



**" HEMODYNAMICALLY SIGNIFICANT PATENT DUCTUS ARTERIOSUS":
INDICATOR TO DETERMINE NEONATAL WELL BEING.**

Moonisah Rafiq*	MD Department of Radiology, SKIMS SOURA, J&K, INDIA. *Corresponding Author
Sheikh Riaz Rasool	MD (Professor), Department of Radiology, SKIMS SOURA, J&K,INDIA.
Javaid Iqbal	MD Department of Radiology, SKIMS SOURA, J&K, INDIA.
Naseer Ahmad Choh	MD (Professor), Department of Radiology, SKIMS SOURA, J&K,INDIA

ABSTRACT

Introduction: The Patent ductus arteriosus is associated with hemodynamic alteration in preterm newborns has been linked to neonatal morbidity and mortality, although yet controversial. We aimed to investigate the relationship between hemodynamically significant PDA and morbidity in a prospective preterm study group. **Methods:** A prospective study including neonates consecutively admitted to neonatal intensive care unit (NICU) with gestational age of <32weeks over a period of two years, subsequently segregated into hemodynamically significant Patent ductus arteriosus (hsPDA) and hemodynamically insignificant PDA (hisPDA) cases and further assessed the relation of hsPDA with morbidity and mortality of preterm newborns. **Results:** We considered 70 newborns eligible for our study. 34 were males (48.6%) and 36 were females (51.4%) ,with mean Gestational age of 29 weeks (range from 27-31 weeks) with mean birth weight of 1025 gm ranged from 860-1180 gm (+/-0.142).The median Apgar score at 1min was 6 (0-10) and at 5mins was 9 (range 7-10). 56 (80%) preterm infants were having PDA and 14 cases(20%) were without PDA. The hemodynamically significant PDA was present in 18 cases and 38 cases were having hemodynamically insignificant PDA. Among the 18 cases of hsPDA 14 (77.8%) were females and 4 (22.2%) were males. The morbidity and mortality was statistically significant in hsPDA patients. Multivariate analysis showed that morbidity significantly depend on hsPDA. **Conclusion:** The occurrence of the main morbidities of prematurity depend on hsPDA . Persistence of a hsPDA in preterm low birth weight infants increases the potential for cerebral injury due to shunting of blood through the hsPDA and alterations in cerebral perfusion and have a higher risk for intraventricular haemorrhage , Respiratory Distress Syndrome, Bronchopulmonary Dysplasia, Necrotising enterocolitis.

KEYWORDS : Necrotising enterocolitis (NEC), Bronchopulmonary Dysplasia (BPD), Respiratory Distress Syndrome (RDS), Intraventricular haemorrhage (IVH).

INTRODUCTION

The World Health Organisation (WHO) defines preterm birth as any birth before 37 completed weeks of gestation⁽¹⁾. The Ductus Arteriosus is a central vascular shunt connecting the pulmonary artery to the aorta, allowing oxygenated blood from the placenta to bypass the uninflated fetal lungs and enter the systemic circulation. Failure of ductus arteriosus closure, termed patent ductus arteriosus (PDA), is primarily an affliction of prematurity, with the ductus. Before the use of antenatal corticosteroids⁽²⁾.

Cerebral Hemodynamics In Newborn Infants

Arterial hemodynamics in the cerebral circulation are affected by normal maturational events in the healthy new-born. Persistence of a hemodynamically significant patent ductus arteriosus (hsPDA) in preterm very low birth weight (VLBW) infants may increase the potential for cerebral injury due to left-to-right shunting of blood through the hsPDA and alterations in cerebral perfusion.

Preterm infants with a hsPDA have lower regional cerebral oxygenation levels and have a higher risk for intraventricular haemorrhage (IVH), cerebral white matter injury^(2,3), Respiratory Distress Syndrome, Bronchopulmonary Dysplasia, Necrotising enterocolitis (NEC), Gastroesophageal reflux (GER).

The purpose of this study was to investigate the association between presence of hsPDA and the occurrence of morbidities in very low birth weight (VLBW) newborn with Gestational age \leq 32weeks.^(4,5,6,7)

Study Methods:

This is a prospective longitudinal study. All the Preterm infants of less than 32weeks of Gestational age admitted in NICU were included in the study. Preterm infants with congenital

malformations and chromosomal anomalies (Patent Ductus Arteriosus was not considered a congenital malformation in this cohort of very preterm infants) were excluded from the study. All the preterm infants included in the study during the study period were subjected to echocardiographic assessment for anatomical, physiological and hemodynamic assessment of PDA, results were compare, and further were segregated into hsPDA and hemodynamically non significant PDA.

The Patent Ductus Arteriosus Was diagnosed by cardiologist and the following criteria was deemed to label the PDA as hemodynamically significant which included, Ductal Size >2mm, Left atrium to aortic root diameter of >1.6, and pulsatile flow pattern of Patent ductus arteriosus. The Patency and the direction of the ductal shunt were evaluated by colour flow mapping, with parasternal short axis view The Demographic, perinatal and postnatal data was also taken into account and its association with hemodynamically significant PDA was ascertained. Informed consent for the study was obtained from the parents and infants were studied in presence of at least one parent. Studies were performed with the infants either sleep or eyes open with no gross body movements.

Demographic, Perinatal And Postnatal Data:

Demographic, Perinatal and Postnatal Data was also collected which included gender, birth weight, gestational age, mode of delivery, Apgar score at 1 min and at 5 mins, antenatal steroids, presence of respiratory distress and need for respiratory support and mode of respiratory support, duration of mechanical ventilation and duration of oxygen therapy, presence of germinal matrix haemorrhage, sepsis, necrotising enterocolitis, bronchopulmonary dysplasia and survival or death.

Data Analysis

The data was analysed by the principal investigator with advice from a statistician.

Descriptive data were analysed by frequencies and categorical data by percentages and continuous variables by means and standard deviations. Continuous variables were compared using Student's t test (for parametric test) or Mann-Whitney U test (for non-parametric test) as appropriate. Group comparisons were done by χ^2 tests. For Qualitative data, chi-square test or Fisher's exact test have been performed as appropriate.

For all comparisons, a p value of less than 0.05 was considered to indicate a statistical significance. All statistical analyses were done by the SPSS statistical software (release 23.0, SPSS Inc.; Chicago, III).

OBSERVATIONS AND RESULTS

We considered 70 newborns eligible for our study. We also took patient characteristics including demographic, perinatal and postnatal data and following results were obtained;

Out of 70, 34 were males (48.6%) and 36 were females (51.4%), with mean Gestational age of 29 weeks (range from 27-31 weeks) with mean birth weight of 1025 gm ranged from 860-1180 gm (+/-0.142).The median Apgar score at 1min was 6 (0-10) and at 5mins was 9 (range 7-10).49 (%) infants were born by caesarean section and 21 (%) were born vaginally. All the preterms enrolled had undergone institutional delivery. Out of 70, 40patients were administered with prenatal steroids.

56 (80%) preterm infants were having PDA and 14 cases(20%) were without PDA. The hemodynamically significant PDA was present in 18 cases and 38 cases were having hemodynamically insignificant PDA. Among the 18 cases of hsPDA 14 (77.8%) were females and 4 (22.2%) were males

Common complications associated with hsPDA were:

Mild respiratory distress syndrome was present in 1 patient (5.6%) and Severe RDS was present in 17 patients (94.4%). 17 patients (94.4%) required mechanical ventilation, 10 patients were given Non-invasive positive pressure ventilation. Germinal matrix haemorrhage was present in 10(55.5%) hsPDA patients .NEC was present in 8cases (44.4%). Sepsis in 14 patients (77.8%) and Bronchopulmonary dysplasia was present in 2 patients (11.1%) among the 18 hsPDA patients. Only 2patients were administered with prenatal steroids.14 patients among hsPDA were given surfactant.All the hsPDA patient received hospital stay for significant duration of time which last for >3days. Out of 18hsPDA patients 8 (44.4%) were discharged and 10 patients (55.6%) got expired.

DISCUSSION

In our study population with gestational age of <32weeks, occurrence of main morbidities of prematurity seems to be associated with HsPDA. We found that hsPDA represents a risk factor for the occurrence of prolonged ventilation, BPD, IVH, ROP and hypotension.

However we experience different scenario for birth weight in our study, the mean birth weight was 1047 grams (ranging from 700-1350gms) in the study group. mean Birth weight in case of hsPDA was 9978gms +/- 142 gm and the Mean birth weight of hsPDA patients were 1063 gms +/- 121 gm with p-value of 0.06 (>0.05), which reveal that there is no statistical significance of PDA with respect to birth weight. Our findings were in concordance with the study conducted by **Reem M. Soliman et al**⁽⁸⁾ who found the association of birth weight with PDA was insignificant.

Among 70 cases ,36 were female (51.4%) and 34 were males (48.6%) with mean Gestational of 29 weeks (range from 27-31

weeks) fig 1. 56 (80%) preterm infants were having PDA and 14 cases (20%) were without PDA. The hemodynamically significant PDA was present in 18 cases and 38 cases were having hemodynamically insignificant PDA (Table-1). Among the 18 cases of HsPDA 14 (77.8%) were females and 4(22.2%) were males. Our results showed that PDA is more prevalent in females than males, which is in concordance to the study done by **maria livia ognean, et al.**⁽⁹⁾ who found PDA prevalent in females.

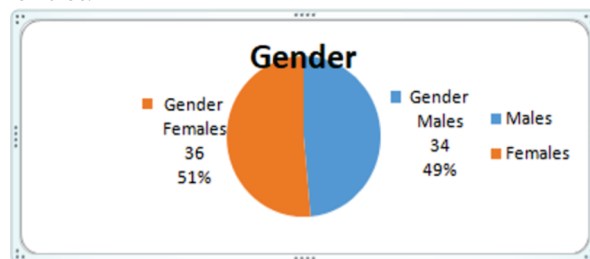


Fig.1: Pie chart depicts distribution of patients with respect to gender. (p-value 0.01)

Table 1: Showing Presence And Absence Of Pda And Hspda In Study Group:

		HAEMODYNAMICALLY SIGNIFICANT PDA		Total
		Absent	Present	
PDA	Absent	14	0	14
		26.9%	0.0%	20.0%
	Present	38	18	56
		73.1%	100.0%	80.0%
Total		52	18	70
		100.0%	100.0%	100.0%

P-value 0.009

we observed that the preterm infants with PDA were associated with relative poor Apgar score of <5 at 1 min (ranging from 3-7) when compared to non-PDA cases. Among the PDA cases the Apgar score was more towards lower side with mean score of <4 at 1min. 55% of the hsPDA were associated with Apgar score of 3, 12% with 5 and 43% with Apgar score of 7, where as the mean Apgar score in non PDA patients was 6 at 1 min . These results are complemented by the study done by **Reem M. Soliman et al.**⁽⁸⁾ who found the poor Apgar score in PDA patients than in non-PDA patients with median Apgar score of <5 at 1 min.

The Comorbidities of the study population: (Table-1)

1. Respiratory distress syndrome:

The respiratory distress syndrome was present in all the 70 preterm cases. Among 18 hsPDA 17patients (94%) presented with Moderate-Severe RDS and 1 patient (6%) was with mild RDS, and among 52 hisPDA patients 38 pts (73%) were having moderate to severe RDS and 14 pts (27%) presented with mild RDS. The Severity of RDS was more marked in case of hsPDA Infants which shows positive correlation with Significant p value- 0.05. Our results are complemented by many previous studies. **Fujji et al**⁽¹⁰⁾ conducted a study on 50 preterm infants, they found that infants with PDA were associated with greatest risk of RDS than non-PDA patients.

2. Ventilation requirements:

Among 70 preterm infants, 48pts (68.6%) required mechanical ventilation, among 18hsPDA patients 17 (94.4%) were put on mechanical ventilation and among 52 hisPDA cases, 38 (73.1%) cases required mechanical ventilation. The preterm babies having hsPDA had more RDS and complications, therefore the need for mechanical ventilation (94.4% vs 73.1%, p-value 0.05) and CPAP/NIPPV were higher in hsPDA patients compared to Non-PDA patients. Our results are in

concordance with the study done by Okur et al,⁽¹¹⁾ who reported similar results and found that duration of mechanical ventilation was longer in hsPDA group when compared with non-hsPDA group.

3. Necrotising Enterocolitis:

Among the 52 hisPDA, 10 (55.6%) presented with NEC and 8 (44.4%) hsPDA presented with NEC. However there was no correlation between NEC with PDA with statistically insignificant p-value 0.25. Our study was in concordance with study done by Reem M Soliman Et al.⁽⁶⁾ conducted study in 150 preterm infants they found NEC in 19.5% PDA cases and 21.5% Non-PDA cases with insignificant p value – 0.767.

4. Sepsis:

Sepsis was present in 77.8% of HSPDA cases and 50% in hisPDA patients. There was a positive correlation between Sepsis and hsPDA with p-value 0.03. our findings were complemented by previous studies done by Visconti et al who found more infants suffering from late sepsis in hsPDA group.

5. Germinal matrix-intraventricular Haemorrhage:

Among the (70 cases) 13 patients (30.6%) presented with IVH, Out of 18 hsPDA patients 10 cases (55%) were having IVH, and only 3patients with hisPDA presented with IVH.

5 patients presented with Grade I IVH, 3patients with Grade II IVH, 5 patients with Grade III IVH. There was a positive correlation of IVH with hsPDA which was statistically significant (p value <0.05). The hsPDA were relatively associated with severe IVH (Grade-3) in one-third of the cases (33%). Our results were in concordance with the study conducted by Heather O’Leary et al⁽¹²⁾ they found significant association between high magnitude cerebral pressure passivity (increased RI values) with Development of GMH/IVH.

6. Bronchopulmonary dysplasia:

In our study group Bronchopulmonary dysplasia was present in 11.1% of HSPDA cases and 3.8% in hisPDA patients, which was statically significant with p-value of 0.04. Our findings are consistent with results of study done by Ronald et al⁽¹³⁾ they concluded that hsPDA was associated with increased risks of BPD but only when infants required intubation >= 10days.

Table 2: Reveals the morbidity associated with hemodynamic significant patent ductus arteriosus.

n- Number of cases n=70	hisPDA cases		hsPDA cases		P -value
	present	absent	present	absent	
1. Moderate-Severe RDS	38 (73.1%)	14 (26.9%)	17 (94.4%)	1 (5.6%)	0.05
2. Ventilation req. (CPAP/NIPPV)	38 (73.1%)	14 (26.9%)	17 (94.4%)	1 (5.6%)	0.05
3. NEC	15 (28.8%)	37 (71.2%)	8 (44.4%)	9 (55.6%)	0.25
4. Sepsis	26 (50%)	26 (50%)	14 (77.8%)	4 (22.2%)	0.036
5. GMH/IVH	3 (5.7%)	49 (94.3%)	10 (55.5%)	8 (44.5%)	0.05
6. BPD	2 (3.8%)	50 (96.2%)	2 (88.9%)	16 (88.9%)	0.005

7. Duration of NICU stay:

Among 18 hsPDA, the duration of stay in 5 patients (27.8%) was 3days-1wk, 9patients (50%) with 1-2weeks , 4 patients (22.2%) with >2weeks. The duration of stay in hisPDA patients was 0-3days in 11 pts (21.2%), 3days-1week in 15 patients (28.8%), 1-2weeks in 13patients (25%), >2weeks in 13 patients (25%). Among the hsPDA infants there was longer duration of

stay compared to non/hsPDA patients. Our finding were in concordance to the study done by okur et al⁽¹¹⁾ and another study done by soliman etal.⁽⁸⁾

8.Outcome of Study group:

Among 70 cases, 26 patients (37.1%) got expired among which 10 patients (55.6%) were having hsPDA and 16 patients (30.8%) were hisPDA/nonPDA. We found that more preterm infants with hsPDA got expired as compared to hisPDA/non PDA patients (55.6% vs 30%, p-value 0.05). This was attributed to more respiratory and cerebral complications associated with hsPDA. Our results were in complete agreement with studies done by Okur et al. and Visconti etal^(11,14) which found that preterm cases with hsPDA are associated with higher mortality rate than hisPDA patients.

Table 3: Depicting The Outcome In Hemodynamically Significant Pda :

Outcome	Discharge	HEMODYNAMICALLY SIGNIFICANT PDA		Total
		Absent	Present	
Death		36	8	44
		69.2%	44.4%	62.9%
Total		16	10	26
		30.8%	55.6%	37.1%
		52	18	70
		100.0%	100.0%	100.0%

P- value 0.05

SUMMARY AND CONCLUSION

PDA remains an important condition among premature infants. The ductus arteriosus shunt play a significant contributory role in pathophysiology of key hemodynamic complications known to occur during this time, and in turn contributes to the significant morbidity and mortality

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