Pulse oximetry as a screening tool for congenital heart disease in neonates: A diagnostic study

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ABSTRACT

Introduction: Many studies have been done for screening of congenital heart disease (CHD) in the neonatal period utilizing pulse oximetry as a screening tool along with routine clinical assessment, but none of them from our province. **Objective:** The objective of the study was to find out the diagnostic accuracy of pulse oximeter at three different sites as a screening tool to diagnose CHD among neonates. **Methods:** A diagnostic study was conducted in neonatal intensive care unit of a tertiary care hospital of Odisha from October 2016 to September 2018 after approval from the Institutional Ethics Committee. Three hundred and seventy-four neonates (both inborn and outborn) with gestational age >34 weeks were included in the study. Oxygen saturation (SpO_2) in the right hand (RH), right foot (RF), and left foot (LF) was estimated by pulse oximeter among all participants after 10 min of postnatal life. All the study subjects were evaluated by two-dimensional (2D) echocardiography for the detection of CHDs. All the diagnostic accuracy tests (sensitivity [Sn], specificity [Sp], positive predictive value, negative predictive value, and diagnostic odds ratio) were calculated taking 2D echocardiography as the gold standard with software, and for all statistical purpose, $p<0.05$ was considered statistically significant. **Results:** Cutoff value of the RH SpO_2 was 90.0% with Sn of 68.80% and Sp of 98.20%; area under curve (AUC) 0.851 (0.766 and 0.914), $p<0.001$, for the RF, SpO_2 was 90.0% with Sn 78.0% and Sp 92.1%; AUC 0.865 (0.782 and 0.925), $p<0.001$, and for LF, it was 87% with Sn 77.1% and Sp 94.0%; AUC 0.864 (0.781 and 0.924), $p<0.001$. **Conclusion:** Along with the clinical skills, pulse oximetry can be used as an early screening tool for the detection of CHD in the neonatal period and of three different sites, RF found to be better.

Key words: *Two-dimensional echocardiography, Diagnostic odds ratio, Oxygen saturation, Sensitivity, Specificity*

Congenital heart diseases (CHDs) are one of the widespread congenital problems of neonates and are an important cause of morbidity and mortality in the infancy period. A lot of children born with CHD in developing countries cannot be recognized early to avoid irreversible pulmonary vascular disease [1,2]. Very often, it happens that newborn babies, who are discharged as normal, are diagnosed later on with CHD, which makes it important to detect them before getting discharged from hospital. Hence, all CHDs should be regarded as main targets of neonatal screening in developing countries, especially like ours and it becomes important to detect those babies who are normal at birth, but with CHD to prevent the mortality and morbidity. As such, some have proposed that pulse oximetry be considered as a vital sign equivalent in importance to pulse, respiration, and blood pressure [3]. For this, if we use pulse oximetry screening soon after delivery, we can detect some of the CHDs.

In the past few years, many studies have been done for the screening of CHD in the neonatal period and few of them have utilized pulse oximetry for the screening of CHD along with routine clinical assessment [4-9]. However, most of these studies have been done in developed countries and very few studies have been done in developing countries [10,11], among which only a few Indian studies [3,12] are available which detected CHDs using pulse oximetry saturation. A study from the United States showed that 25% of the infants with critical CHD were not diagnosed until after discharge from the newborn nursery [13].

Critical CHD, which by definition required surgery or catheter intervention in the 1st year of life and duct dependent critical CHD includes coarctation of the aorta, interrupted aortic arch, hypoplastic left heart syndrome, pulmonary atresia, and tetralogy of Fallot with severe pulmonary stenosis [10]. These CHDs may manifest with sudden and profound worsening clinical status in the 1st day and week of life corresponding to changes in pulmonary vascular resistance and closure of the ductus. Critical CHD in the newborn may have borderline low oxygen saturation (SpO_2) with unrecognized cyanosis clinically.

Pulse oximetry has the potential to identify hypoxemia that might not otherwise produce visible cyanosis. Pulse oximetry is highly specific for the detection of critical CHDs with moderate sensitivity (Sn) that meets criteria for universal screening [9]. Pulse oximetry monitoring is also capable of detecting other conditions that include hypoxia including some lung conditions and persistent pulmonary hypertension of the newborn (PPHN). The investigators observed that pulse oximetry is much more effective in identifying infants with critical CHD and is more accurate and much less expensive than screening all newborns with echocardiography. Hence, our objective was to find out the diagnostic accuracy of pulse oximeter at three different sites as a screening tool for CHDs among neonates.

METHODS

The present Phase-II diagnostic study was conducted in NICU of a tertiary care hospital situated in the western part of Odisha, from October 2016 to September 2018 after getting approval from the Institutional Ethics Committee. Minimum sample size calculated was 374 using n Master v2.0 taking the Sn of pulse oximetry as 58.33% [14] and with an absolute precision of 5% and 95% confidence interval after satisfying predefined inclusion and exclusion criteria. Inclusion criteria were both inborn and outborn neonates with gestational age >34 weeks, whereas exclusion criteria were neonates with respiratory illnesses, congenital lung abnormalities, or malformations.

All consecutive newborns admitted to NICU satisfying the predefined inclusion criteria were enrolled in the study after taking written informed consent from parents and/or legal heir and were assessed for SpO_2 monitoring with pulse oximetry after 10 min of birth in case of inborn and at time of admission for outborn (Fig.1). Two-dimensional (2D) Doppler echocardiography (Phillips HD 11 XE, New York, USA) was done in each baby for the detection of CHD in the department of cardiology and was taken as the gold standard for estimating the accuracy of pulse oximetry. Data were collected regarding the pre-ductal (right hand [RH]) and post-ductal (right foot [RF] and left foot [LF]) SpO_2. Pre-ductal site conventionally RH was taken due to non-significant difference in SpO_2 level between RH and LH as per previous research article by Ruegger *et al*. [15].

Difference between pre-ductal and post-ductal SpO_2 (%) was calculated for each case. The cutoff values were calculated by applying receiver operating characteristic (ROC) curve with relevant statistics such as Sn, specificity (Sp), area under curve (AUC), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio

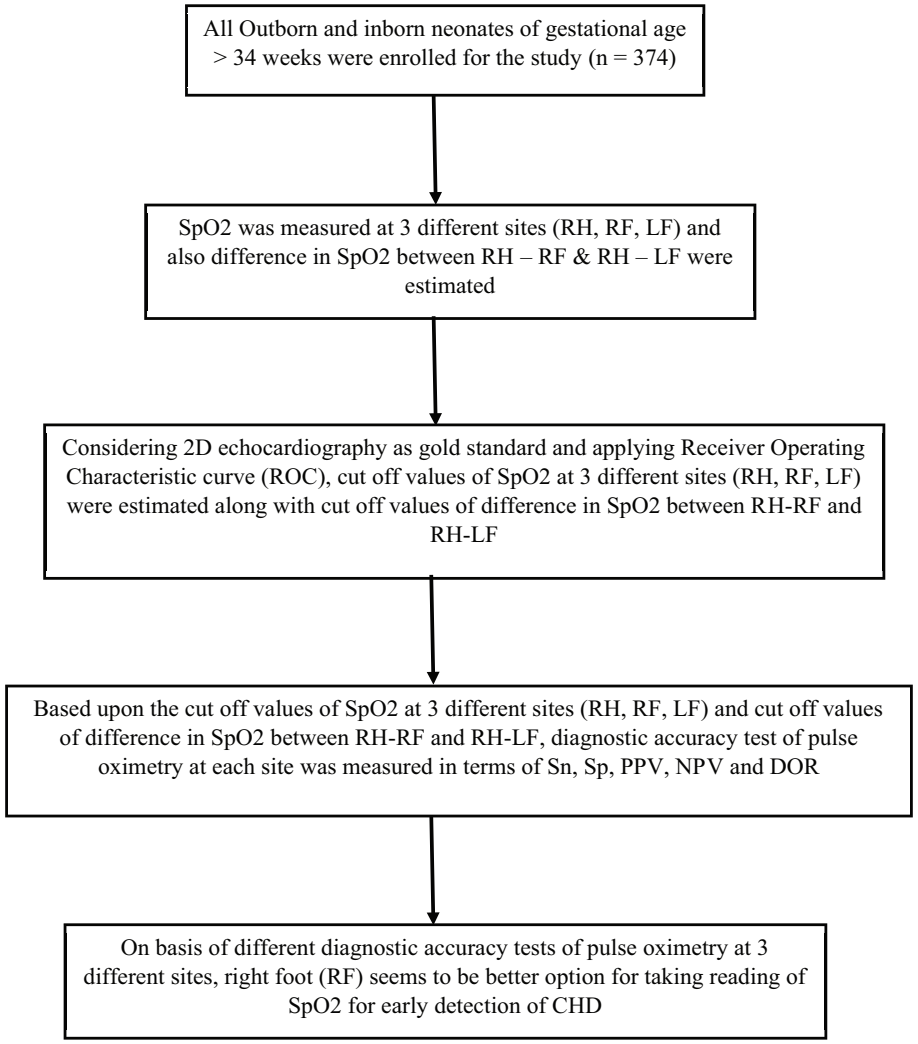

Figure 1: Study flow chart

Table 1: Diagnostic accuracy parameters of RH, RF, LF, RH-RF, and RH-LF

Different Sites	Sn[@]	Sp[#]	PPV[$]	NPV[$$]	LR[+]**	LR[−]**	DOR***	YI****	Sn[@]
LF	80.6	92.6	80.6	92.6	10.919	0.21	52.083	0.732	80.6
RF	77.8	93.2	82.4	91.2	11.494	0.238	48.222	0.71	77.8
RH	69.2	93.7	80.9	88.8	10.995	0.328	33.485	0.629	69.2
RH-LF	83.2	71.9	54.3	91.4	2.961	0.234	12.658	0.551	83.2
RH-RF	75.5	78.7	58.4	89.0	3.548	0.312	11.39	0.542	75.5

[@]Sensitivity (%), [#]Specificity (%), [$]Positive predictive value (%), [$$]Negative predictive value (%), *Positive likelihood ratio, **Negative likelihood ratio, ***Diagnostic odds ratio, ****Youden index, RH: Right hand, RF: Right foot, LF: Left foot

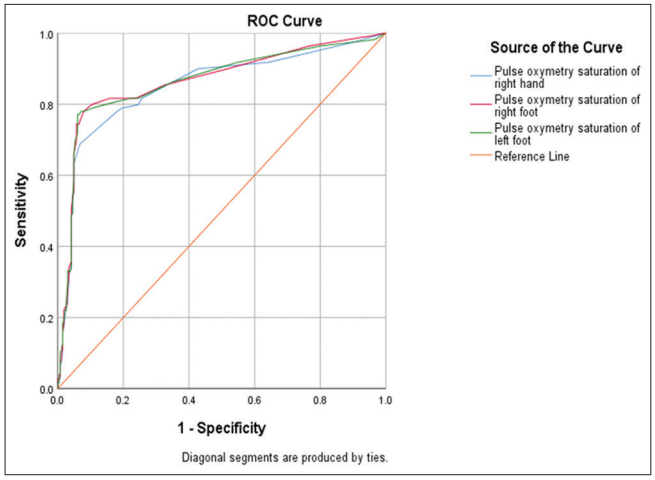

Figure 2: Receiver operating characteristic curve of the right hand, right foot, and left foot

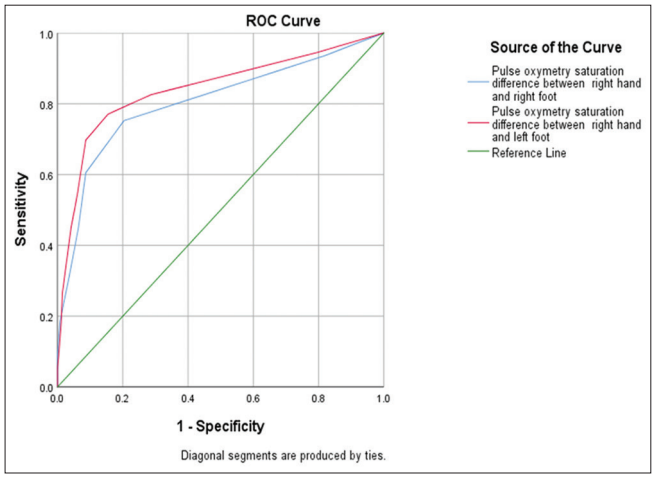

Figure 3: Receiver operating characteristic curve of the right hand-right foot and RH-left foot

(LR−) of RH, RF, and LF, and difference between RH and RF and between RH and LF using the SPSS v25 (IBM, New York) and Dxt v1.0 (BRTC, Bagayam, Vellore). Based on these, we have calculated the Sn, Sp, PPV, NPV, LR+, LR− and diagnostic odds ratio (DOR) of RH, RF, and LF, and difference between RH and RF, and RH and LF. For all statistical purpose, $p<0.05$ was considered statistically significant.

RESULTS

Among 374 neonates included in our study, the male-to-female ratio was 1.04:1. The mean gestational age was 37.51±1.69 weeks, whereas mean postnatal age was 11.85±5.78 h. The mean SpO_2 of the RH was 90.38±12.64%, whereas mean SpO_2 of the RF and LF was 88.98±14.13% and 88.39±14.82%, respectively. The mean difference of SpO_2 between RH and RF was 1.87±1.89% and between RH and LF was 2.48±2.63%. Of 374 neonates screened with 2D echocardiography, 109 (29.14%) neonates were detected with CHDs. Of 109 neonates with CHD, 103 neonates were having acyanotic CHD (59 patent ductus arteriosus, 37 ventricular septal defects, and seven arterial septal defects) and rest six had cyanotic CHD (four PPHN, one transposition of great arteries, and one tricuspid atresia). All six cyanotic CHDs were having poor saturation.

Cutoff value of the RH SpO_2 was 90.0% with Sn 68.80% and Sp 98.20%; AUC 0.851 (0.766 and 0.914), $p<0.001$, LR+=10.13, and LR−=0.335 (Fig. 2). Cutoff value of the RF SpO_2 was 90.0% with Sn 78.0% and Sp 92.1%; AUC 0.865 (0.782 and 0.925), $p<0.001$, LR+=9.845, and LR−=0.239 (Fig. 2). Cutoff value of the LF SpO_2 was 87% with Sn 77.1% and Sp 94.0%; AUC 0.864 (0.781 and 0.924), $p<0.001$, LR+=12.764, and LR−=0.244 (Fig. 1).

Cutoff value of difference in SpO_2 between RH and RF was 2 with Sn 75.23% and Sp 79.63%; AUC 0.805 (0.713 and 0.877), $p<0.001$, LR+=3.692, and LR−=0.311 (Fig. 3). Cutoff value of difference in SpO_2 between RH and LF was 3 with Sn 77.06% and Sp 85.52%; AUC 0.842 (0.755 and 0.907), $p<0.001$, LR+=4.981, and LR−=0.271 (Fig. 3).

Based on the above parameters, we have calculated the Sn, Sp, PPV, NPV, LR+, LR−, and DOR of RH, RF, and LF and are shown in Table 1. Sn of difference between RH and LF was highest among all (83.2%), but DOR was highest for LF (52.083). LR+ was highest for RF (11.494). Applying clinical knowledge along with the statistical parameters, it is assumed that it is better to take RF for screening of CHDs in newborns.

DISCUSSION

Neonates with CHD can be diagnosed on the basis of physical findings. However, these findings are not always evident before hospital discharge or within the first 48 h of life. Newborns with CHD, especially critical CHD, are susceptible to a sudden worsening in clinical status without an accurate diagnosis [13]. Early diagnosis of CHD can significantly impact the outcome; hence, it becomes vital to identify, evaluate, and design strategies to improve early detection. In developing countries like India [3,12], this method can be very helpful in the early detection

of CHD as fetal echocardiography is not routinely done. A study by Levesque *et al.,* in 2000, described the normal range of SpO_2 in term newborns in the 1st day of life [16]. These investigators evaluated normal oximetry values at sea level, from admission to the newborn nursery to discharge.

In the scientific statement from the American Heart Association and the American Academy of Paediatrics, Mahle *et al*. evaluated the statistical analysis of pulse oximetry screening with data from 10 different studies [17]. Analysis of the studies with infants who were evaluated after 24 h of age showed 18 false positives, along with 7 false negatives and 51,063 true negatives. From these data, the Sn of pulse oximetry was 69.9% and Sp was 99.9%, with an NPV of 99.9% and a PPV of 47% [17] which is more or less similar to our present study.

However, the DOR was highest for LF in our study, which means, of three different sites for measuring SpO_2 among neonates, the RF is the better option. The Sn of pulse oximetry of our study coincides with the previous studies [11,18-20] but higher than the study done in Thailand in January 2019 [10]. The reason may be due to the fact that they have taken only critical CHDs, but the present study was aimed for the screening purpose, i.e., we have taken all neonates with and without CHD.

Although there were different studies regarding pulse oximetry as a screening tool for CHD in neonates [21-23], the present study is quite different because all previous studies were taken a proposed algorithm for screening and no study evaluated parameters such as individual limb oximetry and attempted to find out a cutoff in terms of the difference between oximetry in different limbs.

Like other studies, the current study is also not devoid of limitations. Since this is a Phase II diagnostic study, the level of evidence is low. As it is a hospital-based study in a tertiary care center, its result could not be generalized. Since the non-probability sampling technique was used, errors and biases could not be avoided. Hence, in a future, Phase III diagnostic study is required to boost upon the existing knowledge.

CONCLUSION

Early diagnosis of CHD is important for appropriate management of potentially critical (yet often treatable) conditions. Echocardiography is the best, but is expensive, and requires considerable expertise, and is not easily available at most centers. Along with the clinical skills, pulse oximetry can be used as an early screening tool for the detection of CHD in the neonatal period and of three different sites, the RF seems to be a better option for early recognition.

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