RESEARCH PAPER

Pulse Oximetry Screening to Detect Cyanotic Congenital Heart Disease in Sick Neonates in a Neonatal Intensive Care Unit

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Received: November 29, 2014; Initial review: January 01, 2015; Accepted: July 01, 2015.

Objective: To evaluate pulse oximetry for detection of congenital cyanotic heart disease in sick neonates using echocardiography as gold standard.

Methods: Pulse oximetry readings were taken at admission from 950 neonates from right upper limb and either foot with infant breathing room air. Pulse oximetry was considered abnormal if oxygen saturation at room air measured <90% or difference between right hand and foot was more than 3%. Persistent abnormality was considered positive result. Echocardiography was performed on all neonates with positive pulse oximetry (study group) and on one subsequent neonate with negative screen for each neonate with positive screen (controls).

Results: Pulse oximetry was positive in 210 neonates. It detected 20 out of 21 (95.2%) true positives. The sensitivity, specificity, positive predictive value, negative predictive value and odds ratio (95% CI) of pulse oximetry was 95.2%, 52.4 %, 9.5, 99.5 and 22 (5.3, 91.4), respectively.

Conclusion: Pulse oximetry screening is useful in detecting cyanotic heart diseases in sick newborns.

Keywords: Cyanosis, *Duct-dependent lesions, Oxygen saturation*, Screening.

Congenital heart diseases (CHDs) account for 6 -10 % of all the infant deaths, and 20 - 40 % of all infant deaths from malformations [1]. About 25% of CHDs are life threatening and manifest before the first routine clinical examination [1,2]. Challenges in managing CHD in developing countries include delay in diagnosis, transport of sick neonate to tertiary centre, and limited availability of state of the art pediatric cardiac centres [3,4].

The existing pulse oximetry monitoring protocol to detect critical congenital heart disease, is restricted to neonates 24 to 48 hours of age in well infant nursery [5]. A simple algorithm for units catering to sick newborns is challenging because of heterogeneity of underlying conditions; need of studies across a broad range of newborn delivery systems has been expressed [5]. Pulse oximetry as a screening test for congenital cyanotic heart disease has been evaluated among well neonates [2,6-10], but not in sick neonates.The present study was designed to evaluate the utility of pulse oximetry screening in detecting congenital cyanotic heart disease among sick neonates in a referral neonatal unit catering to outborn neonates.

METHODS

The study was conducted in the Referral Neonatal Unit of a teaching hospital between April 2013 and January 2014. The unit caters exclusively to outborn sick neonates referred from community hospitals of Delhi and surrounding states, or to those born at home and transported to the hospital directly by the parents. All neonates admitted to the unit during the study period were eligible for inclusion. Neonates in whom stable pulse oximeter signals could not be obtained were excluded. Informed written consent was obtained from the parents of all enrolled subjects. The study was approved by the Institutional ethical committee.

All neonates at admission were clinically evaluated by a resident doctor for temperature, heart rate, respiratory rate (RR), chest retractions, central cyanosis, femoral pulses, other peripheral pulses, capillary filling time, peripheries (cool or warm) and clubbing. Presence of either tachypnea (RR >60/min), retractions, central cyanosis, poor femoral pulses, precordial pulsations, hepatomegaly or murmur was considered as positive clinical examination suggestive of congenital heart diease

[11]. Pulse oximetry readings (BPL Excello oximeter with reusable Nellcor Oximax probe accuracy of ± 2 %) were taken at admission from right upper limb and either foot with infant breathing room air. The recordings were noted two minutes after stable signals were obtained. Pulse oximetry was considered abnormal if oxygen saturation at room air or on oxygen therapy measured <90% or there was more than 3% difference between right hand and foot [5]. All neonates with abnormal pulse oximetry were subjected to three observations each, separated by at least 1 hour. Screen was considered positive only if the abnormality persisted till the last reading. Echocardiography (Philips iE33 xMATRIX echocardiography system) was performed by a pediatric cardiologist on all neonates with a positive pulse oximetry screen (study group) and on one subsequently enrolled neonate with negative screen per neonate with positive screen (controls).

Data were analyzed using Statistical Package for Social Sciences software (version 21). Student-t test was used for continuous variables and Chi-square test was used for comparing proportions. Multivariate logistical regression (using the forward logistical regression model) was done to find predictors of cyanotic heart disease. Sensitivity, specificity, positive and negative predictive value, positive likelihood ratio and negative likelihood ratio of pulse oximetry in detecting cyanotic heart disease in sick neonates were calculated.

RESULTS

A total of 950 neonates admitted in referral neonatal unit during the study period were screened. Pulse oximetry was positive in 210 neonates, and in five neonates, stable pulse oximeter signals could not be obtained. ***Fig.* 1** shows flow of the study. Out of the 210 controls, 11 neonates (3 with shock, 3 with transient tachypnea of newborn and 5 with pneumonia) had an initial saturation of <90%, but repeat readings were >90%.

***Table* I** compares the baseline demographic and clinical characteristics of cases and controls. Pulse oximetry was positive in 20 out of 21 (95.2%) neonates with echocardiography proven cyanotic heart disease. This included lesions with increased pulmonary blood flow (d-transposition of great arteries, *n*=8), lesions with decreased pulmonary blood flow (tetrology of Fallot, *n*=5; double outlet right ventricle with pulmonary atresia/ severe pulmonary stenosis, *n*=3; single ventricle with pulmonary stenosis, *n*=1) and lesions with pulmonary venous hypertension (obstructed total anomalous pulmonary venous connection, *n*=3). Pulse oximetry was negative in 1 neonate with tetralogy of Fallot with mild pulmonary stenosis and large left to right shunt.

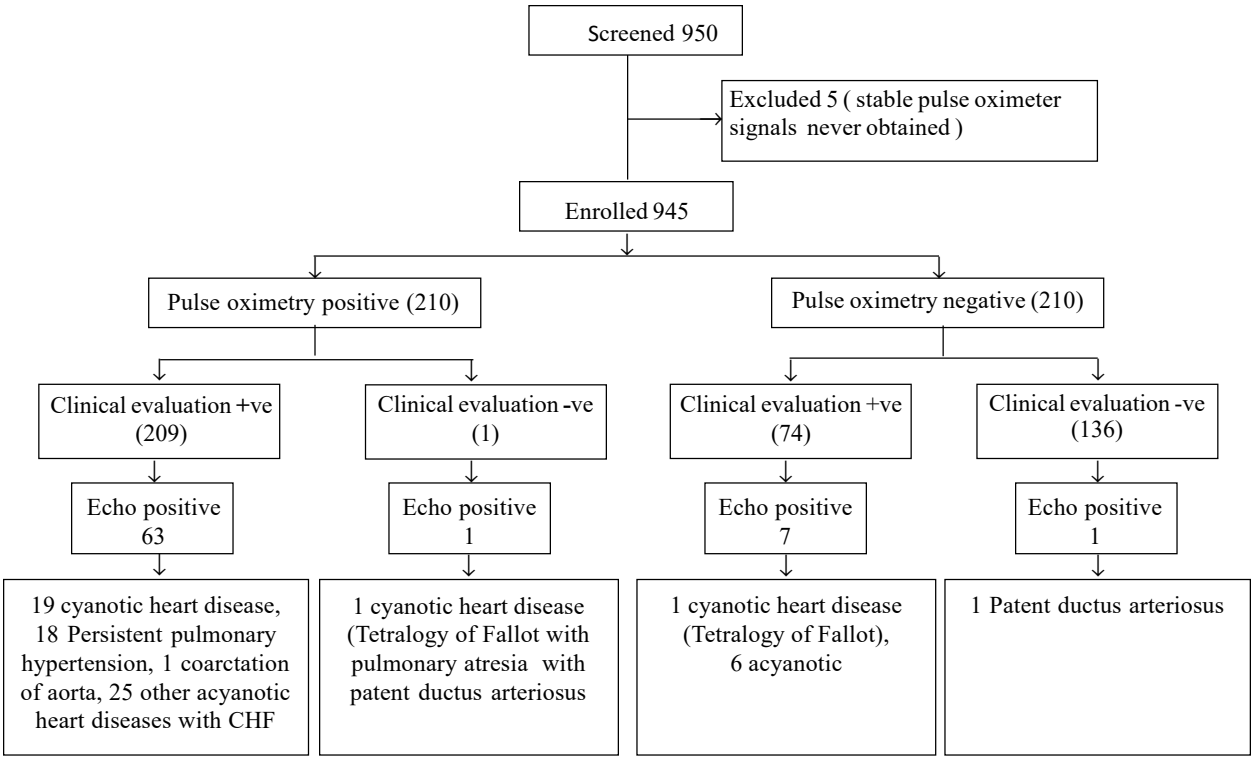

FIG. 1 *Flow of participants in the study.*

TABLE I COMPARISON OF CHARACTERISTICS OF CASES AND CONTROLS

Characteristic	*Cases (n=210)*	*Controls (n=210)*
Age (h), median (IQR)	72 (24, 183)	120 (48, 240)
Male, No. (%)	137 (65.2)	125 (59.4)
Gestational age (wk), mean (SD)	37.7 (2.2)	37.4 (2.5)
#Weight (g), median(IQR)	2500 (2081,2900)	2335 (1800, 2786)
Family h/o smoking, No.(%)	9 (4.3)	12 (5.7)
Clinical signs, No. (%)		
Tachycardia >160/min	33 (15.7)	6 (2.9)
Tachypnea >60/min	143 (68.1)	25 (11.9)
Chest retractions	114 (54.3)	69 (32.9)
Central cyanosis	46 (21.9)	0
Murmur	47 (22.4)	10 (4.8)
Feeble femoral pulses	32 (15.2)	9 (4.3)
Hepatomegaly	37 (17.6)	14 (6.7)
Disease categories		
Cyanotic heart disease	20 (9.5)	1 (0.5)
Acyanotic heart disease	26 (12.4)	7 (3.3)
Persistent pulmonary hypertension	18 (8.6)	0
Respiratory diseases	115 (54.8)	24 (11.4)
Shock	31 (14.8)	9 (4.3)
Others	0	169* (80.4)

**Sepsis 89, hypoxic ischemic encephalopathy 30, hyperbilirubinemia 29, healthy preterms 17, hemorrhagic disease of newborn 4; #Admission weight.*

The sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio and odds ratio (95% CI) of pulse oximetry to detect cyanotic congenital heart disease was 95.2%, 52.4% 9.5%, 99.5%, 2.0, 0.1 and 22 (5.3, 91.4), respectively . The sensitivity of pulse oximetry to detect critical congenital heart disease (cyanotic heart disease, *n*=21 and critical duct dependent systemic lesion, *n*=1) and PPHN (*n*=18) was 97.5 % (39/40) with negative predictive value of 99.5% (209/210).

***Table* II** shows pulse oximetry findings in study population. The pre-post ductal difference was >3% only in cases of cyanotic heart disease, coarctation of aorta and persistent pulmonary hypertension of newborn.

On univariate analysis significant predictors of cyanotic heart disease among sick neonates was positive pulse oximetry, male gender, history of consanguinity, history of pregnancy induced hypertension in mother, family history of congenital heart disease and smoking, and presence of tachycardia, central cyanosis, murmur or hepatomegaly. The significant predictors of cyanotic heart disease among sick neonates on multivariate analysis are outlined in ***Table* III**.

DISCUSSION

In the present study, all congenital heart diseases with different hemodynamics, except one case of tetralogy of Fallot, were detected using pulse oximetry screen. The sensitivity and negative predictive values of pulse oximetry screening to detect cyanotic heart disease and critical congenital heart disease were high. Murmur, central cyanosis, male gender, consanguinity, family history of smoking and history of pregnancy induced

TABLE III PREDICTORS OF CYANOTIC HEART DISEASE IN SICK NEONATES

Predictor	*P value*	*OR (95% CI)*
Positive pulse oximetry screen	< 0.001	12.9 (3.4, 49.9)
Male gender	0.023	89.3 (1.9,4194.1)
Consanguinity	0.003	282.3 (6.6,11254.9)
PIH	0.003	62.8 (4.2, 94.1)
Family history of smoking	0.011	45.5 (2.4,858.5)
Central cyanosis	<0.001	653.3 (30.5, 13998.8)
Murmur	<0.001	962.8 (30.0, 30889.1)

PIH – Pregnancy induced hypertension.

TABLE II PULSE OXIMETRY FINDINGS IN STUDY POPULATION

	SpO_2 <90 %	*Pre-post ductal difference >3%*	*SpO_2 90-<95%*	*SpO_2 ≥95%*
Cyanotic heart disease (*n*=21)	20 (95.2%)	5 (23.8%)	1 (4.8%)	0
Acyanotic heart disease (*n*=33)	26 (78.8%)	1 (3.0%)	4 (12.1%)	3 (9.1%)
Persistent pulmonary hypertension (*n*=18)	18 (100%)	8 (44.4%)	0	0
Respiratory diseases (*n*=139)	115 (82.7%)	0	13 (9.4%)	11 (7.9%)
Shock (*n*=40)	31 (77.5%)	0	8 (20%)	1 (2.5 %)
Others (*n*=169)	0	0	95 (56.2%)	74 (43.8%)

WHAT THIS STUDY ADDS?

- Pulse oximetry screening is useful in detecting cyanotic heart diseases, critical duct-dependent systemic lesions and persistent pulmonary hypertension in sick neonates.

hypertension were significant predictors of cyanotic heart disease.

Majority of the studies done in well infant nurseries had used the saturation cut-off of less than 95% for abnormal pulse oximetry [7,9,10]. The working group [5] recommended any saturation below 90% as abnormal for pulse oximetry screening in well infant nursery, and recommended three repeated saturations taken hourly if the saturation is between 90% and 95%. In our study, only one case of cyanotic heart disease (teralogy of Fallot) had a saturation persisting between 90% and 95% . Considering a persistent saturation value of <95% as criteria for positive pulse oximetry screen would have led to 120 additional referrals for echocardiography. Specificity of pulse oximetry was low because it was also positive in cases of respiratory diseases, acyanotic heart diseases with congestive heart failure, shock and persistent pulmonary hypertension which are common in neonatal intensive care settings. Persistent pulmonary hypertension and hypoxic cardiac conditions have been considered as secondary targets of pulse oximetry screening [5,9,12].

The limitations of present study include single center-based enrolment, and no *a priori* sample size calculation. Also, echocardiography was done only on selected controls rendering calculations of sensitivity, specificity and predictive values inaccurate.

To conclude, pulse oximetry screening is useful in detecting cyanotic heart diseases in a setting catering to sick out born neonates. Negative predictive value of pulse oximetry is high, making it useful to reliably rule out critical congenital heart disease or PPHN among sick neonates, thus avoiding need for an urgent echocardiography.

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