Screening of Retinopathy of Prematurity in Khartoum City, Sudan, 2011-2012

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Abstract

Retinopathy of prematurity (ROP) is a proliferative retinopathy that develops in premature infants due to incomplete vasculogenesis of the retina at the time of birth. It can be mild with no visual defects, or it may become aggressive with new blood vessel formation (neovascularization) and progress to retinal detachment and blindness. The objective was to estimate the incidence of ROP in preterm infants in the Neonatal Intensive Care Unit (NICU) and to identify the risk factors which predispose to ROP. A ROP prospective screening survey was performed enrolling premature infants admitted to Alsiwadi hospital Neonatal Intensive Care Hospital, nursery of Soba and nursery of Alribat hospitals, from November 2011 to September 2012, with a gestational age of 32 weeks or less at birth and a birth weight of 1500 g or less. A total of 60 infants (21 males and 39 females) had retinal evaluation by indirect ophthalmoscopy from the fourth postnatal week. Risk factors for ROP were assessed using statistical analysis. Out of the studied 60 infants, 19 infants (31.7%) developed ROP in one or both eyes; of which 17 babies (89%) had severe ROP. Incidence of ROP from all according to hospitals was 68.4% in Soba, 26.3% in Alsiwadi, 5.3% in Alribat. Statistical analysis showed that there was a significant relationship between the occurrence of ROP and stay in hospital more than 15 days ($P = 0.012$), nasal cannula and nasal continuous positive airway pressure (NCPAP) as mode of oxygen delivery ($P = 0.002$). However, an insignificant relationship was found between the occurrence of ROP and gestational age, birth weight, sex, respiratory distress syndrome, patent ductus arteriosus, intraventricular hemorrhage, hyaline membrane disease, apnea, blood transfusions, necrotizing enterocolitis, meningitis, consanguinity, and age of the mother (all $P > 0.05$). Incidence of ROP in our study was the same as most of the other reported studies in developing countries. Our results suggest that ROP is an important emerging cause of preventable childhood blindness in our country.

Keywords: ROP, Neovascularization, Neonatal Intensive Care Unit, oxygen delivery

INTRODUCTION

ROP is a vasoproliferative disorder of the eye affecting premature neonates, can progress to vetroretnial haemorrhage and tractional retinal detachment, which can result in functional or complete blindness (American Academy of Pediatrics, American Association for Pediatric Ophthamlology and Strabismus, American Aca-
deemy of Ophthalmology, 2001; Quinn, 2010) both of which carry a high financial cost for the community and but a high individual cost by affecting the normal motor, language, conceptual and social development of the child (Piccioni et al., 1997; Mets, 1999). In developing countries worldwide, ROP is now a leading cause of childhood blindness. ROP Of significant complications in preterm neonates despite advances in neonatal care remains a major cause of Childhood blindness worldwide (Campbell, 1950). Due to improved obstetrical and neonatal care, survival of small babies increased. Over the past 60 years, 3 epidemics of ROP have been described. The first in 1940-1950, which was due to unrestricted use of supplemental oxygen (Campbell, 1950). The second, in late 1960 was due to improved survival of Extremely Low Birth Weight (ELBW) (Gibson et al., 1989) now ROP is becoming more significant cause of blindness in developing countries (third epidemic of ROP) (Gilbert et al., 1997).

The WHO ‘Vision 2020’ program (Gilbert and Foster, 2001) targeted ROP as an avoidable disease requiring early detection and treatment to prevent blindness and inherent costs to the individuals and the community (Gilbert and Foster, 2001). Because of the sequential nature of ROP progression and the proven benefits of timely treatment in reducing the risk of visual loss, effective care now requires that ‘at-risk’ infants receive carefully timed retinal examinations by an ophthalmologist who is experienced in preterm infants examination for ROP and that all pediatricians who care for these ‘at-risk’ preterm infants be aware of this timing.

Although many causative ROP factors have been proposed, only low birth weight, low gestational age, and supplemental oxygen therapy following delivery have been consistently associated with the disease.

The International Classification of Retinopathy of Prematurity (ICROP) adopted a well structured classification of ROP (ICROP (International Committee for the Classification of Retinopathy of Prematurity), 2005) in 1984; revised in 1987 (Committee for the Classification of Retinopathy of Prematurity, 1987). Then an international group of pediatric ophthalmologists and retinal specialists has developed a consensus document that revises some aspects of ICROP in 2005. The classification was based on the severity (stage) and anatomic location (zone) of the disease (ICROP (International Committee for the Classification of Retinopathy of Prematurity, 2005; Committee for the Classification of Retinopathy of Prematurity, 1987).

The Stages describe the ophthalmoscopic findings at the junction between the vascularized and avascular retina: stage 1 is a faint demarcation line, stage 2 is an elevated ridge, stage 3 is extraretinal fibrovascular tissue, stage 4 is sub-total retinal detachment, and stage 5 is total retinal detachment.

**MATERIALS AND METHODS**

A prospective, hospital-based study; screening of ROP was performed in Metropolitan Khartoum city, Sudan during the period from November 2011 to September 2012. 40 premature infants from Alsiwadi Hospital; which is a highly equipped NGO tertiary Neonatal Intensive Care Hospital in Khartoum, with a capacity of 40 incubator-beds and 35 patients per month turnover rate; only devoted for premature babies with a capacity of 60 modern incubators and highly specialized staff; were enrolled in this study. Other 20 premature babies were added from another two nurseries within general hospitals in Metropolitan Khartoum city; 18 babies from Soba hospital and 2 from Aribat hospitals. There are big differences in equipments; oxygen monitoring and premature baby’s capacity between the three hospitals.

We included all babies of gestational age of 32 weeks or less, birth weight of 1500 g or less and infants whose gestational age was >32 weeks or birth weight was >1500 g with a course of instability (sepsis or they were under continues ventilation). A total of 60 infants, 21(35%) males and 39 (65%) females had retinal evaluation by indirect ophthalmoscopy and +28 diopter lens; from the fourth postnatal week. Then we followed up the babies on regular schedule bases; over the whole study period. The Risk factors for ROP were assessed using statistical analysis. We exclude infants with fatal systemic anomaly, unilateral or bilateral retinal or choroid disease; other than ROP, infants with a media opacity precluding fundus visualization (e.g., cataract) or if there was refusal of initial consent from the parents. Data was analyzed by the Statistical Package for the Social Sciences (SPSS for windows, version 20). Descriptive statistics included the mean and standard deviation for numerical variables, and the percentage of different categories for categorical variables. The incidence rate of ROP was described in simple proportion. A P value of 0.05 or less was considered statistically significant.

**RESULTS**

In this study; sixty Sudanese neonates (n=60); 21(35%) males and 39 (65%) females (Figure 1) with significantly low birth weight; the mean birth weight of all neonates was1182.3 g (range from 740 to 1900 g; SD 245.3 g) (Figure 2). The mean gestational age was 29.87weeks (range from 27 to 34 weeks, SD ± 1.91 weeks) (Figure 3).

Out of the studied 60 infants, 19 infants (31.7%) developed ROP in one or both eyes; of which 17 babies
(89%) had severe ROP warrant intervention (Figure 4). Number of ROP cases detected in Alsiwadi Hospital was only 5 cases out of total 40 babies examined; giving a 12.5% incidence of ROP from the total study group and incidence of 8.33% from the number of premature within this specialized Hospital. 14 cases were detected in the other two nurseries; 13 neonates in Soba nursery, and one in the ‘two-bed nursery’ in Alribat hospital; showing an incidence of 23.33% in these two nurseries.

Bilateral ROP was detected in 17 (89.5%) babies and unilateral disease was found in 2 babies (10.5%) from the total study group (n=60). Spontaneous regression was observed in only 6 (10%) babies; 3 babies in Alsiwadi Hospital and the other 3 in Soba hospital.

10 (16.7%) of the affected babies were treatment: 5 babies (8.3%) by indirect ophthalmoscope-mounted-laser, 4 babies (6.7%) were treated by Intravitreal Avastin injections (Anti-Vascular Endothelial Growth Factor; bevacizumab) and one baby (1.7%) met the criteria of Pars Plana vitrectomy retinal surgery. Loss of follow up was recorded in 3 babies. We did not record any case of Stage 5 ROP.

Statistical analysis showed that there was a significant relationship between the occurrence of ROP and stay in
hospital more than 15 days ($P = 0.012$), nasal cannula and CPAP as mode of oxygen delivery ($P = 0.002$).

However, an insignificant relationship was found between the occurrence of ROP and gestational age, birth weight, sex, respiratory distress syndrome (RDS), patent ductus arteriosus, intraventricular hemorrhage (IVH), hyaline membrane disease, apnea, blood transfusions, necrotizing enterocolitis, meningitis (NEC), consanguinity, and age of the mother (all $P > 0.05$). ROP as a result of multiple pregnancies were 21% and 79% from a single pregnancy.

The presence of sepsis among babies with ROP was high; up to 89%. 84% of ROP patients received of blood transfusion during their hospital coarse. About 89% of ROP patients were developed respiratory distress syndrome.

**DISCUSSION**

Retinopathy of prematurity is a disorder of retinal vascular development in preterm infants. It continues to be a significant complication in preterm neonates despite advances in neonatal care. It remains a major cause of childhood blindness worldwide.

In Sudan’s current situation: there is only one specialized Neonatal Intensive Care Hospital “Alsiwadi hospital” which is well equipped with well trained staff dealing only with premature babies. Other centers although they have well trained staff but they are smaller units within general hospitals (Omdurman Maternity, Soba, Alribat, Bahri and Military hospitals etc…). These units are smaller in capacities and less facilities for controlling oxygen delivery, monitoring saturation and avoidance of fluctuation, so there is a difference in ROP incidence between the chosen hospitals:

To our knowledge; this is the first ROP screening study conducted in Sudan, so there is no available national data to compare with.

The overall incidence of ROP in the current study was 31.7% which was almost in agreement with the south of Iran study which reported an incidence of 32.4% (Afarid et al., 2012). But slightly less than Bassiouny and colleagues from Oman who reported an incidence of 34% (Bassiouny, 1996), King Abdul-Aziz University Hospital of Saudi Arabia study which reported an incidence of 37.2% (Al-Amo et al., 2003), Aga Khan University of Pakistan study 37.4% (Taqui, 2008) and Kuwait study 38.9% (Vivek, 2008).

The report from Al -Minya University Hospital study documented a lower incidence of 19.2% (Abdel et al., 2012), possible due to improved facilities and well controlled oxygen saturation. This situation is similar to our highly specialized tertiary Neonatal Intensive Care
Hospital “Alsiwadi Hospital” in Khartoum which reported only 5 cases out of total 40 babies examined; giving a 12.5% incidence of ROP from the total study group and incidence of 8.33% from the number of premature within this specialized Hospital. This emphasizes the benefit of having special Neonatal Intensive Care Hospitals.

In this study there were 15 neonates (79 %) as an outcome of single pregnancy and 4 neonates (21%) of multiple pregnancy (figure 3.2), this in contrary of literature where the incidence of ROP in multiple pregnancies is higher than in single ones.

In our study, we found that stay in hospital more than 15 days was significantly associated with the development of ROP, explained by associated other complications of prematurity like RDS, IVH and NEC, which need treatment with oxygen and other modalities of treatment and close follow up for long periods, in addition to prematurity per se.

We found that nasal cannula and nasal continuous positive airway pressure (NCPAP) as mode of oxygen delivery (Figure 5) were significant risk factors for ROP (Figure 5) and this disagreed with Murthy et al. (Chaudhari et al., 2003), who found that nasal CPAP was a significant risk factors for ROP. It is explained by the fact that fixed concentration of oxygen varies on the flow rate by only nasal cannulas. On the other hand, NCPAP designed to deliver higher concentrations of oxygen to premature babies who have trouble maintaining good oxygen levels in their blood that can cause hyperoxia, which induced neovasclarization. However, early nasal CPAP is associated with lower rates of chronic lung disease and ROP (Kirchner et al., 2005), some researchers claimed that ventilator support and NCPAP may be associated with development of ROP; which can be explained by delayed treatment onset.

In our study, low-gestational age (LGA) is insignificant risk factor, which was in disagreement with the results reported by Shah (Vinekar et al., 2007) and Karna (Arroe and Peitersen, 1994). This may be explained by the small number of patients and there were babies with smaller gestational age e.g. 26 weeks without ROP, in addition to the presence of concomitant medical problems shared in the development of ROP even when gestational age is more than 32 weeks.

It has been reported that infants of low birth weight (LBW) may be more likely to develop ROP (Shah et al., 2005). This was not confirmed in our study, as we found that birth weight was an insignificant factor for the development of ROP which concurs other reported studies like “Arroe and Peitersen” (Palmer et al., 2005).

But this was in disagreement with some studies (Vinekar A, Dogra M, Sangtam T) (Vinekar et al., 2007) which reported that LBW was significantly associated with development of ROP, and explained that by more susceptibility for oxygen therapy, prolonged ventilation, sepsis, and blood transfusion in very low birth weight infants.

It is imperative for studies to explore the association between ROP and risk factors other than the three well recognized risk factors: LGA, LBW and supplemental oxygen, especially in developing countries because it is known that larger more mature infants are developing advanced ROP in countries with low levels of development compared to developed countries (Shah et al., 2005). A plausible explanation for this observation is that risk factors like sepsis which is more prevalent in developing countries, account for the advanced ROP in infants with relatively large gestational age and good birth weight.

In our study, oxygen therapy was not significantly associated with the development of ROP, explained by the fact that there was babies received oxygen and did not develop ROP. This was in agreement with Palmer and his group (Murthy and Nagendra, 2006). They reported that ROP may develop in cases that did not receive oxygen therapy.

In this study, we found that sepsis was not significantly associated with the development of ROP. This was in agreement with results of Chaudhari and colleagues (Smith, 2002) and Smith (Deepak et al., 2008). On the other hand, this was in disagreement with (Shah et al., 2005) and (Vinekar et al., 2007).

In our study, we found that blood transfusions are not a risk factor for development of ROP, this disagreed with Deepak and colleagues (Hirano et al., 2001). While Hirano and his co-workers (2001) (Darlow et al., 2005) stated that it is controversial and iron overload rather than number of transfusions may contribute to the development of ROP.

Our study revealed insignificant relationship between sex and occurrence of ROP, in contrast to Darlow and his group (Lokesh et al., 1942) who found that male sex is a significant risk factor.

Bilateral ROP was detected in 17(89.5%) babies and unilateral disease was found in 2 babies (10.5%) which are more than elsewhere e.g. Indian Uttar Pradesh region which was found to be 73% (Taqui et al., 2008).

Other risk factors including RDS, patent ductus arteriosus (PDA) , IVH, necrotizing NEC, meningitis, hyaline membrane disease and apnea, showed insignificant relationship with the occurrence of ROP, explained by small number of study sample. Similarly with Taqui and fellows (2008); reported insignificant relation between ROP and PDA and IVH, but observed a significant relation between RDS and the development of ROP and related this to the fact that systemic hypoxia results in retinal hypoxia and more need for oxygen therapy. On the other hand, Shah and his group (Shah et al., 2005) reported a significant relation between ROP development and PDA and IVH.

Surprisingly consanguinity was observed only in 35% among study population, and it is insignificant risk factor, may be due to consanguinity marriage decreased in our countries in the last years.
In our country average age of marriage is small in most of the state, resulting in decreased maternal age at childbirth, so age of the mother is insignificant risk factors for occurrence of ROP, this disagreed with results of Gung Memorial Hospital study, done in Taiwan (Wu, 2010).

**CONCLUSION**

The incidence of ROP in our study, which was 31.7%, was comparable to other studies. Stay in hospital more than 15 days and NCPAP as mode of oxygen delivery were the most important risk factors, whereas other risk factors including gestational age and birth weight were insignificant factors in our study.

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**Disclaimers**

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**REFERENCES**


