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Role of Perfusion Index on the First Day of Life in prediction of Early Discharge of Newborns

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ABSTRACT

Background: Assessment of maintenance of the tissue oxygen supply adequacy should be considered as the primary objective in neonatal intensive care unit (NICU).

Objective: The aim of this study was to evaluate the value of perfusion index for predicting early discharge of newborns from NICU.

Patients and methods: Our study was conducted on 248 neonates. We measured the perfusion index (PI) for Full term neonates aged ≥37 weeks, appropriate for gestational age with APGAR score >7 at 5 minutes. Newborns included in the study were divided into two groups: Group (1): included neonates admitted to NICU for whom PI was measured daily until discharge or death. Group (2): included neonates discharged to home for whom PI measured at birth.

Results: Among admitted survived cases the median pre-ductal PI was 0.9 and post-ductal PI was 0.8 while among admitted non-survived cases the median pre-ductal PI was 0.5 and post-ductal PI 0.4. Pre and post-ductal PI were significantly increased among survivors (0.94±0.35, 0.85±0.35) than non survivors (0.56±0.23, 0.48±0.21) respectively (P<0.001). Post-ductal PI was significantly increased among survivors than non-survivor patients (P<0.001), Also, SpO2 was significantly increased among survivors than non survivors (P<0.001). PI levels were significantly lower in the patients who needed support with inotropes than those who don't need (P<0.001).Perfusion index was significantly decreased among admitted patients (0.84±0.37) than discharged patients 2.24±0.49 (P<0.001).Perfusion index was significantly decreased among non survivors 0.68±0.36 than survivors 0.89±0.34 (P=0.003).

Conclusion: It could be concluded that the perfusion index measured in the first day of life plays a role in the prediction of early discharge of neonates that have good values of PI. On the other hand, it predicts the admission of neonates that have lower values of PI. Follow-up of PI may help the clinician to identify high risk neonate who need closer monitoring and more aggressive treatment.

Keywords: Perfusion Index, First Day of Life, Early Discharge, Newborns.

INTRODUCTION

Assessment of the appropriate preservation of tissue oxygen delivery adequacy should be the primary objective of the neonatal intensive care unit (NICU). A contributing factor to the peripheral perfusion of NICU patients is the redistribution of the oxygen supply to the brain, heart, and adrenal glands, as well as the marginal cardiac output. Consequently, in order to prevent tissue hypoxia, it is essential to promptly identify impaired organ perfusion, perhaps leading to the failure of vital organs. An early indicator of hypoperfusion of the vital tissue could be the monitoring of the perfusion of these less critical tissues (skin, subcutaneous tissue, muscle, and gastrointestinal tract). Noninvasive monitoring techniques facilitate the evaluation of perfusion in peripheral tissues [(1)].

Clinically, global tissue perfusion can be assessed biochemically through the use of serum lactate and central venous oxygen saturation, as well as through the detection of cutaneous chill, paleness, mottling, and a prolongation of capillary retention time. The most appropriate method for tissue perfusion should be non-invasive, rapid, and easily quantifiable [(2)].

Over the past few decades, the practice of pulse oximetry has been considered non-invasive, painless, rapid, and a low-cost method that accurately represents the percentage of oxygenated hemoglobin in the blood. It also illustrates hypoxia scales in severe cyanotic heart disease that are not clinically apparent [(3)].

The pulsatile flow's non-pulsatile flow rate is defined as the Perfusion Index (PI), a non-invasive technique. PI operates by utilizing a pulse oximeter to examine fluctuations in peripheral perfusion in the fingers.is a potential screening instrument for the detection of congenital heart malformations [(4)].

Hypo perfusion triggers the regional pulsatile signal detected by the sensor is reduced by a reflex peripheral vasoconstriction. The non-pulsatile signal remains constant, resulting in a decrease in the PI value [(5)].

The PI has the potential to be utilized as an assessment instrument in a variety of infant health-related areas, as evidenced by research conducted in the neonatal population [(5)].

The aim of this investigation was to assess the efficacy of the perfusion index in predicting the early discharge of infants from the NICU.

PATIENTS AND METHODS

This prospective observational cohort study included a total of 248 neonates, attending at the Neonatal Intensive Care Unit (NICU), El-Shohadaa Central Hospital and Menoufia University Hospital.

Inclusion Criteria:

- Full term ≥37weeks
- Appropriate for gestational age
- APGAR score >7 at 5minutes

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- Within 6 hours of life.

Exclusion Criteria:

- Need for neonatal resuscitation.
- Infants exhibiting symptoms of prenatal/perinatal asphyxia (event with hypoxia or ischemia that occurs immediately before or during labor or delivery) which are:
  1. A score of less than 5 on the Apgar scale at the 10-minute mark of life.
  2. Acidemia in the fetal umbilical artery is defined as a pH level of less than 7 or a base deficit of at least 12.
  3. MRI images that exhibit a unique basal-ganglia-thalamus, watershed, or near-total cortical lesion pattern and were acquired between 24 and 96 hours and up to day 10.
  4. Cardiac, renal, hepatic, metabolic, hematologic, and gastrointestinal dysfunction, including multisystem organ failure, is present.
- Newborns with known congenital malformations/ chromosomal anomalies.

The included neonates were divided into two groups; **Group (1)** included 136 neonates admitted in NICU for whom PI was measured daily until discharge or death., **Group (2)** included 112 neonates discharged home measured PI at birth.

All patients that admitted to NICU subjected to the following:

a) Medical history:

1. Gestational age: Antenatal ultrasonography, Ballard method, or the last menstrual period (LMP) were employed to ascertain the gestational age of the neonates, if it was known.
2. History of perinatal conditions, including the history of cyanosis or convulsions, maternal illness, mode of delivery, gestational age, infant weight, gender, and Apgar score.
3. Postnatal information.

b) Clinical examination:

Neurological examination, anthropometric measurements, and vital signs were the primary focus of both general and systemic examinations.

c) Peripheral oxygen saturation and Perfusion index were calculated and recorded (preductal and postductal):

Perfusion index (PI) was measured at the first day of life within 6 hours. PI was measured with pulse oximeter **(granzia (pulsox-307). PI** was measured pre-ductal and post-ductal. Pre-ductal reading was measured with sensor placed on right hand of the neonate, while post-ductal reading was measured with sensor placed on either feet of the neonate. In order to mitigate artifacts, for a minimum of 10 seconds, the PI scores were determined after a pulse wave remained stable.

Ethical Consideration:

This study was ethically approved by Research Ethics Committee, Faculty of Medicine, Menoufia University's [IRB NO:2/ 2023 PEDIA 10]. Parents' informed assent was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

SPSS version 22 for Windows® was used to code, process, and analyze the gathered data. The Shapiro Walk test was used to determine whether the data had a normal distribution. Frequencies and relative percentages were used to illustrate the qualitative data. To determine the difference between two or more sets of qualitative variables, use the X2-test. The mean ± SD (standard deviation) was used to express quantitative data. Quantitative data from the groups under study were compared using the independent t-test and the Mann-Whitney U test, respectively. Receiver Operating Characteristic (ROC) curve analysis is used to assess a test's diagnostic performance, or its ability to distinguish between patients that are ill and those that are not. The curve's sensitivity and specificity were identified, and cross-tabulation was used to determine the PPV, NPV, and accuracy. P values were considered statistically significant if they were less than 0.05.

RESULTS

The study population, total 267 patients assessed for certification. The study excluded a total of 19 patients, with nine patients being excluded as their parents refused to participate in the study and to give us a written consent and 10 patients did not meet the inclusion criteria), so the number of eligible patients in the study was 248 patients**.**

Our investigation demonstrated that: Compared to discharged patients, admitted patients exhibited a significant decrease in gestational age, birth weight, and Apgar score at the first and first five minutes, While there was no significant difference among discharged and admitted cases concerning gender and age. Furthermore, there was a substantial disparity between cases that were discharged and those that were admitted in terms of use of antenatal steroids and maternal diseases, where use of antenatal steroids was found in 66.2% of discharged patient and in 8.0% of admitted patient. Among admitted cases, the most common maternal diseases were PROM found in 8.0% then UTI 6.3% followed by HTN 2.7%, DM 1.8%, placenta Previa 0.9% **(Table 1**).

Table (1): Demographic data of the studied groups (n=248).

Variable	patients				*Test of sig.*	*P value*
	Discharged (n=136)		**Admitted (n=112)**			
G.A (weeks) Mean± SD Median (range)	38.17±0.83 38.0 (37.00-40.00)		37.55±.69 37.0 (37.00-40.00)		**U** 6.105	<0.001*
Age (hrs.) Mean± SD Median (range)	4.00±1.32 4.0 (1.00-6.00)		4.13±1.23 4.0 (1.00-6.00)		t 0.771	0.441
Birth weight (Kg) Mean± SD Median (range)	3.07±0.40 3.0 (2.00-4.30)		2.84±0.33 2.8 (2.50-3.80)		**U** 4.92	<0.001*
Sex	**N**	**%**	**N**	**%**	X^2 1.595	0.207
Male	68	50.0	65	58.0		
Female	68	50.0	47	42.0		
Mode of delivery					X^2 3.216	0.073
Cesarean section	100	73.5	93	83.0		
Normal vaginal delivery	36	26.5	19	17.0		
Apgar score at 1st min Mean± SD Median (range)	6.99±0.12 7.0 (6.00-7.00)		6.28±0.60 6.0 (5.00-7.00)		U= 10.68	<0.001*
Apgar score at 5 min Mean± SD Median (range)	9.00±0.00 9.0 (9.00-9.00)		8.74±0.63 9.0 (7.00-9.00)		U= 4.84	<0.001*
Use of antenatal steroids	**N**	**%**	**N**	**%**	X^2 86.566	<0.001*
Yes	90	66.2	9	8.0		
No	46	33.8	103	92.0		
Maternal diseases					X^2 32.26	<0.001*
No	136	100.0	88	78.6		
PROM	0	0.0	9	8.0		
UTI	0	0.0	7	6.3		
DM	0	0.0	2	1.8		
HTN	0	0.0	3	2.7		
DM+HTN	0	0.0	2	1.8		
Placenta Previa	0	0.0	1	0.9		
Consanguinity					X^2 8.459	0.004*
Positive	1	0.7	9	8.0		
Negative	135	99.3	103	92.0		
Order in family					X^2 6.536	0.257
1st	55	40.0	30	26.8		
2nd	34	25	29	25.9		
3rd	23	16.9	28	25		
4th	20	14.7	21	18.8		
5th	2	1.5	3	2.7		
6th	2	1.5	1	0.9		

Premature rupture of membranes (PROM) UTI: urinary tract infection, HTN: Hypertension, DM: diabetes mellitus, G.A.: Gestational age, Mann: U Whitney U test, t: Independent t test, X2: Chi square, *: Significant.

Respiratory diseases were the common cause of admission for patients 48.2% followed by sepsis 38.8%, congenital heart disease 9.8% and finally persistent pulmonary hypertension 7.14%. Regarding respiratory diseases, 30 of patients had transient tachypnea of newborns (TTN), and 20 of patients had meconium aspiration syndrome and 4 of patients had respiratory distress syndrome. Regarding congenital heart disease, 4 of patients had ventricular septal defect (VSD) and 4 of patients had atrial septal defect (ASD), and 3 of patients had patent ductus arteriosus (PDA). Regarding need of inotropes,59.82%of admitted cases need inotropes while 40.18% not need inotropes, while respiratory support, 40.2% of admitted cases were treated with nasal cannula, 30.4% were treated with CPAP, 29.5% were treated with mechanical ventilation. Regarding patient Outcome, 72.3% of admitted cases were survived, 27.7% of admitted cases were non survived **(Table 2)**.

Table (2): Clinical data of admitted neonates (n=112).

Variable	Admitted patients (n=112) N %	
Cause of admission (initial diagnosis)		
Respiratory diseases	54	48.2
Sepsis	39	34.8
Congenital heart disease	11	9.8
Persistent pulmonary hypertension	8	7.14
Length of Hospital stay (days)		
Mean± SD	13.81±11.24	
Median (range)	10.0 (1.00-58.00)	
Need of inotropes		
Yes	67	59.82
No	45	40.178
Respiratory support		
Nasal cannula	45	40.2
CPAP	34	30.4
Mechanical ventilation	33	29.5
Patient Outcome	81	72.3
Survived	31	27.7
Non survived		

CPAP: Continuous positive airway pressure

Pre-ductal and post-ductal perfusion index(es) (PI) were significantly increased among survivor than non survivors respectively (P<0.001). PI was substantially increased among survivors instead of non-survivor patients (P<0.001), Also, SpO_2 significantly enhanced among survivor and non-survivor patients (P<0.001). Admitted patients had significantly lower perfusion index (0.84±0.37) than discharged patients (2.23±0.49) (P<0.001) (**Table 3).**

Table (3): Comparison of pre ductal and post ductal perfusion index and SpO_2 (%) between the admitted group (survivors and non survivors) (n=112).

Variable	Admitted		U	P value
	Non survivors (n=31)	Survivors (n=81)		
Pre-ductal PI				
Mean± SD	0.56±0.23	0.94±0.35	6.691	<0.001*
Median (min-max)	0.5 (0.2-1.6)	0.9 (0.3-2)		
Post-ductal PI				
Mean± SD	0.48±0.21	0.85±0.35	6.800	<0.001*
Median (min-max)	0.4 (0.2-1.5)	0.8 (0.3-1.9)		
Perfusion index PI (%)				
Mean± SD	0.68±0.36	0.89±0.34	2.98	0.003*
Median (Min-Max)	0.4(0.2-1.8)	0.7(0.3-2)		
SpO_2 (%)			2.197	0.036*
Mean± SD	94.48±6.75	97.16±1.07		

SpO_2: Oxygen saturation, U: Mann Whitney U test, *: Significant.

Perfusion index was significantly decreased among non-survivor patients than survivor patients (P=0.003) **Table 4.**

Table (4): Comparison of perfusion index between admitted and discharged patients

Variable	Patients		U	P value
	Discharged (n=136)	Admitted (n=112)		
Perfusion index PI (%)				
Mean± SD	2.23±0.49	0.84±0.37	13.1	<0.001*
Median (Min-Max)	2.20 (0.80-3.40)	0.8 (0.20-2.00)		

PI: perfusion index, U: Mann Whitney U test, *: Significant

In those who required assistance with inotropes, The PI levels of those who did not were significantly lower than those who did (P<0.001)**.** The mean perfusion index was 0.726±0.34 in patients needing inotropes while, the mean perfusion index was 1±0.33 in patients do not need inotropes (**Table 5).**

Table (5): Comparison of the perfusion index between patients who needed support with inotropes and those who don't need.

	Need for inotropes		Mann-Whitney U test	P-value
	Yes N=67	No N=45		
Perfusion index PI%			U	
Mean±SD	0.726±0.34	1±0.33	4.23	<0.001
Median (min-max)	0.7 (0.2-1.8)	1 (0.3-2)		

The cutoff point of perfusion index of day 1 as a diagnostic marker for predicting of early discharge in newborns from NICU was 1.65, with sensitivity of 91.2%, specificity of 97.3%, PPV of 97.6%, accuracy of 94% and AUC of 0.983 (**figure 1).**

With a sensitivity of 84%, specificity of 51.6%, PPV of 81.9%, accuracy of 75%, and AUC of 0.682, the perfusion index of day 1 was a diagnostic marker for predicting neonatal mortality at a cutoff point of 0.55 (**figure 2).**

Among admitted cases, in the survivor group A significant negative correlation was observed between index PI and hospital stays (r = -0.378, P=0.001)., while in non-survivor group there was significant positive correlation between perfusion index PI and hospital stays (r = 0.389, P=0.030)**.**

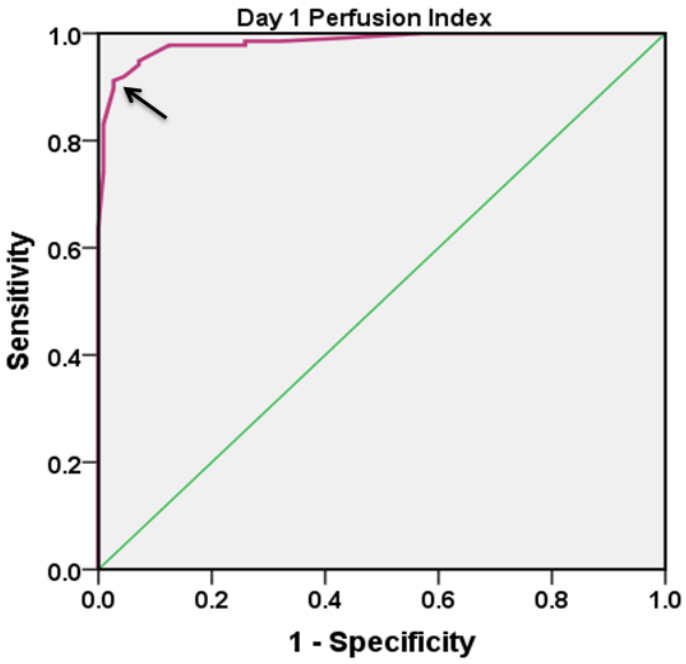

Fig. (1): ROC curve of perfusion index as a marker for predicting early discharge of newborns from NICU.

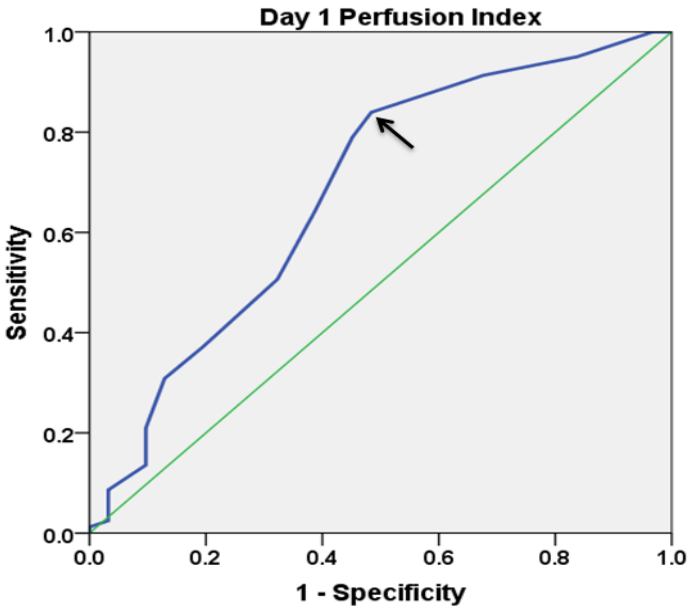

Fig. (2): ROC curve of perfusion index as a marker for predicting of neonatal mortality.

DISCUSSION

Regarding demographic data, the current investigation demonstrated that the Apgar score and birth weight at 1 and 5 minutes were significantly decreased among admitted patients compared to discharged neonates. This is consistent with the research conducted by **Hakan *et al.* [6], Hua *et al.* [7] and Ibrahim and Mohamed [8].**

In the current study, respiratory diseases were the most common cause of admission for our patients 48.2%. Also, in the study done by **Ibrahim and Mohamed [8]**, respiratory distress 44.6% constituted the primary reason for admission. Morbidity and mortality in the neonate during the early stages of development are primarily caused by respiratory diseases, which are also the most common reason for both term and preterm neonates are admitted to the special care nursery **Pramanik *et al.* [9]**. For neonates who are experiencing respiratory distress, the risk of mortality is 2–4 times greater than that of those who are not **Swarnkar and Swarnkar [10].**

In our study 59.82% of admitted patients were treated with inotropic drugs, while in the study done by **Ibrahim and Mohamed [8],** Inotropic drugs were used for 36.6% patients. Inotropic drugs used more in our study because most of patients had respiratory and /or cardiac problems while other study not the same.

Regarding respiratory support, 30.4% of admitted patients were treated with CPAP and 29.5% were treated with mechanical ventilation**,** In the study done by **Mathew *et al.* [11]** which done on admitted patients in NICU**,** CPAP was administered to 14.5% of patients, while 27.5% were advised to undergo mechanical ventilation treatment.

Regarding patient Outcome, among admitted patients 72.3% survived and 27.7% died. This is supported by the WHO report that in 2022, the eastern Mediterranean and African regions exhibited the highest neonatal mortality rates, with 26 and 25 deaths per 1000 live births, respectively [12].

In our investigation, among survivors median preductal PI was 0.9 and post ductal PI was 0.8 while among non survivors the median pre-ductal PI was 0.5 and post-ductal PI 0.4. In a study conducted by **Hakan *et al.* [6],** the median pre ductal PI was 1.34 and post ductal PI 0.90.

In our study, SpO_2 was significantly increased among survivors than non-survivor patients (P<0.001**),** 97.16±1.07 was the mean ±SD of SpO2 among survivors and 94.48±6.75 among non survivors**.** Also the mean ± SD of SpO2 was 95.1±3.9% among neonates had low severity illness and 93.3±5.4% among neonates had high severity illness (P<0.0001) in the investigation conducted by **De Felice *et al.* ([13].**

Perfusion index was significantly decreased among admitted patients 0.84 than discharged patients 2.24 (P<0.001). A study conducted by **Mathew *et al.* [11]**, PI was 1.47 among discharged neonates and 0.75 among neonates who subsequently perished or were discharged against medical advice (DAMA) with (p <0.001).

Perfusion index was significantly decreased among non survivors 0.68±0.36 than survivors 0.89±0.34 (P=0.003), this is supported by the study done by **Mathew *et al.* [11],** at which the low severity group had a PI of 1.94 ± 1.36, the high severity group had a PI of 0.85 ± 0.64. The high severity group had a PI of 0.85 ± 0.64, while the low severity group had a PI of 1.94 ± 1.36).

In our study, the mean ± SD of PI was 0.84±0.37 and range 0.20-2.00 among admitted patients, while in the study done by **De Felice *et al.* [13]**, among the admitted patients, 1.54±0.80 was the mean±SD of PI, with a range of 0.22–5.22. Due to the fact that our

investigation encompassed neonates with more severe conditions

In our study , the median PI was 2,20 in healthy discharged neonates ,while in the study done by **Ostman-Smith and Granelli [(14)]**, 1.70 was the median PI in healthy discharged neonates and in study done by **Hakan *et al.* [(6)]**, the median of PI was 1.0 which was performed on term and preterm neonates who were hemodynamically and clinically stable.

In our study, the mean ±SD of PI was 0.727±0.34 and 1 ±0.33 ($p < 0.001$), respectively, for inotropic use. This is supported by the study done by **Ibrahim and Mohamed [(8)]**, the mean ±SD of PI was 1.03±0.57 and 1.51± 0.76, respectively (p=0.001) for inotropic use. The patient who required inotrope support had substantially lower PI levels than those who did not ($P<0.001$)**,** and PI had a significant relation with the use of inotropes and neonatal outcome Patients who used inotropes and passed away had a significantly lower PI than those who didn't in both day 1 and 3**.**

In our study ,The cut-off point of perfusion index of day 1 as a diagnostic marker for predicting of early discharge in newborns from NICU was 1.65, with sensitivity of 91.2%, specificity of 97.3%, accuracy of 94% and AUC of 0.983**.**While cut-off point of perfusion index was ≤1.25 with sensitivity 63.4% and specificity 60.6% for day 1 in the study done by **Ibrahim and Mohamed [(8)]**, Also in the study done by **Hakan *et al.* [(6)],** The disease severity was accurately predicted by the perfusion index cut-off point of ≤1.24%, which had a sensitivity of 95.5% and a specificity of 93.7%.

Cutoff point of perfusion index of day 1 as a diagnostic marker for predicting of neonatal mortality was 0.55, with sensitivity of 84%, specificity of 51.6%, accuracy of 75% and AUC of 0.682**,** while the validity of the PI to predict mortality using the receiver operating characteristics curve revealed a cut off value of perfusion index was ≤1.25 with sensitivity 75.9% and specificity 61.4% for day1 in the study done by **Ibrahim and Mohamed [(8)].**

In our study, among admitted patients, In the survivor group, the perfusion index PI was significantly negatively correlated with the duration of hospital stay ($P=0.001$, $r = -0.378$), while the hospital stay was significantly positively correlated with the perfusion index PI in the non-survivor group ($P=0.030$, $r = 0.389$).

CONCLUSION

It could be concluded that the perfusion index measured in the first day of life plays a role in the prediction of early discharge of neonates that have good values of PI. On the other hand, it predicts the admission of neonates that have lower values of PI. Follow-up of PI may help the clinician to identify high risk neonate who need closer monitoring and more aggressive treatment.

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REFERENCES

1. **Lima A and Bakker J (2005):** Noninvasive monitoring of peripheral perfusion. Intensive Care Medicine, 10: 131-141.
2. **Hasanin A, Mukhtar A, Nassar H (2017):** Perfusion indices revisited. Journal of Intensive Care, 5(1): 1-8.
3. **Movahedian, Mosayebi Z, Sagheb S (2016):** Evaluation of Pulse Oximetry in the Early Detection of Cyanotic Congenital Heart Disease in Newborns. The Journal of Tehran University Heart Center, 11(2): 73-77.
4. **Jegatheesan P, Song D, Angell C *et al.* (2013):** Oxygen saturation nomogram in newborns screened for critical congenital heart disease. Pediatrics, 131(6): 1803-1810.
5. **Piasek C, Van Bel F, Sola A (2014):** Perfusion index in newborn infants: a noninvasive tool for neonatal monitoring. Acta Paediatrica, 103(5): 468-473.
6. **Hakan N, Dilli D, Zenciroglu A *et al.* (2014):** Reference values of perfusion indices in hemodynamically stable newborns during the early neonatal period. European Journal of Pediatrics, 173: 597-602.
7. **Hua W, Niu C, Xuan Y *et al.* (2023):** Peripheral perfusion index in well newborns at 6 to 72 h of life at different altitudes: a multi-center study in China. European Journal of Pediatrics, 182(2): 907–915.
8. **Ibrahim M, Mohamed M (2023):** Validity of perfusion index in prediction of circulatory compromise and mortality in neonates. Ain Shams Medical Journal, 74(1): 57-64.
9. **Pramanik A, Rangaswamy N, Gates T (2015):** Neonatal respiratory distress: A practical approach to its diagnosis and management. Pediat Clin N Am., 62: 453–69.
10. **Swarnkar K, Swarnkar M (2015):** Neonatal respiratory distress in early neonatal period and its outcome. Int J Biomed Adv Res., 6(9): 643–47.
11. **Mathew J, Bada Shekarappa C, Nanyam Rao S (2019):** Correlation between perfusion index and CRIB score in sick neonates admitted to a tertiary center. Journal of Tropical Pediatrics, 65(1): 84-89.
12. **WHO (2024):** Levels & trends in child mortality: report 2023. Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation. New York, Geneva, Washington, DC:United Nations Children's Fund, World Health Organization,World Bank Group, United Nations Department of Economic and Social Affairs, Population Division; pp. 1-80. https://childmortality.org/wp-content/uploads/2023/01/UN-IGME-Child-Mortality-Report-2022.pdf
13. **De Felice C, Flori M, Pellegrino M *et al.* (2002):** Predictive value of skin color for illness severity in the high-risk newborn. Pediatr Res., 51: 100–105.
14. **Granelli A, Östman-Smith I (2007):** Noninvasive peripheral perfusion index as a possible tool for screening for critical left heart obstruction. Acta Paediatrica, 96(10): 1455-1459.