe,^[5] and South Africa.^[6] India has unique geographic, socioeconomic, and health-care access-related hurdles, which makes it difficult to compare data from other countries.^[7] However, data from a similar time frame from India suggest that children with CHD suffered more during the pandemic. The admissions for acute

Table 1: Potential concerns and consequences of COVID-19 among children with heart disease

Supply-side
Closure of OPD, inpatient services
Diversion of resources for COVID-19 care
Postponement of elective surgeries
Changing hospital priorities and policies
Restrictions posed by the local government
Healthcare personnel safety
Need for social distancing
Demand side
Fear of acquiring COVID-19
COVID-19 infection in caregivers
Lack of transportation/ambulances
Need to travel longer distances to reach a CHD-care centre-logistic issues
Affordability due to job cuts (out-of-hospital expenses)
Potential consequences for CHD surgeries
Increased death rate for children with CHD
Late presentation
Higher risk candidate for delayed surgery
Become inoperable in CHD-PAH situations
Poorer neuro-developmental outcome

CHD: Congenital heart disease, OPD: Outpatient department, PAH: Pulmonary arterial hypertension

myocardial infarction in India decreased by 35%^[8,9] and acute heart failure hospitalization by 50%.^[10] Moreover, the utilization rate of coronary angiography and percutaneous coronary intervention decreased only by 11.3% and 5.9%, respectively, during a similar time frame from across the country.^[9] In challenging situations, care for children gets lesser priority, which is a major learning from the pandemic.

On the positive side, emergency procedures including arterial switch surgery, total anomalous venous connection repair, and balloon atrial septostomy showed the least decline during this period. Government-funded tertiary care centers reported a greater reduction^[3,9] for obvious reasons and took a long time to normalize services. Data are needed on how these missed opportunities affect the natural history of CHD. Worryingly, the care of children with heart disease during the pandemic resulted in higher in-hospital mortality in India^[3] and other LMIC countries but was not universally reported.^[6,11] A greater proportion of complex surgeries, neonatal surgeries, emergency surgeries, and operating on patients with an active or recent COVID-19 infection are likely reasons for the higher postoperative mortality during the pandemic.^[3,12] Furthermore, India and other LMIC countries had a higher proportion of unoperated children admitted during the COVID-19 pandemic.^[3] Interestingly, adverse events related to pediatric cardiac catheterization did not increase, despite a high-severity case mix in the US during the pandemic.^[4] The quantum of impact and outcomes could be different during the subsequent waves of the pandemic; however, systematic studies are lacking.

OUTCOMES OF CHILDREN WITH HEART DISEASE AND COVID-19

There is evidence to suggest that children with CHD were not at a higher risk of acquiring COVID-19 infection.^[13] However, many studies suggested a higher risk of morbidity among children with COVID-19 admitted to hospitals.^[14,15] A large analysis of 339 cardiac patients from 35 international centers, who had a recent COVID illness^[16] reported a 25% hospitalization rate and 15% of children required ICU care. The study reported an overall mortality of 5%, mostly from the non-US centers.^[16] A large retrospective study from India,^[12] which included 94 hospitalized patients, however, reported a high mortality rate (13.8%). The study is one of the largest and represents real-time, cross-sectional practice across India. The chance of survival was the poorest among children from lower socioeconomic backgrounds, children with severe cyanosis, and those who needed immediate ventilation on arrival. Most of the studies identified infants, cyanotic CHD, recent cardiac procedures, complex anatomy, advanced physiological

state, and higher sickness at admission as the predictors of outcomes among COVID-19-infected children with heart disease.^[12,17,18] Other factors reported included male sex,^[18] pulmonary hypertension,^[18] obesity,^[18] and the presence of comorbidities.^[17,18]

Concerns of a higher risk for MIS-C and pulmonary hemorrhage following cardiopulmonary bypass posed significant challenges in operating among children with CHD presenting with a COVID-19 infection.^[19] However, only a handful of studies reported the outcome of COVID-19-positive children who underwent cardiac surgery. Sen *et al.*^[20] reported the outcome of early cardiac surgery among 13 children after a mean interval of 25 days of an illness. They reported one death and a thrombotic complication. In the current issue of APC, Sujana *et al.*^[21] reported the outcome of 18 children who developed MIS-C-like illness following major cardiac surgery. The incidence of unsuspected MIS-C was 3.9%, despite 2 negative RT-PCT COVID-19 tests documented before elective cardiac surgery. The children developed unusual postoperative worsening associated with ventricular dysfunction and coronary dilatation associated with a positive antibody response to COVID-19. Two children died despite intravenous immunoglobulin (IVIG), steroids, and antiplatelet drugs. Such unexpected inflammatory illness has been reported following ASD device closure also.^[22] A high index of suspicion and early aggressive anti-inflammatory treatment improved outcomes. In the unlikely event of emergency surgery during a COVID-19 illness, a florid inflammatory illness may be prevented by a multipronged strategy using steroids, IVIG, hemofiltration, use of cytokine-adsorbing hemofilter during cardiopulmonary bypass, and early peritoneal dialysis.^[23]

The ideal interval following COVID-19 infection before elective cardiac surgery is not known. However, we may extrapolate from noncardiac surgery databases. A large, multicenter, prospective cohort study from the COVIDSurg Collaborative suggested that a nonemergent surgery should be delayed for at least 7 weeks following COVID-19 infection.^[24] A separate analysis suggested that LMIC countries reported further poorer outcomes during the pandemic times.^[25] However, pediatric surgeries had the best outcomes.^[26] Several risk stratification guidelines for CHD were published for triaging cardiac procedures.^[27,28]

MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN IN INDIA—CARDIAC MANIFESTATIONS AND OUTCOME

In the 2020 issue of *Annals*, Ferrero *et al.*^[29] reported one of the earliest cardiac descriptions of MIS-C from Italy. The

authors noted all the essential features including similarity with Kawasaki disease and myocardial dysfunction associated with transient ECG and echocardiographic abnormalities. Subsequently, numerous case series from different Indian institutions reported manifestations and outcomes of MIS-C.^[30-33] Cardiac involvement is reported among 54%–60% of children in a systematic review^[34] and a large multisite retrospective Indian study.^[35] The common and uncommon cardiac manifestations of MIS-C are summarized in Table 2. In the current issue, Shah *et al.*^[42] report the medium-term outcomes of 144 children with MIS-C. It was reassuring that complete resolution of cardiac manifestations was seen in the majority (92%) of children within 3 weeks of illness. A multinational meta-analysis involving 547 children with MIS-C reported a mortality of 2.5%.^[43] Persistent left ventricular (LV) dysfunction at 6 months was found only in 2% of children, compared to 47% in the acute phase. Coronary abnormalities were observed in 25% during the acute phase, however, persisted only in 5% at 6 months. Strain imaging, cardiac MRI (magnetic resonance imaging), or the use of biomarkers picked up more cardiac involvement in MIS-C. In a recent study, the longitudinal left atrial stain was abnormal in all 6 children despite normal LV systolic and diastolic function parameters.^[44]

Whitworth *et al.*^[45] reported a 6.5% incidence of thrombosis in children with MIS-C. The thrombosis rates were 0.7% and 2.1% among symptomatic COVID-19 and asymptomatic SARS-CoV-2 infection children, respectively. Mehta *et al.*^[38] reported the rare occurrence of complete heart block in two children, of whom one recovered and one needed pacemaker implantation. The authors have summarized all the uncommon electrophysiology abnormalities seen in association with MIS-C. The conduction system blocks in MIS-C are like those encountered in diphtheria and Lyme disease.^[46]

Table 2: Cardiac manifestations of multisystem inflammatory syndrome in children

LV dysfunction 50%
Shock
Coronary artery dilatation 25%
Mitral regurgitation
Pericardiac effusion
Thrombotic complications
Intracardiac thrombosis - in MIS-C ^[36]
Arrhythmias
Ventricular tachyarrhythmias
Atrial tachyarrhythmias
Atrial fibrillation ^[37]
First-degree and second-degree heart block
Complete heart block ^[38]
Vascular complications
Renal artery narrowing ^[39]
Ascending aortic pseudoaneurysm ^[40]
Infective endocarditis ^[41]

LV: Left ventricular, MIS-C: Multisystem inflammatory syndrome in children

Pediatric cardiologists are forced to make decisions without randomized controlled trial (RCT) evidence, and the COVID-19 pandemic exemplified the conundrum. The treatment strategies for MIS-C were mostly extrapolated knowledge from the management of Kawasaki disease. Corticosteroids, IVIG, and anticoagulation formed the cornerstone of therapy. A few multicenter studies tried to compare the outcomes of various regimens with conflicting results,^[47,48] and an RCT, the SwissPed recovery trial^[49] was underpowered. Not doing a large adequately powered RCT to compare the various treatment modalities for MIS-C is a missed opportunity for pediatricians and pediatric cardiologists. Effective networks must be established, to quickly answer important therapeutic decisions in future pandemics, as it was done in adults during the pandemic.

The COVID-19 pandemic also had a positive impact on health-care infrastructure, research and publications, medical education,^[50] and patient perception of doctors. This presented a unique opportunity for collaboration and many national and international multicenter studies were carried out and reported during this period. Publication timelines were fast-tracked internationally to allow the available research findings to become publicly available, and this led to an early clinical impact with treatment guidelines being updated at regular intervals throughout the pandemic. The forward momentum must be carried forward and we should not simply go back to our old ways at the end of the pandemic.

COVID-19 PANDEMIC: KEY LEARNINGS

Some of the key learnings from the pandemic include the fact that things evolve very quickly than health systems ever imagined in the era of artificial intelligence, big data, and modern communication. The public is more adaptable than some health-care systems. Fear, risk, and goals are continuously redefined. Health-care systems have a huge capacity for adaptation and resilience. The ability of the frontline systems to rationalize and optimize the available resources with resilience during the crisis is the most important lesson learned during the crisis. Telemedicine revolution, personal hygiene, and reinforcement of infection control were the major gains during the pandemic. We need direction to rethink the way health care is delivered. Some of the solutions^[51,52] that we would like to implement in a future crisis are summarized in Table 3.

For Indian children with CHD, we need to improve outcomes by defining appropriate care during future pandemics. Furthermore, everyone is not treated equally,^[53] especially in a pandemic and the inequality widens. Indian children with CHD requiring cardiac surgery are more vulnerable. We need to reorganize the way acute care for these children is delivered with

Table 3: Solutions for future challenges

Implement new care models
 Realigning resources - space, personnel and supplies
 Revamp governance
 Rapid and timely policy change
 Shared goals
 Improve decision-making
 Task sharing/task shifting
 Incentivize and improve productivity
 Semi-elective/urgent routine should continue
 Essential acute care departments to function optimally
 Transport and logistics of acute emergency care
 Digital solutions
 Telemedicine
 Remote care for even hospitalized patients
 No contact triaging
 Standardized data and analytics
 Setting up registries and starting relevant RCTs
 Continuous monitoring of pandemic and nonpandemic-related outcomes

RCTs: Randomized controlled trials

a focus on transport, finances, and logistics. Leadership and guidance would play a major role. Societies such as the Pediatric Cardiac Society of India should come up with registries, RCTs, position statements, guidelines, and evidence-based recommendations on treatment protocols with regular updates based on the available scientific research during such pandemics. We need to maintain public trust and protect the staff as well as the patients. We need to apply digital solutions more widely. The successful use of televideo consultations and outpatient management should be carried forward even during nonpandemic times. The launch of the e-sanjeevani outpatient department by the government is in the right direction. Indian pediatric cardiology community should make the best use of it.

India is struggling with a huge burden of children with CHD needing intervention with limited health-care resources. Over the past few decades, the government has made efforts to reduce the cost and provide insurance coverage to the vast majority of the Indian poor. The recent pandemic has brought this newly found energetic movement to slow down significantly. Pediatric cardiac set-ups in India, especially the pay-for-service hospitals, faced an existential crisis. Pediatric cardiac surgery in India is very sensitive to the economic milieu. These hospitals faced supply-side constraints, cash flow problems, higher costs, quarantine protocols, and loss of revenue. Fortunately, most of them were able to innovate, restructure, and bounce back rather quickly from the pandemic. The government on its part, never stopped the support schemes for emergency surgeries.

However, in a country like India, COVID-19-related backlog cannot be cleared by returning to pre-COVID-19 capacity. A recent study^[54] showed the pandemic-related backlog of procedures for severe aortic stenosis in adults and suggested strategies to overcome the crisis.

We must leverage additional capacity and implement evidence-based strategies to minimize complications and prevent deaths among children awaiting cardiac surgery in India.

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