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Editorial

COVID-19 in children with congenital heart disease in Asia: clinical features and recommendations for management

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Globally, around 1.35 million children are born with a congenital heart disease's every year.[1] Making CHDs one of the world's most common congenital anomaly and, thus, a significant global health issue. The CHD prevalence rate is highest in Asia (9.3 per 1000 live births) which is followed by Europe (8.2 per 1000 live births) and lowest in Africa (1.9 per 1000 live births).[1] The existing high CHD burden on pediatric health infrastructures around the world has been worsened due to the global coronavirus (COVID-19) pandemic. Approximately, a total of 22.9 million children and adolescent cases of COVID-19 have been recorded.[2] The highest infectivity rate has been in children under 3 years of age.[3] 90% of reported pediatric cases have been categorized as mild or moderate disease, 5.2% as severe and 0.6% as critical.[4] Over 12,300 children and adolescents have died due to COVID-19.[5] Of these deaths, 58% have occurred in the 10-19 age group and 42% in the 0-9 age group.[5] Which can prove to be exceedingly detrimental in Low to Middle Income regions, such as Asia, where the medical infrastructure is less robust and usually poorly accessible.[5] According to a systematic review on the association of COVID-19 and pediatric co-morbidities, around 5.1% of severely ill children have had an underlying comorbidity, such as CHD.[6] However, at present, the data from Asia is very limited. There are only a handful of large, observational cohort studies. These have been conducted primarily in China, Iran, and India.[3,4,6-8]

Additionally, sparse research has been conducted on the specific correlation of COVID-19 and pediatric CHD (PCHD) patients.

Symptoms in PCHD COVID-19 patients

Patients are divided as asymptomatic, mild, moderate, severe, and critically ill. The percentage distribution of critical COVID-19 cases from Asia has been 0.8% to 5.3% in Singapore, Malaysia, Japan, and China, 16% in India, 37.5% in Indonesia, and 78% in Pakistan.[8] A child is diagnosed as severe when he or she presents with dyspnea, severe cyanosis, and/or less than 92% oxygen saturation.[4] It is estimated that 40% of children infected with COVID-19 remain asymptomatic.[8] In the case of symptomatic disease, the nature of the symptoms is flu-like. According to a large cohort study incorporating eight hospitals in seven countries in Asia (China, Japan, Singapore, Malaysia, Indonesia, India, and Pakistan) the most common symptoms are fever (64%), cough (39%), and coryza (23%).[8] Other symptoms, which may or may not occur, include myalgia, encephalopathy, nausea, poor feeding, and diarrhea.[9,10] Symptoms in PCHD COVID-19 children have been similar across Asia.[8] Children with cyanotic CHDs, however, often have heightened or new-onset cyanosis, such as circumoral cyanosis.[4,10]

Risk stratification

The risk of severe illness is greater in children with CHDs because of the effects of the SARS-CoV-2 virus on an existing pressure or volume-overloaded heart. In Asia, the highest (14%) risk ratio of death due to due to COVID-19 in CHD children has been recorded in Pakistan.[11] Several case reports from Asia detail certain specific factors associated to this. Firstly, studies suggest risk stratification by age group. According to multicenter

studies from Iran (34%) and China (1.6%), infants under one year are more prone to severe or critical disease.[12,13] Whereas children in the age group 11-15 have been least critically ill (4.1%).[13] This could be because of the low maturation and expression of the angiotensin-converting enzyme 2 (ACE2) receptors in younger children when compared to older children and adults. Second, is the type of CHD.[14] Children with cyanotic CHDs are particularly at risk.[14] These children develop worsening COVID-19 induced hypoxemia due to an already compromised cardiopulmonary system. Prognosis is further exacerbated in patients with complex heart defects and additional co-morbid conditions, such as pulmonary hypertension and immunodeficiencies.[14] High risk complex heart defects include hypoplastic left heart syndrome (HLHS), tricuspid atresia, pulmonary atresia, unbalanced atrioventricular canal, Glenn anastomosis and Fontan procedure.[14] Large ventricular septal defect and large atrioventricular septal defect are the only two common acyanotic CHDs that have been associated with an increased risk of COVID-19 sequalae.[14] Other vulnerable groups include children who have had aorto-pulmonary window surgery, a modified Blalock-Taussig shunt, Waterson anastomosis, Potts anastomosis and pulmonary artery banding.[14] Finally, CHD patients on heart failure medication have poor prognosis due to the worsening hemodynamic impact of SARS-CoV-2 associated myocardial injury and lung involvement.[14]

Complications in PCHD COVID-19 patients

Multicenter studies from Asia report the predominant role of cardiovascular involvement in PCHD COVID-19 related complications.[10,15,16] The percentage division of these cardiovascular complications according to case reports from China, Iran and India include cardiogenic shock (53%), myocardial dysfunction (52%), coronary artery dilation (15%), heart failure (9%), arrhythmias (3%), stroke (3%), pulmonary hypertension (3%) and myocardial injury (1%).[10,15,16] Serious complications include hyperinflammatory conditions such as Kawasaki disease and Multisystem Inflammatory Syndrome in children (MIS-c).[17] These conditions can cause diarrhea, vomiting, conjunctivitis and rashes on the torso.[17] MIS-c is a severe complication associated with COVID-19 in children.[18] Studies report MIS-c in 28% of Asian children infected with COVID-19. MIS-c associated cardiac complications include depressed ventricular function and arrythmias.[18] In terms of pulmonary complications in PCHD COVID-19 patients, according to a retrospective, observational study including 24 paediatric cardiac centres in India, 14.5% of COVID-19 positive children developed acute respiratory distress syndrome (ARDS) and hypoxia.[4] ARDS and pneumonia are of greater concern in regions such as Asia because they are already prevalent in the region with an associated mortality rate of 7.3%.[5] Finally, COVID-19 in PCHD patients can also result in chronic complications, such as myocardial injury. Particularly in those children who recover from MIS-c. 20-45% of these patients have been reported to have a mildly depressed ejection fraction even after recovery.[18] These chronic complications may be so severe which may require lifelong monitoring and management.[4] MIS-c is a severe complication associated with COVID-19 in children.[18] Studies report MIS-c in 28% of Asian children infected with COVID-19. MIS-c associated cardiac complications include depressed ventricular function and arrythmias.[18] While most patients with these complications usually recover, owing to a greater severity in PCHD children, they may be fatal.

Mortality in PCHD COVID-19 patients

In Asia, the highest PCHD COVID-19 related mortality rates have been reported from India and Pakistan (2.3%).[8] A multicenter study from India has shown a higher percentage of COVID-19 deaths in unoperated children with critical heart disease (13.8%).[4] The predominant in hospital mortality predictor in PCHD COVID-19 patients is the severity of disease at admission.[4] Other factors include (i) cyanosis (ii) tachypnea (iii) shock (iv) ARDS and (v) the possibility of intubation.[4] Some studies have also linked COVID-19 mortality to the complexity of CHD in children.[4] Univariate analysis on the type of CHD reported in death cases of PCHD COVID-19 children has shown cyanotic CHDs (17.9%) as the most common, acyanotic (6.5%) as secondary and obstructive lesions as the least (8.3%) common cause of death.[4] Common mortality cases in the younger pediatric age group have been reported more in children with atrioventricular septal defect (AVSD) and double inlet left ventricle (DILV).[4,19,20] In the older pediatric group, cases of hypoplastic left heart syndrome (HLHS), Eisenmenger syndrome, and severe aortic stenosis associated mortality have been recorded in COVID-19 children.[4,10,20] All of which are complex defects.

Management in PCHD COVID-19 patients

There are currently no guidelines tailored specifically towards PCHD COVID-19 patients. However, recent studies agree on case management according to a patient's baseline cardiac status. This is assessed according to the patient's oxygen saturation, the status of cardiac preload, and/or the presence of right heart failure or an intracardiac shunt.[21] In the case of an adverse event, such as cardiogenic shock, mechanical ventilation paired with vasoactive medication are used to maintain oxygen saturation and organ perfusion.[21] For patients with a moderate infection, the standard management protocol involves close monitoring of the patients, oxygen therapy and antiviral drugs, such as Remdesivir.[20] However, antiviral therapy should be started with caution in PCHD patients. This is due to treatment side effects, such as arrythmias.[20] Additional care should also be taken for patients with a cyanotic CHD. In these cases when the oxygen saturation is below 90%, supplemental oxygen therapy is given by low-flow nasal cannula, followed by oxygen delivery through a face mask or high flow nasal cannula if hypoxemia continues to persist or worsen.[20]

Recently, the COVID-19 vaccination has been approved for use in children aged 5 to under 12. Children in this age group should, therefore, be fully vaccinated to prevent transmission in the region.

CONCLUSION

The PCHD population is more vulnerable to COVID-19 infection and has a higher tendency of poor progression of disease. Identifying risk factors specific to PCHD patients can assist in timely management and prevent severe complications in CHD children, who already require more advanced healthcare management. This is particularly important for Asia, a low-and middle-income continent, due to a weak healthcare infrastructure, a high prevalence of CHD in the region, and economic unpredictability due to the pandemic.

Recommendations

COVID-19 management in children with CHD should be adapted to case prioritization by risk and clinical status. CHD surgeries should be timed accordingly. Should surgical correction be inevitable, preoperative COVID-19 testing is essential due to the asymptomatic nature of the infection in some children. Specific precautionary measures need to be taken by parents/guardians of children with a CHD due to the heterogenous nature of the SARS-CoV-2 virus in this subgroup. Particularly parents/guardians with children with complex CHDs, cyanotic CHDs, and children with pulmonary hypertension. Some measures include (i) parents/guardians and children aged 5 years and above being fully vaccinated against COVID-19 (ii) social distancing, particularly in Asian countries where there is overcrowding and high infectivity rates (iii) wearing protective masks and (iv) hand washing and general hygiene.[22] Due to a comparatively lower Human Development Index in Asia and lack of learning facilities, parents/guardians need to be educated on PCHD and COVID-19 through special awareness campaigns.[22] Awareness needs to be centered on the high-risk characteristics in patients and added precautionary measures catered towards these groups. Recently, mutation of the SARS-CoV-2 virus has resulted in the transmission of variants called the Delta and Omicron variants.[23] Due to the unpredictability of the nature of transmission and effects of these variants, school going CHD children can be home schooled and clinical consultations can be made through telemedicine. These policy changes should be implemented according to the percentage of case sequences per variant in Asia. At present, the highest reported cases in Asia have been from Japan and India.[23] Management strategies from healthcare professionals need to be two pronged. Efforts should be extended to managing the treatment backlog of PCHD patients as well as to managing PCHD COVID-19 patients. Heightened disease surveillance can assist in early identification and treatment of PCHD COVID-19 patients. Timely treatment can help reduce the risk of extensive complications leading to death. Treatment backlog presents a challenge particularly due to the diversion of funding and resources towards the pandemic. Enhancing global advocacy and awareness on the impact of COVID-19 in the PCHD sector in Asia can help secure some of this funding towards this sector, for example. Finally, the limitation of data on PCHD COVID-19 patients warrants further research and large-scale studies on the impact of COVID-19 in CHD children in Asia.

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