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ORIGINAL ARTICLE

TITLE: RETINOPATHY OF PREMATURITY IN ABUJA; OUR EXPERIENCE

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ABSTRACT

Introduction/Background: Retinopathy of prematurity is one of the avoidable causes of blindness in children. Prematurity and several other risk factors have been linked to

]this sight threatening condition, with varying incidence from region to region. The aim of this study is to determine the frequency of ROP, its severity, risk factors and the outcome of treatment.

Subjects and Methods: This retrospective analysis of records of all preterm infants who underwent screening for ROP at the special care baby unit (SCBU) and eye clinic between January 2020 and December 2023.

Results: This study included 122 infants with a mean birth weight of 1251.28±291.52g. and a mean gestational age of 30.02±2.00 weeks who underwent ROP examinations. Of these, 11 infants (9%) developed ROP, out of which 6 (4.9%) developed type 1 and 5 (4.1%) developed type 2 ROP. One child delivered at 34 weeks with a birth weight of 2000g had aggressive ROP. four infants (3.3%) underwent successful treatment. ROP

was found to be associated with lower gestational age(< 30 weeks), low birth weight (< 1250g) and prolonged use of supplemental oxygen.

Conclusion and recommendation: The prevalence of ROP in our cohort is similar to global rates, there is need to further reduce the incidence by careful monitoring of oxygen therapy, continued improvement in prenatal, perinatal and neonatal care while providing timely screening for at risk infants and prompt treatment for infants with type 1 ROP.

Keywords: ROP, Gestational age, Supplemental Oxygen , Preterm infants

INTRODUCTION

Retinopathy of prematurity (ROP) is a proliferative disorder of the blood vessels of the developing retina in preterm infants that leads to neovascularization in the retina resulting in retinal detachment and blindness.[1] Retinopathy of prematurity as a preventable cause of blindness remains one of the leading causes of vision loss in children.[1] it occurs commonly in preterm infants but can also occur in term infants with immature retinal vessels at birth,[2] occurring at the boundary between the vascular and avascular retina.[1] ROP occurs in two phases: The first phase is due to delay in physiologic retinal vascular development in preterm babies and damage to newly developed capillaries in the setting of oxygen and other stresses like oxidative stress, poor nutrition and post-natal growth. The second phase is via abnormal neovascularization growing into the vitreous instead of into the retina due to increased expression of vascular endothelial growth factor.[3]

Retinopathy of prematurity is the most common ocular abnormality seen in preterm infants and occurs more in infants born before 32weeks of gestation and with a birth weight of less than 1500g.[4] Other potential risk factors are multiple births, blood transfusion, respiratory distress syndrome (RDS), sepsis, intraventricular hemorrhage (IHV), anemia and poor weight gain. The sicker the baby, the higher the risk of developing ROP. High unregulated administration of oxygen and fluctuations in oxygenation, in early life, remains the most studied risk factor for ROP.[5]

In Nigeria, over the last decade, there had been notable improvement in the human and technical resource capacity for improved survival of infants born premature as a result of several government and development partner initiatives with respect to neonatal care. The improvement in survival of babies borne premature without a corresponding increase in routine screening for ROP has resulted in an increase in the number of ROP cases and ROP related blindness seen in hospitals and eye clinics in Nigeria.[6-8] The incidence of ROP varies from region to region; with incidence from previous studies ranging from 5.5% – 47.2%[9-13]

The incidence of sight threatening ROP (Type 1 ROP) requiring treatment range from 4% - 22% in infants with ROP.[11 – 13] Blindness from this sight threatening ROP can be reduced with appropriate screening and treatment strategies deployed in a timely manner. [14,15]

Retinopathy of prematurity and the blindness that results from it, which typically occurs

before 6 months of life can be prevented with good neonatal care (including administration of blended oxygen) and a planned screening and treatment program starting within 30 days of life. The economic burden of blindness from an early age is huge, given the many years such persons will live with visual impairment.

Lack of screening in a timely manner is a major cause of blindness that leads to significant medico-legal issues globally.[16-18]

This study aimed to review our ROP screening and treatment experience and document the frequency of ROP, its severity and risk factors and the outcome of treatment at University of Abuja Teaching Hospital, Gwagwalada, Abuja. Few studies on retinopathy of prematurity have been done in Nigeria and none from Abuja, this study will add to the body of knowledge regarding the proportion of infants with the disease and the risk factors associated with it.

MATERIALS AND METHODS

Study design

The study was a retrospective review evaluating records of all preterm infants who underwent screening for ROP at the special care baby unit (SCBU) and eye clinic between January 2020 and December 2023.

Study population

Records of all preterm babies screened for ROP within the study period were included.

Inclusion criteria

Inclusion criteria included infants born at the gestational age of less than 34 weeks and birth weight of less than 1500g. Other preterm infants born outside the above criteria but have severe comorbidities and risk factors such as severe sepsis, prolonged exposure to oxygen, respiratory distress syndrome, multiple blood transfusion as determined by the neonatologists were also included. Infants with congenital ocular anomalies and other conditions preventing posterior segment examination were excluded.

Data collection procedures

Records of all preterm infants who underwent ROP screening both in the SCBU and the eye clinic between January 2020 and December 2023 were retrieved and reviewed. Clinical information was extracted from the ROP evaluation forms filled during the screening and from electronic medical records of all the infants screened. The form had 5 sections,

Section A contained the demographic characteristics of the babies including age of the infants in weeks, (gestational age, postnatal age and post conceptual age i.e gestational + postnatal ages), birth weight, and multiple births among others. **Section B** contained information on maternal risk factors like prenatal steroid use, gestational diabetes and maternal hypertension. **Section C** contained information on neonatal risk factors like number of days on 100% oxygen (No blended oxygen available) , presence of intraventricular haemorrhage, RDS, phototherapy, sepsis and blood transfusion. **Section D** had data on ocular examination findings included are the presence of active iris vasculature, tunica vasculosa lentis and rigid pupils. Posterior segment findings like mature or immature retinal vessels, zone

where vessels are located, presence of ROP, the stage, zone and clock hours involved. **Section E** contained the diagnosis, treatment offered, outcome of treatment and follow up dates.

Screening protocol

Eligible infants were first screened for ROP at 3-4 weeks post-delivery or at discharge (whichever came first) in the Special Care Baby Unit (SCBU) by a trained ophthalmologist. Infants who were discharged before the screening but reported for follow up visits were screened in the eye clinic.

The neonatal team identified infants who fit the criteria for screening and informed the ophthalmology team. Following aseptic procedures, pupillary dilatation was achieved using 2 drops of tropicamide plus (Tropicamide 0.4% + Phenylephrine 2.5%) applied into each eye 15 minutes apart, the excess eye drops that overflowed unto the checks were wiped off with sterile cotton wool. Screening was then done 30 minutes after instillation of the second eye drops. Topical anaesthetic eye drops (tetracaine hydrochloride) was instilled into the eye prior to insertion of the lid speculum. The anterior segment was examined using a pen torch while the posterior segment was examined with an indirect ophthalmoscope (HEINE 200) , a Volks 20 Dioptre lens (V20LC) and a Vectis loop (Appasamy loop) was used as a scleral depressor. The location of the disease in any of the 3 zones of the retina were noted, the extent was defined as twelve (12) sections using clock-hour designations, the stage and presence or absence of plus disease were also documented. Any iris neovascularisation, hazy vitreous and rigid pupils (Signs of plus disease or progressive vascular incompetence) were also documented.

A neonatal nurse was present during each screening exercise and monitored the vital signs of the babies before, during and immediately after the screening exercise.

The stage of the disease was determined based on the revised version of the International Classification of ROP.[19] Infants were classified according to the most advanced stage of ROP in the worse eye.[13,19] Infants found to have type 1 ROP were advised to have treatment and treated immediately once consent was provided. Babies with Type 2 ROP were examined weekly until regression or progression to type 1 ROP where immediate treatment was provided. Infants with incomplete vascularisation of the retinal vessels in zone 3 or type 2 ROP seen in zone 3 were re - examined 2 -3 weekly until regression.

Treatment given was intravitreal injections of anti- vascular endothelia growth factor (anti-VEGF), either intravitreal Bevazicumab (0.625mg) or Ranibizumab (0.25mg) within 48 - 72 hours of diagnosis based on patients' affordability. Successful treatment is defined as complete resolution/ regression of features of Retinopathy of prematurity.

Ethical considerations

The study protocol adhered to the tenants of the Helsinki declaration. The study was approved by Health Research Ethics committee (HREC) of University of Abuja Teaching Hospital, Gwagwalada

(UATH/HREC/PR/457). Written informed consent was obtained from all parents or caregivers.

Data analysis

Statistical analysis was done using SPSS Statistical Software version 21 (IBM Corp. 2012. IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY, USA). Descriptive summary statistics such as mean and standard deviation were computed for continuous and discrete quantitative variables such as age while proportions and frequencies were computed for categorical (qualitative) variables.

Results were presented in form of tables. For categorical variables, Chi-square was used while t-test and ANOVA test were used for appropriate continuous variables. A p-value of <0.05 was considered significant.

RESULTS

A total of 122 infants were screened during the period under review. The mean gestational age of the infants was 30.02±2.00 weeks while the mean birth weight was 1251.28±291.52g. were 56 (45.9%) males, giving a male to female ratio of 1:1.18. Sixty (60) infants (49.2%) were products of multiple gestations. Seventy three (73) infants (59.8%) were treated for sepsis,

ROP was found in 11 infants (9%). Six infants had type 1 ROP requiring urgent treatment, while 5 infants had type 2 ROP (Table 1)

One infant with birth weight of 2000g and gestational age of 34 weeks had aggressive ROP (A-ROP) and was successfully treated with intravitreal Anti -VEGF injection.

Of the 6 infants with type 1 ROP requiring treatment, 4 infants were successfully treated with intravitreal Anti-Vascular Endothelial Factor (Anti – VEGF), one declined treatment and one child could not afford treatment and was lost to follow up.

Table 1 Types, location and severity of ROP

Type of ROP	No (122)	Percentage (%)
Type 1	6	4.9
Type 2	5	4.1
No ROP	111	91
Total	122	100
Stage of ROP in type 2 ROP (No :5)		
Stage 1, Zone 3	3	60
Stage 2, Zone 3	2	40
Total	5	100
Stage of ROP in infants with type 1 ROP (No: 6)		
Aggressive Posterior ROP	1	16.7
Stage 3 ROP in zone 1 with plus disease	3	50
Stage 3 ROP in zone 2 with plus disease	2	33.3
Total	6	100

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Of the 6 infants with type 1 ROP requiring treatment, 4 infants were successfully treated with intravitreal Anti-Vascular Endothelial Factor (Anti – VEGF), one declined treatment and one child could not afford treatment and was lost to follow up.

The remaining 5 infants with stages 1 and 2 ROP in zone 3 were observed and followed up until there was complete regression of the disease. None of them progressed to Type 1 ROP.

The mean gestational age of infants with ROP (28.7 ±2.2) weeks was significantly lower than infants without ROP (30.1±1.9) weeks (p = 0.02).The mean birth weight of the infants who had ROP was lower (1173.6±342.1g)) when compared with 1259.1(±286.6g) for ROP-free infants (p = 0.35) though not significant as shown on Table 2 below.

Table 2: Association between mean Birth Weight/Gestational Age and occurrence of ROP

Variable	No ROP Mean±SD	ROP Mean±SD	t-test	*p-value*
Birth wt(g)	1259.11±286.58	1173.64±342.12	0.926	0.356
GST age (wk)	30.14±1.94	28.73±2.240	2.280	0.024

The mean birth weight of infants with type 1 ROP (1151.67±434.53g) was lower than that of infants with type 2 ROP (though not significant).

The mean gestational age of infants with type 1 ROP (28.33±3.01) was lower than that with type 2 ROP (29.20±0.84) (p = 0.024) (though not significant) as shown on table 3.

Table 3: Association between Mean Birth Weight / Gestational Age among babies with type 1 ROP and type 2 ROP.

VARBL	Type2ROP not-requiring treatment Mean±SD (n=5)	Type1ROP requiring treatment Mean±SD (n=6)	t-test	*p-value*
Birthwt (g)	1200±234.52	1151.67±434.53	0.222	0.829
GST age(wk)	29.20±0.84	28.33±3.01	0.619	0.551

Table 4 below shows the association between infant characteristics and occurrence of ROP, Gestational age less than 30 weeks, birth weight less than 1250g and prolonged oxygen therapy for more than 2 weeks were significantly associated with the occurrence of ROP

Table 4: Association between infant characteristics and occurrence of ROP

Variables	No ROP	ROP	X^2	p-value
Gestational age				
<30 weeks	41(83.7)	8(16.3)	5.334	0.021*[f]
>30 weeks	70(95.6)	3(4.1)		
Birthweight				
<1250g	53(85.5)	9(14.5)	4.409	0.036*[f]
≥1250g	56(96.6)	2(3.4)		
Days on oxygen				
< 2 weeks	85(95.5)	4(4.5)	13.886	*<0.001*[f]*
> 2weeks	16(69.6)	7(9.8)		
Surfactant use				
Yes	46(86.8)	7(13.2)	1.235	*0.266*[f]
No	65(94.2)	4(5.8)		
RDS[×]				
Yes	38(86.4)	6(13.6)	2.337	*0.126*
No	73(93.6)	5(6.4)		
IVH[××]				
Yes	2(100)	0 (0)	0.204	*0.652*[f]
No	109(90.8)	11(9.2)		
Sepsis				
Yes	63(86.3)	10(13.7)	3.299	*0.06*[f]
No	48(98.0)	1(2.0)		
Phototherapy use				
Yes	85(91.4)	8(8.6)	0.000	*0.989*[f]
No	26(89.7)	3(10.3)		

×: Respiratory distress syndrome.××: Intraventricular haemorrhage.f: Fischer exact test, $X^{2:}$: Chisquare test statistic

DISCUSSION

The proportion of infants with ROP in our facility was (9%). This is in keeping with findings from previous reports in Lagos and Ibadan Nigeria that reported 15%[12] and 12.2%[13] respectively but was significantly lower than the 47.2% [11] reported in a study in Port Harcourt, Nigeria. This observed difference may be because of the smaller sample size of the Port Harcourt study and the differences in screening criteria. The Port Harcourt study used a smaller gestation age of <32 weeks.

A study in India reported the presence of ROP in 18.8 % of infants screened for ROP.[20] This is significantly higher than the proportion of ROP in our study. The observed difference may be because of the different screening criteria employed by the 2 studies.

The proportion of ROP requiring treatment (Type 1 ROP) in our study (4.9%) was similar to the report of a study in Lagos (7.5%) [12] .and similar to the findings reported by Garcia et al, in a systematic review, with a pooled prevalence of severe ROP (Type 1 ROP) of 7.5%.[21.]The G-ROP study by Quinn et al also found a similar prevalence of 6.1% [22].These findings are in keeping with increasing improvement in neonatal practice and deployment of modern technology in the management of preterm babies who survive to develop ROP. However this rate still needs to be reduced or eliminated completely if possible from the population. There is therefore the need to look at other factors like monitoring of oxygen administration. Few other studies from Port Harcourt and Ibadan in Nigeria reported much lower prevalence of 1.89%[11] and 2.7%[13] respectively.

One infant in our study weighing 2000g with a gestational age of 34 weeks developed aggressive ROP. The infant had severe and

multiple comorbidities and had oxygen therapy for about 1 month. More effort therefore needs to be made to ensure that older infants with severe co-morbidities who fall outside the recommended birth weights and gestational ages are also routinely screened for ROP.

Gestational age (less than 30 weeks) was found to be significantly associated with the development of ROP in our study similar to the findings by Mamta et al [20] who found that the incidence of ROP rose as the gestational age decreased. Chang-Yo Yang *et al* [23] also found a significant association between low gestational age and development of ROP. Several other studies found a significant association between low gestational age and development of ROP.[24,25.] The immaturity of the retinal vessels of preterm babies with lower gestational age makes the retina susceptible to oxidative damage and other factors like hypoxia, sepsis and blood transfusion.

Of the eleven infants found to have ROP in our study, 9 (81.8%) had birth weight less than 1250g and low birth weight was found to be significantly associated with development of ROP. This is similar to the findings reported by several other authors. [21, 26, 27]

We also found a significant association between prolonged use of supplemental oxygen and development of ROP as infants who had supplemental oxygen for more than 2 weeks developed ROP compared to babies who had oxygen for a shorter period. Adio et al in Port Harcourt, Nigeria reported a similar finding where majority of the infants who developed ROP had been given supplemental oxygen.[11] Hakeem et al in Egypt also found a significant association between supplemental oxygen therapy and ROP.[25] Supplemental oxygen therapy has been implicated in the development and rapid progression of ROP necessitating close monitoring of preterm infants on oxygen therapy and ensuring they are not given 100% oxygen. Neonatologists are encouraged to blend the oxygen given to preterm infants and to monitor all preterm infants on oxygen. These infants should not be left a day longer than necessary on oxygen. Oxygen therapy should be monitored using pulse oximetry (Sp02) and Partial pressure of oxygen (arterial blood gases). Blindness from ROP can be prevented by prompt regular screening using recommended guidelines and prompt treatment of type 1 ROP.

Other risk factors implicated in the development of ROP like respiratory distress syndrome, intraventricular haemorrhage, sepsis and phototherapy showed insignificant relationship with development of ROP in our study. Some studies found an association between these factors and ROP,[11, 28.] While some studies did not find any association between these factors and development of ROP, [12,13 25] further multicentre studies are required to identify the most common risk factors for development of ROP in Nigeria.

LIMITATIONS

The limitations of our study include the small sample size, the fact that the study was retrospective in nature and the babies were not examined by a single ophthalmologist which could introduce bias.

CONCLUSION

The proportion of ROP in our cohort was found to be associated with lower gestational

age, low birth weight and use of supplemental oxygen. The proportion of ROP in our cohort requiring treatment was 4.9%, which is in keeping with global rates. There is need to further reduce the incidence by careful monitoring of oxygen therapy, continued improvement in prenatal, perinatal and neonatal care. Providing timely screening of at risk babies and prompt treatment of babies with type 1 ROP will also go a long way in reducing severe visual impairment and blindness from this condition.

AUTHORS CONTRIBUTION

	A1	A 2	A 3	A 4	A5	A6	A7	A8	A9	A10	A11	A12
Concepts	X	X	X	X		X	X					
Design	X	X	X	X	X	X	X	X	X	X	X	X
Definition of intellectual content	X	X	X	X	X	X	X	X	X	X	X	X
Literature search	X	X	X	X		X	X	X	X	X		X
Clinical studies	X	X	X	X		X	X	X	X	X	X	X
Experimental studies												
Data acquisition	X				X	X	X	X	X	X	X	X
Data analysis	X				X		X					
Statistical analysis	X				X							
Manuscript preparation	X	X	X	X	X	X	X	X	X	X	X	X
Manuscript editing	X	X	X	X	X							X
Manuscript review	X	X	X	X	X	X	X	X	X	X	X	X
Guarantor	X											

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