The impact of COVID-19 on the practice of pediatric cardiology: a narrative review

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Background and Objective: Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome virus 2 (SARS-CoV-2), is a global pandemic evolving in real time and affecting persons of all ages. Contemporary pediatric data demonstrate that children of all ages are susceptible to SARS-CoV-2, and that infants under 1 year of age are at risk for severe disease although this still is a relatively rare outcome. This narrative overview discusses the impact of the COVID-19 pandemic on various aspects of pediatric cardiology, and proposes strategies to mitigate disruptions, so as to better future-proof our practice.

Methods: PubMed, EMBASE and Google Scholar databases were searched for literature in English from year 2020 through April 2021.

Key Content and Findings: There is an overall decreased in ambulatory clinic volume with clinical visits restricted for emergency purposes. Cardiovascular services including transthoracic echocardiography, fetal echocardiography, cardiac catheterization and intervention, and cardiac surgeries have been reported to have declined and performed on a priority basis. Infants and young children with hemodynamically significant congenital heart disease, cyanosis and pulmonary hypertension may constitute a vulnerable group with known susceptibility to acute infectious viral illnesses, and could be considered high-risk for complications related to COVID-19 infection. Associated with SARS-CoV-2, the newly described multisystem inflammatory syndrome in children have led to serious and life-threatening illness in previously healthy children and adolescents.

Conclusions: COVID-19 has had a profound impact on the practice of pediatric cardiology and will continue to affect all aspects of patient care. As pediatric cardiologists play an important role in the care and outcomes of these patients, the approach to the evaluation and management of children with heart disease in the COVID-19 era, will evolve as the pandemic rages on. Strategies incorporating new technology-enabled options, maintaining staff well-being, both physically and mentally, and ensuring adequate supply of consumables including personal protective equipment (PPE) and machines are imperative for us to fight the challenge.

Keywords: Coronavirus disease 2019 (COVID-19); children; cardiovascular disease; congenital heart disease (CHD); pediatric cardiology

Received: 31 May 2021; Accepted: 09 October 2021; Published: 28 November 2022.
doi: 10.21037/pm-21-64
View this article at: https://dx.doi.org/10.21037/pm-21-64

Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome virus 2 (SARS-CoV-2), is gripping the world. Over 160 million individuals have been infected at time of this writing, with more than 3.3 million reported deaths (1). Since the start of the COVID-19 pandemic 18 months ago, there has been tremendous improvement in our knowledge about this disease. An unprecedented public health threat, with ongoing fluctuations in disease prevalence and spread, COVID-19 requires us to nimbly adapt our strategies in practice management.

We have observed that healthy children appeared less severely affected than adults during SARS-CoV-2 infection (2-7). Socio-economically disadvantaged and/or minority children are more likely infected, and there is increased risk for severe disease and complications, in the very young or in those with chronic medical conditions (7). There is obvious concern over increased risks in children with heart disease because of underlying physiologic and anatomic abnormalities; yet these cases have been only rarely reported. Although children seem less predisposed to serious illness during the acute infection, a subset develop multi-system inflammatory syndrome in children (MIS-C), with potential hemodynamic compromise and myocardial dysfunction, which may be severe enough to require support with extracorporeal membrane oxygenation (8).

As our understanding evolves, we set out to discuss the impact of the COVID-19 pandemic on the delivery of various pediatric cardiology services. This narrative overview also proposes potential strategies to adapt the practice of pediatric cardiology to the challenges posed by the pandemic in order to mitigate disruptions, so as to future proof our practice. We present the following article in accordance with the Narrative Review reporting checklist (available at https://pm.amegroups.com/article/view/10.21037/pm-21-64/rc).

Methods

A multi-database search was performed (PubMed, EMBASE and Google Scholar) using the following search terms: ("COVID-19" OR "SARS-CoV-2") AND ("pediatric cardiology services" OR "pediatric cardiac intervention" OR "pediatric echocardiography" OR "fetal cardiology" OR "fetal echocardiography" OR "congenital heart disease" OR "multisystem inflammatory syndrome" OR "Kawasaki"). Articles published in the English language from January 2020 through April 2021 were reviewed. All articles retrieved from the initial search were transferred to Mendeley Reference Manager (Version 1.19.8, Elsevier) where duplicates were identified and removed. Articles were excluded if the studies were not relevant to the effects of COVID-19 on pediatric cardiology services, staff, procedures, and surgeries (*Table 1*).

Discussion

Effects of the COVID-19 pandemic on pediatric cardiology services

Ambulatory clinic volume

Reduced clinical visits

Initial concerns that elective clinic visits and procedures could fuel propagation of the infection, along with incomplete knowledge of the best strategies of mitigating transmission risk, led to a dramatic reduction in clinical visits (9). Only emergency cases were facilitated and brought to the hospital, in accordance to institutional protocol. One study highlighted a 93% decrease in the outpatient presentation (10), resulting in an almost complete absence of patients at the outpatient setting (10,11). Patients were advised not to visit the hospital for follow-up and to avail telemedicine services where applicable, in order to reduce physical contact and subsequent risk of exposure (10,11). A reduction in higher risk group patient presentation was noted for cardiac diseases comprising decompensated heart failure, and endocarditis which in itself could prove harmful (12-14). Learning from previous infectious disease outbreaks, such cancellation of outpatient clinic visit and reduced patient presentation might lead to a loss to follow-up, and poorer overall outcome in vulnerable pediatric patients (15,16).

Telemedicine as a solution, a bridge to reviewing patients safely

Previous work alluded to the potential for using telemedicine in disasters and public health emergencies (17). In an effort to mitigate the transmission risk and ensure effective cardiac care, healthcare providers have adapted to video consultations and virtual clinics to manage patients. With restrictions in place on the number of caregivers who accompany a patient, the use of telemedicine allows crucial support persons to join in a virtual consult. It has also enabled an option for multidisciplinary consultation with relevant teams.

In a dedicated pediatric cardiology unit in North India, physical outpatient services were replaced by

Table 1 The search strategy summary

Items	Specification
Date of search	1 May 2021
Databases and other sources searched	PubMed, EMBASE, Google Scholar
Search terms used	(“COVID-19” OR “SARS-CoV-2”) AND (“pediatric cardiology services” OR “pediatric cardiac intervention” OR “pediatric echocardiography” OR “fetal cardiology” OR “fetal echocardiography” OR “congenital heart disease” OR “multisystem inflammatory syndrome” OR “Kawasaki”
Timeframe	1 Jan 2020–30 Apr 2021
Inclusion and exclusion criteria	Inclusion criteria
	1. All study types including case reports and case series were included
	Exclusion criteria
	1. Non-English literature
	2. Studies not relevant to the effects of COVID-19 on pediatric cardiology services, staff, procedures, and surgeries
Selection process	Articles were screened independently by CK Chen and YP Lim, and adjudicated by CK Chen

teleconsultations. The authors noted that systematic teleconsultation in conjunction with local evaluation and investigations achieved better management of children with congenital heart disease (CHD). Notably however, the number of patients availing successful teleconsultation was only 15% of the total number of patients attending physical outpatient services during a corresponding period in the preceding year (11). Telemedicine had also been employed effectively to monitor and manage infants with CHD prior to surgery, and shown to help relieve anxiety and stress among parents (18).

Non-invasive cardiac testing

Decreased cardiac imaging

Prioritization of urgent cases and deferring non-urgent imaging studies have resulted in >50% reduction in investigations being performed, such as electrocardiograms (ECGs) and outpatient echocardiograms (10). The pandemic has necessitated sonographers to rapidly adapt their workflow, including safe measurement measures, and echocardiographic examination protocols. Young children remain less compliant with facemasks and have difficulty cooperating, especially during the long examination to assess complex CHD. Optimal safe distancing is difficult to achieve in a small echocardiography examination room with child, caregiver, and sonographer.

Other investigations such as the exercise test (ET) and dobutamine stress test were also affected. Computed tomography (CT) angiography was noted to decrease by 63% with reduction noticed in transesophageal echocardiography (TEE). These may have consequences on patients, leading to worsening of symptoms and increased mortality due to delayed care (19).

Impact on fetal cardiology services

In the current pandemic, a significant decrease in fetal cardiology visits at multiple centers (by approximately 20–35%) and decreased referrals have been reported with consequent less face-to-face counseling (20). In order to minimize risk of exposure, the American Society of Echocardiography (ASE) recommended a triaging system for scheduling fetal echocardiographic examinations and consultations. This recommendation takes into consideration the risk for CHD, significant fetal arrhythmia, or anomaly by referral indication, while being mindful of the scheduling limitations imposed by decision-making during pregnancy, and perinatal and neonatal management planning (21). Importantly, a neonate with critical CHD born to a COVID-19-positive mother should be managed in a timely fashion, and that testing for COVID-19 does not delay transfer to a tertiary center (22).

In recent times, some centers have begun resumption of fetal cardiology scheduling practices, and allow more support persons to accompany the patient. However, with sporadic increases in infection rates, some centers

Table 2 Tier-level classification of common procedures performed on children and young adults with congenital heart disease based on the severity of the underlying condition

Tier level	Description	Examples of lesions/procedures
1A (urgent/emergent)	Any inpatient or patient transferred from another inpatient/outpatient setting, requiring an urgent cardiac catheterization procedure due to haemodynamic/impending haemodynamic compromise	Pericardiocentesis; atrial septostomy for TGA; atrial septal decompression for HLHS; atrial septal decompression on ECMO; Impella (Abiomed) placement; thrombectomy for symptomatic PE with significant RV strain; coiling of AP collaterals/bronchial arteries due to haemoptysis
1B (urgent/emergent)	Any inpatient awaiting a cardiac catheterization required prior to inpatient cardiac surgery OR in order to be discharged	PDA/RVOT stenting for decreased pulmonary blood flow; balloon valvuloplasty of critical or severe AS/PS; perforation of PV for PA/IVS; PDA closure in premature infants; biopsy in HTx for acute rejection; surveillance after recent HTx
2 (semi-elective)	Significantly symptomatic outpatients OR patients who are asymptomatic whose trajectories indicate that a delay in procedure (>30 days) could be detrimental	Pulmonary vein stenosis and significant RV dysfunction; heart failure and a large PDA or muscular VSD; increasing aortic valve/pulmonary valve gradients that already meet the threshold for intervention; venous interventions to treat occlusions/stenosis to alleviate symptoms
3 (elective)	Asymptomatic OR "mildly" symptomatic patients whose wait times would be longer than 1 month per routine	Secundum ASD; PDA without significant heart failure; moderate pulmonary/aortic valve stenosis; pulmonary valve dysfunction awaiting pulmonary valve replacement; pre-surgical catheterization (pre-Fontan catheterization); routine surveillance biopsy post-HTx

Adapted from reference (24). AP, aortopulmonary; AS, aortic stenosis; ASD, atrial septal defect; ECMO, extracorporeal membrane oxygenation; HLHS, hypoplastic left heart syndrome; HTx, heart transplantation; PA/IVS, pulmonary atresia with intact ventricular septum; PDA, patent ductus arteriosus; PE, pulmonary embolism; PS, pulmonary stenosis; PV, pulmonary valve; RV, right ventricle; RVOT, right ventricular outflow tract; TGA, transposition of the great arteries; VSD, ventricular septal defect.

have reinstated strategies that are more restrictive, depending on local conditions (20). Undoubtedly, pregnant mothers experience increased psychosocial stress related to regulations limiting in-person support during these consultations. As our knowledge improves, and strategies for protection of sonographers and pregnant women are enhanced, re-opening of fetal cardiology services would be in order. Obstetricians should continue to perform fetal cardiac screening for low-risk indications, and images made available for review by the fetal cardiologist where necessary. However, it is crucial for certain patients to be assessed by a fetal cardiology team with in-person consultation for appropriate evaluation and management. These include fetuses at high risk for CHD, those already diagnosed or suspected to have complex fetal cardiac diagnoses, significant extracardiac malformation, fetal anomalies requiring intervention or affecting the fetal heart, hydrops fetalis, or significant fetal arrhythmias (20).

Cardiac catheterization and interventions

Decreased procedure volume

A study from a high-volume pediatric cardiac catheterization laboratory in New York revealed an almost 75% reduction in the number of catheterization procedures compared to the same period in the preceding year (23). A similar trend was reported from a center in India where pediatric catheterization procedures decreased by 84% during the COVID-19 pandemic (11).

Recommendations on the safe performance of cardiac catheterization

Morray and colleagues, at the start of the pandemic, provided timely guidance on case selection, based on a multi-institutional online survey of pediatric interventional cardiologists (24). This allowed the categorization of patients according to disease severity, using a tiered schema to facilitate case selection (*Table 2*). Urgent/emergent procedures (tier 1A, tier 1B) must be performed in a timely fashion, while semi-elective procedures (tier 2) should be scheduled within 1–3 months and elective procedures (tier 3) may be postponed for >3 months.

Leading associations such as the American College of Cardiology (ACC) and the Society for Cardiovascular Angiography and Interventions (SCAI) have published guidelines on the implementation of protocols to continue non-elective cardiac catheterizations (25,26). Although these guidelines focus on adult patients, many recommendations can be applied to pediatrics, including facilitating bedside procedures when possible, intubation prior to arrival in the catheterization laboratory, avoiding elective procedures, limiting personnel physically in the lab, and utilizing appropriate personal protective equipment (PPE).

The CDC recommends that babies born to mothers with known COVID-19 at the time of delivery should be considered to have suspected COVID-19 (27). Urgent procedures such as balloon atrial septostomy (BAS) can be performed safely when proper precautions are taken by the intensive care, interventional, and imaging staff involved. Occupational transmission of SARS-CoV-2 during urgent neonatal cardiac interventions can be avoided by safe management measures including wearing PPE, physical distancing, designating separate delivery and transport teams, and limiting the number of providers in direct contact with the patient (28).

Pediatric cardiac surgery

Reduction in elective surgical patients

Hospitals reserved their finite healthcare resources for COVID-19 by decreasing elective pediatric cardiac surgery, and reserving only for those deemed urgent. In a global multi-societal consortium involving 176 congenital heart surgery programs in 52 countries, approximately half of the programs surveyed reported >50% reduction in surgical volumes (29). A multi-institutional national online survey involving 46 centers in Brazil revealed a significant decrease in surgical volume (ranging from 24% to 75% reduction) in over 70% of the centers. Additionally, there was a shift in case-mix profile towards more complex cases in 89.1% of centers with a resultant increased mortality during the pandemic (30). Experience from a congenital cardiac surgical center in Turkey showed a 33% contraction in monthly surgical volume, but a decrease in postoperative hospital length of stay during the pandemic (31). The shorter postoperative hospital stay could be a reflection of the preferred early discharge after the cardiac surgery to minimize the risk of nosocomial COVID-19 transmission, as well as the need to free up hospital beds. On the other hand, a dedicated pediatric cardiology unit in North India reported a 90% contraction of total CHD surgeries (40% for emergency CHD surgeries) during the pandemic compared to preceding year. Other centers, however, opted to optimize their healthcare resources by innovating their congenital cardiac care system through re-organization. In the Northern Italy region of Lombardy, CHD surgeries were diverted from secondary satellite units (“spoke centers”) and concentrated to a single unit (“hub center”) in a “Hub-and-Spoke” model of care (32). In so doing, the immediate needs of the patients could be met without increased mortality or COVID-19 exposure for the patients and providers.

Triaging for cardiac surgery

Specifically in children, surgical prioritization can be based on the type of CHD, and divided into three classes of urgency: emergent (24–48 hours), urgent (1–2 weeks), and elective (beyond 2 weeks) (*Table 3*) (33,34). Despite the recommendations, it remains imperative to exercise sound clinical judgment for individual patients. Shared decision from a multidisciplinary team (including medical and surgical) is essential to optimizing the timing for CHD intervention, especially when fewer resources are available.

New challenges emerging during COVID-19

COVID-19 in patients with CHD

Although pediatric data have shown that most COVID-19 cases in children are less severe than cases in adults, serious COVID-19 illness does occur, particularly among infants and children with underlying co-morbidities (35,36). Most of the deaths and critical disease reported in children have occurred in those with underlying co-morbidities. During previous viral epidemics, CHD was associated with increased hospitalization and complications (37). It might be surmised that children with pre-existing cardiovascular conditions are at increased risk of severe disease if they are infected with the SARS-CoV-2 (38-40). As the pandemic continues to progress globally, we expect infections in children to increase, and specialized management of children with cardiovascular disease will be necessary to minimize their risk.

Although there is concern of increased risk in children with CHD owing to the underlying anatomic and physiologic abnormalities, these cases have been only rarely reported. Most cardiovascular complications occur in CHD patients with confirmed, as opposed to suspected, COVID-19 cases (41). These complications included heart failure (55%), arrhythmias (22%), and stroke (22%). In a series of 7 CHD patients aged 3 months to 19 years, 5 (71%) required ICU admission and there was 1 death (42). A retrospective review of all individuals with CHD followed at a large CHD center in New York City revealed 53 COVID-19-positive patients with CHD, 10 (19%) of whom were <18 years of age (median age 3 years). Two of

Table 3 Congenital heart disease and surgical priorities (33,34)

Emergent (in 24–48 hours)	Urgent (in 1–2 weeks)	Elective (beyond 2 weeks)
For newborns		
Obstructive TAPVR	TGA with IVS	TGA + VSD
Obstructed cor triatriatum	Symptomatic TOF	Stable truncus arteriosus
TOF with spell	Ebstein resistant to medical therapy	HLVS
Coarctation unstable with PGE	Coarctation stable with PGE	
Aortic stenosis unstable with PGE	Aortic stenosis stable with PGE	
HLHS with restrictive ASD	PA + IVS with PDA (stenting not possible)	
Shunt thrombosis	HLHS	
	Shunt stenosis	
For infants		
Acute unstable aortic regurgitation	VSD + CHF resistant to medical therapy	VSD + CHF
Prosthetic valve thrombosis	TOF with spell (despite medical therapy)	TOF resistant to medical therapy
Shunt thrombosis	Shunt stenosis	AVSD + trisomy 21 + pulmonary overcirculation resistant to medical therapy requiring surgery
	DCM resistant to medical therapy, restrictive CMP	Ebstein anomaly + right heart failure
		Mitral insufficiency + CHF
		Symptomatic aortic insufficiency + enlarged left ventricle/decreased LVEF
		Symptomatic aortic stenosis/LVOTO + decreased LVEF
		RVOTO + impaired right ventricular function
		Despite shunting, increased cyanosis, or shunt stenosis in bidirectional cavopulmonary anastomosis candidates
For children		
Acute unstable aortic insufficiency	Worsening CHF with DCM despite medical therapy	Symptomatic heart failure + mitral insufficiency despite medical therapy
Prosthetic valve thrombosis	ARCAPA/ALCAPA + angina with minimal exercise	Aortic insufficiency + decrease in LVEF/LV enlargement
Severe RV dysfunction in patients with RV-PA conduits/conduit stenosis with ventricular arrhythmia	Severe stenosis in RV-PA conduit	Symptomatic AS/LVOTO + decrease in LVEF
Despite maximal medical therapy, endocarditis in cardiogenic, or septic shock	Stable but uncontrolled endocarditis with ongoing infection	Worsening right heart failure in patients with RV-PA conduits
ARCAPA/ALCAPA + resuscitated cardiac arrest		Fontan candidates with worsening cyanosis

ALCAPA, anomalous left coronary artery origin from pulmonary artery; ARCAPA, anomalous right coronary artery origin from pulmonary artery; AS, aortic stenosis; ASD, atrial septal defect; AVSD, atrioventricular septal defect; CHF, congestive heart failure; CMP, cardiomyopathy; DCM, dilated cardiomyopathy; HLHS, hypoplastic left heart syndrome; HLVS, hypoplastic left ventricle syndrome; IVS, intact ventricular septum; LV, left ventricle; LVEF, left ventricular ejection fraction; LVOTO, left ventricular outflow tract obstruction; RV, right ventricle; RVOTO, right ventricular outflow tract obstruction; PA, pulmonary artery; PGE, prostaglandin E; TAPVR, total anomalous pulmonary venous return; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

these 10 children had moderate/severe infection (defined as need for hospitalization and/or respiratory support) but no deaths (43). The authors noted that across all age groups, CHD patients with a genetic syndrome, and adults at advanced physiological stage (44) were at highest risk (43). In adults with CHD, a large study involving 58 adult CHD centers worldwide, identified 1,044 infected patients (87% laboratory-confirmed SARS-CoV-2 infection) with 24 COVID-related deaths. The authors concluded that COVID-19 mortality in adults with CHD (case fatality 2.3%; 95% CI: 1.4–3.2%) was commensurate with the general population. Factors associated with mortality included male sex, diabetes, cyanosis, pulmonary hypertension, renal insufficiency, and previous hospital admission for heart failure. The most vulnerable patients were those with worse physiological stage (44), such as cyanosis and pulmonary hypertension, whereas anatomic complexity did not predict SARS-CoV-2 infection severity (45).

Much remains unknown regarding CHD surgery and the associated risks of peri-operative COVID-19. In patients undergoing cardiac surgery, patients with peri-operative SARS-CoV-2 infection had an overall postoperative mortality of 34% and pulmonary complications in 94.1% (46). The predictors of poor outcome include male gender, age 70 years or older, ASA grades 3–5, surgery for malignant disease, emergency surgery, and major surgery. These findings were corroborated by the COVIDSurg Collaborative study in that patients with more serious cardiovascular disease are at an increased mortality risk if infected (46). In the global multi-societal consortium, 5 children were COVID-19 positive pre-operatively, and underwent congenital heart surgeries; in 4 of the 5, the outcome was not affected (29). In the same study, 12 congenital heart programs reported COVID-19 infection during the postoperative period in a total of 19 patients, and in one-third (6/19) of these, the surgical outcome was "adversely affected" (29). Nearly half (43.5%) of the 46 centers in Brazil involved in a multi-institutional national online survey reported at least one patient with SARS-CoV-2 infection in the post-operative period. This study observed a high number of post-operative infection (48 patients) with a significant mortality rate of 45.8%. Postoperative COVID-19 manifestations were varied, ranging from asymptomatic to hypoxemia and respiratory insufficiency. Notably, those who survived had mild or no symptoms (30).

Multisystem inflammatory syndrome in children (MIS-C) and Kawasaki disease (KD)

First reported in the United Kingdom in April 2020, the MIS-C shares features similar to KD and toxic shock syndrome. The phenomenon is frequently accompanied by hemodynamic instability, and is associated with previous COVID-19 infection in otherwise healthy children (8). MIS-C, also known as pediatric multi-system inflammatory syndrome (PMIS), is characterized by fever and laboratory markers of inflammation (including elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase, interleukin-6 (IL-6), neutrophilia, lymphopenia and hypoalbuminemia) with multisystem (>2) organ involvement (including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs). (see *Table 4* for RCPCH, CDC and the WHO case definition for MIS-C) (8,47,48). In the United States, there have been 3,742 reported cases of MIS-C and 35 deaths (49). Most children were 1 to 14 years of age (mean 8 years), but infantile cases have been reported as well.

MIS-C manifestation is temporally associated with SARS-CoV-2, appearing approximately 3–4 weeks after the acute COVID-19 infection (50,51). It was frequently observed that these children had positive antibodies to SARS-CoV-2, but a negative RT-PCR on swab analysis at the time of MIS-C presentation. Although the basis of MIS-C appears to be an increased inflammatory reaction, MIS-C differs from other pediatric inflammatory syndromes such as KD, KD shock syndrome, and toxic shock syndrome (52). The major laboratory findings described to characterize a potential MIS-C in comparison to KD include: (I) anemia, lymphopenia; (II) leucocytosis and neutrophilia; (III) normal or low platelets; (IV) elevated fibrinogen and ferritin; (V) elevated cardiac troponin, NT-proBNP; (VI) hypoalbuminemia; (VII) elevated IL-6, C-reactive protein; (VIII) lymphocytic myocarditis (53).

Cardiac involvement may manifest in three predominant presentations, often overlapping: (I) atypical KD-like spectrum (with particularly prominent gastrointestinal symptoms); (II) vasodilatory or hyper-inflammatory shock with normal cardiac function; or (III) cardiogenic shock from ventricular dysfunction [usually left ventricular (LV)] (54). Owing to the potential for pan-carditis, there should be a low threshold for performing or repeating echocardiography. Interestingly, MIS-C has not been

Table 4 Case definitions for SARS-CoV-2-associated MIS-C (8,47,48)

Royal College of Paediatrics and Child Health (RCPCH), UK	Centers for Disease Control and Prevention (CDC), USA	World Health Organization (WHO)
A child presenting with persistent fever (>38.5 ℃), inflammation (neutrophilia, elevated CRP, and lymphopenia) and evidence of single or multiorgan dysfunction (shock, cardiac, respiratory, kidney, gastrointestinal, or neurological disorder) with additional features*	An individual aged <21 years presenting with fever*, laboratory evidence of inflammation**, and evidence of clinically severe illness requiring hospitalization with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)	Children and adolescents 0–19 years of age with fever ≥3 days
This may include children fulfilling full or partial criteria for KD	AND	AND two of the following:
Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice)	No alternative plausible diagnoses	• Rash of bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet)
SARS-CoV-RT-PCR test results may be positive or negative	AND	• Hypotension or shock
*Additional features:	Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test, or COVID-19 exposure within 4 weeks prior to the onset of symptoms	• Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echo findings or elevated troponin/NT-proBNP)
✧ Clinical:	*Fever ≤38 ℃ for ≥24 h, or report of subjective fever lasting ≥24 h	• Evidence of coagulopathy (by PT, PTT, elevated d-dimers)
• Most: oxygen requirement, hypotension	**Including, but not limited to, one or more of the following: an elevated CRP, ESR, fibrinogen, procalcitonin, d-dimer, ferritin, LDH, or IL-6 elevated neutrophils, reduced lymphocytes and low albumin	• Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)
• Some: abdominal pain, confusion, conjunctivitis, cough, diarrhea, headache, lymphadenopathy, mucus membrane changes, neck swelling, rash, respiratory symptoms, sore throat, swollen hands and feet, syncope, vomiting	Additional comments:	AND
✧ Laboratory:	• Some individuals may fulfil or partial criteria for KD but should reported if they meet the case definition of MIS-C	Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin
• All: abnormal fibrinogen, high D-dimers, high ferritin, hypoalbuminemia	• Consider MIS-C in any pediatric death with evidence of SARS-Cov-2 infection	AND
• Some: acute kidney injury, anemia, thrombocytopenia, coagulopathy, high IL-10, high IL-6, proteinuria, high CK, high LDH, high TG, high troponin, transaminitis		No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes

Table 4 (*continued*)

Table 4 (*continued*)

Royal College of Paediatrics and Child Health (RCPCH), UK	Centers for Disease Control and Prevention (CDC), USA	World Health Organization (WHO)
✧ Imaging:		AND
• Echo and ECG: myocarditis, valvulitis, pericardial effusion, coronary artery dilation;		Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19
• CXR: patchy symmetrical infiltrates, pleural effusion;		Consider this syndrome in children with features of typical or atypical KD or toxic shock syndrome
• Abdo USS: colitis, ileitis, lymphadenopathy, ascites, hepatosplenomegaly		
• CT chest: as for CXR. May demonstrate coronary artery abnormalities if with contrast		

APTT, activated partial thromboplastin time; CK, creatine kinase; COVID-19, coronavirus disease 2019; CXR, chest X-ray; CRP, C-reactive protein; echo, echocardiography; ESR, erythrocyte sedimentation rate; IL, interleukin; KD, Kawasaki disease; LDH, lactic acid dehydrogenase; MIS-C, multisystem inflammatory syndrome in children; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PT, prothrombin time; PTT, partial thromboplastin time; RT-PCR, reverse transcriptase-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TG, triglycerides.

described in patients with known pre-existing congenital or acquired heart disease (54).

In this group of patients, myocardial dysfunction may range from mild to severe. LV systolic dysfunction, as measured by ejection fraction, has been described in 33% to 75% of patients with MIS-C. As high as 90% of patients have been reported to have abnormal global longitudinal strain (GLS) (52,54-56). Notably, impaired LV GLS and LV apical 4-chamber longitudinal strain (<16.4%) at initial presentation independently predicted a higher risk of adverse clinical course and persistent subclinical LV dysfunction at 10 weeks follow-up, suggesting they could be applied to identify higher risk children with MIS-C (57). Right ventricular dysfunction has also been described (44,58). Beyond global systolic dysfunction, regional abnormalities such as apical hypokinesia resembling Takotsubo cardiomyopathy have been reported (58). Diastolic dysfunction has been observed with abnormal findings on Doppler tissue imaging (56). Other cardiac manifestations included pericardial effusion (8% to 25% of patients), mitral valve regurgitation (50%), and tricuspid valve regurgitation (60%) (56). In 6% to 24% of patients, coronary artery dilation occurred, although true aneurysms are uncommon (50,52,54,55,59-61). Thrombosis has been observed in the setting of severely impaired ventricular function, coronary artery aneurysm, or pulmonary embolism; however, this complication seemed to be less prevalent in MIS-C compared to the thromboembolic phenomena and coagulopathy reported in acute COVID-19 infections in adults. Serial echocardiographic examinations would be in order during the acute illness, as ventricular function can worsen precipitously in the first 24 to 48 hours after admission, occurring around seventh day of illness (56,58). Fortuitously, ventricular dysfunction improves in most patients, although residual dysfunction can persist, with abnormal GLS potentially persisting even in the face of normal ejection fraction (54,56,58,61,62).

Treatment strategies of MIS-C include supportive care with focus on early recognition and aggressive management to reverse shock. Anti-inflammatory therapies include intravenous immunoglobulin (most commonly used), steroids (variable doses reported), and anti-platelet therapy, particularly in patients who also meet KD criteria and in those with coronary artery involvement. Immuno-modulators, which may include anti-IL-6 (tocilizumab) or anti-IL-1Ra (anakinra) therapy, have been used (50,53). To date, there is no evidence on the most effective treatment strategy, although several observational studies and registries are currently ongoing.

Long-term implications of disruption in pediatric cardiology services

A reduction of essential pediatric cardiac services could culminate in adverse short-term and long-term implications. A study conducted in the UK demonstrated that the second interval of the pandemic had seen a gradual increase in patients referred to cardiology services, and a rise in the investigation and diagnosis of myocardial infarctions compared to the first wave of the pandemic. Hence, the cessation of cardiology services during the COVID-19 outbreak could result in a rebound of patients referred to cardiology services, which in turn would lead to an increased burden on cardiology services (63).

Reduction in diagnostic services could portend a remarkable increase in the number of patients with severe cardiac complications down the line (64). In most countries, the deferment of elective cardiology procedures has caused a backlog of cases (65). Triaging systems may cause delay in care (66,67). This is an area of concern as patients are at a much greater risk of developing more severe complications. In this silent void of care, as attention has been diverted to COVID-19, CHD patients are at risk of dying at home or developing complications. They are potentially the hidden victims of the COVID-19 pandemic (68).

It has been estimated that the cancellation or delay in approximately 50% of elective surgical cases could potentially harmful (14), culminating in a lower quality of life, and exacerbation of symptoms. One concern is the impact of delayed surgery. Although the CHD population may not be severely affected by the SARS-CoV-2 virus itself, the impact of the strategies taken to reduce transmission has not been well defined. The possibility that patients may deteriorate, albeit temporary, will have an impact on the outcome vis-à-vis morbidity and mortality. In one survey, majority (85%) of respondents believed that postponement of elective surgeries would have a negative impact on their patients, and 92% estimated resumption of elective procedures would be delayed by one to four months (29). Furthermore, travel restrictions and border closures have also affected the ability of patients from countries without pediatric cardiac services to receive care elsewhere, or by visiting teams (29,31). This further aggravates uneven distribution of cases within and between countries and leads to inequalities in care (69). As it is, low-income countries and low-to-middle-income countries already have a significant lack of access to cardiac surgery, resulting in premature death from rheumatic heart disease and CHD (70).

How long the COVID-19 pandemic would last is unknown. Some patients with CHD may not be able to wait till the pandemic is over to receive care. The risk of patients who may be lost to follow-up or delayed for intervention because of COVID-19 can be mitigated now by reaching out to patients and families in a timely fashion. Although we must be mindful of protecting our patients from COVID-19 infection, the healthcare system must continue to care for those whose lives will be affected without timely management.

Proposed considerations to minimize the disruption in pediatric cardiology services

Looking ahead, several strategies can be adopted and/or maintained in order to mitigate the havoc that the COVID-19 pandemic has wreaked on the practice of pediatric cardiology.

Usage of appropriate personal protective equipment (PPE)

All healthcare providers must wear the appropriate PPE during all aerosol-generating procedures including TEE, cardiopulmonary resuscitation (CPR), intubation, extubation, ventricular tachycardia ablation, and echocardiography (71). Institutions need to ensure that their PPE equipment includes all the necessary components. Training of all healthcare providers on the donning and doffing of PPE is essential (72).

Precautions for high-risk CHD patients

The British Congenital Cardiac Association has suggested that adults and children with high-risk CHD, such as those with severe cyanosis, pulmonary hypertension, or heart failure, should be considered more vulnerable to COVID-19, and should therefore be particularly strict in following the physical distancing and hygiene measures. Based on definitions of physical distancing, it would be recommended that attendance at nurseries, school, college, or universities as well as socializing with extended family, going to restaurants, and children's parties be avoided (73).

Cardiac imaging

Imaging procedures put the staff and patients at risk of transmission as well as contamination of equipment. In addition to PPE, the following measures may be employed during imaging:

- ❖ Limiting caregiver to one individual per patient whenever possible.
- ❖ Maintaining thorough sanitation protocols for machines, probes, rooms, and workstations.
- ❖ Physical distancing in waiting areas or staggered entrance.

Cardiac procedures and surgeries

Although most elective and non-urgent cardiac procedures and surgeries have been postponed, it should be cautioned that a system that facilitates continual, serial re-evaluation of patient candidacy would be developed in order to maintain best practices in a prolonged pandemic, as a semi-elective or elective case can become an urgent one if untreated for a sustained period of time (24). As the pandemic trajectory improves, staged re-expansion of the cardiac intervention services and surgeries would be in order to clear backlogged cases. This can be incorporated into triage procedures to ensure delivery of the necessary care to the patients who need it. Negative pressure procedure rooms and proper disinfection of the equipment before and after procedure must not be overlooked. Ideally, all patients must be screened for COVID-19 before any interventional or surgical procedures. Within the wards, separate rooms can be allotted to COVID-19 positive patients (26).

Cardiac critical care/CPR

Patients with cardiac arrest should be moved to negative-pressure rooms expediently to mitigate the risk of aerosol generation. A compressions-only CPR can be performed en route to a negative-pressure room. An oxygen mask with a flow of 10 L/min should be used to cover the mouth and nose of the patient, and additional layer can be added over the mouth using a towel or cloth (74).

Telemedicine

By leveraging on new technology-enabled options, patients would have access to the care conducted with both patient and clinician at home, greatly limiting travel and exposure, and permitting uninterrupted care of patients. As much as possible, virtual visits and remote monitoring should be encouraged. Moreover, telemedicine can help improve access to rural areas, especially during the pandemic (18).

Smart weighing devices can be used to monitor the sudden increase in weight, especially in children with heart failure (75). In children and adolescents with arrhythmia, smart-watch and smartphone applications can monitor patients' heart rhythm up to a certain extent (76,77). In children with cyanotic CHD, home monitoring of oxygen saturation allows for earlier detection of extreme hypoxemia (78).

Availability and adoption of fetal tele-echocardiography may contribute a significant role during and beyond the COVID-19 pandemic. With fetal tele-echocardiography, the obstetric sonographers can be guided through a complete evaluation remotely, in conjunction with a telehealth consult with the family. In addition, fetal tele-echocardiography permits a timely approach to diagnosis with maternal-fetal-medicine (MFM) in conjunction with a pediatric cardiologist. Tele-medicine software and the use of video capture adapters provides a relatively simple approach to live imaging, as fetal echocardiographic images can then be streamed to a picture archiving and communication system (PACS), for reading. Following imaging, tele-consult may be scheduled with a pediatric cardiologist and a congenital heart surgeon.

Management of hospital staff and resources

Institutions need to manage resources by predicting needs and managing shortages through enhancing co-ordination among hospitals (79). It is paramount for each program to develop contingency plans if physicians and other healthcare workers in the program are infected or quarantined, so that business continuity can be maintained. Strategies to reduce overall exposure include scheduling providers in on-off rotations ("split team" arrangement), maintaining adequate PPE and surveillance via widespread testing of asymptomatic healthcare providers (33). Healthcare workers need to monitor themselves daily for fever or respiratory symptoms. If symptoms occur, such workers need to be immediately removed and be screened for SARS-CoV-2 (80).

To optimize staff welfare, strategies to ensure reasonable patient load and sufficient rest between patients include (81):

- ❖ Staggering cases with longer duration of time between echocardiography appointments.
- ❖ Daily and weekly rotating shift adjustments.

Leadership decisions must be communicated to healthcare providers in real time to ensure that teams retain confidence that their well-being is of highest priority.

Vaccination

Finally, the value of vaccination cannot be over-emphasized. Although the age recommendations currently may preclude young children from lack of data, it is essential that older children and ACHD patients, healthcare workers and all caregivers—indeed those eligible—should be vaccinated to provide herd immunity and reduce the risk and severity of infections.

Conclusions

COVID-19 has had a profound impact on the practice of pediatric cardiology and will continue to affect all aspects of patient care. Short- and long-term sequelae on pediatric cardiology services need to be taken into consideration. As pediatric cardiologists play an important role in the care and outcomes of these patients, the approach to the evaluation and management of children with heart disease in the COVID-19 era, will evolve as the pandemic rages on.

Strategies incorporating new technology-enabled options, maintaining staff well-being, both physically and mentally, and ensuring adequate supply of consumables including PPE and machines are imperative for us to fight the challenge. Moving forward, the lessons we have learnt and the successes we have had during this tumultuous period must be remembered such that this turning point in history will be useful in mitigating future crises and keep our health care sustainable in the long term.

Acknowledgments

The authors wish to thank Tan Wei Loong Wildon for helping with editing, formatting and in submission of the manuscript for publication.
Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Pediatric Medicine* for the series "Advances in Pediatric Cardiology". The article has undergone external peer review.

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://pm.amegroups.com/article/view/10.21037/pm-21-64/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://pm.amegroups.com/article/view/10.21037/pm-21-64/coif). The series "Advances in Pediatric Cardiology" was commissioned by the editorial office without any funding or sponsorship. SCQ serves as an unpaid editorial board member of *Pediatric Medicine* from September 2022 to August 2024 and the unpaid Guest Editor of the series. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/pm-21-64
Cite this article as: Chen CK, Grignani RT, Lim YP, Quek SC. The impact of COVID-19 on the practice of pediatric cardiology: a narrative review. Pediatr Med 2022;5:39.

