RESEARCH PAPER

Clinical Screening for Congenital Heart Disease at Birth: A Prospective Study in a Community Hospital in Kerala

BALU VAIDYANATHAN, GAYATHRI SATHISH, SINIMOL THOPPIL MOHANAN, KARIMASSERY RAMAIYAR SUNDARAM*, KARUKAPPILLY KRISHNAN RAGHAVA WARRIER† AND RAMAN KRISHNA KUMAR

*From the Departments of Pediatric Cardiology and *Biostatistics, Amrita Institute of Medical Sciences and Research Center, AIMS Ponekkara PO, and †Department of Pediatrics, Lakshmi Hospital, Kochi, Kerala, India.*
Correspondence to: Dr Balu Vaidyanathan, Clinical Professor, Pediatric Cardiology, Amrita Institute of Medical Sciences, AIMS Ponekkara PO, Kochi, Kerala, 682 041, India. baluvaidyanathan@gmail.com
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Objective: To develop a clinical strategy for detection of Congenital heart disease (CHD) in the newborn through a combination of clinical signs and pulse oximetry.

Design: Prospective longitudinal study.

Setting: Community level hospital in the city of Kochi, Kerala.

Participants and interventions: All consecutive newborns between June 2006 and February 2009 were prospectively screened for CHD, 48 hours after birth. The on-site pediatrician performed clinical screening. A study nurse recorded pulse oximetry in a lower extremity; value of <94% was defined as abnormal. Echocardiography was performed on site by a trained research officer. A 6-week clinical follow-up evaluation was done for all.

Main outcome measure: Detection of CHD by echocardiography.

Results: Of 5487 babies screened, 425 (7.75%) had CHD. 17 (0.31%) had major CHD, two of whom (one ALCAPA and one large VSD) were missed during the initial evaluation. The rest were minor CHD (408 patients, 7.44%), most of which normalized by 6 weeks. On multivariate analysis, murmur, central cyanosis, abnormal precordial pulsations and abnormal pulse oximetry emerged as significant predictors of CHD. The sensitivity of clinical evaluation and pulse oximetry combined was 19% for all CHDs and 20% for major CHD; specificity was 88%.

Conclusions: In the community setting of a developing country, clinical evaluation and pulse oximetry after birth had a very low sensitivity for detection of CHD. Though an abnormal screening warrants prompt echocardiography, a 6-week clinical evaluation is recommended to ensure that major CHD is not missed.

Key words: *Congenital heart disease, India, Newborn, Pulse oximetry, Screening.*

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Congenital heart diseases (CHD) account for about 10% of infant deaths and about half of deaths due to congenital malformations in developed countries [1]. The prevalence of CHD diagnosed in the first 12 months is estimated at 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 delay in referral and increased mortality and morbidity [5]. Several studies have documented the lack of sensitivity of routine neonatal examination in detecting CHD [6-10]. Recent studies have reported a high sensitivity and specificity for pulse oximetry for early detection of CHD in newborn babies [11-16]. Combining pulse oximetry with clinical examination can enhance the clinician's ability to detect life-threatening CHD in a timely manner [17,18].

Accompanying Editorial: Pages 17-18

With advances in perinatal care, congenital malformations are emerging as one of the leading

causes of neonatal and infant mortality, even in developing countries [19]. Challenges for CHD management in developing countries include early diagnosis, transport of a sick neonate with CHD to a tertiary cardiac center, and limited availability of state-of-the-art pediatric cardiac centers [20]. The present study, conducted in a community hospital, attempted to identify a strategy based on clinical signs and pulse oximetry that best predicts CHD in newborns immediately after birth.

METHODS

This was a prospective hospital-based study (June 2006-February 2009) conducted in a secondary level hospital (Lakshmi hospital) in Kochi, Kerala. The study personnel were given one-month training at the coordinating centre (Amrita Institute of Medical Sciences). All consecutive babies (including pre-mature infants) were screened for CHD according to a pre-designed protocol. Out-born babies were excluded. Clinical evaluation was performed by the on-site pediatrician within the first 48 hours of life. Pulse oximetry was recorded in a lower extremity by a study nurse using portable equipment (Oximax *N*-65; Nellcor Puritan Bennett, Pleasanton, CA) at 48 hours after birth. Bedside echocardiography was done by the research officer, using a portable machine (Cyprus-Acuson, Siemens Medical Solu-tions, USA). All babies with abnormal bedside echo-cardiography were evaluated by a pediatric cardio-logist (major CHD – immediately; minor CHD – at 6 weeks). For the normal babies, a follow-up evalua-tion (clinical evaluation, questionnaire or telephonic interview of parents) was performed at 6 weeks. If this was abnormal, echocardiography was repeated.

Definitions of CHD: Patients were categorized into those with and without CHD based on echocardiography [2]. Any CHD that was likely to require early intervention was categorized as major CHD. Minor CHD was defined as any atrial septal defect (ASD) >5mm, patent ductus arteriosus (PDA) >2mm, restrictive ventricular septal defect (VSD) with gradient >30mm Hg, valvular aortic/ pulmonary stenosis with gradients <25 mm Hg, and pulmonary artery branch stenosis with gradients <20 mm Hg. All others (including patent foramen ovale or ASD <5 mm, PDA <2 mm) were categorized as normal variants. Abnormal pulse oximetry was defined as oxygen saturation <94% [11].

Statistical analysis: For analysis, all patients with CHD, including the ones detected during follow-up were considered. Univariate analysis was performed using Chi-square test. All variables which were significant with P <0.2 (80% confidence) were entered into a stepwise logistic regression model for multivariate analysis. Results were expressed as Odd' ratios for association with CHD (with 95% confidence limits) as well as P values. P value of <0.05 was considered significant. Sensitivity, specificity, positive and negative predictive values were computed for clinical signs, pulse oximetry and echocardiography.

An informed consent was obtained from one of the parents before initial screening. The study protocol was approved by the ethics committees of the Institute and the Indian Council of Medical Research.

RESULTS

A total of 5487 consecutive newborn babies were included in the study. Of these, 5086 (92.7 %) were well babies and 401 (7.3%) required admission in the neonatal intensive care unit. 2688 (49%) were males. The mean birthweight was 2.93 ± 0.53 Kg. ***Table* I** summarizes the baseline demographic charac-teristics of the study population.

TABLE I BASELINE CHARACTERISTICS OF THE STUDY POPULATION

Variable	Number (%)
Gestational age: Term	4940 (90.3)
Pre-term	528 (9.7)
Family history of CHD	43 (0.8)
Consanguinity	107 (2)
Maternal diabetes mellitus	542 (10)
Pregnancy induced hypertension	571 (10.6)
Infections during pregnancy	264 (4.9)
Exposure to teratogenic drugs	18 (0.3)
Parental smoking	672 (12.5)

A CHD was detected in 425 neonates (7.75%). Seventeen patients (0.31%) were classified as major (large perimembranous VSD 5, sinus venosus ASD 2, large PDA 2, dTGA 2, Tetralogy of Fallot 2, Primum ASD 1, double aortic arch 1; the rest (408 patients, 7.44%) were minor CHD. Four patients were detected during the 6-week follow-up evaluation. Two of these had major CHD, presenting with heart failure between 4-6 weeks of age (1, anomalous left coronary from the pulmonary artery, requiring surgery and 1, large VSD). Two other patients presented with asymptomatic murmur at 6 weeks (both had moderate sized ASDs). Majority (71.3%) of the minor CHDs normalized by 6-weeks follow-up. ***Fig.* 1** summarizes the findings of the initial screening and 6-week follow-up.

A total of 157 patients (2.9%) had positive clinical evaluation, the most common being murmur (84 patients, 1.6%). Clinical evaluation was positive in only 3 patients (17.6%) with major and 32 patients (7.8%) with minor CHD. Abnormal pulse oximetry was found in 549 (10%) patients, of which 55 (10%) had CHD on echocardiography (2 major, 53 minor). Abnormal pulse oximetry was detected in only 2 patients (11.8%) with major CHD; 4 whereas four patients had cyanotic CHDs. 53 patients with minor CHD (none with cyanotic CHD) had abnormal pulse oximetry. ***Figure* II** summarizes the results of pulse oximetry and its association with clinical signs and echocardiography.

The overall sensitivity for the clinical signs and abnormal pulse oximetry combined was 19% for all CHDs and 20% for major CHD. (***Table* II**). Fourteen patients (82.3%) with major CHD had normal clinical evaluation and pulse oximetry. Bedside echocardiography had a sensitivity, specificity and negative predictive value of 88.2%, 92.6% and 99.9%, respectively for major CHD.

On univariate analysis, maternal diabetes mellitus (O.R 1.39, 95% C.I 1.03-1.89; *P*=0.029), family history of CHD (O.R 2.37, 95% C.I 1.04-5.35; *P* = 0.05), history of ante-natal exposure to teratogenic drugs (O.R 3.47, 95% C.I 1.14-10.64; *P* 0.05), murmur (O.R 24.39, 95% CI 3.62-9.35, *P* <0.001), respiratory distress(OR 2.76; 95% CI 1.27-5.99, *P* <0.017), central cyanosis (OR 8.18, 95% CI 1.37-50, *P* 0.05), abnormal precordial pulsations(O.R 24.39, 95% C.I 3.62-9.35, *P* 0.005) and abnormal pulse oximetry (OR 1.39, 95% CI 1.01-1.91, *P* <0.042) were found to be significantly associated with all CHD. The results of multivariate analysis are summarized in ***Table* III**.

DISCUSSION

The results of this study bring out the inherent limitations of clinical screening for CHD in newborns immediately after birth, especially in the context of limited resource environments. The overall prevalence of CHD reported in this study is higher than that reported previously from various population-based studies [2]. This is accountable by

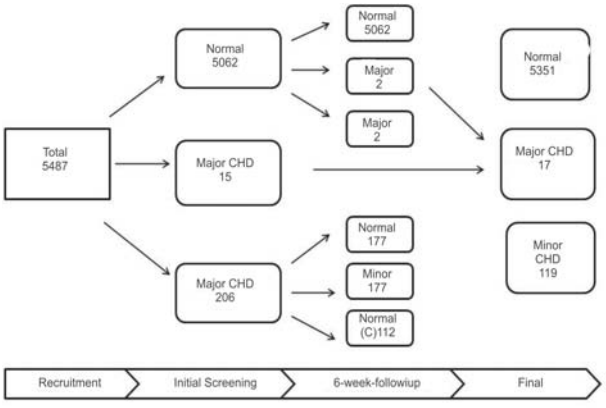

FIG. 1 *Details of CHD diagnosed on initial screening and 6-week follow-up.*

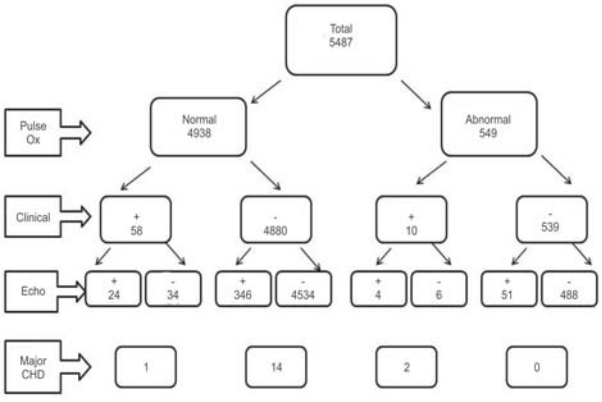

FIG. 2 *Association of pulse oximetry with clinical evaluation and echocardiography.*

TABLE III MULTIVARIATE ANALYSIS OF PREDICTORS OF CHD

Variable	Odds ratio (95% CI)	*P* value
Murmur	5.61 (3.31-9.52)	<0.001
Central cyanosis	15.52 (1.22-197.6)	0.035
Abnormal precordial pulsations	20.22 (1.55-263.21)	0.022
Abnormal pulse oximetry	1.41(1.01-1.97)	0.047
Male sex	1.3 (1.04-1.62)	0.021
Family history of CHD	2.74 (1.19-6.29)	0.018

CHD: Congenital heart disease.

the detection of minor, self- resolving lesions due to use of echocardiography for screening all babies. Though murmur, cyanosis and abnormal pulse oximetry were identified as predictors of CHD, the sensitivity of these signs to detect CHD were very low (combined clinical evaluation and pulse oximetry had a sensitivity of <20%).

Previous studies have reported low sensitivity of clinical examination for detection of CHD in the newborn [4-10]. This study reports a poor sensitivity for pulse oximetry, as well, for detection of CHD [11-17]. Pulse oximetry was also found to have a low predictive value. This may be due to the fact that only four patients in this study had critical CHD with cyanosis. In addition, technical and human factors may also have contributed to the low sensitivity of pulse oximetry, as previously reported [21]. Hence, repeated testing and adequate training of manpower is required before pulse oximetry can be recommended for clinical screening of CHD on a mass level [22]. These issues may limit the widespread use of pulse oximetry as a screening tool for CHD in developing countries.

Though echocardiography is the gold standard for diagnosis of CHD and can be performed by neonatologists with acceptable accuracy, it is not feasible as a routine screening tool, especially in developing countries [23-25]. In this study, even after echocardiography, two patients with major CHD, including a potentially life threatening condition ALCAPA, were missed after the initial screening. This demonstrates the limitations of echocardio-graphy for detection of CHD in the neonates, especially when performed by personnel with limited training, and its potential pitfalls in picking up critical lesions like congenital coronary abnormalities before symptoms have set in.

This study suggests that the presence of abnormal clinical signs like murmur should warrant a prompt cardiac evaluation. With training and repeated testing, pulse oximetry may potentially emerge as a useful adjunct to clinical evaluation, especially for cyanotic CHD. Even if the initial screening is normal, it is mandatory to have a follow-up clinical evaluation at 6 weeks. A comprehensive approach consisting of improved awareness, refining of clinical skills and training of personnel in newer diagnostic techniques (pulse oximetry and echocardiography) is required to ensure that major CHDs do not go undetected in the newborn before discharge from hospital. Large studies are needed for testing the conclusions derived from this study.

This study did not address the impact of fetal echocardiography on the prevalence of major CHD in the population studied. It is possible that the most complex forms of CHDs may have been terminated after a prenatal diagnosis. A follow-up echocardiogram at 6 weeks was not routinely performed for

TABLE II SENSITIVITY, SPECIFICITY, AND POSITIVE AND NEGATIVE PREDICTIVE VALUE OF CLINICAL SIGNS

Variable	All CHDs				Major CHDs			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
Clinical	9.26	97.4	23.3	92.8	13.3	96.9	1.1	99.7
Pulse oximetry	11.4	90.9	9.4	92.8	13.3	90.7	0.3	99.7
Combined	19	88	12	92	20	87.9	0.4	99.7

CHD: congenital heart disease, NPV: negative predictive value, PPV: positive predictive value; All values in percentage.

WHAT IS ALREADY KNOWN?

- Clinical evaluation has a very low sensitivity for detection of CHD in asymptomatic newborns.

WHAT THIS STUDY ADDS?

- In the setting of low resource environments, the utility of pulse oximetry as a screening tool for CHD is limited.
- Training of personnel in the technique of pulse oximetry is essential before it can be recommended for mass screening for CHD in developing countries.

most patients with minor CHD as well as those with normal screening.

In the community setting of a developing country, clinical evaluation and pulse oximetry after birth had a very low sensitivity for detection of CHD. Though an abnormal screening warrants prompt echocardio-graphy, a 6-week clinical evaluation is recommended to ensure that major CHD is not missed.

Contributors: BV designed the study, analyzed the data and wrote the manuscript and shall act as the guarantor for the paper; GS collected the data, helped in data analysis and manuscript preparation; STM collected the data and helped in analysis; KRS performed the statistical analysis; KKRV critically reviewed the manuscript, and RKK designed the study and critically reviewed the manuscript.
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