

# A Systemic Analysis of Referral Indications for Paediatric Cardiac Evaluation and Impact of COVID-19 Pandemic in a Tertiary Care Hospital in Uttar Pradesh

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## ABSTRACT

**Introduction:** Study aimed to determine the basis of referral for cardiac evaluation in children in a tertiary care hospital, impact of covid pandemic on referral pattern and confirmation of cardiac involvement by echocardiography in a tertiary care government hospital, Uttar Pradesh, India.

**Material and methods:** A retrospective analytical study was conducted on children referred by paediatrician to cardiologist with suspected cardiac diseases from January 2019 to December 2021. Referral pattern was retrospectively analysed for 3 consecutive years (January 2019-December 2021) to compare referral pattern, effect of COVID waves on cardiology referral and echocardiographic diagnosis in pre-COVID and 1<sup>st</sup> and 2<sup>nd</sup> COVID waves.

**Result:** Total outpatient visits over study period were 3494 with male female ratio of 2.13 and median age of 8 months. The most common indication for cardiology referral was congenital heart disease (CHD) (43.6%); acquired heart disease (AHD) accounted for 21% of cohort. MIS-C emerged as a new form of AHD and formed main AHD cohort. Other common indications of referral were post cardiac intervention (5.9%), functional echo in neonatal intensive care unit (9%) while cardiac clearance in case of associated systemic illness (syndromic association, preop clearance or intercurrent systemic illness etc.) contributed to 20% of cohort. Covid-19 pandemic had major impact on cardiac services.

**Conclusion:** Commonest indication of cardiology reference was congenital heart disease. The COVID pandemic, a rare epidemiological entity with contrasting behaviour of agent, host and environment across the world, had definite effect on paediatric cardiology services and that include OPD footfall, indication of referral and emergence of new entity MIS-C especially during 2<sup>nd</sup> wave of COVID-19 pandemic.

**Keywords:** Congenital Heart Disease, RHD, MIS-C, COVID-19, Cardiomyopathy, Pediatric Cardiology Referral

## INTRODUCTION

Miscellaneous cardiac lesions affect children but their relative frequency of presentation to paediatricians is yet unaddressed in India. Prevalence of congenital heart defect (CHD) is traditionally stated as 8-12/1000 term-live births. Our current birth rate is 16.949 per 1000 people and latest population number is 1,416,236,963. Above numerals point towards a gigantic cohort of CHD in India [1]. Early diagnosis and treatment offer 95% survival with good long-term outcome [2]. Acquired heart diseases (AHD) in children are another silent entity with significant public health

concern. Both communicable (eg. Rheumatic heart disease, diphtheria, tuberculosis, sepsis etc) and non-communicable AHDs (eg. severe anaemia, vitamin D deficiency, electrolyte imbalance, hypertension, renal, hepatic and thyroid diseases) are emerging [3].

Cardiac involvement (ischemia, myocarditis, arrhythmia, cardiomyopathy) post SARS-CoV-2 infection in previously healthy adults versus those with pre-existing comorbidities was repeatedly published in recent literature [4, 5, 6, 7]. Global head-to-head comparative data in paediatrics is sparse. 34% of Spanish children with COVID were admitted in PICU due to cardiac dysfunction [8]. Furthermore, from April 2020, a novel entity called MIS-C (ICD code M35.81) was described secondary to dysregulated immune system [9-14]. The cardiac involvement post MIS-C in India was published in few scientific researches [15].

**Aim of study:** This study aimed to evaluate the pattern of children with cardiac concerns presenting to paediatricians before and during pandemic, the reason for their referral to paediatric cardiologists, impact of pandemic on cardiac care and confirmation with classification of their diagnosis by advanced ECG and echocardiography. Uttar Pradesh, the most populous state in India, was chosen as the sample.

## MATERIAL AND METHODS

**Study design:** This retrospective, observational, single-centre study was conducted in paediatric cardiology unit of a tertiary care public hospital on consecutive children (n=3494) between January, 2019 and December, 2021. The study period was divided into three groups: 1. 2019 (pre COVID), 2. Year 2020 (1<sup>st</sup> wave of COVID-19) and 3. Year 2021 (2<sup>nd</sup> wave of COVID-19)

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**How to cite this article:** Kanika Bansal, Munesh Tomar, Maitri Choudhuri, Vikas Aggarwal, Vijay Jaiswal A systemic analysis of referral indications for paediatric cardiac evaluation and impact of COVID-19 Pandemic in a tertiary care hospital in Uttar Pradesh. International Journal of Contemporary Medical Research 2023;10(5):E1-E7.



Demographic, clinical, ECG and echocardiographic data were collected. In group B, the records were specifically reviewed to identify all children with acute COVID-19 or MIS-C.

## STATISTICAL ANALYSIS

Chi-square test was used to test the significance in association between categorical variables. Mann-Whitney test was used to test the association between categorical and continuous variables.

### Cardiac evaluation

**Electrocardiogram:** Twelve lead ECG was done when clinically indicated like history of arrhythmia, syncope, chest pain, cardiomyopathy, family history of unexplained death, and bradycardia or tachycardia noted during cardiac evaluation.

**Echocardiography** was done with GE VIVID™ E95 with the use of broad band transducers (12S, 6S, M5Sc) according to American Society of Echocardiography guidelines [16]. Structural defects, cardiac dimensions and function, coronary artery origin and Z score, valvar regurgitation, pulmonary hypertension (PH), pericardial effusion (PE), and presence of vegetation or thrombus were recorded.

## RESULTS

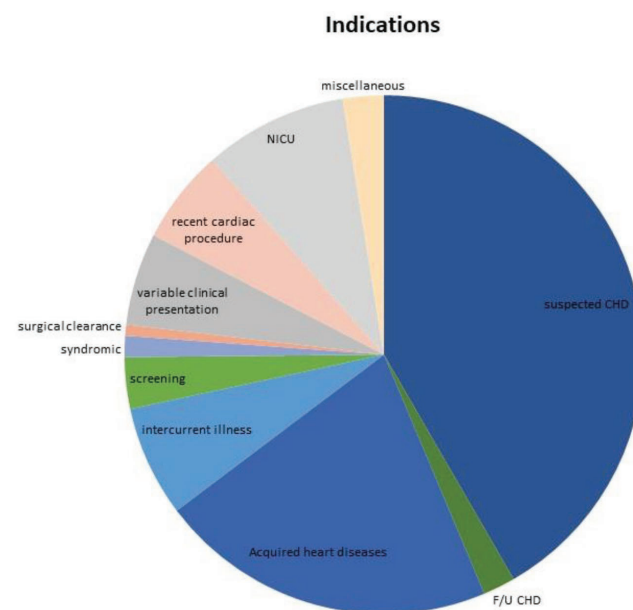
A total of 3494 children were screened in the study period with footfalls in consecutive years being 1219, 482 and 1793 in year 2019, 2020, and 2021 respectively. Median age of total cohort was 8 months, 58.2% (n=2034) were infants, of which 38.2% (n=776) were neonates. Sixteen neonates had abnormal fetal echocardiographic diagnoses and 296 (8.5%) consultations were emergent, performed in NICU. Male patients comprise of 68.1% (n=2380) while 31.8% (n=1114) were female, and with male: female ratio of 2.13. A total of 85.4% presented to OPD while remainder (14.6%) were admitted patients. The indications for referral are detailed in figure 1.

The most common reason for referral was CHD (43.6%); suspected (41.6%) or previously known (2%). Clinical presentations of CHD were murmur, cyanosis, feeding difficulty, failure to thrive, recurrent chest infections, cardiomegaly in chest X-ray and increased precordial pulsations. AHD accounted for 21% of cohort (Figure 1 and 2). Traditional lesions were RHD, cardiomyopathies, suspected myocarditis, Kawasaki disease, pericardial diseases, arrhythmias, hypertension and PH. MIS-C emerged as a new indication for referral as awareness increased among physicians and there was an exponential rise in MIS-C from zero case in 2019, 1.2% in 2020 to 24% of total referral in 2021 and contributed to 12.5% of total cohort. Other referral indications were post cardiac intervention (5.9%), functional echo in neonatal intensive care unit (9%) while 20% referral for cardiac clearance in case of associated systemic illness. Last group included cardiac evaluation in syndromic child, preop clearance, concurrent non-cardiac illness, non-cardiac congenital anomalies, dysmorphism and variable clinical symptoms. Children with variable clinical presentation

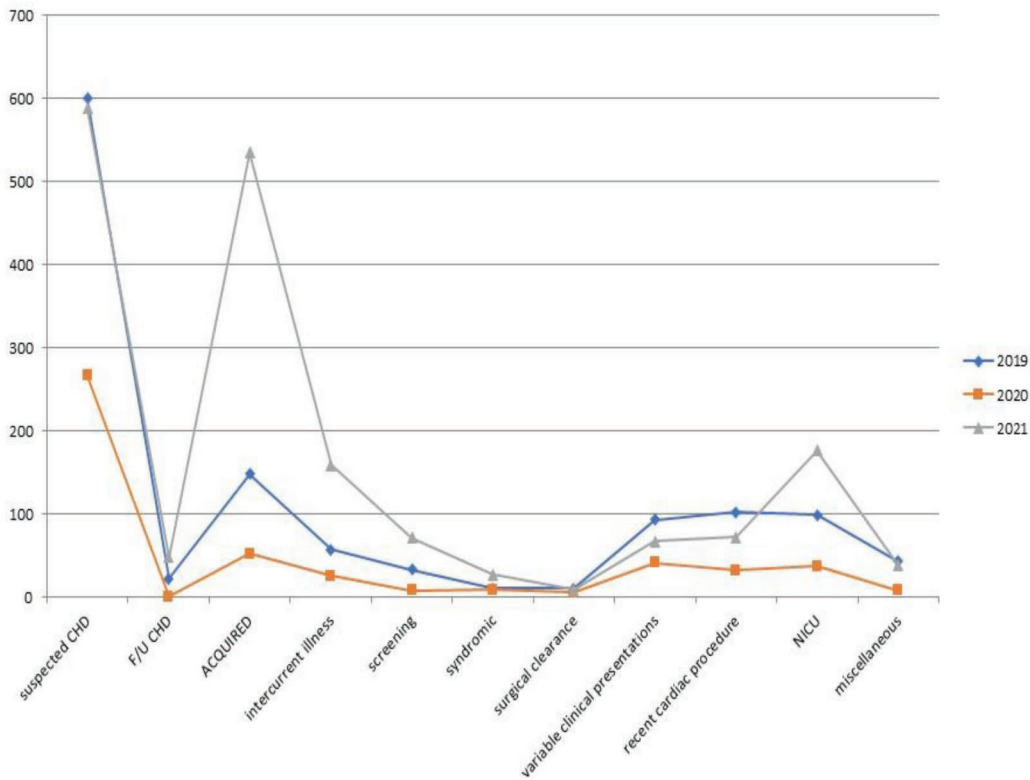
had anemia, fast breathing and heart rate, chest pain, palpitation, syncope and breath holding spells constitute. Small percentage of cohort was screened for miscellaneous reasons like arteriovenous malformation, cardiac tumor, deep vein thrombosis, cerebrovascular accident, and ataxia telangiectasia.

**Impact of COVID-19:** There was noteworthy temporal influence of pandemic on referral numbers and heterogeneity of aetiology as graphically demonstrated in figure 2. The least footfalls were in 2020 13.8% (n=482) in contrast to 34.8% (n=1219) in 2019. The commonest reason for consultation was suspicion of CHD in all groups but absolute numbers of cardiology referrals were inversely related to increasing COVID cases. In 2021, consultations increased to 51.4% (n=1793) and a significant proportion of them were clinically suspected MIS-C. The distributions of final diagnosis are shown in figure 3.

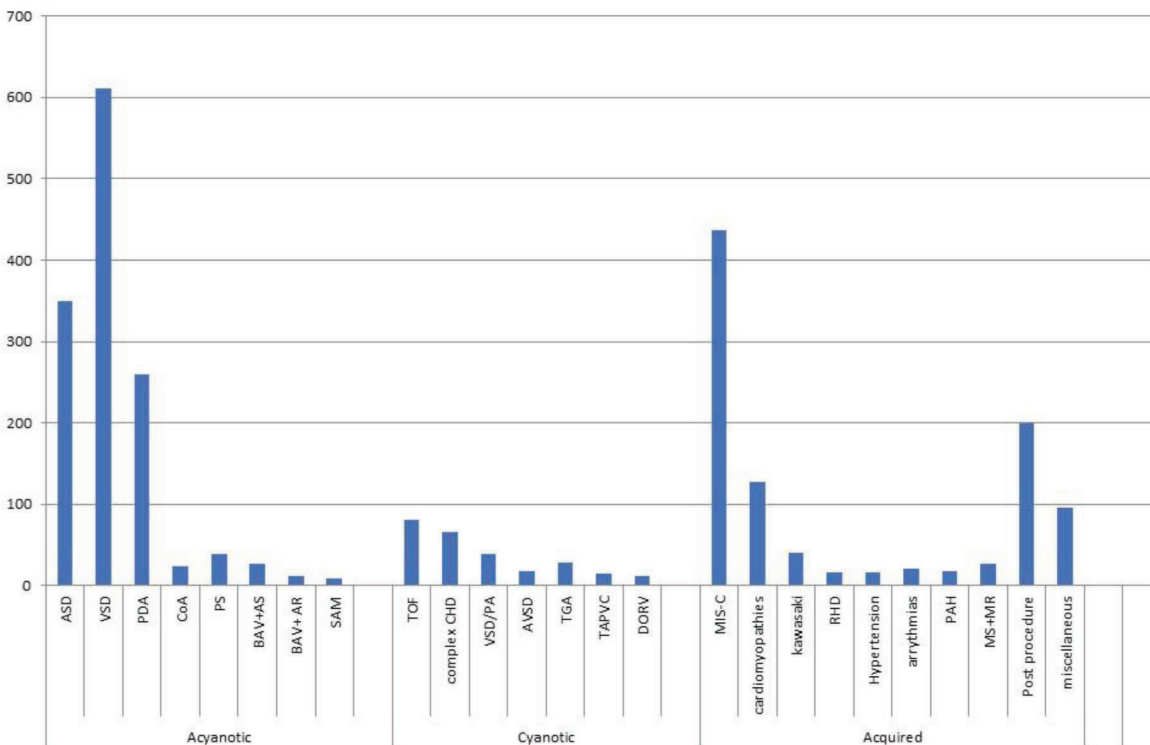
**Echocardiographic Diagnosis:** Abnormal cardiac findings were noted in 76% (n=2653) while 24% (841) were found to have structurally and functionally normal heart. Cyanotic CHD was noted in 39.2% (n=1367) children, out of which VSD (44.6%) was the most common defect followed by ASD (25.6%), PDA (19%), isolated valvar PS (2.8%), and CoA 1.8% (n=24). Bicuspid aortic valve (BAV) was found in 5.4% (n=73) with AS and/or AR (n=30), associated CoA (n=18) and Shone complex (n=6) while 2 patients were diagnosed to have Aortopulmonary window (APW). Normal functioning isolated BAV was detected in 17. Cyanotic CHD was diagnosed in 7.7% (269), out of which Tetralogy of Fallot (TOF) (30.1%) was the most common followed by complex CHD (24.5%), VSD/PA was 14.5%, complete TGA 10.8% and 6.7% were AVSD with PS. Rest 13.4% constitute DORV, TAPVC, tricuspid atresia and Ebstein's anomaly.



**Figure-1:** Pie chart showing different indications of cardiology referrals



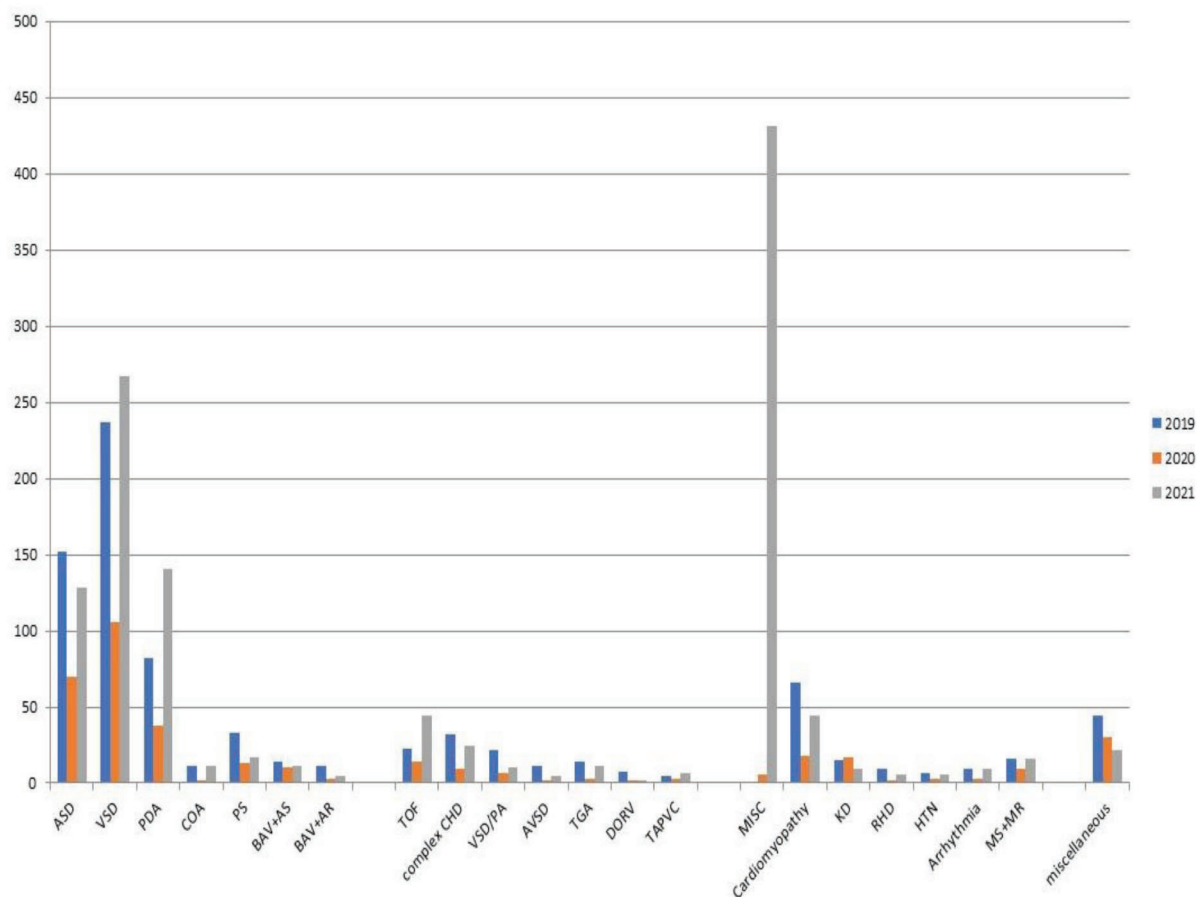
**Figure-2:** Graphic demonstration of temporal influence of pandemic on referral numbers and heterogeneity of aetiology over three consecutive years (year 2019, 2020 and 2021)



**Figure-3:** Bar diagram showing cardiac diagnosis (congenital acyanotic, congenital cyanotic and acquired heart diseases) confirmed by echocardiography

A substantial number of AHD (n=694, 21%) were diagnosed in the study period, of which 62.9% were MIS-C. Cardiomyopathies (CMP) were diagnosed in 18.4% (n=128);

DCM with LV dysfunction was most common (n=109) followed by LV noncompaction (n= 9) ,RCMP (n=4), and HCMP (n=3). Two children had CMP due to glycogen storage



**Figure-4:** Bar diagram showing temporal influence of pandemic on type of heart disease over three consecutive years (year 2019, 2020, and 2021)

diseases (Pompe's) and one post diphtheria. 5.9% cohort was formed by Kawasaki disease. Three evaluations were for arrhythmias mainly SVT. RHD was diagnosed in 2.4% (n=17) mostly associated with MR. Sixteen consultations were done for severe hypertension; all had LVH with 50% of them having LV dysfunction on echo. Eighteen children were referred with outside diagnosis of primary pulmonary arterial hypertension in age range of 8 months to 72 months and same was confirmed. Rest were valvular heart diseases including 3.9% (n=27) congenital MS with MR and seven with isolated TR because of dysplastic TV (n=2), ruptured chordae with anterior tricuspid leaflet prolapse (n=4) and Uhl's anomaly in one.

A total of 5.7% (n=200) were evaluated as a follow up after cardiac procedure (open heart surgery and catheter interventions). Commonest reason for post operative evaluation (n=105) was VSD surgical closure (n=40), followed by TOF total correction (n=17), PDA ligation (n=08), ASD surgery (n=05), AV canal repair (n=02), BT shunt (n=07), TAPVC repair (n=05), arterial switch (n=03), Rastelli (n=03), single ventricle palliation (n=05), CoA repair (n=03), ALCAPA (n=2) and valvar repair /replacement in 5 children. A total 95 children were seen post catheter intervention, commonest being PDA device closure (n=38), followed by ASD device (n=22), balloon aortic valvotomy (n=17), CoA balloon/stent (n=12), and post balloon pulmonary valvotomy

(n=06).

Rest 2.7% (n=96) were in miscellaneous group and diagnosed as PPHN (n=48) in NICU, mild LV dysfunction due to other systemic causes (n=22), cardiac mass (n=07) (myxoma and rhabdomyosarcoma), Takayasu arteritis (n=04), ALCAPA (n=04), pulmonary embolism (n=02), vascular ring (n=02), vegetations (n=05) and idiopathic dilation of main pulmonary artery (n=02).

Since the spread of COVID-19, pediatric patients were initially considered less affected by SARS-COV-2, but current literature reported subsets of children with different cardiac manifestations and labelled as Multisystem Inflammatory Syndrome in Children (MIS-C) [17]. Covid-19 pandemic has major impact on cardiac evaluation as shown in figure 4. In 2020, there is significant difference in number of hospitalization/outpatient visit which decreased to 13.8% (n= 482) as compared to corresponding period in 2019 (34.8%) (n= 1219). Consultations then increased again in 2021 by 51.4% (n= 1793) as normal OPDs resumed in hospitals, thus followup cohort increased. MIS-C emerged as a new indication for referral to cardiologist as awareness increased among paediatricians. There was an exponential rise in MIS-C from zero case in 2019, 1.2% in 2020 to 24% of total referral in 2021.

## DISCUSSION

Our study documents the issues prompting cardiac

consultation in a tertiary care multi-speciality hospital in India. Although a variety of conditions were assessed, some diagnosis were encountered more frequently. According to Robert L. Geggel,[18]and Subramanian J. Murugan[19] evaluation of a murmur was the most frequent basis for consultation. Our study confirmed CHD with referrals due to murmur, cyanosis, feeding difficulty, failure to thrive, recurrent chest infections, cardiomegaly noted on chest X-ray and increased precordial pulsations remained the leader in the study period.

In recent decades, the incidence of CHD appear to be increased due to advancements in antenatal and postnatal screening technologies [20, 21]. Clinical diagnosis by paediatrician when confirmed by echocardiography in referred suspected CHD cohort showed 24% with structurally normal hearts, 39.2% cyanotic CHD and 7.7% cyanotic CHD respectively. Recent studies also reported increasing incidence of paediatric DCM and myocarditis [22,23]. An Indian study by Aggarwal N [24] on incidence of AHD in children reported RHD in one-third, cardiomyopathies and/or myocarditis combined in another third and the residual third were due to other causes, including pericardial diseases and metabolic or genetic disorders. Our study data found 21% children with AHD out of which cardiomyopathies, MIS-C, KD, arrhythmias, RHD, myocarditis, pericardial diseases, endocarditis and arrhythmias. MIS-C (n= 437) accounted significantly to AHD cohort in last two years.

Far-reaching consequences of COVID pandemic are being reported globally both in acute, short-term and mid-term datasets. From the first case identified in December 2019 in Wuhan City in China [25], most children in the initial period of the pandemic were either asymptomatic or mildly symptomatic with fever and cough; this changed with the emergence of multisystem inflammatory syndrome in children (MIS-C) [26-28]. Since late April 2020, children began presenting with fever, gastrointestinal symptoms, and features of myocarditis, including some with coronary artery aneurysms (CAAs), as clustered cases in the Western hemisphere [29]. More than 80% of MIS-C patients present with cardiac involvement which include cardiac dysfunction (28–62%), shock (35–50%), myocarditis (17–22%), and coronary vasculopathy (8–24%), with a miniature proportion having electrophysiological abnormalities[30-35]. These manifestations are triggered primarily by the massive dysregulated immunological response to the virus[35].

A study from India did reviewed impact of COVID-19 on paediatric cardiac services and showed that the outpatient visits across the 24 participating pediatric cardiac centers decreased by 74.5% in 2020 (n = 13,878) as compared to the corresponding period in 2019 (n = 54,213). The reduction in the number of hospitalizations, cardiac surgeries, and catheterization procedures was 66.8%, 73.0%, and 74.3%, respectively. In our study from a single centre, we found a similar statistical trend in 2020 as compared to 2019. Analysis of questionnaires filled by families revealed reasons like stricter nationwide lockdown, fear due to the pandemic, long travel distances to reach a hospital and the conversion

of major hospitals to COVID care facilities. However, 2021 showed a significant increase in number of consultations of which MIS-C was a dominant theme.

Limitations: As the sample volume consisted of patients referred by paediatricians to paediatric cardiology, referral bias cannot be excluded. Diagnosis was made primarily on clinical, laboratory, ECG and echocardiographic results. Advanced and expensive cardiac imaging (MRI, CT angiography) could not be performed due to financial restraints. The diagnosis of myocarditis and cardiomyopathies were not confirmed with endomyocardial biopsy. Although latter is gold standard, the procedural risks and resource limitations excluded its use.

## CONCLUSION

The COVID pandemic was a rare epidemiological entity with contrasting behaviour of agent, host and environment across the world. Our analysis targeted the impact on pediatric cardiology services in India with a large tertiary government medical college as the study centre. The response of families, public health care system and paediatricians to the new disease, the emergence and prompt referral of MIS-C, the importance of AHD in pediatric cardiology, heterogeneity of causes of AHD were collated in two temporal groups divided by SARS-CoV-2. The sample volume was minuscule compared to the silent cohort in India. More well-designed, multi-centric, long-term prospective studies across the nation is the need of the hour.

## ABBREVIATIONS

CHD – congenital heart disease, AHD - acquired heart disease, RHD - rheumatic heart disease, ASD - atrial septal defect, VSD - ventricular septal defect, PDA - patent ductus arteriosus, AVSD - atrioventricular septal defect, TGA - transposition of great vessels, TOF - tetralogy of Fallot, PA-pulmonary atresia, DORV - double outlet right ventricle, TAPVC - total anomalous pulmonary venous connection, BAV - bicuspid aortic valve, AS-aortic stenosis, AR - aortic regurgitation, MS - mitral stenosis, MR - mitral regurgitation, DCM - dilated cardiomyopathy, RCMP - restrictive cardiomyopathy, HCMP - hypertrophic cardiomyopathy, SVT-supraventricular tachycardia, TV-tricuspid valves, TR-tricuspid regurgitation, ALCAPA - anomalous origin of left coronary artery from pulmonary artery, COA - coarctation of aorta, SAM - subaortic membrane, PS-pulmonary stenosis, PPHN-persistent pulmonary arterial hypertension of neonate, LVH - left ventricle hypertrophy, PICU - pediatric intensive care unit, NICU - neonatal intensive care unit, MIS-C-multisystem inflammatory syndrome in children, OPD - out patient department, PH - pulmonary hypertension

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**Source of Support:** Nil; **Conflict of Interest:** None

**Submitted:** 23-03-2022; **Accepted:** 27-04-2023; **Published:** 30-05-2023