Retinopathy of Prematurity as seen in two major hospitals in Nairobi, Kenya

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Abstract

Aim: To determine the incidence, pattern and risk factors for Retinopathy of Prematurity (ROP) in Kenya (a developing country).
Design: Non-comparative cohort study.
Setting: Kenyatta National Hospital (KNH) and Pumwani maternity hospital (PMH) newborn units, November 2003 to April 2004.
Subjects: 120 consecutive low birth weight preterm babies (55 from KNH and 65 from PMH).
Results: A total of 240 eyes of 120 preterm babies weighing between 800g and 1750g were examined for the presence of ROP. At the end of the follow-up period, 16.7% had developed different stages of the disease (cumulative incidence). Mild ROP occurred in 18 (15.0%) and severe ROP in 2 (1.6%) of the babies. Only one baby (0.8%) had threshold ROP. This study did not find any stage 4 or 5 ROP. Duration of oxygen therapy, gestational age, birth weight, sepsis and blood transfusion were the most important known risk factors. On multivariate logistic regression analysis, only duration of oxygen therapy was independently associated with ROP. The study did not find any significant statistical association between the considered maternal risk factors and ROP.
Conclusions: Incidence of ROP in this cohort of preterm black African babies was lower compared to centres in developed countries and presented as mild ROP. The duration of oxygen therapy was found to independently predispose the babies to ROP.
Recommendations: There is need to monitor the trend of ROP in Kenya. Newborn babies on continuous oxygen administration should be closely monitored. Routine screening of babies above 32 weeks gestation may not be required.

Introduction

Retinopathy of prematurity is the disease of low birth weight preterm babies with prematurity and low birth weight being the definite risk factors reported.[1-4] Neonatal units have different incidence of the disease noted even within the same racial and geographical centres.

However, it has been noted that black infants with similar or even shorter gestation period are less likely to have any stage of ROP.[4] Despite the efforts being made in developed countries to unravel the cause and risk factors for ROP, little or nothing is being done in

developing countries. The incidence of ROP is under reported in developing countries especially in Africa.[14] It has emerged as a cause of blindness in children in industrialized countries during the late 1940's and 1950's owing to improvement in neonatal intensive care (NICU), which included supplemental oxygen and increased survival of pre-term babies.[5] Current researchers have concluded that the increasing risk of ROP is related to other risk factors other than low birth weight, low gestational age and receiving oxygen therapy.[1-4]

In view of the fact that the risk of blindness or visual impairment can be decreased with therapy, many countries have developed national screening programmes with serial retinal examinations to identify the few infants with threshold ROP. However, most developing countries especially in Africa have not done much in this area. Taking into consideration the tremendous improvement in neonatal care in these developing countries, there is continuous increase of survival of preterm born infants.[5] Retinopathy of prematurity is a disease of the retina which affects small premature babies by interruption of the developing retinal vessels by constriction and obliteration of the advancing capillary bed followed by neovascularization of the retina.[8-13] The general objective of the study was to report the incidence of ROP in newborn preterm babies at Kenyatta National Hospital and Pumwani Hospital nursery, identify the risk factors for ROP and establish common presenting patterns of ROP in these preterm babies.

Materials and Methods

This was a non-comparative cohort study involving screening of consecutively born infants with gestational age of 35 weeks or less and weighing 1750g or less at birth. It was conducted from November 2003 to April 2004 at Kenyatta National Hospital (KNH) and Pumwani Maternity Hospital (PMH) newborn units. Kenyatta National Hospital is a national referral hospital located in Nairobi. It is a public hospital offering services to Nairobi residents and referral cases from elsewhere in the country. Pumwani Hospital is largest maternity hospital in Nairobi, catering mainly for the population of the city slums.

Eye examination was done by the principle investigators using indirect ophthalmoscope and 20D Heine loupe after dilating the pupils of the babies with 2.5% phenylphrine and 1% tropicamide eye drops. A flashlight evaluation of adnexa and anterior segment was done before instilling the dilating drops. While awaiting dilation over the next 10-15 minutes, all the data about the baby was obtained and recorded. The WHO screening criteria for ROP was applied.[8] The infants who had immature (incomplete) retinal vasculature and in Zone II but no disease (ROP) was present, follow up examination was done 2 weekly until vascularization proceeded into Zone III. Those infants with ROP or immature vessels detected in Zone I were examined weekly until normal vascularization proceeded to Zone III or the risk of attaining threshold conditions was passed. The infants with threshold disease, (stage 3 ROP, Zone I and II in 5 or more continuous clock hours or 8 cumulative clock hours with the presence of "plus disease"), were referred to eye clinic for laser

therapeutic intervention. A pre-tested questionnaire was used to collect the data and record examination results.[12] The questionnaire was pre-coded and the data entered in the SSPS database software and analyzed statistically using student t-test for continuous variables and Chi-Square test for categorical variables.[22] Stepwise logistic regression analysis was used to determine the predictors associated with the development of the disease.[23]

Results

During the study period, all the preterm babies admitted were of black African origin. 200 preterm live born babies admitted with gestational age of 35 weeks and less and weighing 1750g and less. 116 were admitted at KNH New Born Unit and 84 at Pumwani Maternity Hospital New Born Unit. Forty nine infants died before the first examination was carried out leaving 151 infants with survival rate of 75.5% (151/200). Thirty one infants were excluded from the study because they died before 32 weeks post conceptual age or before attaining the 4 postnatal weeks or whichever came first at first examination.

This gave a drop out rate of 20.6%. Of the remaining 120 infants included in the study, 55 were from KNH and 65 from Pumwani Maternity Hospital. 47 (39.2%) were male and 73 (60.8%) female. The ratio of male: female was 1:1.3. 78 (65.0%) of the babies were of gestational age of 27 to 32 weeks (65%) while 15(12.5%) were 27 weeks and 27(22.5%) above 32 weeks. The shortest gestation period was 24 weeks. The mean gestational age for both hospitals was 30 weeks. There was no statistically significant difference, (p value=0.5), in gestational age between babies from KNH and those from Pumwani. There were 89 babies with birth weight less than 1500 grams of whom 45 were from KNH and 44 from Pumwani (p = 0.2.). The mean birth weight for KNH was 1314g, Pumwani 1435g and overall of 1375g. There was a statistically significant difference (p value = 0.007) between the mean birth weight of the two hospitals. The lightest baby enrolled in the study weighed 800g.

Table 1: Summary of fundus findings and fate of the babies in the study

Gestational age (weeks)	Complete vascularization	Incomplete vascularization	ROP	Total	Died
24	4	1	3	8	4
25	0	0	2	2	1
26	4	0	1	5	1
27	1	0	3	4	2
28	11	5	4	20	8
29	7	5	2	14	5
30	12	4	1	17	5
31	4	2	0	6	2
32	14	1	2	17	1
33	7	0	0	7	0
34	13	1	2	16	1
35	4	0	0	4	0
Total	81	19	20	120	30
%	67.5	15.8	16.7	100	25

Seven (5.9%) of the male babies and 13(10.8%) of the female babies had ROP. There was no significant statistical difference of ROP incidence between male and female babies (p=0.67). ROP was bilateral and symmetrical in all. Six babies had features of plus disease.

Table 2: Cumulative incidence of ROP in various gestational age groups

Stage of ROP	Gestational age (weeks)				
	$\leq$ 26	27-29	30-32	33-35	
No ROP	9	29	37	25	100
Stage 1	0	3	3	1	7
Stage 2	5	6	0	0	11
Stage 3	1	0	0	1	2
Total	15	38	40	27	120
% ROP within age group	40%	23.7%	7.5%	3.7%	

Incidence was higher in babies born at or before 32 weeks (18 out of 20). There was a significant statistical difference between gestational age and incidence of ROP (p value = 0.003).

Table 3: Cumulative incidence of ROP by birth weight

Stage of ROP	Birth weight(g)			
	≤1000	> 1000-1500	>1500-1750	Total
No ROP	5	66	29	100
Stage 1	0	6	1	7
Stage 2	5	6	0	11
Stage 3	1	0	1	2
Total	11	78	31	120
% of ROP within birth category	54.5%	15.4%	6.5%	

Incidence of ROP was lower in the heavier babies >1000g as compared to in those with birth weight <1000g (p=0.000).

Table 4: Stage of ROP and the number of days on oxygen (n=120)

Stage of ROP	Days on oxygen			
	< 7 days	8-14 days	> 14 days	Total
No ROP	48	23	29	100
Stage 1	0	3	4	7
Stage 2	1	1	9	11
Stage 3	0	1	1	2
Total	49	28	43	120
% ROP within the group	2%	17.9%	32.5%	16.7%

Fourteen babies with ROP had been on oxygen for more than 2 weeks (p=0.004).

Table 5: Neonatal risk factors and ROP

Risk factor	Babies without ROP	Babies with ROP	P value
Mean birth weight (g)	1434	1160	0.00
Mean days on oxygen	10	21	0.00
Neonatal sepsis(n=55)	38	17	0.000
Blood transfusion(n=15)	8	7	0.004
RDS(n=70)	51	19	0.000
Apnea(n=90)	70	20	0.003
Apgar score 5min(n=37)	27	10	0.000
Phototherapy (n=9)	4	5	0.006
Fetal distress (n=78)	61	17	0.003
Convulsions (n=3)	2	1	0.424

On multivariate logistic regression analysis, only duration of oxygen therapy was independently associated with ROP.

Table 6: Maternal risk factors and ROP

Risk factor	Babies without ROP	Babies with ROP	P value
Maternal infection (n=11)	7	4	0.086
PROM (n=4)	3	1	0.523
APH (n=14)	10	4	0.248
PIH (n=12)	9	3	4.19
Maternal diabetes (n=1)		1	0.167
Multiple pregnancy(n=10)	9	1	1.000

None of the maternal factors considered was statistically significant as a risk factor for ROP (p=0.424). However some risk factors such as maternal anemia were not looked into because the data was not available.

DISCUSSION

The cumulative incidence of ROP in this study was 16.7% which correlates with published data from other African countries in the region such as South Africa being 24.5%.[12] These two studies had different survival rates and drop out rates, 75.5% in our study versus 64.4% and 20.6% versus 54.2% respectively. Our findings differ greatly from those of a survey done in Ethiopian schools for the blind which found no case of ROP. Their conclusion was that may be the very low birth weight babies do not survive to be admitted in theses schools or most of the cases they diagnosed as bilateral phthisis bulbi were actually the end stage ROP.[12] These findings of the Ethiopian study were also supported by another study done by Gilbert C. et al in some sampled developing countries, which included African countries, which found prevalence of ROP in most African countries ranging from 0% - 38.6%. Their conclusion was that most middle income countries lack intensive care services but ROP is becoming a major cause of potentially preventable blindness among children in those countries that have introduced intensive care services for preterm and low birth weight babies as it is now being evidenced at KNH and Pumwani hospitals in Nairobi. These results may not be exactly comparable to ours, since the Ethiopian study did not consider the preterm babies in their NICU. It must be noted that 81 babies (67.5%) in this study had complete vascularization of the retina by the end of examination without having developed any form of ROP, including the very preterm and those with very low birth weight, contrary to U.S.A cryo ROP study which found that more than 60% of preterm babies born at or less than 32 weeks gestational age will develop some stage of ROP[10]. Mild ROP occurred in 18 of the infants screened (15%) and stage 3 ROP in 2 babies (1.6%) similar to findings of Kalafong Hospital and University of Pretoria, South Africa which found 18.1% mild ROP and 6.4% stage 3 ROP.[12] There was no stage 4 and 5 ROP seen in this study. This is comparable to findings from studies done on black Americans in the U.S.A and black South Africans which also did not find stage 4 and 5 ROP in black premature babies.[11] One baby had threshold ROP giving an incidence of threshold ROP as 0.8%. Published data from the U.S.A cryo ROP study show that black infants have a lower incidence of threshold ROP than their white counterparts (3.2% versus 7.4%) with similar exposure risks. The study done by Delport S.D. et al. in South Africa found an incidence of threshold ROP of 4.3%. Treatment was not offered to the baby found to have threshold ROP because the baby had severe sepsis and died before treatment could be started. This was rather disappointing since the aim of screening was to detect infants with severe ROP, which is before threshold is reached and in time to perform treatment. There were 47 males and 75 female babies (table 1). Seven males and 13 females had ROP. Statistical analysis of these figures did not show any significant sex difference in incidence of ROP (p value= 0.67). This finding concurs with other studies which did not show any sex preference for ROP.[17] However, Larson E.et al, in a study done in Sweden, found a significant sex difference (p value= 0.04) with girls being at a higher risk.[10]

All the patients with ROP in this study had bilateral ROP with no difference between the eyes with regard to the stage of ROP, similar to findings from other studies done elsewhere.[16] No ROP was found in Zone I. Six out of 20 babies with ROP had features of plus disease. Two of the above six babies had stage 3 ROP and 4 had stage 2 ROP. All babies with stage 1 ROP had no posterior pole abnormalities. These results compare with results from a study done by Richard A. Sander et al which found that all severe cases of ROP can be detected just by examining the posterior pole for dilated blood vessels.[14] They suggested that this screening can be successfully done by non-ophthalmologist using direct ophthalmoscope and the suspected ROP cases can then be referred to the ophthalmologist for diagnosis and management. There is a significant association between gestational age and ROP (p value = 0.003). It is worthwhile to note that majority of the babies with ROP were in the age group < 32 weeks (15%) with the highest incidence in the very premature < 26 weeks (40%), 27-29 weeks (23.7%), 30 – 32 weeks (7.5%) and 33 – 35 age group being (3.7%). From the above discussion it emerges that screening babies above 32 weeks gestation may not be required routinely. It is important to note that the two babies who had ROP in this age group, (above 33 weeks), also had sepsis with respiratory distress syndrome and frequent spells of apnea. The highest incidence of ROP 54.5% is recorded in the lightest group (<1000g). There is a significant statistical association between birth weight and ROP (p value= 0.000). Only two babies with birth weight > 1500g developed ROP, one of which had severe ROP contrary to findings of AL-Fissa M. et al who concluded in their study that ROP does occur in babies of birth weight more than 1500g, but in mild form and with good prognosis and screening in this group of babies is not warranted. However it has been demonstrated in this study that severe ROP can occur in babies with birth weight above 1500g especially if they have sepsis. The limitation in this conclusion is that our study had only two babies with ROP in this weight category. All the babies with ROP were exposed to oxygen. The babies with severe ROP had been on continuous oxygen for a period of more than 2 weeks. The baby who developed threshold ROP had been on oxygen for 35 days. On multiple stepwise logistic regression analysis only the number of days of oxygen exposure was found to be an independent neonatal risk factor and hence predictor of ROP. Larson E. et al, found gestational age at birth and birth weight being the only independent neonatal risk factors.[16] Al-Essa. et al, found that none of these neonatal factors was an independent predictor of the disease. When analyzing maternal risk factors, both univariate and multivariate logistic regression analysis showed that none of the risk factors considered in table 12, were an independent predictor of the disease. It was concluded that ROP does occur in premature black African Kenyan babies although at a lower incidence as compared to other centres in developed countries. The most frequent presentation is mild ROP. The duration of exposure of preterm, low birth weight babies to oxygen independently predispose them to developing ROP. The maternal risk factors considered in this study were not found to have any statistical significance in predisposing the preterm babies to ROP. There is need to monitor the trend

of ROP in Kenya. Newborn babies on continuous oxygen administration should be closely monitored. Routine screening of babies above 32 weeks gestation may not be required necessary.

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