Md. Sihan N et al., J Pediatr Perinatol Child Health 2022
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Table 2: Comparison of baseline characteristics of studied neonates (n=70).

Variable	PDA, no (%) (n=20)	No PDA, no (%) (n=50)	p value
Gestational age			
<32 weeks	6 (30)	14 (28)	0.867^{ns}
32-<37 weeks	14 (70)	36 (72)	
Birth weight			
<1500 gm	8 (40)	26 (52)	0.364^{ns}
1500-<2500 gm	12 (60)	24 (48)	
Gender			
Male	12 (60)	31 (62)	0.877^{ns}
Female	8 (40)	19 (38)	
IDM			
Yes	6 (30)	9 (18)	0.269^{ns}
No	14 (70)	41 (82)	
PIH			
Yes	5 (25)	19 (38)	0.301^{ns}
No	15 (75)	31 (62)	
PROM			
Yes	5 (25)	9 (18)	0.508^{ns}
No	15 (75)	41 (82)	
ACS			
None	10 (50)	22 (44)	0.411^{ns}
Incomplete	2 (10)	12 (24)	
Complete	8 (40)	16 (32)	
Fetal growth			
SGA	3 (15)	11 (22)	0.503^{ns}
AGA	17 (85)	37 (74)	
LGA	0 (0)	2 (4)	

Statistical test: Chi square test, IDM: Infant of diabetic mother, PIH: Pregnancy induced hypertension, PROM: Premature rupture of membrane, ACS: Antenatal corticosteroid, s: Significant, ns: not significant.

Table 3: Perfusion Index level among studied group on Day 1.

PI Level	PDA(n=20)	No PDA (n=50)	p value
Pre ductal PI	1.615 ± 0.370	1.518 ± 0.428	0.378^{ns}
Post ductal PI	0.935 ± 0.343	1.104 ± 0.427	0.120^{ns}
Delta PI	0.680 ± 0.164	0.414 ± 0.129	<0.001^{s}

Data are presented as (mean ± standard deviation). Statistical test: Independent t-test. PI level: Perfusion index level. Delta PI level: Difference between pre and post ductal Perfusion index. s: significant. ns: not significant

Table 4: Perfusion Index level among studied group on Day 3.

PI Level	PDA (n=20)	No PDA (n=50)	p value
Pre ductal PI	1.585 ± 0.363	1.566 ± 0.461	0.870^{ns}
Post ductal PI	0.765 ± 0.380	1.050 ± 0.387	<0.01^{s}
Delta PI	0.820 ± 0.216	0.516 ± 0.255	<0.01^{s}

Data are presented as (mean ± standard deviation). Statistical test: Independent t-test. PI level: Perfusion index level. Delta PI level: Difference between pre and post ductal Perfusion index. s: significant, ns: not significant.

Table 5: Echocardiographic finding among PDA group.

PDA size	HsPDA	Non HsPDA	P value
Ductal diameter	2.409 ± 0.610	0.805 ± 0.487	<0.01^{s}

Data are presented as (mean ± standard deviation). Statistical test: Independent t-test. s: significant, ns: not significant.

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Md. Sihan N et al., J Pediatr Perinatol Child Health 2022
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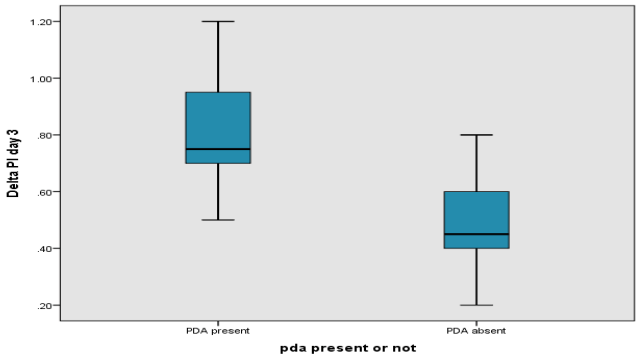

Figure 3: Box diagram of Delta PI among both groups in Day 3.

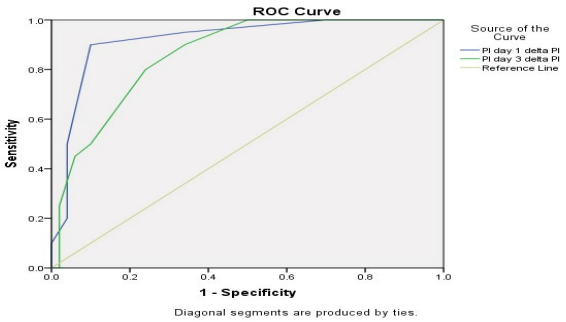

Figure 4: ROC curve for prediction of PDA by ΔPI.

Comparison of preductal and post ductal perfusion index on day 1 between HsPDA and non HsPDA group is presented in Table 6. The pre-ductal PI was slightly higher in the HsPDA group on Day 1 than non-HsPDA group (1.845 ± 0.304 vs. 1.489 ± 0.407). The Post ductal PI of HsPDA group was significantly lower than preductal PI (1.090 ± 0.361 vs. 1.845 ± 0.304). The mean Delta PI in the HsPDA group was higher than the mean DPI in the non-HsPDA group in Day 1 (0.754 ± 0.175 vs 0.440 ± 0.139) indicating the more steal occurring in the Hs PDA group and it is statistically significant. Comparison of preductal and post ductal perfusion index on day 3 between HsPDA and non HsPDA group is presented in Table 4.7. The pre-ductal PI was slightly higher in the HsPDA group on Day 3 than non-HsPDA g r o u p (1.736 ± 0.317 vs. 1.540 ± 0.446). The Post ductal PI of HsPDA group was significantly lower than preductal PI (0.845 ± 0.425 vs. 1.736 ± 0.317). The mean Delta PI in the HsPDA group was higher than the mean DPI in the non-HsPDA group in Day 3 (0.890 ± 0.246 vs 0.549 ± 0.253) indicating the more steal occurring in the Hs PDA group and it is statistically significant. Delta perfusion index (ΔPI) cutoff 0.5 on Day 1 offered a good sensitivity (85%), specificity (89%), positive predictive value (78%), and negative predictive value (93%) with an overall accuracy of 88.5%. The delta perfusion index (ΔPI) cutoff on Day 3 also followed similar trends with 0.7 had good specificity (90%) but less sensitivity (50%), positive predictive value (66.7%), negative predictive value (81.8%) with an overall accuracy of 78.5%.

Data are presented as number (percentage) unless otherwise indicated. IDM: Infant of diabetic mother, PIH: Pregnancy induced hypertension, PROM: Premature rupture of membrane, ACS: Antenatal corticosteroid.

Statistical test: Chi square test, IDM: Infant of diabetic mother, PIH: Pregnancy induced hypertension, PROM: Premature rupture of membrane, ACS: Antenatal corticosteroid, s: Significant, ns: not significant.

Discussion

Patent ductus arteriosus (PDA) is common among preterm babies and a major cause of morbidity and death. When PDA is hemodynamically significant, survival is further compromised. A reduction in PDA related mortality may be possible by identifying PDA earlier and targeting them for optimum management. Currently, echocardiography is the gold standard tool to diagnose PDA. Echocardiography is costly and requires expert cardiologist to perform this procedure. Echocardiography may not be immediately available in many neonatal intensive care units (NICU) of Bangladesh. All neonatal units do have pulse oximeters, which could provide a clue toward the presence of PDA by measuring Perfusion index (PI). This prospective observational study was conducted with an objective to identify PDA by calculating Perfusion index (PI) using pulse oximeter. In this study, total 93 preterm babies were assessed for eligibility. Among these 93 infants 23 were excluded and finally 70 preterm babies were analyzed. Out of them 28.5% had PDA which was similar to a study finding conducted by Benitz W.E. et al., [1] who reported the incidence of PDA ranging from 25%–85% depending on population and diagnostic criteria at first week of life. In our study the incidence of HsPDA was 55% which was also consistent with a study conducted by Hammerman and Kaplan et al., [24]. The increased incidence of hemodynamically significant PDA in this population possibly owing to high incidence of premature delivery (22.3%) and growth restriction (21%) according to Rashed Shah et al. [25] and Bishnupada Dhar et al. [26]. As the availability of echocardiography is not yet available across the country, Perfusion Index, a simple clinical adjunct has been used to suspect its presence.

Specificity and sensitivity of Perfusion Index is proven by several studies and this makes Perfusion Index, a sensitive bedside simple marker important in the early diagnosis of PDA to improve outcomes. In this study, babies <37 weeks old were monitored for the presence of PDA by monitoring Perfusion Index serially. In this present study, the right hand was used to represent preductal site and the right/left foot to represent post ductal site. The baseline characteristics did not differ significantly between the groups. In this study, the pre-ductal PI was higher in the PDA group on Day 1 than non-PDA group (1.615 ± 0.370 vs. 1.518 ± 0.428). The Post ductal PI of PDA group was lower than non-PDA group (0.935 ± 0.343 vs. 1.104 ± 0.427) and it was significantly lower than pre-ductal PI. The mean Delta perfusion index (delta PI) in the PDA group was higher than the mean Delta perfusion index (delta PI) in the non-PDA group in Day 1 (0.680 ± 0.164 vs 0.414 ± 0.129) indicating the steal occurring in the PDA group. Our study finding was consistent with Bianchi et al. [27] who

Md. Sihan N et al., J Pediatr Perinatol Child Health 2022
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Table 6: Perfusion Index level among HsPDA and Non HsPDA group on Day1.

PI Level	HsPDA (n=11)	Non HsPDA (n=9)	p value
Pre ductal PI	1.845 ± 0.304	1.489 ± 0.407	0.035^{ns}
Post ductal PI	1.090 ± 0.361	1.049 ± 0.421	0.759 ^{ns}
Delta PI	0.754 ± 0.175	0.440 ± 0.139	<0.001^{s}

Data are presented as (mean ± standard deviation).Statistical test: Independent t-test, PI level: Perfusion index level, Delta PI level: Difference between pre and post ductal Perfusion index, HsPDA: Hemodynamically significant Patent ductus arteriosus. s: significant, ns: not significant.

Table 7: Perfusion Index level among HsPDA and Non HsPDA group on Day3.

PI Level	HsPDA (n=11)	Non HsPDA (n=9)	p value
Pre ductal PI	1.736 ± 0.317	1.540 ± 0.446	0.171^{ns}
Post ductal PI	0.845 ± 0.425	0.991 ± 0.399	0.274^{ns}
Delta PI	0.890 ± 0.246	0.549 ± 0.253	<0.01^{s}

Data are presented as (mean ± standard deviation), Statistical test: Independent t-test , PI level: Perfusion index level, Delta PI level: Difference between pre and post d`uctal Perfusion index , HsPDA: Hemodynamically significant Patent ductus arteriosus. s: significant, ns: not significant.

Table 8: Screening analysis of delta PI (ΔPI) in diagnosing PDA using the most suitable cut-off point.

	Cut-off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
ΔPI D1	0.5	85%	89%	78%	93%	88.50%
ΔPI D3	0.7	50%	90%	66.70%	81.80%	78.50%

found lower Post ductal PI in babies who required medical closure of PDA (PI 1.29 ± 0.35) or multiple medical treatment/surgical ligation of PDA (PI 1.19 ± 0.20) as compared with babies with spontaneous closure of PDA (PI 1.56 ± 0.55).

This study had higher pre-ductal perfusion index in PDA as well as HsPDA group. Table 4.4 showed the Comparison of preductal and post ductal perfusion index on day 3 between PDA and no PDA group. The pre-ductal PI was slightly higher in the PDA group on Day 3 than non-PDA group (1.585 ± 0.363 vs. 1.566 ± 0.461). The Post ductal PI of PDA group was significantly lower than preductal PI (0.765 ± 0.380 vs. 1.585 ± 0.363). The mean delta perfusion index (delta PI) in the PDA group was higher than the mean delta PI in the non-PDA group in Day 3 (0.820 ± 0.216 vs 0.516 ± 0.255) indicating the steal occurring in the PDA group. Terek et al. [28] also found lower post ductal PI on Day 1 in babies with HsPDA which was similar to our study findings. They also concluded that it becomes normalized after treatment. The mean delta perfusion index (delta PI) in the HsPDA group (Day 1: 0.754 ± 0.175, Day 3: 0.890 ± 0.246) was higher than the mean delta perfusion index in the non HsPDA group (Day 1: 0.440 ± 0.139, Day 3: 0.549 ± 0.253), indicating the more steal occurring in the HsPDA group. This finding was consistent with Khositseth et al. [21] who studied Delta Perfusion Index in 30 preterm infants on Days 1, 3 and 7. On Days 1 and 3 of life, the Delta perfusion index of infants with HsPDA [1.57%, interquartile range (IQR) 0.28–2.32, n ¼ 14, and 1.32%, IQR 0.28–1.83, n ¼ 10] was significantly higher than those without HsPDA (0.14%, IQR 0.03 to 0.30, n ¼ 16, and 0.08%, IQR 0.07 to 0.26, n ¼ 20), p ¼ 0.009 and 0.005, respectively. Granelli and Ostman-Smith et al. [18] found a median perfusion index of 1.70% (IQR, 1.18–2.50) in 10,000 normal newborns at 1st week of age. Cresi et al. [29] reported perfusion index measured at either foot in clinically and hemodynamically stable preterm infants in the first week of life (day 1, 3, and 7 of life) and concluded that perfusion index could be used as an indirect and noninvasive measurement of peripheral perfusion at specific monitoring sites. To use Delta Perfusion Index (delta PI) as a bedside tool for diagnosing PDA, there is need of having a cutoff value. The Delta Perfusion Index (delta PI) cutoff of 0.5 on Day 1 offered a good sensitivity (85%), specificity (89%) and predictive values, while decreasing the cutoff to 0.4 the sensitivity increases to 95% at the cost of specificity 66%.

In this study considering use of 0.4 cutoff in NICU where it is possible to confirm PDA by echo before treatment. However, if echo is not possible or if interpretation of echo is difficult, it would be safer to use the 0.5 cutoff with specificity of 89% before treatment. The Delta perfusion index cutoff on Day 3 also followed similar trends with 0.7, who had good specificity (90%) but less sensitivity (50%). While consider a cutoff of 0.65 had improved sensitivity (80%) at the cost of specificity (76%). However, Day 1 Delta Perfusion Index was more sensitive and specific than Day 3 Delta Perfusion Index. This suggests that it is possible to predict the occurrence of PDA on the first day of life. Khositseth et al. [21] showed that at all time points (Days 1, 3 and 7 of life), Delta Perfusion Index >1.05% had sensitivity, specificity, positive predictive value and negative predictive value of 66.7%, 100%, 100% and 86.4%, respectively. In our study to detect HsPDA, cutoff for delta perfusion index to diagnose HsPDA was lower than other study. This study adds to the existing evidence that Delta Perfusion Index could be useful adjunct for bedside diagnosis of PDA. This study shows that delta perfusion index is a good surrogate marker for diagnosing PDA as well as HsPDA.

Md. Sihan N et al., J Pediatr Perinatol Child Health 2022
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If ductus arteriosus steal a large volume of left ventricular output, it would be at the cost of systemic distal perfusion and thereby reflected in Perfusion Index. When pre-ductal and post-ductal sites are monitored for perfusion, a difference could give insights into the amount of steal and thereby hemodynamic significance.

This study, to the best of my knowledge, is the first study of Perfusion Index in PDA in Bangladesh. In a country where rate of prematurity is high, and preterm infants are being managed in NICU and other centers without universal access to echocardiography but with pulse oximeter, this study could identify the group of babies who would need referral for evaluation and management of PDA. This would result in better and cost-effective management. The other strength of the study is that all perfusion indexes were recorded by the principal investigator. There was no inter-observer bias. Despite some limitations, this study had identified a simple bedside investigation available to all secondary and tertiary care centers, not requiring intensive training for diagnosing PDA.

Conclusion

Assessment of the difference between pre ductal perfusion index and post ductal perfusion index (Delta Perfusion Index -ΔPI) can be used as a diagnostic tool to identify Patent Ductus Arteriosus in preterm infants.

Limitation of the Study

- Single centered study.
- Echocardiographic examination was not done by same cardiologist.

Recommendation

- Delta perfusion index (ΔPI) can be a diagnostic tool to identify PDA in preterm neonates where echocardiography is not available.
- Further multicenter study with large sample size is recommended to validate the present study.

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