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# Clinical Profile, Embryology, Mode of Presentation and Midterm Outcome of Cyanotic Congenital Heart Diseases in Children – A Study from North India

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## ABSTRACT

Background: Although less common than acyanotic congenital heart diseases(CHD), cyanotic group is more significant cause of the associated mortality and morbidity due to its severe nature and poor medical or surgical outcome if the diagnosis is delayed. It is thus important to have detailed information on the clinical profile of various cyanotic CHDs as well as their mode of presentation and outcome for the early detection and timely intervention.

Methods: The study was carried out over a period of two and a half years in 0-18 years age group at three different paediatric cardiac centres at Kashmir valley. All the children referred with complaints or clinical examination suggestive of congenital heart defects were further evaluated with echocardiography. On echocardiography children having cyanotic congenital heart defects were included in this study. The clinical profile and mode of presentation and midterm outcome of various cyanotic CHDs was further studied in detail.

Results: Out of total 2445 children screened on echocardiography, 1315 children had normal scans, while 1130 had CHDs. Among these, 842 (74.5%) had acyanotic CHDs while 288(25.5%) had cyanotic CHDs. Among the cyanotic CHDs, Tetralogy of Fallot (TOF) was the most common lesion (44.8 % of cyanotic CHDs). Other common cyanotic lesions included single ventricle

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11.5%, DORV 11.1%, TGA 8.6% and TAPVC 8 %. Cyanosis along with cyanotic spells was the most common mode of presentation in 77.4 % patients. Many patients were lost to follow-up (19.8%) and among others 23% underwent surgical repair, 43% were medically managed and 14.2% expired.

Conclusion: Detailed study and knowledge about the clinical profile, mode of presentation and outcome of various cyanotic CHDs paves a way for the further research and referral for timely intervention in this group of CHDs with relatively dismal prognosis in absence of surgery.

## Introduction:

Congenital heart disease(CHD) is the single most common group of congenital disorders in children accounting for almost 1 % of all the live births.[1,2] Although less common than acyanotic CHDs, cyanotic group is more significant cause of the associated mortality and morbidity due to its severe nature and poor medical or surgical outcome if the diagnosis is delayed.[3,4] Hence timely diagnosis of cyanotic CHD (CCHD) requires proper knowledge about their clinical presentation and subsequent echocardiographic diagnosis. Few studies have been done describing in detail the CHDs in children from the northern India,[5,6] but only a handful have studi ed in detail about the CCHDs.[7,8] The need for this comprehensive study arises due to the fact that majority of the cases remain undetected until late due to lack of adequate trained manpower, poor socioeconomic status and the lack of parental awareness and treatment seeking behaviour.

## Materials and Methods:

All the children less than 18 years of age suspected of CHDs referred by the paediatricians on the basis of history and clinical examination were included. Basic screening included a SpO2 at room air of 93 or less, visible cyanosis or cyanotic spells, failure to gain weight, intermittent feeding, exertional dyspnoea, history of recurrent chest infections, clubbing, murmur or any other abnormal heart sounds on auscultation. A verbal consent was taken from the parents of the children to participate in the study. Baseline ECG and Chest X-ray was done for all the children with suspected CHD. Echocardiographic evaluation was done to confirm the diagnosis.

From May 2018 to November 2020, a total of 2445 children referred to three different paediatric cardiac clinics were screened using echocardiography. On echocardiography 1315 children had normal scans, while 1130 had CHDs. Among these, 842 (74.5%) had acyanotic CHDs while 288(25.5%) had cyanotic CHDs.

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The Embryological defects can be from various Abbertions in the development of Heart Tube. To generalize we have could see that the adult structures can be malformed as a result of abnormal development of Heart tube components as mentioned below.

## Embryology of Heart

| Embryonic structure | Adult structure |
|---|---|
| **Truncus arteriosus** | ▪ Aorta<br>▪ Pulmonary Trunk |
| **Bulbus cordis☛** | ▪ **Smooth** part of R ventricle<br>▪ **Smooth** part of L ventricle |
| **Primitive ventricle** | ▪ **Rough** part of R ventricle<br>▪ **Rough** part of L ventricle |
| **Primitive atrium** | ▪ **Rough** part of R atrium<br>▪ **Rough** part of L atrium |
| **Sinus venosus** | ▪ **Smooth** part of R atrium<br>▪ **Coronary sinus (Lt horn of sinus venosus)**<br>▪ **Oblique vein of Left Atrium** |

Generalizations from Embryology :

- The primitive atrium gives rise to the trabeculated part of the right and left atria.
- The primitive ventricle gives rise to the trabeculated part of the right and left ventricles.
- The truncus arteriosus gives rise to the proximal portions of the ascending aorta and the pulmonary trunk.
- The 3rd, 4th, and 6th aortic arches and the right and left dorsal aortae contribute to the remainder of the aorta.
- The bulbus cordis gives rise to the right ventricle and the aortic outflow tract.
- The left horn of the sinus venosus gives rise to the coronary sinus.
- The right common cardinal vein gives rise to the superior vena cava.
- The right horn of the sinus venosus gives rise to the smooth part of the right atrium

All patients with suspected cyanotic CHD were provisionally included in this study. All the children with cyanosis due to other causes like peripheral cyanosis, Eisenmenger's syndrome, primary PAH, pulmonary arteriovenous

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fistula, and methemoglobinemia etc. were excluded. A prospective observational study at three pediatric cardiac centers was done over a period of 2.5 years. Spectrum of disease, common symptoms at presentation, age, and clinical outcome and follow-up were recorded for each case.

Results:

Cyanotic heart defects constituted 25.50% of total CHDs. Table 1 shows the demographic characteristics of the patients with CCHDs. There were 288 children with CCHD with a male to female ratio of 1.42:1. The children were aged from newborns to 18 years of age. 70 (24.3 %) patients presented in the neonatal period (<1 month of age), however majority of the patients were in the age group of 1 month -1 year of age (120 patients - 41.7%). Seventy-four patients (25.7 %) were between 1 -5 years at the time of presentation. Thus by 5 years of age, approximately 91.7% of the children with CCHDs had been diagnosed owing to the earlier onset of symptoms and earlier referral for this much severe subset of CHD.

**Table 1: Demographic details of patients with Cyanotic congenital heart disease.**

| Age group | Males | Females | Total n, (%) |
|---|---|---|---|
| 0-1 month | 44 | 26 | 70 (24.3) |
| 1-12 months | 68 | 52 | 120 (41.7) |
| 1-5 years | 39 | 35 | 74 (25.7) |
| 5-18 years | 18 | 6 | 24 (8.3) |
| Total | 169 | 119 | 288 |

Table 2 represents the clinical spectrum in accordance with age and gender distribution of CCHDs detected. Among CCHDs, five most common cyanotic

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lesions were Tetralogy of fallot (TOF) constituting 44.8 % of the total, Single Ventricle 11.5%, DORV 11.1%, TGA 8.6% and TAPVC 8 %, thus constituting about 84% of the total load of CCHDs.

**Table 2: Clinical profile and spectrum of various cyanotic congenital heart diseases in accordance with age and sex distribution.**

| S. no. | Diagnosis | Less than 1 month | | 1-12 month | | 1-5 years | | 5-18 years | | Total(%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | M | F | M | F | M | F | M | F | |
| 1 | TOF | 10 | 7 | 28 | 23 | 24 | 22 | 10 | 5 | 129(44.8) |
| 2 | SV | 8 | 5 | 9 | 7 | 1 | 2 | 1 | 0 | 33(11.5) |
| 3 | DORV | 4 | 2 | 7 | 6 | 6 | 5 | 1 | 1 | 32(11.1) |
| 4 | TGA | 5 | 3 | 5 | 4 | 3 | 3 | 2 | 0 | 25(8.6) |
| 5 | TAPVC | 6 | 4 | 4 | 4 | 2 | 1 | 2 | 0 | 23(8) |
| 6 | TA | 3 | 2 | 3 | 4 | 1 | 0 | 1 | 0 | 14(4.8) |
| 7 | PA | 2 | 1 | 4 | 2 | 1 | 1 | 0 | 0 | 11(3.8) |
| 8 | HLHS | 2 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 6(2) |
| 9 | E A | 1 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 5(1.7) |
| 10 | CCTGA | 1 | 0 | 2 | 0 | 1 | 0 | 0 | 0 | 4(1.4) |
| 11 | Truncus | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 3(1) |
| 12 | Common Atrium | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 3(1) |
| | Total | 44 | 26 | 68 | 52 | 39 | 35 | 18 | 6 | 288 |

TOF = Tetralogy of fallot, SV =Single ventricle, DORV=double outlet right ventricle, TGA= Transposition of great vessels, TAPVC =Total anomalous pulmonary venous connection TA = Tricuspid atresia, PA= pulmonary atresia,

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HLHS = Hypoplastic left heart syndrome, Ebsteins anomaly, TA= Truncus arteriosus, CCTGA= congenitally corrected TGA

Tetralogy of Fallot (TOF): TOF was the most commonly detected cyanotic heart lesion seen in 44.8% of the CCHD. There were a total of 72 males and 57 females with TOF with the male: female ratio of 1.26:1. Most of the patients presented with cyanosis alone in infancy or beyond infancy with cyanotic spell or cyanosis with exertional dyspnoea in later age group. Three patients had cerebral abscess with history of stroke. Down syndrome was seen in 6 patients with TOF. TOF had the most favourable natural history among all the CCHDs and 61 out of 129(47%) TOF cases presented beyond infancy. In comparison, rest of cyanotic lesions were common during infancy.

Single ventricle: SV was seen in 11.5% of the CCHD. Pulmonary stenosis was seen in 20 out of 33 patients. Two patients had underlying Downs syndrome.

DORV: it was seen in 11.1 % of the CCHDs. 23 out of 32 cases had associated pulmonary stenosis. Downs syndrome was seen in two of the patients with DORV-VSD-PS.

TGA: Out of 25 patients (8.6% of CCHD) with TGA 8 had intact interventricular septum (IVS) while 10 had associated VSD and 7 had associated VSD-PS.

TAPVC: among 288 patients with CCHDs 23 (8%) had TAPVC. 13 had supracardiac TAPVC, 7 had cardiac TAPVC and 3 had infracardiac TAPVC.

TA: Tricuspid atresia was seen in 14 patients (4.8%) with 9 having associated VSD-PS and 5 having large VSD with unrestrictive pulmonary blood flow.

PA: Pulmonary atresia with large VSD was seen in 7 patients while 4 had intact interventricular septum.

HLHS: Two patients with HLHS had mitral atresia/aortic atresia with hypoplastic arch, two had aortic atresia with patent mitral valve and hypoplastic arch and two had mitral stenosis with aortic stenosis. Prognosis was dismal in HLHS with 3 dying in infancy and two were lost to follow-up where outcome was not known. One patient with successful operation is on regular follow-up.

E A: All the 5 patients with Ebsteins anomaly had ASD, two of them are on medical follow-up as they did not have an indication for surgery as yet while three were advised surgery. Among these three only one patient went for the surgical treatment while two were lost to follow-up.

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CCTGA: Among the 4 patients with CCTGA 2 had VSD-PS, one had VSD and one had intact IVS without PS.

Truncus: Three patients were diagnosed with Truncus in which 2 had type I and one had Type II truncus. Two patients expired and one was lost to follow-up.

Common Atrium: Three patients with common atrium were diagnosed during this time period in which 2 were operated and one was lost to follow-up.

Clinical presentation and indication for cardiac evaluation:

Cyanosis was the most consistent presenting clinical feature noted being present in 68.8 % . The children presented with distinct clinical features as depicted in table 3 and some had more than one feature. Most of the newborns were referred from the neonatal units after the basic screening for spo2 and 12 newborns were referred due the abnormal fetal echocardiography report where the lesion was already diagnosed in the perinatal life.

**Table 3: Mode of presentation in various cyanotic congenital heart diseases.**

| s.no | Clinical features | Number of patients | %age of all the patients |
|---|---|---|---|
| 1 | Cyanosis | 198 | 68.8 |
| 2 | Spells | 25 | 8.6 |
| 3 | Intermittent feeding | 55 | 19.1 |
| 4 | Exertional dyspnea | 25 | 8.6 |
| 5 | Tachypnoea | 21 | 7.3 |
| 6 | Failure to thrive | 18 | 6.2 |
| 7 | Congestive heart failure | 9 | 3.1 |
| 8 | Murmur | 46 | 16 |
| 9 | Recurrent chest infections | 16 | 5.5 |
| 10 | Associated chromosomal anomalies | 10 | 3.5 |
| 11 | Family history of CHD in a sib | 5 | 1.7 |

Mid-term outcome and Outlook for cyanotic congenital heart disease:

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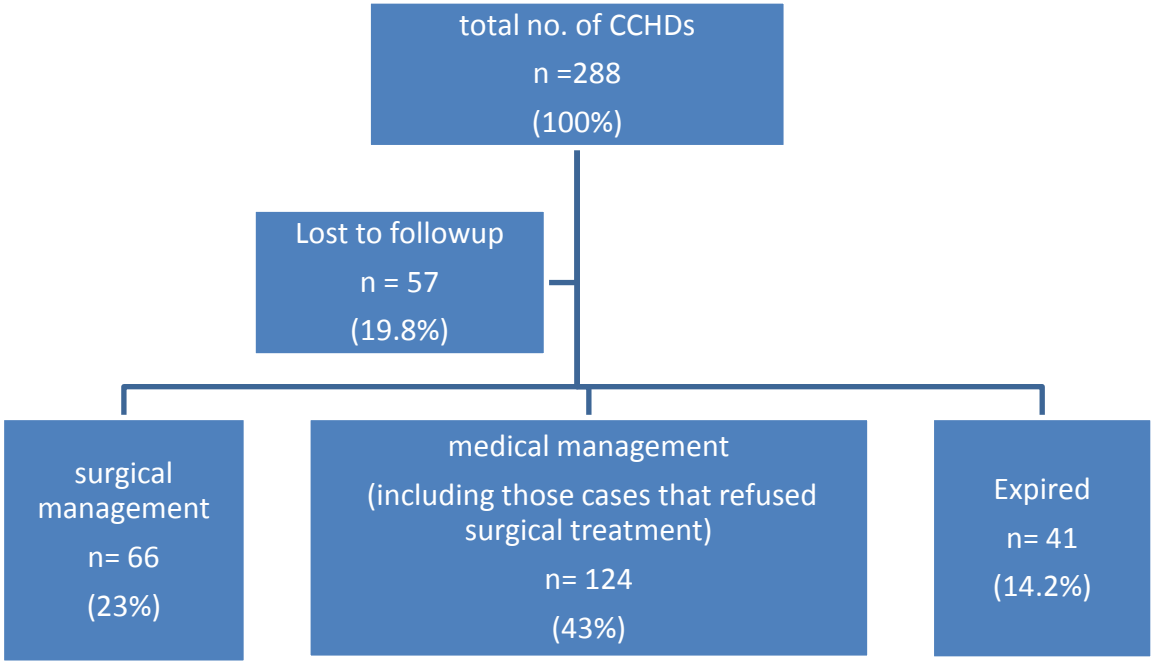
Figure 1 represents the midterm outcome in various CCHDs. Out of the total 288 patients 57 (19.8%) were lost to follow-up. In the remaining 231, only 66 (23%) went to the higher centres for surgical repair whether corrective or palliative. Medical management was done in 124 (43%) and included those patients who refused the surgical intervention on basis of either non-affordability or non-availability of trained manpower at their native place. Mortality during this time period was seen in 41 patients (14.2 %).




**Discussion:**

In the present study CCHDs constitute 25.5 % of the total load of CHDs detected. Similar distribution has been reported in all the literature with acyanotic heart disease more common than cyanotic heart disease.[1,2,3] Our study showed a male preponderance with M: F ratio of 1.42:1 for the CCHDs which in accordance with the studies done by Gupta et al and Kumar et al.[7,9]

In 65% of the cases CCHD was diagnosed under 1 year of age and in 91.7% by five years of age. This agrees with the studies by Hussain et al.[10] In developing countries most cases are not diagnosed until late in infancy. Some cases are not even diagnosed until 5 years of age or older. Common reasons for such late presentation includes difficulty in assessing specialized paediatric cardiac care, affordability and poor health seeking behaviour among the low to middle class groups.[11,12]

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Among the different types of cyanotic heart lesions, TOF was the most common lesion (44.8%) of all the CCHDs. The finding is consistent and widely established in literature.[13,14]

The most common mode of presentation and reason for cardiac evaluation was cyanosis and cyanotic spells in 77.4 %, followed by intermittent feeding (19.1%) exertional breathlessness (8.3%) and tachypnoea (7.6 %). Murmur on auscultation as observed by the paediatricians was the reason for referrel in 16 % of the patients. This was in agreement with other studies done by Animasahun BA et al, Humayun et al and Dorfman et al.[15,16,17] Downs syndrome was seen in 10 patients with cyanotic heart diseases. It has been observed in various studies that 40 to 63.5% of Downs syndrome patients have CHD associated with them. [18]

In our study 14.2 % of children with cyanotic CHD expired during the study period. This mortality rate is comparable to study by Shah et al which showed mortality rate of 20%. Other studies showed much higher rates of 36.4% by Humayun et al[16]. The difference may be due the difference in the study population (age group of 0-18 years in our study as compared to neonatal cases only in other studies) and the higher number of patients that were lost to follow-up (19.8 %) many among whom would also have succumbed to CCHDs eventually and were thus unaccounted for.

Only 23% of the patients underwent surgery. Poverty and the lack of cardiac care facilities mainly the surgical care for these CCHDs is the main reason for this. In addition, lack of parental awareness also attribute to lower number of patients getting the surgical treatment.[15]

CCHDs impose a significant financial burden on the family and the lack of critical cardiac surgical care in Kashmir valley is a major obstacle to the way forward. Among those referred to higher dedicated centres for cardiac surgeries many are lost to follow-up. In addition, robust screening programmes and dedicated paediatric cardiology units must be set for the early detection and management of lesions which have an excellent outcome after surgery and the child can live a near normal life.

Limitation of the study:

As the data is not population based and depended only on referrals, so it is not a true representative of profile of CCHDs, however due to the limited paediatric cardiac care facilities available in this part of India, this data would be useful when extrapolated to the general paediatric population and will prove to be a useful guide in framing the need for the paediatric cardiac surgical facilities

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which is the mainstay treatment for these type of congenital cardiac lesions.This study is important for low resource settings such as ours where it can provide a basis for further studies and the need to develop appropriate clinical interventions.

## Conclusion:

One should be aware of Embryology of Heart as a clinician. Cyanotic congenital heart disease is common among Kashmiri children with most of them being detected in infancy. Males are more affected. Diagnosis is still made late in most of the cases due to delayed referrals and lack of awareness. Definitive surgical correction is not readily available. TOF is the most common among CCHDs seen and constituted 44.8% of the cases. Cyanosis is the most common mode of presentation. Clinical features are protean; thus a high index of suspicion is required to make an early diagnosis and appropriately manage the cases.

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