Echocardiographic Evaluation in Neonates with Heart Murmurs

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Abstract

Auscultation of the heart is one of the most important tools of physical examination in neonates, which is very helpful in the diagnosis or rejection of congenital heart diseases (CHDs). The aim of this study is to investigate the causes of heart murmur in neonates hospitalized in neonatal unit in Imam Reza Hospital, Kermanshah, Iran. This cross-sectional study was conducted within the period of 18 months on neonates hospitalized in neonatal unit whose heart murmur, diagnosed through examination, and echocardiography was conducted to investigate the existence of CHD. In 62.1% of the cases, murmuring was auscultated within the first week after birth. Among 172 neonates with heart murmur, 25 subjects (14.5%) had normal echocardiogram, and others had abnormal echocardiogram in which ventricular septal defect (31.4%) was the most common CHD. Patent ductus arteriosus (23.3%) was the second common CHD found. Other defects were atrial septal defect, persistent foramen ovale, pulmonary stenosis, and tricuspid regurgitation. Among the neonates with CHD, 55 subjects were females and 92 cases were males. There was CHD history in previous siblings in 10 cases. In 73 neonates with CHD, the mother had not taken folic acid in the first trimester of pregnancy. A total of 14.5% of the hospitalized neonates suffered from innocent murmur, and the rest with heart murmur had abnormal echocardiography and suffered from CHD (85.5%). Heart murmur in neonates could be a symptom of CHD, and timely echocardiography is very important in diagnosing the type of disease.

Keywords

- neonates
- murmur
- echocardiography

Introduction

Congenital heart diseases (CHDs) are the most common congenital anomalies in neonates with the incidence of 0.8 in 1,000 live neonates.¹ Murmur could be the first symptom of a serious heart disease in neonates.^{2,3} Heart murmurs are divided into innocent and pathologic (organic) types.⁴ Some of the neonatal and many pediatric murmurs do not have pathological importance, and they are considered as innocent.⁵

Diagnosing murmur requires experience, skill, precision, and spending enough time when examining the neonates.⁶ Auscultation of heart murmur in neonates is the most common cause of referring to pediatric cardiologist.^{7,8} Accurate physical examination of neonates and careful auscultation of the heart along with timely echocardiography plays an important role in early diagnosis of heart diseases and starting treatment measures. The prevalence of murmur in neonates is 0.9 to 77.4%, and it seems that it is affected by the type of different studies conducted in this field.^{2,8}

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Neonatal heart murmur remains one of the most common reason for pediatric cardiologist consultation in the neonatal intensive care units and nurseries.⁷ Two-thirds of normal newborns possess innocent murmurs several days after birth.⁹ However, a normal neonatal examination includes CHD, and routine examination may fail to show more than half of the cases of CHD.^{9,10}

Unrecognized heart disease of neonates carries a serious risk of avoidable mortality, handicap, and morbidity. The dynamic nature of neonatal circulation causes the difficulty in assessing heart murmurs in the neonate as compared with other pediatric age groups. Neonates' assessment with heart murmurs based on the clinical examination alone without the use of echocardiograph may not be complete.^{11,12}

The goal of this cross-descriptive study was to investigate the cause of heart murmur in neonates hospitalized in neonatal unit in Imam Reza Hospital, Kermanshah, Iran, conducting echocardiography on them.

Materials and Methods

This cross-sectional and descriptive study was conducted in neonatal unit of the Imam Reza Hospital, Kermanshah, Iran; a big academic and referral hospital west of Iran, within the period of September 2013 to March 2014. All neonates were visited by a neonatologist daily. Among 1,668 neonates hospitalized, 172 subjects (10.3%) suffered from heart murmur. A file was prepared for each neonate with cardiac murmur, which consisted of demographic details, including birth weight, fetal age, and history of folic acid intake by the mother in the first trimester. Echocardiography was conducted by neonatal cardiologist, in the same hospital, for all of the neonates with heart murmur. According to the results of echocardiography, neonates were classified into two groups: one group with normal echocardiogram and no structural heart problems, under the title of group with innocent murmur. The other group had abnormality in the echo and was named as the group with pathologic murmur. Data were inserted in SPSS, and statistical analysis of data was conducted. The significance level was selected as $p < 0.05$.

Results

Average age of the neonates with murmur was 8.9 ± 3.6 days with the average weight of $2,654 \pm 478$ g, and they were mostly term neonates (71%). The initial clinical diagnosis of the heart murmur by the neonatologists was 62.1% of murmur cases heard during the first week after birth. Among 172 neonates with heart murmur, 25 cases (14.5%) had normal echocardiogram, and the rest had abnormal echocardiogram. With regard to CHD, 55 neonates were females, and 92 subjects were males. In 10 cases, there was a family history of CHD in pervious children. In 73 neonates with CHD, their mother had not taken folic acid regularly during the first trimester of pregnancy.

A total of 172 neonates were enrolled during the study period. The initial clinical diagnoses of the heart murmur by the neonatologists were innocent in 22 neonates, pathological

Table 1 Initial evaluation by neonatologist and cardiologist of 75 neonates with heart murmur

Clinical diagnosis	No. of neonatologist assessments (%)	No. of cardiologist assessments (%)
Innocent murmur	22 (13)	20 (12)
Pathological murmur	129 (75)	139 (81)
Possible pathological murmur	21 (12)	12 (7)
Total	172 (100)	172 (100)

in 129, and possible pathological in 21 patients (►Table 1). After echocardiography (►Table 2), the diagnosis of innocent murmur was changed to pathological in 15 patients. Of the 129 neonates with the initial clinical diagnosis of pathological murmur, the diagnosis of 30 of them was changed to innocent murmur after echocardiography. Of the remaining 21 infants with the clinical diagnosis of possible pathological murmur, the diagnosis of 9 of them was changed to innocent and that of 12 of them was changed to pathological after echocardiography. The initial clinical diagnoses of the heart murmur by the cardiologists were innocent murmur in 21, pathological in 139, and possible pathological in 12 neonates. After performing echocardiography (►Table 3), the diagnosis of innocent murmur was changed to pathological in 14 neonates, that of pathological murmur was changed to innocent in 27, and for the diagnosis of possible pathological murmur, 3 neonates were changed to innocent, and 9 were changed to pathological murmur. The results were analyzed by means of 2×2 tables, considering echocardiography as the gold standard to assess the accuracy of the clinical examination. For the neonatologists, the sensitivity to detect a pathological murmur was 78% and the specificity was 33%; the positive predictive value was 77% and the negative predictive value was 37%.

For the cardiologists, the accuracy of the clinical examination showed a sensitivity of 83% in detecting a pathological murmur and a specificity of 25%; the positive predictive value was 80% and the negative predictive value was 29%. There was no significant difference between the two groups for all

Table 2 Changes in neonatologist clinical diagnosis after performance of echocardiography

Clinical diagnosis	No. of neonatologist assessments (%)	Innocent murmur (%)	Pathological murmur (%)
Innocent murmur	22 (13)	7 (4)	15 (9)
Pathological murmur	129 (75)	30 (18)	99 (57)
Possible pathological murmur	21 (12)	9 (5)	12 (7)
Total	172 (100)	46 (27)	126 (73)

Table 3 Changes in cardiologist clinical diagnosis after performance of echocardiography

Clinical diagnosis	No. of neonatologist assessments (%)	Innocent murmur (%)	Pathological murmur (%)
Innocent murmur	21 (12)	7 (4)	14 (8)
Pathological murmur	139 (81)	27 (16)	111 (65)
Possible pathological murmur	12 (7)	3 (2)	9 (5)
Total	172 (100)	37 (22)	135 (78)

parameters. The kappa coefficient to assess the agreement in auscultation between the two groups was 0.62 (95% confidence interval, 0.41–0.83). In the group with pathologic murmur, ventricular septal defect (VSD) was the most common CHD disease in 54 cases (31.4%) and patent ductus arteriosus was the second common type in 40 cases (23.3%) (► **Tables 4 and 5**).

Discussion

Heart murmur detection relies on the examiners' experience and skill, the timing and frequency of the examination, and the state under which the examination takes place. Failure to identify pathological murmur may lead to a delay in crucial

Table 4 The type and frequency of CHD according to echocardiogram results

Type of defect	Number (%)
VSD	54 (31.4%)
PDA	40 (23.3%)
ASD	30 (17.5%)
TR	5 (3%)
PS	4 (2.3%)
Other	4 (2.3%)

Abbreviations: ASD, atrial septal defect; CHD, congenital heart disease; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TR, tricuspid regurgitation; VSD, ventricular septal defect.

Table 5 Indications for early fetal echocardiography in 54 cases of this series

	N	Cases with CHD
Family history of CHD	21	2
Previous child with CHD	18	1
Previous child with a rare syndrome	1	1
Pregestational diabetes	2	0
No increased risk for CHD	19	0

Abbreviation: CHD, congenital heart disease.

medical or surgical intervention and cause unwanted sequences. Therefore, diagnosis is important in a neonate with a heart murmur. The neonatal examination detects only 44% of cardiac malformations that present in infancy, and if a murmur is heard, there is a 54% chance of an underlying cardiac malformation.¹³ Our study showed that 75% of neonatal murmurs referred to pediatric cardiology from a neonatal tertiary care center were secondary to organic heart disease.

Only 25% of patients had innocent heart murmur; most were secondary to pulmonary artery branch stenosis or tricuspid regurgitation (TR). The most common murmur diagnosis in the neonatal intensive care unit was VSD in contrast with Geggel report⁷ in a similar study. In older children and infants, clinical cardiovascular examination is a very accurate and sensitive method of screening for the underlying heart disease, and echocardiogram is less likely to reveal clinically unsuspected heart disease.^{14–16} This condition did not hold true in neonates with heart murmur, in whom echocardiography is important whenever CHD is suspected.^{11,12}

Our study showed that in a neonatal tertiary care center, the sensitivity of clinical examination alone in detection of pathological murmurs by a neonatologist and cardiologist was only 78 and 83%, respectively, whereas both groups' accuracy (neonatologists and cardiologists groups) in detection of innocent murmurs was unsatisfactory. This supports the fact that echocardiography has drastically improved the accuracy of neonate's diagnosis of CHD, and it is a good tool in neonates with heart murmur evaluation.

Our study showed that there were only little differences between the cardiologists and neonatologists in the initial clinical evaluation of neonates with heart murmur; similar comparison between such groups was not found in the literature.

Previous studies have assessed the diagnostic accuracy of pediatricians' clinical auscultation skills to assess murmurs in children and cardiac simulators. Hansen et al¹⁷ concluded that general pediatricians were good at diagnosing innocent murmurs, whereas McCrindle et al¹⁸ concluded that pediatric cardiologists have excellent diagnostic accuracy. However, Gaskin et al¹⁹ showed that pediatric residents had only 33% diagnostic accuracy. Farrer and Rennie²⁰ showed that the sensitivity of the senior house officer's examination to assess the clinical significance of the neonatal murmur was 71% and the specificity was 91%; the positive predictive value was 71% and the negative predictive value was 91%.

These results are similar to those reported in this study. That is, a trained neonatologist is able to assess the significance of, and determine appropriate management for, neonatal heart murmurs, although echocardiogram is still needed to reach the accurate diagnosis of CHD in neonates even if a pediatric cardiologist is consulted.

At birth, CHD may not have any major sign and symptoms. Physical examinations and noticing the heart sounds and diagnosing heart murmur play an important role in early diagnosis of these diseases in neonates.²¹ In this study, 172 neonates with heart murmur were diagnosed by cardiac examination, 85.5% of whom suffered from structural problems of heart according to echocardiogram results. Many studies showed the increase chance of structural heart disorders for approximately 39 to

84% in neonates having heart murmur. In this study, this increase is higher, which could be the result of the type of study and investigation of the hospitalized neonates. Mohammad et al²² showed that 68% of neonates with heart murmur suffered from structural heart disorders, and 32% had innocent murmur. Moss et al²³ showed that 70% of neonates with heart murmur had structural heart disorder. It would be better not to evaluate the murmur cause in neonates by an adult cardiologist, and in this study, all echocardiographic cases were conducted by pediatric cardiologist who were experienced for neonates' cases. Tanasan et al²⁴ showed that there is no difference in the diagnosis of heart murmurs by neonatologist and pediatric cardiologist, and echocardiography is still considered as the golden standard and the best method to diagnose heart murmur. In this study, evaluating the precision of murmur was not conducted by the two groups of specialties. However, for all of the cases diagnosed by neonatal specialist as murmur, echocardiography was conducted by pediatric cardiology specialist.

TR may play a physiological crucial role in right ventricular (RV) development in pulmonary atresia with intact ventricular septum (PA-IVS). It was observed that the severity of TR was related with tricuspid inflow duration and tricuspid valve annulus dimension, signifying that the physiology of moderate-to-severe TR may be promising for the development of RV growth and development.²⁵

Several types of echocardiographic nomograms were proposed for the pediatric age group from early 1980s to date. Nevertheless, the precision of some of these previous reports has been limited by the small number of assessed healthy subjects, the rare distinction among age groups (from birth to 18 years), and the lack of methods of measurements standardization.

In spite of the current development, pediatric echocardiographic nomograms employed for valvular and arterial dimensions continue to be restricted. Pediatric echocardiographic nomograms for systolic and diastolic functional indices are restricted by small sample size and an inconsistent procedure. Cantinotti et al²⁶ established pediatric nomograms for pulsed wave Doppler (PWD), tissue Doppler imaging (TDI), and mitral valve (MV) velocities. They reported a normal range for TDI, PWD, and MV velocities that were derived from a large Caucasian children population. The variability of diastolic patterns, particularly those at lower ages, was taken into account. Cantinotti et al²⁷ investigated healthy Italian children using a two-dimensional (2D) echocardiography. They reported echocardiographic nomograms for arterial and valvular dimensions derived within a large Caucasian children population. The integration of results obtained with those of previous investigations would permit an understanding of pediatric 2D echocardiographic nomograms for the measurement of 2D cardiac structures. However, the limitation of this study is that the duration of the study is short and the sample size is minimal.

Conclusion

Heart murmur is one of the clinical symptoms that imply CHD in neonates. Therefore, it is important to pay special attention to heart sound auscultation in neonates, although innocent

and pathologic murmur could not be distinguished from each other only through auscultation. Since 85.5% of the hospitalized neonates suffered from pathologic murmur, conducting timely echocardiography by experienced pediatric cardiologist is necessary for the diagnosis of this type of heart defect and deciding about the type of treatment to be considered.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 declaration of Helsinki and its later amendments or comparable ethical standards.

Conflict of Interest

The authors deny any conflict of interest in any terms or by any means during the study.

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