Retinopathy of Prematurity in the University of Calabar Teaching Hospital, Calabar, Nigeria: An Early Report of a Screening Service

Abstract

Background: Retinopathy of prematurity (ROP) is an important cause of childhood blindness worldwide. This blindness is avoidable through regular screening of preterm infants and prompt intervention for those with the condition. **Aims/Objectives:** This study aimed to determine the pattern of presentation of ROP and the risk factors for its development among preterm infants in the Neonatal Unit of the University of Calabar Teaching Hospital, Calabar, Nigeria. **Design of Study:** This study is a prospective, longitudinal study. **Settings:** The study was carried out in the Special Care Baby Unit, Sick Baby Unit, and Neonatal Clinic of the Department of Paediatrics and Child Health, University of Calabar Teaching Hospital, Calabar, Nigeria. **Materials and Methods:** All preterm infants whose mothers had given informed consent to participate were enrolled. Ocular examination was performed by a trained ophthalmologist. ROP was staged and documented using the revised version of the International Classification of ROP. Data were entered into a questionnaire and analysed using IBM SPSS version 22. **Results:** Of the 53 neonates recruited into the study, ROP was detected in 11 (21%) neonates, of which 9 (82%) had stage 1 disease, 2 (18%) had stage 2, and none had stage 3. ROP was more common in females, 7 (63.6%), than their male counterparts 4 (36.4%). ROP was higher among those with gestational age (GA) ≤30 weeks [9 (81.8%)] when compared with those with GA >30 weeks [2 (18.2%)] ($P = 0.016$). Other risk factors for ROP assessed by this study were found not to be significantly associated with the occurrence of ROP. **Conclusion:** ROP was present in 21% of the neonates, and the majority had stage 1 disease. This finding emphasizes the need for screening of all preterm neonates for ROP in order to forestall avoidable blindness which could result from this condition.

Keywords: *Infants, pattern, preterms, retinopathy of prematurity, risk factors, screening*

Introduction

Retinopathy of prematurity (ROP) is a potentially blinding and yet treatable vaso-proliferative disorder of the premature retina affecting preterm and very low birth weight (BW) infants.[1] The World Health Organization (WHO) Vision 2020 programme had prioritized ROP as an important cause of childhood blindness worldwide.[1-5] More than 60% of the world's 15 million preterm births are reported in Sub-Saharan Africa and South Asia.[6] Blindness in babies and infants is often not perceived by parents, most health workers, and the general public as being preventable.[7] As such, there is a perception that babies are born blind, and very little can be done in terms of public health preventive measures.[7] Contrary to this perception, blindness from ROP is avoidable; hence, regular screening and timely treatment are essential for improving anatomical and functional outcomes of the disease and should therefore be part of routine neonatal care. With the increasing survival rates of preterm babies in middle-income countries, screening for ROP is even more important for these groups of high-risk babies.[8,9]

ROP screening is an important and essential aspect of delivering high-quality neonatal care as the natural history of ROP is well understood.[10] Two vital aspects of screening for ROP which have been elucidated are as follows: who to screen and the appropriate timing of the examination.[3,10] The knowledge of risk factors for the development of ROP helps to identify babies who need to be screened, and these risk factors for ROP are divided into two groups: prenatal and postnatal.[11] Prenatal factors include gestational age (GA) and BW, whereas postnatal factors include prolonged exposure to oxygen and other identified markers of neonatal illness severity in the preterm baby.[1,3] The WHO advocates

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examining the eyes of premature babies at risk of ROP, treating premature babies with severe/sight-threatening ROP, and promoting oxygen monitoring to all premature babies receiving oxygen therapy.[3]

The aim of this study was to determine the pattern of presentation of ROP and the risk factors for its development among preterm infants in the Neonatal Unit of the University of Calabar Teaching Hospital (UCTH), Calabar, Nigeria.

Materials and Methods

A prospective study was conducted over a 3-month period at the Special Care Baby Unit (SCBU) (for babies whose mothers had routine orthodox antenatal care and given birth to in UCTH), Sick Baby Unit (SBU) (babies delivered at home whose mothers did not have orthodox antenatal care or other facilities and brought to UCTH), and Neonatal Clinic of the UCTH between March 1 and May 31, 2021. All preterm babies who received medical care in the Neonatal Unit of the Department of Paediatrics, UCTH, Calabar, Nigeria who met the Nigerian National ROP Screening Criteria[12] and whose mothers had given informed consent to participate in the study were enrolled in the study. This included all preterm neonates born on or before 34 weeks of gestation and or with a BW of 1500 g or less admitted into the SCBU or SBU of the UCTH, Calabar. All preterm neonates who met the screening criteria but whose parents refused to give consent for ophthalmologic examination after appropriate counselling or who had congenital eye abnormalities were excluded from the study. Also excluded from the study were preterm neonates who were too ill to be examined or who died before their ophthalmologic examinations could be carried out. ROP screening was performed at about 4–6 weeks of life or any time before discharge whichever came first. Neonates discharged before 4 weeks of age or requiring repeat examinations had their eyes examined on an outpatient basis at the Neonatal Clinic. Written informed consent for ROP screening was sought from parents; and in cases in which there was an initial parental refusal, it was documented in the records of the baby to enable the neonatologist counsel further in order to ensure that no baby was denied due to ROP screening.

Ocular examination

Ocular examinations were performed by a subspecialty trained ophthalmologist. These included external eye, anterior segment, and posterior segment examinations. Pupillary dilatation was achieved with the use of one to two instillations of dilating drops (tropicamide 0.5% and phenylephrine 2.5%) applied 10 min apart over 30–45 min before ocular fundus examination. Gentle pressure was applied over the medial canthal region to reduce systemic absorption of topical eye drops. Care was taken to wipe (with sterile cotton wool) eyedrops that overflowed onto the cheeks. Tetracaine hydrochloride (0.5%) eye drops were instilled into each eye to achieve topical anaesthesia prior to insertion of a sterile reusable paediatric eyelid speculum to aid eye examination.

Anterior segment examination was performed using a pen torch and a handheld slit lamp biomicroscope, whereas the posterior segment (retina and vitreous) was examined using a binocular indirect ophthalmoscope with a 20-dioptre lens. Scleral indentation was performed to examine peripheral retina. All examinations were done with the neonatology team including a trained Neonatal Intensive Unit (NICU) nurse. The NICU nurse monitored the preterm baby's vital signs during and after the eye examination.

ROP staging

Staging of the disease was done and documented using the revised version of the International Classification of ROP.[13] Neonates were classified according to the most advanced stage of ROP in the worse eye. Scheduled subsequent ROP screening examinations were performed to ascertain disease progression or regression. Repeat eye examinations were done either weekly or fortnightly as indicated by the maturity of the retinal vasculature or severity of the disease. Neonates with type 2 ROP disease were examined every fortnight until it regressed or progressed to type 1 at which time treatment was instituted within 48–72 h.[14-16]

The study adhered to the tenets of the Declaration of Helsinki. Neonates' demographic characteristics as well as information on GA at birth, BW, oxygen therapy, and presence of other risk factors were retrieved from their hospital records. Data were analysed with the use of IBM SPSS version 22. With regard to bivariate analyses, Fisher's exact test was used for categorical variables, whereas Student's t-test was used for continuous variables. A P-value ≤ 0.05 was considered statistically significant.

Results

Infant characteristics

A total of 53 infants were screened during the period of this study. There were 23 (43.4%) males and 30 (56.6%) females giving a male-to-female ratio of 0.76:1. The mean BW was 1400 (±0.27) g with a range of 800–2100 g. The mean GA at birth was 30.91 (±2.52) weeks with a range of 27–36 weeks. The mean corrected GA at screening for ROP was 34.06 (±2.52) weeks with a range of 29–40 weeks, as seen in Table 1.

Incidence of ROP

ROP was detected in 11 (21%) neonates out of the 53 neonates studied.

Pattern of ROP in study participants

Of the 11 neonates with ROP, 9 (82%) had stage 1 disease, 2 (18%) had stage 2, and none was found with stage 3, 4, or 5.

Risk factors for retinopathy of prematurity

Of the 53 infants studied, 40 (75.5%) received supplemental oxygen, 31 (58.5%) received phototherapy, 23 (43.3%) received blood transfusion, 10 (18.9%) were products of multiple gestations, and 3 (5.7%) had intraventricular haemorrhage.

From this study, 5 (9.4%) mothers had premature rupture of membranes (PROM). Other risk factors are as displayed in Table 2.

Association among infant characteristics, risk factors, and occurrence of retinopathy of prematurity (*n* = 53)

Table 3 shows that the proportion of neonates with ROP was higher among those with GA ≤30 weeks [9 (81.8%)] compared with those with GA >30 weeks [2 (18.2%)] (*P* = 0.016). SBU had the higher proportion of infants with ROP [10 (90.9%)] when compared with the SCBU [0 (0.0%)] and Neonatal Clinic [1 (9.1%)] with *P* = 0.024. ROP was more common in females [7 (63.6%)] than their male counterparts [4 (36.4%)]. None

of the other risk factors was significantly associated with the occurrence of ROP.

Association between infant characteristics (risk factors) and severity of retinopathy of prematurity (*n* = 11)

Table 4 shows that among the infants who developed ROP, 7 (100.0%) of the females developed stage 1 ROP when compared with males who recorded 2 (50.0%) each with stage 1 ROP and stage 2 ROP (*P* = 0.109). Similarly, 7 (100.0%) of the infants with BW < 1500 g developed stage 1 ROP, whereas infants of BW ≥ 1500 g were 2 (50.0%) each with stage 1 ROP and stage 2 ROP (*P* = 0.109). None of the other infant characteristics or risk factors was significantly associated with the severity of ROP.

Discussion

This study has ascertained the occurrence of ROP in preterm babies admitted to the NICU in UCTH, Calabar, Nigeria. The incidence of ROP in this study was found to be 21%, of which 82% had stage 1 disease and 18% had stage 2 disease.

The incidence of ROP in our hospital at 21% is higher than earlier reports from Ibadan, Nigeria (12.2%),[1] Lagos, Nigeria (15%),[17] Ghana (13.7%),[18] Rwanda (7.3%),[8] but much less than the 30% reported from Iran,[19] Port Harcourt, Nigeria (47.2%),[4] Kenya (41.7%),[20] and Oman (46.4%).[21] However, the incidence recorded in this report is similar to the 19.2% reported in Egypt.[22] Reasons for these differences are not clear though a variation in sample size may play a role. Further research from other NICUs in Nigeria is needed to provide some clarity.

The increase in the incidence of ROP in developing countries including Nigeria is alarming, constituting what has been referred to as the 'third epidemic of ROP'.[23] The increase observed in Nigeria is likely due to an increase in awareness of the condition. On the contrary, the incidence of ROP is on the decline in developed countries, and this is attributable to the improvement in neonatal care and screening.

The mean GA and mean BW of neonates in our study were 30.91 ± 2.52 SD weeks and 1400 g, respectively. In comparison,

Table 1: Infant characteristics

Variables	Frequency (*N*=53)	Percentage (%)
Sex		
Male	23	43.4
Female	30	56.6
Screening site		
SCBU	15	28.3
SBU	36	67.9
Neonatal Clinic	2	3.8
Birth weight (g)		
800–1200	16	30.2
1300–1700	33	62.3
1800–2200	4	7.5
Mean weight ± SD	1400±0.27	
Gestational age (weeks)		
27–29	19	35.8
30–32	19	35.8
33–35	12	22.6
≥36	3	5.7
Mean age ± SD	30.91±2.52	
Corrected gestational age (weeks)		
27–29	1	1.9
30–32	14	26.4
33–35	23	43.4
≥36	15	28.3
Mean age± SD	34.06±2.52	

Table 2: Risk factors for retinopathy of prematurity

Variable	Yes frequency (%)	No frequency (%)	Total
Oxygen therapy	40 (75.5)	13 (24.5)	53 (100)
Ventilator	3 (5.7)	50 (94.3)	53 (100)
Phototherapy	31 (58.5)	22 (41.5)	53 (100)
Surfactant	6 (11.3)	47 (88.7)	53 (100)
Multi-birth	10 (18.9)	43 (81.1)	53 (100)
Apnoeic episodes	14 (26.4)	39 (73.6)	53 (100)
Blood transfusion	23 (43.3)	30 (56.6)	53 (100)
PROM	5 (9.4)	48 (90.6)	53 (100)
Respiratory distress syndrome	20 (37.7)	33 (62.3)	53 (100)
Sepsis	39 (73.6)	14 (26.4)	53 (100)
Intraventricular haemorrhage	3 (5.7)	50 (94.3)	53 (100)
Jaundice	40 (75.5)	13 (24.5)	53 (100)

Table 3: Association between infant characteristics (risk factors) and occurrence of retinopathy of prematurity (*n* = 53)

Variable	Occurrence of ROP		*P*-value (Fisher's exact test)
	Yes, *n* (%)	No, *n* (%)	
Gender			
Male	4 (36.4)	19 (45.2)	0.738
Female	7 (63.6)	23 (54.8)	
Birth weight (g)			
< 1500	7 (63.6)	20 (47.6)	0.501
≥ 1500	4 (36.4)	22 (52.4)	
Gestational age (weeks)			
≤30	9 (81.8)	16 (38.1)	**0.016***
>30	2 (18.2)	26 (61.9)	
Corrected gestational age			
≤34	9 (81.8)	22 (52.4)	0.097
>34	2 (18.2)	20 (47.6)	
Screening site			
SCBU	0 (0.0)	15 (35.7)	**0.024***
SBU	10 (90.9)	26 (61.9)	
Neonatal Clinic	1 (9.1)	1 (2.4)	
Apgar score at 1st minute			
1–3	0 (0.0)	1 (2.3)	1.000
4–6	4 (36.4)	13 (31.0)	
≥7	7 (63.6)	28 (66.7)	
Apgar score at 5th minute			
1–3	0 (0.0)	0 (0.0)	0.324
4–6	6 (14.3)	0 (0.0)	
≥7	36 (85.7)	11 (100.0)	
Oxygen therapy			
Yes	9 (81.8)	31 (73.8)	0.711
No	2 (18.2)	11 (26.2)	
Ventilator			
Yes	1 (9.1)	2 (4.8)	0.510
No	10 (90.9)	40 (95.2)	
Phototherapy			
Yes	6 (54.5)	25 (59.5)	1.000
No	5 (45.5)	17 (40.5)	
Surfactant			
Yes	1 (9.1)	5 (11.9)	1.000
No	10 (90.9)	37 (88.1)	
Multi-birth			
Yes	2 (18.2)	8 (19.0)	1.000
No	9 (81.8)	34 (81.0)	
Apnoeic episodes			
Yes	3 (27.3)	11 (26.2)	1.000
No	8 (72.7)	31 (73.8)	
Blood transfusion			
Yes	7 (63.6)	16 (38.1)	0.177
No	4 (36.4)	26 (61.9)	
PROM			
Yes	0 (0.0)	5 (11.9)	0.571
No	11 (100.0)	37 (88.1)	
Respiratory distress syndrome			
Yes	3 (27.3)	17 (40.5)	0.503
No	8 (72.7)	25 (59.5)	
Sepsis			
Yes	7 (63.6)	32 (76.2)	0.453
No	4 (36.4)	10 (23.8)	
Intraventricular haemorrhage			
Yes	1 (9.1)	2 (4.8)	0.510
No	10 (90.9)	40 (95.2)	
Jaundice			
Yes	10 (90.9)	30 (71.4)	0.257
No	1 (9.1)	12 (28.6)	

Table 4: Association between infant characteristics (risk factors) and pattern of retinopathy of prematurity (*n* = 11)

Variable	Pattern of ROP		*P*-value (Fisher's exact test)
	Stage 1, *n* = 9 (%)	Stage 2, *n* = 2 (%)	
Gender			
Male	2 (50.0)	2 (50.0)	0.109
Female	7 (100.0)	0 (0.0)	
Birth weight (g)			
<1500	7 (100.0)	0 (0.0)	0.109
≥1500	2 (50.0)	2 (50.0)	
Gestational age (weeks)			
≤30	8 (88.9)	1 (11.1)	0.345
>30	1 (50.0)	1 (50.0)	
Corrected gestational age (weeks)			
≤34	8 (88.9)	1 (11.1)	0.345
>34	1 (50.0)	1 (50.0)	
Screening site			
SCBU	0 (0.0)	0 (0.0)	1.000
SBU	8 (88.9)	2 (11.1)	
Neonatal Clinic	1 (100.0)	0 (0.0)	
Apgar score at 1st minute			
1–3	0 (0.0)	0 (0.0)	1.000
4–6	3 (75.0)	1 (25.0)	
≥7	6 (85.7)	1 (14.3)	
Oxygen therapy			
No	2 (100.0)	0 (0.0)	1.000
Yes	7 (77.8)	2 (22.2)	
Ventilator			
No	8 (80.0)	2 (20.0)	1.000
Yes	1 (100.0)	0 (0.0)	
Phototherapy			
No	4 (80.0)	1 (20.0)	1.000
Yes	5 (83.3)	1 (16.7)	
Surfactant			
No	8 (80.0)	2 (20.0)	1.000
Yes	1 (100.0)	0 (0.0)	
Multi-birth			
No	7 (77.8)	2 (22.2)	1.000
Yes	2 (100.0)	0 (0.0)	
Apneoic episodes			
No	7 (87.5)	1 (12.5)	0.491
Yes	2 (66.7)	1 (33.3)	
Blood transfusion			
No	4 (100.0)	0 (0.0)	0.491
Yes	5 (71.4)	2 (28.6)	
Respiratory distress syndrome			
No	7 (87.5)	1 (12.5)	0.491
Yes	2 (66.7)	1 (33.3)	
Sepsis			
No	2 (50.0)	2 (50.0)	0.109
Yes	7 (100.0)	0 (0.0)	
Intraventricular haemorrhage			
No	8 (80.0)	2 (20.0)	1.000
Yes	1 (100.0)	0 (0.0)	
Jaundice			
No	1 (100.0)	0 (0.0)	1.000
Yes	8 (80.0)	2 (20.0)	

GA and BW was lower at 29 weeks and 1400 g, respectively, for the Port Harcourt study[4]; babies were younger and weighed less at 30 weeks and 1260 g, respectively, in the Lagos study[17]; and babies were younger at 29 weeks and 1260 g, respectively, in the Ibadan study.[1] The study in Egypt[22] included infants with higher GA (>32 weeks) and BW (up to 2000 g), whereas the mean age in the ROP group in a study in Rwanda is somewhat similar to that in the index study at 30.1 weeks.[8] However, reasons for the variances in the incidences of ROP from these different studies can be alluded to the difference in the GA used, in addition to other yet-to-be determined factors.

The frequency and severity of ROP are inversely associated with GA and weight at birth. This was the observation in our study [Table 3], in which the frequency was 36.0% for babies delivered at ≤ 30 weeks of gestation and less than 7.1% for babies delivered at >30 weeks of gestation ($P = 0.016$). This finding in our study implies that the more preterm the baby, the more the likelihood of developing ROP. This is in agreement with recommendations of professional bodies in the USA including the American Academy of Ophthalmology, the American Academy of Paediatrics, and other work.[4,21,24] However, this is in contrast to what has been found in Ibadan[1] where ROP was more frequently detected in older preterm infants.

Also, for the index study, ROP was seen in 25.9% of babies weighing ≤ 1500 g and 15.4% of babies delivered with BW >1500 g, suggesting that ROP could be more commonly found in smaller preterm infants (the results were the same using the mean weight of our study, 1400 g). A similar trend is reported in some reports from Ibadan, Nigeria[1]; Accra Ghana[18]; and Hamadan, Iran.[19] It is noteworthy that in Rwanda, nearly a fifth of all babies with ROP were larger than the American Academy of Ophthalmology guideline.[8]

In contrast, stage 1 and stage 2 ROP were encountered during the duration of the study. Of the 11 preterm neonates with any ROP, 9 (77.8%) had stage 1 ROP, 7 (77.8%) of which were seen with BW <1500 g [Table 4]. Similarly, in the Port Harcourt, Nigeria study, stage 1 ROP was by far the most frequently encountered category [21 (84%)]. This trend is repeated in preterm babies who had neonatal jaundice, neonatal sepsis, or neonates who were given oxygen therapy. Although the findings were not statistically significant, a higher proportion of neonates who had stage 1 ROP and all neonates who had stage 2 ROP in our study (100%) received oxygen therapy. This is similar to what was reported from some African studies.[1,8]

Zero (0.0%) babies weighing <1500 g were diagnosed with stage 2 ROP, whereas 50.0% of babies weighing ≥1500 g and delivered at >30 weeks of gestation were diagnosed with stage 2 ROP. Note the low incidence of babies coming down with stage 2 ROP [2 (18.0%)] in our study as in the Port Harcourt, Nigeria[4] study but at variance with what was encountered in Ibadan, Nigeria,[1] in which the largest proportion of ROP was stage 2 disease. Again, no preterm had stage 3, 4, or 5 ROP in our study. Comparatively, in Ibadan, Nigeria, and Port Harcourt, Nigeria, stage 4 and stage 5 diseases were not encountered. Reasons for these may be related to the suggestion that very sick at-risk preterm babies may have died before their eye examination, relatively small sample size, among others.[4] Our findings also support the suggestion that the quality of neonatal care practice in Nigeria needs to be standardized and improved.[25,26]

Although no preterm neonates examined in the SCBU ICU had any ROP during the study, 10 (90.9%) had ROP with the larger portion [8 (72.7%)] being stage 1 ROP encountered in neonates in the SBU NICU [Table 4]. The association between the presence of ROP and the ROP screening site in our study, viz., SBU vs. SCBU, was statistically significant ($P = 0.024$). The SBU accommodates babies from very low-income segments of society whose mothers did not receive routine orthodox antenatal or delivery services and so had an increased risk of prematurity.[27] Increased incidence of prematurity and improved neonatal care increase the likelihood of developing ROP.[25,28] The risk of developing ROP is also increased in low-income settings.[26,28]

The contribution of the use of a ventilator, administered oxygen therapy, use of surfactant, apnoeic episodes, respiratory distress, multiple gestation, administration of blood transfusion, neonatal sepsis, PROM, and neonatal jaundice, all well-recognized risk factors for ROP were found not to be significantly associated with the occurrence of ROP in our study. The comparatively small number of babies screened, relatively short study duration, quality of neonatal care, and the fact that our ROP screening service had only just commenced could be contributing factors. Likewise, the Lagos study[17] did not find any associations between these recognized risk factors and ROP. However, the Ibadan study[1] found a statistically significant association between the development of ROP and necrotizing enterocolitis only, whereas the Port Harcourt study[4] found that supplemental oxygen therapy, sepsis, and blood transfusions were significantly associated with ROP. Further studies are essential to further explore the risk factors for ROP in Nigerian premature infants. The recognition of such risk factors would aid the modification of the country-specific ROP screening criteria and guidelines.

In conclusion, with the reported high prevalence of premature births in Sub-Saharan Africa, ROP may be an eye disease of public health importance in our environment. ROP was present in 21% of our study population. This study further validates the need to sustain and improve ROP screening services and emphasizes the need for better antenatal and newborn care in order to forestall avoidable blindness which could result from this condition.

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Conflicts of interest

There are no conflicts of interest.

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