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RESEARCH ARTICLE

Incidence of Stage Five Retinopathy of Prematurity in A Tertiary Private Retina Specialty Eye Center in Erbil Kurdistan Region of Iraq

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ABSTRACT

Retinopathy of prematurity (ROP) is a significant contributor to childhood visual impairment on a global scale. This research aimed to ascertain the occurrence and identify the variables contributing to progressive ROP in a specialist ophthalmic facility in Erbil, Iraq. In this cross-sectional research, a total of 277 preterm newborns were examined for ROP between the time frame of January 2021 to May 2023. The researchers reviewed medical records to gather data on the staging of ROP, gestational age, birth weight, duration of neonatal intensive care unit admission, and several other parameters. The findings indicate that out of the 277 newborns that underwent screening, 82 of them, accounting for 29.6% of the total, were diagnosed with stage 5 ROP. A significant correlation existed between lower birth weight, less than 1500g, and an elevated likelihood of stage 5 ROP (p=0.014). The incidence of stage 5 ROP was significantly greater in cases referred by ophthalmologists than those referred by pediatricians (p:0.008). The duration of neonatal intensive care unit stay was found to be significantly greater in newborns diagnosed with stage 5 ROP compared to those with other stages of ROP (mean duration of 27.6 days vs. 21.3 days, p:0.012). Advanced ROP was substantial among this specific cohort of Iraqi individuals. Significant risk variables were lower birth weight, referral to an ophthalmologist, and a more extended stay in the neonatal intensive care unit. The results above underscore the need for enhanced newborn care and focused ROP screening in Iraq to mitigate the risk of visual impairment.

INTRODUCTION

Retinopathy of prematurity (ROP) is a major cause of preventable blindness in infants that occurs only in premature newborns. However, timely diagnosis and treatment can prevent this condition. Globally, ROP causes blindness in over 20,000 infants annually [1, 2]. Additionally, around 12,300 infants were reported to have temperate to moderate seeing impairment because of ROP. As neonatal maintenance skills continue to improve, more premature newborns persist. However, the increasing rates of blindness in ROP are mainly attributed to inconsistent standards of neonatal care, lack of or delayed screening, and a shortage of trained ophthalmologists to screen and treat ROP [3-5]. The incidence of ROP leading to blindness is significantly associated with socioeconomic development and the accessibility and quality of healthcare services. ROP accounted for two-thirds of all patients of visual impairment in Brazil, India, Indonesia, Mexico, China, Thailand, Turkey, Iran, the USA, and

the Russian Federation in 2010, underscoring its profound worldwide impact [6]. The incidence of ROP causing blindness is rapidly increasing in middle-income countries, with a growing increase in low-income patients. Bowe et al have proposed that the criteria for ROP screening should be adjusted according to the capabilities and unique challenges of each country's NICU (neonatal intensive care unit). This customization improves the effectiveness of ROP screening programs and reduces the prevalence of blindness caused by ROP [7].

According to recent findings from 2019, ROP is becoming a more significant lead to blindness in sub-Saharan Africa, particularly in Kenya and Nigeria, as neonatal care improves. As more African nations create highly sophisticated neonatal critical care, a new ROP epidemic will likely occur within the next decade. Key strategies for preventing permanent blindness caused by establishing establish effective screening programs. Screening aims to identify preterm at risk of developing ROP and those requiring treatment. Although not all preterm infants require treatment, ROP is a visually threatening disease that can lead to blindness, so appropriate and timely screening is essential for diagnosing and treating infants at risk [8, 9].

The content analysis technique helps draw accurate conclusions about the context of written texts. Medical researchers have long relied on content analysis of medical records to gain insights into health issues [10, 11]. Unlike patient recall, medical records do not rely on memory or subjective interpretations of events and are less prone to errors or omissions. Additionally, medical records can be used to track changes in a patient's health status, monitor the effectiveness of treatments, and identify potential risk factors or predictors of disease. As a result, medical records are a valuable tool in medical research and are often used to inform clinical decision-making and improve patient care [12-14].

Other factors associated with an increased risk of ROP include sepsis, intraventricular hemorrhage, and respiratory distress syndrome. In addition to identifying risk factors, researchers have also explored the potential pitfalls in ROP screening and management. These include delayed or missed screenings, inadequate documentation of examination findings, and insufficient follow-up care. Addressing these potential pitfalls is crucial in ensuring timely and effective treatment for infants at risk of developing advanced ROP. Overall, the literature on ROP highlights the importance of early detection and appropriate management of the disease. Identifying and addressing risk factors and potential pitfalls in screening and management can help reduce the incidence of advanced ROP and prevent blindness in premature infants [15-19].

PATIENTS AND METHODS

Study Design and Setting: This was a cross-sectional study, in which a total of 277 newborn premature babies were screened in our study. This screening was done at a tertiary private retina specialty eye center in Erbil Kurdistan Region of Iraq and carried out from the beginning of January 2021 until mid-May 2023. We reviewed medical records of all retinopathy of prematurity babies who were screened and staged. We determined and evaluated the incidence of Stage 5 ROP in our tertiary eye care center.

Method and Data Collection: Patients were referred to the American Eye & Retina Center (AERC) for evaluation and treatment from all over Iraq. Detailed past medical history including gestational age in weeks, birth weight in grams, days of admission to NICU, comorbidities like intracranial hemorrhage or blood transfusion and ocular history were obtained from the family and relatives of the premature babies. We screened 277 premature babies at AERC--Erbil from January 2021 to May 2023. Babies were referred as soon as they were discharged from the NICU, within 4 weeks post-delivery, or when they learned about late staging of the disease. Screening was performed according to the standard normal practice of ROP screening guidelines. Pharmacologic dilatation of the pupils done using a combination of eyedrops of relatively low concentration (cyclopentolate 0.2% and

phenylephrine 1%). The screening was performed in the operation room with two nurse technicians along with a nurse anesthetist. A sterile lid speculum was placed and the patient had 360 indirect peripheral retinal exams using 28 Diopter lens and a scleral depressor. All patients were graded and staged according to the most recent AAO ROP Guidelines and given the appropriate treatment or follow-up.

Post op artificial tears and sometimes low dose steroids were given if there have been any conjunctival injection or hemorrhage. The babies were placed in the recovery area for 30 minutes prior to discharge to verify that their oxygen saturation and breathing were regular.

Inclusion criteria: All babies of gestation age of 38 week or less at birth.

Exclusion criteria: All cases of gestational age above 38 weeks or ROP babies with staging between 0 and 4B.

Data management and statistical analysis:

The data recorded on a specially designed questionnaire, collected and entered in the computer via Microsoft Excel worksheet (Excel 2016) and then analyzed using appropriate data system which is called Statistical Package for Social Sciences (SPSS) version 28 and the results were compared between patients with different variables, with a statistical significance level of ≤ 0.05. The results presented as rates, ratio, frequencies, percentages in tables and figures and analyzed using t-test, and Chi square tests.

Ethical considerations:

This study was submitted to the Research Protocol Ethics and Scientific committees of Pediatrics program at Kurdistan Higher council of Medical Specialties for scientific and ethical approval which was granted. This study was explained for each patient's parents and a verbal consent was obtained from each parents. Confidentiality and anonymity of data were ensured.

RESULTS

A total of 277 subjects enrolled in the study, more than half (54.2%) of cases were male, 45.8% of them were female babies, 57.8% of infants were > 1 month and less than half (42.2%) of them were ≤ 1 month at presentation, most (59.9%) of babies were ≤ 30 weeks and 40.1% of them were > 30 weeks regarding their gestational age, 57% of newborns weighed < 1500 gram while 43% of cases were ≥ 1500 grams at birth. See Table 1.

Table 1: Background variables of participants.

Variables	Categories	Frequency	Percent
Gender	male	150	54.2
	female	127	45.8
age at presentation	≤ 1 month	117	42.2
	> 1 month	160	57.8
gestational age	≤ 30 weeks	166	59.9
	> 30 weeks	111	40.1
birth weight (grams)	< 1500 gram	158	57
	≥ 1500 grams	119	43
Total		277	100%

Table 2 reveals that 29.6% of babies had stage 5 ROP following by 19.5% of neonates were at stage 0 and only 7.2% of them reported as stage 2 ROP, less than half (47.7%) of them diagnosed with OU ROP following by 15.9% of them had OD retinopathy of prematurity, only 17% of neonates had ROP in OS side.

Table 2: Retinopathy of prematurity stages.

Variables	Categories	Frequency	Percent
ROP stages	0	54	19.5
	1	31	11.2
	2	20	7.2
	3	48	17.3
	4	42	15.2
	5	82	29.6
ROP side	No ROP	54	19.5
	od (right)	44	15.9
	os (left)	47	17
	ou (both)	132	47.7
Total		277	100%

Table 3 shows that 38.3% of babies referred by ophthalmologist followed by 37.5% of cases referred by pediatrician, majority (84.5%) of them were single babies, 11.9% were twins and only 3.6% were triple babies, less than half (48.7%) of neonates had jaundice, 17% of them diagnosed with jaundice and sepsis, only 0.4% of newborns had intracranial haemorrage.

Table 3: Referral and comorbidities of patients.

Variables	Categories	Frequency	Percent
Referral	Pediatrician	104	37.5
	Ophthalmologist	106	38.3
	Parents	67	24.2
Twin	Single baby	234	84.5
	Twin	33	11.9
	Triple	10	3.6
Comorbidities	No other comorbidity	75	27.1
	Jaundice	135	48.7
	Sepsis	17	6.1
	jaundice and sepsis	47	17
	blood transfusion	2	0.7
	intracranial haemorrage	1	0.4
Total		277	100%

Findings of OD show that 36.1% of babies diagnosed with immature retina, 20.2% of them had total retinal detachment, only 5.8% of babies had presence of ridge. According to findings of OS more than one quarter (35.4%) of cases diagnosed with immature retina, 15.5% of them had ridge with extraretinal fibrovascular proliferation, only 5.8% of newborns had presence of ridge, in accord to treatment plan OD, most (60.6%) of babies treated with follow up after 4 weeks, 20.2% of them treated with realities, poor prognosis, vitrectomy was done to 7.6% of babies, only 2.2% of them dealt with intravitreous injection, regarding treatment plan OS, , most (58.5%) of babies treated with follow up after 4 weeks, 16.2% of them treated with realities, poor prognosis, intravitreous laser was done to 7.6% of babies and finally only 2.2% of them underwent intravitreous injection treatment. See Table 4.

Table 4: Findings of OD and OS.

Variables	**Categories**	**Frequency**	**Percent**
Findings of OD	Immature retina	100	36.1
	Demarcation line between vascularized and neovascularized retina	26	9.4
	Presence of ridge	16	5.8
	Ridge with extraretinal fibrovascular proliferation	42	15.2
	Partial retinal detachment	37	13.4
	Total retinal detachment	56	20.2
Findings of OS	Immature retina	98	35.4
	Demarcation line between vascularized and neovascularized retina	35	12.6
	Presence of ridge	16	5.8
	Ridge with extraretinal fibrovascular proliferation	43	15.5
	Partial retinal detachment	36	13
	Total retinal detachment	49	17.7
Treatment plan OD	follow up after 4 weeks	168	60.6
	Intravitreous laser	13	4.7
	Intravitreous injection	6	2.2
	vitrectomy	21	7.6
	realities, poor prognosis	56	20.2
	lensectomy, ppv, poor prognosis	13	4.7
Treatment plan OS	follow up after 4 weeks	162	58.5
	Intravitreous laser	27	9.7
	Intravitreous injection	6	2.2
	vitrectomy	23	8.3
	realities, poor prognosis	45	16.2
	lensectomy, ppv, poor prognosis	14	5.1
Total		277	100%

Findings of Table 5 show that there was a non-significant statistical association between stage 5 ROP and gender and gestational age, p-value was > 0.05. There was a statistically significant association between stage 5 ROP and age at presentation, most (78%) of ROP stage 5 group were > 1 month while only (22%) of stage 5 group were ≤ 1 month at presentation. There was a statistically significant association between stage 5 ROP and birth weight, most (68.3%) of ROP stage 5 cases weighed < 1500 gram while only 31.7% of ≥ 1500 gram infants had ROP stage 5. There was a significant statistical association between stage 5 ROP and referral, more than half (51.2%) of ROP stage 5 group referred by ophthalmologist while more than one quarter (25.6%) of stage 5 cases referred by pediatrician. Chi square test was significant and p-value was < 0.05.

Table 5: Association between stage 5 ROP and gender, age, weight and referral.

Variable	**Categories**	**ROP stage 5**		**p-value**
		No or other ROP stages	**ROP stage 5**	
Gender	male	105 (53.8%)	45 (54.9%)	0.896
	female	90 (46.2%)	37 (45.1%)	
Age at presentation	≤ 1 month	99 (50.8%)	18 (22%)	<0.001
	> 1 month	96 (49.2%)	64 (78%)	
Gestational age	≤ 30 weeks	117 (60%)	49 (59.8%)	0.970
	> 30 weeks	78 (40%)	33 (40.2%)	
Birth weight (grams)	< 1500 gram	102 (52.3%)	56 (68.3%)	0.014
	≥ 1500 gram	93 (47.7%)	26 (31.7%)	
Referral	Pediatrician	83 (42.6%)	21 (25.6%)	0.008
	Ophthalmologist	64 (32.8%)	42 (51.2%)	
	Parents	48 (24.6%)	19 (23.3%)	
Total		195	82	
		100%	100%	

Table 6 shows that, there was a significant statistical difference between ROP stage 5 patients and other cases, ROP stage 5 cases had higher (mean of 27.63) in comparison to mean other ROP stages or no ROP at all was 21.34. t-test was significant and p-value was 0.012.

Table 6: Difference in NICU admission in days between ROP stage 5 patients and other cases.

ROP stage 5	**N**	**Mean**	**Std. Deviation**	**p-value**	**t-test**
No or other ROP stages	195	21.34	18.707	0.012	Significant
ROP stage 5	82	27.63	19.440		

DISCUSSION

According to the Table ROP stages, which indicates all stage's retinopathy of prematurity, 45.5% of cases are classified as stages 3, 4, or 5, which indicate considerable aberrant development and possible retinal detachment. [20] Most cases occur at Stage 5, the final and most severe stage. [21] The milder stages (stages 0-1) account for about 38% of all diagnoses. [22]

The analysis of the ROP side offers valuable insights into the distribution patterns of retinopathy in prematurity (ROP) patients, explicitly concerning the affected side of the eye and the presence or absence of the disease. [23] The findings indicate a high prevalence of ROP, with a significant proportion of cases exhibiting bilateral involvement. This underscores the importance of diligent surveillance and the implementation of suitable medical interventions to mitigate the risk of visual impairment or blindness. Approximately 65.6% of cases exhibit some manifestation of ROP in either one or both eyes. In the cohort of patients diagnosed with ROP, more cases exhibit ROP in both eyes (OU) instead of instances presenting ROP in just one eye (OD or OS). A significant proportion of the sample, precisely 19.5%, exhibits no indications of ROP. The present investigation highlights the extensive occurrence of ROP and its consequential effects on the ocular health of premature newborns. The significance of regular eye examinations, early therapies, and ongoing monitoring is underscored by the variable degrees of involvement and the predominance of bilateral ROP to achieve optimal visual outcomes for these infants.

This study also examines the sources of referrals for instances with ROP. Out of a total of 277 cases, pediatricians made referrals for 37.5% of the cases, ophthalmologists made referrals for 38.3% of the cases, and parents made referrals for 24.2% of the cases. The diverse sources of referrals for ROP cases underscore implementing a collaborative approach involving medical professionals and parents. [24] Pediatricians and ophthalmologists have significant responsibilities in the identification and referral of cases, thereby guaranteeing a thorough evaluation. The significance of raising awareness about symptoms of ROP is underscored by the substantial contribution of parental engagement, which accounts for around 25% of referrals. The collaborative endeavor results in prompt identification, timely care, and enhanced outcomes for neonates impacted by ROP. [25] The analysis of the incidence of ROP in various birth scenarios provides valuable insights into the prevalence of ROP in single births, twins, and triplets. [26] Although single births are more prevalent, it is essential to acknowledge that multiples, while less common, constitute a significant part. This investigation highlights the importance of early detection of ROP and individualized care for all premature children, irrespective of their birth circumstances, to achieve the best visual health outcomes. The phenomenon of single births refers to the delivery of solitary offspring instead of multiple births. Within the cohort of ROP cases, a significant proportion of instances (84.5%) involved single births. The prevalence of single births is notably high about the occurrence of ROP.

Twins accounted for approximately 11.9% of the observed instances. Although twin births constitute a minority of cases, they remain a substantial component. Including twin children within the dataset emphasizes the significance of closely monitoring premature infants born as part of multiple births for the occurrence of ROP. The dataset has a limited proportion (3.6%) of instances of triplets. While triple births are uncommon, they provide valuable insights into retinopathy of prematurity (ROP) cases in multiple births. [27]

The obtained p-value of 0.896 suggests insufficient evidence to establish a statistically significant relationship between the incidence of stage 5 ROP and gender within the examined cases. This finding implies no significant difference in the probability of having stage 5 ROP between male and female infants in the analyzed sample. [28]

The obtained p-value of 0.970 suggests insufficient evidence to support a statistically significant relationship between the occurrence of Stage 5 ROP and gestational age within the examined cases.

[29] This finding indicates no statistically significant difference in the dataset's probability of developing Stage 5 Retinopathy of Prematurity (ROP) among cases with varying gestational ages.

Among cases with a birth weight of < 1500 grams, 102 cases did not exhibit stage 5 ROP, while 56 cases did have Stage 5 ROP. Among cases with a birth weight of ≥ 1500 grams, 93 had no stage 5 ROP, and 26 displayed Stage 5 ROP. The overall distribution consists of 195 cases with no stage 5 ROP and 82 with Stage 5 ROP. The p-value of 0.014 indicates a statistically significant association between stage 5 ROP and birth weight among the cases studied. [30] This suggests that the likelihood of stage 5 ROP significantly differs between cases with birth weights of < 1500 grams and those with≥ 1500 grams.

The patients submitted by pediatricians, 83 instances were devoid of stage 5 Retinopathy of Prematurity, whereas 21 cases were diagnosed with stage 5 ROP. Out of the patients submitted by ophthalmologists, 64 cases were devoid of stage 5 ROP, while 42 instances exhibited the presence of stage 5 ROP. Of the instances referred by parents, 48 cases were devoid of stage 5 ROP, while 19 cases were identified as having stage 5 ROP. The distribution of cases in the study encompasses a total of 195 instances without Stage 5 ROP, with 82 instances with Stage 5 ROP.

The p-value of 0.008 suggests a statistically significant relationship between the occurrence of stage 5 ROP and the origin of case referral within the examined patients. This finding indicates a notable variation in the probability of developing Stage 5 retinopathy of prematurity (ROP) across cases recommended by various sources, including pediatricians, ophthalmologists, and parents. [31]

Based on the total number of single-baby births, 160 instances were observed where stage 5 ROP was absent, but 74 were recorded where stage 5 ROP was present. Out of the total number of twin births, 27 instances were observed where stage 5 ROP was absent, but in 6 cases, stage 5 ROP was observed. Out of the total number of triple births, it was observed that eight instances did not manifest stage 5 Retinopathy of Prematurity, but 2 cases did present with stage 5 ROP. The total distribution encompasses 195 instances without stage 5 ROP and 82 instances with stage 5 ROP.

The p-value of 0.227 suggests insufficient evidence to establish a statistically significant relationship between Stage 5 ROP and the incidence of twin or multiple births within the examined cases. [30] This finding indicates no statistically significant difference in the probability of developing Stage 5 Retinopathy of Prematurity (ROP) depending on various birth circumstances as observed in the dataset.

Among the instances without other comorbidities, 56 cases lacked stage 5 ROP, whereas 19 cases were identified as having stage 5 ROP. Out of the total number of infants presenting with jaundice, 96 cases were devoid of stage 5 retinopathy of prematurity, while 39 exhibited stage 5 ROP. Within the cohort of sepsis patients, it was observed that 10 cases did not manifest stage 5 retinopathy of prematurity (ROP), while seven instances did present with stage 5 ROP. Of the instances presenting with jaundice and sepsis, 31 cases were devoid of Stage 5 retinopathy of prematurity (ROP), whereas 16 cases were diagnosed with stage 5 ROP. The dataset had a minimal proportion of cases involving blood transfusion and cerebral bleeding, indicating a limited occurrence of such instances. The distribution of cases in the study encompasses a total of 195 instances without stage 5 ROP, with 82 instances with Stage 5 ROP.

CONCLUSION

the present research reveals a notable incidence of advanced stage 5 retinopathy of prematurity (ROP) at 29.6% among preterm newborns who underwent screening at a specialist eye facility in Erbil, Iraq. Significant risk factors for developing stage 5 retinopathy of prematurity (ROP) include lower birth weight, referral by ophthalmologists, and an extended stay in the neonatal intensive care unit (NICU). The findings of this study emphasize the need for enhanced newborn care quality and

the establishment of efficient retinopathy of prematurity (ROP) screening initiatives in this area. These measures are crucial in facilitating the timely identification and treatment of high-risk children. The use of focused therapies designed explicitly for newborns with low birth weight and extended stays in the neonatal intensive care unit (NICU) can potentially alleviate the impact of advanced retinopathy of prematurity (ROP) and the resulting visual impairment among this particular group.

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