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Incidence and Prevalence of Retinopathy of Prematurity in a Tertiary Care Centre of North India

Choudhary MAMTA[a], Sharma JANARDAN[a], Dulani NISHA[b], Solanki MEGHNA[c], Dulani HARISH[a, c]

[a]Pediatrics Department, Govt. R.D.B.P. Jaipuria Hospital, Attached with RUHS College of Medical Sciences, Jaipur, India

[b]Department of Ophthalmology, RUHS College of Medical sciences, Jaipur, India

[c]ESIC Model Hospital, Jaipur, India

ABSTRACT

Purpose: *The goal of the current study was to shed light on the previous research on retinopathy of prematurity (ROP) among infants born before 34 weeks of gestation or those with birth weights (BW) under 2000 g and gestational ages between 34 and 36 weeks, with emphasis on prevalence and incidence.*

Methods: *A prospective hospital based observational study was conducted on 160 neonates after ethical clearance within a period of four months. The study population comprised neonates less than 34 week of gestational age and those with BW less than 2000 gm and gestational age between 34-36 weeks.*

Statistical analysis: *Categorical/nominal variables were expressed as number and percentage and were analysed using Chi square test or Fischer exact test. Continuous variables were expressed as mean and standard deviation. Relevant statistical software like SPSS (Statistical Sciences Package for Social) were used for all statistical analysis.*

Results: *Screening of all 160 neonates included in the present study revealed the presence of ROP in 30 of them, with a rate of 18.8% for ROP. Most of the neonates screened for ROP were delivered at a gestational age of 33-34 weeks (56.9%), followed by 30-32 weeks (28.8%); 16 (10%) neonates were delivered at gestational age <30 weeks, while seven (4.4%) had >34 weeks. Among the 30 neonates with ROP, 10 (33.3%) were delivered at gestational age <32 weeks and 20 (66.7%) at gestational age >32 weeks. A significant association was found between gestational age <32 weeks and occurrence of ROP (p=0.044). Among the 30 neonates with ROP, 24 (80%) had a BW of <1500 g and six (20%) >1500 g. Birth weight of <1500 g and occurrence of ROP (p <0.001) were found to be significantly associated.*

Conclusions: *Most of the neonates screened for ROP were delivered at gestational age of 33-34 weeks (56.9%), followed by 30-32 weeks (28.8%). Gestational age of <32 weeks (p=0.044) and BW of <1500 g (p <0.001) were significantly associated with the occurrence of ROP.*

Keywords: retinopathy of prematurity (ROP), birth weight, gestational age, risk factors, prevelance, North India.

Address for correspondence:
Dr. Meghna Solanki
D-840, sector 8, Malviya Nagar, Jaipur-302017, India
Email: solankimeghna@gmail.com

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INTRODUCTION

Retinopathy of prematurity is a vaso-proliferative condition caused by oxygen therapy usually affecting premature infants (ROP). It is a serious cause of preventable blindness in both affluent and developing nations (1, 2) affecting around 50,000 children worldwide. Even though premature infant survival increased in the ensuing decades and monitoring techniques for oxygen supplementation were improved, ROP was found to have a rising incidence (second epidemic) (3). In low-income nations, the incidence of ROP blindness has been on the rise during the past ten years. In India, 500 children are thought to go blind from ROP each year (1). Due to escalated survival rates among very low birth weight preterm neonates or those with birth weights ≤ 1500 g, who are most at risk for developing ROP, the condition has received substantial research on a global scale. The better prenatal care may be responsible for these higher numbers.

The condition is brought on by aberrant vascular proliferation in the developing retina, which results from insufficient vascularization of the retinal tissue brought on by hyperoxia, which kills endothelial cells and inhibits VEGF. The developing retinal tissue becomes ischemic and hypoxic as a result of the closure of emerging capillaries. Neovascularization results from this process' upregulation of VEGF (4-6). Retinopathy of prematurity can proceed to a severe form, which is linked to a higher risk of retinal detachment-related blindness. Macular folds, refractive amblyopia and strabismic amblyopia are possible further problems (7-11).

A successful screening approach is the most pivotal factor of any ROP management program (12). The most recent ROP guidelines propose screening of all children born ≤34 weeks and those >34 weeks with risk factors, if the GA is known, or all infants ≤2000 g BW, if GA is unknown. In the newborn intensive care unit (NICU), screening is done before discharge or by 30 days of age, whichever comes first.

Risk factors for ROP, some of which can result in development of severe ROP, include birth weight, gestational age, supplemental oxygen, prolonged mechanical ventilation, Apgar score, pulmonary complications, anaemia, intraventricular haemorrhage (IVH), necrotizing enterocolitis, and sepsis.

The stages of ROP show the level of vascular changes as follows:
- stage 1 - demarcation line between the vascular and avascular retina
- stage 2 – demarcation line growing to form a ridge
- stage 3 - extra retinal fibrovascular proliferation with ridge
- stage 4 - subtotal retinal detachment
- stage 5 - total retinal detachment.

Plus disease is a measure of disease severity and is defined as posterior pole vessels tortuosity and dilatation.

Pre-plus disease is defined as posterior pole vascular dilation and tortuosity, more than normal but less than plus disease.

Aggressive posterior ROP is a rare, fast progressing ROP variant characterised by its posterior location, severe plus disease, and flat intraretinal neovascularization. If not treated immediately, it can rapidly progress into stage 5 ROP and blindness.

The goal of the current study was to shed light on the previous research on ROP in infants born before 34 weeks of gestation or in infants born with birth weights under 2000 g and gestational ages between 34 and 36 weeks with emphasis on their prevalence and incidence. ❑

METHODS

This study was a hospital based prospective observational study conducted on 160 neonates after ethical clearance within a period of four months. The study population included neonates less than 34 week of gestational age and those babies with BW less than 2000 g and gestational age between 34-36 weeks with risk factors admitted to NICU during the study period.

Data was collected using a semi structured proforma. To seek information from subjects, relevant history was taken from parents after a written informed consent was obtained from them.

We included all neonates of both sexes born less than 34 weeks of gestation and all neonates of both sexes born between 34-36 weeks of gestation and babies weighing less than 2000 g admitted in NICU with the following risk factors: hyperglycemia/hypoglycemia; oxygen therapy given *via* mechanical ventilator/CPAP/HFNC/NASAL PRONGES/HOOD for any duration; multiple pregnancy; blood component transfusion; anemia in mother or baby; sepsis; apnea of prematurity;

respiratory distress syndrome; shock/use of inotropes; patent ductus artrieosus, and neonatal jaundice.

Babies with ocular disorders which hinder with fundus examination, those who were not ensuing up till complete vascularisation of retina, and babies with hereditary retinal abnormalities were all excluded from the present study.

Written informed consent was obtained from parent/guardian before inclusion into the study. All neonates included in the study were subjected to following:

1) Detailed maternal history, details of assessment of intrauterine fetal wellbeing, Gestational age at birth, sex and weight of baby, mode/duration/fio2 given for oxygen therapy and other risk factor of the baby were recorded on the predesigned proforma.

2) Thorough clinical and neurological examination was done; babies were then screened by an ophthalmologist for the presence of retinopathy of prematurity.

3) Investigation like complete blood counts, blood culture, CRP, peripheral smear were done in the central lab to establish the risk factors for ROP.

4) They were followed up till 40 weeks of post menstrual age or till retina maturation was completed, or treatment started.

5) First screening examination was done after three weeks in babies born before 28 weeks and after four weeks in babies born after 28 weeks of gestation and whichever earlier.

Procedure of ophthalmologic examination

- Pupils were dilated with Phenylephrine 2.5% and Tropicamide 0.5%. One drop of Tropicamide was instilled four times (every 10-15 minutes) commencing one hour before the scheduled time for examination, followed by one drop of phenylephrine, just before the examination. Repeated instillation of phenylephrine was avoided for the fear of hypertension.
- Screening of ROP involved a wide angle digital pediatric retinal imaging system (RETCAM) by an experienced ophthalmologist.

Statistical analysis

All data originating from this study were entered into performa and then into a MS Excel sheet, cleaned and verified.

Categorical/nominal variables were demonstrated as number and percentage and were examined using Chi square test or Fischer exact test as applicable. Fischer exact test was used when one of the cells in 2x2 contingency table has expected value <5.

Continuous variables were expressed as mean and standard deviation (SD) and were analyzed using independent sample t test for comparison between the two groups.

P value <0.05 was considered statistically significant. Statistical software like SPSS (Statistical Sciences Package for Social) was used for all statistical analyses. ❑

RESULTS

Most of the neonates screened for ROP were delivered at gestational age of 33-34 weeks (56.9%), followed by 30-32 weeks (28.8%); 16 (10%) neonates were delivered at gestational age <30 weeks, while seven (4.4%) had >34 weeks (Table 1). Among the 160 neonates screened for ROP, 83 (51.9%) were males and 77 (48.1%) females. The male to female ratio was 1.08:1.

Gestational age (week)	N	Percentage
<30 weeks	16	10.0
30-32 weeks	46	28.8
33-34 weeks	91	56.9
>34 weeks	7	4.4
Total	160	100

TABLE 1. Distribution of study subjects according to gestational age

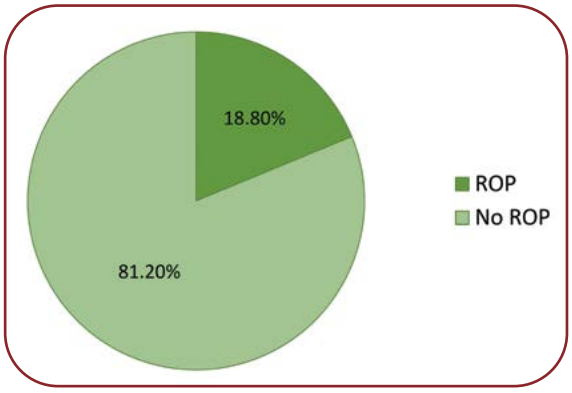

FIGURE 1. Distribution of study subjects according to presence of retinopathy of prematurity (ROP)

TABLE 2. Distribution of study subjects according to stage of retinopathy of prematurity (ROP)

Stage of ROP	N	Percentage
Stage 1	20	66.7
Stage 2	7	23.3
Stage 3	2	6.7
Stage 4	1	3.3
Stage 5	0	0
Total	30	100

TABLE 3. Distribution of study subjects according to aggressive retinopathy of prematurity (ROP)

ROP	N	Percentage
Stage ROP	25	83.3
APROP	5	16.7
Total	30	100

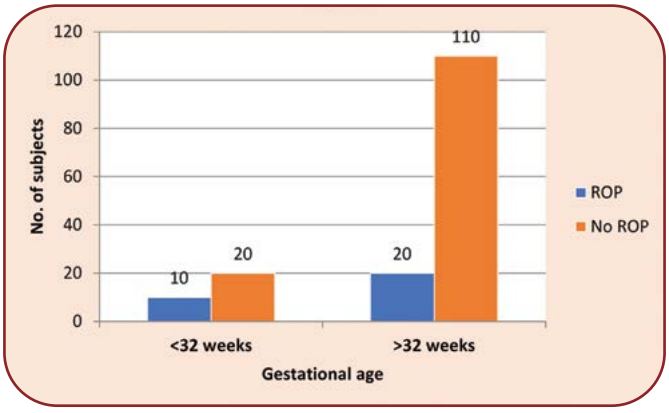

FIGURE 2. Retinopathy of prematurity (ROP) in relation to gestational age of study subjects

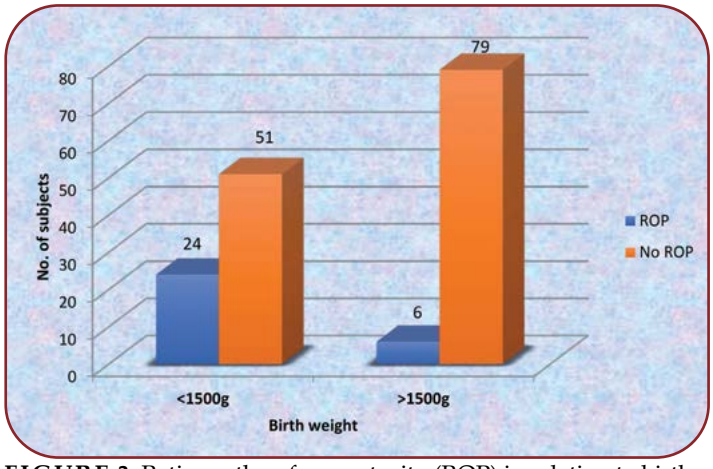

FIGURE 3. Retinopathy of prematurity (ROP) in relation to birth weight of study subjects

Among the 160 neonates screened, 30 subjects were found to have ROP, giving a rate of 18.8% for ROP (Figure 1). Among the 30 neonates with ROP, 20 (66.7%) had stage 1 ROP, seven (23.3%) stage 2 ROP, two (6.7%) stage 3 ROP, and one (3.3%) stage 4 ROP, with none of them having been found with stage 5 ROP (Table 2). Of the 30 neonates found to have ROP, 5 (16.7%) had aggressive posterior retinopathy of prematurity (APROP) (Table 3).

Among the 30 neonates with ROP, 10 (33.3%) were delivered at gestational age <32 weeks and 20 (66.7%) at gestational age >32 weeks, while among the 130 neonates without ROP, only 20 (15.4%) were delivered at gestational age <32 weeks and most of them (84.6%) at gestational age >32 weeks. A significant association was found between gestational age <32 weeks and occurrence of ROP (p=0.044) (Figure 2).

Among the 30 neonates with ROP, 24 (80%) had a BW of <1500 g and six (20%) >1500 g. Contrary to this, among the 130 neonates without ROP, 51 (39.2%) had a BW of <1500 g and 79 (60.8%) >1500 g. Significant association was found between the BW of <1500 g and occurrence of ROP (p<0.001) (Figure 3). ❑

DISCUSSION

The present study stated that most of the neonates screened for ROP were delivered at gestational age of 33-34 weeks (56.9%), followed by 30-32 weeks (28.8%). The value of the mean gestational age was 31.4±2.2 weeks in a study conducted by Chaudhari *et al* in 2009 (12) and 26.4±1.3 weeks in a study performed by Gordon SK *et al* (13).

Among the 160 neonates screened, 30 neonates were found to have ROP, giving a rate of 18.8% for ROP. In a previous study by VA Shah *et al* (15), ROP was diagnosed in 165 (29.2%) of very low BW infants. In 2011, Chang-Yo Yang *et al* (16) conducted a retrospective study on 252 very-low-birth-weight (VLBW) infants, of which about 99 (40%) were found to have ROP. Kumar *et al* (17) screened 704 neonates, of which 84 (11.9%) and 33 (4.7%) had mild or severe ROP, respectively. Gloria Isaza *et al* (18) observed a higher rate of about 40%. Saravanan Jothi *et al* (19) found that out of 259 infants, 142 (54.8%) had ROP in varying stages. Crystal Le *et al* (20)

also reported a prevalence of ROP in 2.3% (n = 66) of subjects.

Our findings showed that among the 30 neonates with ROP, 20 (66.7%) had stage 1 ROP, seven (23.3%) stage 2 ROP, two (6.7%) stage 3 ROP, and one (3.3%) stage 4 ROP, with none of them having stage 5 ROP.VA Shah *et al* (16) showed that 49% of their subjects had stage 1 illness, 24% stage 2, and 27% stage 3 or greater. Abdel H. A. A. Hakeem *et al* (21) also found similar proportions in each stage of ROP. Eduardo Gonçalves *et al* (22) reported that stage I ROP had the highest incidence among the studied newborns, followed by stage III ROP and stage II ROP. Saravanan Jothi *et al* (19) also found that the majority of infants with ROP (66.9%) had stage 1 ROP.

In our study, among the 30 neonates with ROP, 10 (33.3%) were delivered at gestational age <32 weeks and 20 (66.7%) at gestational age >32 weeks, while among the 130 neonates without ROP, only 20 (15.4%) were delivered at gestational age <32 weeks and the majority (84.6%) at gestational age >32 weeks. A remarkable association between gestational age <32 weeks and occurrence of ROP (p=0.044) was found by us. On univariate analysis, gestational age <32 weeks (OR=2.750) was found to be significantly associated with ROP, in line with the findings reported by Chaudhari *et al* (12), who observed that the incidence of ROP rose as gestational age decreased (P=0.003). Chang-Yo Yang *et al* (16) also found an association between low gestational age and ROP. Similar findings were reported by Abdel H. A. A. Hakeem *et al* (21), who observed that ROP incidence was significantly correlated with gestational age. Kumar *et al* (17) also found a significant association of similar nature with gestational age ≤ 30 weeks. Gloria Isaza *et al* (18) noticed that the average gestational age was about 26 weeks (23 to 31 weeks) among newborns with ROP and 28.5 weeks (24 to 36 weeks) among those without ROP. Further logistic regression demonstrated that gestational age was one of the most significantly adjusted risk factors for ROP (odds ratio: 2.64, 95% confidence interval 1.73 to 4.03). Rao KA *et al* (23) also observed that low gestational age was significantly associated with ROP. Saravanan Jothi *et al* (19) reported that gestational age was an autonomous risk factor for the development of ROP by multiple logistic regression analysis. Rania M.R. Bassiouny *et al* (24) found that premature infants screened for ROP had a mean gestational age of 31.5± 2.3 weeks (range: 24–36 weeks). Dhaivat Vasavada *et al* (25) observed that the average gestational age at delivery was 30.6 + 1.97 weeks (with a range of 26 to 35 weeks).

In our study, among the 30 neonates with ROP, 24 (80%) had a BW of <1500 g and six (20%) >1500 g. Contrary to this, among the 130 neonates without ROP, 51 (39.2%) had a BW of <1500 g and 79 (60.8%) >1500 g. A significant association was found between the BW of <1500 g and occurrence of ROP (p <0.001). On univariate analysis, BW <1500 g (OR=6.196) was found to be significantly associated with ROP. Chaudhari *et al* (12) similarly observed that the mean BW of their subjects was 1306 ±267 g. Kumar *et al* (17) noted that infants with severe ROP had mean birth weights of 1113± 438 g and found a significant association between ROP and BW of 1000 g. Gloria Isaza *et al* (18) reported that Children with ROP had a mean BW of 840 g (500 to 1,890 g), which was considerably lower than the mean BW of infants without ROP, which was 1,191 g (470 to 2,460 g). Further, logistic regression demonstrated that BW was one of the most significant adjusted risk factors for ROP (odds ratio: 1.90, 95% confidence interval 1.34 to 2.69). Rao KA *et al* (23) also observed that low BW was significantly associated with ROP. Saravanan Jothi *et al* (19) reported that low BW was an autonomous risk factor for the development of ROP by multiple logistic regression analysis. Rania M.R. Bassiouny *et al* (24) found that the average BW was 1514±391 g. (range: 600–2860 g). ❑

CONCLUSION

Among the 160 neonates screened for ROP in our study, 30 (18.8%) had ROP, of which five (16.7%) had aggressive posterior ROP, 20 (66.7%) stage 1 ROP, seven (23.3%) stage 2 ROP, two (6.7%) stage 3 ROP, and one (3.3%) stage 4 ROP. A significant association was found between the occurrence of ROP and gestational age <32 weeks (p=0.044) for a birth weight of <1500 g (p<0.001). ❑

Conflicts of interest: none declared.
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