

Retinopathy of prematurity: Prevalence and risk factors among infants in rural Kenya

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ABSTRACT

Background: Retinopathy of Prematurity (ROP) is a potentially blinding eye disorder that is seen in premature infants. Data is scanty on prevalence rates in Africa. This study was done to determine the prevalence and risk factors for ROP in a rural hospital in Kenya.

Design: A prospective cohort study.

Methods: The study was carried out at the Jaramogi Oginga Odinga Teaching and Referral Hospital, Kisumu, Kenya between March 2015 and April 2016 in the neonatal unit and outpatient eye clinic. Infants less than 32 weeks gestation and/or weighing less than 1500 grams at birth, plus those with an unstable clinical course had a dilated fundoscopic examination starting at 28 days of life. Exam findings were recorded using standard IC-ROP classification. Examinations were repeated every 1-2 weeks until mature vasculature in zone III was confirmed. Infants were excluded if they died before the ROP outcome or if they did not show up for the first outpatient exam.

Results: One hundred and thirty one neonates were included in the study, with a male to female ratio of 1:0.95 (64/67). Mean gestational age was 30.64 ± 3.6 weeks and mean birth weight was 1478 ± 414.08 grams. Of these, 91 (69.5%) had been on oxygen, with a mean of 4.6 ± 5.9 days on oxygen. Four babies developed ROP (a prevalence of 3.05%). Three (75%) had zone II, stage 1 ROP and one (25%) had zone II, stage 2 ROP; all regressed without treatment. No infant developed vision-threatening ROP. Peri-natal risks identified in this group included respiratory distress syndrome, prolonged oxygen administration, intra-ventricular haemorrhage and seizures.

Conclusion: ROP prevalence was much lower than that reported in other studies, with all cases of ROP regressing without treatment. The presence of ROP in this setting however, makes a case for screening in hospitals in rural areas.

INTRODUCTION

Retinopathy of Prematurity (ROP) is a potentially blinding eye disorder characterized by abnormal vessel growth in the retina of premature infants. Data is scanty on prevalence rates in Africa. Some African studies have shown high prevalence rates¹ while others have reported low prevalence rates that present a barrier to developing screening programs. While ROP screening is currently ongoing in some urban hospitals in Kenya, many premature infants are not screened as no universal policy has been established in the country. The Jaramogi Oginga Odinga Teaching and Referral Hospital in Kisumu, is a government hospital situated in the western part of Kenya. Kisumu county has a population of 968,909 living in an area of 805m². The main economic activities are fishing and farming. Despite a recent revamping of its neonatal unit, an ROP screening program has not been established. The neonatal unit admits 50-100 neonates per month and

has a bed capacity of 30. The unit is run by a team of paediatricians and there is no resident neonatologist. This study was carried out to determine the prevalence and risk factors for ROP in a rural hospital in Kenya.

MATERIALS AND METHODS

This was a prospective cohort study carried out at the Jaramogi Oginga Odinga Teaching and Referral Hospital, Kisumu, Kenya. It was conducted between March 2015 and April 2016 in the neonatal unit and outpatient eye clinic. All infants aged less than 32 weeks gestation and/or weighing less than 1500 grams, plus those with an unstable clinical course were identified on admission to and during their stay at the neonatal unit. Examinations were started at 28 days post-natal (PNA) and were carried out every one-two weeks in the neonatal unit or eye clinic. Those discharged prior to achieving 28 days PNA were followed up with a phone call reminder and provision of transportation to the hospital to reduce the risk of drop out. Dilatation

was achieved by installation of a mydratic cocktail drop (cyclopentolate 0.1% + phenylephrine 0.25% OR tropicamide 1% + phenylephrine 0.5%) instilled three times at 5 minute intervals in both eyes. Fundoscopic exam was then carried out 30- 40 minutes after the last drop was instilled. This was done with a Heine© Indirect ophthalmoscope and 28D Volk© lens. Fundus findings were then recorded in a questionnaire that contained a pictorial representation of the fundus. ROP was classified according to the International Classification of ROP revisited (ICROP)³. Other findings recorded on the questionnaire included days on oxygen, weights (at birth and at examination), anterior segment findings, neonatal risk factors (respiratory distress syndrome, anaemia/transfusions, IVH, neonatal sepsis, jaundice/ phototherapy, seizures, other congenital malformations) and maternal risk factors (multiple gestation, premature rupture of membranes, infection/sepsis, eclampsia, preterm labour and others). Exams were performed at two-week intervals if there was immature retina or stage 1 ROP in zone 2 without plus disease, at one-week intervals if there was immature retina in zone 1 or ROP without plus disease in zone 2 and continued until 50 weeks PMA or until vascularization in zone 3 was achieved. The majority (85%) of the eye examinations were carried out by a paediatric ophthalmologist, while the rest (15%) were done by a general ophthalmologist trained to carry out ROP evaluations.

RESULTS

There were 836 infants admitted in the neonatal unit during the study period. Of these, 303 were classified as premature (less than <37 weeks of gestation). Two hundred and fourteen fulfilled the criteria for inclusion in the study. Out of these, 131(61.2%) were examined. Those not examined (83/214; 38.8%) included deaths before the first exam (27/214; 12.6%), those discharged who did not come for any review (54/214; 25.2%) and those transferred out to other centers (2/214; 0.9%).

The male to female ratio was almost equal, with 64/131 (48.9%) males and 67/131 (51.1%) females. The mean gestational age was 30.64 weeks, calculated from the mother's last menstrual period, with a range of 22-39 weeks. Median age was 31 weeks and modular age 32 weeks. Birth weight of participants ranged from 600 - 3500 grams, with a mean age of 1478 grams. Figure 1 shows the distribution of gestational age and birth weight among infants respectively. The mean maternal age was 25 years, with a range of 17- 33 years.

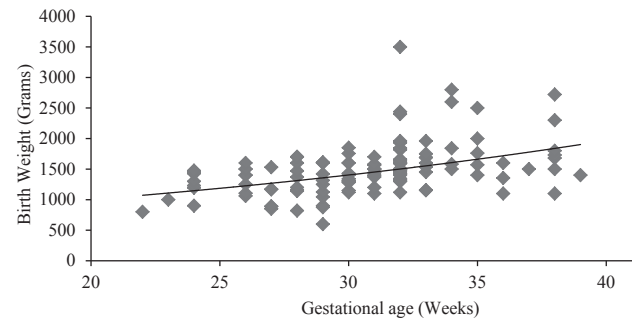


Figure 1: Distribution of birth weight vs gestational age (n=131)

Table 1: Distribution of perinatal risks among 131 included infants

Perinatal risk	No. (%)*
Anaemia	1 (0.6)
IVH	1 (0.6)
Jaundice	18 (10.3)
RDS	112 (64.0)
Seizures	1 (0.6)
Sepsis	15 (8.6)
Transfusion	0 (0.0)
Phototherapy	19 (10.9)
Malformation	0 (0.0)
Other (HIV-exposed, n=7, aspiration pneumonia, n=1)	8 (4.6)

*Percentage values have been rounded up and may not add up to 100

Out of the 131 neonates, 91 (69.5%) had oxygen administered during their hospital stay. The average days on oxygen was 4.6 ± 5.9 days with a range of 1-43 days. Table 2 shows gender distribution versus days of oxygen use. Of note is that there was no system of oxygen monitoring in this neonatal unit and all infants received 100% oxygen by nasal cannula.

Table 2: Oxygen use in days vs gender, (N=131)

Days on O ₂	Male	Female	Totals
None	18	22	40 (30.5%)
1- 3	36	25	61 (46.6%)
4- 7	8	11	19 (14.5%)
>7	2	9	11 (8.4%)

Four neonates were found to have ROP (3.05%; 99% CI 0.05 to 0.093%), with a total of 6 eyes being affected (2.29%; 99% CI 0.06 to 0.059%). All of these had either stage 1 or 2 ROP in zone II, and they all regressed without treatment, none developed vision

threatening ROP. Table 3 gives a description of ROP found in each patient. The risk factors identified in this group are as shown in Table 4. Due to the small number of ROP patients, statistical analysis was not performed.

Table 3: Rop descriptions, stage and zone. (N=4 patients)

	Right eye			Left eye			Inpatient or outpatient at diagnosis
	Stage	Zone	Plus	Stage	Zone	Plus	
Patient 1	1	II	-	0	II	-	Inpatient
Patient 2	1	II	-	1	II	-	Inpatient
Patient 3	2	II	-	2	II	-	Inpatient
Patient 4	1	II	-	0	II	-	Inpatient

Table 4. Biodata and Risk factors among neonates with ROP. (N= 4 patients)

Patient	Sex	GA (wks)	BWT (grams)	Days ON O ₂	Gestational risks	Perinatal risks	PMA and weight at diagnosis	
1	M	24	900	2	HIV exposed	*RDS	28wks	1390g
2	F	29	600	3	-	*RDS, sepsis	33wks	1530g
3	M	34	2800	43	HIV exposed	*IVH, *RDS seizures	46wks	3950g
4	M	26	1250	2	Twin	*RDS	34wks	2600g

*RDS- Respiratory Distress Syndrome *IVH- Intra-Ventricular Haemorrhage

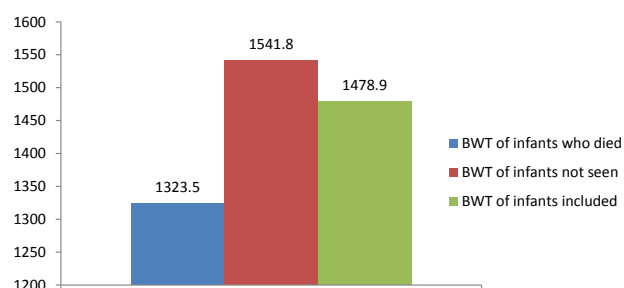


Figure 2: Comparison of average birth weight between infants who died, those never seen and those included.

Finally, a comparison was done between the included infants (n=131) and those who were never seen (n=56) or died before their first exam (n=27). It was found that those who died had a lower average weight than the other two groups, as demonstrated in Figure 2.

DISCUSSION

Retinopathy of prematurity in low and medium income countries has been identified as an upcoming epidemic due to recent improvements in neonatal care^{4,5}. Scanty data on prevalence rates in many developing countries has hampered the development of screening and treatment guidelines. Studies done in schools for the

blind in East Africa, in which Kenya was included, showed 0% blindness from ROP⁶⁻⁸. The conclusion was that neonates in these countries were not surviving long enough to develop the blinding disease.

The first prevalence study in Kenya, carried out in two urban hospitals, reported an ROP prevalence of 16.7%⁹. Other African studies have reported a prevalence ranging from 18.6%¹⁰ to 47.2%¹. Our study found a much lower prevalence of ROP (3.05%) than what has been reported. ROP prevalence may vary significantly even within one country depending on the level of neonatal care in each hospital, its location and setting (urban vs rural)⁴ and its survival rates at lower gestational age. In this study, the high mortality rates (12.6%) and high dropout rates (25.2%) could have also contributed to the low ROP prevalence found. It is important to stress that in our study, majority of the ROP screening examinations were done in the outpatient setting. Neonates were discharged from the neonatal unit once they achieved a weight of 1700 grams, which was usually before they achieved 4 weeks of life. Most babies therefore received their first eye examinations in the outpatient clinic. Higher risk infants usually remain in the hospital under medical care¹¹ thus have longer hospital stays. All four infants found to have ROP were diagnosed while undergoing in-patient care

in the NICU. Additionally, this hospital does not have paediatric surgery services, therefore patients that required surgery (2/214; with gastroschisis and cardiac disease) were transferred to other centers for treatment and thus not examined.

A comparison of the average birth weight between those who were included and those who were not (those who died or were never seen), revealed a lower average birth weight among the infants who died. Low birth weight has been identified as a risk factor for development of ROP. This could explain the low prevalence, as those more likely to develop the disease died before examination. On the other hand, those who never showed up for examination had the highest average birth weight. It could be extrapolated that this group of infants fared well at home after discharge and therefore their parents did not see the need to bring them to the clinic for examination.

All the babies in our study were of black African descent. Black race has been suggested as a protective factor for the development of ROP. Studies that have included race as a predictor variable have shown that black race infants have a lower prevalence of ROP blinding disease or ROP requiring treatment when compared to Caucasian infants^{12,13}. Good *et al*¹⁴ attempted to explain this racial variation, attributing it to Beta-adrenergic receptor polymorphisms in African-Americans as a protective factor. This theory can be explored for treatment of vision-threatening ROP. In a Nigerian study¹, despite a high ROP prevalence of 47.2%, none of the babies had stage 4 or 5 disease and all ROP cases regressed spontaneously. Wanjala *et al*⁹, in a Kenyan study with a prevalence of 16.8%, found no cases of stage 4 or 5 disease after examining 120 infants. While this could explain the low prevalence in this study, other factors including level of neonatal care need to be considered.

Gestational age and low birth weight have been consistently identified as risk factors for development of ROP. Our study was not an exception. Two-thirds of the infants that developed ROP had a gestational age of less than 30 weeks and birth weight of equal to/less than 1250 grams, which is consistent with current guidelines for screening. However, it is important to note that the infant with the worse stage of ROP had a GA of 34 weeks and BW of 2800 grams. This infant, the “forgotten baby”, escaped the nurses’ attention due to her large birth weight and gestation. She was later discovered by the ophthalmologist and provided the opportunity to emphasize screening of high risk infants who fell outside normal screening criteria. The most important risk for ROP development in this patient was clearly a very prolonged oxygen administration of 43 days.

Gilbert *et al*⁴ and Quinn¹⁵ have shown that in low and middle income countries, ROP develops in infants with larger GA and BW and it has been argued that expanded screening criteria should be used. The

forgotten baby is a clear example of how infants falling outside normal screening criteria can develop ROP. However, in Kenya, Wanjala *et al*⁹, after using an expanded screening criteria of <35 weeks GA and BW ≤1700 grams, found that only one infant 34 weeks GA and 1500 grams BW developed ROP. This infant had been on oxygen for 35 days and was on treatment for neonatal sepsis. He recommended screening at < 32 weeks and 1500 grams, with expanded screening criteria for those with prolonged oxygen administration, blood transfusions and neonatal sepsis.

In this study, the most consistent risk factor among the four babies with ROP was respiratory distress syndrome. Other risk factors identified were HIV exposure, multiple birth, sepsis and intra-ventricular haemorrhage. Comparable studies^{1,9} have listed low birth weight, oxygen administration, neonatal sepsis, blood transfusion, apnea and phototherapy as risk factors in univariate analyses. Due to the small numbers of ROP in this cohort we could not perform a meaningful analysis of each contributing risk factor.

While this study may question the necessity of having an ROP screening program in rural Kenya and other similar low income countries, it also confirms the emergence of ROP in this setting including Stage 2 ROP in a larger GA infant due to unregulated oxygen exposure. Improved neonatal care may reduce mortality and increase prevalence of ROP in rural government hospitals. Since ROP is a treatable condition with life-long implications for vision and disability if undetected, it seems prudent to continue with ROP screening of high-risk infants to avoid missing any case of this potentially blinding disease.

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