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Original Research Paper

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EFFECTIVENESS OF ROUTINE PULSE OXIMETRY SCREENING TO DETECT CRITICAL CYANOTIC CONGENITAL HEART DISEASE IN NEONATES AFTER BIRTH– A RETROSPECTIVE STUDY

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ABSTRACT

Objective Pulse Oximetry in newborns to detect the Critical Cyanotic Congenital Heart Diseases (CCHD) has become a standard of care in many developed countries after recent guidelines. Several large randomized trials have shown that the use of universal pulse-oximetry screening (POS) at the time of discharge from birth hospital can help in early diagnosis of these infants. This study was conducted to evaluate its feasibility in Indian circumstances. **Setting** Tertiary Maternity Hospitals in Bangalore, India. **Participants** All healthy babies born above 36 weeks at the hospital and not requiring Neonatal Intensive Care Unit (NICU) admission were included in this study. **Results** Screening by Pulse Oximetry was done for a total of 12,204 neonates between July 2020 and July 2023 (study period). Thorough clinical examination done by the neonatologists for the 10 neonates who failed screenings, revealed that two babies had a pulmonary condition requiring treatment (false positive cases) and 8 babies were investigated with an Echocardiography by a Paediatric Cardiologist. One infant had a PDA with no other abnormalities, one had a VSD with a small PDA, but no other abnormalities, and the remaining six infants were diagnosed with CCHD: three were found to have Transposition of Great Vessels (TGV); one baby was found to have Fallot's Tetralogy (TOF); one baby was found to have Total Anomalous Pulmonary Venous Drainage (TAPVD); one baby had a VSD, an ASD and Patent Foramen Ovale with pulmonary hypertension. **Conclusion** Through our study we conclude that Pulse Oximetry screening of apparently healthy newborns in India is effective for early diagnosis of newborns with CCHD and thus helps to improve their prognosis.

KEYWORDS : Congenital Heart Disease (CHD), Critical Cyanotic Congenital Heart Disease (CCCHD), newborn, Pulse Oximetry screening.

INTRODUCTION

Congenital heart disease is an important cause of mortality and morbidity in early childhood with a prevalence of 5-10 per 1000 live births worldwide.1 One-fourth of these have major CHD (Critical congenital heart disease defined as requiring surgery or catheter intervention in the first year of life). In India, heart disease in young children accounts for more than 10% of all childhood deaths due to late presentation or diagnosis.2,3 Early diagnosis can prevent progression to cardiac failure, cardiovascular collapse, neurological sequelae and death.2,3 Currently, screening for CHD relies on antenatal ultrasonography in the mid-trimester and post-natal clinical examination. Antenatal scans have a diagnosis rate of up to 44%, while newborn examination diagnoses are less than 50% of CHD and have a false positive rate of 1.90%.4,5 The combination of antenatal ultrasonography and clinical examination of the newborn lead to discharge 30% of cases of CCHDs before diagnosis, with mortality rates up to 50%.

Pulse Oximetry screening (POS) of newborns has been shown to be a non-invasive test that increases the ability to identify infants with major CHD before clinical presentation with collapse, which may result in long term complications.2,5 POS is a simple, non-invasive and painless tool that measures oxygen saturation, and therefore could detect CCHDs with ductal-dependent systemic or pulmonary blood flow that usually present with hypoxemia.

Seven severe lesions are considered as primary targets for screening by POS; those are hypoplastic left heart syndrome, pulmonary atresia, tetralogy of Fallot, total anomalous pulmonary venous return, transposition of the great arteries, tricuspid atresia, and truncus arteriosus. Other clinical conditions which can be identified and not screenable through POS are tabulated in Table 1.

Table 1: Summarises various clinical conditions which can be screened through POS.

Primary targets	Secondary targets	Possibly screenable	Not screenable
Hypoplastic left heart syndrome	Interrupted aortic arch/ aortic atresia	Aortic stenosis with PDA	Coarctation of aorta without PDA
Pulmonary atresia	Coarctation of aorta with PDA	Pulmonary stenosis	Ebsteins anomaly without right to left shunt
Total anomalous pulmonary venous connection	Ebsteins anomaly	Complete atrioventricular canal	Aortic stenosis without PDA
Transposition of great arteries	Double outlet right ventricle		Other left to right shunting lesions
Tetralogy of Fallot	Single ventricle physiology		
Tricuspid atresia			
Truncus arteriosus communis			

The screening of CCHD by pulse oximetry involves taking advantage of its ability to detect clinical and more importantly subclinical levels of hypoxemia that should raise suspicion for a CCHD. The concerns about false-positive rates (FPRs) and the perception that this will place an undue burden on parents and limited health-care resources led to an intense debate about the appropriateness of adding POS to the universal newborn screening panel. In 2012, a chain of tertiary maternity hospitals in India reviewed the published evidence of the benefit and decided to implement this practice into routine care.

We present our Indian experience of effectiveness of Pulse Oximetry screening of well newborns at Tertiary care hospitals and its implications.

METHODS

The study population included all babies born at the two maternity tertiary care hospitals between July 2020 and July 2023. Tertiary maternity hospitals in Bangalore (one each at Malleshwaram and Jayanagar)}, delivering over 5,000 babies a year, provide Maternal Fetal Medicine service, including screening for high-risk births and cardiac screening.

Pulse Oximetry Screening

Pulse Oximetry screening was performed by specially-trained nurses between 24 – 48 hours of age or at the time of discharge, which is usually after 48hours. For babies who were discharged before 24 hours, the oximetry was performed prior to discharge and then repeated within the first 3-5 days during follow up.

According to the Royal College of Paediatrics and Child Health (RCPCH) recommendations, the Pulse Oximeter sensor was placed initially on one foot, obtaining a post-ductal oxygen saturation reading, and then immediately moving the sensor to the right hand to obtain a pre-ductal oxygen saturation reading.6,7 The oximeter was switched on and oxygen saturation documented when the reading stabilized with a strong plethysmographic signal. This typically took between 2 and 4 min. The saturation readings were recorded in hospital clinical records and baby's personal health record. The probe was cleaned between babies with 70% isopropyl alcohol wipes. Screening data was collected from July 2020 to July 2023 in both hospitals.

A neonate was categorized as having passed the screening if SaO2 was more than 95% in all limbs and if the difference was less than 3%. Readings between 90% and 95% lead to a repeat saturation measurement in the next 2 to 6 hours.

According to the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC)protocol [8],

Screening Was Considered Positive If:

1. Oxygen saturation measure is <90% in either the right hand or either foot.
2. Oxygen saturation is <95% in the right hand and foot on three measures, each separated by one hour; or
3. Persistent >3% difference exists in oxygen saturation between the right hand and foot on three measures, each separated by one hour.

When screening was positive, the neonate underwent a thorough physical examination by a neonatologist and, if indicated, a chest radiograph and an electrocardiogram was done. If no pulmonary condition was found, the neonate was immediately referred for a complete echocardiogram by a pediatric cardiologist, as applicable.

We collected all saturation readings from the hospital electronic, clinical database. Medical records were searched if further information was needed. Information was collected on the oxygen saturation, the subsequent management, the review by a senior neonatologist, further management and need for echocardiography. We calculated the sensitivity, specificity, positive and negative predictive values, and false-positive rate.

Data Collection and Analysis

The results of screening were entered into the HIS (Hospital Information System) database and stored. For this study we derived descriptive statistics for the number of babies screened, their demographics, the results of the screening, and the associated variables.

Ethics and IRB Approval

Informed consent was taken from the parents or guardians of each child prior to the screening.

Ethical committee approval for retrospectively analyzing the stored screening data was obtained.

RESULTS

There were a total of 12,204 babies born after 36 weeks in the study period. Of the 12,204 babies screened, 12,186 (99.9%) passed the test, and 18 babies (0.1%) were referred. These were babies who had failed the screening protocol, as their initial saturations were difficult to obtain for whatever reason or was <90% or 90-95% on two occasions. Of the 18 cases who were referred, repeat saturation monitoring after a few hours was normal in eight babies, and abnormal in 10 babies. Of the 10 babies with abnormal saturations, an examination by a neonatologist found that two had low saturations secondary to a previously unrecognized pulmonary cause, which was diagnosed following review - these included Persistent Pulmonary Hypertension of the Newborn in one and congenital pneumonia with sepsis in the other. The other 8 babies who failed oxygen saturation screening underwent a detailed echocardiography by the Paediatric Cardiologist, and One infant had a PDA with no other abnormalities, one had a VSD with a small PDA, but no other abnormalities, and the remaining six infants were diagnosed with CCHD: three were found to have Transposition of Great Vessels (TGV); one baby was found to have Fallot's Tetralogy (TOF); one baby was found to have Total Anomalous Pulmonary Venous Drainage (TAPVD); one baby had a VSD, an ASD and Patent Foramen Ovale with pulmonary hypertension.

Among these 8 infants, 4 had been picked up by antenatal scans by our Fetal Medicine specialists in the anomaly scans. All the infants were followed up by the Paediatric Cardiologist and 4 were referred for emergency cardiac surgery. Three underwent surgery on the 3rd Day of Life (DoL), and are currently alive and thriving. One underwent surgery on Day 7, and is currently doing well.

Analyzing the accuracy of Pulse Oximetry screening in the detection of major CHD, the sensitivity was 88%; specificity was 99.6%; positive predictive value was 0.7% and a negative predictive value was 99.9%. The false positive rate was 0.12%.

DISCUSSION

CCHD broadly comprises cyanotic congenital heart defects and left-sided obstructive lesions, in which cyanosis may or may not be a predominant clinical presentation. Currently, Congenital heart disease (CHD) is 1 of the most frequently diagnosed congenital disorders afflicting approximately 0.8% to 1.2% of live births worldwide. This increase in the prevalence of CHD is a result of an increase in true incidence as well as increase in our ability to detect and diagnose. True increase in prevalence of CHD is attributed to various factors such as advanced maternal age; illnesses during pregnancy such as diabetes, infections, and PKU; increased exposure to drugs during pregnancy such as anticonvulsants, steroids, and alcohol; and environmental exposures such as organic solvent, dichlorodiphenyltrichloroethane (DDT), and other chemicals. There has been an increasing recognition over the years that a significant proportion of neonates and infants requiring cardiac surgery have adverse neurodevelopmental outcomes.9,10 Although it is likely that the early detection and treatment of CCHD will decrease neurological injury by providing a more stable perioperative status, the studies published so far have not specifically evaluated the impact of early detection of CCHD on long-term neurodevelopmental outcome of these infants.

The first opportunity for a postnatal diagnosis is at the time of clinical examination by health-care providers after birth. But it has limitations like lack of specificity of heart murmurs in newborns, absence of any cardiac findings including murmur in nearly half of all infants with CCHD, and limited newborn physician experience in differentiating physiological from pathological murmur. A retrospective review from UK of all potentially life-threatening cardiovascular malformations reported that nearly 30% of these infants were diagnosed after discharge from their birth hospital and that diagnosis of CCHD was made in 5% after death.11

In our study Pulse Oximetry screening of healthy newborns provided early alerts to diagnose - life-threatening conditions,

both cardiac and respiratory. Successful Pulse Oximetry screening needs appropriate equipment and training.

In 2009, the American Academy of Pediatrics (AAP) and the American Heart Association (AHA) did meta-analysis of ten studies with a total of 123,846 infants reported a FPR of 0.87% but the FPR was 0.035% if screening was done after 24 hours. A FPR of 0.035% means that approximately 3–4 infants out of every 10,000 screened infants will have a false-positive screen. a systematic review and meta-analysis of pulse oximetry screening for CCHD in the newborn nursery, which included 13 studies with 229,421 infants.28 Sensitivity of pulse oximetry was 76.5% (95% CI 67.7–83.5) and specificity was 99.9% (95% CI 99.7–99.9) for the detection of CHD, with the average false-positive rate for these infants being 0.14% (95% CI 0.16–0.33).12

Our study showed similar accuracy to those reported in the recent meta-analysis of 13 studies, which showed a sensitivity of 76.5%, specificity of 99.5% and a low false positive rate of 0.14%.

The 8 cases with major CHD who were identified by Pulse Oximetry were all identified prior to discharge from our service with the clinical alert in all being triggered by the saturation reading, although our foetal medicine experts had picked up 4 cases antenatally.

We opine that implementation of Pulse Oximetry screening as one more test in normal newborn examination would help in timely diagnosis and management of cardiac conditions and in optimizing the prognosis for these babies.

The low false positive rate in our study was consistent with the rest of the literature. Even though its false positive, this indicates that baby must be having for hypoxaemia due to other causes, which ia as important as identifying CCHD.

Grenelli et al showed that a low false positive rate of 0.17%, and that 31/69 'false positives' had other pathology. Our data are consistent with this, as there were 2 of 10 cases with low saturations and a normal heart that had previously unrecognised respiratory pathology, in which timely management was equally important.

Earlier screening (<24h) results in more false positives, but many of these are important non-cardiac pathology. A late screening results in a lower false positive for CHD and may be more accurate for diagnosis of obstructive left heart lesions, particularly Coarctation of the Aorta. Prudhoe et al showed that Pulse Oximetry is relatively insensitive in detection of coarctation of aorta/interrupted aortic arch (95% Confidence Interval (CI) 24-50%) and TOF (95% CI 24-58%). The AAP recommends screening at 24-48 h. Hence we performed screening after 24 hrs of birth.

There is increasing evidence to justify Pulse Oximetry screening as the standard of care.9,10,11,12,13 As a screening tool, Pulse Oximetry fulfills the requirements. It is inexpensive and easy to use, has a low false-positive rate and allows diagnosis of an important disease process (CCCHD) which has a defined natural history, a suitable confirmatory test, and is treatable.

Table 2 Summarises Comparison of four large multicenter prospective studies on use of POS for detection of CHD. 16,17,18,19.

Country	Germany[16]	Norway[17]	Swedan[18]	UK[19]
Total infants	41,455	50,008	39,821	20,055
Age at screening	24-72hrs	1-21 hrs	1-406 hrs	Before discharge
Pulse oximetry site	Postductal	Postductal	Pre and postductal	Pre and postductal
Oxygen saturation cutoff	>/= 96%	>/= 95%	>/=95%	>/= 95%
Sensitivity	77.8	77.1	62.07	75
Specificity	99.9	99.4	99.82	99.12
Positive predictive value	25.9	8.3	20.69	9.23
Negative predictive value	99.99	99.98	99.97	99.97
False positive rate	0.10	0.6	0.17	0.8

Based on the findings of these studies, it is estimated that the use of POS can reduce the diagnostic gap from 30% to 5%–10%. After excluding prenatally detected infants, it is estimated that nearly 50%–70% of infants born with undiagnosed CCHD can be detected by POS. A large majority of cases missed by POS are duct-dependent systemic circulation such as coarctation of the aorta, severe aortic stenosis.

Limitations of POS. The primary limitation of POS is its relatively low sensitivity in most studies, ranging from 62% to 78% (Table 2). It is important for health-care providers and parents to understand that a normal screen at birth does not eliminate the possibility of CCHD. Large majority of false negatives are cases of duct-dependent systemic circulation such as coarctation of the aorta, severe aortic stenosis.

There are multiple sources of potential artifacts, which are particularly relevant for neonates and can cause false readings. These include motion artifacts, poor perfusion and cold skin at the site of measurement, irregular rhythms, ambient light, phototherapy or electromagnetic interference, skin pigmentation and jaundice, inappropriate probe positioning (penumbra effect), venous pulsation, intravenous dyes, and presence of abnormal hemoglobin molecules

CONCLUSIONS

We conclude that Pulse Oximetry screening is efficient, feasible method to identify hypoxemic babies in Indian practice. This screening practice helps in assessing neonatal well-being, not just for CHD. Each type of CHD affects cardiopulmonary circulation differently, and pulse oximetry is a good screening tool to detect lesions that cause hypoxemia in the first few days of life. CHD with impaired perfusion rather than oxygenation will, though, remain undetected by pulse oximetry

REFERENCES

1. Strobel AM, Lu Le N. The Critically ill infant with congenital heart disease. Emerg Med Clin North Am. 2015; 33(3): 501-18.
2. Bakshi K D , Vaidyanathan B , Sundaram K R , Roth S J , Shivaprakasha K, Rao SG, et al.. Determinants of early outcome after neonatal heart surgery in a developing country. J Thoracic Cardio Vascular Surgery. 2007: 134: 765-71.
3. Aamir T, Kurse L, Ezeakudo O. Delayed diagnosis ofCritical congenital malformations (CCVM) and Pulse Oximetry screening of newborns. Acta Paediatr. 2007; 96: 1146-9.
4. Roberts TE, Barton PM, Auguste PE, Middleton LJ, Furmston AT, Ewer AK. Pulse Oximetry as a screening test for congenital heart defects in newborn infants: a cost-effectiveness analysis. Arch Dis Child. 2012 Mar; 97(3): 221-6.
5. Thangaratinam S, Brown K, Zamora J, Khan KS, Ewer AK. Pulse Oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis. Lancet. 2012 Jun 30;379(9835):2459-64.
6. Jegatheesan P, Song D, Angeil C, Devarajan K, Govindaswami B. Oxygen saturation nomogram in newborns screened for c r i t i c a l congenital heart disease. Pediatrics 2013; 131 (6): e1803-1810. DOI: 10.1542 /peds.2012-3320.
7. Iyengar H, Kumar P, & Kumar P. Pulse-oximetry screening to detect critical congenital heart disease in the neonatal intensive care unit. Pediatric Cardiology 2014;35(3),406-410 Doi:10.1007/s00246-013-0793-2.
8. Kemper AR, Mahle WT, Martin GR, et al. Strategies for implementing screening for critical congenital heart disease. *Pediatrics*. 2011;128 (5):e1259–e1267.
9. Singh A, Ewer AK. Pulse Oximetry screening for critical congenital heartdefects: a UK national survey. Lancet 2013; 381: 535.
10. Liberman R.F., Getz K.D., Lin A.E., Higgins C.A., Sekhavat S, Markenson G.R. & Anderka M. Delayed diagnosis of critical congenital heart defects. Tends

and associated factors. Pediatrics 2014; 134 (20) e373-e381. Doi:10. 1532/peds.2013-3949.
11. Zhao QM, Ma XJ, Ge XL, Liu F, Yan WL, Wu L, et al. Pulse Oximetry with clinical assessment to screen for congenital heart disease in neonates in China. A prospective study. Lancet 2014; 384: 747-54.
12. Reich JD, Connolly B, Bradley G, Littman S, Koeppel W, Lewycky P, Liske M. The reliability of a single Pulse Oximetry reading as a test for congenital heart disease in otherwise asymptomatic newborn infants. Pediatr Cardiol. 2008; 29: 885-889.
13. Thangaratinam S, Brown K, Zamora J, Khan KS, Ewer AK. Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis. *Lancet*. 2012;379 (9835):2459–2464.
14. Bhola K, Kluckow M, Evans N. Post implementation review of Pulse Oximetry screening of well newborns in an Australian tertiary maternity hospital. J Paediatr Child Health. 2014; 50: 920-25.
15. Scholler GF. Pulse Oximetry screening of newborns: Not just a screening test for congenital heart disease. J Paediatr Child Health 2014; 50: 864-5
16. de-Wahl Granelli A, Wennergren M, Sandberg K, et al. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39,821 newborns. *BMJ*. 2009;338:a3037.
17. Riede FT, Wörner C, Dähnert I, Möckel A, Kostelka M, Schneider P. Effectiveness of neonatal pulse oximetry screening for detection of critical congenital heart disease in daily clinical routine – results from a prospective multicenter study. *Eur J Pediatr*. 2010;169(8):975–81.
18. Meberg A, Brügmann-Pieper S, Due R Jr, et al. First day of life pulse oximetry screening to detect congenital heart defects. *J Pediatr*. 2008;152(6):761–5.
19. Ewer AK, Middleton LJ, Furmston AT, et al; PulseOx Study Group. Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study. *Lancet*. 2011;378(9793):785–94.