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Original Article

Relationship between Retinopathy of Prematurity (ROP) and Bronchopulmonary Dysplasia (BPD): A Retrospective-Analytical Study

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Abstract

Background: Retinopathy of prematurity (ROP) and Bronchopulmonary dysplasia (BPD) share the common risk factors of perinatal inflammation and oxidative stress exposure. Moreover, both diseases have a genetic background. **Aim of work**: is to explore the ROP prevalence and severity among preterm infants diagnosed with BPD and to identify and examine the shared risk factors. **Patients and methods:** This was a retrospective case-control study consisting of 44 preterm infants with BPD and 62 gestational age-matched controls. Infants' birth and postnatal medical records were revised. **Results:** BPD and ROP corresponded with the duration of administration of CPAP, oxygen blender, head box, incubator oxygen, mechanical ventilation, duration of admission, oxygenation, caffeine citrate, TPN, administration and duration of inhaled steroids, inotropic support, surfactant administration, PDA, ICH, PRBCs and plasma transfusion, LOS and infectious episodes. Severe cases of ROP occurred in BPD cases, and this connection extended to varying grades in both diseases. The use of inotropic support was the most predisposing factor to BPD. By contrast, utilizing mechanical ventilation was the most predisposing factor to ROP. **Conclusions:** BPD and ROP share common risk factors, and there is a connection between them in regard to the varying grades of severity. Though, hemodynamic instability, longer inotropic support, hemodynamically significant PDA, prolonged mechanical ventilation act as cofactors.

Key words: BPD, ROP, inotropic support, preterms, mechanical ventilation

Introduction

Retinopathy of prematurity (ROP) is a developing retina disease. More premature neonates are predisposed to severe stages of ROP [1,2]. Despite it being the leading cause of infantile blindness all over the world, the disease is avoidable [3,4]. There has been an increase in global incidence [3] and severity [4] of ROP. Consequently, ROP is a significant disease that deserves further concern.

Bronchopulmonary dysplasia (BPD) is one of the commonest complication of prematurity with a rising global incidence. There is an inverse proportionality between the incidence of BPD on one hand, birth weight and gestational age on the other [5,6]. BPD and ROP share common risk factors of inflammation and oxidative stress exposure [7–11]. Moreover, both diseases have a genetic background [12,13]. Results from a previous study conducted at our center established a relationship between the incidences of ROP among BPD patients [14]. Therefore, it was decided that this connection should be investigated further.

The aim of this study is to research the ROP prevalence and severity among preterms diagnosed with BPD and to examine the shared risk factors between ROP and BPD

Methods

This case-control study consisted of 44 preterm infants (cases) of less than or equal to 32 weeks gestation who had developed BPD and were admitted to the Neonatal Intensive Care Unit (NICU) of Aburreesh El-Mounira, Cairo University Children Hospital between January 1, 2019, and December 31, 2020. In addition, 62 gestational age-matched controls who were admitted during the same period were also included in the study. Infants who died before being diagnosed with BPD and newborns with congenital anomalies were excluded. In all preterms, the presence and staging of

ROP in both eyes were documented retrospectively.

Risk factors associated with the development of BPD and ROP were documented in accordance with medical records, and the shared risk factors were identified. The data analyzed included gestational age in weeks, birth weight in grams, sex, duration of admission in days, early onset sepsis (EOS), late onset sepsis (LOS) and premature rupture of membranes (PROM), patent ductus arteriosus (PDA), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), duration of mechanical ventilation, CPAP, oxygen blender, head box and incubator oxygen. In addition, the duration of oxygen in days, duration of TPN, caffeine citrate, and inotropes together with inhaled steroids were documented. Moreover, surfactant therapy, the number of blood transfusions and infectious episodes were also documented.

BPD diagnosis and severity were determined by using BPD severity-based criteria proposed by the National Institute of Child Health and Human Development (NICHD) [15]. At the time of diagnosis, infants who did not require oxygen were considered as mild BPD cases. Moderate BPD was considered for cases requiring less than 30% oxygen, and severe BPD was considered for cases needing positive pressure and/or oxygen support ≥30% [15].

ROP was diagnosed by a neonatologist and confirmed by an ophthalmologist according to the American Academy of Ophthalmology definition [16]. Based on the diagnosis and staging of ROP, all preterm infants were classified into the following groups: absent, low grade (stage 1 or 2) severe ROP (more than stage 2 with or without plus disease).

Sepsis was considered following a positive blood culture result and evident symptoms. Early-onset sepsis is sepsis occurring before seven days and late-onset sepsis is sepsis occurring seven days or more after birth. NEC was considered according to symptoms,

radiographic findings, and the staging criteria modified by Bell et al. [17]. Moreover, PDA was considered by assessing symptoms and echocardiography results. Furthermore, Intracranial hemorrhage (ICH) was identified by performing a brain ultrasound [18–20].

Ethical considerations

This study's protocol was accepted by the Ethical Committee of the Faculty of Medicine, Cairo University, and corresponded with the provision of the Declaration of Helsinki in 1964 and its later amendments or comparable ethical standards. Informed signed consent was collected from the parents of each preterm before their inclusion in the study

Statistical analysis

Data analysis was studied using the IBM SPSS Statistics program version 21. Quantitative variables were displayed as mean, standard deviation (SD), median, and interquartile range (IQR), while qualitative variables were defined as numerical values and percentage. Comparison between quantitative variables was done using independent T test if variables were normally distributed or using mannwhitney test in case of non-normally distributed variables A chi-square test was employed to compare qualitative variables and the Pearson correlation coefficient (PCC) was used to test the linear relationship between variables. Post hock test with Bonferroni adjustment was used in comparing qualitative variables of more than two categories. A p-value less than or equal to 0.05 was considered significant. In contrast, a p-value less than or equal to 0.01 was deemed highly significant. Multiple stepwise backward logistic regressions were conducted to detect the significant predictors for BPD and ROP.

NB Stepwise regression was conducted through several steps. In each step, the insignificant variables were excluded from the model. Accordingly, those reported in the last

step were only the significant variables.

Results

During the two-year study period, 106 premature infants with less than or equal to 32 weeks gestation were included in the study. There were 44 cases and 62 gestational age-matched controls as shown in figure (1). The BPD cases when compared to controls: (a) average gestational age was 30.77±1.41 (mean ± standard deviation); (b) average birth weight in grams was 1262.56±216.7; (c) average admission period in days was 59.25±24.31; median48(40.5:79) (d) average duration of oxygen in days was 44.68±20.3; median 38(32:47) (e) average duration of mechanical ventilation, CPAP, oxygen blender, head box, and incubator oxygen were 24.18 ± 22.67 median 13(7:35), 15.11 ± 9.2 , median 14.5 (11:18), 8.18±4.43, median 8.5 (6:12), 3.09 ± 2.24, median 3(1:5), 2.91 ± 2.15, median 3(1.5:4), respectively. Furthermore, the average duration of TPN in days was 24.73±15.17 median 22.5(12:40); (f) average duration of caffeine citrate was 42.68±22.84; median37.5(23.5:54) (g) average intake of inotropes duration in days was 14.11±10.02; median16(11:24) (h) average inhaled steroids duration in days was 27.23±17.9 median 23(14:38); (i) the average BPD regimen duration in days was 14.7±9.8 Finally, (j)the average infectious episodes were 3.5±1.66 ,median 3(2:5); and the average intake of PRBCs was 2.67±1.8 median 2(1:4) times as shown in Table 1(A)

BPD cases were significant to birth weight in grams and intake of PRBCs with a p value of 0.004 for both. BPD cases were highly significant ($p < 0.001$) to admission duration, oxygenation duration, durations of mechanical ventilation, CPAP, oxygen blender, head box and incubator oxygen. BPD cases were highly significant too to durations of total parenteral nutrition and medications administration in the form

of caffeine citrate, inotropes, and inhaled steroids(P<0.001). BPD cases correlated highly to plasma intake and infectious episodes (p<0.001) as shown in Table 1(A).

BPD cases were consistent with administration of TPN regardless of duration (p0.029) and were highly significant (p<0.001) to administration of mechanical ventilation, CPAP, inhaled steroids and inotropic support regardless of duration too. Regarding the clinical course of the preterms involved, surfactant administration, presence of PDA, development of NEC, IVH, and pneumothorax correlated significantly to BPD (p<0.001) as shown in Table 1(B).

ROP cases were correlated with administration of oxygen blender (p 0.003) head box (p0.005), incubator oxygen (p 0.012), inotropic support (p 0.01), surfactant (p0.004), and plasma transfusion (p 0.004). Presence of PDA (p0.036) and development of IVH (0.042) correlated too to ROP cases. They highly correlated with administration of mechanical ventilation, CPAP, inotropic support, inhaled steroids, PRBCs transfusion and BPD regimen (p<0.001). Presence of PDA and development of LOS highly correlated with ROP (p<0.001) as shown in Table 2(A). Distribution of ROP cases is displayed in figure (2)

ROP cases showed statistical significance to birth weight (p0.025) and duration of incubator oxygen (p0.019). They were highly significant to durations of ; admission, oxygenation, oxygen blender and CPAP administration (p0.001). They were also highly significant to durations of; mechanical ventilation (p0.004), head box (p0.002), caffeine citrate (p0.005) and total parenteral nutrition. Regarding infectious episodes ROP cases were highly significant to them (p0.003) as shown in Table 2(B)

Both BPD and ROP corresponded with the durations of the administration of CPAP, oxygen blender, head box, incubator oxygen, mechanical

ventilation, duration of admission, oxygenation, caffeine citrate, TPN, administration and duration of inhaled steroids, inotropic support, surfactant administration, PDA, ICH, PRBCs and plasma transfusion, LOS and infectious episodes as shown in Table (1) and Table (2). Severe cases of ROP occurred in BPD cases, and this connection extended to varying grades of both diseases as shown in Table (3) and Figure (3). The use of inotropic support was the most predisposing factor to BPD as shown in the multiple regression analysis in Table (4) The model showed significance for BPD at X2 (85.71) and p-value <0.001. Significant predictors in the model were PDA, intake of inotropes, ROP and the duration of admission in days. The most significant predictor was the intake of inotropes denoting that patients who took inotropes were five times more prone to develop BPD than those who did not (OR 5.959). By contrast, utilizing mechanical ventilation was the most predisposing factor to ROP according to the multiple regression analysis. Significant predictors for ROP in the model were mechanical ventilation, oxygen intake and admission duration in days. The most significant predictor was mechanical ventilation (MV). This confirmed that patients who were mechanically ventilated were five times more prone to develop ROP than those who were not (OR 5.959) as shown in Table (5)

Discussion

Our study revealed a link between the incidence of ROP in preterm infants with the incidence of BPD. This is consistent with the findings presented by Guven et al., [21], Kornacka et al., [22], Higgins et al., [23] and Leviton et al., [24]. The presence of BPD necessitates oxygen therapy that in turn results in increased incidences of ROP due to immaturity of the antioxidant systems together with the use of steroids. Unfortunately, targeting oxygen saturation below 90% is correlated with a higher risk of death [25]. Therefore,

neonatologists are obliged to target higher levels, especially ROP is treatable. Consistent with the study results, severe cases of ROP occurred in BPD cases, and this relationship extended to varying grades of both diseases. This finding corresponded with the results of Krzysztofowicz et al., and many other studies [26-29].

According to Shah et al., [28] and Allegaert et al., [29], it was concluded that extended duration of mechanical ventilation and/or nasal continuous airway pressure (nCPAP) played a significant role in developing severe forms of ROP. Yang et al., [30] and Seiberth et al., [31] concluded that mechanical ventilation increases the severity of ROP. Previous studies [32–34] concluded that developing BPD and ROP is affected by free radicles generated secondary to oxygen excess and increased partial oxygen pressure during mechanical ventilation and oxygenation. This primarily applied to this study, where both BPD and ROP were associated with durations of CPAP, oxygen blender, head box, incubator oxygen and mechanical ventilation, admission duration and oxygenation. Another explanation is that it may be related to the fact that our center is a tertiary center. The nature of the cases referred to us from other hospitals under weak transport facilities exposes patients to alternate episodes of hypoxia, hyperoxia, hypothermia and hypotension, and this adds to the unstable preterm infants from the start. Mohamed et al., [35] mentioned that alternating hypoxia and hyperoxia were more dangerous than hypoxia or hyperoxia alone. As for BPD, alternating hypoxia and hyperoxia precipitates oxidative stress causing more cellular and pulmonary inflammation. In case of ROP, after weaning from oxygen the retina becomes relatively hypoxic inducing angiogenic factors causing vasoproliferation of retinal vessels and worsening of the grades of ROP[35],[36]. In addition, Yue et al., [37] stated that smaller gestational age, lower blood

pressures, decreased Apgar score at 5 min, increased respiratory rate, patent ductus arteriosus, increased C-reactive protein levels, all of which were classified as significant risk factors of adopting mechanical ventilation in preterms. These factors were shared by the vast majority of preterms included in our study, many of whom ended up in mechanical ventilation, which may impose a clue to ending up in both diseases.

Both BPD and ROP were associated with the administration and duration of caffeine citrate and inhaled steroids [14], which is typically the routine for younger preterms that require a longer duration of admission and respiratory support. Extended caffeine and inhaled steroids duration reflected a younger preterm. In an animal study, Poon et al., [38] discovered that hyperoxia could cause injury to the brain, lungs and retinas, adding that more significant lung injuries were correlated with more significant retinal and brain injuries.

Both BPD and ROP share common pathogenesis [39-45], and both have dysfunction of angiogenic signaling pathways [39-50], disruption of which causes altered development and vasculature of both retinal and pulmonary vessels.

According to Podraza et al., [27], Del Vecchio et al., [51], Fortes et al.,[52], Northway et al.,[53], Englert et al., [54], and Gomaa & Abdelkhalik [55], frequent blood transfusions were found to increase the risk of both BPD and ROP, and these results were confirmed in this study. Oxidative injury caused by a blood transfusion increases non-transferrin bound iron. Furthermore, the inflammatory mediators present in stored blood products may explain the association between ROP and BPD on one hand and plasma transfusion on the other. However, another explanation may be due to the use of plasma and PRBCs as colloids during resuscitation of unstable preterms with hypotension. Blood transfusions increase the risk

of ROP by two mechanisms: (a) by an increase in retinal oxygen supply and (b) by an increase in oxygen free radicals through free iron overload.

In the multiple regression analysis, PDA was found to be a risk factor for BPD and this coincided with Kim et al., Ding et al., and Abuelhamd et al., [56-58]. Terrin et al., [59] stated that hemodynamically unstable PDA is a predictor for BPD, IVH, ROP, increased mechanical ventilation duration and hypotension and added that together with birth weight, gestational age, and prenatal steroids, there is a significant association between hypotension and hemodynamically unstable PDA that may partly explain the higher incidence of inotropic support and duration in this study. El Sayed and Fraser [60] stated that hemodynamic instability caused by PDA may predispose to a variety of organ injuries causing clinical complications. Additionally, ROP was an independent risk factor in our study. The intake of inotropes and the duration of admission in days [58]were independent risk factors for BPD. The intake of inotropes was the most significant predictor denoting that preterms who received inotropes were five times more likely to develop BPD than those who did not [61]. Whether this is solely related to inotropes, hemodynamic instability and hypotension [56] associated with prematurity or with a hemodynamically significant PDA needs further investigation. Regarding ROP, mechanical ventilation, intake of oxygen and the duration of admission in days were independent risk factors in the multiple regression analysis, with mechanical ventilation being the most significant factor.

Ventilated preterms were five times more likely to develop ROP than those who were not ventilated. This was in accordance with a study conducted by Madhu et al., [62].

Limitations: The limitation of this retrospective study is the improper

recording of data that would have helped achieve better results. Moreover, better outcome would have have been achieved with more number of patients

Conclusions

BPD and ROP share common risk factors, and there is a connection between them as regards the varying grades of severity. Though, there is some evidence that hemodynamic instability, longer inotropic support, hemodynamically significant PDA, prolonged ventilation act as cofactors between both diseases.

Recommendations

It is of the utmost importance to limit duration of admission, oxygenation, ventilation and TPN. Emphasis should be made on judicious use of inotropes and minimizing their duration to the least possible. Beginning with the end in mind, should be the slogan when ventilating a neonate or administering inotropes. Though, we have to admit a compromise is difficult owing to the link between inotropes, PRBCs and plasma transfusions on one hand together with ROP and BPD on the other. Further research is needed to correlate between ROP and BPD and the aforementioned results

Abbreviations

BPD: Bronchopulmonary Dysplasia

ROP: Retinopathy of Prematurity

EOS: Early-Onset Sepsis

LOS: Late-Onset Sepsis

NEC: Necrotizing Enterocolitis

PDA: Patent Ductus Arteriosus

ICH: Intracranial Hemorrhage

IUGR: Intra-Uterine Growth Restriction

TPN: Total Parenteral Nutrition

GA: Gestational Age

BW: Birth Weight

RBC: Red Blood Cells

PRBC: Packed Red Blood Cells

NICU: Neonatal Intensive Care Unit

CPAP: Continuous Positive Airway Pressure

MV: Mechanical Ventilation

PROM: Premature Rupture of membranes

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Author's contributions

NG: Data collection, acquisition, design of the study, interpretation of data, drafting, writing, revising, finally approving the manuscript for submission and publication. AS: Data collection, acquisition, interpretation of data, drafting, revising and final approval of manuscript for submission and publication

Conflict of interest

The authors have no conflict of interests to declare.

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Table 1A: Clinical and demographic data of cases and controls

Item		Control	Case	p-value
Gestational age in weeks	Mean± SD	31.15±1.14	30.77±1.41	0.211
	Median (IQR)	32(30:32)	31(30:32)	
Birth weight in grams	Mean± SD	1374.84±168.78	1262.56±216.7	0.004**
	Median (IQR)	1370(1260:1480)	1300(1100:1450)	
Multiple Gestation	Mean± SD	0.31±0.53	0.45±0.7	0.294
	Median (IQR)	0(0:1)	0(0:1)	
Duration of Oxygen in days	Mean± SD	11.06±7.99	44.68±20.3	<0.001**
	Median (IQR)	12(4:18)	38(32:47)	
CPAP Duration	Mean± SD	4.05±3.99	15.11±9.22	<0.001**
	Median (IQR)	4(0:7)	14.5(11:18)	
Blender Duration	Mean± SD	3.11±2.57	8.18±4.43	<0.001**
	Median (IQR)	3(1:5)	8.5(6:12)	
Mechanical Ventilation Duration	Mean± SD	4.73±2.57	24.18±22.67	<0.001**
	Median (IQR)	4(3:7)	13(7:35)	
Head box Duration	Mean± SD	1.47±1.51	3.09±2.24	<0.001**
	Median (IQR)	1(0:2)	3(1:5)	
Incubator Oxygen Duration	Mean± SD	1.63±1.66	2.91±2.15	<0.001**
	Median (IQR)	1(1:2)	3(1.5:4)	
Total Parenteral Nutrition duration in days	Mean± SD	8.69±6.01	24.73±15.17	<0.001**
	Median (IQR)	9.5(5:13)	22.5(12:40)	
Intake of Plasma	Mean± SD	0.84±1.36	4.07±4.24	<0.001**
	Median (IQR)	0(0:1)	2.5(1:7)	
Maternal age	Mean± SD	27.16±4.87	25.5±4.87	0.087
	Median(IQR)	27(23:31)	24(22:30)	
Infectious episodes	Mean± SD	1.5±1.02	3.55±1.66	<0.001**
	Median (IQR)	2(1:2)	3(2:5)	
Duration of caffeine citrate	Mean± SD	27±11.86	42.68±22.84	<0.001**
	Median (IQR)	24(19:30)	37.5(23.5:54)	
Inotropes Duration in days	Mean± SD	6.69±4.27	17.25±8.23	<0.001**
	Median (IQR)	5(4:9)	16(11:24)	
Intake of PRBCS	Mean± SD	1.6±1.17	2.67±1.8	<0.004**
	Median (IQR)	1(1:2)	2(1:4)	
Inhaled Steroids Duration	Mean± SD	10.75±4.44	28.52±17.28	<0.001**
	Median (IQR)	12(7:14)	23(14:38)	

*significant **highly significant

Table 1B: Continued Clinical and Demographic Data between cases and controls

Item	Controls=62 N(%)	Cases=44 N(%)	P value
Sex			
Female	30(48.3%)	23(52.3%)	0.691
Male	32(51.7%)	21(47.7%)	
CPAP	40(64.5%)	42(95.5%)	<0.001**
Blender	49(79%)	39(88.6%)	0.149
MV	11(17.7)	28(63.6)	<0.001**
Head Box	41(66.1)	35(79.5)	0.131
Incubator Oxygen	49(79)	37(84.1)	0.512
Early Onset Neonatal Sepsis	25(40.3)	25(56.8)	0.094
Late onset Neonatal Sepsis	43(69.4)	43(97.7)	<0.001**
Patent Ductus Arteriosus	8(12.9)	28(63.6)	<0.001**
Development of pneumothorax	0(0)	11(25)	<0.001**
Necrotizing Enterocolitis	4(6.5)	23(52.3)	<0.001**
Intake of Inhaled steroids	40(64.5)	42(95.5)	<0.001**
Intake of Surfactant	5(8.1)	20(45.5)	<0.001**
Total Parenteral Nutrition	48(77.4)	41(93.2)	0.029*
Severity of ROP			
Absent ROP	33(53.2)	5(11.4)	<0.001**
Low grade ROP	24(38.7)	32(72.7)	
Severe ROP	5(8.1)	7(15.9)	
Intraventricular hemorrhage	8(12.9)	18(40.9)	<0.001**
Intake of Inotropes	15(24.2)	36(81.8)	<0.001**
Intake of Inhaled steroids	40(64.5)	42(95.5)	<0.001**

*significant **highly significant

Table 2A: Clinical and demographic data associating ROP cases

Item	ROP N(%)		P value
	Absent N=38	Present N=68	
Sex			
Female	19(50)	34(50)	0.316
Male	19(50)	34(50)	
Premature Rupture Of Membranes	8(21.1)	13(19.1)	0.694
Antenatal Steroid Use	8(21.1)	22(32.3)	0.257
Patent Ductus Arteriosus	8(21.1)	28(41.2)	0.036*
Necrotizing Enterocolitis	6(15.8)	21(30.9)	0.087
Intraventricular hemorrhage	5(13.2)	21(30.9)	0.042*
Development of pneumothorax	1(2.6)	10(14.7)	0.93
Early Onset Neonatal Sepsis	15(39.5)	35(51.5)	0.235
Late Onset Neonatal Sepsis	27(71.1)	59(86.8)	0.047*
CPAP	22(57.9)	60(88.2)	<0.001**
Oxygen blender	26(68.4)	62(91.2)	0.003**
Mechanical Ventilation	5(13.2)	34(50)	<0.001**
Head box	21(55.3)	55(80.9)	0.005**
Incubator Oxygen	26(68.4)	60(88.2)	0.012*
Total Parenteral Nutrition intake	30(78.9)	59(86.8)	0.293
Intake of BPD regimen	3(7.9)	31(45.6)	<0.001**
Intake of Inotropes	12(31.6)	39(57.4)	0.011*
Intake of RBC	20(52.6)	57(83.8)	<0.001**
Intake of plasma	16(42.1)	48(70.6)	0.004**
Intake of Inhaled steroids	22(57.9)	60(88.2)	<0.001**
Intake of Surfactant	3(7.9)	22(32.4)	0.004**

*significant **highly significant

Table 2B: Clinical and demographic data associating ROP cases

Item	**ROP Absent**	**ROP Pesent**	P value
	Median(IQR)	Median(IQR)	
Gestational age in weeks	32(31:32)	31(30:32)	0.108
Duration of admission in days	28.5(24:40)	43.5(32.5:59)	0.001**
Birth weight in grams	1355(1300:1500)	1300(1155:1450)	0.025*
Duration of oxygen in days	10(0:20)	30(17:43)	0.001**
CPAP duration	4(0:7)	11(4:16)	0.001**
Blender duration	3(0:6)	6(3:9)	0.001**
Mechanical ventilation duration	8(5:8)	19(9:37)	0.004**
Head box duration	1(0:2)	2(1:4)	0.002**
Incubator oxygen duration	1(0:2)	2(1:4)	0.019*
Infectious episodes	2(1:3)	2(2:4)	0.003**
Total parenteral nutrition duration	11(5:13)	14(8:28)	0.008**
BPD regimen duration	10(10:10)	10(6:27)	0.604
Duration of caffeine citrate	23(19:31)	28(23:44)	0.005**

*significant **highly significant

Table 3: Severity of BPD in relation to ROP

Item	**Severity of ROP**						**P value**
Severity of BPD	**Absent ROP**		**Low grade ROP**		**Severe ROP**		
	N	**%**	**N**	**%**	**N**	**%**	
Absent BPD	33	86.8	24	42.9	5	41.7	0.002**
p-value	<0.001		0.0005		0.194		
Mild	1	2.6	1	1.8	1	8.3	
p-value	0.689		0.920		0.617		
Moderate	4	10.5	16	28.6	4	33.3	
p-value	0.036		0.072		0.764		
Severe	0	0	15	26.8	2	16.7	
p-value	<0.001		0.012		0.134		

** Highly Significant;
Bonferroni adjusted p value= 0.000417

Table 4: Multiple regression analysis to detect the predictors of BPD

Item	B	p-value	OR	95% C.I. for OR	
				Lower	Upper
PDA	1.599	0.02*	4.949	1.289	19.001
Intake of Inotropes	1.785	0.008**	5.959	1.597	22.232
ROP	1.644	0.021*	5.177	1.279	20.949
Duration of admission in days	0.095	0.003**	1.1	1.034	1.17
Constant	-6.953	0	0.001		

*significant **highly significant

Variable(s) entered on step 1: Birth weight in grams, MV, Incubator oxygen, Late onset neonatal Sepsis, TPN, PDA, Intake of Inotropes, Intake of Surfactant, ROP, Duration of admission in days.

Table 5: Multiple regression analysis to detect the predictors of ROP

Item	B	p-value	OR	95% C.I.for OR	
				Lower	Upper
Mechanical Ventilation duration	1.672	0.004**	5.323	1.689	16.777
Duration of Oxygenation	1.555	0.012*	4.736	1.405	15.957
Duration of admission in days	0.043	0.009**	1.044	1.011	1.078
Constant	-2.857	0.001**	0.057		

*significant **highly significant

Variable(s) entered on step 1: Birth weight in grams, Mechanical Ventilation duration, Incubator Oxygen, Late onset neonatal Sepsis, TPN, PDA, Intake of Inotropes, Intake of Surfactant, Duration of admission in days.

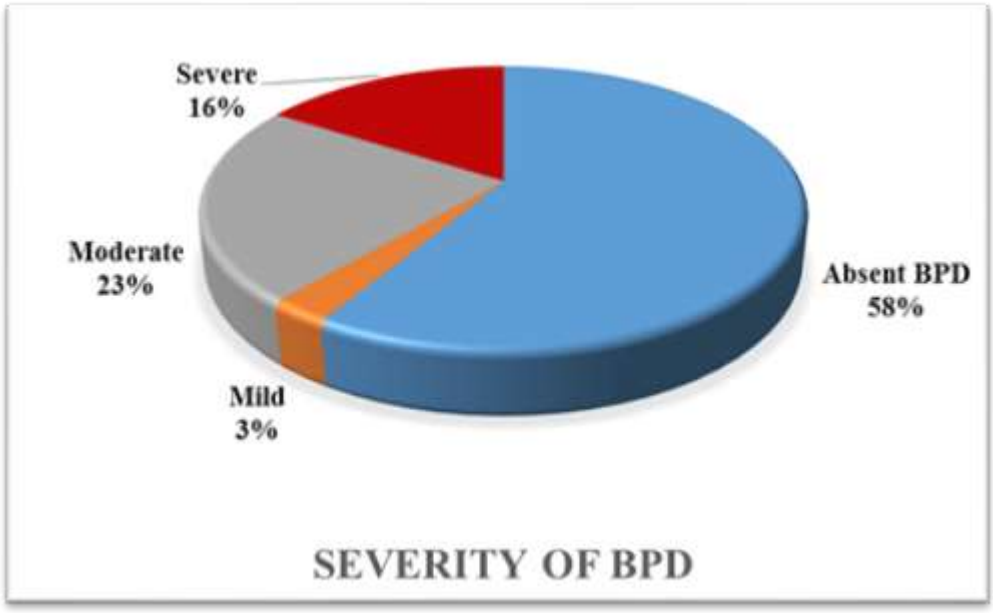

Figure (1) Distribution of BPD cases

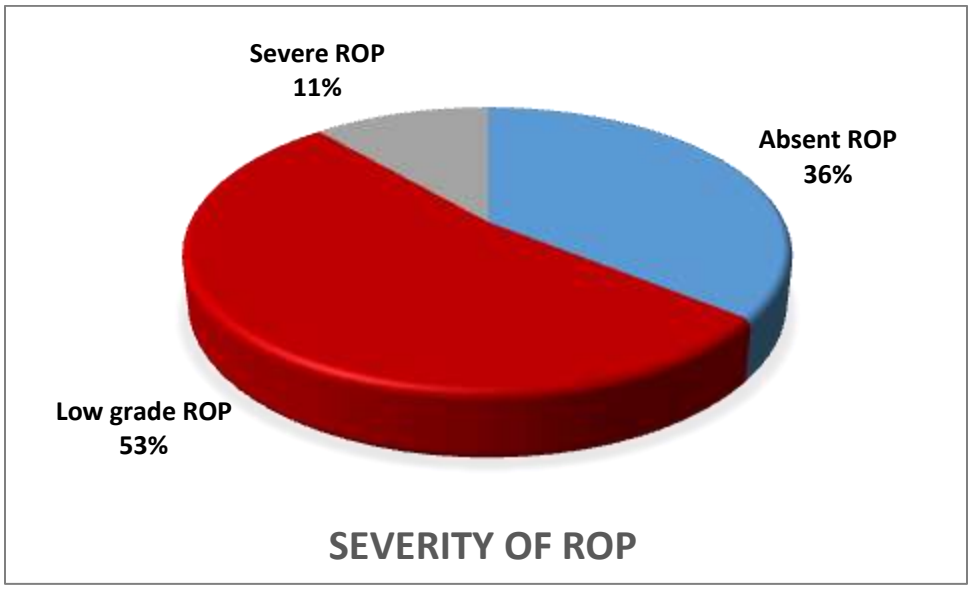

Figure (2) Distribution of ROP cases

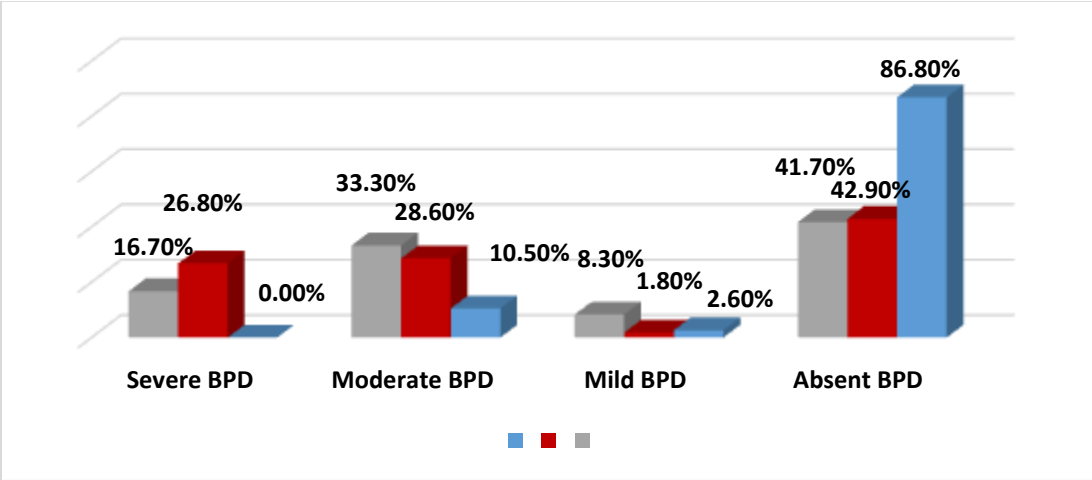

Figure (3) Varying grades of severity of ROP in relation to BPD severity

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