Original Articles

Comparison of pulse oximetry screening versus routine clinical examination in detecting critical congenital heart disease in newborns

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Abstract

Introduction: Critical congenital heart disease (CCHD) in newborns has a worldwide prevalence of 1-2 per 1000 live births and often remain asymptomatic pre-discharge, leading to significant morbidity and mortality. Screening depends on physical examination (PE) and pulse oximetry (PO) which is proposed as a novel method.

Objective: Evaluate efficacy and suitability of PO as a screening strategy of CCHD compared to PE in the Sri Lankan setup.

Method: A prospective study was conducted in 5435 asymptomatic newborns, period of amenorrhoea (POA) ≥34weeks, aged ≥24 hours, in Castle Street Hospital for Women, Colombo. Pre-ductal and post-ductal oxygen saturation (SpO_2) measurements in right hand (RH) and right foot (RF) along with PE were performed. Babies without SpO_2 thresholds of ≥95% in RH and RF and ≤3% difference between RH and RF or with abnormal PE, underwent 2D echocardiogram.

Results: Detection rate of CCHD by PO and PE were 91% and 82% respectively. Addition of PO screening to PE detected 02 missed cases. PO and PE sensitivities were 90.9% and 81.8% (p=0.54) and 100% in combination (p=0.8), and specificities were 99.9% and 98.2% respectively (p=0.37) and 98.1% in combination. Positive predictive value and positive likelihood ratio were higher in PO compared to PE (71.4% vs 8.6%, p=0.0001) and 1232.7 vs 46.2), whereas false positive rate was substantially lower in PO compared to PE (0.07% vs 1.76%, p=0.0001).

Conclusions: CCHD prevalence of newborns was 2.02 per 1000 live births. PO improved ruling in and ruling out of CCHD, whereas PE ruled out than ruled in owing to detection of non CCHD. PO is a simple, non-invasive, cost-effective, feasible, and reliable test, which also detects non-cardiac causes of hypoxaemia and our study provides evidence of superiority of PO over PE for CCHD detection,

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(Key words: Critical congenital heart disease, pulse oximetry, physical examination, newborns)

Introduction

Congenital heart disease (CHD) is the most common congenital malformation[1-6] accounting for 28% of major anomalies[1] and 6-10% of infant deaths[3,7,8]. Prevalence has increased substantially over time to 1.35million newborns annually[1,10] with 5-10 per 1000 live births[1,2,8-11,14-17] with the highest prevalence in Asia and categorized into four basic categories: critical, serious, significant and non significant[4,7,14]. Critical congenital heart disease (CCHD) is defined as "any potentially life threatening duct dependant disorder within first 28 days of life"[4,7,13-16,18] and the incidence is 1.2-1.7:1000 live births[3,6,8,19,20] accounting for 10-15% cases of CHD[8]. Current increasing tendency of early discharge of asymptomatic newborns[2,3,15,21-24] before 24 hours[7,18] has raised concern[15,21,22,24], since the effects of duct closure may not be apparent[3,11,13,21,25], thereby making many babies with CCHD leaving hospital undiagnosed[4,5,7,17,21], allowing 1/3 of babies to be symptomatic at home[2,3,18,21,24] and 1 in 4 (25%) to die[15,16,24].

Missed or delayed diagnosis of CCHD is associated with significant morbidity[2,5-9,11,19] and 12 times[15,16] higher mortality during infancy[2-11,15,17-20,26] and over 80% deaths in early neonatal period[24]. Timely diagnosis of CCHD, by 2D echocardiography, provides opportunity for timely intervention[5-8,11,22,23] in order to improve survival[5,7,11,15,23] and to

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reduce morbidity[4,5,7,9,11-23]. CCHD represents a newborn condition that would be ideally suited to a screening programme[5,6,8,16,17,23], thus evaluation of strategies to enhance early detection is of paramount importance[5,11,25]. Current screening strategies to detect CCHD include antenatal anomaly scan[3-8,11,26] and physical examination (PE) of the newborn[2-9,11-18,23-26]. PE is performed before discharge mainly focusing on visible central cyanosis, weak femoral pulses and cardiac murmur[2-5,9,11,17]. Since each strategy has a fairly low detection rate of<50%[2-5,7-23,26], screening newborns with non-invasive measurement of pre and postductal[3,4,8,9,14,21,22] oxygen saturation of blood[16,20,28,29] by pulse oximetry (PO) has been proposed as an aid for early detection[3,5,16-18,25] to reduce the postnatal diagnostic gap of CCHD in newborns[7,23].

Literature shows that developed countries have abundant research on pulse oximetry screening (POS), whereas there are few studies in developing countries. Effectiveness of POS in detecting CCHD in newborns along with suitability and limitations in local settings is worth finding out. Therefore, our study aimed to compare novel POS with routine PE for detection of CCHD in newborns admitted to post-natal wards in Castle Street Hospital for Women (CSHW), Colombo. This is the first published study of this nature comparing pulse oximetry with clinical detection in Sri Lanka.

Objectives

General objective

To evaluate the efficacy and suitability of pulse oximetry as a screening strategy in the detection of CCHD in newborns in CSHW compared to routine clinical examination.

Specific objectives

1) To obtain an estimate of the prevalence of CCHDs in newborns in CSHW as detected by PO and PE.
2) To assess the rate of detection of CCHD with POS compared to PE in newborns in CSHW.

Method

Design: Hospital based prospective study.

Study period: 6 months from 01/11/2018 to 30/04/2019.

Setting: Five postnatal wards in CSHW, which is the main tertiary care hospital providing maternal and newborn care across the country with catchment of both rural and urban populations in the region, in which around 1000 deliveries are occurring per month with majority from November to January.

Study population and sampling method: Sampling was universal. Newborns delivered during study period, after application of inclusion and exclusion criteria, were included.

Inclusion criteria: All asymptomatic newborns at the age ≥24 hours with period of amenorrhoea (POA) ≥34weeks

Exclusion criteria:

- Ill late preterm and term babies
- Preterm babies of POA<34weeks.
- Newborns with multiple dysmorphic features.
- Babies with a prenatal diagnosis of CHD.

Data collection tools

- Neonatal routine clinical examination data sheet prepared based on the neonatal examination method described in Rennie & Roberton's Textbook of Neonatology (5th edition).
- Pulse oximetry screening summary sheet prepared based on the algorithm provided by the Sri Lanka College of Paediatricians.

PE was done at ≥24 hours of age by an experienced medical officer to identify any visible central cyanosis, weak/absent femoral pulses or cardiac murmur. All examiners were blinded to POS results. In case of suspicious CHD, re-examination was performed by consultant neonatologist and 2D echocardiogram was arranged within 48 hours.

Motion tolerant new generation high performance PO, reporting functional oxygen saturation and validated for use in low perfusion conditions, and having 2% root mean square accuracy, with low intra observer and inter observer variability, with 8-10 seconds of averaging time [Radical7 Masimo SET pulse oximeter with rainbow technology] and manufacturer recommended PO probes (a multisite reusable sensor $LNOPY_1$), cleaned with 70% alcohol swabs in between each use, and adhesive tapes (Bespoke disposable tape) were used. Comprehensive one day training was given to all nursing officers and medical officers in postnatal wards, week prior to testing, by the consultant neonatologist, focusing on proper use of PO along with the algorithm to be followed (Figure 1). Test was done according to the standard algorithm by trained nursing officers at the time of discharge, in a calm, quiet warm place free of artefacts. Pre-ductal and post-ductal SPO2 were measured in right hand (RH) and right foot (RF) respectively. First, the probe was placed on RF to ensure minimum disturbances to baby followed by RH. Readings were recorded after 1-2 minutes in a non-fussy baby, having a stable PO plethysmography waveform. Positive and negative tests were defined accordingly. Experienced medical officer was informed immediately in case of a positive test, in order to exclude non cardiac related hypoxaemia.

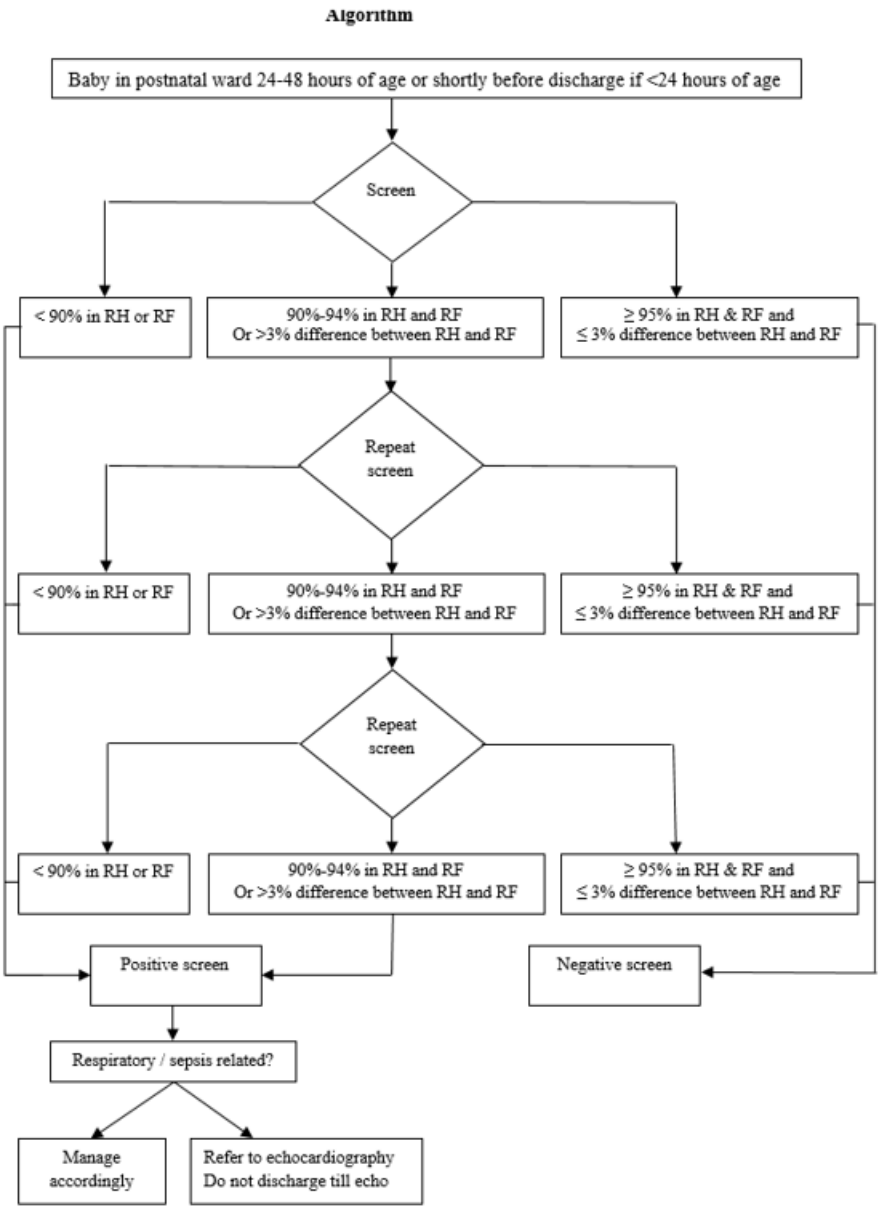

Figure 1: ***Pulse oximetry screening protocol***

Following comprehensive evaluation, 2D echocardiogram, the gold standard test in diagnosing CCHD, was performed by a consultant paediatric cardiologist, within 48 hours. All newborns born during study period were given follow up plans to attend neonatology clinic at CSHW for at least one month.

Ethical issues: Ethical clearance was obtained from the Ethical Review Committee of Castle Street Hospital for Women, Colombo 8 (ERC/223/01/2018). Informed written consent was obtained from the mothers using information sheet and consent form following description of the procedure by a nursing officer at the time of admission to post-natal ward.

Statistical analysis: Data were analysed using SPSS 22.0 version with regards to prevalence of CCHDs and main outcome measures; sensitivity, specificity, detection rate (DR), false positive rate (FPR), positive and negative predictive values (PPV, NPV) along with positive likelihood ratio (+LR) and negative likelihood ratio (-LR) for each test alone and in combination along with 95% confidence intervals and p values.

Results

We analysed a total of 5435 newborns at ≥24 hours (median age at screening=25 hours) of age. Healthy babies had a median SPO2 of 99% (interquartile range 98%-100%). Of all 11 babies with CCHD, 10 had positive PO results and 9 had positive PE results. 2 cases of CCHD would have been missed if only routine PE was performed (Table 1).

Table 1: ***Performance of screening tests in detection of CCHD in newborns (n=5435)***

Result	Pulse oximetry (PO) alone	Physical examination (PE) alone	PO+PE
True positive (n)	10	09	11
False negative (n)	01	02	0
False positive (n)	04	96	98
True negative (n)	5420	5328	5326

CCHD: Critical congenital heart disease

The baby with missed CCHD by POS had SPO2 96%-98% in both RH and RF while PE had detected a systolic murmur. 2D echocardiogram had shown CCHD with DDPC (morphologically univentricular heart). Therefore, POS had detection rate (DR) =91% with false positive rate (FPR) =0.07% while DR of PE=82% with relatively high FPR=1.76% which was statistically significant compared to POS (p=0.0001). This was owing to the detection of non-critical CHDs as opposed to CCHDs by PE. Out of basic 3 clinical features, presence of heart murmur is the main feature that has led to high FPR, whereas poor/absent femoral pulses and presence of gross cyanosis had led to low false positivity. However, routine PE has helped early identification of CHD with a DR=1.37% and 20 cases were clinically significant needing early interventions or close follow-ups, that would otherwise have led to significant morbidity and mortality later in life, making routine PE additionally advantageous over POS (Figure 2).

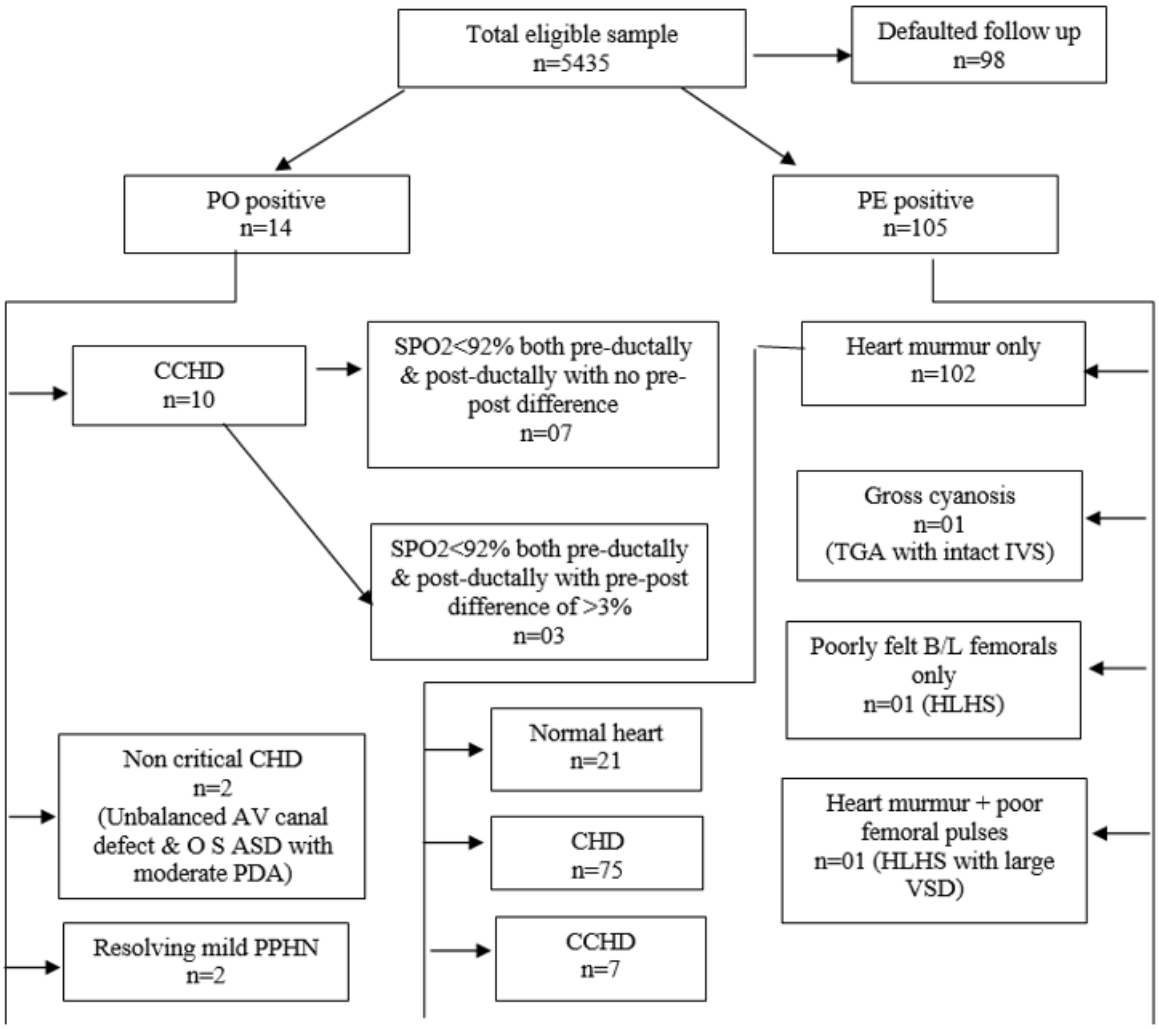

Figure 2: ***Summary of test positive newborns***

Combination of PO+PE for screening of CCHD had DR=100% with FPR=1.8%, suggesting that, combination have led to a better DR of CCHD at the expense of relatively higher FPR, which was statistically significant compared to POS alone (P=0.0001), owing to 25 fold higher FPR of PE

over POS. PPV of PE was significantly lower than POS (8.57% vs 71.4%; P=0.0001) and +LR was also lower (1232.7 vs 46.2).

In our study; POS, PE and combination had got higher sensitivity values of 90.9%, 81.8% and 100% and higher specificity values of 99.9%, 98.2% and 99.8% respectively. Prevalence of CCHD in our study sample was 2.02 per 1000 live births.

The DR of individual CCHD is shown in Table 2.

Table 2: Detection rate of individual critical congenital heart disease (CCHD)

Lesion	Detection rate			
	Number	POS alone	PE alone	POS+PE
Pulmonary atresia (PA)	02	02 (100%)	**01 (50%)**	02 (100%)
Double outlet right ventricle (DORV)	01	01 (100%)	01 (100%)	01 (100%)
Transposition of Great Arteries (TGA)	01	01 (100%)	01 (100%)	01 (100%)
Hypoplastic left heart syndrome (HLHS)	02	02 (100%)	02 (100%)	02 (100%)
Single ventricle	01	**0 (0%)**	01 (100%)	01 (100%)
Total anomalous pulmonary venous drainage (TAPVD)	-	-	-	-
Truncus arteriosus	=	-	-	-
Interrupted aortic arch	-	-	-	-
Critical coarctation of aorta	-	-	-	-
Critical pulmonary stenosis (PS)+Univentricular heart	01	01 (100%)	**0 (0%)**	01 (100%)
DORV + PA	01	01 (100%)	01 (100%)	01 (100%)
Complex cyanotic heart disease	02	02 (100%)	02 (100%)	02 (100%)
Total	11	10 (91%)	09 (82%)	11 (100%)

Discussion

CCHDs are detrimental to newborns in both short and long term and therefore early recognition is of crucial importance since clinical presentation and deterioration may be sudden[2]. Detection rate (DR) of POS is 75%[3,4,18,21] in comparison to 91% in our study and the missed case of CCHD was a single ventricle with significant left to right shunting of blood. It is well documented that some heart lesions can be missed especially in the context of high pulmonary blood flow by POS[23].

The major limitation of PO is to miss the diagnosis of duct dependent systemic circulation (DDSC) than duct dependent pulmonary circulation (DDPC)[3,4,18,21]. Our study did not miss HLHS which is the only lesion of DDSC noted during study period. This may be due to either low sample size, short study period or low birth prevalence of lesions with DDSC compared to lesions with DDPC in Asia[1], leaving only one case for analysis. The DR of PE in our study is 82%, higher than 62%[2], possibly due to involvement of the experienced neonatology team.

Missed cases of CCHDs, referred to as the diagnostic gap of CCHD, is narrowed when POS is included, increasing DR to >90% (92-94%)[23], favouring the use of both in combination than each method alone. Proving this further, our study has a DR=100% in combination which had detected all CCHD cases, as each missed case by one screening strategy was detected by other.

Relatively higher sensitivity of both POS=91% and PE=82% in our study compared to sensitivity of POS=66%[3] and PE=62%[3], may be due to either relatively low sample size, short study period, defaulted follow up of some neonates leading to missed cases at the community or lower incidence of DDSC in Asia. However, the prevalence of CCHDs in our study is 2:1000 live births which is compatible with other worldwide studies[3,15,25](1.2-1.3/1000 live births), suggesting that missing cases of CCHDs at the community in our study may be unlikely. Moreover, the relatively higher prevalence of CCHD in our study may be due to the aggregation of complicated fetal and neonatal cases from across the country at CSHW.

Although high sensitivity is considered essential for a screening test, for cardiac disease, specificity is more imperative as it would generate costly follow up testing, making screening prohibitively expensive[17]. The specificity=99.9% of POS in our study is compatible with most of the studies worldwide (99.9%[7] and 100%[17]). FPR of PE in our study=1.76 and in combination FPR=1.8 which are compatible to 1.9%[3], 2.09%[3] respectively. Relatively higher FPR associated with PE and in combination is due to the fact that routine PE could detect not only CCHDs but also non critical CHDs. DR of CHDs in our study was 71% by PE and 27% of them needed either early interventions or close follow ups, favouring the need of thorough PE of newborn in addition to POS despite high FPR in detecting CCHDs. Furthermore, PPV=71.4% of POS in our study, compatible with 66.7%[17] while PE and both in combination showed significantly low PPVs of 8.6%,10.09% respectively(P=0.0001), compatible to PPV of combination=9.6%[21] owing to higher false positivity of PE.

NPV of POS vs PE in our study has not shown a statistical significance, inferring that CCHD can safely be excluded by each screening method[3,21] in 99% of cases. +LR of our study for POS=1232.7% compatible with +LR=1823.1%[17], whereas PE and both in combination=46.2% and 55.35% respectively, inferring that POS alone is best compared to either PE alone or in combination for ruling in CCHDs. Moreover -LR of PE=0.19% and POS=0.09% which is compatible to 0.13%[17], suggesting that each negative test result rules out CCHD. Furthermore, POS is a feasible and convenient test[3,7] as it took only 5 minutes along with little alteration in nursing routine in our study.

POS as a combined strategy with newborn PE should be implemented as a basic routine at discharge for every newborn in maternity units island-wide, while scientific evaluation of POS protocol is continued to allow for modifications in terms of optimal timing of testing and the method. However, POS needs further large scale, multicentre studies in our country to assess accuracy, suitability, cost-effectiveness and validity for our neonatal populace, thereby reducing morbidity and mortality of neonates with CCHDs in SL.

Furthermore, adding POS is cost effective than the expenses associated with short and long term morbidities and mortality of undiagnosed CCHDs. Therefore for the purpose of detecting CCHDs early, this study provides evidence in favour of superiority of PO over PE. Nevertheless, since PE could detect clinically significant CHDs and other gross abnormalities, POS is neither intended to serve as a substitute nor replace thorough PE of newborns. Capability in identifying equally devastating sinister pathologies has made POS additionally advantageous and is a non-invasive, feasible test with high accuracy; hence introduction is suitable even to a developing country like ours.

Conclusions

Prevalence of CCHD in our study was 2.02 per 1000 live births. Using POS as an adjunct to routine PE can substantially reduce the diagnostic gap in CCHD as combined approach has an additive effect resulting in more efficient screening. However, routine PE is better for ruling out CCHD than ruling in whereas POS is better for both.

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