

REVIEW ARTICLE

COVID-19 and Children with Congenital Heart Disease: Pandemic Implication

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Abstract

While the global coronavirus crisis worsens, a surprising feature of the disease appears that children might be immune from the worst form of it. Studies suggest that COVID-19 is more likely to infect older adult men, particularly those with comorbidities. There is only limited data detailing the effects of COVID-19 on the pediatric population. Patients with underlying cardiovascular comorbidities are at increased risk of morbidity and mortality from SARS-CoV-2 infection. Certain adult patients with congenital heart disease (ACHD) and with complex congenital heart disease can be considered as high risk for complications related to COVID-19 infection on the basis of decreased functional reserve. While no study on COVID-19 has been included paediatric patients with congenital heart disease, it stands to reason that patients with congenital heart disease can be considered at higher risk for complications from COVID-19. Given the increased risk for severe COVID-19 in adults with underlying cardiac disease, there is concern that patients with congenital heart disease (CHD) may likewise be at increased risk for severe infection, as they are known to have higher risk for complications with viral illnesses including respiratory syncytial virus and influenza.

Keywords: COVID-19, children, CHD.

Introduction

An outbreak of pneumonia of an unknown origin developed in Wuhan of Hubei Province, China during December, 2019.¹ By January 7, 2020, Chinese scientists confirmed that the outbreak was caused by a novel coronavirus, renamed as severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), and the disease is now termed coronavirus disease 2019 (COVID-19).²⁻⁴ On January 30, 2020, WHO declared a public health emergency of international concern (PHEIC) and pandemic on 11 March 2020.⁵

While the global coronavirus crisis worsens, a surprising feature of the disease appears that children

might be immune from the worst form of it. Studies suggest that COVID-19 is more likely to infect older adult men, particularly those with chronic comorbidities.⁶ There are only limited data detailing the effects of COVID-19 on the paediatric population. A review of 72,314 cases by the Chinese Center for Disease Control and Prevention showed that <1% of COVID-19 cases were in children younger than 10 years.⁷ In Bangladesh among confirmed cases 3% of children <10 years were identified as COVID-19.⁸ No study described children with congenital heart disease (CHD) and COVID-19, and thus the effect of the virus on this specific patient population is not clear. The mechanism by which children seem less

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susceptible to severe infection caused by SARS-CoV-2 has yet to be revealed. It has been theorized that the ACE2 (the binding protein for SARS-CoV-2) in children is not as functional as it is in adults, and thus SARS-CoV-2 is less infectious.⁸

Patients with underlying cardiovascular comorbidities are at increased risk of morbidity and mortality from SARS-CoV-2 infection.⁷ Studies so far have not detailed in a granular fashion the risk of individual cardiovascular complications in patients with underlying cardiovascular disease who are infected with SARS-CoV-2. While no studies on COVID-19 have included patients with congenital heart disease, it stands to reason that patients with congenital heart disease could be considered at higher risk for complications from COVID-19. Certain adult patients with congenital heart disease and complex congenital heart disease could be considered high risk for complications related to COVID-19 infection on the basis of decreased functional reserve.⁹

Since this is an emerging infectious disease, there is limited data on the effects of this infection on patients with cardiovascular disease, particularly so for those with congenital heart disease.¹⁰ Importantly, the pandemic has stretched healthcare systems and many care team members are at risk for contracting and possibly transmitting the disease which may further impact the care of patients with congenital heart disease. Despite numerous recently published articles on the topic, understanding of the virus and the disease is incomplete, and robust data specifically in the setting of congenital heart disease are lacking.

Viral effects on the heart and on patients with cardiovascular conditions

Previous coronavirus epidemics (SARS and MERS) showed that they mainly cause pulmonary issues like pneumonia and acute respiratory distress syndrome.¹¹ They also cause direct myocardial injury and myocarditis caused by both influenza and coronaviruses.¹² Furthermore, patients with underlying heart disease (both congenital or acquired) seem to have increased morbidity and mortality related to viral infections.¹³ There are also some data to suggest that patients with underlying heart disease may be more susceptible to contracting coronavirus infection.¹⁴

COVID-19 and myocardial injury

Mechanism of cardiac injury in COVID-19 and its effects on the cardiovascular system are not fully understood. In some studies, cardiac injury (manifested as an increase in troponin levels) was found in admitted patients and cardiac injury was more common in critically-ill patients.¹⁵⁻¹⁸

Mechanisms of cardiac injury in COVID-19

- COVID-19 may cause cardiac injury indirectly due to an overwhelming immune inflammatory response and cytokine storm.¹⁹
- SARS-CoV-2 viral invasion of cardiomyocytes and direct damage via this process, but this has not been proven.²⁰
- Severe hypoxia from acute respiratory damage caused by the virus may result in oxidative stress and myocardial injury from increased myocardial oxygen demand in the presence of severe hypoxia due to acute lung injury (ARDS).¹⁰
- Furthermore, ACE2 is expressed in the heart, and the SARS-CoV-2 virus uses this enzyme as a receptor for entry into the cell.²¹ It is unclear that SARS-CoV-2 binding alters ACE2 expression or causes dysregulation of the RAAS (renin-angiotensin-aldosterone system) pathway.

COVID-19 and Kawasaki like disease

Reports of a multisystem inflammatory syndrome (MIS-C) in previously well children temporally associated with COVID-19 infection have emerged.²² MIS-C shares similarities to severe Kawasaki disease (KD), including the development of giant coronary aneurysms. At least initially, myocardial involvement appears to be reversible and thought to be related to myocardial stunning and edema rather than inflammatory myocardial injury. Thus, although initial cardiac dysfunction may be severe, most of the patients seem to recover their ventricular function. However, the long term prognosis of coronary involvement, and whether the response to therapy is similar to KD, remain to be seen.²³

COVID-19 and adult congenital heart disease (ACHD)

At present, the number of ACHD patients affected by COVID-19 is unknown. Combining available real-time epidemiological data of confirmed patients with COVID-19²⁴ with current estimates of CHD prevalence suggests that approximately 4800 ACHD patients currently actively infected in Europe and

about 5600 patients in the USA and Canada as of 22 May 2020. These numbers assume a prevalence of 6.12/1000 adult population (6.16 for the USA)^{25,26} and that ACHD patients are infected at a comparable rate as the general population and require confirmation by prospective data. So in Bangladesh we also expect same scenario. Adults with ACHD may be at high risk in the case of COVID-19. Due to the heterogeneity of ACHD and secondary complications, risk profiles are, however, not uniform.

A pragmatic approach is proposed to categorising patients into low-risk, intermediate-risk and high-risk groups.²⁷

Infection with SARS-CoV-2 should be suspected in ACHD patients presenting with fever, onset or worsening of dyspnoea, lower than usual peripheral oxygen saturation but also in case of unexplained worsening of ventricular function or new arrhythmia. Rarely these patients may present with overt cardiogenic shock.²⁸

Comparison of current and previous oxygen saturations, ECGs, complete blood cell counts, NT-Pro-BNP and troponin may be helpful. A chest X-ray or CT scan may provide additional information in selected patients. Echocardiography should be focused on obtaining information of immediate clinical value such as pericardial effusion or ventricular function in the current situation avoiding prolonged direct physical contact with patients.²⁹

Other infections should not be overlooked, and especially endocarditis remains prevalent in ACHD patients.²⁹

If ACHD patients are tested positive for SARS-CoV-2, management should be guided by patient risk and clinical status. Parameters of oxygenation, blood pressure, heart rate and ECG should be recorded, and baseline laboratory testing performed. Point of care echocardiographic assessment may be helpful in this situation. Stable patients with low or moderate risk and without signs or symptoms of respiratory or cardiovascular deterioration may be cared at home with supportive measures, instructed to self-isolate and be remotely followed up through teleconsultation. Impairment of lung function is prevalent in ACHD patients and its severity is related to the complexity of the underlying heart defect and the surgical history.³⁰

High-risk patients or those with signs of respiratory or cardiovascular impairment require admission ideally at a tertiary ACHD center. Especially patients with complex, cyanotic disease, heart failure and arrhythmias require particular attention. Treatment in patients with cyanotic heart disease should be guided by the relative degree of desaturation compared with baseline and lactate levels rather than absolute oxygen saturation levels. Patients with right heart dilatation or dysfunction are potentially at increased risk of right heart failure as mechanical ventilation and acute respiratory distress syndrome can lead to increase in pulmonary arterial pressures.²⁷

COVID-19 and children with congenital heart disease

There are no published studies on COVID-19 in children with congenital heart disease. Thus, all of the current management strategies are extrapolated from what is known about the effect of COVID-19 on adult patients and adult patients with cardiovascular disease. Efforts are under way through the Adult Congenital Heart Association and the International Society of Adult Congenital Heart Disease to gather data on the number of suspected and confirmed cases both in the United States and globally and to better understand outcomes among adult congenital heart disease population.¹⁰ In the absence of data to help guide care it is difficult to make any definitive recommendations.

Risk stratification

Based on observations made in older adults with underlying congestive heart failure, it is likely that patients with underlying CHD may be at risk for more severe disease related to the viral infection. It is important to recognize that there is a broad range of anatomical and physiological abnormalities among patients with CHD, and it is likely that not all are at similar risk for severe disease. In general, patients with impaired ventricular function and those with abnormal pulmonary blood flow/pulmonary hemodynamics are believed to be at higher risk.³¹ Based on anatomy and additional physiological factors including symptoms, exercise capacity, heart failure, pulmonary hypertension and cyanosis, a pragmatic approach is proposed to categorising patients into low-risk, intermediate-risk and high-risk groups.^{27,31}

High-risk lesions

- Unpalliated cyanotic CHD.
- Unpalliated shunt lesions with significantly elevated pulmonary blood flow.
- Lesions associated with sequestered lung segments (abnormal venous drainage with arterial supply coming from bronchial vessels).
- Palliated univentricular heart disease.
- Fontan physiology.
- Congenitally corrected transposition of the great arteries (CCTGA).
- Dextro-transposition of the great arteries (d-TGA) palliated by atrial switch procedures (Mustard or Senning).
- Eisenmenger syndrome or pulmonary arterial hypertension (PAH).
- Any lesion with poor systemic ventricular function.
- Heart failure and severe valvular heart disease.

Moderate to low-risk lesions

- Corrected septal defects and other shunt lesions with no residual defect, absence of pulmonary hypertension, and normal systemic ventricular systolic function.
- Palliated tetralogy of Fallot with good ventricular function and competent pulmonic valve.
- D-TGA palliated with arterial switch and normal ventricular function.
- Isolated bicuspid aortic valve (BAV) or valvar pulmonary stenosis (PS) with normal ventricular function and no symptoms.

Management strategy

Shortages of hospital capacity, manpower and supplies are reported even from highly developed countries. Many tertiary cardiac centres and specialized cardiologists had to shift focus of care, postponing or rerouting specialised cardiac procedures to provide adequate resources for general COVID-19 patients. As the focus of the medical community has shifted toward patients suffering from COVID-19, taking care of CHD patients has become extremely challenging. If patients suffer cardiovascular complications from COVID-19 requiring either percutaneous or surgical intervention, each case must be assessed on an individual basis. Each institution should develop

protocols for appropriate triage, isolation and treatment of COVID-19 patients who may need such interventions.

Hospital responses in this situation for CHD include^{32,33}

- Replacing in-person office visits with telemedicine.
- Implementing universal masking for everyone.
- Practicing social distancing as much as possible in the hospital environment.
- Requiring additional hygiene procedures to protect patients and health care employees.
- Requiring temperature and symptom screenings for visitors and employees. All parents entering the hospital or clinic should be screened for symptoms suggesting SARS-CoV-2 (including cough or fever) as well as for contact with known positive cases.
- Performing routine microbiologic test screening depends on a multitude of factors, including local prevalence. Parents of cardiac patients should follow local guidance in accordance with the CDC guidance.
- Clinical need for imaging, invasive and surgical interventions must be weighed against the risk of infecting healthcare workers.
- Laboratory assessment for cardiac injury is not recommended on a routine basis, patients who show signs and symptoms of myocardial injury (ST-segment changes on an electrocardiogram for example), acute coronary syndrome (chest pain), unstable arrhythmias, or heart failure should be evaluated thoroughly.
- Only a limited goal-directed examination should be performed in emergency life-saving situations, ideally with the transesophageal echocardiography (TEE) probe in a protective sleeve.
- There are reports demonstrating chest CT abnormalities in adults during asymptomatic/pre-symptomatic disease; however, the role of chest CT in relation to COVID-19 in children remains undifferentiated at this time. It should be reserved for clinical indication based on symptoms.
- Postponing elective surgeries and procedures which require inpatient resources and preserve those resources for acute needs.

- Preoperatively testing patients for COVID-19. If preoperative testing is required, PCR-based testing of respiratory secretions is the most widely accepted approach.
- Using personal protective equipment (PPE).
- Minimizing the number of personnel. It may become necessary to re-deploy staff to help cover more acute case load if we begin seeing staff become infected with COVID-19.

Prevention of aerosolization and airborne transmission during procedure

The risk of aerosolization and airborne transmission of SARS-CoV-2 during aerosol-generating medical procedures (AGMPs) is especially pertinent to the pediatric cardiac anesthesiologist or intensivist given the high viral loads within the nose and nasopharynx of COVID-19 positive patients.³⁴

- Aerosol formation during AGMP may be divided into procedures that induce the patient to produce aerosols (e.g., bronchoscopy, intubation, cough-like force during cardiopulmonary resuscitation) and procedures that mechanically generate aerosols themselves (e.g., bag-mask ventilation, nasotracheal suctioning, tracheostomy tube change, noninvasive ventilation, high-frequency oscillatory ventilation).³⁵ Among them tracheal intubation was associated with the highest risk of transmission of acute respiratory infections to HCWs.³⁶ The use of a 3-layered clear plastic drape configuration during extubation in a simulated mannequin model has been shown to limit aerosolization and droplet spray significantly.³⁷ The first layer was placed under the head of the mannequin, a second torso-drape layer was applied from the neck down covering the chest, and finally, an overhead top drape was placed over the mannequin's head to prevent contamination of the surrounding surfaces, including the HCW.
- For transesophageal echocardiography (TEE) the pediatric cardiac anesthesiologist will be called on to help with placement of the TEE probe in COVID-19 patients because it is considered a significant AGMP.³⁸ An experienced airway proceduralist, such as a cardiac anesthesiologist, may be the best HCW to pass the echocardiography probe, in full recommended PPE.³⁹⁻⁴²

Care of COVID-19 patients in the cardiac catheterization laboratory^{43,44}

- During procedures in the catheterization laboratory, the risk of radiation necessitates wearing a protective lead apron and thyroid shield before donning PPE.
- Remove all possible emergency medications that may be required during the procedure from the anesthesia workstation. This will prevent the reopening of the anesthesia workstation and potential contamination of all anesthetic supplies in the workstation. Ideally, the anesthesia workstation should be covered in a plastic sheet as a barrier to reentry to help minimize cross-contamination.
- Catheterization laboratories and cardiac operating rooms use positive ventilation systems and are not designed for infection isolation. Therefore, these rooms will require conversion to an air neutral or negative-pressure room to care for COVID-19 patients safely. In addition, the room will require a terminal clean at the end of the procedure.

Outpatient care of paediatric cardiac patients^{23,45-48}

Caring for CHD patients is a shared responsibility and requires a great deal of coordination. The importance of communication between patient and the physicians is paramount so to avoid unnecessary delays in providing appropriate medical or surgical therapy. While CHD patients are inherently a higher risk population, we must weigh the risks of failing to address a cardiac abnormality with that of exposure to COVID-19. Following can be done to help bridge the current gap between patients and hospitals due to the COVID-19 pandemic:

- Utilize telemedicine visits to stay under the care of the pediatric cardiologist and to ensure that timely decisions can be made regarding necessary tests or procedures. The advent of wearable technology and wide availability of blood pressure, heart rate, and oximetry equipment for home use can be a reasonable substitute for in-clinic vital sign measurements.
- Hand-held and easily sterilized echocardiographic equipment can also be a 'handy' substitute for traditional comprehensive

echocardiography, and the inevitably higher rate of exposure in a frequently visited echo lab.

- The clinician must be cognizant of QT prolonging effects of some of the medications like ritonavir/lopinavir that are used in COVID-19 therapy, including hydroxychloroquine and azithromycin. They should be used cautiously especially when combined with hypokalemia, hypomagnesemia, myocarditis, or other QT prolonging medications.
- The WHO and the European Medicines Agency currently approve the use of ibuprofen and NSAIDs in COVID-19. The British Congenital Cardiac Association suggested avoiding NSAIDs to treat fever in COVID-19.
- It is recommended that all cardiac medications, including aspirin, anticoagulants, ACE inhibitors, angiotensin receptor blockers, beta blockers, diuretics and antiarrhythmic medications be continued during COVID-19 illness, unless a clear contraindication develops.
- Coagulation cascade abnormalities and disseminated intravascular coagulation are reported in patients hospitalized with severe COVID-19 disease. So continuing anticoagulation in mild cases with monitoring from the prescribing physician and adjusting anticoagulation can be done as needed in cases of severe COVID-19. Aspirin is commonly used in the pediatric and adult population with CHD for its antiplatelet effects at a low dose of 3 to 5 mg/kg per day. There are no reports of Reye syndrome in patients on low dose aspirin typically used with CHD or with COVID-19. Because of that currently there is no need to stop aspirin in children or adults with CHD and COVID-19.

Effect of COVID-19 on cardiac team members⁴⁷

Based on the COVID-19 pandemic trends it is expected that many of the cardiovascular care team members will be exposed to patients with COVID 19 in the coming weeks and months. In anticipation of the spread of COVID-19, many hospitals and cardiology practices have changed their care models and policies to accommodate the care of patients impacted by COVID-19 and prevent the spread of the disease.

What CHD (and other) patients must do/expect during the COVID-19 pandemic and beyond^{49,50}

- Social distancing (all, until further notice).

- Shielding of high-risk patients (i.e., single ventricle physiology, pulmonary arterial hypertension, immunosuppressed/compromised patients, other specific patients).
- Regular updates/information sharing about COVID-19.
- Mental and psychosocial well-being, exercise, lifestyle modification.
- Patients with congenital heart disease should be vaccinated against influenza and pneumococcal pneumonia.

Conclusion

Children with CHD are more susceptible to COVID-19. At this point, data are insufficient to suggest specific preventive measures in patients with congenital heart disease and all patients with CHD, irrespective of which group they are in, follow routine public health guidelines with regard to social distancing, scrupulous handwashing and avoiding unnecessary contact.

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