VALIDITY OF PERFUSION INDEX IN PREDICTION OF CIRCULATORY COMPROMISE AND MORTALITY IN NEONATES

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ABSTRACT:

Background: *Early prediction of circulatory compromise in neonates is a cornerstone in improving neonatal outcome. Proper functioning circulatory system is indicated by adequate tissue perfusion. Perfusion index (PI) can identify the state of peripheral tissue perfusion which is a window to the perfusion of the body.*

Aim of the work: *To validate the use of the perfusion index in predicting risk of circulatory compromise in neonates, to help in guidance of accurate, properly timely management.*

Patients and Methods: *This prospective observational study was done on 112 neonates. PI at the day of admission and after 3 days of hospital stay. The hospital course was followed up especially the need for inotropic support, hospital stay and mortality.*

Results: *Patients who used inotropes and passed away had a significantly lower PI than those who didn't in both day 1 and 3. Mean and SD (1.03(±0.57) vs 1.51(± 0.76) p=0.001 respectively for inotropic use in day 1, 1.09 (±0.57) vs. 1.87 (±0.68) p<0.001 for inotropic use in day 3, 0.91(±0.53) vs. 1.48(±0.74) p<0.001 respectively for outcome in day 1. 0.91 (±0.42) vs. 1.82 (±0.69) p<0.001 respectively for outcome in day 3. A significant inverse correlation was found between duration of hospital stay and perfusion index on day 3(r= -0.253, p= 0.007).* ***Conclusion:*** *perfusion index can be used as an early predictor of the need of inotropes, duration of hospital stay and mortality in neonates.*

Keywords: perfusion index, neonate, inotropes, mortality, circulation

INTRODUCTION:

Identification of prognosis of critically ill neonates, in an objective way, is a cornerstone in determination of the quality of care provided in Intensive Care Units (ICUs)[1].

Early diagnosis of ineffective tissue perfusion is crucial in neonates in any Neonatal Intensive Care Unit (NICU). This facilitates proper institution of timely management, to prevent the development of shock [2].

The perfusion index (PI) translates the actual alterations of the signal of the pulse oximetry of the circulation peripherally. It is an easy, useful, non-invasive, and continuous score that can reflect variations in the vasomotor tone and the cardiac output**.** By monitoring the microcirculation of tissues of decreased vitality, it could detect early hypoperfusion of vital tissue before the development of organ failure and decompensated shock[3].

PI helps to indicate ineffective peripheral perfusion in critically diseased

new-borns. low PI is an accurate predictor for severe disease affection in neonates[4].

A decrease in PI In both preterm and full-term infants, with oxygen saturation and heart rate, reflects a deterioration in the clinical condition. PI can accurately detect diseased neonates in sub-clinical chorioamnionitis. It has also been used as a tool to screen critical obstruction of the left side of the heart and predict decreased flow in the superior vena cava in neonates with very low birth weight. PI is considered a non-invasive and simple tool to detect different neonatal conditions[5].

The PI is a numerical score that is the result of dividing the pulsatile blood flow signal in the arteries, and the non-pulsatile signal from the skin, subcutaneous tissue, surrounding tissues and blood flow in the veins[6].

AIM OF THE STUDY:

Our aim was to study the validity of PI to identify its feasibility in being a good tool for assessing the need for inotropic support, duration of hospital stay and outcome in neonates.

PATIETS AND METHODS:

This prospective observational study was done on 112 neonates admitted in the neonatal intensive care unit (NICU) at Ain Shams University hospitals regardless of diagnosis. neonates less than 28 days both full term and preterm were included in the study. Neonates discharged in less than 24 hours of admission were excluded. For each neonate, demographic data, complete history taking from the legal guardians (medical, obstetric, perinatal, mode of delivery, resuscitative data and Apgar score), Detailed physical examination and Diagnosis were collected. The neonate's hospital course was followed up to determine the use of inotropes with doses used and duration, Length of hospital stay and mortality.

For each neonate the **Perfusion index (PI)** was measured at the first day of admission and after 3 days of hospital stay. PI was measured with Masimo Radical-7 SET® (Masimo Corp) and the recorded values were in the range of 0 - 2[7]. PI was measured post-ductal with the sensor placed on either feet of the neonate. The PI scores were taken after obtaining a stable pulse wave for 10 seconds at least, to decrease artifacts.

In full term neonates, a value of >1.24 was considered adequate but a value of <1.24 was considered an indicator for inadequate tissue perfusion. [8] For preterm neonates median PI value of 0.89 (0.62-0.97) was as an accurate predictor for inadequate tissue perfusion and measures above this were considered adequate[7].

Consent and Ethical Considerations:

An oral informed consent was taken from legal guardians or parents of the patients before enrolment in this study. This study was in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies dealing with humans.

Data management and analysis:

Data were analyzed using SPSS 23. Mean, standard deviations and range were used for parametric data and median, inter-quartile range (IQR) for non-parametric data. Also, number and percentages for qualitative variables. The comparison between groups used Student T Test to assess the difference between the means of two study group. Correlation analysis (using Spearman's rho was done to correlate between two quantitative variables. *Receiver operating characteristic curve (ROC)* was done to identify the best cut off point, sensitivity, specificity, positive and negative predictive value and Area under curve (AUC) for the studied marker. The 95%

confidence interval and 5% margin of error were used. $p > 0.05$ was Non-significant. $p < 0.05$ was Significant and $p < 0.01$was highly significant.

RESULTS

Data were collected prospectively on 112 neonates admitted to the NICU at Ain Shams University hospitals regardless of diagnosis. The mean post-natal age was 5.54 (±6.81) days, The mean weight was 2.53(±0.66) kg. 57(50.9%) were males and 55 (49.1%) were females. Preterm neonates represented 46.4% (n=52) and full-term neonates represented 53.6% (n=60) of the total number of participants. Respiratory distress (44.6%) constituted the major cause of illness at the time of admission, followed by neonatal jaundice (19.6%), congenital anomalies (12.5%), sepsis (8%), growing premature babies (4.5%). Others included Convulsion, postoperative, hypoglycemia, inborn error of metabolism (IEM) and hemorragic disease of newborn (HDN). Inotropic drugs were used among 41 (36.6%) patients, with mean duration of 6.9 ±2.96 days. Mean hospital stay was 8.67 (±5.55) days. Out of the 112 patients, 83(74.1%) survived and 29 (25.9%) died. (Table 1)

Table 1: General characteristics of the studied neonates:

n=(112)		**Range**	**Mean (±SD)**	**n (%)**
Post Natal Age (days) on admission		(1-28)	5.54(±6.81)	
Weight (kg)		(1.090-3.800)	2.53(±0.66)	
Sex	Male			57(50.9%)
	Female			55(49.1%)
GA	Preterm			52(46.4%)
	full term			60(53.6%)
Initial Diagnosis	RD			50 (44.6%)
	Sepsis			9 (8.0%)
	Jaundice			22 (19.6%)
	Convulsions			4 (3.6%)
	Hypoglycemia			2 (1.8%)
	Postoperative			4 (3.6%)
	Congenital anomalies			14 (12.5%)
	Preterm Grower			5 (4.5%)
	IEM			1 (0.9%)
	HDN			1 (0.9%)
Use of inotropes	No			71 (63.4%)
	Yes			41 (36.6%)
Duration of inotropes (days)		(3-14)	6.90 (±2.96)	
Hospital stays (days)		(3-34)	8.67 (±5.55)	
Patient Outcome	Survived			83(74.1%)
	Died			29(25.9%)

Number & percent for sex, gestational age, diagnosi , use of inotropes and patient outcome, Mean (SD) for parametric data.

SD= standard deviation, n= number, GA= Gestational age, RD= Respiratory distress, IEM=Inborn error of metabolism HDN=Hemorrhagic disease of newborn

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. Mean and SD (1.03(±0.57) vs 1.51(± 0.76) p=0.001 respectively for inotropic use in day 1, 1.09 (±0.57) vs. 1.87 (±0.68) p<0.001 for

inotropic use in day 3, 0.91(±0.53) vs. 1.48 (±0.74) p<0.001 respectively for outcome in day 1. 0.91 (±0.42) vs. 1.82 (±0.69) p<0.001 respectively for outcome in day 3. (Table 2)

The validity of the PI to predict the need for inotropes using the receiver operating characteristics curve revealed a cut off value of ≤1.25 with sensitivity 63.4% and specificity 60.6% for day 1 and ≤1.35 with sensitivity 70.7% and specificity 80.3% for day 3. The validity of the PI to predict mortality using the receiver operating characteristics curve revealed a cut off value of ≤1.25 with sensitivity 75.9% and specificity 61.4% for day1 and <1.35 with sensitivity 86.2% and specificity 78.3% for day 3. Day 3 cut off values revealed to be more sensitive and specific. (Tables 3&4 and figures 1&2)

A significant inverse correlation was found between duration of hospital stay and perfusion index on day 3(r= -0.253, p= 0.007), but not for day 1. (Table 5)

Table 2: Relation between PI and inotropes used and outcome of the neonates at day1 & day 3:

Items		PI day 1		t*	P value	PI day 3		t*	P value
		Mean	SD			Mean	SD		
Inotropes used	No	1.51	0.76	3.53	0.001	1.87	0.68	6.15	<0.001
	Yes	1.03	0.57			1.09	0.57		
Patient Outcome	Survived	1.48	0.74	4.52	<0.001	1.82	0.69	8.36	<0.001
	Died	0.91	0.53			0.91	0.42		

*Student t test P-value > 0.05: Non -significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

Table 3: Validity of PI for prediction of inotropic use at day 1 and day 3:

Test Result Variable(s)	Area Under the Curve					Best cut off value	Sen-sitivity	Spe-cificity
	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval				
				Lower Bound	Upper Bound			
PI score day1	0.694	0.051	0.001	0.595	0.794	≤ 1.25	63.4%	60.6%
PI score day3	0.805	0.043	0.000	0.721	0.889	≤ 1.35	70.7%	80.3%

Table.4: Validity of PI for prediction of mortality:

Test Result Variable(s)	Area Under the Curve					Best cut off value	Sen-sitivity	Spe-cificity
	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval				
				Lower Bound	Upper Bound			
PI day1	0.735	0.052	0.000	0.633	0.837	≤ 1.25	75.9%	61.4%
PI day3	0.859	0.037	0.000	0.786	0.932	<1.35	86.2%	78.3%

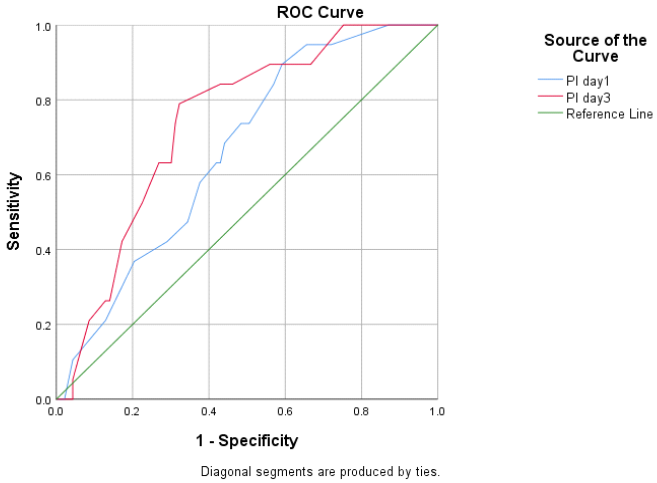

Diagram.1: ROC curve for Validity of PI for prediction of inotropic use at Day 1 and 3.

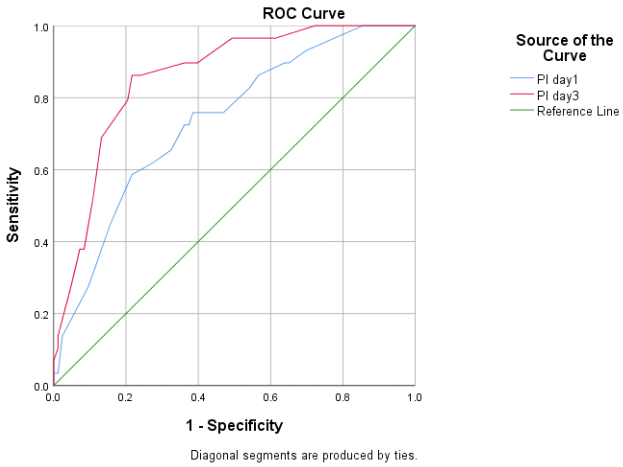

Diagram.2: ROC curve for Validity of PI for prediction of mortality.

Table 5: Correlation between hospital stay and perfusion index (Spearman's correlation):

Hospital stay (day)		
PI day1	r	-0.127
	P value	0.181
PI day3	r	-0.253
	P value	0.007

DISCUSSION:

Prediction of patient's mortality risk and outcome is important for patients and their families, as it allows the medical team to evaluate the patient's prognosis, decide the management plan and help in evaluating the ICU performance[9].

Skin perfusion of neonates is greater than its need of oxygen. When diseases are present cardiac output is redirected to supply the needed oxygen to important organs such as the heart, the brain, and the adrenals. Hence, the monitoring of the PI is of utmost

importance in determining the neonatal status (healthy or ill)[10].

In this prospective study, we studied the total hospital course of 112 neonates admitted to NICU. Perfusion index was used, being an indicator of peripheral circulation, to assess the need of inotropic support, duration of hospital stay and mortality. It was measured in day 1 and day 3 of admission.

PI had a significant relation with the use of inotropes and neonatal outcome. Patients who used inotropes. A cut off value of ≤ 1.25 with sensitivity 63.4% and specificity 60.6% for day 1 and ≤ 1.35 with sensitivity 70.7% and specificity80.3% for day 3. This cut off value for day 1 and especially on day 3 of admission can prompt clinicians in charge of the neonates to reassess the clinical condition of the patient and redirect their management plan to include inotropic support.

A low perfusion index indicates defective peripheral perfusion which indicates that a circulatory compromise is present that has led to deviation of circulation from the unimportant peripheral circulation to the central organs. Physicians should be prompted to reassess the circulatory status of the patient and properly investigate the subtle changes in the vital data that can apprehend the circulatory compromise. If the proper support is not initiated early central perfusion will soon be affected. [4]

Mathew *etal*., noted that there was a significan decrease of PI scores in neonates with clinical signs of shock, who required a bolus of fluids and inotropic support. [2] In **Rasmy *et al*.**'s study, la decreased PI indicated vasopressor need in adults in severe sepsis. A PI ≤ 0.3 had a sensitivity of 100%and specificity of 93% for determining the need for vasopressor. The discrepancy in the cut off value can be attributed to the fact that adults were included to the study which normally tend to have a decreased peripheral circulation than preterm neonates[11].

In assessment of the circulation, **Takahashi et al.[12]** found a positive correlation between PI and flow in the superior vena cava. Scores less than 0.44 are indicators of decreased flow in the superior vena cava in neonates with very low birth weight, indicating a circulatory compromise. [12] The difference in the cut off value is due to the difference in the weight of the neonates enrolled in their study and ours.

Patients who passed away had a significantly lower PI than those who survived in both day 1 and 3. A cut off value of ≤ 1.25 with sensitivity 75.9% and specificity 61.4% for day1 and <1.35 with sensitivity 86.2% and specificity 78.3% for day 3 is indicative of fatal outcome among neonates admitted in NICUs. Day 3 cut off values revealed to be more sensitive and specific than day 1. Day 3 values can also be used to indicate the effectiveness of the management plan given, if the PI doesn't improve above the cut off value reassessment to the treatment should be done.

De felice *etal*., stated a PI of 1.24 is indicative of severe disease in new-born infants[8]/ **Van Laere *etal*.**, reported that PI of decreased readings and decreased variability of short duration on day 1 are linked to adverse neonatal outcome[13].

A significant inverse correlation was found between duration of hospital stay and perfusion index on day 3(r= -0.253, p= 0.007), but not for day 1. No similar studies have assessed this relation before.

PI can be easily used in neonates in NICUs with the predefined cut off values to help clinicians initiate the circulatory support needed to maintain proper circulation. PI should be done on day 1 and confirmed on day 3 of admission. If on day 3 of admission the perfusion index did not improve above the cut off value indicated,

grave prognosis and prolonged hospital would be expected to occur. Prompt management with accurate monitoring of PI and quick decision making is needed to improve neonatal outcome.

Conclusion:

Perfusion index measured in day 1 and more specifically in day 3 of NICU admission can be used to predict the need for inotropic support in neonates. Perfusion index can also predict mortality and duration of hospital stay.

Conflicts Of Interest and Funding:

The authors declare that there were no conflicts of interest. There was no funding for the study from any source.

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صحة مؤشر التروية في التنبؤ بالقصور في الدورة الدموية والوفاة لدى الأطفال حديثي الولادة

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مقدمة: يعد التنبؤ المبكر بالقصور في الدورة الدموية لدى الأطفال حديثي الولادة محور أساسي في تحسين النتائج المرجوة من علاج الأطفال حديثي الولادة. يدل تروية الأنسجة الكافي الى عمل نظام الدورة الدموية بشكل صحيح. يمكن لمؤشر التروية (PI) تحديد حالة تروية الأنسجة المحيطة والتي تعد نافذة على تروية الجسم.

الهدف: التحقق من صحة استخدام مؤشر التروية في التنبؤ بالقصور في الدورة الدموية لدى الأطفال حديثي الولادة ، للمساعدة في توجيه خطة علاج دقيقة , في الوقت المناسب و بشكل صحيح.

الطرق: أجريت هذه الدراسة القائمة على الملاحظة على ١١٢ طفل حديثي الولادة . تم قياس مؤشر التروية في يوم الدخول الطفل وبعد ٣ أيام من الإقامة في المستشفى. تمت متابعة الطفل خلال الأقامة بالمستشفى خاصة الحاجة إلى الأدوية الداعمة الى القلب , مدة الإقامة في المستشفى ونسبة الوفاة.

النتائج: المرضى الذين استخدموا الأدوية الداعمة الى القلب وتوفوا كان لديهم مؤشر التروية أقل بكثير من أولئك الذين لم يستخدموا ذلك في كل من اليوم الأول والثالث خلال الأقامة بالمستشفى. تم العثور على ارتباط عكسي مهم بين مدة الإقامة في المستشفى ومؤشر التروية في اليوم الثالث.

الخلاصة: يمكن استخدام مؤشر التروية كمؤشر مبكر للحاجة إلى إلى الأدوية الداعمة الى القلب, مدة الإقامة في المستشفى ونسبة الوفاة لدى الأطفال حديثي الولادة .