Original Research Article

A study on clinical and echo cardiographic evaluation of neonatal cardiac murmurs and their follow up at 6 weeks of age

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Abstract

Background: The echocardiogram permits early accurate anatomical diagnosis either to reassure parents that the heart was normal, or to detect a heart disease and explain the nature of the abnormality and make an early referral for definitive treatment. **Aim:** Assessment of neonatal cardiac murmurs clinically and by echocardiogram at birth and at 6 weeks of age. **Materials and Methods:** A prospective longitudinal study was conducted on neonates for a period of one year at Government Mohan Kumaramangalam Medical College Hospital, Salem. Cardiac murmur was graded between 1 and 6 based on the intensity of the murmur. All neonates underwent an echocardiographic examination by Cardiologists at 1st week and later at 6 weeks. **Results:** The incidence of murmur in the first week of life was 23/1000 live births and the incidence of congenital heart disease was 12.6/1000 live births and at 6 weeks it was 6.6/1000 live births. The most common congenital heart disease during the 1st week examination was found to be VSD, followed by ASD and PDA. Identifying a pathological murmur and its association with structural congenital heart disease was found to be statistically significant ($p<.05$), whereas identifying an innocent murmur and its association with a normal heart did not show a statistical significance and so it infers that all the innocent murmurs has to be followed up with a echocardiogram to rule out structural heart disease in the neonates. **Conclusion:** It is important to evaluate all neonatal cardiac murmurs with echocardiogram before they become symptomatic.

Keywords: Congenital heart disease, Murmur, Echocardiogram
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Introduction

Congenital heart disease is one of the most common congenital malformations. It remains the major cause of death in babies with congenital malformations. The most common presentations of the neonates with congenital heart disease are heart murmur, respiratory distress, cyanosis and congestive cardiac failure. They may also have abnormal chest x-ray and ECG findings. Congenital heart diseases account for about 10% of infant deaths and in that about half of the deaths are due to congenital malformations [1].

The estimated prevalence of CHD in the first 12 months was 6-8 per 1000 live births [2]. About 25% of CHDs are life-threatening and may manifest before the first routine clinical examination [3,4]. Failure to identify these critical lesions immediately after birth leads to increased mortality and morbidity [5]. The difficulties in detecting heart disease at neonatal examination are well known [6]. The neonatal examination takes place at a time of rapid change within the cardiovascular system as part of adaptation to extra uterine life [7]. These changes may produce murmurs which can be mistaken for heart disease [8]. Similarly, if transitional changes are slow to occur, presentation of congenital heart disease may be delayed.

Some murmurs in neonates, many in infants and most in childhood are 'benign' or 'innocent' [9,10]. The reported prevalence of murmurs in neonates varies from 0.6% to 77.4% [11]. Differentiation of such murmurs from those due to structural cardiac disease, so called 'pathological' murmurs, is largely clinical. Paediatricians are capable of differentiating one from

the others, provided a detailed evaluation is done. Thus, detection of a murmur depends on the examiner's skill and experience, the timing and frequency of examination and the condition under which examination takes place. One of the major challenge in the management of congenital heart disease is its early diagnosis as very few validated investigatory tools being available.

Most babies presenting with an innocent heart murmur usually have a mid systolic ejection murmur which is of grade 1–2/6 in intensity, located in the pulmonary area, radiates to the axillae and the back, and typically disappears by 3–6 months of age, which suggests that the origin is a branch of the pulmonary artery based on the hypothesis supported by clinical and angiographic studies [12]. However, not many studies had reported the echo cardiographic findings of newborn babies with an innocent heart murmur in the first days of life.

The echocardiogram permits early accurate anatomical diagnosis either to reassure parents that the heart was normal, or to detect a heart disease and explain the nature of the abnormality and make an early referral for definitive treatment.

Based on the echocardiography findings the neonates can be categorised as either having structural heart malformations; a physiological variant which would account for the murmur (such as left pulmonary artery branch stenosis or patent ductus arteriosus); a finding that in itself would not cause a murmur (such as cardiac hypertrophy secondary to maternal diabetes); or a completely normal echo-cardiogram [13].

Aim

Assessment of neonatal cardiac murmurs clinically and by echocardiogram at birth and at 6 weeks of age.

Methodology

Study design: Prospective longitudinal study

Study area: Government Mohan Kumaramangalam Medical College Hospital, Salem.

Study period: One year

Sample size: 98 neonates

Sampling: All babies born during the study period

Inclusion criteria: All term babies delivered in our hospital with cardiac murmurs on clinical examination were included in the study.

Exclusion Criteria: Preterm babies and all sick and moribund newborn babies who cannot be completely evaluated were excluded from the study. The study was conducted after getting the clearance from the institutional ethical committee and the informed consent from the parents of the newborn. Details of the neonates with precordial murmurs were taken into a structured data collection sheet which included socio-demographic variables such as maternal age, period of gestation, maturity and the sex of the baby, ethnicity and geographical area. Dysmorphology assessment of the neonate was done by history, physical examination of growth parameters, ectodermal features such as skin and hair, skull, face regions and overall face impression, hands and feet, joints and skeleton, and genitals and anus. Those with features suggestive of Down Syndrome (DS) were confirmed by karyotyping.

A thorough clinical examination was conducted which was later followed by ECG and Chest X-ray. Cardiac murmur was graded between 1 and 6 based on the intensity of the murmur. The intensity of the heart murmur was gauged using the system originally proposed by Levine [14]. Respiratory distress as defined as respiratory rate >60/min with chest wall recessions and grunting. Following which all neonates underwent an echocardiographic examination by Cardiologists. Echo included two-dimensional, M-mode, and Doppler measurement in the standard projections: subcostal view, four-chamber view, five chamber view, long- and short-axial parasternal views, and suprasternal view, with examination of the anatomy of the atriums, atrioventricular valves, ventricles, and septums. The semilunar valves, outflow tracks, and the great vessels were evaluated and flow in the ductus arteriosus examined-mode measurements were for evaluation of left and right ventricular dimensions, thickness and motion of the ventricular walls, left ventricular ejection fraction, and fractional shortening. Echocardiogram was performed initially at the 1st week after birth and later during the follow-up visit at 6 weeks. Then neonates were then classified as having innocent murmur and structural heart defect and the structural heart defect was further subdivided into physiological variant or with significant heart disease.

Statistical Analysis: All data were entered and analysed by using SPSS version 21, for all the quantitative variables mean and standard deviation was derived and for all the non-parametric variables chi-square test was used for assessing the association between them considering $p < .05$ as statistically significant.

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Results

The total number of live births occurred during the study period was 4116 and among them 98 neonates were found to have murmur during auscultation and only those 98 neonates were included in our analysis. Based on the neonates birth weight they were classified as appropriate for gestational age, small for gestational age and large for gestational age. The gender and birth weight wise distribution of the neonates was shown in table 1. It is seen from the table that the male and female neonates were almost in equal number with a M:F ratio of 0.9:1. More than 80% of the study subjects were appropriate for age and only 15% of the study subjects were small for gestational age and 3% were large for gestational age. The signs and symptoms for the neonates were assessed during the 6th week of the follow-up period and the major symptoms were fast breathing and difficulty in feeding and the major sign was found to be respiratory distress and cyanosis (table 2). The presence of congenital heart disease was confirmed by echocardiogram. The association of grading of murmur and the presence of congenital heart disease was shown in table 3. It is inferred from the table that as the grading of murmur increases the possibility of having congenital heart disease was found to be higher as there is a statistical significant association exist between the grading of murmur and the presence of CHD ($p<.05$).

Based on the echocardiogram findings of the 98 neonates with murmur 52 of them were found to have a structural heart disease during the first week of examination and all the 98 neonates were asked to come for a follow-up visit at 6 weeks, in that out of 98 only 84 had come for the follow-up visit and among them 35 neonates were confirmed to have a structural congenital heart disease by performing a echocardiogram. The most common congenital heart disease during the 1st week examination was found to be VSD, followed by ASD and PDA followed by cyanotic heart disease, physiological pulmonary stenosis and patent foramen ovale were found to be present in 6 and 2 neonates respectively. During the follow-up visit in the 6th week both the patients with physiological pulmonary stenosis were found to become normal and out of 6 patients with patent foramen ovale 3 patients had become normal and one patient with cyanotis heart disease had died before the 6th week (table 4). The various associated anomalies that were presented in patients with congenital heart disease were tabulated in table 5. Only 10 patients with CHD had an associated anomaly out of which Down's syndrome was present in two patients and the other anomalies were cleft lip, anal atresia, diaphragmatic hernia, etc. Among the various risk factors associated with CHD, consanguineous marriage, presence of CHD in mother, father or sibling found to have a statistical significant association with CHD whereas any type of chronic morbidities in the antenatal period like diabetes, hypertension, pre-eclampsia did not had a statistical significant association with the development of congenital heart disease (table 6). The association between presence of murmur and the congenital heart disease was shown in table 7. Identifying a pathological murmur and its association with structural congenital heart disease was found to be statistically significant ($p<.05$), whereas identifying an innocent murmur and its association with a normal heart did not show a statistical significance and so it infers that all the innocent murmurs has to be followed up with an echocardiogram to rule out structural heart disease in the neonates.

Table-1: Gender and birth weight wise distribution of the study subjects

Birth weight	Gender		Total	P value
	Male	Female		
Appropriate for gestational age	38 (80.8%)	42 (82.3%)	80 (81.6%)	0.794
Small for gestational age	8 (17%)	7 (13.7%)	15 (15.3%)	
Large for gestational age	1 (2.1%)	2 (3.9%)	3 (3%)	
Total	**47 (100%)**	**51 (100%)**	**98 (100%)**	

P value derived by applying Chi-square test

Table-2: Distribution of the study subjects based on the symptoms and signs at 6 weeks of follow-up

Symptoms	Frequency	Signs	Frequency
Bluish discoloration of the body	6 (17.6%)	**Cyanosis**	5 (13.8%)
Fast breathing	16 (47%)	**Low oxygen saturation**	9 (25%)
Feeding difficulty	9 (26.4%)	**Edema**	4 (11.1%)
Sweating	3 (8.8%)	**Respiratory distress**	12 (33.3%)
		Bounding pulse	6 (16.6%)
Total	34 (100%)	**Total**	36 (100%)

Table-3: Association of grading of murmur and presence of CHD based on echocardiogram.

Murmur	Echocardiogram findings		P value
	CHD present	**CHD absent**	
Systolic grade 1 (n=4)	0	4 (100%)	<.001
Systolic grade 2 (n=32)	4 (12.5%)	28 (87.5%)	
Systolic grade 3 (n=42)	19 (45.2%)	23 (54.7%)	
Systolic grade 4 (n=11)	6 (54.5%)	5 (45.4%)	
Systolic grade 5 (n=5)	4 (80%)	1 (20%)	
Systolic grade 6 (n=4)	4 (100%)	0	

P value derived by applying Chi-square test

Table-4: Types of congenital heart disease presented among the study subjects based on the echocardiogram findings at 1st week and 6th week

CHD confirmed by ECHO	1st week (n=98)	6th week (n=84)	P value
Normal	46 (46.9%)	49 (57.1%)	<.01
VSD	12 (12.2%)	8 (9.5%)	0.0314
ASD	9 (9.1%)	7 (8.3%)	0.318
Cyanotic heart disease	6 (6.1%)	5 (5.9%)	0.981
PDA	7 (7.1%)	3 (3.5%)	<.05
PFO	6 (6.1%)	3 (3.5%)	<.05
ASD+PDA	3 (3%)	3 (3.5%)	0.819
ASD+VSD	2 (2%)	2 (2.3%)	0.791
Physiological pulmonary stenosis	2 (2%)	0	<.05
Mild TR	2 (2%)	1 (1.1%)	0.918
ASD+TR	1 (1%)	1 (1.1%)	0.991
VSD+PDA	1 (1%)	1 (1.1%)	0.991
VSD+TR	1 (1%)	1 (1.1%)	0.991

P value derived by applying Chi-square test

Table-5: Distribution of the study subjects based on the presence of associated anomalies

Associated anomaly	Frequency	Percentage
No anomaly	88	89.8%
Absent radius	1	1%
Anal atresia	1	1%
Cleft lip	1	1%
Diaphragmatic hernia	1	1%
Downs syndrome	2	2%
Esophageal atresia	1	1%
Polydactyly	1	1%
Skin tag	2	2%
Total	98	100%

Table-6: Risk factors association between CHD among the study subjects.

Risk factors	CHD present	Percentage	P value
Consanguineous marriage (n=35)	20	57.1%	<.01
CHD in mother (n=3)	2	66.6%	<.001
CHD in father (n=2)	1	50%	<.01
CHD in sibling (n=1)	1	100%	<.01
Morbidities in Antenatal period like diabetes, hypertension, eclampsia etc (n=20)	3	15%	0.518

P value derived by applying Chi-square test

Table-7: Association between murmur and presence of CHD at 1st and 6th week among the study subjects

Time of examination	Clinical diagnosis of murmur	Echocardiogram diagnosis		P value
		Structural heart disease	Normal heart	
1st week	Pathological (n=44)	42 (95.4%)	2 (4.5%)	<.001
	Innocent (n=54)	10 (18.5%)	44 (81.4%)	0.548
6th week	Pathological (n = 40)	30 (75%)	10 (25%)	0.0251
	Innocent (n=44)	6 (13.6%)	38 (86.3%)	0.683

P value derived by applying Chi-square test

Discussions

Based on the results of the present study the incidence of murmur in the first week of life was 23/1000 live births and the incidence of congenital heart disease was 12.6/1000 live births and at 6 weeks it was 6.6/1000 live births. The overall percentage of structural heart disease among the neonates with murmur was 53.06%. In our study population 80 neonates were appropriate for gestational age. 3 were LGA (large for gestational age) and 15 were SGA (small for gestational age).

AGA (appropriate for gestational age) is taken as reference category. There is no significant relationship between birth weight and CHD. This is similar to study done by Mehrdad Mirzharahimi M D [15]. Reports have shown that murmurs in the neonatal period had shown a varying incidence between 0.3-77.4% with incidence depending on various factors such as study size, auscultatory conditions and the skill of the examiner [11]. An Iranian study, within 24-hour neonatal examination among 2,928 neonates had revealed the prevalence of murmurs as 31 per 1,000 live births.

Furthermore, the same study had shown that the prevalence of cardiovascular malformations as 16 per 1,000 live births [15]. However not all neonates with congenital heart disease will be found to have a murmur during the immediate postnatal period check and similarly the vice versa, as most of the congenital heart disease remains asymptomatic in the early neonatal period [16]. History of consanguinity was present in parents of 23 newborns (23.4%). History of CHD in family members is present in 11 newborns. When there is history of consanguinity in parents or history of CHD in family members there is three times more chance of getting CHD. Correlation between family history and CHD is significant. This is similar to studies by Becker S M and Ramegowda whose findings revealed increased incidence of CHD among babies of consanguineous parents [17,18].

Neonates with murmur also had clinical feature which assisted in the classification of murmur as innocent or pathological. Clinical features suggestive of CHD are respiratory distress (most common finding), cyanosis, low oxygen saturation, edema and bounding peripheral pulses. 19 out of 52 babies with CHD had clinical features at birth. At 6 weeks of follow up neonates with positive clinical features in addition to murmur had persistent structural heart disease.

This correlation between clinical features and CHD at birth and at 6 weeks follow up was statistically significant. E. Clarke et al in their study suggested checking oxygen saturation in any neonate with suspicion of CHD [19]. Cyanosis can be easily missed. Some of the congenital anomalies, trisomies and dysmorphisms are seen in babies in the study. They are Down syndrome, neonate with absent radius, anal

atresia, cleft lip, esophageal atresia with tracheoeso-phageal fistula, diaphragmatic hernia, polydactyly and skin tag. E. Clarke et al suggested to consider a murmur as pathological when it is associated with dysmorphic features [19]. In our study Chest X-ray showing cardiomegaly is taken as a positive finding and 10 out of 11 babies who had cardiomegaly were found to have structural heart disease. ECG abnormalities were found in 10 babies and in which 9 had structural heart disease.

In the study of Swenson JM et al chest X -ray and ECG helped in diagnosis of heart disease in 4 patients who were thought to have no heart disease [20]. They recommended ECG and Chest X -ray as valuable tools for heart disease evaluation.

A study conducted by Preethi S. Pillai etal in Kerala on 72 new-borns with murmur 75% had cardiac disease, of which 94.5% were acyanotic heart disease and 5.5 % had cyanotic heart disease and the prevalence of cyanotic heart disease and acyanotic heart disease was almost similar to the present study and few other studies done in various other parts of the world had also shown an almost similar results [21-24]. Thus, a need for early assessment in neonates with murmurs has been recommended. In our study the most common structural heart disease was ventricular septal defect which is of muscular type and several other studies had also shown VSD as the most common congenital heart disease.

In the present study 13% of innocent murmur at 6th week of follow-up was found to have structural heart disease which was almost in par with the results of the other studies [25,26]. Most of the babies (75.5%) in our study had grade 2 or grade 3 murmur. This was in agreement with other studies [27]. There was a strong association between the degree of murmur and the significance of cardiac disease as none of the babies with Grade 1 or 2 murmurs had severe cardiac disease and most of the babies with grade 3, 4 or 5 murmur had moderate to severe heart disease. In our study subjects none of the babies had a diastolic murmur. So it infers a skillful auscultation in recognizing a murmur in neonate is a mandate in routine neonatal examination.

Conclusion

Our study proves that the incidence of cardiac murmur is 23/1000 live births and if a murmur is detected there is a 53% chance of having structural heart disease. 7.7% of our study subjects had severe form of cardiac disease. Hence it is important to evaluate all neonatal cardiac murmurs before they become symptomatic. Prompt early referral for echocardiography is necessary for diagnosis and appropriate management to reduce morbidity and mortality. Structurally normal heart in echocardiography helps in authoritative re-assurance of parents.

Contribution by Authors

- Dr. Saranya Ravichandran – Designing the whole study and examining the patients
- Dr. Sampath Kumar Dhanaraj – Writing the manuscript and examining the patients
- Dr. Shankar Radhakrishnan – Statistical analysis and deriving the statistical inference

What this study adds to existing knowledge: Referring the neonates with cardiac murmurs for echocardiogram at the earliest would prevent most of the morbidity and mortality due to cardiovascular diseases.

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