

The Association Between Clinical Signs and Detection of Congenital Heart Disease by Echocardiography in Neonates: Systematic Review

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ABSTRACT

Background: Background and objective: Congenital heart disease (CHD) is a leading cause of death in newborns. Accurate clinical 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. This systematic review aimed to evaluate the correlation and diagnostic value of clinical signs in predicting echocardiographic findings in neonates.

Patients and Methods: This systematic review was conducted based on PICO Format study design questions according to PRISMA guidelines. A comprehensive search of online databases was conducted, including Scopus, PubMed, and Cochrane Library. Full text, English language, peer-reviewed, prospective and retrospective cohort, observational and cross-sectional articles were included if they evaluated the correlation and diagnostic value of clinical signs in predicting echocardiographic findings in neonates.

Main Findings and conclusion: A significant proportion of neonates presenting with heart murmurs or cyanosis had CHD on echocardiography. Ventricular septal defect and patent ductus arteriosus were the most commonly diagnosed anomalies. Clinical examination showed moderate-to-high sensitivity and specificity in detecting CHD. However, echocardiography significantly improved diagnostic accuracy. While targeted echocardiography in symptomatic neonates proved beneficial, routine screening in asymptomatic neonates was associated with an increased rate of clinically insignificant findings. Echocardiography should be employed in neonates with heart murmurs or cyanosis for early detection of CHD. A clinically guided approach is recommended over routine screening to avoid over-diagnosis and unnecessary interventions.

Keywords: Echocardiography, clinical signs, neonates, systematic review

1. INTRODUCTION

Congenital heart disease (CHD) is a leading cause of death in newborns (1), (2). CHD prevalence in newborns has increased globally from 0.6 per 1000 live births to 9.410 per 1000 live births, according to several recent reports (3), (4). Echocardiography has become a bedside tool in the pediatric intensive care unit (PICU) and neonatal intensive care unit (NICU) (5). It has become indispensable in diagnosis because of its real time ability to visualize the heart, lack of invasiveness and because it does not need specific installation precautions (6). Echocardiography provides confirmation of disease suggested by clinical findings, or rules it out (7). Echocardiography has limitations and the most important limitation is that it is operator dependent and needs training to achieve the required skill. Yet, echocardiography is not a replacement for physical examination and clinical assessment for hemodynamic stability while making clinical decisions (8). Despite antenatal screening processes using fetal echocardiogram (Echo), more than 50% of newborns with CHD are unrecognized at birth (9), (10). As undiagnosed CHD can lead to life-threatening cardiovascular collapse and cardiac arrest, which are the primary causes of death in infants, screening newborns' cardiac health is vital (11). Cardiac assessments, including physical examinations, have been performed for newborns after birth; however, the use of Echo for diagnosing CHD has been a subject of debate (12), (13). Echo, which pediatricians use to evaluate heart function, uses sound waves to produce pictures of the movement of different parts of the heart; thus, it has become the gold standard for diagnosis of CHD in pediatric patients with cardiac murmurs and its use has expanded with advances in technology (14), (15). Almost all pediatricians

agree with performing Echo for newborns with cardiorespiratory symptoms, such as cyanosis and tachypnea; chromosome abnormalities, including Down syndrome; or other non-cardiac anomalies to rule out CHD (16). The appropriate criteria for the use of Echo in children and adolescents with cardiac murmurs are well established (17), (18). 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. Therefore, this systematic review aimed to comprehensively evaluate the correlation and diagnostic value of clinical signs in predicting echocardiographic findings in neonates.

1. Patients and Methods

This systematic review was conducted based on PICO Format (Population/patient: Neonates, Intervention: Clinical findings, Comparison: Echocardiographic findings, Outcome: Correlation/diagnostic value) study design questions according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (19).

Search Strategy: A comprehensive search of online databases was conducted, including Scopus, PubMed, and Cochrane Library, utilizing a combination of text keywords such as infant, newborn, neonates, echocardiography, clinical signs, heart murmur, cyanosis, congenital heart disease. The electronic searches were restricted to investigations published in English and involving human subjects. Furthermore, we performed a manual examination of the reference lists from the involved clinical trials & prior reviews to identify supplementary investigations

Selection criteria: Full text, English language, peer-reviewed, prospective and retrospective cohort, observational and cross-sectional articles were included if they evaluated the correlation and diagnostic value of clinical signs in predicting echocardiographic findings in neonates.

Exclusion Criteria: 1) reviews, comments, editorials, conference abstracts or papers, letters, and notes, 2) studies did not perform echocardiogram, or didn't report clinical signs, 3) studies not in English were excluded

Data extraction: the following data was extracted, the name of author, year of publication, study location, type of study, sample size, age, sex and outcomes.

2. Results

During the first search, 825 studies were found. After excluding duplicates, the screening list comprised 630 titles. Of the 630 articles, 600 articles were excluded at title and abstract screening level. The remaining 30 articles were obtained at full text. Ultimately, this systematic review included 7 studies.

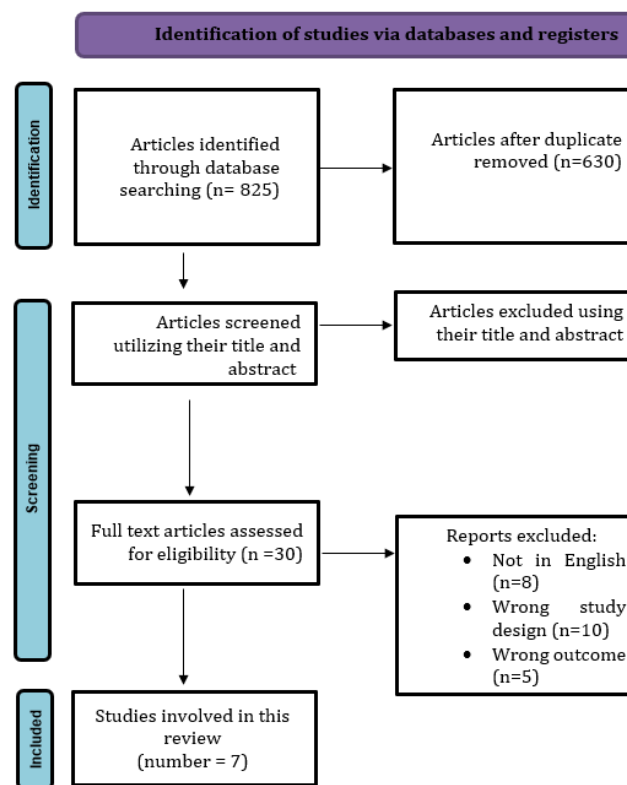


Figure 1 Flow diagram of the investigation involved in the systematic review.

Table (1): Baseline characteristics of the included studies in this systematic review

Study ID	Year	Country	Study Design	Sample size	Age	Sex (M/F)
Azhar et al., (20)	2006	Canada	Prospective study	75 neonates	1–28 days	NA
Singh et al., (21)	2012	UK	Retrospective study	350 neonates	NA	NA
Tehrani et al., (22)	2015	Iran	Descriptive analytic study	113 neonates	NA	60.18% / 39.82%
Al-Ammouri et al., (23)	2016	Jordan	Retrospective study	309 neonates	NA	167 / 142
Khalilian et al., (24)	2016	Iran	Cross-sectional study	7113 neonates	NA	NA
Ahmadipour et al., (25)	2018	Iran	Cross-sectional study	172 neonates	8.9 ± 3.6 days	NA
Kondo et al., (26)	2018	Japan	Retrospective chart review	3434 newborns	NA	NA

Table (2): The main findings of the included studies

Study ID	Outcomes
Azhar et al., (20)	Echocardiography has dramatically improved the accuracy of diagnosis of congenital heart disease in neonates, and it is an essential tool in the evaluation of neonates with heart murmur.
Singh et al., (21)	They found that 74% of newborns with a heart murmur had CHD. Predischage echocardiography service for postnatal heart murmurs provided by neonatologists has the benefit of providing an early diagnosis, counselling of the parents and arranging appropriate follow-up.
Tehrani et al., (22)	Echocardiographic findings were normal in 20 newborns and abnormal in 93 cases. Tricuspid regurgitation was the most common disorder by a prevalence of 54.84% followed by PDA (52.69%). Murmur and cyanosis were reasons for referral to cardiologist in 45 (39.82%) newborns, of which 42 (93.33%) newborns had CHD. Their results highlighted the importance of physical examination and clinical manifestations, especially murmur and cyanosis in detection of congenital heart diseases by Echocardiography.
Al-Ammouri et al., (23)	22% of babies with asymptomatic heart murmurs had structural heart disease on echocardiography. The most common abnormality was ventricular septal defect. The presence of murmurs on pre-discharge physical examination is a useful, yet slightly insensitive tool for the early detection of CHD. They recommended echocardiographic screening of newborns with heart murmurs before discharge from the hospital.
Khalilian et al., (24)	Echocardiography showed that the most prevalent CHD was VSD. There was a significant relationship between central cyanosis, auscultated murmur and prevalence of CHD. Sensitivity of 79.7%, specificity of 88.5%, positive predictive value of 87%, negative predictive value of 81.8%, were obtained for detection of CHD in clinical examinations.
Ahmadipour et al., (25)	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%). Ventricular septal defect (31.4%) was the most common CHD followed by Patent ductus arteriosus (23.3%). Other defects were atrial septal defect, persistent foramen ovale, pulmonary stenosis, and tricuspid

regurgitation. Heart murmur in neonates could be a symptom of CHD, and timely echocardiography is very important in diagnosing the type of disease. Their results supported that echocardiography had drastically improved the accuracy of neonate's diagnosis of CHD, and it is a good tool in neonates with heart murmur evaluation.

Kondo et al., (26)

Echocardiography screening within the first 5 days of life did not help improve critical CHD detection rate in newborns without prenatal diagnosis or clinical signs of CHD. Echocardiographic screening may be associated with increased rate of false-positives (defects resulting in clinically non-significant CHDs) in newborns without prenatal diagnosis or suspicion of CHD.

2. DISCUSSION

Early diagnosis and timely management of CHD in newborns are critical to improve clinical outcomes (4), (27). Hence, this systematic review comprehensively evaluated the correlation and diagnostic value of clinical signs in predicting echocardiographic findings in neonates.

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 (28). In the study by Ahmadipour et al., (25), 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. Mohammad et al., (29) showed that 68% of neonates with heart murmur suffered from structural heart disorders, and 32% had innocent murmur. Moss et al., (30) showed that 70% of neonates with heart murmur had structural heart disorder. The variation in these studies can be attributed to the populations studied and variable definition of CHD. Also, Tehrani et al., (22) highlighted the importance of signs and symptoms to diagnosis of CHD neonates. They reported that prevalence of CHD was 28.7% and PDA was the most common disorder (52.69%). The most common reasons to perform echocardiography were cyanosis and murmur in physical examination, in which CHD of most was verified by echocardiography. While other reasons including diabetic mother, asphyxia, bradycardia, tachycardia, arrhythmia, and respiratory distress were uncommon, but were associated with high probability of CHD. These results indicated the importance of clinical symptoms and precise physical examination to diagnose CHD at birth. Similarly, systematic review conducted by Yoon et al., (31) identified the incidence of CHD diagnosed with Echo and determine whether Echo should be used in the proper management of CHD in newborns with asymptomatic non-syndromic cardiac murmurs (ANCM). The incidence of cardiac murmurs ranged from 0.6–8.6%. Among newborns with ANCM, 37.3% were diagnosed with Echo as having CHD, and ventricular septal defect was the most common congenital malformation. More than 50% of the newborns showed moderate CHD necessitating outpatient cardiology follow-up, and 2.5% had severe CHD requiring immediate interventions, such as cardiac catheterization and heart surgery. They concluded that a high incidence of CHD in newborns with ANCM was detected using Echo. This indicated that the use of Echo for diagnosing CHD in healthy newborns with cardiac murmurs could be helpful in earlier detection of CHD, thereby improving clinical outcomes for newborns with severe CHD. In addition, Abd El Massih et al., (32) determined the validity of clinical indications for requesting bedside pediatric bedside echocardiography in critically ill children to confirm the presence of echocardiographic abnormalities. They concluded that echocardiographic evaluation was a valuable tool, and the requirement of echocardiographic assessment increases according to clinical severity. The most commonly encountered indication for requesting bedside echocardiography was screening for hemodynamically significant patent ductus arteriosus in the neonatal intensive care units and assessment of cardiac function in the pediatric intensive care units. Clinical signs of pulmonary hypertension were the most sensitive parameter reflecting cardiac problems in neonatal intensive care unit, while clinical signs of impaired cardiac contractility were found to be the most sensitive parameter reflecting cardiac problems in pediatric intensive care units. In the neonatal intensive care units, the number of echocardiograms that revealed no cardiac abnormalities outnumbered those that revealed a cardiac problem. Furthermore, Bandyopadhyay et al., (33) evaluated the correlation between functional echocardiography and clinical parameters in term neonates with shock. They demonstrated that functional echocardiography provides an adjunct information to the clinical assessment of shock and helps in monitoring the response to treatment.

3. CONCLUSION

This systematic review demonstrated a strong association between clinical signs especially heart murmurs and cyanosis, and positive echocardiographic findings in neonates. While physical examination remains an important initial screening tool, it was not sufficiently sensitive or specific to rule out or confirm CHDs. Echocardiography substantially enhanced diagnostic accuracy and should be employed promptly in neonates presenting with suspicious clinical signs. However, indiscriminate echocardiographic screening in asymptomatic neonates without clinical indicators may lead to over-diagnosis and

unnecessary interventions. Targeted echocardiography based on clinical findings offers a balanced approach to early and accurate CHD detection. A clinically guided approach is recommended over routine screening to avoid over-diagnosis and unnecessary interventions.

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