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Original Article

Significance of Cardiac Murmurs in Symptomatic and Asymptomatic Neonates by Correlation with Echocardiogram

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Abstract

Introduction: Congenital heart disease (CHD), one of the commonest congenital anomaly in neonates, might result in adverse neonatal outcome if not detected and treated on time. Clinically, these neonates may present with murmurs. Neonatal physical examination aided by echocardiography has improved diagnostic yield.

Methods: A descriptive observational study was conducted over 18 months in a medical college hospital in Mangalore, India. Neonates with murmurs during their routine clinical examination or on follow up visits within the first 28 days of life were enrolled. Subsequently, they were categorized based on whether the symptoms were present or absent. Echocardiograms were performed by a paediatric cardiologist within 24 hours of the detection of murmurs and were correlated with the murmur and clinical features.

Results: The study identified cardiac murmurs in 70 (3.7%) out of 1880 neonates examined. Ejection systolic murmurs were predominant (71.4%) and commonly detected within the first two days (67.1%). Sixty percent of the neonates were symptomatic. Echocardiography revealed significant CHD in 30% of symptomatic and 5.7% of asymptomatic neonates. Symptomatic neonates at presentation were twice as likely to exhibit abnormal echocardiograms (Odds ratio: 2.071, with 95% confidence interval: 0.36-4.79), and additional physical examination features tripled the likelihood of abnormal echocardiograms (Odds ratio: 3.187, with 95% confidence interval: 1.542–6.612).

Conclusions: Cardiac murmurs were observed in 3.7% of neonates. In addition to murmurs, those who were symptomatic increased the likelihood of having CHD. Therefore, symptomatic neonates need cardiac evaluation before discharge.

Introduction

Congenital heart diseases (CHD) present a diverse array of issues as defects involving the heart walls, valves, or blood vessels. They are characterized by dynamic developmental processes from the early embryonic stage and are incredibly intricate.[1] Regrettably, congenital cardiac diseases constitute prominent contributors to infant mortality.[2] Globally, CHD is estimated to affect 6 – 12 per 1000, contributing to 1.35 million CHD cases worldwide annually.[3-6] Within this global context, over 200,000 CHD births occur in India.[2,5]

Efforts to identify significant CHD after delivery are ongoing.[3] A common misperception is that neonatal heart murmurs are mostly innocent.[6] A baby's murmur could be the first clue to indicate they have a CHD.[7] However, interpreting these murmurs presents challenges. When no structural defects exist, they are called innocent or physiological murmurs. On the other hand, irregular vascular and cardiac flow patterns caused by CHD can produce pathological murmurs.[6-9]

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The complexity of distinguishing innocent murmurs from those indicative of structural defects underscores the need for more precise diagnostic methods.[9,10] Data from prior studies show that over half of children with CHD cannot be diagnosed by a standard clinical examination.[2,11] For the diagnosis of CHD, in addition to clinical examination, electrocardiography and chest radiography have been used.[2,12] In light of this, the objective of the study was to estimate neonatal murmur frequency, identify the significance by correlating with echocardiogram diagnosis, and determine the clinical features aiding in diagnosis and correlating with the echocardiogram diagnosis. By emphasizing the pivotal role of key clinical features in CHD screening in resource limited settings, we wish to contribute to a more precise diagnostic approach, improving outcomes in paediatric cardiology.

Methods

A descriptive observational study was carried out at a medical college hospital in Mangalore, Karnataka, India for 18 months, starting in January 2021 to July 2022. The institutional ethics committee approved the protocol (Ref No.FMIEC/CCM / 66 / 2021). Written consent was obtained from the parents. The sample size of 69 (when a 99.9% confidence level is considered) was rounded to 70. Sample size was calculated using the formula N = [DEFF*Np (1-p)] / [(d^2/Z^2 1-□/2*(N-1) + p*(1-p)]. Population size (for finite population correction factor, or fpc) (N): 1000000. Hypothesized % frequency of the outcome factor in the population (p):1.6% ± 5%.[13] Confidence limits as % of 100 (absolute +/- %) (d): 5%. Design effect (for cluster surveys, DEFF): 1(4). Neonates were included if a murmur was detected on a daily routine clinical examination or on follow-up visits within the first 28 days of life. They were excluded if an echocardiogram couldn't be performed or if they were out born. The initial cardiovascular examination was focused on pulses, apical impulses, oxygen saturation, abnormal heart sounds, murmur character, and grading. Thorough medical history, physical assessment, and overall appearance, data were noted. Neonates showing signs of distress or heart failure were categorized as symptomatic, while asymptomatic neonates showed no such signs. An echocardiogram was usually done within 24 hours of the detection of a murmur by a paediatric cardiologist, and the echocardiogram diagnosis was correlated with the murmur and clinical features. The

CHD was classified as follows.[2,6,7,13,14]

Normal: no echocardiographic abnormality.

Insignificant congenital heart diseases: neonate with patent ductus arteriosus (PDA) < 2 mm in size, atrial septal defect (ASD) < 5 mm without left and right ventricular volume overload, respectively.

Significant congenital heart diseases: These were divided into acyanotic and cyanotic CHDs.

Data were analyzed using SPSS 23 version software. The statistical analysis was done using the mean and Fisher's exact test for categorical variables, and the odds ratio was used for binary variables.

Results

Of the 1880 neonates who were analyzed, 70 had murmurs, making the frequency of 3.7%. Among these, 57.2% were male neonates. The neonates were grouped as preterm and term, with 42.8% being in term gestation (37 – 40 weeks). The mean gestational age was 34.5 weeks. A maternal history of gestational diabetes mellitus was present in 10%, and none of the mothers had a history of prior cardiac disease [Table 1].

Table 1: The demographic characteristics

Gender	Number (N = 70)	Percentage
Male	40	57.2%
Female	30	42.8%
Gestational age		
37 - 40 weeks	30	42.8%
34 - 36 weeks, 6 days	15	21.4%
32 - 33 weeks, 6 days	11	15.7%
28 - 31 weeks, 6 days	8	11.5%
less than 28 weeks	6	8.6%
Maternal history		
Nil significant	57	81.4%
GDM	7	10%
Hypothyroidism	5	7.1%
PIH	1	1.4%

Most murmurs were detected within the first two days of life (67.1%). Only one case was identified on day 15 and two cases on day 26 during the follow-up period. The mean age for murmur presentation was 3.3 days. Ejection systolic murmurs were the most common (71.4%), with the majority falling in the 2 / 6 category of grading (72.8%) [Table 2].

Table 2: The murmur characteristics

Day of detection	Number (N = 70)	Percentage
< 24 hours	8	11.4%
24 – 48 hours	39	55.7%
48 – 72 hours	9	12.8%
> 72 hours	14	20%
Type of murmur		
Continuous	19	27.1%
Ejection systolic	50	71.4%
Pansystolic	1	1.4%
Grade of Murmur		
2 / 6	51	72.8%
3 / 6	19	27.1%

Sixty percent of neonates were symptomatic, with respiratory symptoms (55.7%) being the predominant one. Physical examination findings were present in 30% of neonates [Table 3].

Table 3: The clinical presentation characteristics

Symptoms at presentation	Number (N = 70)	Percentage
Asymptomatic	28	40%
Symptomatic	42	60%
Respiratory symptoms	39	55.7%
Feeding problem	1	1.4%
Bluish discoloration of skin	1	1.4%
Edema	1	1.4%
Physical examination findings		
Nil	49	70%
Poor activity	2	2.9%
Desaturation (SpO_2 < 94%)	6	8.5%
Dysmorphic facies	2	2.9%
Tachycardia	9	12.8%
Others	2	2.9%

Critical CHDs were seen in 8.5% of symptomatic neonates. Chest X-rays were done on 55 neonates. Bilateral haziness was noted at 10%. None showed a diagnosis of any specific CHD. [Table 4].

Table 4: Echocardiogram and chest X ray findings

Echocardiogram findings		
Asymptomatic neonates	**Number (N = 17)**	**Percentage**
ASD (< 5 mm)	7	41.1%
ASD (< 5 mm), PDA (< 2 mm)	3	17.6%
PDA (< 2 mm)	3	17.6%
PDA	4	23.5%
Symptomatic neonates	Number (N = 32)	Percentage
ASD (< 5 mm)	4	12.5%
ASD (< 5 mm), PDA (< 2 mm)	4	12.5%
PDA (< 2 mm)	3	9.3%
PDA	14	43.8%
VSD, ASD, and PDA	1	3.1%
Coarctation of Aorta (COA)	1	3.1%
Severe Aortic Stenosis (AS)	1	3.1%
Hypoplastic Right ventricle,(HRV)	1	3.1%
Hypoplastic Left ventricle (HLV), DORV	1	3.1%
Hypoplastic pulmonary valve (HPV), small PDA	1	3.1%
Chest X-ray findings	Number (N = 55)	Percentage
Normal	50	90%
Abnormal	5	10%

Table 5: Correlation between murmur type and echocardiogram diagnosis

Echocardiogram diagnosis											
Type of murmur (N = 70)	**Normal**	**PDA**	**PDA with ASD**	**ASD**	**VSD, ASD, and PDA**	**COA**	**Severe AS**	**HRV**	**HLV, DORV**	**HPV, small PDA**	**TGA with ASD**
Continuous murmur	1	16	1	0	0	0	0	0	0	1	0
Ejection systolic murmur	20	8	6	11	0	1	1	1	1	0	1
Pansystolic murmur	0	0	0	0	1	0	0	0	0	0	0
Fisher's exact test p-value of 0.000 is highly significant											

There was a strong association between the type of murmur and the echocardiogram diagnosis. A continuous type of murmur was seen mostly in PDA. The majority of neonates with ejection systolic murmurs had normal echocardiogram findings. Others were found to have ASD [Table 5].

It was noted that symptomatic neonates with murmurs were twice as likely to exhibit abnormal echocardiograms. Additionally, the presence of additional physical examination findings tripled the likelihood of abnormal echocardiograms [Table 6].

Table 6: Correlation between symptoms at presentation and echocardiogram findings, and between physical examination findings and Echocardiogram findings

	Echocardiogram normal	Echocardiogram abnormal
Symptoms at presentation	10	32
Symptoms absent	11	17
Odds ratio: 2.071, 95 % CI: 0.36 - 4.79		
	Echocardiogram normal	Echocardiogram abnormal
Examination findings present	3	18
Examination findings are absent	18	31
Odds ratio: 3.187, 95% CI: 1.542 – 6.612		

Discussion

CHD continues to be a significant contributor to newborn mortality, highlighting the necessitating early detection and intervention for improved outcomes. In the present study, out of 1880 neonates screened, 70 had cardiac murmurs, and the frequency was 3.7%. The prevalence varies from as low as 0.9 to 77.4%.[14] These variations are due to geographical location, socioeconomic status, and healthcare infrastructure. In the study, the ratio between males and females in the study was 1.33:1 [Table 1]. Jayawardana et al obtained similar results, with a male to female ratio of 1.40:1.[13]

According to our study, 60% of newborns had symptoms at the time of presentation. The predominant symptoms were respiratory (55.7%), like fast breathing and chest indrawing. Thirty percent of the newborns had additional physical examination findings, including tachycardia (12.8%), desaturation of SpO_2 (8.5%), etc [Table 3]. In comparison, Ramhari et al reported respiratory distress (51.8%), followed by cyanosis (11.8%). Other non-cardiac anomalies were cleft lip and palate in 5.9%, Down syndrome in 3.5%, etc.[15] These disparities in the studies are due to variations in clinical presentations and examiner skills.

Surprisingly, our study found that 70% of murmurs were associated with structural cardiac defects. Only 5.7% of asymptomatic neonates, and 30% of symptomatic neonates had a clinically significant CHD with critical CHD in 8.5% of symptomatic neonates [Table 4]. In contrast, Iyad et al reported a 26% incidence of significant CHD in asymptomatic neonates.[16] The rationale for referral for echocardiography was to detect critical CHD necessitating urgent intervention. The need for an echocardiogram before discharge is still debatable. In resource-limited settings without a paediatric cardiologist, evaluating asymptomatic neonates depends on murmur characteristics, oxygen saturation and follow-up feasibility. This approach helps optimizes resource allocation and minimizes the risk of missing critical CHD. This study highlighted the limited diagnostic utility of the chest X-ray alone in identifying specific CHD [Table 4]. This aligns with findings from Bernard et al, highlighting the low accuracy of chest X-rays alone in diagnosing cardiac lesions.[17]

Our study revealed most neonates (28.5%) detected to have an ejection systolic murmur had a normal echocardiogram, indicating innocent murmurs. A continuous type of murmur (22.8%) was seen mostly in PDA [Table 5]. A study by Duz D et al concluded that 16% of neonatal cardiac murmurs were innocent, and the rest (84%) had significant heart defects.[18] This research underscores the importance of echocardiography in providing a definitive diagnosis.

In the current study, symptoms at presentation were two fold more likely to cause an abnormal echocardiogram (Odds ratio of 2.071 with a 95% confidence interval of 0.36 - 4.79) [Table 6]. However, the large confidence interval indicates variability in the results, necessitating cautious interpretation. These results were consistent with the study by Ken Chen et al, in which the diagnosis of CHD was made using a combination of clinical findings and showed a sensitivity of 91.23% and a specificity of 95.26%.[19] Similarly, McConnel et al concluded that symptomatic newborns with a cardiac murmur have a greater likelihood of cardiac disease.[20] This reinforces the importance of evaluating murmurs, particularly when associated with symptoms.

Additionally, neonates with physical examination findings were three times more likely to exhibit an abnormal echocardiogram (Odds ratio: 3.187, with a 95% confidence interval of 1.542 – 6.612) [Table 6]. However, a careful interpretation is warranted due to the large confidence interval. This finding aligns with the research by Sean B et al, which demonstrated a 54% increased likelihood of CHD in neonates with combined examination findings and murmurs.[13] This highlights the critical role of comprehensive physical assessments in the early detection of CHDs. Additionally, the broad confidence interval highlights the need for further larger-scale studies for a better understanding of the association between symptoms at presentation, physical examination findings, and abnormal echocardiograms in neonates.

A key question remains regarding the management of asymptomatic neonates with murmurs: should they all require immediate evaluation, or can a watchful

waiting approach be considered? This dilemma calls for further research to determine the optimal management strategy, especially in resource-limited settings. A single center study with a small sample size and limited period of follow-up are the limitations of this study.

Conclusions

Murmurs are often encountered in routine neonatal evaluations. Early identification and evaluation of murmur are crucial. Symptomatic neonates were twice as likely to have an abnormal echocardiogram, while those with additional physical examination findings increased this likelihood threefold. This emphasize the evaluation of all symptomatic neonates before discharge. However, the approach for asymptomatic infants is debatable, depending on saturation, blood pressure, murmur characteristics, and follow-up feasibility.

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