

# Retinopathy of prematurity:- Prevalence, demographic characteristics, and outcomes at a tertiary care center in central India.

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**Received:** 01 June, 2022, Manuscript No. AAJCP-22-61880; **Editor assigned:** 02 June, 2022, PreQC No. AAJCP-22-61880(PQ); **Reviewed:** 05 June, 2022, QC No. AAJCP-22-61880; **Revised:** 13 June, 2022, Manuscript No. AAJCP-22-61880(R); **Published:** 25 June, 2022, DOI:10.35841/0971-9032.26.6.1448-1453.

## Abstract

**Introduction:** Retinopathy of Pre-maturity (ROP) is one of the leading causes of preventable childhood blindness in India. Neonatologist have been playing the major role to recognize infants for screening ROP and also counsel parents regarding seriousness of issue, possible findings and consequences.

**Aim:** To evaluate the prevalence of Retinopathy of Prematurity (ROP), demographic characteristics and treatment outcomes among infants admitted to the Neonatal Intensive Care Unit (NICU).

**Material and Methods:** A single-centre retrospective hospital based observational study was carried out among infants with screening for ROP performed in all preterm neonates who are born <34 weeks gestation and/or <1750 grams birth weight; as well as in babies 34-36 weeks gestation or 1750-2000 grams birth weight if they have risk factors for ROP. We collected information from Medical Record Department (MRD) through Case Record Form (CRF). The collected data was tabulated and all statistical analysis was performed.

**Results:** 106 were eligible for ROP screening in which 15 infants developed ROP. Out of the 15 infants with ROP, 7 were male and 8 were female. Prevalence of ROP was 14.15%. The mean gestational age was found to be 31.26 weeks and mean birth weight was recorded 1.348 kg. Amongst 15 ROP cases, 12 (80.00%) were classified into classic, 02 (13.34%) into aggressive posterior retinopathy of prematurity (APROP), and 01 (06.66%) into hybrid.

**Conclusion:** Demonstrated high prevalence of APROP which was 13.34%. Successful screening and appropriate action cease the progression of ROP to last stages, for this role of treating pediatrician/neonatologist, obstetrician and ophthalmologist has become predominant.

**Keywords:** Aggressive Posterior Retinopathy of Prematurity (APROP), Hybrid, Neonatal Intensive Care Unit (NICU).

Accepted on 18th June, 2022

## Introduction

Retinopathy of Pre-maturity (ROP) has increasingly been recognized in the past few decades as one of the most important avoidable causes of blindness and visual impairment in children found in developing countries especially low and middle-income [1-3]. The proportion of blindness in children attributable to ROP ranges from 10% to 37.4% worldwide [4,5]. Globally, there are at least 50,000 children blind from ROP, which remains an important cause of childhood blindness in high-income countries and is also emerging as a major cause of childhood blindness in middle-income economies, such as Latin America, Eastern Europe, India, and China [6].

ROP is a multifactorial vaso-proliferative retinal disorder that increases in incidence with decreasing gestational age. Approximately 65% of infants with a birth weight <1,250 g and 80% of those with a birth weight <1000 g will develop some degree of ROP. ROP screening is recommended in premature infants weighing <2,000 g and/or <34 weeks' gestation at birth (Indian population data) [7]. The risk for ROP increases with decreasing gestational age. Other risk factors include prolonged or labile oxygen exposure and increased illness severity. There

is variation in the incidence of ROP even in urban and rural centers of India [8]. Studies done on ROP in India is from urban or rural parts of the country shows that data are lacking from rural areas, which has recently seen an increased survival of pre-term infants due to improvement in neonatal health care facilities by Special Neonatal Care Unit (SNCU).

SCNUs have been scaled up in many rural districts of the country. The United Nations Children's Fund (UNICEF) provided technical and financial support during the initial phase in establishing eight units [9]. Early treatment of disease with cryotherapy, laser photocoagulation, and Anti-Vascular Endothelial Growth Factor (AVEGF) therapy has improved visual outcomes for patients; however, early recognition through screening is critical. Prevention of ROP requires a multidisciplinary approach beginning before the infant is born and continuing throughout childhood [10].

Thus, the aim of this study was to evaluate the prevalence of Retinopathy of Prematurity (ROP), demographic characteristics, and treatment outcomes among infants admitted to the Neonatal Intensive Care Unit (NICU). In addition, the present research aims to encourage and facilitate uniform

screening guidelines programs in Low-Income and Middle-Income Countries (LMICs) like India.

## Material and Methods

This was a single-centre retrospective hospital based observational study of all NICU admissions between 1st July 2020 to 30th June 2021 at Indira Gandhi govt. medical college, Nagpur a tertiary care center in central India. The institutional ethical committee approval was obtained. Infants were diagnosed with ROP identified and other information that increases their risk of ROP development is recorded. The stage of ROP at the time of diagnosis, treatment intervention, and treatment outcomes was documented.

### Inclusion criteria

- Infants admitted with  $\leq 34$  weeks gestation.
- Birth weight  $\leq 2000$  g.
- Gestational age between 34 to 36 weeks but with risk factors such as Respiratory Distress Syndrome (RDS), neonatal sepsis, apnea, oxygen therapy, multiple blood transfusion, intraventricular haemorrhage.

### Exclusion criteria

- Infants born at  $>34$  weeks of gestational age without risk factors.
- Birth Weight  $>2000$  grams without the risk factor.

## Methods

### Data collection

The information of ROP developed in infants and treatment for same was retrieved from case record forms through the Medical Record Department (MRD). The data including birth weight, gestational age, history of sepsis, history of multiple blood transfusions, history of transient tachypnea of the newborn, apnea of prematurity, oxygen therapy, respiratory support, neonatal sepsis, intraventricular hemorrhage, and necrotizing enter colitis. ROP cases were classified as per their mode of presentation.

### Procedure

All babies who satisfied any one of the inclusion criteria were enrolled for the study. Demographic history and risk factors

ROP	n	%
Present	15	14.15
Absent	91	85.85
Total	106	100

**Table 1.** Prevalence of Retinopathy of Prematurity (ROP).

In the present study 01 (06.67%) infant was extreme preterm, 09 (60.00%) were very preterm, 04 (26.66%) were moderately

(mention above) were documented using a study proforma. The pupils were dilated with a mixture of phenylephrine 2.5% and tropic amide 0.5% instilled 3 times at 10 minutes intervals about 1 hour before the scheduled examination [11].

### Method of examination

The examination was done under aseptic precautions in a temperature-controlled room by an ophthalmologist in the presence of a neonatologist. The indirect ophthalmoscopy examination was done. One drop of topical paracrine eye drops was used to anesthetize the cornea [11].

### Follow-up protocol

If no ROP was detected at the initial examination, the infants will be re-evaluated once every two weeks until vascularization is complete. If ROP will be detected, the examinations will be performed weekly for stage 1-2 disease and more frequently for stage 3 disease, till the disease start resolving or progress to the threshold stage. Babies showing evidence of regression were followed up till vascularization was complete. Babies progressing to the threshold stage will be advised treatment. Infants were sent to a Retina specialist for further treatment. The follow-up examinations were done at the neonatal intensive care unit itself if the baby had to stay there for some other reasons. The discharge babies were called up for follow up as advised by the pediatrician and ophthalmologist [11].

**Statistical analysis:** The data was entered in an EXCEL sheet was tabulated and was analyzed further.

## Result

Out of 210 infants admitted in a Neonatal Intensive Care Unit (NICU) in above mention 1-year duration, 106 were eligible for ROP screening those who fulfilled inclusion criteria in which 15 infants developed ROP. The present study demonstrates the prevalence of ROP to be 14.15%.

Out of the 15 infants with ROP, 7 were male and 8 were female. The mean gestational age was found to be 31.26 weeks and mean birth weight was recorded at 1.348 kg (Table 1).

preterm and 01 (06.67%) was late preterm. Respiratory distress syndrome (12 (80%)) was one of the biggest comorbidities responsible for the development of ROP followed by neonatal sepsis 02 (13.33%) and then Intra Ventricular Hemorrhage

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(IVH) 01 (06.67%) among the study population (Tables 2 and 3).

Demographic characteristics of ROP cases	Results
Total cases (n)	15
Males (%)	07 (46.67%)
Female (%)	08 (53.33%)
Mean birth weight (in kg)	1.348 kg
Mean Gestational age (in weeks )	31.26 weeks
Gestational age (%)	
a) Extreme preterm (< 28 wks)	01(06.67%)
b) Very preterm (28-32wks)	09 (60.00%)
c) Moderately preterm (33-34wks)	04 (26.66%)
d) Late preterm (35-37wks)	01 (06.67%)
e) Term (>37wks)	00 (00.00%)
Birth weight	
a) <1kg	01(06.67%)
b) 1-1.5kg	09 (60.00%)
c) 1.5-2kg	05 (33.33%)
d) >2kg	00 (00.00%)

**Table 2.** Demographic characteristics of ROP cases.

S.no	ROP	n	%
1	Respiratory Distress Syndrome (RDS)	12	80
2	Neonatal sepsis	2	13.33
3	Intraventricular Haemorrhage (IVH)	1	6.67
	Total	15	100

**Table 3.** Co-morbidities among study population as a risk factor for development of ROP

Amongst 15 ROP cases, 12 were classified into classic, 02 into Aggressive Posterior Retinopathy of Prematurity (APROP), and 01 into a hybrid. Advised treatment modalities for ROP were laser, Inj. (Anti VEGF) Anti-Vascular Endothelial Growth Factor + laser, and Inj. (Anti VEGF) Anti-Vascular Endothelial Growth Factor + laser and surgery required 10, 03 and 02

infants respectively. ROP regressed in 13 infants over the period after treatment and did not regress in 02, in which one 01 infant had developed retinal detachment and other infant had vitreous hemorrhage and were referred to higher center for surgery (Table 4).

ROP classification	n	%
Classic	12	80
APROP	2	13.34
Hybrid	1	6.66
Total	15	100

**Table 4.** Classification of ROP. APROP: Aggressive Posterior Retinopathy of Prematurity.

## Discussion

In India, recently survival of preterm neonates increased with the establishment of a Special Newborn Care Unit (SNCU) in almost every district as part of the national health mission under Rashtriya Bal Swasthya Karyakam (RBSK) and also advancement in neonatal care [12]. This study was done in tertiary care hospitals in which infants were admitted from the various interior parts of central India to include hilly areas and

referred from another district rural area predominantly for further management. The American and British guidelines recommend screening for ROP for all infants born weighing  $\leq 1500$  g or present at  $\leq 30$  weeks gestational age. The guidelines further recommend that infants with a birth weight of 1500–2000 g who experience an unstable course requiring cardiorespiratory support should also be screened [13] (Table 5).

S.no.	Treatment modalities	n	%
1	Laser	10	66.67
2	Inj. Anti-VEGF + laser	3	20
3	Inj. Anti-VEGF + laser + surgery	2	13.33
	Total	15	100

**Table 5.** Treatment modalities of ROP. VEGF= Vascular Endothelial Growth Factor.

The prevalence of ROP in the present study was 14.15% which is near to similar as compared with a study done by Nikhil R et al. [11] in 2019 in which 19.2% was prevalence noted and found lower as compared with Dwivedi A et al. in 2019 in which 30% prevalence was present [14]. The present study shows that ROP occurred almost equally were in both male 07

(46.67%) and female 08 (53.33%) but female predominance as compared with Dwivedi et al. in 2019 in which female 47.7% near to similar findings was noted. Another study was done by Aahuja et al. [15] in 2018 and Le et al. [16] in 2021 were showed male predominance 54% and female 46% and 59% males and 41% females respectively (Table 6).

S.no.	Outcome	n	%
1	ROP regressed	13	86.67
2	ROP not regressed*	2	13.33
	Total	15	100

**Table 6.** Outcome of ROP. \*: 02 patient required further management at higher center for surgery, out of which one infant had retinal detachment and other infant had vitreous haemorrhage.

All infants who developed ROP in the present study weighed  $<2000$  grams at birth. The mean birth weight was recorded in the present study was 1.348 kg which is similar to 1.355 kg by Gopal et al. [17] in 1995, 1.315 kg by Padhi et al. [18], and 1.34 kg by Dwivedi et al. [14] in 2019. The mean birth weight was slightly higher compared with 0.884 kg, 1.113 kg, 1.274 kg, 1.282 kg, 1.285 kg, and 1.285 kg by Nikhil et al. [11] in 2019, Kumar et al. [19], by Freitas et al. [20], by Aggarwal et al. [21], by Charan et al. [22], and Aahuja et al. [15] respectively and lower as compared with 1.555 kg by Hungi et al. [8] and 1.6 kg by Patel et al. [23].

Prematurity is one of the most common risk factors for developing ROP in infants. Prevalence and severity of ROP are inversely related to gestational age. Mean gestational age (31.26 weeks) in the present study is higher than the mean gestational age of other studies like 27.60 weeks in Nikhil et al. [11], 29 weeks in Kumar et al. [19], 29.71 weeks in Aahuja et al. [15], 30.3 weeks in Aggarwal et al. [21], 30.7 weeks in Padhi et al. [18], 30.7 Freitas et al. [20], weeks in 31 weeks in Le et al. [16], and 31.05 weeks in Dwivedi et al. [14] and lower than like following studies, 31.6 weeks in Maini et al. [24], 32 weeks in Hungi et al. 08, and 33.33 weeks in Patel et al. [23].

In the present study, the most prevalent postnatal comorbidities in infants responsible for the development of ROP is Respiratory Distress Syndrome (RDS) was 80% which is higher than other studies like Aahuja et al. was 25.47%, Dwivedi et al. [14] was 51.2%, Le et al. was 58%, and Sivaramudu et al. was 61.7% and lower than studies like Freitas et al. was 83.8%. Other comorbidities like neonatal sepsis in the present study were found to be 13.33% which is higher than studies like Aahuja et al. [15] in which 3.78%, and lower than studies like Sivaramudu et al. [25], Le et al. [16], and Freitas et al. [20] were 28.8%, 33%, and 83.5% respectively. In the present study, intraventricular hemorrhage was found to be 06.67% which was slightly close with Le et al. was 4.54% and very small as compared with Freitas et al. was 26.7%.

The present study, classified ROP into classic, Aggressive Posterior Retinopathy of Prematurity (APROP) and hybrid 80%, 13.34%, and 6.66% respectively which was low as resemblance with Dwivedi et al. [14] in which classic, APROP, and hybrid were 26.08%, 13.04% and 3.34% respectively. Vinekar et al. found to be APROP was 3.1% which is lower compared with the present study. Treatment modalities used for

ROP included Laser, Inj. Anti-VEGF (VEGF Vascular Endothelial Growth Factor) + laser, and Inj. Anti-VEGF + Laser + Surgery were 66.67%, 20.00%, and 13.33% respectively. The present study demonstrated, 13 (86.67%) ROP were regressed after the above-given treatment and 02 (13.33%) ROP not regressed\*. \*02 infants required further management at higher center for surgery, out of which one infant developed retinal detachment and other infant had a vitreous hemorrhage.

As there was an improvement in the neonatal intensive care unit which leads to increased survival of the preterm infant, low birth weight infant, and also another risk factor responsible for the development of ROP in infants especially in lower-middle-income countries like India [12]. Severe Retinopathy of Prematurity (ROP) leads to long-term vision loss and potential blindness, so timely treatment is vital. Traditional treatment options for ROP include cryotherapy and surgery, though these are related to complications. Lifelong monitoring of ROP is required thanks to a variety of associated eye problems which can occur later in life. Laser is current standard of look after ROP, but it is invasive, resource-intensive procedure utilized in advanced disease only. More recently, anti-VEGF therapy is getting used for the treatment of ROP, especially in Zone 1.

## Conclusions

Present study, demonstrated a high prevalence of APROP was noted 13.34%. Both prevalence and severity of ROP were inversely related to birth weight and gestational age. In lower middle-income countries like India, all infants less than 2000 grams and less than 34 weeks should be screened whatever of risk factors.

Lack of prompt ROP screening was most susceptible to grow ROP in an infant. Successful screening and appropriate action cease the progression of ROP to the last stages, for this role of treating pediatrician/neonatologist, obstetrician and ophthalmologist have become predominant. Evolution of neonatal care services throughout the country, the special newborn care units that were already established in almost every district of the country are leading to put a big burden on at-risk babies for ROP screening. We recommend gear up to encourage and facilitate uniform ROP screening guidelines program in the Low-Income and Middle-Income Countries (LMICs) like in India and establishing Retinopathy of Prematurity (ROP) screening before discharge from the neonatal intensive care unit or called follow-up for ROP screening if discharge early.

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