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Prevalence of retinopathy of prematurity in a urban based tertiary hospital in central India: A prospective observational study

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Abstract---Background: Retinopathy of prematurity (ROP) is an important cause of preventable blindness in children. It is a serious and underestimated complication of prematurity treatment among preterm and low-birth weight babies and is preventable cause of blindness unless recognized and treated early. Objective: The objective of this study was to estimate the prevalence of ROP in preterm infants and low-birth weight in the Neonatal Intensive Care Unit (NICU) of a tertiary hospital and to increase the awareness of early screening of ROP among parents and doctors. Materials and Methods: A ROP prospective screening survey was performed enrolling all prematures and low-birth-weight Neonates delivered at Index Medical College Hospital & Research Centre from July 2018 to June 2021, with a gestational age of 37 weeks or less at birth and a birth weight of 1700 g or less. One Hundred and Eighty Six(186) preterm infants (i.e.372 eyes) were included for ROP screening .Out of these 186 preterm infants (372eyes), Forty eight (48)preterm infants (i.e.96 eyes) developed Retinopathy of Prematurity. Descriptive statistics included the mean and standard deviation for numerical variables, and the percentage of different categories for categorical variables. Results: The prevalence of disease in this study was 25.80%.Out of these 186 infants (i.e.372 eyes), the48 preterm infants (.i.e.96 eyes) developed ROP. Of these 48 infants,27(14.52%) had stage I disease;16(8.60%) had stage II disease; 5 (2.69%)had stage III disease and none of them

had stage IV(0%) and V(0%)disease at the time of examination. Conclusion: The prevalence of ROP in this study was 25.80%. low gestational age, low birth weight, sepsis, oxygen therapy, hypoxia and frequent blood transfusions were significant risk factors for ROP.

Keywords---low birth weight, prematurity, awareness, screening, retinopathy of prematurity, prevalence.

Introduction

Retinopathy of prematurity is a disease that occurs in premature infants and affects the blood vessels of the developing retina. It results in the development of vascular shunts, neovascularisation, and in its more severe forms, tractional retinal detachment. Retinopathy of prematurity (ROP) is an important cause of preventable blindness in children. It is believed to account for 6-18% of childhood blindness in developed countries.[1,2]In India, it has been estimated that 0.2% of childhood blindness is because of ROP. Of the 26 million children born each year in India, 7.8 million are low-birth-weight infants-1.68 million are less than 2500gms and 0.36 million are less than 1500gms and they are at risk of developing ROP.[1,3]

The unique feature of ROP relates to its occurrence only in premature infants with immature and incompletely vascularised retina. ROP is mild and undergoes spontaneous regression with no visual sequelae in the majority of the affected infants. However, progression to advanced ROP does occur in a significant number of infants and can lead to severe visual impairment and even complete blindness in some infants. Thus most important factor in management of ROP is its early screening followed by proper management. In the absence of proper screening strategy, increasing number of premature infants who should have been successfully treated may turn irreversibly blind. This can lead to increase in social and economic burden of the society; especially in developing country like India, it can worsen the situation.

Retinopathy of prematurity was first described in 1942 by Terry[4]. He described an abnormal growth of fibroblastic tissue and blood vessels behind the lens, seen those days only in severe forms of ROP. This histological description led to the term Retrolental Fibroplasia (RLF).

Classification Of ROP according to international classification of retinopathy of prematurity [ICROP] Is as Follows: (1984, 87)

ICROP was published in 2 parts, first in 1984 and later expanded in 1987 to include a classification of retinal detachment and the sequelae of this condition. ICROP characterizes progression of ROP and has given one common language for research in ROP. It describes the early levels of severity of ROP based on several parameters: a) Zone, b) Stage, c) Extent of ROP, and d) Presence of Plus Ds.[5,6,7]

Classification of ROP according to the location

For the purpose of defining the antero-posterior location of ROP, three concentric zones centred on the optic disc are described.

- ZONE 1 is bounded by an imaginary circle the radius of which is twice distance from the disc to the centre of the macula.
- ZONE 2 extends concentrically from the edge of zone 1; its radius extends from the centre of the disc to the nasal ora serrata. (at 3-o'clock position in the right eye and the 9-o'clock position in the left eye).
- ZONE 3 consists of a residual temporal crescent anterior to zone 2.
- The approximate temporal extent of zone 1 can be determined by using a 25 or 28 D condensing lens. By placing the nasal edge of the optic disc at one edge of the field of view, the limit of zone 1 is at the temporal field of view.

Classification of ROP according to the extent

Extent of involvement is determined by the number of clock hours of retina involved (30 sectors). As the observer looks at each eye, the 3-o'clock position is to the right and nasal in the right eye and temporal in the left eye, and the 9-o'clock position is to the left and temporal in the right eye and nasal in the left eye. The boundaries between sectors lie on the clock hour positions; that is, the 12-o'clock sector extends from12o'clock to 1o'clock. (As seen in fig.I)

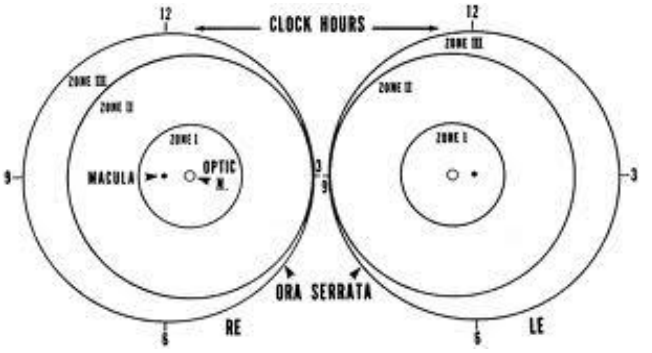


Fig 1.

Classification of ROP according to the staging

The following five stages are used to describe the abnormal vascular response at the junction of immature avascular peripheral retina and vascularised posterior retina. Because more than one ROP stage may be present in the same eye, staging for the eye as a whole is determined by the most severe manifestation.

- Stage 1 consists of demarcation line which is a thin, flat, tortuous, grey-white line running roughly parallel with the ora-serrata. It is more prominent in the temporal periphery. There is abnormal branching or 'arcading' of vessels leading up to the line.
- Stage 2 consists of ridge which arises in the region of the demarcation line, has height and width, and extends above the plane of the retina. Blood

vessels enter the ridge and small isolated neo-vascular tufts ('popcorn') may be seen posterior to it.

- Stage 3 consists of extra-retinal fibro-vascular proliferation which extends from the ridge into the vitreous. It is continuous with the posterior aspect of the ridge, causing ragged appearance as the proliferation becomes more extensive. The severity of stage 3 can be subdivided into *mild*, *moderate* and *severe* depending on the extent of extra-retinal fibrous tissue infiltrating the vitreous. The highest incidence of this stage is around the post-conceptual age of 35 weeks.
- Stage 4 consists of partial retinal detachment which is divided into extra-foveal (stage 4A) and foveal (stage 4B). The detachment is generally concave and circumferentially orientated. In progressive cases the fibrous tissue continues to contract and the detachment increases in height and extends anteriorly and posteriorly.
- Stage 5 consists of a total retinal detachment. ROP was defined as the incomplete or abnormal vascular proliferation of the retina, The ROP was classified by location on the retina (zone 1–3), and severity (stage 1–5), according to the criteria established by the International Committee for Classification of ROP.[8]

The ophthalmological examinations were initiated at the 4th week of life and were repeated weekly or biweekly, using the schedule for follow-up recommended by AAP, AAO, and AAPO[9] until full vascularization of the retina reached zone 3 (the most peripheral temporal retinal zone), or until full remission of ROP after treatment. Follow-up examination schedule was done according to defined by ETROP study. Our study was carried out after approval by the ethical committee of the institute. The aim of this prospective study was to estimate the prevalence of ROP in preterm infants at Index Medical College Hospital and Research Centre,Indore a tertiary centre to identify the risk factors which predispose to ROP, and to assess the association of ROP with its risk factors.

Materials and Methods

This prospective study was conducted in Department of Ophthalmology and Department of Paediatrics, Index Medical College,Indore.

Inclusion Criteria

The study population included 186 neonates; preterm and low-birth weight babies of less than or equal to 1700 and/or grams and less than 37 weeks gestational age, born in Index Medical College Hospital& Research Centre, Indore ,from July 2018 to June 2021 and admitted in the Neonatal Intensive Care Unit, Surviving at the post natal age of 3 weeks, and Attending neonatal follow up clinic.

Exclusion Criteria

Infants born outside of this institute, with <37 weeks of gestational age but >1700 grams birth weight, and who fulfilled the inclusion criteria but did not survive till first eye examination for Retinopathy of Prematurity (ROP). Gross

congenital malformations & lost during follow-up were excluded from this study. The parents were explained about the nature of the examination. Informed Parental consent regarding screening was taken.

Place

The place for the screening examination was a temperature controlled room, since premature neonates are susceptible to hypothermia. The screening was done in the presence of a neonatologist at Eye OPD so that any systemic complication can be handled easily. Those babies in incubators or on oxygen therapy were examined in the nursery with the ophthalmologist taking care to prevent contamination. The usual complications were bradycardia or a decrease in the oxygen saturation which was easily reversible.ROP screening examinations can have short-term effects on blood pressure, heart rate and respiratory function in the premature baby.[27] The examinations was kept as short as possible and precautions were taken to ensure that emergency situations can be dealt with promptly and effectively. Eye examination during ROP screening may cause considerable pain to the neonate. A systematic review and meta-analysis comprising four studies has reported that oral sucrose reduces pain during eye examination.[27] Of two studies reporting the role of topical proparacaine drops one has observed significant pain reduction. Discomfort to the baby was minimized by administering oral sucrose just before examination, pretreatment of the eyes with a topical proparacaine and swaddling the baby. Baby was not fed just before examination to avoid vomiting and aspiration. Hand washing should be done and asepsis maintained.

Local eye examination

Pupils are dilated with Phenylephrine 2.5% and Tropicamide 0.5%. One drop of Tropicamide is instilled every 10-15 minutes for 4 times starting 1 hour before the scheduled time for examination.[26] Screening for ROP was carefully done by indirect ophthalmic examination of the peripheral retina. Since the infant's eyes are small, a pediatric wire speculum was helpful in keeping the eyelids apart.Though Indirect Ophthalmoscopy was performed with a 20D lens, a 28D lens was helpful in examining the periphery especially in mid-dilated pupil.

- Descriptive statistics included the mean and standard deviation for numerical variables, and the percentage of different categories for categorical variables

Result

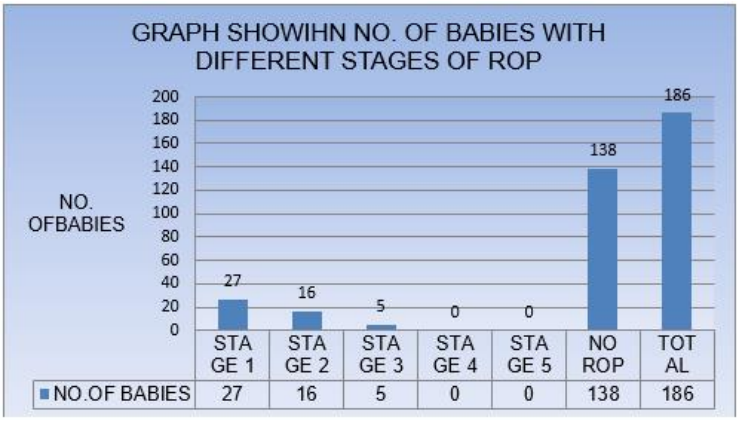
Among 186 (372 no. of eyes) babies, 48 premature infants had ROP i.e. (96 no. of eyes) had different stages of ROP. All the cases had similar stages of ROP in both the eyes. Among the 48 number of ROP cases, distribution of different stages were as follows:

Table 1

STAGE OF ROP	NO.OF BABIES
STAGE 1	27(14.52%)
STAGE 2	16(8.60%)
STAGE 3	5(2.69%)
STAGE 4	0(0%)
STAGE 5	0(0%)

Table 2

STAGE OF ROP	NO.OF BABIES
STAGE 1	27
STAGE 2	16
STAGE 3	5
STAGE 4	0
STAGE 5	0
NO ROP	138
TOTAL	186



Graph 1

Results

In our study, One Hundred and Eighty Six(186) preterm infants (i.e.372 eyes) of <37weeks and/or birth weight ≤1700gms were included for ROP screening between July 2011 to June 2013 .Out of these 186 preterm infants (372eyes), Forty eight (48)preterm infants (i.e.96 eyes) developed Retinopathy of Prematurity of any stage. The prevalence of disease in this study was 25.80%.Out of these 186 infants (i.e.372 eyes), the48 preterm infants (.i.e.96 eyes) developed ROP. Of these 48 infants ,27 had stage I disease;16 had stage II disease; 5 had stage III disease and none of them had stage IV and V disease at the time of examination Our observations in this Prospective Study among 186 infants are as follows:

Range of Birth Weight: 900gms to 1700gms
Mean 1470.935gms±219.91gms

Range of Gestational Age: 28wks to 36.6wks
Mean 33.61wks±2.15wks
Range of Post Conceptional Age first examination: 30wks to 49wks
Mean 37.15wks±3.19wks
Out of 186 babies 103(55%) were male and 83(45%) were female. (Tab.3)

Table 3

MALE	103
FEMALE	83
TOTAL	186

Out of 186 babies 40(22%) were ≤32 wks of gestational age and 144(78%) were between 32 and 37 wks. (Tab.4)

Table 4

GA(WKS)	NO.OF CASES
≤32WKS	40
32-37WKS	144
TOTAL	186

Discussion

Retinopathy of prematurity is a disorder of retinal vascular development in preterm infants. It continues to be a significant complication in preterm neonates despite advances in neonatal care and remains a major cause of childhood blindness worldwide.[9]

Prevalence

In our study, we have reported the prevalence of ROP as 25.80%, which was comparable to other data in literature.[10,11,12,13,14] The prevalence of ROP in the west has been reported to be5-8%.[10] There was wide variation of prevalence in studies taken place in India as well as in those undergone in the western countries. This wide range of variations in prevalence was mostly due to difference in selection criterion, protocol for retinal examination, and other methodological factors. In studies where there was large number of survivors, the prevalence was also high. This was mostly due to increase in the incidence of the disease in those studies which was directly related to the prevalence. So increase in number of the low birth weight babies lead to increase in the incidence of the ROP, which lead to increase in the prevalence of the disease.

Our study shows 25.80% of the prevalence, which was comparable to many other reports; 24% in India,[15]29.2% in Singapore,[16] and 32.4% in Pakistan.[17]. Other factor responsible for the decreased prevalence may be due to the fact that our study was done in one centre, thus limiting the number of cases. Other important factor noticed during our study was that there was absence of ROP Stage IV and Stage V. The absence of the advanced and severe stages of ROP may be explained by the early timing of first eye examination. In our study mean post-

conceptional age of 1st eye examination is 37.15wks± 3.19wks.This means that a large number of infants are effectively being screened at post-conceptional age of 37-40 wks.

American Academy of Paediatrics (AAP), the American Association of Ophthalmology and Strabismus (AAOS) and the American Academy of Ophthalmology(AAO)have issued a policy statement in September (2006)[18] for screening of premature infants for ROP recommends screening of infants with <28wks and/or <1500gms birth weight (BW). But several studies in India and other middle income countries concluded that by following AAP guidelines of screening, some cases may be missed. [19-25]Our inclusion criteria considered this, and we have taken ≤1700gms as cut-off value for birth weight in our study. Our efforts to increase the awareness of ROP among Parents:

- Informed consent is signed by parents before ROP Screening.
- Parents are informed about ROP by a two way communication to relieve their stress about the screening procedure.
- Communication is "parent-friendly"
- Parents are made aware that mild ROP is common and it gets resolves spontaneously.
- A brief statement as a written information is given on admission to NICU to make parents aware of early stage ROP screening.

Our efforts to increase the awareness of ROP among Neonatologists:

- We have communicated with NICU staff about "which babies to be screened?"
- We have prescribed them to send the "at-risk" infants for ROP screening timely.
- We have informed them how to prepare baby before screening. (i.e. timely instillation of Tropicamide).

Conclusion

On the basis of this study, following conclusion was drawn:

- Prevalence of ROP in Index Medical College, Hospital & Research Centre was 25.80%.
- This prevalence of ROP in our Hospital in the selected group was comparable to other Indian studies.
- Mean Post conceptional age at 1st examination in our study was 37.15wks± 3.19wks. So, screening at 34-37 weeks of post conceptional age made it possible to detect the infants early before they develop advance stages of ROP (Stage 4, Stage 5). It is because of this reason that we did not record any case of Stage 4 and Stage 5 ROP.
- This study is a minor step in this field, where lack of knowledge is prevalent among common man, especially in the country like India. This study increases the awareness of ROP, not only amongst the Pediatricians and the Ophthalmologists, but also in the parents of preterm infants.

- Preventing blindness due to ROP is a race against time and by avoiding risk factors and managing it timely reduces the incidence of ROP.

We are aware that a limitation of this study is the small number of patients. In conclusion, the prevalence of ROP in this study was 28.50%. The timely retinal screening of high-risk preterm infants is important to prevent the development of advanced ROP. Since ROP may produce serious sequelae up to complete blindness, all efforts must be made to prevent the development of advanced ROP through elimination of preterm births, changes in the neonatal care, and improvement in detection of threatening ROP markers.

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