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ORIGINAL ARTICLE

Critical congenital heart disease screening by pulse oximetry in a neonatal intensive care unit

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OBJECTIVE: Critical congenital heart disease (CCHD) screening is effective in asymptomatic late preterm and term newborn infants with a low false-positive rate (0.035%). (1) To compare 2817 neonatal intensive care unit (NICU) discharges before and after implementation of CCHD screening; and (2) to evaluate CCHD screening at < 35 weeks gestation.
STUDY DESIGN: Collection of results of CCHD screening including pre- and postductal pulse oximetry oxygen saturation (SpO_2) values.
RESULT: During the pre-CCHD screen period, 1247 infants were discharged from the NICU and one case of CCHD was missed. After 1 March 2012, 1508 CCHD screens were performed among 1570 discharges and no CCHDs were missed. The pre- and postductal SpO_2 values were $98.8 \pm 1.4\%$ and $99 \pm 1.3\%$, respectively, in preterm and $98.9 \pm 1.3\%$ and $98.9 \pm 1.4\%$, respectively, in term infants. Ten infants had false-positive screens ($10/1508 = 0.66\%$).
CONCLUSION: Performing universal screening in the NICU is feasible but is associated with a higher false-positive rate compared with asymptomatic newborn infants.

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INTRODUCTION

Critical congenital heart disease (CCHD) is generally defined as congenital heart defect that requires surgery or catheter intervention within the first year of life or may cause significant morbidity and mortality in the first weeks of life.[1] Universal newborn pulse oximetry screening to detect CCHD was added to the recommended uniform screening panel (RUSP) by the Health and Human Services Secretary in 2011. CCHD screening through pulse oximetry (SpO_2) is being implemented by many states and is shown to be cost-effective for asymptomatic newborn infants.[2] The false-positive rate among asymptomatic newborn infants is low (0.035%).[3,4]

Approximately 10 to 12% of all newborn infants are admitted to neonatal intensive care units (NICU). Many NICUs including ours routinely monitor SpO_2 for all admissions. Limited data are available regarding CCHD screening in the NICU. Iyengar *et al.*[5] reported 250 patients discharged from the NICU with CCHD screening at Northwestern University but did not report any positive screens. A recent commentary suggested three options for screening in the NICU: (i) consider that all NICU patients, by default, already undergo screening and not perform additional screening by pre–post ductal oxygen saturation difference; (ii) perform screening similar to that in normal newborn nursery in infants 35 weeks and higher gestation; or (iii) screen all infants admitted to the NICU.[6] Many state governments recommend universal screening and do not differentiate between infants cared in the NICU vs those admitted to newborn nursery.

Before initiation of CCHD screening, infants in our NICU did not undergo simultaneous pre- and postductal SpO_2 monitoring unless there was suspicion of persistent pulmonary hypertension of the newborn (PPHN) or congenital heart disease (CHD). Our objective is to describe our experience with CCHD implementation in the NICU and to evaluate and report compliance with this procedure/process. We aim to report the frequency of CCHD diagnoses among NICU discharges. We evaluated readmissions with a primary diagnosis of CCHD to the Emergency Department or Pediatric Intensive Care following discharge from the NICU before and after implementation of CCHD screening. We also evaluated the results of CCHD screening and false-positive rate among NICU discharges born at < 35 weeks and $\geqslant 35$ weeks postmenstrual age (PMA).

METHODS

The NICU at Women and Children's Hospital of Buffalo serves as the regional perinatal center for Western New York. There were 61 869 births in Western New York between 1 January 2010 and 31 December 2013 (average 15 467 per year). Of these, 6944 infants were admitted over the 4-year period to any level 2/3 neonatal intensive care (11.2%) and had SpO_2 monitoring during their stay in the NICU (average 1736 per year). Of these, 3152 patients (average 788 patients per year) were admitted to the NICU at the Women and Children's Hospital of Buffalo. Only discharges from this NICU were evaluated in this study. The unit policy during this period was to maintain SpO_2 between 91% and 95%, respectively, in both preterm and term infants requiring supplemental oxygen.

Routine CCHD screening was implemented for all NICU discharges in early 2012. We conducted screening using Masimo Rad 7 pulse oximeters (Masimo Corporation, Irvine, CA, USA) and disposable probes. All patients in our NICU are continuously monitored with a pulse oximeter throughout their stay. The same probe was used sequentially to determine the right upper limb and a lower limb SpO_2. Each screening attempt was conducted over a 3-min period with the infant in the supine position. The pulse oximetry measure was considered complete once the wave form on the plethysmograph was stable.[7] Infants discharged in 2010 and 2011

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(pre-CCHD screen) were compared with NICU discharges from March 2012 to March 2014 (post-CCHD screen). All discharges were screened according to AAP guidelines.[7] The screen was performed 24 to 48 h before discharge from the NICU and at least 24 h after weaning to room air (if the infant required supplemental oxygen). An echocardiogram was performed if the infant met the following criteria: (i) failed CCHD screen on room air (and if a prior echocardiogram was not performed during the NICU stay for other indications). Failed CCHD screen was defined as an $SpO_2 < 90\%$ in any extremity, a persistent SpO_2 of 90 to 94% in both pre- and postductal sites on three attempts or a persistent preductal to postductal SpO_2 difference $> 3\%$,[7,8] (ii) unexplained need for oxygen (unable to maintain $SpO_2 \geqslant 90\%$ in room air), or (iii) inability to wean oxygen before discharge. A revised algorithm currently in use in our NICU was published.[9] To detect false negatives, encounters and referrals to pediatric cardiology office, emergency department, pediatric intensive care unit and coroner's office were evaluated.

Statistical analysis: The demographic features, incidence of echocardiographic evaluation in the pre- and post-CCHD screening epochs and among preterm and term infants were analyzed by unpaired '*t*' test or χ^2 test as appropriate. Significance was accepted at $P < 0.05$.

RESULTS

Comparison between pre-screen and post-CCHD screen periods

During the pre-CCHD screen period, 1533 infants were admitted to the NICU at Women and Children's Hospital of Buffalo and 1247 of them were directly discharged home (Table 1). Excluding prenatally suspected CCHD, 12 infants were diagnosed with CCHD based on clinical presentation during this period. Four hundred and sixty-five infants (37.3% of discharges) underwent echocardiography for clinical indications during this period. Sixty-eight infants (5.5% of discharges) were sent home with oxygen supplementation. Five of these infants had moderate bronchopulmonary dysplasia and did not have an echocardiogram before discharge. One infant with interrupted aortic arch and anomalous left subclavian artery was not diagnosed and discharged from the NICU in spite of continuous SpO_2 and blood pressure monitoring.[10] The precise site of pulse oximetry probe placement (pre- or postductal) could not be ascertained from our medical records. This infant was noted to have absent femoral pulses at 1 week of age at the pediatrician's office, and was referred to cardiology for an echocardiogram, which led to the diagnosis. The echocardiogram demonstrated complete interruption of the arch beyond the right subclavian artery. The left subclavian artery and descending aorta were supplied exclusively by the ductus arteriosus.

In early 2012, CCHD screening was reviewed with community pediatricians, hospital faculty, residents/fellows, nurse practitioners/physician assistants and nurses. A PowerPoint presentation with a flow chart and a color-coded saturation chart[10] were used in the NICU.

Between March 2012 and March 2014, 1508 CCHD screens were performed among 1570 discharges (Figure 1). During the first month of implementation, nursing compliance with CCHD screen was 68%, improved to 92% by the 6th month and was 100% in 2013–2014. Excluding prenatally diagnosed CCHD, 16 infants were diagnosed with CCHD based on abnormal physical examination and transferred to cardiac surgical service. Five hundred and five (32.2% of discharges) underwent echocardiogram for medical indications before discharge. Sixty-four infants were discharged home with supplemental oxygen. Five of these infants did not have an echocardiogram for medical indications. These infants underwent echocardiogram to determine the etiology of oxygen need as per the modified CCHD algorithm. Four of these infants had a normal echocardiogram (1-patent ductus arteriosus (PDA)/patent foramen ovale (PFO); 3-PFO). One infant had supracardiac total anomalous pulmonary venous return (TAPVR). The pre- and postductal SpO_2 were 88% and 91%, respectively, before oxygen supplementation in this infant.

Results of pulse oximetry screen

The median pre- and postductal SpO_2 values were 99% (range: 90 to 100%) and 100% (range: 92 to100%), respectively. No infant had a SpO_2 value $< 90\%$ (by unit policy, these 64 infants were on supplemental oxygen). Eighteen infants in room air did not meet pass-criteria (18/1508 = 1.2%) on first attempt of pulse oximetry screening (Figure 1). One infant had both pre- and postductal SpO_2 between 90 and $< 95\%$ and did not change with repeated screening attempts. Four infants had preductal $SpO_2 >$ postductal value by $> 3\%$. Postductal SpO_2 exceeded preductal SpO_2 by $> 3\%$ in 13 infants. After repeat pre- and postductal SpO_2 measurements, 10 infants (0.66%; Figure 1) failed the screen (1– $< 95\%$, 3-preductal > postductal SpO_2 by $> 3\%$ and 6-postductal > preductal SpO_2 by > 3%). Echocardiogram showed mild pulmonic stenosis, AV malformation and PFO or PDA (PFO/PDA) or PPHN in these infants. Postductal SpO_2 exceeded preductal SpO_2 by $> 3\%$ in 6 infants. Three infants had normal anatomy (PFO ± PDA), and one had tricuspid regurgitation. Two infants whose postductal saturations were 100% and preductal were 96% on final repeat screen were labeled as passed and discharged

Table 1. Patient characteristics pertaining to CCHD at Women and Children's Hospital of Buffalo NICU during period 1 (January 2010 to December 2011—no CCHD screening) and period 2 (March 2012 to March 2014—CCHD screening)

	No CCHD screening (January 2010–December 2011)	*CCHD screening (March 2012–March 2014)*
Total number of admissions	1533	1975
Number of direct discharges home (excluding transfers, transfer of service and deaths)	1247	1570
Number of CCHD diagnosed during the NICU course (excluding antenatal diagnosis)	12	16
Number of CCHD screens performed	N/A	1508 (96.1% of discharges)
Infants with echocardiograms performed for clinical indications	465 (37.3% of discharges)	505 (31.8% of discharges)
Infants discharged home on oxygen (or unable to wean off oxygen prior to CCHD screen)	68	64
Infants unable to be weaned to room air prior to screen who have not had an echo for clinical indication	5	5
True positives	N/A	1—TAPVR (unexplained oxygen requirement)
Missed patients—readmissions and underwent intervention	1—Interrupted aortic arch	0

Abbreviations: CCHD, critical congenital heart disease; NICU, neonatal intensive care unit; N/A, not applicable; TAPVR, total anomalous pulmonary venous return.

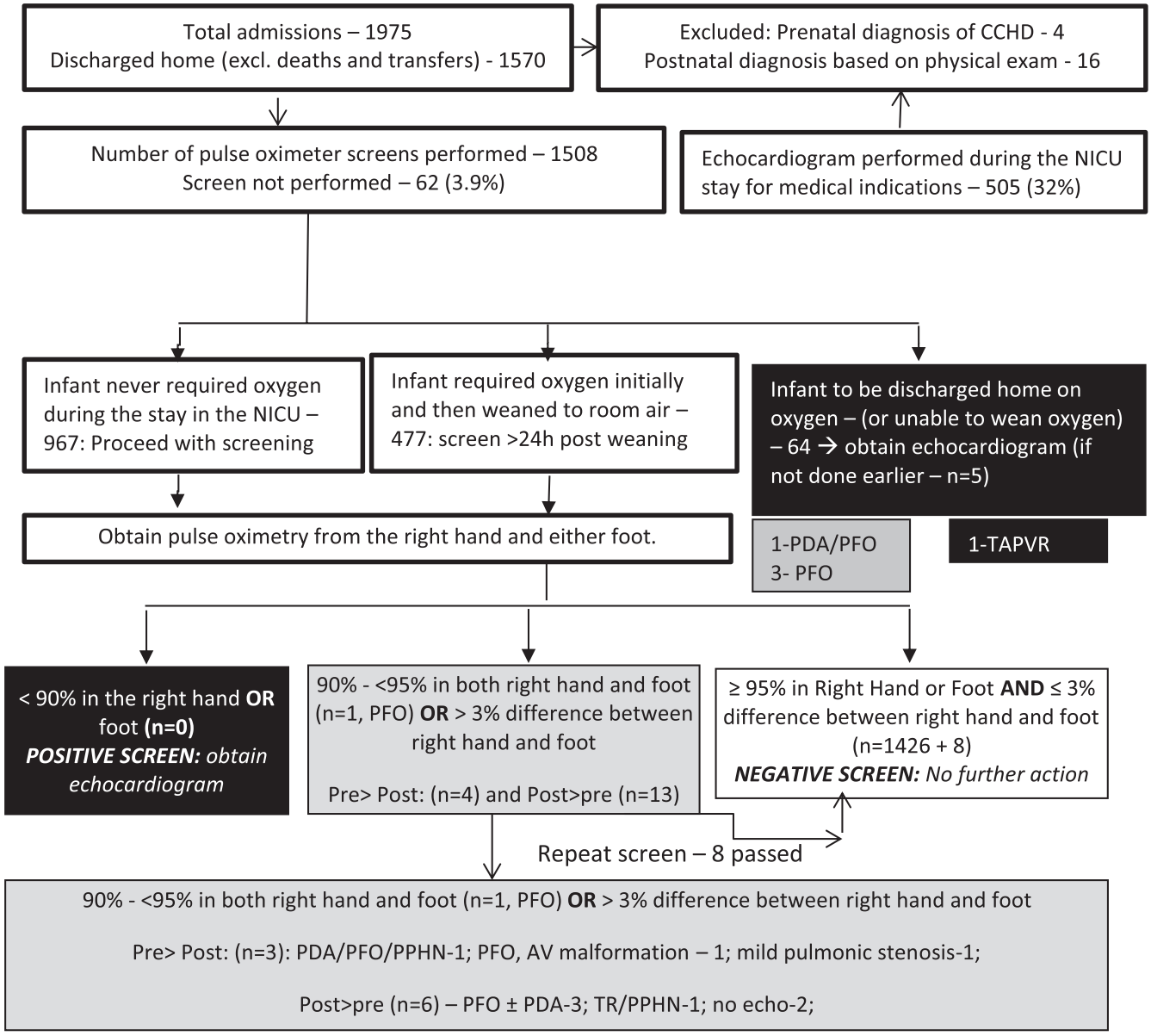

Figure 1. Flowchart showing distribution of patients based on universal screen conducted in the NICU from March 2012 to March 2014. CCHD, critical congenital heart disease, NICU, neonatal intensive care unit; PDA, patent ductus arteriosus; PFO, patent foramen ovale; PPHN, persistent pulmonary hypertension of the newborn; TAPVR, total anomalous pulmonary venous return.

home without an echocardiogram. None of the infants discharged from the NICU were diagnosed to have CCHD on follow-up visits to their pediatrician/family practitioner, emergency department/pediatric intensive care unit or readmission during the period of CCHD screen. Of note, one infant discharged from a level 1 nursery after a normal CCHD screen was readmitted and transferred to us with CCHD during the same period (ventricular septal defect with transverse arch hypoplasia and coarctation of the aorta). Two infants with failed CCHD screens in level 1 nursery were transferred to the NICU during this period (one with tetralogy of Fallot and another with TAPVR).

Differences between pre- and postductal SpO_2

Fifty-two percent of infants had the same pre- and postductal SpO_2. Preductal saturations were higher than postductal in 18% of infants and less than postductal in 30% of infants. The frequency distribution of the difference between pre- and postductal oxygen saturations is shown in Figure 2.

Differences between preterm and term neonates in the NICU

There was no significant difference in SpO_2values in preterm (< 35 weeks PMA) and term ($\geqslant 35$ weeks PMA) infants. The cutoff of 35 weeks was chosen as all infants < 35 weeks PMA are initially admitted to the NICU in our institution. More preterm infants had at least one prior echocardiogram for clinical indications (43% vs 27%, $P < 0.01$ by χ^2 test). The false-positive rate was not significantly different between preterm and term infants (Table 2).

DISCUSSION

Many states including the state of New York have mandated universal pulse oximetry screening of all newborn infants. March of Dimes estimates that about 10 to 15% of US babies spend time

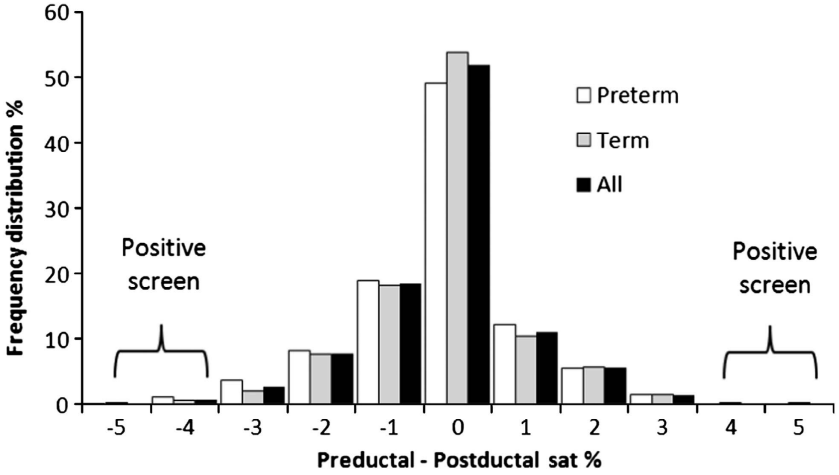

Figure 2. The frequency distribution (%) of the difference between pre- and postductal saturations in preterm (⩽34 weeks, 6/7 days PMA) and term neonates (⩾35 weeks, 0/7 days PMA) and all infants. PMA, postmenstrual age.

Table 2. CCHD screen characteristics at < 35 weeks gestation and ⩾ 35 weeks gestation at birth (data are shown as mean (s.d.))

	'Preterm' < 35 weeks	*'Term' ⩾ 35 weeks*
N	619	889
Gestational age weeks	31.1 (2.8) Range: 22–34	38 (1.7) Range: 35–41
Birth weight (g)	1700 (598) Range: 438–5081	3146 (679) Range: 1318–6010
Race		
Caucasian	385	554
Black	168	205
Hispanic	39	44
Asian/other	27	86
Postmenstrual age at CCHD screening (weeks)	36.9 (2.5) Median: 36.4 Range: 33.3–46.7	39.4 (2.2) Median: 39.3 Range: 35.6–50
Preductal SpO_2	98.8 (1.4)% Median: 99% Range: 92–100%	98.9 (1.3)% Median: 99% Range: 93–100%
Postductal SpO_2	99.1 (1.3)% Median: 100% Range: 94–100%	98.9 (1.4)% Median: 99% Range: 92–100%
Pre–post difference	−0.23 (1.2)%	−0.14 (1.3)%
Echocardiogram for clinical indications	264 (43%)	241 (27%)*
Echocardiogram as baby was being discharged on oxygen (and had not had an echocardiogram before for clinical indication)	2/57 Patients not weaned off oxygen by discharge	3/7 Patients not weaned off oxygen by discharge
False-positive screen	3 (0.48%)	7 (0.78%)
True-positive screen	0	1

Abbreviations: CCHD, critical congenital heart disease; SpO_2, pulse oximetry oxygen saturation.
*$P < 0.01$ by χ^2 test.

in an NICU each year. These infants undergo multiple physical examinations and are continuously monitored by pulse oximetry. There is limited literature on the use of pulse oximetry screening in the NICU.[5,6,10] To our knowledge this study represents the largest series of universal CCHD screening among the NICU population.

Universal screening for CCHD was implemented initially in our NICU as a quality improvement measure following the discharge of a term infant with interrupted aortic arch.[10] It is not clear if we would have detected this patient by CCHD screening. Detection rates for coarctation of aorta are < 60% by CCHD screening.[3] Although precise detection rates for interrupted aortic arch by pulse oximeter screening are not known and this diagnosis has been missed by CCHD screen,[8] we speculate that the saturations in the left upper limb and lower limbs (ductal-dependent systemic circulation) in this infant would be < 90%. Simultaneous pre- and postductal SpO_2 measurement at CCHD screen may be beneficial in the NICU. Moreover, infants already have a disposable pulse oximeter probe reducing the cost of CCHD screen in the NICU.

Approximately a third of the discharges from our NICU had a prior echocardiogram for medical indications. In the current study, these infants were also screened; we have recently revised our protocol and infants who have had prior echocardiograms in the NICU are not screened. Instead, the date of the echocardiogram and the main findings are recorded in the CCHD screen folder of the electronic medical record significantly reducing the number of screens required in the NICU.

During the 2-year period of screening, only one patient with CCHD (TAPVR) was diagnosed using the screen algorithm. This term infant was symptomatic with an unexplained oxygen need and this echocardiogram would have been performed as part of his medical evaluation irrespective of the CCHD screening protocol. As TAPVR would have likely been diagnosed even without CCHD screening in place, the probability of a new CCHD diagnosis from a screening program in the NICU is not known with certainty. Pooled data from many NICUs are needed to evaluate the precise true-positive rate of CCHD screening in the NICU and the costs involved per additional CCHD diagnosed. There were no cases of CCHD detected among NICU discharges in the Pediatrician/family practitioner's office, cardiology or emergency department/pediatric intensive care unit. The Women and Children's Hospital of Buffalo is the only pediatric emergency department/pediatric intensive care unit and neonatal/pediatric transport team in Western New York.

One notable difference when compared with non-NICU neonates in the current study is the high rate of false-positive screens in the NICU population. Meta-analyses of large population-based studies of newborn pulse oximetry screening conducted after the first 24 h after delivery among asymptomatic newborn infants demonstrate a low false-positive rate of 0.035 (ref. 4) to 0.05%.[11] The false-positive rate in our study was significantly higher at 0.66% in a high-morbidity NICU population. As almost a third of patients undergo echocardiography in our NICU, this false-positive rate results in a small additional need for echocardiograms. Similar high false-positive rates are documented for high-risk population

with endocrine/metabolic newborn screen (1.05% in term infants vs 6.9% in preterm infants, 6% for low birth weight and 4.9% for infants with chronic illness).[12]

Two-thirds of these false-positive screens were secondary to a postductal SpO_2 in the 99–100% range and a preductal SpO_2 of 95–96% ($n = 13$ on first attempt and 6 after subsequent attempts). In infants with both pre- and postductal $SpO_2 \geqslant 95\%$, if preductal to postductal difference of $>3\%$ was not a criterion for screen failure, the false-positive rate in our NICU would be reduced to 0.07%, similar to the rate in asymptomatic newborn infants. It is interesting to note that among studies conducted >24 h of life, Riede *et al.*[13] evaluated foot oximetry only in 41 445 births and demonstrated a sensitivity of 77.8% and a false-positive rate of 0.1%. In contrast, de-Wahl Granelli *et al.*[8] conducted simultaneous pre- and postductal oximetry in 39 821 births with a sensitivity of 62% and a false-positive rate of 0.17%.

Ten neonates had postductal SpO_2 exceed preductal SpO_2 by $>3\%$ on the first attempt suggesting reverse differential 'cyanosis'. Two CCHD lesions are associated with reverse differential cyanosis. The first is transposition of great arteries associated with PPHN[14] or transposition of great arteries with coarctation/interrupted aortic arch.[15,16] The SpO_2 in these patients is often $<80\%$. The second condition reported in one case with reverse differential cyanosis is supradiaphragmatic TAPVR.[17] The preductal SpO_2 was 80% and postductal SpO_2 was 93% on 60% inspired oxygen in this patient. Patients with both pre- and postductal $SpO_2 \geqslant 95\%$ in room air are highly unlikely to suffer from transposition of great arteries or TAPVR. Should infants with postductal SpO_2 exceeding preductal SpO_2 by $>3\%$ and with baseline pre- *and* postductal SpO_2 of $>95\%$ on room air be considered to have passed the screen (with no possibility of CCHD)?

Approximately half of the NICU patients had no difference between pre- and postductal SpO_2 (Figure 2), but postductal SpO_2 was significantly higher than preductal values in the NICU population ($99 \pm 1.3\%$ vs $98.8 \pm 1.4\%$, $P < 0.0001$). Interestingly, a similar trend was observed in normal newborn infants 24 h after birth.[18]

In spite of presentations and color charts readily available in the NICU with the correct algorithm for the screen, two infants with failed screens (with postductal SpO_2 of 100% and preductal SpO_2 of 96%) were erroneously labeled as passed and were discharged without an echocardiogram. Intensive and repeated educational efforts and close collaboration between neonatal and cardiology services can mitigate such errors. There are several limitations to this study. First, we did not evaluate the optimal timing for CCHD screen in the NICU. We performed the screen 24–48 h before discharge along with other screening tests such as car-seat challenge and hearing screen. It is possible that screening may be conducted earlier (at 24 to 48 h of age for neonates in room air and 24 h after weaning to room air in infants requiring supplemental oxygen/respiratory support). Second, not all NICUs monitor patients SpO_2 continuously throughout the length of stay. Finally, the incidence of CCHD is low and the current single-center study is underpowered to make any definitive conclusions in this population.

We conclude that performing universal screening in the NICU is feasible but may not be effective as a stand-alone tool. A thorough history and physical examination will provide clues to the diagnosis of CCHD in many infants. Pulse oximetry screening may enhance the effectiveness of CCHD diagnosis by clinical examination. CCHD can potentially be missed by not performing a pre- and postductal SpO_2 screen before discharge in the NICU. The false-positive rate for CCHD screen is higher in the NICU compared with asymptomatic newborns in a level 1 nursery and is mainly due to $>3\%$ difference in pre- and postductal SpO_2. Data analyses from multiple units are needed to determine the precise false- and true-positive rate and effectiveness among neonates admitted to the NICU.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Veena Manja drafted the initial manuscript, conducted analysis and approved the final manuscript as submitted. Bobby Mathew collected data, revised the manuscript and approved the final manuscript as submitted. Vivien Carrion implemented the protocol, collected data, revised the manuscript and approved the final manuscript as submitted. Satyan Lakshminrusimha conceptualized and designed the study, implemented the protocol, collected data, critically reviewed the manuscript and approved the final manuscript as submitted.

REFERENCES

1 Frank LH, Bradshaw E, Beekman R, Mahle WT, Martin GR. Critical congenital heart disease screening using pulse oximetry. *J Pediatr* 2013; **162**(3): 445–453.
2 Peterson C, Grosse SD, Oster ME, Olney RS, Cassell CH. Cost-effectiveness of routine screening for critical congenital heart disease in US newborns. *Pediatrics* 2013; **132**(3): e595–e603.
3 Mahle WT, Newburger JW, Matherne GP, Smith FC, Hoke TR, Koppel R *et al.* Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the American Heart Association and American Academy of Pediatrics. *Circulation* 2009; **120**(5): 447–458.
4 Mahle WT, Newburger JW, Matherne GP, Smith FC, Hoke TR, Koppel R *et al.* Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the AHA and AAP. *Pediatrics* 2009; **124**(2): 823–836.
5 Iyengar H, Kumar P, Kumar P. Pulse-oximetry screening to detect critical congenital heart disease in the neonatal intensive care unit. *Pediatr Cardiol* 2013; **35**(3): 406–410.
6 Suresh GK. Pulse oximetry screening for critical congenital heart disease in neonatal intensive care units. *J Perinatol* 2013; **33**(8): 586–588.
7 Kemper AR, Mahle WT, Martin GR, Cooley WC, Kumar P, Morrow WR *et al.* Strategies for implementing screening for critical congenital heart disease. *Pediatrics* 2011; **128**(5): e1259–e1267.
8 de-Wahl Granelli A, Wennergren M, Sandberg K, Mellander M, Bejlum C, Inganas L *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.
9 Lakshminrusimha S, Sambalingam D, Carrion V. Universal pulse oximetry screen for critical congenital heart disease in the NICU. *J Perinatol* 2014; **34**(5): 343–344.
10 Lakshminrusimha S, Turkovich S, Manja V, Nair J, Kumar VH. Critical congenital heart disease screening with pulse oximetry in the neonatal intensive care unit. *E-J Neonat Res* 2012; **2**(2): 96–101.
11 Thangaratinam S, Daniels J, Ewer AK, Zamora J, Khan KS. Accuracy of pulse oximetry in screening for congenital heart disease in asymptomatic newborns: a systematic review. *Arch Dis Childhood Fetal Neonat Ed* 2007; **92**(3): F176–F180.
12 Tarini BA, Clark SJ, Pilli S, Dombkowski KJ, Korzeniewski SJ, Gebremariam A *et al.* False-positive newborn screening result and future health care use in a state Medicaid cohort. *Pediatrics* 2011; **128**(4): 715–722.
13 Riede FT, Worner C, Dahnert I, Mockel 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): 975–981.
14 Martin TC. Reverse differential cyanosis: a treatable newborn cardiac emergency. *Neoreviews* 2011; **12**(5): e270–e273.
15 Buckley MJ, Mason DT, Ross J Jr, Braunwald E. Reversed differential cyanosis with equal desaturation of the upper limbs. syndrome of complete transposition of the great vessels with complete interruption of the aortic arch. *Am J Cardiol* 1965; **15**: 111–115.
16 Aziz K, Sanyal SK, Goldblatt E. Reverse differential cyanosis. *Br Heart J* 1968; **30**(2): 288–290.
17 Yap SH, Anania N, Alboliras ET, Lilien LD. Reversed differential cyanosis in the newborn: a clinical finding in the supracardiac total anomalous pulmonary venous connection. *Pediatr Cardiol* 2009; **30**(3): 359–362.
18 Jegatheesan P, Song D, Angell C, Devarajan K, Govindaswami B. Oxygen saturation nomogram in newborns screened for critical congenital heart disease. *Pediatrics* 2013; **131**(6): e1803–e1810.