Clinical score to detect congenital heart defects: Concept of second screening

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ABSTRACT

Introduction : **Neonatal screening for congenital heart defects at birth can miss some heart defects, sometimes few critical ones, and the scenario is even worse in those neonates who had never undergone a neonatal checkup (home deliveries). Immunization clinic can serve as a unique opportunity as the second checkpoint for the screening of the children. A history- and examination-based test can serve as an effective tool to screen out children with heart defects.**

Aims and Objectives : **The aim of this study was to establish the sensitivity and specificity of a clinical screening tool for the identification of congenital heart defects at the first visit of an infant after birth for immunization.**

Materials and Methods : **This is a cross-sectional observational study which the consecutive children presenting at 6 weeks of age for immunization or any child presenting for the first time (outborn delivery) till 6 months of age in the immunization clinic were subjected to detailed history and examination and findings were recorded on a predesigned pro forma and a clinical score was calculated. All these children were then subjected to echocardiography for confirmation of the diagnosis of congenital heart disease (CHD), and the sensitivity and specificity of the test were recorded**

Observations and Results : **A total of 970 babies were screened, out of them 31 were diagnosed with CHD and 18 had undergone neonatal screening at birth. A clinical score of 3 or more had more chances of detecting CHD. The sensitivity of the cutoff score as 3 was 96.77% and specificity was 98.72, with a positive predictive value of 71.43%, a negative predictive value of 99.89%, and an accuracy of 98.66%.**

Conclusions : **The history- and examination-based tool is an effective method for early identification of CHD and can easily be used by peripheral workers working in remote places with poor resources enabling prompt referral.**

Keywords : Clinical score, congenital heart defects, echocardiography, immunization clinic

INTRODUCTION

The prevalence of congenital heart disease (CHD) diagnosed in the first 12 months is estimated at 6–8/1000 live births.[1] About 25% of CHDs are life-threatening and may manifest before the first routine clinical examination.[2] Fetal screening can identify

Access this article online

Quick Response Code:

Website: www.annalspc.com

DOI: 10.4103/apc.APC_113_19

How to cite this article: Izhar FM, Abqari S, Shahab T, Ali SM. Clinical score to detect congenital heart defects: Concept of second screening. Ann Pediatr Card 2020;13:281-8.

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Submitted: 02-Aug-2019 **Revised:** 07-May-2020 **Accepted:** 27-Jun-2020 **Published:** 01-Sep-2020

many structural heart diseases, but it is highly variable, depending on operator expertise, gestational age, fetal position, and the type of cardiac defect, and can miss some of the CHDs including few critical ones.[3] Neonatal screening programs have incorporated pulse oximetry for early diagnosis of CHDs and have been cleared by the FDA for use in newborns.[4] However, pulse oximetry screening does not detect all CHDs, so it is possible to still have a congenital heart defect with a negative screening result.

The detection rate for CHD by prenatal ultrasound is approximately 25%–50% and by postnatal newborn physical examinations is approximately 25%–50%.[4] The combination of physical examination with pulse oximetry increases the sensitivity and specificity, as shown by Saxena *et al.*[5]

Several studies have documented the low sensitivity of routine neonatal examination in detecting CHD.[6-9] A study has been done for screening of CHD at birth by clinical examination,[10] but a large number of cases remain undiagnosed at birth which may present with severe life-threatening complications at a later age.[11] Hence, there is a need to create a clinical score based on simple history taking and examination which can be applied in the next contact with the infant usually when the infant comes for the immunization. The immunization clinic provides a unique opportunity to act as a second checkpoint to screen out these missed and undiagnosed cases.

MATERIALS AND METHODS

This is a cross-sectional observational study done in the Division of Pediatric Cardiology, Department of Pediatrics, Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh, Uttar Pradesh, from July 2017 to December 2017 on the immunization days in the Pediatric Outpatient Department (OPD). The immunization clinic receives children delivered within the hospital (inborn) as well as children born outside (other hospitals/clinics/peripheral centers). All the consecutive children presenting in the OPD at 6 weeks of age for immunization or any child presenting for the first time (outborn delivery) till 6 months of age in the immunization clinic were subjected to detailed history and examination and findings were recorded on a predesigned pro forma and a CHD score [Table 1] was recorded. The scoring system was made based on the common signs and symptoms associated with CHD. The score was given based on the association of symptoms with CHD. Since 96.7% of cases of murmur had CHD, it was given a score of 2. Similarly, SpO_2 of <95% , bluish discoloration, and cyanotic spell were most commonly associated with CHD and also easy to catch by the peripheral worker, they were given double score as compared to others. All these children were then subjected to echocardiography for confirmation of the diagnosis of CHD, and the sensitivity and specificity of the test were calculated at different cutoff scores [Figure 1].

Place of study

This study was conducted in the Pediatric OPD (Immunization Clinic, Well Baby Clinic, and Cardiology Clinic), Department of Pediatrics, Jawaharlal Nehru Medical College, AMU, Aligarh.

Inclusion criteria

Any infant (both inborn and outborn) presenting for the first time in the immunization clinic after discharge at 6 weeks of age or any child presenting for the first time (outborn) up to the age of 6 months in the clinic was included in the study.

Exclusion criteria

- Parents not giving consent
- Diagnosed cases of congenital heart defect were excluded from the study.

Definitions

Undiagnosed cases

Children presenting for the first time to our hospital including home deliveries and other hospital deliveries (where neonatal screening was not done) were detected as a case of CHD on echocardiography.

Missed cases

Cases who were presumed to have undergone neonatal screening (babies born at JNMC or other SNCUs) and were missed initially and later at second screening were diagnosed as CHD by echocardiography.

Data analysis

Statistical analysis was done using the Statistical Package for Social Sciences (SPSS 20) for Windows Software (SPSS Inc, Chicago, Illinois, USA). Continuous variables were expressed as means, standard deviation (SD), 95% confidence intervals (CIs), frequency, and range. Independent sample *t*-test, Chi-square test, Fisher's exact test, and Kolmogorov–Smirnov test were used. Sensitivity and specificity were calculated, and receiver operating characteristic (ROC) curve was plotted for the cutoff score.

Institutional ethical and research committee clearance

Approval was taken on July 17, 2017, by the Ethics Committee of Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh.

OBSERVATIONS AND RESULTS

A total of 970 children in our study were screened by echocardiography, in whom 872 were institutional deliveries and presumed to have undergone neonatal

Table 1: Congenital heart disease score used in the study

History	Score	Examination	Score
Bluish discoloration	2	Clinical stigmata of specific syndromes	1
Difficulty in feeding (slow/interrupted, sweating/tiring easily)	1	Pulse volume (normal or decreased) and any discrepancy	1
Difficulty in breathing (tachypnea and retractions)	1	Discrepancy in blood pressure	1
Increased precordial activity/pulsations	1	Pulse oximetry abnormality (SpO_2<95%)	2
Failure to thrive	1	Hepatomegaly	1
Cyanotic spells	2	Abnormality in precordium examination - visible precordial pulses, position of apex beat and character (hyperdynamic or heaving), or presence of a thrill.	1
History of consanguinity	1	Auscultation - Abnormal heart sounds (S2, S3, and clicks)	1
Family history of CHD	1	Murmurs	2

CHD: Congenital heart defect

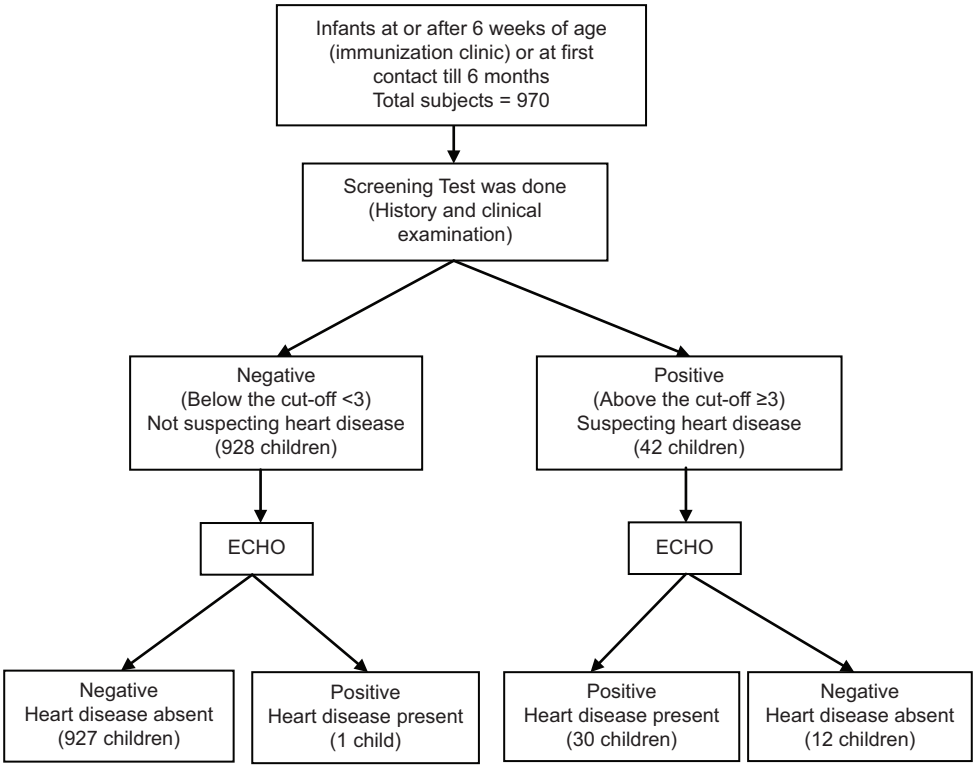

Figure 1: Flowchart of the study

screening at birth, and 18 out of 872 were found to have CHD at subsequent screening and therefore were labeled as missed cases [Figure 1]. Ninety-eight babies did not have any screening test at birth (home deliveries), of which 13 were diagnosed as CHD at presentation. These were considered as undiagnosed cases. The prevalence of CHD was 2.1% in children who had undergone neonatal screening at birth, whereas it was 13.3% in children who had not undergone any neonatal screening.

Table 2 shows that more than half (57%) of the children in the study were in the age group of 6–12 weeks, whereas only about one-fifth (23.8%) were in the age group of 19–24 weeks who came for immunization for the first time. The number of males (57.7%) among study participants was more than the females (42.3%). There were 34 (3.5%) children with a history of consanguinity. The children coming from urban areas (63.4%) for immunization were almost double to that of coming from rural areas (36.6%). Majority of the children coming for immunization were institutional born (89.9%).

The most common CHD detected was ventricular septal defect (VSD) (15), followed by tetralogy of Fallot (TOF) (5), atrial septal defect (ASD) (2), patent ductus arteriosus (PDA) (2), VSD + ASD (2), ASD + PDA (2), tricuspid atresia (TA) (2), and atrioventricular (AV) canal defect (1), as shown in Table 3. A total of 828 children had a clinical score of 0, whereas none of the children with CHD had a score of 0. Ninety-four children had a score of 1. There was

one child with CHD (ASD) who had a score of 2. There were 15 children with a clinical score of 3, and only 5 of them were diagnosed with CHD. Out of the 7 children with a score of 4, 5 were diagnosed with CHD. All the children with a score of 5 or more had a CHD.

There was one baby with dilated cardiomyopathy with severe LV dysfunction with a clinical score of 4 and another of left ventricular (LV) hypertrophy with a score of 3. It was seen that the mean score for ASD and PDA was 3.5 which increased to 5 for VSD and further increased with the severity of the disease (e.g., 10 for TOF and TA).

By applying one-sample Kolmogorov–Smirnov test, the observations were normally distributed and the mean score was 0.34 with a SD of 1.245.

Hence, an independent *t*-test was applied to find the association between total score and CHD.

Table 4 shows that the most common symptom of CHD was failure to thrive (FTT, 80.6%), followed by feeding difficulty (71.6%) and breathing difficulty (71.6%), and the most common sign was murmur (93.5%), followed by tachycardia (38.7%) and desaturation (32.3%).

Our study found that the maximum sensitivity for detection of CHD was that of murmur (93.6%), followed by FTT (80.7%), feeding difficulty (71%), and breathing difficulty (71%), and the specificity was that of murmur (99.9%), followed by bluish discoloration (99.9%), low saturation (99.8%), and tachycardia (99.6%). All other variables had a high specificity, but sensitivity came out to be very low [Table 4].

Table 5 shows the children with various scores, and all the children with a score of >4 have congenital heart defects.

In this study, the mean score ± SD came out to be 6.13 ± 2.68 in children with CHD and 0.15 ± 0.48 in normal children and was statistically significant by *t*-test [Figure 2]. The area under the ROC curve [Figure 3] was 0.984 ± 0.008 (95% CI). On ROC, the cutoff score of 3 was found to have maximum sensitivity as well as specificity; therefore, a clinical score of 3 or more was taken as a cutoff point for the detection of CHD. Thirty children with a score of 3 or more had CHD, whereas 12 children with a score of 3 were normal. The sensitivity of the cutoff score as 3 was 96.77% and specificity was 98.72%, with a positive predictive value of 71.43%, a negative predictive value of 99.89%, and an accuracy of 98.66%.

Table 2: Demographic distribution of study participants (*n*=970)

Variable	*n* (%)
Age group (weeks)	
6-12	553 (57.00)
13-18	186 (19.2)
19-24	231 (23.8)
Sex	
Male	560 (57.7)
Female	410 (42.3)
Consanguinity	
Yes	34 (3.5)
No	936 (96.5)
Area of residence	
Urban	615 (63.4)
Rural	355 (36.6)
Place of delivery	
Institutional	872 (89.9)
Home	98 (10.1)

Table 3: Spectrum of congenital heart disease with their mean score

Congenital heart disease	*n* (%)	Mean score
VSD	15 (1.6)	4.9±1.8
TOF	5 (0.5)	10.0±1.4
ASD	2 (0.2)	3.5±2.1
PDA	2 (0.2)	3.5±0.7
VSD + ASD	2 (0.2)	7.0±1.4
ASD + PDA	2 (0.2)	6.5±0.7
Tricuspid atresia	2 (0.2)	9.5±2.1
Common AV canal defect	1 (0.1)	7.0±0
Total	31 (3.2)	

VSD: Ventricular septal defect, TOF: Tetralogy of Fallot, ASD: Atrial septal defect, PDA: Patent ductus arteriosus, AV: Atrioventricular

Table 4: Association of clinical features with congenital heart defects

Clinical features	CHD, *n* (%)			Fisher's exact test		Accuracy (%)	
	Yes	No	Total	χ^2	*P*	Sensitivity	Specificity
Bluish discoloration	7 (87.5)	1 (12.5)	8	185.3	<0.05	22.6	99.9
Feeding difficulty	22 (40.7)	32 (59.3)	54	260.5	<0.05	71.0	96.6
Breathing difficulty	22 (59.5)	15 (40.5)	37	393.6	<0.05	71.0	98.4
Abnormal precordial activity	5 (100.0)	0 (0.0)	5	152.2	<0.05	16.1	100.0
Failure to thrive	25 (41.7)	35 (58.3)	60	305.9	<0.05	80.7	96.3
Syndromes	1 (50.0)	1 (50.0)	2	14.2	>0.05	3.2	99.9
SpO_2 <95%	10 (83.3)	2 (16.7)	12	252.2	<0.05	32.3	99.8
Murmur	29 (96.7)	1 (3.3)	30	874.3	<0.05	93.6	99.9
Tachycardia	12 (75.0)	4 (25.0)	16	271.1	<0.05	38.7	99.6
Hepatomegaly	1 (14.3)	6 (85.7)	7	2.8	>0.05	3.2	99.4
Abnormal heart sound	2 (100.0)	0 (0.0)	2	60.7	<0.05	6.5	100.0
Consanguinity	4 (11.8)	30 (88.2)	34	8.4	>0.05	12.9	96.8
Family history	0 (0.0)	14 (100.0)	14	0.5	<0.05	0.0	98.5

CHD: Congenital heart defect

DISCUSSION

A total of 970 children coming for immunization were screened by history and clinical examination, and echocardiography was done to confirm the diagnosis. Out of these, 31 were diagnosed with CHD with a prevalence of 3.2% which was much more than the reported prevalence of CHD or as per reported by Hoffman and Kaplan,[1] Ferencz *et al.*,[12] and Khalil *et al.*[13] However, this will not be the true representation of prevalence in the community as the study was conducted among children visiting the hospital for immunization. The majority will visit the hospital whenever the child has some complaints, otherwise they would prefer the local community center for vaccination.

The proportion of infants with CHD among total females screened was higher (4.1%) than that of total males screened (2.5%), whereas studies by Chadha *et al.*,[14] Bidwai *et al.*,[15] and Jain *et al.*[16] showed a male preponderance. The mean weight of study participants was 5.4 ± 1.2 kg and mean length was 60.4 ± 5.2 cm.

Table 5: Relationship of clinical score with congenital heart defects

Score	Number of children	Children with CHD	Percentage within CHD
0	828	0	0
1	94	0	0
2	6	1	3.2
3	15	5	16.1
4	7	5	16.1
5	2	2	6.5
6	6	6	19.4
7	3	3	9.7
8	2	2	6.5
9	4	4	12.9
11	2	2	6.5
12	1	1	3.2

CHD: Congenital heart defect

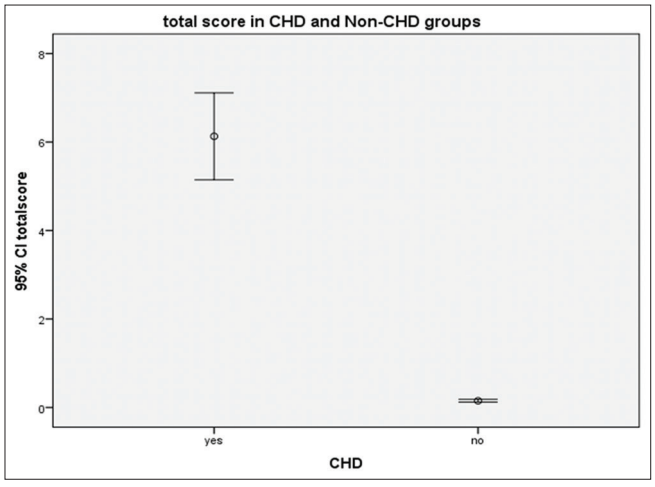

Figure 2: Error bar graph for the total score and congenital heart disease

This study showed that there was significant poor growth among children with CHD than other normal children of that age. This observation was consistent with other studies which had shown the prevalence of malnutrition higher among children with CHD.[17,18]

In our study, the most common symptom of CHD was FTT (80.6%), followed by feeding difficulty (71.6%) and breathing difficulty (71.6%), and the most common sign was murmur (93.5%), followed by tachycardia (38.7%) and low saturation (32.3%). These findings were consistent with various other studies, as shown in Table 6.

Phuljhele *et al.*[21] in their study took history and examination of 400 children with CHD and found the major symptoms as cough (60%), difficulty in breathing (60%), poor weight gain (72%), suck-rest-suck cycle (46%), bluish discoloration of body (36%), and consanguinity (2.5%).

Similarly, Harshangi *et al.*[23] reported 50 patients as CHD, and the most common symptoms among them were breathlessness (78%), lower respiratory tract infection (60%), FTT (40%), and cyanosis (26%) and the most common signs were murmur (96%), tachypnea (88%), and tachycardia (76%). Various studies reported that breathing difficulty, feeding difficulty, and FTT were the most consistent symptoms and murmur, tachypnea, and tachycardia were the most common signs of CHD.[20,24]

Spectrum of congenital heart disease and scoring

The most common CHD in our study was VSD (15), followed by TOF (5), ASD (2), PDA (2), VSD + ASD (2),

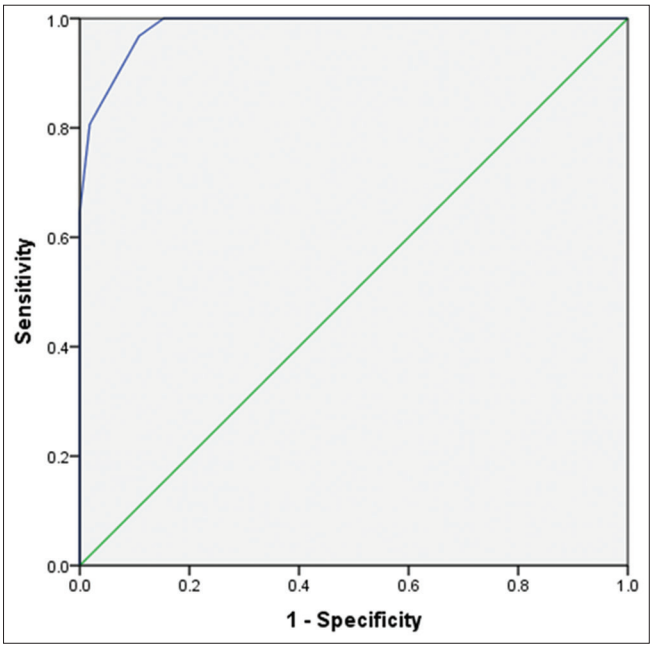

Figure 3: Receiver operating characteristic curve for the sensitivity of the clinical score (total score ≥1)

ASD + PDA (2), TA (2), and AV canal defect (1). There was one baby with dilated cardiomyopathy with severe LV dysfunction with a clinical score of 4 and another of LV hypertrophy with a score of 3. Other studies[20,23] also showed that VSD is the most common CHD. It was seen that the mean score for ASD and PDA was 3.5 which increased to 5 for VSD and further increased with the severity of the disease (e.g., 10 for TOF and TA). This shows that the score is directly related to the severity of the defect, and even with the child with LV dysfunction and no structural heart defect, a high score meant an early detection and subsequent treatment of the condition.

Diagnostic accuracy of different clinical features

Our study found that the maximum sensitivity for detection of CHD was that of murmur (93.6%), followed by FTT (80.7%), feeding difficulty (71%), and breathing difficulty (71%), and the specificity was that of murmur (99.9%), followed by bluish discoloration (99.9%), pulse oximetry (99.8%), and tachycardia (99.6%). All other variables had a high specificity, but sensitivity came out to be very low. Similarly, in a study by Vaidyanathan *et al.*,[10] Kochi, Kerala, has reported low sensitivity of clinical examination (9.26%) and pulse oximetry (11.4%), whereas specificity was high (97% and 91%, respectively).

This study shows that neonatal screening can miss quite a few heart defects and is especially important in our region since routine use of pulse oximetry in neonatal screening is still not universally implemented. Besides, lots of studies have shown that even with a robust neonatal screening program, a lot of CHDs are missed and detected late, as shown in Table 7. A study by Wren *et al.*[8] who reported that 82% of babies with CHD who had undergone routine examination at birth were discharged with no diagnosis and 54% remained undiagnosed at 6 weeks of age and 36% by 12 weeks of age. A similar finding was reported by Meberg *et al.*,[6] where they screened 35,218 newborns at birth by clinical examination, and 269 of them were confirmed as CHD at birth by echo and 84 were diagnosed with CHD on subsequent examination. Gregory *et al.*[26] also had a similar study where they screened 5906 newborns at birth and found 11 neonates with CHD, and on follow-up at 6 weeks, another 24 were diagnosed with CHD. In a prospective study by Patton and Hey,[27] 14,572 babies were screened between 1996 and 2003, in whom 150 were diagnosed to have CHD at birth and 26 were diagnosed by 1 year of age [Table 6].

Alexander Nada has given a score for the detection of CHD on the basis of clinical evaluation very early in the 1950s–1960s. Nada's criteria have four major and five minor components. Major criteria include systolic murmur of Grade 3 or more, diastolic murmurs, cyanosis, and congestive cardiac failure. Minor criteria include systolic murmur of Grade <3, abnormal second sound, abnormal electrocardiogram, abnormal X-ray, and abnormal blood pressure. There has to be one major or two minor criteria to label CHD. A study by James *et al.*[29] in Kerala reported the sensitivity of Nada's criteria for detecting CHD (in children with Grade >2 murmur) as 87.87% and specificity as 83.3%.

Vaidyanathan *et al.*[10] in their study had shown a very low sensitivity of clinical examination for detection of CHD at birth and recommended a 6-week clinical evaluation to ensure that major CHDs are not missed. Pulse oximetry is now a part of neonatal screening, and abnormality in it (SpO_2 <95% beyond 24 h) can detect few critical CHDs but can miss few heart defects which do not present immediately after birth. As is clear from Table 7, a second screening is warranted for the children to detect these missed cases which can later on present with one or the other complications. The attempt of the study was to design a clinical parameter which can be utilized by various field workers to suspect heart defect in a child and followed up by early referral. The clinical score pro forma can provide a checklist to the workers in which complaints of the child can be ticked during their field visits for immunization and the child can be referred early. In our study, a score of 3 or more had

Table 6: Comparison of various studies on the clinical spectrum n (%) of congenital heart defects

Study	Total CHD	Cyanosis	Murmur	Tachycardia	FD	BD	FTT	Features of CHF	Syndrome
Meshram and Gajimwar 2018[19]	430	172 (40)	420 (97)	382 (89)	163 (38)	377 (88)	209 (49)	205 (47.7)	73 (17)
Mahapatra *et al.*, 2017[20]	231	44 (19)	196 (85)	96 (41)	-	84 (36)	-	Edema 21 (9) Hepatomegaly 41 (18)	-
Phuljhele *et al.*, 2016[21]	400	18 (4.5)	-	-	23 (5.8)	31 (7.8)	36 (9.0)	-	-
Meena *et al.*, 2016[22]	390	SpO_2<95,335 (86)	-	-	-	-	131 (33)	-	
Harshangi *et al.*, 2013[23]	50	13 (26)	48 (96)	38 (76)	-	39 (78)	20 (40)	Edema 9 (18)	12
Shah *et al.*, 2008[24]	84	17 (20)	-	-	-	58 (69)	10 (12)	46 (55)	-
This study, 2018	31	7 (22.6)	29 (93.5)	12 (38.7)	22 (71.6)	22 (71.6)	25 (80.6)	-	1 (3.2)

FD: Feeding difficulty, BD: Breathing difficulty, FTT: Failure to thrive, CHF: Congestive heart failure, CHD: Congenital heart defect

Table 7: Review of literature of studies on missed and undiagnosed cases

Study	Total babies screened	CHD diagnosed at birth	CHD undiagnosed at birth	Remarks
Meberg *et al.*, 1999[6] Norway	35,218	269	84	Screened 35,218 newborns (in three 5-year cohorts with either one or two examinations in newborn period) and missed cases were detected on follow-up (2 weeks-11 years)
Wren *et al.*, 1999[8] UK	1061 confirmed cases of CHD	476 (abnormal neonatal examination)	585	Total 1061 children with CHD were retrospectively reviewed for the sensitivity of clinical examination at birth to detect CHD
Vaidyanathan *et al.*, 2011[10] Kerala	5487	425 (major - 17, minor - 408)	Echo was done at birth	5487 newborns were screened at 48 h by clinical examination and pulse oximetry, and echo was also done and was followed at 6 weeks. Out of 17 major CHDs, 14 had a normal clinical examination and PO
Abu-Harb *et al.*, 1994[25] Newcastle	1009 cases of CHD (108 cases of LVOTO)	45 (LVOTO at birth)	63 (diagnosed subsequently)	34 were diagnosed at initial examination and 11 at a second examination before discharge
Gregory *et al.*, 1999[26] Newcastle	5906 (examined at 6-8 weeks)	47 had murmur (11 had CHD)	6 had CHD with no murmur	Clinical examination was done in 5906 children at 6-8 weeks and was followed up
Patton and Hey 2003[27] UK	14,572	150	26	Neonatal screening was done in all newborn delivered during study period and was followed at 1 year of age
Ng and Hokanson 2010[28] Wisconsin	3,45,573 (live births)	-	14 (deaths or rehospitalization)	Neonates brought dead, or rehospitalization during the first 2 weeks of life due to CHD was reported
This study, 2018	970	-	31	All babies coming to immunization clinic between 6 weeks and 6 months were screened with history and clinical examination and confirmed with echo. Eighteen were missed and 13 were undiagnosed cases of CHD

CHD: Congenital heart defect, LVOTO: Left ventricular outflow tract obstruction

a high sensitivity as well as specificity for the detection of CHD. However, a large community-based study is required for the evaluation of validity of the score.

CONCLUSION

The history and examination based tool is an effective method for early identification of CHD and can easily be used by peripheral workers working in remote places with poor resources enabling prompt referral. The cut off score of ≥3had more chances of detecting CHD. Its sensitivity was 96.77% and specificity was 98.72, with a PPV of 71.43%, NPV of 99.89% and an accuracy of 98.66%.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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