



Original Research Article

Ophthalmic manifestations of 500 consecutive cases of premature birth

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ABSTRACT

Aim: To find out prevalence of Retinopathy of prematurity (ROP) and congenital malformations in a series of consecutive 500 premature babies, and to study various risk factors associated with ROP.**Materials and Methods:** Hospital based prospective observational study of 500 consecutive premature babies admitted to the specialized newborn care unit and attending to the eye OPD having gestational age less <37 weeks over a period of one year. All the babies were examined following four weeks of birth. Risk factors such as gestational age, birth weight, twin pregnancy, history of oxygenation and systemic illness were assessed. Infants having signs of ROP were referred to vitreo-retina specialist.**Results:** A total of 500 premature consecutive babies were examined. Incidence of ROP was found to be 6.8% (n = 34), the majority of whom (20) had Stage I ROP. Seven (22%) of the infants having ROP weighed <1000 g. The percentage of twin pregnancy was (11.8%). Prevalent postnatal risk factors included oxygen treatment (67%) and respiratory distress syndrome (41%) sepsis 26.5%. 8% babies also developed retinal haemorrhages. 31 babies were found to have some or other forms of Congenital ocular anomalies.**Conclusion:** Retinopathy of prematurity is the leading cause of blindness in the premature infants. Staging the disease correctly and following the national treatment guidelines and timely screening could help in reducing the burden.© 2019 Published by Innovative Publication. This is an open access article under the CC BY-NC-ND license (<https://creativecommons.org/licenses/by/4.0/>)

1. Introduction

Advances in medical technology and understanding over the last several decades have resulted in significant improvements in the survival of premature infants. Preterm birth can impose challenges on the developing ocular system, resulting in the various visual manifestations of varied significance and pathological scope.

The ocular condition commonly associated with preterm birth is retinopathy of prematurity, which has the potential to result in severe vision loss. Retinopathy of prematurity (ROP) also called retrolental fibroplasia is disease of the developing retinal vasculature of the premature infants, first described by Terry¹ in 1942 in a premature infant who had greyish white vascular membranes behind the lens in both the eyes. Its incidence is higher in babies of low gestational

age and birth weight.^{2,3} Risk factors of ROP other than prematurity include hyperoxia, sepsis, blood transfusions, acidosis, antioxidant deficiency, patent ductus arteriosus, apnoea and intraventricular haemorrhage.

In the Indian scenario, ROP screening should be performed in all preterm neonates who are born <34 weeks of gestation and/or <1750 g birth weight; as well as in babies 34-36 weeks of gestation or 1750-2000 g birth weight if they have risk factors for ROP. Screening should start by one month after birth, and as early as 2-3 weeks of age in infants born <28 week or <1200g birth weight.⁴ The overall extremely low birth weight (<1000gms) infants are three times more likely to have a vision of less than 6/60 than those born at term.⁵ Congenital ocular anomalies are also commonly encountered in premature babies. Most congenital anomalies are present long before the time of birth, some in the embryonic period (up to the 7th week

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of gestation) and other in the fetal period (8th week to term). Various ocular congenital anomalies which are commonly seen are Microphthalmos, Microcornea, iris and choroid coloboma, congenital cataract, and congenital nasal duct obstruction etc. The immature eye differs in many respects from that of a child born at term and certainly can be much different than the adult eye. An understanding of these differences is important to the ophthalmologist, paediatrician, primary care provider, and the parents. Careful coordination between the neonatologist, and the ophthalmologist is required.⁶

2. Materials and Methods

This hospital based prospective observational study was conducted between September 2018 to August 2019 and approved by the ethical Committee at our institution. Study included total 500 consecutive premature infants having gestational age of less than 37 weeks. All infants admitted to the SNCU and babies attending to eye opd were screened for ROP and examined for congenital ocular anomalies. Data including demographic profile, birth weight, gestational age, history of sepsis, respiratory distress syndrome, oxygen therapy were recorded. Prenatal risk factors measured include multiple gestations. The pupils were dilated using 2.5% phenylephrine and 0.5-1% tropicamide, instilled twice at an interval of 15 minutes. The infant was wrapped warmly to prevent them from hypothermia. Pediatric wire speculum was used to separate the lids. Screening was performed under aseptic conditions, using an indirect binocular ophthalmoscope with a + 20 diopter lens. Examination was done under supervision of a pediatrician. Fundus findings were classified according to International Classification of ROP ICROP. A strict protocol was adopted for follow-up of these infants. Infants having immature retina were followed till the peripheral retinal vascularization was complete, while Infants having signs of ROP were referred to vitreoretinal clinic for further management.

3. Result

A total of 500 consecutive premature babies were examined admitted to the SNCU between September 2018 and August 2019. 34 (6.8%) infants were diagnosed with ROP. Patients with ROP showed a slight female predominance (52.9% female, 47% male). All infants with ROP weighed <1900 gm at birth, with 47% (16) weighing between 1000 to 1499gms and, 32% (11) between 1500 and 2000 g, and 20% (7) less than 1000gm. The average birth weight of babies developing ROP was 1.317 k g (range: 0.54-1.9, SD, 0.329). The average GA of babies developing ROP was 28.47 (range: 24-36, SD 2.312). Bilateral ROP was detected in 30 (34.7%) babies and unilateral disease was found in 4 babies only. Percentage of the infants having ROP was

maximum 73.5% (25) in gestational age of less than 28 weeks, and 11% (4) in 29-32 weeks, (5) 14% in more than 32 weeks of gestational age as shown in Table 4. Maximum cases were seen in Zone III i.e. 20 (60%), 10 (30%) in Zone II and remaining cases 4 (10%) were noted to occur in Zone I. The most prevalent postnatal risk factors among patients with ROP were RDS, Sepsis and use of oxygen therapy. The most prevalent postnatal risk factors seen in our study among patients with ROP were Respiratory distress syndrome (RDS) and use of oxygen therapy. Forty one percent of patients with ROP experienced RDS and 67% needed oxygen therapy. Mean duration of oxygen therapy required was 3 days (range: 0-15 days). Other postnatal risk factors noted were presence of sepsis in 9 babies (26.5%), and in patients with no ROP it was 3(0.6%) and only one infant had patent ductus arteriosus. Twin pregnancy was found in (35) 7%. 40 infants (8%) were found to have retinal haemorrhages without any signs of ROP which later get resolved. 31(6%) babies had some or other forms of congenital ocular anomalies with slight male predominance as given in Table 5.

4. Discussion

ROP may lead to permanent visual loss, if left untreated resulting in decreased quality of life for the individual as well as a significant financial burden on the individual and the community.⁷ In India, approximately, 1 in 1000 children is blind, and the incidence of ROP is reported between 24% and 47%.⁸

Our study discovered ROP among preterm infants of less than 37 weeks of gestation to be much lower at 6.8%. This is because most of the infants who are included in the study belongs to higher gestational age as well as higher birth weight range and small sample size which might have resulted in the lower incidence of ROP. A decreasing incidence has been observed by some authors⁹⁻¹¹ and this is because of Surfactant use¹⁰ or to the improved neonatal care and better monitoring of oxygen saturation.¹¹ Gilbert et al.¹² observed that in less developed countries, babies with higher birth weight may develop severe ROP as compared to more developed countries. All infants who developed ROP weighed <1,900 g at birth. majority (47%) of the infants had birth weight between 1000-1500gm, and 32% of the infants weighed 1500–2000gm. The average birth weight of the infants who developed ROP was 1317gm which is lower than the average birth weight of babies who did not develop any ROP which is 1762gm. Similarly, the average gestational age of infants who developed ROP was 28 weeks (range: 24-36 weeks) which is quite lower as compared to the average gestational age of the infants who did not develop any ROP which is 32 weeks (range: 24-37weeks). This shows the higher incidence of ROP in lower birth weight, gestational age as shown in Table 1. We found significant relationship between lower gestational

Table 1: Univariate analysis of risk factors associated with ROP

	ROP Present	ROP Absent	SD	P Value
Mean GA	28.47	32.33	2.312	0.000
Mean BW	1.317	1.762	0.329	0.00
Mean duration of O2	3.76	0.61	3.947	0.00

Table 2: Stage wise data and mean gestational age

	ROP Present	% In Total	Mean GA	SD	P Value
Stage 1	20	4.2%	28.30	2.364	0.00
Stage 2	10	2%	29.60	1.838	0.004
Stage 3	4	0.8%	26.50	1.915	0.000

GA gestational age (in weeks), SD standard deviation

Table 3: Risk factors associated with ROP

	ROP Present	ROP Absent	Total	P value
RDS +	14 (41.2%)	1 (0.2%)	15 (3%)	0.00
SEPSIS +	9 (26.5%)	3 (0.6%)	12 (2.4%)	0.00
TWIN +	4 (11.8%)	31(6.7%)	35(7%)	0.285
Total	34 (6.8%)	466	500	

(RDS respiratory distress syndrome)

Table 4: Gender distribution of congenital anomaly

Congenital anomaly	Female	Male	Total
Present	13 (41.9%)	18 (58.1%)	31(6.02%)

Table 5: Congenital ocular anomalies

CNLDO	12 (1 U/L)
Iris choroid coloboma	7
Microcornea	6
Congenital cataract	6 (4 B/L)
Microphthalmos	2
Congenital glaucoma	2
Limbal Dermoid	1
Capillary haemangioma	1
Congenital ptosis	1
Congenital esotropia	1

(CNLDO, congenital nasal duct obstruction)

age and the severity of ROP. Infants developing stage 3 had mean gestational age of 26.50 weeks as compared to the infants who developed stage 1 (28.30 weeks) as depicted in Table 2. This was in agreement with the results of studies done by Shah et al.,¹³ Karna et al.,¹⁴ and Fortes et al.¹⁵ and other studies showing that lower gestational age was significantly associated with severe ROP. This was explained by immaturity of vascularization that induces an increased susceptibility of the retina to oxidative damage and to a number of perinatal factors which include hyper and hypoxia, blood transfusions, and sepsis. We found slight female predominance of 52.9%, and a male predominance 47%. Male gender predominance in ROP has been documented before. Our research contains small sample size to comment on this potential phenomenon.

The cryotherapy for ROP study showed the likelihood of developing threshold ROP disease to be 36% greater in multiple gestation births.¹⁶ We found the incidence of ROP among multiple gestations to be 11%. A larger sample size of infants resulting from multiple gestations needs to be done to confirm this hypothesis. In our study the percentage of ROP among babies with birth weight of less than 1251 g was 12%, which is very low as compared to 65.8% noted in the CRYO- ROP study and 68% in Early Treatment of Retinopathy of Prematurity (ETROP) incidence study.⁷ This can be explained because of very low birth weight babies included in that study. The aim of our study included identifying the risk factors for the development of ROP. Several factors were found to be significant for the development of any ROP by Univariate analysis (see

section on Results). The most prevalent postnatal risk factors among patients with ROP are RDS (41%) and use of oxygen therapy (67%) and sepsis (26.5%) as shown in Table 3. Taqui et al.¹⁷ observed a significant relation between respiratory distress syndrome and the development of ROP and related this to the fact that systemic hypoxia results in retinal hypoxia and more need for oxygen therapy. This was in agreement with our study showing 41% babies had RDS among ROP. Oxygen therapy was an independent risk factor for the development of ROP.^{18,19} We found insignificant relationship between the occurrence of ROP and use of oxygen therapy, which was in agreement with the results of Dutta et al.,²⁰ and there was no significant relationship between oxygen therapy and stages of ROP also. 67% babies among ROP needed oxygen therapy. On the other hand, Palmer et al.¹⁶ reported that oxygen therapy was not significant factor for occurrence of ROP. Their report shows that ROP may develop in cases who did not receive oxygen therapy. Some studies reported that a duration of oxygen therapy more than 7 days was a significant risk factor for development of ROP.^{13,21} Apart from ROP 39 congenital ocular malformations were found in 31 (6%) babies, which is higher as compared to a study conducted by Stoll, et al²² (0.75%), and Singh, et al²³ (0.105%), and Bermejo, et al²⁴ (0.037%). Various congenital ocular anomalies were found in our study (given in Table 4) of which the Congenital nasolacrimal duct obstruction 12 was found to be the commonest eye malformation followed by iris and choroid coloboma 7, microcornea 6. Epidemiological studies report that the prevalence of CNLDO ranges from 5% to 20% in the early phase of childhood. Moreover, the higher prevalence of CNLDO reported in premature infants compared with ones at full-term suggests the importance of the physiological development of the nasolacrimal drainage system during intrauterine life, in order to ensure the patency of the NLD.²⁵ While usually unilateral, CNLDO occurs bilaterally in 20% of cases²⁶ Microphthalmos was reported as the second commonest congenital ocular anomaly by Stolle et al.,²² but we found only 2 cases. One baby with microphthalmos had coloboma of the iris and choroid, and another was isolated. In present study Microcornea was seen in association with iris and choroid coloboma in Six babies and one baby also had Nystagmus. Animal experiments have shown that vitamin A deficiency can produce anophthalmos, microphthalmos, and hair lip in the developing embryo.²⁷ Reports are also available to indicate the relationship of maternal vitamin A deficiency and microphthalmos.²⁸ Other causes of Microphthalmia include intrauterine infections, chromosomal anomalies and teratogenic drugs. Cataract was the most common congenital ocular anomaly reported in several studies and its does not appear in the newborn period but at a later date. We found the same in 6 babies of them only one was found to have Down syndrome. So, every child should undergo

a thorough systemic examination to detect anomalies in other systems also. Age distribution of babies with ocular anomalies was from birth to 3 months. Gender distribution showed male to female ratio of 1.38, while study by Chukka-Okosa, et al²⁹ reported a male preponderance with male to female ratio of 1:1.2. and 1:1.22 by Stoll, et al.²²

5. Conclusion

Low birth weight and premature babies are at high risk of development of ROP. Combined role of Neonatologist (improved care, monitoring and management of systemic illness) and Ophthalmologist is necessary. ROP screening and proper management is crucial for the prevention of development of sight threatening ROP.

6. Source of funding

None.

7. Conflict of interest

None.

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