INCIDENCE AND RISK FACTORS OF PREMATURITY RETINOPATHY AMONG PRETERM INFANTS IN NEONATAL INTENSIVE CARE UNIT

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ABSTRACT:

Background*: A primary cause of blindness that affects about 50,000 children worldwide is prematurity retinopathy. The degree of perinatal care and the presence of screening programs for early diagnosis affect the disease's incidence, which differs among nations. Several antenatal, postnatal, and other risk variables have been found with their relationship to the severity of the disease, including low birth weight, small gestational age, and other risk factors.*

Aim*: This research aimed to determine the incidence and risk factors of prematurity retinopathy among preterm infants in the neonatal intensive care unit.*

Patients and methods*: This study included 200 preterm infants admitted to neonatal intensive care units at Sohag University Hospital in the period from April 2021 to April 2022. Fundus examination was done using indirect ophthalmoscopy and a 28 D lens, and fundus images were captured using a wide-field digital fundus camera.*

Results*: Out of the 200 screened preterm babies, (57%) cases had prematurity retinopathy, among whom (43%) had stage 1, (48%) had stage 2, (6%) had stage 3, (and 3%) had aggressive posterior retinopathy. GA, BW, oxygen therapy, sepsis, multiple birth, and cesarean section were factors found to be significantly associated with the disease.*

Conclusion *prematurity retinopathy occurred in 57% of all screened preterm babies. The main risk factors for the development of prematurity retinopathy were GA, BW, oxygen therapy, and sepsis.*

Keywords*: birth weight, gestational age, oxygen, preterm, retinopathy of prematurity*

INTRODUCTION:

Because of aberrant vascular growth in the developing retina of preterm newborns, prematurity retinopathy—which is regarded as a serious public health issue in low- and middle-income nations like Egypt, Brazil, and India - is one of the main causes of blindness in children [1]. The majority of research on the risk factors for preterm retinopathy concentrated on low birth weight (BW) and small gestational age (GA)[2,3]. Investigations are being done right now to identify other risk variables that can be used to forecast the stages of cancer that need treatment[4,5]. Worldwide improvements in neonatal care have raised premature baby survival rates while concurrently raising the prevalence of ROP. Early detection through appropriate screening could increase the effectiveness of the cure and lessen illness consequences[6-7].

Prematurity retinopathy has been linked to several risk factors, including low birth weight, low gestational age, sepsis, apnea, and prolonged use of supplemental oxygen. 7 There aren't many studies that examined the scope of this health issue in Egypt. In Egypt, there is no established screening procedure. Additionally, we decided to broaden our inclusion criteria to include infants with birth weights of up to 2000 g and gestational ages (GA) of up to 34 weeks because we had screened infants weighing more than 1500 g at a gestational age (GA) of more than 32 weeks and discovered signs of prematurity retinopathy. Therefore, this study aimed to determine the incidence and risk factors of prematurity retinopathy among preterm infants in the neonatal intensive care unit.

AIM OF THE STUDY:

This study aimed to determine the incidence and risk factors of prematurity retinopathy among preterm infants in the neonatal intensive care unit.

PATIENTS AND METHODS:

These infants <37 weeks) this infant (aged 37 weeks) was admitted to the neonatal critical care unit at the Sohag University Hospital between April 2021 and April 2022. Examination as well as potential risk factors like sex, GA, BW, oxygen therapy, sepsis, jaundice, surfactant, respiratory distress syndrome, total parenteral nutrition, multiple births, maternal age, antenatal steroid, and cesarean section (CS), were reviewed. Following recommendations from the American Academy of Pediatrics[10], the first examination was timed based on the GA at birth. Half an hour before inspection, both eyes' pupils were dilated with drops containing a combination of cyclopentolate (100 mg/ml) and phenylephrine (10 mg/ml) (one drop, 5–10 min apart). Using a sterile pediatric eye speculum, an ophthalmological examination was carried out following pupillary dilatation (Barraquer wire speculum 9 mm blade; S1-500-00 PK], after applying 0.4% benoxinate hydrochloride eye drops for topical anesthetic. Wide-field digital fundus camera was used to take pictures of the fundus after the fundus was examined using indirect ophthalmoscopy with a 28 D lens and scleral depression (Retcam III; Clarity Medical Systems, Inc., Pleasanton, CA). The International Classification of Prematurity Retinopathy, which includes stage, zone, and the presence or absence of plus disease, was used to categorize each infant's prematurity retinopathy status[11]. Depending on the zone and degree of the disease, infants with prematurity retinopathy had repeated examinations[10].

Statistical analysis:

Utilizing the Statistical Package for the Social Sciences, data were examined (version 21.0, SPSS Inc., Chicago, Illinois, USA). Quantitative data were described using percentages and numbers. Using Fisher's exact tests or two-tailed tests, associations between categorical variables were examined. For parametric data, continuous variables were given as mean ± SD, and an independent t-test was used to test them. Statistical significance was defined as a P value of less than or equal to 0.05. For relevant variables, a logistic regression model employing a backward stepwise procedure was applied. Additionally determined for each potential risk factor were the odds ratio and 95% confidence interval.

Ethical Consideration:

The Sohag University Hospital’s ethical committee in Egypt accepted the study. Every participant’s mothers consent was obtained before their neonates, participation and after being informed of the purpose of the study at the time of enrollment.

RESULTS:

In **table 1** 200 preterm infants in all were checked for prematurity retinopathy, and (57%) of the examined preterm infants had the condition. There were 56% more boys. Their median gestational age was 33.26 weeks with a mean gestational age of 2.69 weeks. 1956.34689.39 g was the average BW.

The incidence of prematurity retinopathy was seen to decrease with an increase in GA and BW (**Figs. 1 and 2**), and both were considerably lower in the prematurity retinopathy group (P 0.001) than in the non-ROP group.

Table 2 demonstrates that among the risk factors for prematurity retinopathy, there was a significant correlation between LBW (1500 gm) and low gestational age (32 weeks) and oxygen supplementation provided by a nasal cannula, continuous positive airway pressure (CPAP), or mechanical ventilation (OR: 6.9, CI: 3.8-12.4), (OR: 13.7, CI: 5.7–33.2). Along with thrombocytopenia (OR: 2, CI: 0.7-6.7), phototherapy for jaundice, and apnea, prematurity retinopathy alterations were also significantly increased by these risk factors (OR: 15.7, 8.0-30.3). (OR: 2.3, CI: 1.3–3.6).

Table 3 demonstrates a statistically significant negative connection between GA and BW and the severity of prematurity retinopathy.

Table 4 shows that stage 1, stage 2, stage 3, and aggressive posterior retinopathy were present in 43%, 48%, and 6% of the preterm children that were investigated.

Table 1 Demographic and clinical data of the studied group of preterm Infants

Demographic and clinical data	**Number of preterm infants =200**
Gender	Boys 112 (56%) Girls 88 (44%)
Gestational age	(33.26±2.69)
Birth weight	836–5500 g (1956.34±689.39)
Without ROP	114 infants (57%)
With ROP	86 infants (43%)

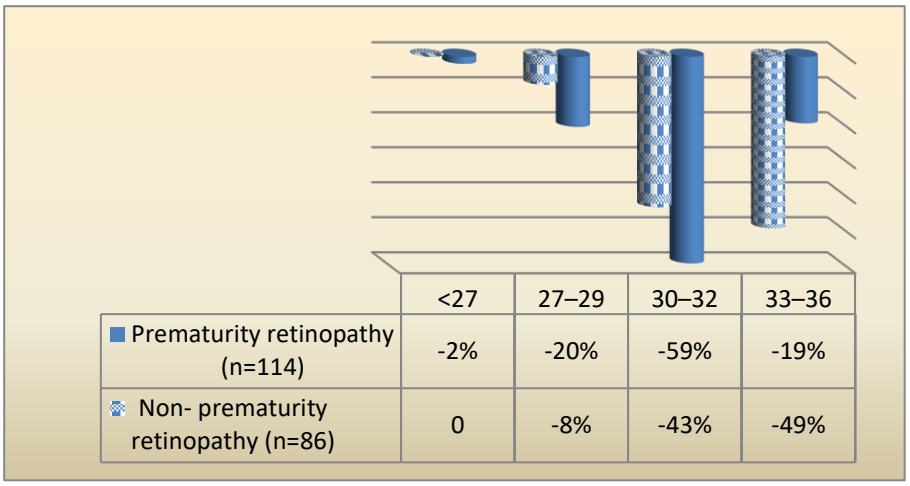

Figure 1 percentage of the studied groups' preterm infants regarding their gestational age categories

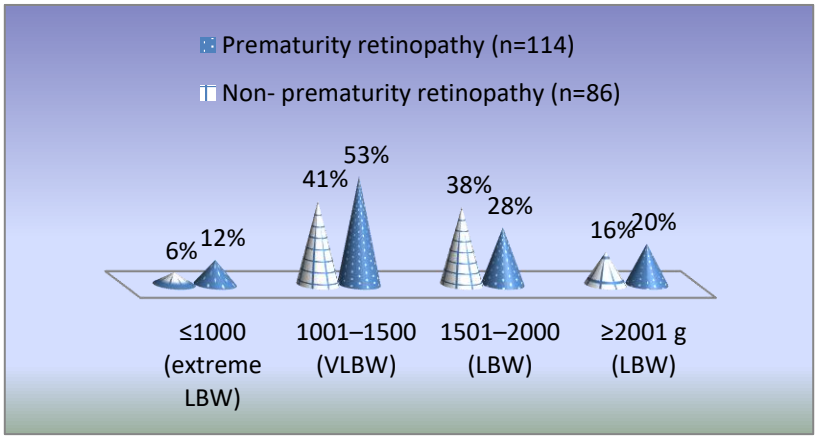

Figure 2 percentages of the studied groups' preterm infants regarding their birth weight
BW, birth weight; LBW, low birth weight; VLBW, very low birth weight *P<0.001.

Table 2 Logistic regression analysis of risk factors of prematurity retinopathy among the studied preterm infants

Risk Factors	OR	95CI%	*P*
Birth weight equal to or less than 1500 g	4.31	2.4–7.4	<0.001*
Gestational age equal to or less than 32 weeks	6.9	3.8–12.4	
Apnea	15.7	8.06–30.3	
Nasal cannula	3.89	1.15–13.6	
CPAP	17.8	5.6–62.8	
Mechanical ventilation	13.7	5.7–33.2	
Sepsis	1.3	5.7–2.16	
Thrombocytopenia	2	0.7–6.7	
Blood transfusion	1.20	0.6–2.4	
Exchange transfusion	0.8	0.07–10.8	
Phototherapy	2.3	1.3–3.6	

Abbreviations: OR, odds ratio; CI, confidence interval.

Table 3 Correlation between retinopathy ofprematurity severityand gestational age and birth weight

The severity of prematurity retinopathy stages

Risk factor	*r*	*P*
GA	−0.3	<0.001*
BW	−0.17	0.006*

BW, birth weight; GA, gestational age *P≤0.05, statistically significant.

Table 4 Distribution of stages among the studied group of preterm infants regarding prematurity retinopathy

Stages	ROP group (*n*=114) (*n* [%])
Stage 1 (*n*=86)	43.0

Stage 2 (*n*=96)	48.0
Stage 3 (*n*=12)	6.0
APROP (*n*=6)	3%

APROP, aggressive posterior retinopathy of prematurity

DISCUSSION:

In both developing and wealthy countries, prematurity retinopathy is a significant contributor to juvenile blindness that may be prevented. The condition has become more common as neonatal care has improved. For the early discovery and treatment of preterm newborns with this blinding condition, several nations have embraced their screening protocol. However, preterm retinopathy screening in Egypt is still in its infancy. For Egypt, no screening standards have been made available. As a result, all of our inclusion criteria were premature infants (GA 37 weeks).

The current study found that approximately 35% of the preterm newborns tested had prematurity retinopathy. In several studies, the disease's incidence ranged from 12.4% to 71%. In wealthy nations, a lower prevalence of between 12.4% and 29.2% was recorded[2,12&13]. There is no prior analogous research describing the prevalence of ROP in the governorates of Mansoura and Dakahlia. However, many research were carried out in various parts of Egypt. Research conducted in a neonatal ICU run by a non-governmental organization in Cairo found a 23% incidence[14]. An additional study conducted in Alexandria found a 34.4% incidence[15].

These findings are consistent with those of Bassiouny[16] and Maheshwari et al[17], who both reported incidences of 27% in India and 34% for prematurity retinopathy in Oman, respectively. While Al- Amro et al.[19] reported an incidence of 37.4% in the neonatal intensive care unit at King Khalid University Hospital in Riyadh in 2003, Binkhathlan et al.[18] reported an incidence of 56% for ROP in Saudi Arabia in 2008.

The current study found that the mean GA was 33.26 weeks, plus or minus 2.69 weeks. The mean BW was higher than that in earlier investigations at 1956.34689.39 g. The average gestational age was reported to be 29.1 2.1 weeks by Goble et al.[20] and 29.7 2.2 weeks by Shah et al.[21].

According to the study's findings, both the incidence and prevalence of prematurity retinopathy were considerably lower in the prematurity retinopathy group (P 0.001) than in the non-prematurity retinopathy group. A risk factor for the development of preterm retinopathy was gestational age equal to or less than 32 weeks. Only 19% of infants delivered after 32 weeks acquired prematurity retinopathy, according to our research, compared to 59% of infants born before this time. Other investigations [22] also supported this. However, several investigations observed lower results in comparison to the current study, indicating that in low- and middle-income countries, preterm retinopathy may affect more mature newborns[6].

As a result of the study's findings, it should be standard practice for every infant with a birth weight less than 2000 g to undergo a thorough examination by a qualified ophthalmologist to rule out ROP. This is in contrast to Hadi and Hamdy's[23] recommendation to keep the highest limit of a baby's ROP screening at 1500 g.

Regarding the potential contribution of apnea, oxygen supplementation (nasal cannula, CPAP, mechanical ventilation), infections, thrombocytopenia, blood transfusion, exchange transfusion, and phototherapy to the emergence of

prematurity retinopathy. The development of prematurity retinopathy was positively correlated with the use of an oxygen supplement, whether by a nasal cannula, CPAP, or mechanical breathing. Our findings are consistent with prior research that found a connection between the risk of prematurity retinopathy and using CPAP[21] and mechanical ventilation[24]. A key risk factor for the development of prematurity retinopathy, including newborn apnea and phototherapy for jaundice, is the presence of thrombocytopenia [25&26].

According to the study, prematurity retinopathy and oxygen delivery are strongly correlated. Other studies where oxygen was mentioned as a risk factor had earlier described this association[27&28]. Furthermore, there was a strong correlation between retinopathy, high oxygen pressure, and the length of oxygen therapy. However, some research found no connection between oxygen and the development of prematurity retinopathy[29]. According to some authors, the length of oxygen therapy was directly correlated with the development of ROP. A substantial risk factor for the disease was also known to be the variation in oxygen exposure that results in hyperoxia (>3 episodes) and hypoxia (2-4 episodes)[27].

Sepsis was shown to be a significant risk factor for prematurity retinopathy in the current study using univariate analysis. This was consistent with earlier research that found sepsis to be a crucial and essential predictor of the emergence of severe prematurity retinopathy. They demonstrated that early sepsis detection and prophylaxis may reduce the frequency of ROP requiring treatment[30]. According to Weintraub et al.[31], sepsis may increase oxygen demand and interfere with oxygen tension, which in turn may exacerbate retinal ischemia and lead to prematurity retinopathy. Sepsis also raises the likelihood of developing prematurity retinopathy by a factor of 12 (i.e., a 12-fold increase). That is most likely due to endotoxin-induced retinitis, which results in inflammation and leaking due to increased active leukocyte adherence to the vascular endothelium of retinal blood vessels[27]. Many other researchers, however, believed that sepsis has no clinical significance[32].

Prematurity retinopathy severity showed a strong negative connection with both GA and BW. According to Celebi et al.[33], the severity of ROP was inversely associated with GA and BW at birth. The retina is more vulnerable to oxidative damage and several prenatal variables, such as hyperoxia and hypoxia, as well as sepsis, due to immature vascularization, which may be the cause of this[33].

More than two-fifths of the preterm infants investigated in this study had stage 1 and stage 2, according to the study. The high prevalence of stages 1 and 2 may suggest that earlier prematurity retinopathy stages were more frequently detected through early screening, which could account for the study's overall incidence results. Babaei et al.[34] observed an incidence of 45.5% for both stage 1 and stage 2, which was in agreement with what was said here. Celebi et al.[33] reported an incidence of stage 1 and stage 2 in babies with extremely low BW of 25.9% and 11.06%, respectively. These numbers were lower than those found in the present study. The majority of cases were categorized as stage 2 in another Iranian study (63.77%), but the number was stage 1 in another investigation was 16.99% [35]. This was also found by Singh et al.[27], who reported 14.28 and 64.28% for stage 1 and stage 2, respectively.

Conclusion:

In Egypt, premature retinopathy is a significant public health issue. Prematurity, low birth weight, early gestation, oxygen administration, apnea, thrombocytopenia, and jaundice are significant risk factors for the development of prematurity retinopathy.

Recommendations:

To prevent the devastating complications of this serious condition, which has a high incidence among neonates in Egypt, cooperation between neonatal specialists and trained ophthalmology subspecialists is strongly advised. The use of oxygen and a strict screening program is essential to decrease blindness as well as long-term visual morbidity in these infants. Prematurity retinopathy incidence must be decreased, risk factors must be avoided, and protocols must be improved to guarantee that all babies at risk receive a timely screening check.

Ethical approval:

NA

Data Availability Statement:

Data of this research will be available upon reasonable request.

Conflict of interest:

Authors state no conflict of interest.

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عوامل الإصابة والمخاطر المتعلقة باعتلال الشبكية بين حديثى الولادة في وحدة العناية المركزة لحديثي الولادة

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المقدمة: السبب الرئيسي للعمى الذي يصيب حوالي ٥٠٠٠٠ طفل في جميع أنحاء العالم هو اعتلال الشبكية الخداجي. تؤثر درجة رعاية الفترة المحيطة بالولادة ووجود برامج فحص للتشخيص المبكر على حدوث المرض ، والذي يختلف بين الدول. تم العثور على العديد من متغيرات المخاطر قبل الولادة وبعدها وغيرها من المتغيرات مع علاقتها بخطورة المرض ، بما في ذلك انخفاض الوزن عند الولادة ، وصغر عمر الحمل ، وعوامل الخطر الأخرى.

الهدف: يهدف هذا البحث إلى تحديد الوقوع وعوامل الاختطار لاعتلال الشبكية الخداجي بين حديثى الولادة في وحدة العناية المركزة.

المرضى والطرق: تضمنت هذه الدراسة ٢٠٠ حديثى ولادة تم إدخالهم إلى وحدات العناية المركزة لحديثي الولادة في مستشفى جامعة سوهاج في الفترة من أبريل ٢٠٢١ إلى أبريل ٢٠٢٢. تم إجراء فحص قاع العين باستخدام تنظير العين غير المباشر وعدسة ٢٨ D ، وتم التقاط صور قاع العين باستخدام كاميرا رقمية واسعة المجال.

النتائج: من بين ٢٠٠ طفل حديثى ولادة تم فحصهم ، (٥٧٪) كان لديهم اعتلال الشبكية الخداجي ، من بينهم (٤٣٪) لديهم المرحلة الأولى ، (٤٨٪) لديهم المرحلة ٢ ، (٦٪) لديهم المرحلة ٣ ، (و ٣٪) كان لديه اعتلال الشبكية الخلفي العدواني. تم العثور على عوامل مرتبطة بشكل كبير بالمرض GA، BW ، العلاج بالأكسجين ، تعفن الدم ، الولادة المتعددة ، والولادة القيصرية. الاستنتاج حدث اعتلال الشبكية الخداجي في ٥٧٪ من جميع الأطفال حديثى ولادة الذين تم فحصهم. كانت عوامل الخطر الرئيسية لتطوير اعتلال الشبكية الخداجي هي GA، BW ، العلاج بالأكسجين ، والإنتان.