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ORIGINAL ARTICLE

Frequency of retinopathy of prematurity in preterm low birth weight vs preterm very low birth weight admitted to Abbasi Shaheed Hospital, Karachi, Pakistan.

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ABSTRACT… Objective: To determine the prevalence of retinopathy of prematurity (ROP) in preterm low birth weight (LBW) versus very low birth weight (VLBW) among admitted infants. **Study Design:** Prospective Observational study. **Setting:** The Pediatric Department, Abbasi Shaheed Hospital, Karachi, Pakistan. **Period:** January 2025 to June 2025. **Methods:** A total of 100 preterm newborns (50 LBW, and 50 VLBW) of any gender, admitted to the NICU within 48 hours, and without congenital ocular abnormalities were included. All infants were examined and managed for ROP using standard protocols. Data were analyzed using SPSS version 26.0. Stratification of effect modifiers was done to observe their effect on ROP. Inferential statistics were applied taking p<0.05 as significant. **Results:** In 100 preterm newborns, 51 (51.0%) were females, and the mean age was 11.4±5.5. ROP was found in 61 (61.0%) infants. Those with ROP had significantly lower birth weight (1390.2±286.8 g vs 1604.6±361.3 g, p=0.001) and gestational age (29.7±2.0 vs 31.1±1.1 weeks, p<0.001), with VLBW seen in 67.2% versus 23.1% without ROP (p<0.001). Cesarean section delivery (80.3% vs 43.6%, p<0.001), lower Apgar scores, surfactant (34.4% vs 7.7%, p=0.002), steroid use (9.8% vs 0%, p=0.047), longer oxygen therapy and NICU stay, and all deaths (14.8%) were significantly associated with ROP. **Conclusion:** There is a substantial burden of ROP among preterm VLBW infants, with key risk factors including lower gestational age, lower birth weight, and prolonged oxygen therapy.

Key words: Apgar Score, Cesarean Section, Low Birth Weight, Mortality, Retinopathy of Prematurity.

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INTRODUCTION

Retinopathy of prematurity (ROP) is the most extensively recognized cause of vision impairment after preterm delivery.[1] Preterm newborns with ROP are those who require admission to NICU because of a variety of morbidities, such as sepsis, extremely low birth weight and the resulting underdevelopment of the lungs, and other conditions.[2,3] It has been observed that the retinal vascularization reaches full maturation approximately 40 weeks into the pregnancy, having begun to develop around week 16 of gestation.[4] Premature neonates are naturally undeveloped in the retinal vasculature, and the comparatively high oxygen flow.[5,6] The current American guidelines for ROP detection suggest ROP examinations for infants weighing less than 1500 g or with a gestational age ≤ 30 weeks. Infants with birth weights up to 2000 g may also be added to the list if the attending neonatologist determines that an examination is necessary due to a poor neonatal course. These standards result in a high number of low-yield tests on newborns who are bigger and better developed.[7]

Numerous countries have conducted population-based research on ROP, with varying definitions and reported results. According to research utilizing the pediatric inpatient care databases from USA, the incidence of ROP ranged between 12.8% and 19.9%.[8,9] A study conducted in Taiwan found that the incidence of ROP was 36.6% among premature infants with LOS of more than 28 days.[10] Any stage of respiratory failure was observed in 27-30% of newborns with birth weight ≤1500 g, gestational age ≤32 weeks, or an unstable clinical course in a network of Turkish NICUs.[11,12]

According to a Pakistani study, the prevalence of ROP was found to be 26.8% of these patients, with 25.6% of them having a weight of less than 1 kg, 65.1% having a weight between 1 and 1.5 kg, and 9.3% having a weight of more than 2 kg.[13] However, there is not much literature available in this regard to address the local population.

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The burden of LBW is highly prevalent in South Asia, it becomes importance to study the pattern how ROP burden differs among different categories of LBW. This study was planned to determine the prevalence of ROP in preterm LBW versus VLBW infants admitted to the Abbasi Shaheed Hospital, a tertiary care facility in Karachi. The findings of this study would not only be a valuable addition to the existing literature but also help the clinicians to know the actual burden of the disease among different categories of LBW and opt for the most suitable treatment options for patients falling into those LBW groups for better outcomes of the disease.

METHODS

This prospective observational study was performed at the Pediatric Department, Abbasi Shaheed Hospital, Karachi, Pakistan, from January 2025 to June 2025, after obtaining approval from the institutional ethics committee (letter number IRB/KMDC/KMU/080/2025, dated: 15-1-2025. A sample size of 58 (29 in each group) was calculated using the WHO sample size calculator, considering the anticipated frequency of ROP in LBW and VLBW as 74.7% and 25.6%, respectively[13], at 95% power of the study and 95% confidence level. The calculated sample size turned out to be too small for the study, therefore, it was enhanced to 50 patients in each study arm. Patients' inclusion was carried out following the non-probability consecutive sample technique. The inclusion criteria were infants of any gender, and born with a birth weight ≤2500 grams. Only those with a gestational age ≤37 weeks, admitted to the NICU within 48 hours of birth, and with no congenital ocular abnormalities were made part of this study. The exclusion criteria were infants with major congenital malformations affecting the eyes. Infants who died before their first ophthalmologic examination, or those with incomplete medical records, or those who had insufficient follow-ups were also excluded from the study. Birth weight between 1500 and 2500g was considered LBW, whereas a birth weight <1500g as VLBW.[16] Informed and written consents were obtained from parents/guardians.

Patients either admitted to the NICU or visiting outpatient ophthalmology clinics because of their referral for eye examination were enrolled into the study. Demographical data of the eligible patients like gender, age, birth weight, along with perinatal information were recorded. Information regarding oxygen therapy used, family history of eye disorders, surfactant administration, use of steroids, and maternal medical history were taken. ROP was diagnosed and classified according to the International Classification of Retinopathy of Prematurity (ICROP) criteria.[17] Following pupillary dilation with 0.5% tropicamide and 2.5% phenylephrine, a consultant pediatric ophthalmologist performed indirect ophthalmoscopy at 4 to 6 weeks postnatal age or at 31 weeks postmenstrual age, whichever was later. The presence and severity of ROP were assessed based on the location (zone I–III), stage (1: demarcation line, 2: ridge, 3: extraretinal fibrovascular proliferation, 4: partial retinal detachment, 5: total retinal detachment), and the presence of plus disease (dilatation and tortuosity of posterior pole vessels). The consultant pediatric opthalmologist having at least 5 years of experience examined and treated all patients as per standard protocols. The relevant data was stored on a predesigned proforma.

The collected data was analyzed using "IBM-SPSS Statistics version 26.0". Categorical variables were represented as frequencies and percentages, while the numerical data were shown as mean and standard deviation (SD). Stratification of effect modifiers was done to observe their effect on the outcome (ROP). The post-stratification chi-square or the Fisher's exact test, or independent sample t-test were applied taking $p<0.05$ as significant.

RESULTS

A total of 100 preterm newborns were enrolled, comprising 51 (51.0%) females. The mean age at the time of admission was 11.4±5.5 hours. The overall frequency of ROP was noted in 61 (61.0%) cases. Among those diagnosed with ROP, stage 1 was observed in 26 (42.6%), stage 2 in 17 (27.9%), stage 3 in 15 (24.6%), and stage 4 in 3 (4.9%) infants. Infants with ROP had a significantly lower mean birth weight (1390.2±286.8 g vs. 1604.6±361.3 g, $p=0.001$). The frequency of ROP was significantly higher in the VLBW (67.2% in ROP vs. 23.1% without ROP, $p<0.001$). The mean gestational age was significantly lower in the ROP cases (29.7±2.0

weeks vs. 31.1±1.1 weeks, p<0.001). The mode of delivery was significantly associated with ROP, with cesarean section accounting for 49 (80.3%) of ROP cases, compared to 17 (43.6%) in the non-ROP cases (p<0.001). Infants with ROP had significantly lower Apgar scores both at 1 minute (5.7±0.5 vs 7.3±0.8, p<0.001), and 5 minutes (7.3±0.8 vs 8.3±0.6, p<0.001). Table-I is showing comparison of baseline characteristics with respect to frequency of ROP.

ROP cases were found to have significant association with surfactant administration (34.4% vs 7.7%, p=0.002). Type of oxygen therapy was found to have significant association with the frequency of ROP (p=0.012). The mean duration of oxygen therapy was almost double in the ROP group (24.5±13.3 days vs. 13.1±4.0 days, p<0.001). ROP was significantly associated with the use of steroids (p=0.047). The mean duration of NICU stay was significantly longer for infants with ROP (31.0±15.8 days vs. 18.2±5.6 days, p<0.001). All cases with mortality (n=9, 14.8%) had ROP (p=0.009). Comparison of treatment related aspects and outcomes with respect to frequency of ROP are given in Table-II.

DISCUSSION

This study found a significant association of VLBW with the frequency of ROP with compared to LBW infants. The pronounced frequency of ROP among VLBW infants in this study aligns with the findings reported by Hwang et al.[18], from Korea, who documented an ROP incidence of 34.1% among VLBW infants, with increased risk correlating with lower gestational age, and birth weight. The Korean study also highlighted that 11.6% of infants developed stage 3 or greater ROP, paralleling the higher proportion of severe ROP cases in the present study, where stage 3 or higher accounted for nearly 30% of all ROP cases.[18] Bhuiyan et al.[19], in Bangladesh found a frequency of 23.5% for ROP among VLBW infants, and a striking 44.4% among extremely LBW neonates. The current study's elevated ROP frequency, particularly among VLBW infants may reflect local disparities in neonatal care protocols, higher rates of prematurity, and potentially limited access to preventive strategies such as timely oxygen monitoring and administration of antenatal corticosteroids. Comparison with work from rural India[20], which documented ROP prevalence of 17.4%, further emphasizes the higher burden observed in the present urban tertiary care context.[20]

TABLE-I

Comparison of baseline characteristics (N=100)

Characteristics		Retinopathy of Prematurity (n=61)	No Retinopathy of Prematurity (n=39)	P-Value
Gender	Male	36 (59.0%)	13 (33.3%)	0.012
	Female	25 (41.0%)	26 (66.7%)	
Age (hours)		11.5±5.0	11.1±6.2	0.755
Birth weight		1390.2±286.8	1604.6±361.3	0.001
Birth weight categories	Low birth weight	20 (32.8%)	30 (76.9%)	<0.001
	Very low birth weight	41 (67.2%)	9 (23.1%)	
Gestational age (weeks)		29.7±2.0	31.1±1.1	<0.001
Mode of delivery	Cesarean section	49 (80.3%)	17 (43.6%)	<0.001
	Vaginal delivery	12 (19.7%)	22 (56.4%)	
Apgar score	At 1-minute	5.7±0.5	7.3±0.8	<0.001
	At 5-minutes	7.3±0.8	8.3±0.6	<0.001
Parental history of eye disorders		6 (9.8%)	2 (5.1%)	0.328
History of parental smoking		14 (23.0%)	19 (48.7%)	0.008
Maternal diabetes		12 (19.7%)	10 (25.6%)	0.482
Maternal hypertension		32 (52.5%)	16 (41.0%)	0.264
Pre-eclampsia		14 (23.0%)	2 (5.1%)	0.018

TABLE-II

Comparison of treatment related aspects and outcomes (N=100)

Characteristics		Retinopathy of Prematurity (n=61)	No Retinopathy of Prematurity (n=39)	P-Value
Type of oxygen therapy	Continuous positive airway pressure	36 (59.0%)	13 (33.3%)	0.012
	Mechanical ventilation	25 (41.0%)	26 (66.7%)	
	Mechanical ventilation + Continuous positive airway pressure	18 (29.5%)	3 (7.7%)	
	Nassal cannula	-	5 (12.8%)	
Duration of oxygen therapy (days)		24.5±13.3	13.1±4.0	<0.001
Surfactant administration		21 (34.4%)	3 (7.7%)	0.002
Use of steroids		6 (9.8%)	-	0.047
Sepsis		49 (80.3%)	25 (64.1%)	0.071
Duration of NICU stay (days)		31.0±15.8	18.2±5.6	<0.001
Mortality		9 (14.8%)	-	0.009

Differences in ROP incidence between centers can be attributed to variations in screening criteria, survival rates of extremely premature infants, and quality of perinatal care. In contrast to the present study's high ROP burden, Awan et al.[21], in another local study reported an ROP incidence of only 3.2% among preterm infants with a mean gestational age of 31.9 weeks, and mean birth weight of 1632 g. A study from Bangladesh involving 154 infants <35 weeks gestation and <2000 g, reported an ROP prevalence of 19.5%.[22] Relatively lower prevalence of ROP may result from broader inclusion criteria, later screening initiation, or higher mean birth weights in the screened population.

This study documented significant association between ROP and prolonged oxygen therapy, with infants diagnosed with ROP receiving oxygen for a mean duration of 24.5 days, almost double that of those without ROP ($p<0.001$). This observation echoes findings from Boo et al.[23], in Malaysia, who identified prolonged oxygen therapy, invasive respiratory support, late-onset sepsis, and extreme prematurity as key risk factors of ROP. The relation between cesarean section and increased ROP prevalence in the current cohort stands in contrast to Boo et al.[23], who found vaginal delivery to be independently associated with higher ROP risk. The difference may be related to local clinical practices or underlying maternal and neonatal comorbidities influencing delivery mode selection and subsequent neonatal outcomes. Apgar scores were significantly lower among infants with ROP in this study, a pattern that is supported by Goldman et al.[24], who also identified low Apgar scores at five minutes as an independent risk factor for ROP in VLBW infants. The relationship with surfactant use likely reflects greater pulmonary immaturity among infants who later develop ROP, while the exclusive use of steroids among ROP infants in this study (9.8%) points to the potential dual role of steroids in both respiratory support and modulation of angiogenic processes in the retina. Multicenter analyses by Koc et al.[25], and Boo et al.[23], linked respiratory distress syndrome, bronchopulmonary dysplasia, and prolonged ventilation to increased ROP risk.

Length of NICU stay, and mortality were both substantially higher among infants with ROP. Koc et al.[25] also observed higher rates of morbidity and prolonged hospitalization among VLBW survivors, with major neonatal complications paralleling increased ROP incidence. The association between ROP, and mortality highlights the broader systemic vulnerability of these infants and reinforces the need for targeted surveillance and intervention strategies in the highest-risk subgroups. NICUs must prioritize strict control of oxygen supplementation, minimize unnecessary transfusions, enhance infection control, and promote the use of antenatal corticosteroids to reduce both the incidence and severity of ROP. Interdisciplinary collaboration

between neonatologists, ophthalmologists, and nursing staff is essential to ensure timely diagnosis, follow-up, and intervention.

Expanding future research to a multicenter or national registry would enhance the robustness and external validity of the results. A limitation is the lack of detailed data on the timing, concentration, and duration of oxygen therapy, which could provide further insights into modifiable risk factors. Future research should integrate neurodevelopmental assessment as a routine outcome measure for preterm infants at risk of ROP, enabling more holistic care and targeted early intervention.

CONCLUSION

There is a substantial burden of ROP among preterm VLBW infants, with key risk factors including lower gestational age, lower birth weight, and prolonged oxygen therapy. The identification of these factors supports the need for enhanced preventive strategies and early intervention in high-risk populations. Adoption of uniform ROP screening guidelines, improvements in perinatal and neonatal care, and multicenter data collection efforts can reduce the incidence of severe ROP and its lifelong sequelae in similar resource-limited settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Tayyaba Anwer:** Data collection, drafting.
2	**Shaheen Masood:** Conception, Critical revision.
3	**Urooj Mateen:** Data analysis, methodology.
4	**Ilham Khanam:** Literature review.
5	**Nisha Usman:** Proof reading.
6	**Dua Akhtiar:** Data collection, proof reading.