RESEARCH PAPER

Neurodevelopmental Status of Children Aged 6-30 Months With Congenital Heart Disease

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Background: Children with congenital heart diseases (CHD) are considered to be at high-risk for neurodevelopmental delay, but scant Indian data are available.

Objective: To evaluate the neurodevelopmental status of children with CHD.

Methods: We enrolled consecutive children aged 6-30 months with echocardiographically-confirmed CHD between June 2013 and January 2014. Children with clinically recognizable genetic syndromes or disorders; visual and/or hearing deficits, and microcephaly; and post-cardiac surgery children were excluded. Development was assessed by Developmental Assessment Scale for Indian Infants (DASII) and Developmental delay defined as Development Quotient (DQ) <70 in either the mental or motor scale.

Results: 75 children (53 males) with CHD were enrolled. Acyanotic CHD was seen in 51 children (VSD in 47%), and Tetralogy of Fallot was the commonest cyanotic CHD (25%). Developmental delay was seen in 25% of these children, more in the motor domain (48%) than in mental (12%). Mean motor and mental DQ in acyanotic CHD was 77 and 84, respectively; and 65 and 85, respectively in cyanotic CHD. Mean motor DQ was significantly less than mental DQ in both acyanotic and cyanotic CHD children (P=0.048).

Conclusion: Children with CHD are at an increased risk for developmental delay. Periodic surveillance, screening and evaluation should be instituted in them for early identification and appropriate interventions to enhance later academic, behavioral, psycho-social and adaptive function.

Keywords: *Congenital heart defects, Developmental disabilities, Intervention, Neurodevelopmental delay, Outcome, Surveillance.*

Increasing survival rates in children with Congenital heart diseases (CHD) have been associated with a shift in focus from heart-related morbidity and death to concern for brain integrity, and developmental and neurological outcomes have come under increasing scrutiny [1-3]. These children are at risk of developmental problems due to events that occur during intrauterine life, at surgery, or during the growing years *e.g.*, poor perfusion, shock, acid-base disturbances, hypoxia, and failure to thrive. Neurodevelopmental delay in children with CHD is reported to be more common with cyanotic CHD, and in those requiring surgical intervention [4].

There is very little information available on the neurodevelopmental status of Indian children with CHD. The only Indian study on the topic has addressed neurodevelopmental outcome of infants after cardiac surgery [5]. Thus, the present study was conducted to study the neurodevelopmental status of children with congenital heart disease and elucidate associated factors.

METHODS

This descriptive study was conducted from June 2013 to January 2014 in the Pediatrics department of Lok Nayak hospital, Maulana Azad Medical College, Delhi, after obtaining clearance from the Institutional Ethics Committee. With an expected 25% prevalence of developmental delay in children with CHD, with a 90% precision and 95% confidence, a sample size of 72 was calculated. We planned to enroll 75 children, expecting a 5% loss to follow-up between stabilization and developmental assessment.

All consecutive children in the age group of 6 to 30 month who presented with symptoms and signs suggestive of congenital heart disease, which was confirmed by echocardiography, were approached for inclusion after initial management and stabilization of the child. Children with clinically recognizable genetic syndromes or disorders *e.g.*, Down, Alagille, Turner or Noonan syndrome and VACTERL association; Visual and/or hearing deficits; microcephaly; and, those who were post-cardiac surgery were excluded. Parents were explained about the purpose of the study and a written informed consent was obtained. This process was continued till the *a priori* sample size of 75 children was achieved.

Echocardiography was done after the patient was stabilized, and details of the cardiac problem were recorded in the form. Blood investigations including complete hemogram, serum calcium, serum phosphorus, and alkaline phosphatase were done in all children. Neurodevelopmental assessment was done by Developmental Assessment Scale for Indian Infants (DASII) [6] by a single trained examiner, when the child was clinically stable to undergo the evaluation. Developmental delay was defined on DASII as DQ score ≤70 (≤2SD) in either the mental or motor scale [6]. Anemia was defined as hemoglobin <11g/100mL in acyanotic CHD group and <15g/100mL in cyanotic CHD group. Management of the child's acute condition was done by the pediatricians in the treating unit. All children with developmental delay also underwent thyroid function tests.

Clinical severity of lesion was classified as per criteria suggested by Hoffman and Kaplan [7]. Children were classified as low-, moderate- and high-risk groups for developmental delay based on criteria given by American Heart Association [4]. Appropriate interventions were provided at the Child Development Centre of our institution for all children with developmental delay; and early intervention provided to those in high-risk categories for developmental delay [8].

Statistical analysis: Data were entered in Excel spreadsheets and analyzed using SPSS 16.0 by a statistician. Various anthropometric and clinical factors were compared between CHD patients with or without neurodevelopmental delay by the Chi-square test or Fischer exact test. Mean DQ was compared between cyanotic and acyanotic groups by the Student's t test, and between risk and severity groups by Anova. A *P*-value less than 0.05 was considered significant.

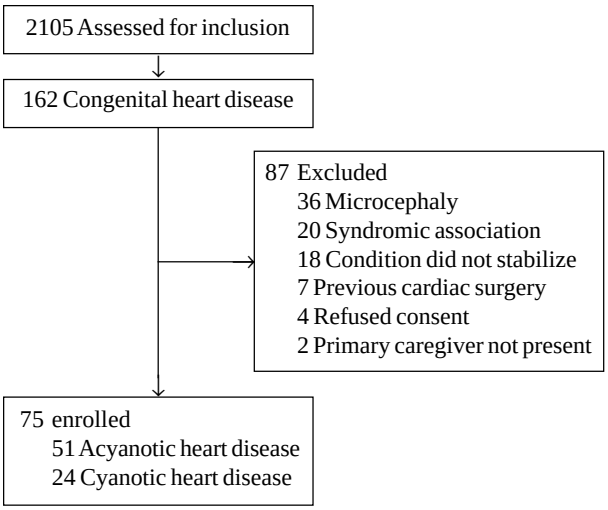

FIG.1 *Flow of participants in the study.*

RESULTS

A total of 2105 children in the described age-group attended the hospital during the study period, of which 75 children (51 acyanotic CHD) were enrolled (***Fig.* 1**). Majority of children (62.6%) in the study group were in the younger age group (6-12 month), with 29.4% older than 18 months. 57.3% had weight <-3 Z score of WHO charts; although there were no age, sex or anthropometric differences between children with cyanotic or acyanotic CHD. Ventricular septal defect was the commonest acyanotic CHD (47%) and Tetralogy of Fallot was the commonest cyanotic CHD (25%) (***Table* I**).

The mean Motor DQ was significantly lower in the cyanotic group than acyanotic group (*P*=0.048). However, mean Mental DQ was not different among acyanotic and cyanotic CHD groups (*P*=0.92) or according to type of acyanotic CHD (*P* = 0.44) (***Table* II**). Delayed motor development was seen in 75% children with cyanotic CHD and 35.3% with acyanotic CHD (*P*=0.001) (***Table* II**). The motor DQ was also found to be significantly affected by type of ACHD (*P* = 0.018), with lower motor DQ in large VSD and complex acyanotic CHD. DQ was not different among various type of cyanotic CHD (*P*=0.223 and 0.526 for mean Motor and Mental, respectively) (Data not shown).

All cyanotic CHD children were in severe group (***Table* III**). As per AHA risk stratification for developmental delay, 35(68%) children were in low and 15 (29%) in moderate risk group among acyanotic CHD. Among cyanotic CHD, 16 (66%) were in moderate risk group and 8 (33%) in high risk group. As expected, motor DQ was found to be significantly lower in the severe group (*P*=0.01), whereas mental DQ was not much

TABLE I CHARACTERISTICS OF CHILDREN WITH CONGENITAL HEART DISEASE (*N*=75)

Characteristic	*ACHD (n=51), No. (%)*	*CCHD (n=24), No. (%)*
Male sex	34 (66.7)	19 (79.2)
Weight <-3 Z score	34 (66.7)	9 (37.5)
Height <-3 Z score	10 (19.6)	2 (8.3)
Anemia	36 (70.6)	17 (70.8)
Hypocalcemia	14 (27.4)	6 (25.0)
Rickets	3 (5.8)	3 (12.4)

ACHD: Acyanotic, and CCHD: cyanotic congenital heart disease.

TABLE II DEVELOPMENTAL STATUS IN CHILDREN WITH CONGENITAL HEART DISEASE (*N*=75)

Characteristic	*ACHD group (n=51)*	*CCHD group (n=24)*	*All children (n=75)*
Development Quotient, Mean (SD)			
Motor	77 (17.9)	65 (17.8)	71 (17.9)
Mental	84 (11.8)	85 (11.7)	84.5 (11.8)
Developmental Delay (DQ≤70), No. (%)			
*Motor	18 (35.3)	18 (75)	36 (48)
Mental DQ	8 (15.7)	1 (4.2)	9 (12)

**P<0.001 for comparison of proportion of children with cyanotic and acyanotic CHD with motor delay.*

different across either the severity groups or the risk categories (***Table* III**).

Neurological abnormalities were found in 6 children, among which 3 children were in high risk category. Most common neurological abnormality found was hypotonia (5 children). USG cranium was normal in all children.

DISCUSSION

In this descriptive hospital-based study of 75 children with CHD (68% acyanotic CHD) assessed by DASII, 48% and 12% children had low (≤70) Motor and Mental DQ, respectively.

The limitations of the present study include smaller number of cyanotic CHD children, lack of non-CHD controls, lesser number of patients in the older age-groups, and absence of follow-up after surgery/control of cardiac failure. There are other psychosocial factors that may have a negative impact on these children including physical restriction, parental overprotection, school absence, and decreased peer-interaction, which were not studied.

TABLE III DEVELOPMENTAL STATUS IN CHILDREN WITH CONGENITAL HEART DISEASE BASED ON SEVERITY CLASSIFICATION AND RISK STRATIFICATION (*N*=75)[#]

Characteristic	*Motor DQ, Mean (SD)*	*Mental DQ, Mean (SD)*
**Severity*		
Mild (*n*=14)	79 (17.9)	85 (11.8)
Moderate (*n*= 23)	75 (17.8)	88 (11.7)
Severe (*n*=38)	64 (17.8)	86 (11.7)
Risk		
Low (*n*=35)	73 (17.9)	87 (11.8)
Moderate (*n*=31)	70 (17.8)	87 (11.7)
High (*n*= 9)	60 (17.8)	83 (12.1)

*#Severity of congenital heart disease as per Hoffman and Kaplan [7], and risk group as per American Heart Association [4]; *For Motor DQ across severity groups P<0.01.*

Nearly half the children (57.3%) had weight <-3 SD of WHO growth chart. Malnutrition in infants with CHD is related to increased energy expenditure and inadequate caloric intake for growth [9]. Mean motor DQ was decreasing with the severity, which was in accordance to previous studies [10] stating that developmental delay increases with the complexity of heart disease. Stratification based on risk for developmental delay has been given by American Heart Association [4]. We found low DQ in high risk groups in all domains compared to moderate- and low-risk groups.

More developmental delay was found in CCHD group in various previous studies due to chronic hypoxia caused by underlying CHD [7]. In a previous study [11] of neurodevelopmental status of newborns and infants with congenital heart disease before and after open heart surgery, newborns with acyanotic defect were more likely to demonstrate neurologic abnormality than those with cyanotic defect. In another study [12] from Canada, gross and/or fine motor delay was documented in 42%, and 23% had global developmental delay. Higher number of children with developmental delay in our study compared to these studies could be due to the high prevalence of uncontrolled CHF; anemia and rickets may also contribute to the same. Similar to our study, others have also found that motor delay is more than mental delay among children with CHD [13,14].

The high rate of developmental delay among children with CHD demonstrated in this study has important implications for practice and research. Future studies need to identify modifiable factors affecting development among these group of children in addition to those previously identified (*e.g.*, congestive cardiac failure and anemia). Screening and evaluation of developmental delay in pediatric CHD population are essential steps to guide appropriate interventions to maximize their overall development.

WHAT THIS STUDY ADDS?

- Developmental delay is common among children with congenital heart diseases.
- Developmental delay it is more common in those with cyanotic heart disease, and in the motor domain.

Contributors: DM: conceived and planned the study, and supervised the conduct of the study and preparation of the manuscript. KL: enrolled subjects, did the neurodevelopmental assessment, analyzed data, and prepared the initial draft of the manuscript. VM: echocardiographic studies. MJ: supervised the neurodevelopmental assessment. VM and MJ: assisted in the planning of the study and preparation of the manuscript. All authors approved the final manuscript for publication.
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