Vol 1| Issue 1| 2011 | 56-60.

e-ISSN 2248 – 9142
print-ISSN 2248 – 9134

International Journal of
Current Pharmaceutical & Clinical Research

www.ijcpcr.com

A STUDY OF RISK FACTORS FOR RETINOPATHY OF PREMATURITY IN A MEDICAL COLLEGE HOSPITAL IN SOUTH INDIA TO EVALUATE THE CRITERIA FOR SCREENING FOR RETINOPATHY OF PREMATURITY

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ABSTRACT

ROP is a major cause of preventable blindness in preterm infants. The incidence of ROP is increasing in developing countries due to increased survival of preterm infants. The profile of ROP differs between various countries. To study the risk factors and screening strategy for ROP. Seventy six preterm infants with birth weight 2000 grams and/ or gestational age 37 weeks were included. Antenatal, perinatal and postnatal data were collected for all infants. Screening for ROP was done at 4 weeks post natal age and continued as per initial finding. Statistical analysis was done by Smith's statistical package. Multiple antenatal, perinatal and postnatal risk factors were identified. Stage 2 ROP was seen in birth weight of 1500 grams ± 0.16 and gestational age of 32 weeks. Stage 3 ROP was seen in birth weight of 1200 grams and gestational age of 32 weeks. ROP occurred in our study in infants above 1500 grams and in gestational age of 32 weeks. American Academy of Paediatrics recommends screening of infants' ≤ 28 weeks of gestational age and ≤ 1500 grams birth weight. Our study shows that ROP screening should be modified for the existing local scenario.

Key words: Blindness, Preterm infants, Gestational age, Birth weight.

INTRODUCTION

Retinopathy of prematurity (ROP) continues to be one of the important preventable causes of childhood blindness[1-4].With the increased survival of premature infants due to improvement in neonatal care there has been an alarming increase in the incidence of ROP especially in the developing countries [5, 6]. ROP is a vasoproliferative disease affecting the eyes of premature infants and it has a multifactorial origin. Low birth weight, lower gestational age, supplemental oxygen therapy, sepsis are among the major risk factors for the development of ROP [2, 7, 8]. Recently studies have shown that poor weight gain in the early neonatal period is a strong predictive factor for the development of ROP [9-11].

There is a difference in the clinical profile of infants with ROP in developing countries like India and that in developed countries [5, 6]. The aim of this prospective study was to evaluate the incidence of ROP in a tertiary care hospital in South India and to analyse the antenatal, perinatal and postnatal risk factors for the development of ROP. The relevance of recommended screening criteria (American Academy of Paediatrics) in Indian scenario was assessed.

METHODS AND MATERIALS

This prospective observational case study was conducted at the department of Optholmology, Sree Balaji Medical College and Hospital,Chrompet,Chennai for a period of two years between June 2009 and June 2011 after obtaining institutional ethical committee clearance. The study group comprised of 76 preterm babies with

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gestational age of ≤ 37 weeks and birth weight of ≤ 2000 grams. At the end of the study period the preterm babies were divided into two groups – Infants with ROP and Infants without ROP for analysis.

A detailed documentation including gestational age (GA), birth weight, antenatal and perinatal risk factors was done. The duration of neonatal intensive care stay and the treatment given and interventions done were also documented. All the preterm infants, after an informed consent from the parents, underwent pupillary dilatation with 0.2% tropicamide and 1.25% phenylephrine eye drops, instilled every ten minutes for three applications. Examination was performed by indirect ophthalmoscopy with 20 diopters lens 30 to 40 minutes later. The first screening was done at four weeks postnatal age. The repeat examinations were based on the initial visit findings. Statistical analysis was done by Chi-square test and ANOVA with Yates correction using Smith's statistical package.

RESULTS

A total of eighty eight infants were screened of which seventy six completed follow up. Completion of follow up was defined as vessels reaching up to Zone III periphery or regression of ROP. Sixteen infants developed any stage ROP. Stage I ROP was seen in ten infants, Stage II in four infants and Stage III in two infants. No Stage IV or V ROP was detected. Eight infants with Stage I ROP had unilateral involvement and rest had bilateral involvement.

Of the 76 infants screened, 5 infants were less than 30 weeks gestational age (GA), 27 infants were between 31-34 weeks GA and 44 infants were more than 34 weeks GA. Among the infants that developed ROP, 2 infants (12.5%) were in less than 30 weeks, 2 infants (12.5%) were in more than 34 weeks and 12 infants (75%) were in 31-34 weeks GA.

Analysis of birth weight and gestational age showed Stage I ROP with birth weight of 1.58 Kilograms (Kg) ±0.26 and GA of 33.6 weeks±1.62. Stage II ROP was seen with birth weight of 1.5 Kg±0.16 and GA of 32 weeks. Stage III ROP was seen with birth weight of 1.2 Kg and GA of 32 weeks.

Twelve infants showed signs of ROP in first visit of four weeks itself and the rest developed at 6 weeks (two infants) and eight weeks (two infants). The four infants with Stage II ROP had the signs of ROP by six weeks and Stage III was reached in two infants by eight weeks. Risk factor analysis was done by comparing between the sixteen infants with any stage ROP (ROP group) and sixty infants without ROP (controls). Analysis of the antenatal problems showed multiple pregnancies and oligohydramnios to be statistically significant in ROP group (Table 1).Perinatal problems found significant in ROP group were prolonged labour, foetal distress, APGAR < 6, Acute Respiratory Distress Syndrome (ARDS), use of endotracheal tube (ETT), meconium stained liquor and premature rupture of membranes (Table 2).

Birth asphyxia, Respiratory Distress Syndrome, sepsis, neonatal jaundice, seizures, apnoea, acidosis, exchange transfusion, phototherapy, pneumonia and duration of NICU stay were the significant neonatal risk factors in the ROP group (Table 3). Duration of ventilator therapy and hood oxygen therapy were also found to be significant in the ROP group (Table 4).There was also a statistically significant correlation between lower GA and lower birth weight for the occurrence of ROP (Table 5).

Table 1: Antenatal Risk factors Analysis

Risk factor	ROP (n=16)	Controls(n=60)	P value
Multiple pregnancy	8	2	0.00
Oligohydramnios	8	6	0.00
Anaemia	8	24	0.47
PIH	8	20	0.21
Placenta previa	6	10	0.07
Elderly primi	1	0	0.05

PIH- Pregnancy induced hypertension. Statistical analysis done by chi-square test with Yates correction

Table 2: Perinatal risk factor analysis

Risk factor	ROP(n=16)	Controls(n=60)	P value
Prolonged labour	8	2	0.00
Fetal distress	10	8	0.00
APGAR <6/10	8	6	0.00
ETT	8	4	0.00
MSL	10	8	0.00
PROM	12	2	0.00

ETT-Active resuscitation at birth with endotracheal tube, MSL- Meconium stained liquor, PROM- Premature rupture of membranes. Statistical analysis done by chi-square test with Yates correction

Table 3: Neonatal risk factor analysis

Risk factor	ROP(n=16)	Controls(n=60)	P value
Birth asphyxia	8	4	0.00
RDS	8	8	0.00
Sepsis	14	10	0.00
Neonatal jaundice	16	24	0.00
Seizures	8	10	0.01
Apnoea	8	10	0.01
Acidosis	4	0	0.00
Pneumonia	4	4	0.03
Hypoglycemia	4	10	0.44
Anaemia	4	14	0.89
Exchange transfusion	6	1	0.00
Phototherapy	14	22	0.00
IV fluids	16	56	0.29

RDS- Respiratory distress syndrome. Statistical analysis done by chi-square test with Yates correction

Table 4: Correlation of duration of Oxygen therapy

Risk factors	ROP (n=16)	Controls (n=60)	P value
Duration of stay in NICU(days)	21.25 $\pm$ 2.74	3.68 $\pm$4.37	0.00
Duration on ventilator(days)	5.75 $\pm$ 0.93	0.38 $\pm$ 0.94	0.00
Duration on CPAP(days)	0.56 $\pm$ 0.96	0.06 $\pm$ 0.25	0.10
Duration in hood(days)	15..06 $\pm$ 3.02	3.23 $\pm$ 3.40	0.00

Statistical analysis done by Anova test with Yates correction.

Table 5: Correlation of birth weight and gestational age between ROP and controls

Risk factors	ROP(n=16)	Controls(n=60)	P value
Birth weight (Kg)	1.37 $\pm$ 0.18	1.60 $\pm$ 0.21	0.00
Gestational Age (weeks)	31.25 $\pm$ 1.18	33 $\pm$ 1.77	0.00

Statistical analysis done by ANOVA test with Yates correction

DISCUSSION

ROP is an important cause of childhood blindness. The incidence of ROP in our study was an overall 21%. Our results are in conformity with the observations of various other studies from our country which ranges from 20 % - 47. 3 % [12-15]. The reported incidence in developed countries where patient care settings are quite different from the developing country scenario ranges from 0.12 % - 27% [16-21]. Heterogeneous patient population, differing inclusion, exclusion criteria and variable sample size could also contribute to the differences in the incidence of ROP.

The risk factors reported as significant in our study include Multiple pregnancy, Oligohydramnios, prolonged labour, foetal distress, APGAR<6, Respiratory distress syndrome (ARDS), Use of Endotracheal tube, meconium stained liquor, premature rupture of membranes, Birth asphyxia, Sepsis, Neonatal jaundice, Seizures, Apnoea, Acidosis, Exchange transfusion, Phototherapy, Pneumonia and duration of neonatal intensive care unit stay. Other studies have also reported similar risk factors indicating that ROP is a disease of smallest and sickest babies [12, 13, 15, 22-25]. Assisted and in vitro fertilization were found to have a significant association especially for severe ROP as shown by *Bergh et al* [26].

The American Academy of Pediatrics recommends screening of all preterm infants $\leq$ 28 weeks of gestational age and $\leq$ 1500 grams birth weight as well as all preterms that the neonatologists consider to have risk factors like sepsis, multiple blood transfusions, respiratory distress and oxygen support for evidence of ROP [27]. But in a developing country like India, a higher birth weight has been advocated as criteria for screening. The onset and progression of the disease is also earlier and more rapid in India [28]. In a study from India by Vinekar et al less than stage 3 ROP occurred in mean birth weight of 1550 $\pm$ 200 grams and GA of 31.1 $\pm$ 1.6 weeks and stage 3 ROP or more in infants with birth weight of 1500 $\pm$ 300 grams and GA of 30.5 $\pm$ 2 weeks. In their study the birth weight ranged from 1251 to 2750 grams and GA from 26 to 35 weeks [29]. Our study included infants with gestational age $\leq$37 weeks and birth weight $\leq$2000 grams. If we consider the gestational age alone 87.5% of infants with any stage ROP was above 30 weeks with 2 infants above 34 weeks of gestational age. Also any stage ROP was seen in infants with birth weight of > 1500 grams also. Though Stage 3 ROP which needs treatment at threshold stage was seen in

our study only in birth weight of 1200 grams we would have missed out lesser stages of ROP if we had kept screening protocol ≤ 1500 grams. Our results are in agreement with the suggestion of and hence we suggest a modification of the screening criteria specific to our region.

This study was conducted in a resource poor setting. However with the limited facilities available for diagnosis we believe that gestational age <37 weeks should be considered a potential risk factor for development of ROP and timely diagnosis would facilitate early interventional strategies leading to prevention of ocular morbidity.

CONCLUSION

To conclude the incidence of ROP was 21% in our population. Every infant with gestational age of <37 weeks and birth weight of < 2000 grams should be considered vulnerable to ROP. Based on our results and those of previous published studies, we believe that the existing guidelines on management of ROP should be modified to lay emphasis on screening of higher gestational age groups and birth weights to facilitate timely interventional strategies.

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