Role of perfusion index in pulse oximetry screening for critical congenital heart disease in neonates

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ABSTRACT

Introduction: Screening for critical congenital heart diseases (CCHD) with oxygen saturation (SpO_2) by pulse oximeter often misses left-sided obstructive heart diseases. **Objective:** The role of perfusion index (PI) along with SpO_2 in CCHD screening was studied. **Methodology:** The Masimo, RADICAL-7 pulse oximeter was used to record the SpO_2 and PI in the right hand and left foot of asymptomatic babies at 24–72 h of life. Babies with SpO_2 <95% or PI <0.7 were rechecked at an hourly interval for three recordings. SpO_2 90–94% or PI <0.7 in all three recordings or SpO_2 <90% at any one recording were considered as screen positive. An echocardiogram was done for screen-positive cases. Screen negative cases were clinically followed for 6 weeks. **Result:** Of 1011 screened babies, four were screen positive. One baby had PI <0.7 and SpO_2 <90%. This baby had single ventricle, transposed great vessels, and interrupted aortic arch. Other three cases had SpO_2 between 90% and 94% in all three recordings. Echocardiogram showed severe right ventricle outflow obstruction in 2 cases and normal heart in one baby. At follow-up, no baby had CCHD. **Conclusion:** In this study with small sample size, only one baby had left-sided obstructive lesion but also had single ventricle physiology. Hence, there was no difference in the diagnostic accuracy between SpO_2 alone and SpO_2 with PI in screening for CCHD. Thus, combining PI with SpO_2 may improve CCHD screening using pulse oximeter, but large-scale study is needed.

Key words: *Critical congenital heart disease, Newborn screening, Oxygen saturation, Perfusion index, Pulse oximetry*

Congenital heart diseases (CHD) requiring intervention in the 1st month of life to ensure survival is considered as critical CHD (CCHD). CCHD has an incidence of about 170 in 100,000 live births. Early diagnosis and timely therapy are crucial to prevent acute deterioration of the affected children [1]. CHD with right-sided obstruction or well-mixing lesion present predominately with cyanosis. These cyanotic CHD initially present with faint cyanosis which may be indistinguishable clinically. Thus, the clinical examination (CE) fails to identify about 50% of CHD in the neonatal period [2]. However, these babies can be identified with low oxygen saturation (SpO_2) in the pulse oximeter. Hence, American Academy of Pediatrics (AAP) has recommended SpO_2 measurement by pulse oximeter as a screening strategy to identify cyanotic CHD [3].

However, left-sided obstructive lesions such as hypoplastic left heart syndrome, interrupted aortic arch, and coarctation of aorta present initially with poor peripheral perfusion. SpO_2 may remain within normal limits at an early stage of the disease and can be missed by pulse oximeter screening [1]. Studies have shown that more than 3% difference in saturation ($DSpO_2$) between pre-ductal and post-ductal regions may give a clue to these left-sided obstructive heart diseases [4]. Granelli and Ostman-Smith have found that peripheral perfusion index (PI) measured with new generation pulse oximeter can help in screening for left-sided obstructive lesions [5]. PI is a measure of the pulsatile blood flow in the underlying tissues and is decreased in babies with reduced peripheral tissue perfusion [6]. PI below 0.7 was suggested as a screening tool for identifying left-sided obstructive heart diseases [5].

This study was planned with a hypothesis that combining PI with SpO_2 may improve CCHD detection. The primary objective was to compare the diagnostic accuracy of SpO_2 alone, with SpO_2 and PI in screening for CCHD among asymptomatic newborn babies at 24–72 h of life. The secondary objective was to find out the diagnostic accuracy of CE in screening for CCHD either alone or in combination with SpO_2 and PI.

METHODOLOGY

This prospective study was done in a tertiary care hospital in the Tamil Nadu state of India. The study was carried out over a period of 4 months from October 2011 to January 2012. The Institutional Ethics Committee approved the study. All babies born during the study period and asymptomatic at 24–72 h of life were included in the study. Asymptomatic babies under evaluation for sepsis due to various perinatal risk factors were excluded from the study.

Parents of all babies who satisfied the inclusion criteria were approached for the study. Written informed consent was obtained from the parents and basic demographic details were collected. Babies were then clinically examined for any dysmorphic features, central cyanosis, respiratory distress, apical impulse location, femoral pulses, and grade ≥3/6 precordial murmur.

The new generation pulse oximeter with signal extraction technology (Masimo, RADICAL-7, Signal extraction pulse Co-Oximeter with rainbow technology) was used for recording functional hemoglobin SpO_2 percentage and PI. The instrument displays the pulse waveform, heart rate, SpO_2, and PI. The reusable neonatal probe was applied in the right hand (Pre-ductal area) and the left foot (Post-ductal area) serially when the baby was calm and quiet. The SpO_2 and PI were recorded, once the monitor's display panel showed regular pulse waves. The probe was cleaned with a compatible disinfectant solution between babies.

If PI was ≥0.7 with SpO_2 ≥95% in the both tested limbs and $DSpO_2$ between the two limbs was ≤3%, the screening was considered negative. If anyone of these readings was abnormal, the test was repeated after 1 h. If the second recording result remained abnormal, it was reconfirmed by repeating the test 3rd time after another hour. Babies who consistently had SpO_2 <95% or PI <0.7 or $DSpO_2$ >3% in all three recordings were declared screen positive. SpO_2 <90% in either limb at any time either in the initial recording or in the repeat recordings was immediately declared as screen positive without further testing. All babies with positive screening and those babies with abnormal clinical findings underwent echocardiography (Philips ER VISION-HD-7 with pediatric probe) by a pediatric cardiologist with 5-year experience in the field. Confirmed CCHD cases were referred to cardiothoracic surgeons for further management.

The screen negative cases were followed up clinically at 6 weeks of age when they attended the well-baby clinic for review and vaccination. Any suspicion of CHD was confirmed by echocardiography. The parents of babies who did not come for follow-up were tracked through phone about the health status of the baby. For those parents who could not be contacted by phone, a letter enquiring the health status of their baby was posted to their mailing address. The babies who could not be contacted by phone or post were considered as dropouts.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for SpO_2, PI, and CE were calculated individually and in combination using OpenEpi, Version 2, open source calculator for diagnostic tests. Categorical data were analyzed with two-tailed Fisher's exact test for small groups and Chi-square test for the large population using SPSS Version 16. $p<0.05$ was considered as significant.

RESULTS

A total of 1011 babies out of 1059 eligible babies were screened. 48 babies were discharged before 24 h of life due to various reasons and were not included in the study (Fig. 1).

Male to female ratio in the study population was 1.03:1. The babies were screened at a mean age of 34 h (±10.5), and their mean birth weight was 2850 g (±440) (Table 1).

Mean SpO_2 in the right hand and left foot was 97.42% (±1.35) and 97.58% (±1.44), respectively, with a mean $DSpO_2$ of 1.07% (±0.86). Mean PI in the right hand and left foot was 2.43 (±1.48) and 2.43 (±1.32), respectively (Table 2).

We had four screen positive cases: One at first recording and other three at the end of three recordings. The baby who was screen positive at first recording had SpO_2 <90% and PI< 0.7 in the right hand. This baby was antenatally diagnosed to have single ventricle. Postnatal echocardiogram of this baby showed transposition of great vessels (TGV), interrupted aortic arch, single ventricle, hypoplastic left atrioventricular valve, and patent ductus arteriosus. Three babies persistently had SpO_2 90–94%

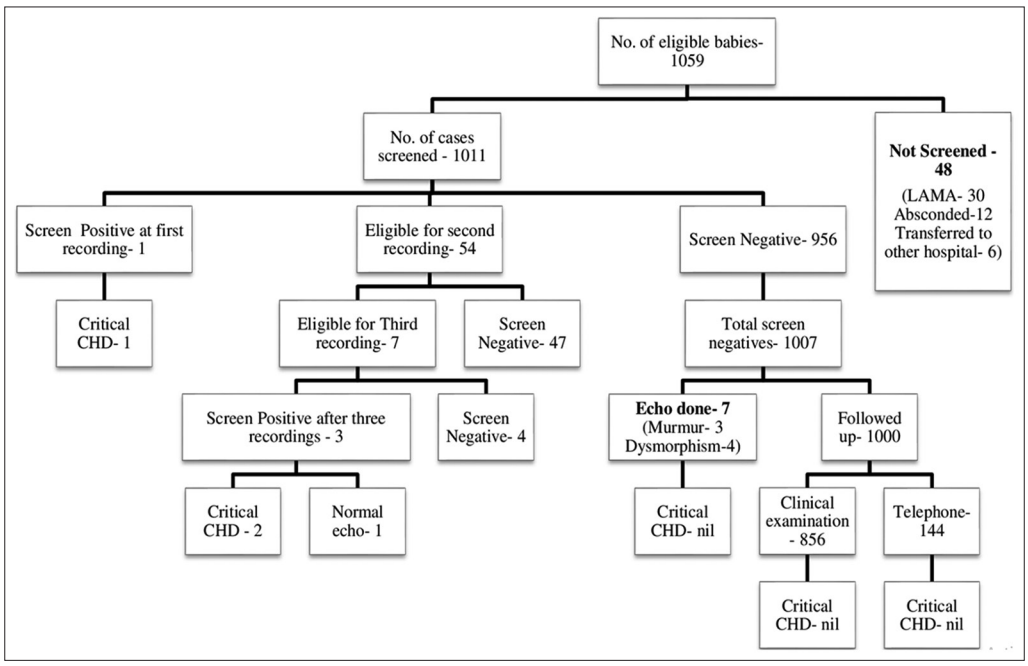

Figure 1: Flow of cases through the study

Table 1: Baseline characteristics of the study population

Characteristics	Observation
Male: female ratio	1.03:1 (p=0.687)
Mean birth weight	2850 (±440) g
Mean age at screening	34.03 (±10.5) h
Mode of delivery	Labor naturale-453; Cesarean section-532; Assisted breech-3; Outlet forceps-17; Vacuum-6

Table 2: Study results

Characteristics	Observation
Mean SpO_2 in right hand	97.42% (±1.35)
Mean SpO_2 in left foot	97.58% (±1.44)
Mean $DSpO_2$	1.07% (±0.86)
Mean PI in right hand	2.43 (±1.48)
Mean PI in left foot	2.43 (±1.32)
Number of babies with dysmorphism	4 (down syndrome-1, Preauricular skin tag-3)
Number of babies with cardiac murmur	4 (CCHD-1, VSD-3)
Number of screen positive cases	4 (Low SpO_2 and low PI-1, low SpO_2-3)
Number of confirmed CCHD	3 (Antenatally detected-2, detected by screening-1)

SpO_2: Pulse oximeter saturation, $DSpO_2$: Difference in pulse oximeter saturation between right upper limb and left lower limb, PI: Perfusion index, CCHD: Critical congenital heart disease, VSD: Ventricular septal defect

at all three recordings. Echocardiogram in these babies showed tetralogy of fallot (TOF) with severe right ventricular outlet obstruction in one baby, right ventricular dysplasia with severe right ventricular outlet obstruction in the second baby and structurally normal heart in another baby. The baby with TOF was antenatally diagnosed to have CHD and postnatally had systolic murmur by CE. The other two cases had normal antenatal scans and normal CE. The screen positive baby with normal echo subsequently had normal SpO_2 before discharge.

Thus, two babies antenatally detected to have CCHD had positive screen by pulse oximeter. Four babies had systolic murmur in CE, and this includes one screen positive baby with TOF. The other three babies with systolic murmur and negative pulse oximeter screening were found to have ventricular septal defect (VSD) by echocardiogram. In addition, four babies with dysmorphic features underwent echocardiography as a part of dysmorphology work up, and all were found to have a structurally normal heart (Table 2).

Other cases were followed up at 6 weeks of age. A total of 856 babies came for follow-up, and none had clinical features of CHD. 144 babies who did not turn for follow-up were contacted by phone and were reported to be healthy without any symptoms suggestive of CCHD. Thus, the incidence of CCHD in our population was 2.97/1000 babies, and the incidence of CHD was 5.93/1000 babies.

The diagnostic accuracy of SpO_2, PI, and CE was calculated individually and in combination. The sensitivity, specificity, PPV, and NPV of SpO_2 alone and SpO_2 with PI were similar. PI alone has low sensitivity but better PPV compared to SpO_2. If the role of PI alone in identifying left-sided obstructive lesions is considered then the sensitivity is 100% and specificity is 100%. CE has low sensitivity and PPV compared to SpO_2. When all three methods of screening are combined, i.e., SpO_2, PI, and CE the sensitivity is 100%, specificity is 99.7%, and PPV is 50% with a false positivity rate of 50% in identifying CCHD (Table 3).

DISCUSSION

In this study, an attempt was made to study the role of combined SpO_2 and PI screening in identifying the CCHD. The results are encouraging since PI has rightly identified one baby with the interrupted aortic arch. Interestingly, this baby also had SpO_2 <90% due to TGV and single ventricle. It can be assumed that even if it had been an isolated interrupted aortic arch, this case would have been picked up by pulse oximeter when both SpO_2 and PI were recorded in all babies. Thus, PI and SpO_2, each have a unique role as a screening tool for identifying left-sided obstructive heart diseases and cyanotic heart diseases, respectively.

de-Wahl Granelli *et al*. have suggested that incorporating cutoff values for PI into routine pulse oximetry screening would probably increase sensitivity for detection of the left heart obstructive disease [4]. In our study, the PI <0.7 has a sensitivity of 33.33%, specificity of 100%, and PPV of 100% in identifying all CCHD. However, it has a sensitivity of 100% and specificity of 100% in identifying CCHD with the left-sided obstructive lesion since there was only one case with the interrupted aortic arch in the study population which was identified by low PI.

de-Wahl Granelli *et al*. stated that in a complex heart disease with a combination of TGV, arch obstruction and duct dependent circulation, the post-ductal saturation may well be >95%, and hence, >3% $DSpO_2$ between pre-ductal and post-ductal regions was included as a screening tool in their study [4]. Although we had one baby with TGV and aortic arch obstruction, the $DSpO_2$ was not significant. Probably this was due to the complex nature of the defect with single ventricle physiology which resulted in SpO_2 <90% in both pre-ductal and post-ductal areas.

There were two babies in this study with antenatally detected CHD whose SpO_2 screening was positive and echo later confirmed the critical cardiac lesions. This supports Richmond *et al.*'s comment that even if the antenatal diagnosis was not made in these babies, the screening saturation measurement would have triggered the evaluation for CHD [7]. Riede *et al*. stated that in babies with the prenatal diagnosis of CCHD, if medical treatment is initiated soon after birth, SpO_2 will be spuriously high because of medical therapy [8]. Koppel *et al*. have noted that in a center where fetal echocardiography is readily accessible, many lesions will be diagnosed prenatally, and therefore, SpO_2 screening may be less useful in detecting new CCHD. However, centers, where fetal echocardiography is performed less frequently, are likely to demonstrate higher yields from pulse oximetry screening [9].

Although CE is said to miss about 50% of CHD in infants, many studies on CHD screening have included the CE in their

Table 3: Evaluation of the screening test

Variables	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
SpO_2	100 (43.85, 100)	99.9 (99.44, 99.98)	75 (30.06, 95.44)	100 (99.62, 100)
PI	33.33 (6.149, 79.23)	100 (99.62, 100)	100 (20.65, 100)	99.8 (99.28, 99.95)
CE	33.33 (6.149, 79.23)	99.8 (99.28, 99.95)	33.33 (6.149, 79.23)	99.8 (99.28, 99.95)
SpO_2 and PI	100 (43.85, 100)	99.9 (99.44, 99.98)	75 (30.06, 95.44)	100 (99.62, 100)
SpO_2 and CE	100 (43.85, 100)	99.7 (99.13, 99.9)	50 (18.76, 81.24)	100 (99.62,100)
SpO_2, PI and CE	100 (43.85, 100)	99.7 (99.13, 99.9)	50 (18.76, 81.24)	100 (99.62, 100)

SpO_2: Pulse oximeter saturation, PI: Perfusion index, CE: Clinical examination, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

protocol [7-10]. In this study, though CE failed to pick up two CCHD, it has identified three screen negative babies with VSD. This stresses the importance of clinical evaluation for CHD in all babies, including the screen negative babies, at least once before discharge. In developing countries, where delay in seeking medical care for sick babies is a common occurrence, early recognition of this non CCHD may also play a key role in influencing CHD related mortality.

Thangaratinam *et al*. on the basis of eight studies have found that in pulse oximeter screening, the summary estimates of sensitivity and specificity were 63% and 99.8%, respectively, yielding a false positive rate of 0.2% [2]. Valmari based on 10 studies found a high specificity (99.9–99.99%), and the overall rate of detection of 15 specified defects with pulse oximetry was 72%, which exceeds that of the CE (58%) [11]. In this study, the diagnostic value of SpO_2 in diagnosing CCHD has a sensitivity of 100%, specificity of 99.9%, and PPV of 75% with the false positivity rate of 25%.

Liske *et al*. have defined CCHD as heart diseases that require intervention or cause death within 1 month of age in contrast to AAP definition of up to 1 year of age [1,3]. The follow-up in this study was limited to 6 weeks of age, as patient compliance with long-term follow-up is poor in this study scenario. Ideally, pulse oximetry and echo have to be done for all babies [12]. However, this is not practically feasible in large community studies. Hence, in most of the studies, authors have done echo only for screen positive cases and have clinically followed the screen negative cases for manifestations of CCHD [4,8].

The study has following limitations: It is a hospital-based study done with small sample size, and clinical follow-up was not available for 15% of babies at 6 weeks of age. Hence, this may not reflect the true screening scenario at the community level. However, this study has tried to address the challenge in identifying left side obstructive heart diseases with pulse oximetry by including PI measurement in the screening protocol.

CONCLUSION

In our study, PI was low in one baby with left-sided obstructive lesion, but due to coexisting single ventricle physiology, SpO_2 was also low. Hence, in this study, there was no difference in the diagnostic accuracy between SpO_2 alone and SpO_2 with PI in screening for CCHD. However, the study was limited by small sample size. Thus, combining PI with SpO_2 may improve CCHD screening using pulse oximeter but large-scale study is needed.

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