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ORIGINAL RESEARCH

Incidence of retinopathy of prematurity among preterm babies undergoing treatment at a tertiary healthcare center's neonatal intensive care unit

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Abstract
Background: Retinopathy of Prematurity (ROP) is a significant cause of visual impairment in preterm infants. This study aims to determine ROP incidence, associated risk factors, and their correlation with disease severity.
Methods: A prospective cohort study was conducted in a tertiary care center. Preterm infants were screened for ROP based on gestational age, birth weight, and risk factors. Data were analyzed using descriptive and inferential statistics.
Results: The study included 122 preterm infants. ROP incidence inversely correlated with birth weight and gestational age. Factors like parenteral nutrition, phototherapy, septicemia, apnoeic spells, and oxygen administration were significantly associated with ROP. Maternal factors showed no significant association. Blood transfusion did not correlate with ROP.
Discussion: The study confirms low birth weight and gestational age as significant risk factors for ROP. Some neonatal factors like apnea and oxygen administration were associated with ROP, while others like blood transfusion showed no significant association. Maternal factors did not significantly influence ROP incidence.
Conclusion: ROP remains a concern in preterm infants, with significant associations found with certain neonatal factors. Tailored screening protocols and multidisciplinary management involving neonatologists and ophthalmologists are recommended for effective prevention and management of ROP.
Keywords: Retinopathy of Prematurity, preterm infants, risk factors, neonatal care, screening, phototherapy, oxygen administration.

Introduction

Retinopathy of Prematurity (ROP) is a vasoproliferative disorder that affects the retina of premature newborns, potentially leading to visual impairment. Initially described in 1984, ROP has a complex pathogenesis influenced by several factors, including oxygen levels.

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Paradoxically, after exposure to high oxygen levels, premature infants experience relative anoxia when returned to normal atmospheric conditions, leading to abnormal vessel growth, retrolental fibrous tissue formation, and retinal detachment[1].

Key risk factors for ROP include low birth weight, low gestational age, and oxygen exposure. Other potential risk factors, such as sepsis, blood transfusions, multiple births, and maternal conditions like preeclampsia and placental issues, require further study[2].

Three ROP epidemics have occurred in developed and medium-developed countries, linked to oxygen therapy use and improved survival rates of extremely low birth weight infants. The first epidemic was noted in the 1940s-1950s when oxygen therapy was introduced. A second epidemic in the 1970s-1980s correlated with the survival of more extremely low birth weight infants. Currently, a third epidemic is observed in medium-developed countries. Effective screening and cooperation between ophthalmologists and neonatologists are crucial for timely intervention[3].

The international classification system for ROP[4], established in 1984, divides the retina into three zones and stages the disease based on vascular changes:

- **Zone I**: Posterior pole, extending twice the distance from the disc to the macula.
- **Zone II**: Extends to the nasal ora serrata and approximately to the anatomic equator.
- **Zone III**: Remaining temporal crescent of the retina anterior to Zone II.

Stages of ROP are:

1. **Stage 1**: Demarcation line separating avascular from vascularized retina.
2. **Stage 2**: Ridge formation with height and width.
3. **Stage 3**: Ridge with fibrovascular proliferation.
4. **Stage 4**: Partial retinal detachment.
5. **Stage 5**: Total retinal detachment, often funnel-shaped.

"Plus" disease indicates advanced vascular changes, while "Pre-Plus" disease represents a spectrum of vascular abnormalities that may progress to Plus disease. Aggressive posterior ROP (AP-ROP) is a severe, rapidly progressing form requiring immediate attention.

In 1987, the classification was expanded to detail retinal detachment:

- **Stage 4A**: Extrafoveal retinal detachment.
- **Stage 4B**: Partial retinal detachment involving the fovea.
- **Stage 5**: Total retinal detachment.

ROP management includes regular follow-up examinations based on retinal findings and the stage of the disease. Criteria for ceasing follow-ups include reaching Zone III retinal vascularization without prior Zone I or II ROP, full retinal vascularization, or a postmenstrual age of 45 weeks without severe ROP.

Residual changes in regressed ROP include vascular and retinal alterations, increased myopia, astigmatism, anisometropia, amblyopia, nystagmus, strabismus, cataract formation, corneal abnormalities, and a higher risk of glaucoma. These complications underscore the need for comprehensive long-term care for affected infants[5].

Enhanced neonatal care in countries like India has increased ROP incidence, highlighting the necessity for improved screening and reporting to manage this condition effectively[6-8].

Aims and objectives

The aim of this study is to determine the incidence of Retinopathy of Prematurity (ROP) in preterm babies, study associated risk factors, and correlate these factors with disease severity and progression.

Material and methods

A prospective cohort study was conducted in the Department of Ophthalmology and NICU of UPUMS, Saifai (Etawah).

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Inclusion Criteria
Screening for ROP was performed in preterm neonates born <34 weeks gestation and/or <1750 grams birth weight, and in babies 34-36 weeks gestation or 1750-2000 grams birth weight with risk factors like respiratory distress, sepsis, multiple blood transfusions, multiple births, and apneic episodes. The first retinal examination was conducted by 4 weeks of age or 30 days of life for infants born ≥28 weeks, and by 2-3 weeks for those <28 weeks or <1200 grams.

Exclusion Criteria
Babies who died before examination, did not complete follow-up, had other ocular disorders, or lacked consent were excluded.

Informed Consent
Informed consent was obtained from guardians, explaining the examination's nature, frequency, and possible complications.

Dilating Procedure
Tropicamide 0.5% with phenylephrine 2.5% or cyclopentolate 0.5%-1.0% were used for pupil dilation. Care was taken to avoid systemic absorption.

Examination Protocol
Examinations were conducted in the NICU or eye department, ensuring a warm, clean environment. Indirect ophthalmoscope with 20D or 28D/30D lens was used, with infants evaluated for retinal abnormalities according to ICROP guidelines. Follow-up examinations were based on initial findings.

Statistical Methods
Descriptive and inferential statistical analyses were performed. Continuous measurements were presented as Mean ±SD, while categorical measurements were presented as Number (%). Significance was assessed at a 5% level using Chi-square/Fisher Exact test and multivariate logistic regression for risk factor prediction. Sample size was calculated using population proportions with a critical value of 1.96 at a 95% confidence interval. The statistical tests included the Chi-Square Test to assess the relationship between categorical variables, the Fisher Exact Test to evaluate contingency tables for treatment outcomes, and multivariate logistic regression to predict ROP using various risk factors. Statistical significance was categorized as suggestive ($p: 0.05<p<0.10$), moderate ($p: 0.01<p\leq0.05$), and strong ($p: p\leq0.01$). The software used for the analysis included SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0, and R ver.2.11.1. Microsoft Word and Excel were utilized for documentation.

Results
Table 1: Incidence of ROP and Neonatal Factors

Variable	Subcategory	Total Patients	ROP Patients	Incidence of ROP	P Value
Birth Weight (gms)	750-1000	2	2	100%	-
	1001-1250	6	3	50%	-
	1251-1500	12	2	17%	-
	1501-1750	15	1	7%	-
	1751 onwards	16	1	6%	-

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Gestational Age (weeks)	≤28	4	3	75%	-
	29	4	1	25%	-
	30	3	1	33%	-
	31	4	1	25%	-
	32	13	2	15.38%	-
	33	7	1	14.28%	-
	34	4	0	0%	-
	35	6	0	0%	-
	36	6	0	0%	-
Gender	Males	69	14		0.48
	Females	53	8		
Parenteral Nutrition	PN present	17	5		0.002
	PN absent	98	2		
Phototherapy	PhT present	41	12		0.02
	PhT absent	81	10		
Septicemia	SEP present	36	12		0.008
	SEP absent	86	10		
Apnoeic Spells	APN present	20	10		0.0003
	APN absent	102	12		
Oxygen Administration	O2 given	62	17		0.004
	O2 not given	60	5		
Respiratory Distress	RD present	48	12		0.14
	RD absent	74	10		
Chronic Lung Disease	CLD present	12	2		1.00
	CLD absent	110	20		
Blood Transfusion	BT present	29	5		1.00
	BT absent	83	17		

The table 1 provides an analysis of the incidence of Retinopathy of Prematurity (ROP) among 122 preterm infants, considering various neonatal factors and their association with ROP. The incidence of ROP is inversely related to birth weight. Infants weighing between 750-1000 grams showed the highest incidence of ROP at 100%, while those weighing 1751 grams or more had a significantly lower incidence of 6%. Similarly, ROP incidence decreases with increasing gestational age. Infants born at 28 weeks or earlier had a 75% incidence of ROP, while those born at 34 weeks or later had no cases of ROP. Gender did not show a significant association with ROP (p=0.48). Factors like parenteral nutrition (p=0.002), phototherapy (p=0.02), septicaemia (p=0.008), apnoeic spells (p=0.0003), oxygen administration (p=0.004) were significantly associated with ROP. However, variables like respiratory distress (p=0.14), chronic lung disease (p=1.00), and blood transfusion (p=1.00) did not show a significant association with ROP.

Table 2: Maternal Factors and Association with ROP

Variable	Subcategory	Total Patients	ROP Patients	P Value
Leaking per vaginum (LPV)	LPV present	20	5	0.55
	LPV absent	102	17	
Bleeding per vaginum (BPV)	BPV present	19	2	0.52
	BPV absent	103	20	
Pre-eclamptic toxaemia (PET)	PET present	19	2	0.68
	PET absent	103	20	

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Placenta previa (PP)	PP present	19	2	0.52
	PP absent	103	20	
Abruption placenta (ABP)	ABP present	19	2	0.52
	ABP absent	103	20	
Meconium-stained liquor (MSL)	MSL present	19	5	0.33
	MSL absent	103	17	
Multiple Births (MB)	MB present	19	2	0.52
	MB absent	103	20	
Seizure Disorder	Seizure present	19	2	0.52
	Seizure absent	103	20	
Icterus	Icterus present	34	8	0.44
	Icterus absent	86	14	
Cyanosis	Cyanosis present	19	2	0.52
	Cyanosis absent	103	20	
Congenital Malformation (CM)	CM present	20	2	0.52
	CM absent	102	20	

The table 2 presents an analysis of the association between various maternal factors and the incidence of Retinopathy of Prematurity (ROP) among 122 preterm infants. The incidence of ROP was not significantly associated with leaking per vaginum (LPV) (p=0.55), bleeding per vaginum (BPV) (p=0.52), pre-eclamptic toxaemia (PET) (p=0.68), placenta previa (PP) (p=0.52), and abruption placenta (ABP) (p=0.52). However, meconium-stained liquor (MSL) showed a suggestive association with ROP (p=0.33), with a slightly higher incidence in infants exposed to meconium-stained liquor. Multiple births (MB) and seizure disorder did not show a significant association with ROP (p=0.52 for both). Icterus, or jaundice, also did not exhibit a significant association with ROP (p=0.44). Similarly, cyanosis (p=0.52) and congenital malformations (p=0.52) did not show a significant association with ROP. Overall, maternal factors like LPV, BPV, PET, PP, and ABP did not significantly influence the incidence of ROP in preterm infants. However, there was a suggestive association with meconium-stained liquor. Multiple births, seizure disorder, icterus, cyanosis, and congenital malformations also did not show significant associations with ROP.

Figure 1 shows the mean birth weight of the 122 babies was1250gms ranged from(750-1750gms) . The babies were divided into 2 groups on the basis of their birth weight.when we compared the incidence of ROP with babies birth weight≤1250gms (n=19)and>1250gms(n=103) the former had higher significant higher incidence (pvalue =0.0002)

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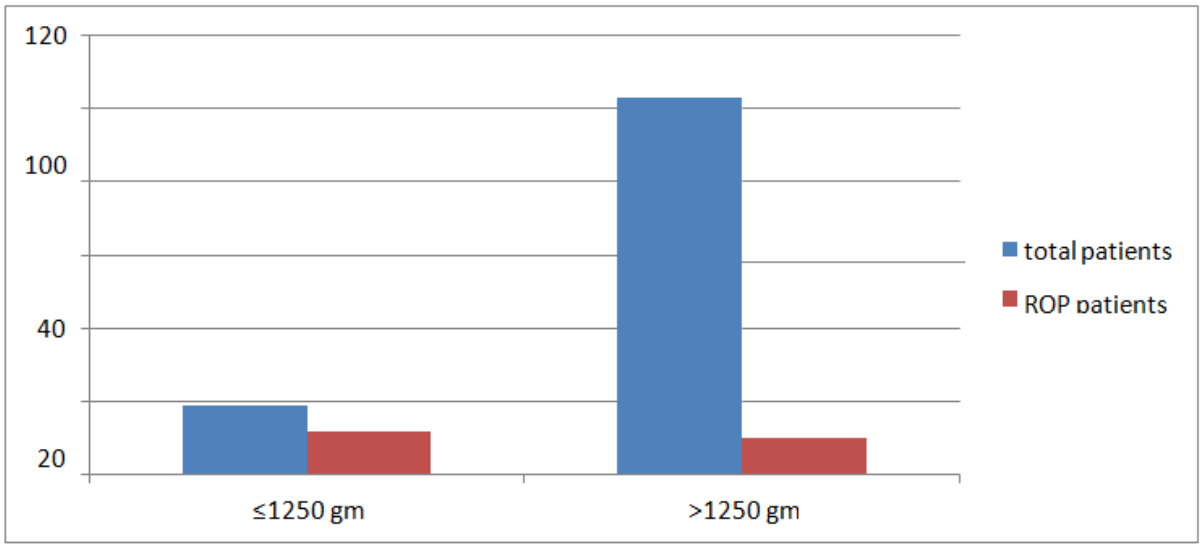

Figure 1 - Incidence of ROP in different ranges of birth weight.

Discussion

Retinopathy of prematurity (ROP) remains a significant concern in neonatal care, particularly with the increasing survival rates of extremely preterm infants. This discussion aims to analyze various factors associated with ROP incidence based on the findings of the study, along with relevant literature references.

ROP, a leading cause of childhood blindness, has garnered attention globally, with initiatives like WHO's VISION 2020 program emphasizing its control and prevention through early screening and treatment. The study reported an ROP incidence of 18.03%, consistent with previous Indian studies (Cooke et al.) and some foreign data (Salks et al.), suggesting variability in incidence rates across regions and over time[9-11].

Maternal risk factors like abruptio placentae, placenta previa, and others were explored but were not significantly associated with ROP in this study, consistent with findings from other authors. The association between maternal hypertension and ROP has conflicting evidence in literature, with some studies suggesting a risk while others showing a protective effect (Sullivan et al.)[12].

Low birth weight and low gestational age are well-established risk factors for ROP. The study confirmed these associations, with ROP occurring more frequently and more severely in infants with lower birth weight and gestational age, aligning with other Indian studies (Sumes et al.)[13]. However, setting the upper limit of gestational age for screening remains a balance between cost-effectiveness and risk[14,15].

Multiple gestations were not significantly associated with ROP in this study, contrary to some literature suggesting higher risk in second-born twins due to low birth weight (Garcia et al.)[16]. Similarly, factors like seizures, cyanosis, and congenital malformations did not show significant associations with ROP in this study.

Various neonatal factors like apnea, oxygen administration, sepsis, and others were investigated. Apnea was significantly associated with ROP, consistent with previous studies suggesting its role in ROP development (Larsen et al.)[17]. Oxygen administration showed a significant association, reflecting the historical understanding of oxygen as a risk factor for ROP, despite challenges in defining safe oxygen levels.

The role of blood transfusions in ROP development is controversial. While some studies suggest a significant association (Friving et al.)[18], this study did not find a statistically significant link. The study's protocol of prophylactic vitamin E supplementation might have influenced the low ROP incidence observed.

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Conclusion

The study highlights ROP's significant impact on preterm infants, with an 18.03% incidence in our tertiary care center. Factors like lower gestational age and birth weight were associated with higher ROP rates, while gender showed no significant difference.

Maternal factors such as hypertension, bleeding per vaginum (BPV), and neonatal factors like multiple births, seizure disorder, and congenital malformations didn't correlate with ROP. However, phototherapy, apnea, and septicemia were significantly associated with ROP development, emphasizing careful management.

Oxygen administration was linked to ROP, though not influencing disease severity. Surprisingly, blood transfusion showed no significant association with ROP, challenging previous findings.

Recommendations

It includes tailored screening protocols starting at 3-4 weeks postnatal age and considering additional indicators like plus disease. A multidisciplinary approach involving neonatologists and ophthalmologists is vital. Each nursery should establish screening programs based on its risk population to ensure timely intervention and prevent blindness. Careful neonatal management, cautious phototherapy and oxygen use, and monitoring for apnea and septicemia are crucial in ROP prevention.

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