

Risk factors and Incidence of Retinopathy of Prematurity in rural area of Bihar, presented at tertiary care center, Muzaffarpur, Bihar

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Abstract:

Objectives: The present study was to evaluate the various risk factors and incidence of retinopathy of prematurity in neonates coming from rural area of Bihar at the tertiary care center, Muzaffarpur, Bihar.

Methods: A total of 250 newborns were enrolled. The anterior segment was examined and pupillary reaction were noted. Then Pupil were adequately dilated with 50% diluted Tropicamide 0.5% with phenylephrine 5% with normal saline instilled thrice every 10 minutes. Proparacaine was instilled in both eyes before examination for anaesthesia. Patient was immobilized by wrapping them in sterile linen. A sterile infant eye speculum (Alfonso) was used during examination. A complete fundus examination was done with Indirect ophthalmoscopy and 20 Dioptre lens. Flynn Scleral depressor was used to see peripheral retina up to ora serrata.

Results: Rate of prevalence of ROP was 17.2%. Among 43 patients diagnosed with ROP, 24(55.81%) patients were male and 19(44.19%) patients were female. Majority of the patients (16 patients) were having gestational age of 28 weeks. Maximum No. of the patients (18 patients) had birth weight between 1.1-1.49 kg. 37 patients' mother had no history of systemic disease like hypertension and diabetes mellitus, while 6 patients had history of any systemic disease in mother. 36 cases had history of respiratory distress syndrome. **Conclusions:** Lower gestational age, low birth weight and longer exposure of oxygen are the major risk factors of ROP. Respiratory Distress Syndrome is highly significantly associated with retinopathy of prematurity in neonates. Maternal factor and safe percentage of oxygen needs to be evaluated.

Key words: Retinopathy of Prematurity, Neonates, Gestational Age, Respiratory Distress Syndrome

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Introduction

ROP is characterized by abnormal neovascular development in the retina of premature infants. These abnormal blood vessels are fragile and can leak or bleed, scarring the retina and pulling it out of position. This causes a tractional retinal detachment, which is the main cause of

visual impairment and blindness in ROP [1]. The stages of ROP 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 an extraretinal fibrovascular tissue, stage 4 is a

subtotal retinal detachment, while stage 5 is a total retinal detachment. In addition, Plus disease, which indicates significant vascular dilation and tortuosity observed at the posterior retinal vessels, may be present at any stage and reflects the increased blood flow through the retina [2].

Recognizing the potential danger of this disease, significant efforts have been made to understand its development, leading to advancements in prevention and treatment strategies [3]. Advances in neonatal care during the 1970s significantly improved the survival rates of extremely preterm infants. However, this success has also led to an increase in the number of children at the highest risk for developing ROP [4,5]. This was followed by a second epidemic, with a greater incidence of ROP [6] and blindness due to ROP in industrialized countries such as the US and Western Europe [7,8]. Since the 1990s, a third epidemic of visual impairment due to ROP has occurred specifically in middle-income countries (MICs), primarily attributable to the development of neonatal care but also caused by unregulated oxygen supply as well as insufficient ROP screening and treatment options [7,9].

Globally, ROP is a leading cause of potential vision impairment in children and remains a major cause of childhood blindness [10]. It affects preterm infants (born before week 37), particularly those with low BW (<1500 g) and low GA (<32 weeks) [11,4]. Prematurity itself is considered the most significant risk factor for the occurrence of ROP [12]. Objectives of the present study was to evaluate the risk factors and incidence of retinopathy of prematurity at a tertiary care centre, Muzaffarpur, Bihar.

Material & Methods

The present cross-sectional study was conducted in the Department of Ophthalmology, with the Collaboration of Department of Paediatrics, SKMCH, Muzaffarpur, Bihar during a period from

July 2019 to December 2022. A total of 250 newborns were enrolled in the present study. Patients were included according to inclusion and exclusion criteria.

Inclusion criteria

1. Neonates of less than or equal to 36 weeks of gestational age and/or less than or equal to 2.5 kg birth weight.
2. ROP screening done according to ICROP guidelines.

Exclusion criteria

1. Any Neonates with more than 36 weeks of gestational age.
2. Any Neonates with more than 2500 gm of birth weight.
3. Any neonate with congenital conditions like – congenital heart diseases, genetic conditions and other ocular diseases like – congenital glaucoma, microcornea, mucopolysaccharidosis.

Methods:

Examination was performed with approval of neonatologist/Paediatrician. The Informed Verbal Consent was taken from Patient's parents or Guardian. History was taken along with risk factors according to proforma.

The anterior segment was examined and pupillary reaction were noted. Then Pupil were adequately dilated with 50% Diluted Tropicamide 0.8% with phenylephrine 5% with normal saline instilled thrice every 10 minutes. Proparacaine was instilled in both eyes before examination for anaesthesia. Patient was immobilized by wrapping them in sterile linen. A sterile infant eye speculum (Alfonso) was used during examination. A complete fundus examination was done with Indirect ophthalmoscopy and 20 Dioptre lens. Flynn Scleral depressor was used to see peripheral retina up to ora serrata. Patient was advised for follow up or was referred to higher centre as required.

Statistical Analysis

Data was analysed by the use of IBM SPSS (Version 26)) software. Chi square test was applied. P-value was taken less than or equal to 0.05 ($p \leq 0.05$ for significant differences).

Results

A total of 250 preterm low birth weight neonates (500 eyes) were enrolled. Out of 250 patients, 135(54%) patients were male

and 115(46%) patients were female patients.

Out of 250 cases, 43 patients were diagnosed with ROP. Rate of prevalence of ROP was 17.2%. Majority of the patients (16 patients) were having gestational age of 28weeks, while (2) least number of patients had gestational age 27 weeks.

Table 1: Distribution of patients according to sex (N=250)

Sex	No. of patients	P-Value
Male	130(52%)	0.371
Female	120(48%)	

Among 43 patients diagnosed with ROP, 24(55.81%) patients were male and 19(44.19%) patients were female.

Table.2: Distribution of patients with ROP according to gestational age

Gestational age (weeks)	Cases of ROP
27	2(4.65%)
28	16(37.21%)
29	4(9.30%)
30	4(9.30%)
31	5(11.63%)
32	9(20.93%)
33	3(6.97%)
Total	43(100%)

Out of 43 patients diagnosed with ROP, majority of the patients (23 patients) had post conceptional age 30-35 weeks, while the least patients (4 patients) had post conceptional age 40-45 weeks.

Table.3: Distribution of patients with ROP according to post conceptional age

Post conceptional age (weeks)	Cases of ROP
30-35	23(53.49%)
35-40	16(37.21%)
40-45	04(9.30%)

Among 43 patients with ROP. Majority of the patients (18 patients) had birth weight between 1.1-1.49 kg, while least number of patients (3) were having birth weight 2.5kg. 38 patients were singlets and 5 patients were twins.

Table 4: Distribution of patients with ROP according to birth weight

Birth Weight (kg)	Cases of ROP
1.1-1.49	18(41.86%)
1.5-1.9	7(16.27%)
2.0-.2.4	15(34.88%)
2.5	3(6.98%)

Among 43 patients diagnosed with ROP, 39 patients did not receive pre natal steroids while, only 4 patients received pre-natal steroids.

Table 5: Distribution of patients with ROP according to Twins status

Twins' status	Cases of ROP	p-value
Singlet	38(88.37%)	<0.0001
Doublet	5(11.63%)	

Table 6: Association of ROP with prenatal steroids administration

Pre-natal steroid administration	Cases of ROP	p-value
Given	4(9.30%)	<0.0001
Not Given	39(90.70%)	

Among 43 patients diagnosed with ROP, in 37 patients' mother had no history of systemic disease like hypertension and diabetes mellitus, while 6 patients had history of any systemic disease in mother.

Table 7: Association of ROP with maternal systemic diseases

Systemic Diseases	Cases of ROP	p-value
Present	6(13.95%)	<0.0001
Absent	37(86.05%)	

Among 43 patients, 19 patients who developed ROP were given oxygen therapy up to 10 days. Whereas 5 ROP positive patients were given oxygen for >40 days.

Among 43 patients of ROP, 16 patients developed ROP had history of phototherapy, while 27 patients who developed ROP had no history of phototherapy.

Table 8: Association of ROP with oxygen therapy

Oxygen therapy given (days)	Cases of ROP
0-10	19(44.19%)
11-20	7(16.28%)
21-30	10(23.26%)
31-40	2(4.65%)
>40	5(11.63%)

Table 9: Association of ROP with Phototherapy given

Phototherapy given	Cases of ROP	p-value
Yes	16(37.21%)	0.018
No	27(62.79%)	

Among 43 ROP cases, majority of cases (16) had stage 2 ROP. Least number of cases (5) had stage 3 ROP.

Table 10: Distribution of ROP according to stages

Stage of ROP	Number of cases
Stage 2	16(37.21%)
Stage 3	5(11.63%)
Stage 4	13(30.23%)
APROP	9(20.93%)

Out of total 18 ROP cases, 15(83.33%) cases had history of respiratory distress syndrome. Only 3(16.67%) cases had not history of RDS.

Table 11: Association of ROP with respiratory distress syndrome

RDS	No of ROP case	p-value
Yes	36(83.72%)	<0.0001
No	7(16.28%)	

Discussions

Retinopathy of prematurity (ROP) is a disease of retinal vascular and capillary proliferation affecting premature infants undergoing oxygen therapy [33]. The pathogenesis of ROP is classically divided into 2 phases. Phase 1 involves hyperoxia-induced vaso-obliteration; phase 2 is characterized by hypoxia-driven pathological neovascularization due to increased expression of vascular endothelial growth factor [34]. These vessels are fragile and prone to leakage, which can lead to fibrovascular proliferation, tractional detachment, and ultimately, retinal detachment if left untreated [35]. Early identification of retinal damage and the institution of appropriate treatment prevent blindness and offer child better overall development [14]. In the present study, incidence of retinopathy of prematurity in our study was 17.2 %, which was less in comparison to other studies done in other parts of India. Others study stated that incidence of retinopathy was 21.7%, 45.1% and 22.3% [15,16,17]. This might be due to difference in exclusion and inclusion criteria, low survival rate of preterm baby, and methodology with other studies.

In our study, all the patients who developed retinopathy of prematurity were given oxygen therapy via nasal prong /Continuous positive airway pressure . It is close to other Asian and Indian studies. According to others studies, oxygen therapy was given in 64.5%, 78.1% and 82.7% ROP neonates [17,13,9]. This variation in the incidence may be due to variability in neonatal care and oxygen therapy practices in various NICU.

In our study, incidence of retinopathy of prematurity in very low birth weight baby (1.1-1.49kg) was 41.86% which was almost similar to other Indian study G Sanghi et al [18] 41.8%.

In our study, prevalence of APROP among babies diagnosed with ROP was 20.93%. It is almost similar to studies done in other parts of India. According to G Sanghi et al [18], Anamika Diwedi et al [19], Tekchandani et al [20], prevalence of APROP were 20%, 27.7% and 22% respectively.

In our study, gestational age of majorities of cases (37.21%) and (20.93%) diagnosed with ROP were 28 and 32 weeks respectively. Which was similar to other studies done in other region of India Parag et al [21] (31.7 ± 3,45 weeks), and Jalali et al [22] (29.6 ± 3.76 weeks). It was seen from our study that as there was increase in gestational age, number of patients with retinopathy were almost same which was consistent with other studies done by Parag et al. [21] and Jalali et al [22]. We were observed that lower the gestational age, higher is the risk of developing ROP because immature vessels are more prone to oxidative stress due to oxygen therapy.

In our study, there were 5 doublet twins and all the twins developed Retinopathy of prematurity (p<0.0001). 4 twins had history of prenatal steroid administration (p <0.0001) which was a significant protective factor against ROP. Reason for occurrence of ROP in all twins was associated with low birth weight and long-term exposure to the oxygen therapy.

In similar study conducted by Rao et al[18] 16.36% of twins developed ROP. In our study, low birth weight and extremely low

birth weight, gestational age \leq 30 weeks and chronic oxygen exposure were important risk factors in pathogenesis of APROP. Few patients with APROP in our study had septicemia which may be an important risk factor for pathogenesis of APROP.

Multiple gestations have been described as an independent risk factor for ROP by Sood et al. [2]. Intraventricular hemorrhage independent risk factor for severe ROP in a study by Watts et al. [24] Aggarwal et al found apnea, clinical sepsis and male sex to be significant risk factors [25]. Seiberth et al found surfactant a significant risk factor, but surfactant was not found to be significant by Chaudhari et al [26,17]. Gender was not identified as a significant risk factor in the present study.

It is known that the risk of premature birth and low gestational age is increased in multiple pregnancies, and consequently, an increased incidence of ROP would be expected [27].

In our patients, multiple births had no significant impact on the risk of developing ROP, as also reported by Blumenfeld et al. [28]. Friling et al. [29] found that, in twin births, the lower birth weight of the second-born twin explained the higher risk. Nevertheless, Li et al. [30] found a higher ROP incidence in twins than in singletons, and Motta et al. [31] demonstrated a higher incidence of any stage of ROP except threshold-ROP in twins and triplets.

Maternal factors for prematurity were could not be documented because of poor record. Most the patients were from low socioeconomic group and smoking in not in culture of mother of low socioeconomic study group. Maternal smoking as an independent risk factor for the development of severe retinopathy of prematurity in very preterm infants [32].

Conclusions

The present study concluded that the lower gestational age, low birth weight and longer exposure of oxygen are the major risk factors of ROP. Respiratory Distress Syndrome is highly significantly associated

with retinopathy of prematurity in neonates. Maternal factor and safe percentage of oxygen needs to be evaluated.

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