Original Article

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Retinopathy of Prematurity (ROP) Screening -A Report from a Tertiary Eye Care Center

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ABSTRACT

Purpose: To evaluate the incidence and severity of ROP and its association with perinatal risk factors.

Method: A cross-sectional observational study of infants born ≤ 37 weeks gestational age and birth weight ≤ 2500 gm, who were screened for ROP between December 2019 to November 2020. ROP screening examination was done with indirect ophthalmoscope by trained Ophthalmologist. Data regarding demography and risk factors were collected from patient referral note or interviewing caregiver.

Result: 428 eyes of 214 patients were screened. Mean gestational age was 33.8±2.43 weeks and mean birth weight was 1590±0.36 gram. Incidence of ROP was 25.47%. Incidence of ROP was increased as gestational age and birth weight decreased. Multiple birth, oxygen therapy, sepsis, respiratory distress syndrome had significant association with ROP.

Conclusion: This is the first study that evaluates the incidence of ROP at medical retina department of Chittagong Eye Infirmary and Training Complex and the incidence is not less. So, early prediction with risk factor analysis and appropriate screening can prevent ROP related morbidity and blindness.

Keywords: Retinopathy of prematurity, Screening, Prematurity, Low birth weight.

Introduction

Retinopathy of prematurity is a proliferative retinopathy of premature and low birth weight infants that causes permanent loss of vision by means of macular dragging and retinal detachment. Onset of ROP is triggered by premature birth, in which abnormal neovascularization occurs instead of normal vascular development of retina[1]. It is a biphasic disorder. Phase 1 involves relative hyperoxia and decreased vascular endothelial growth factor (VEGF) levels; hyperoxia suppresses VEGF expression and results in vaso-obliteration. Meanwhile, in phase 2, VEGF expression is increased due to peripheral retinal hypoxia, leading to neovascularization[2].

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Besides prematurity and low birth weight; sex, oxygen therapy, neonatal sepsis, intra ventricular hemorrhage, phototherapy and blood transfusion are also associated risk factors for the development of ROP[3]. It is the leading cause of childhood blindness in United States and other developed countries and 5th leading cause of bilateral blindness globally[4]. The proportion of blindness due to ROP varies among countries depending on their quality and outcome of neonatal care and availability of ROP screening and treatment services[5]. In the developed countries, ROP accounts for 4% of childhood blindness, whereas 40% in the developing ones[6].

Bangladesh is a developing country and it is improving in all sectors including health. With her improved neonatal care, survival rate of premature infants are increasing with increasing chance of ROP and its related blindness. According to UN (2018) estimation, out of 3 million children born, 0.6 million children are born premature which are all at risk of developing ROP.

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One of the earlier studies for ROP in Bangladesh done over a period of 4 and half year, found an incidence of 5.5% (n=144) with different stages[7]. But a recent study showed 31% incidence with different stages. It was done over a period of 4 year and included 2000 preterm babies.

Blindness in childhood is a curse. It not only causes social dependency but also increases economic burden[8]. Identifying ROP as an important cause of childhood blindness, The World Health Organization (WHO) "Vision 2020: The Right to Sight" programme proposed that infants at risk for ROP should undergo screening by the 4th week of life and get access to prompt treatment[9,10]. This is because timely retinal examination and treatment of high-risk preterm infants can prevent blindness due to ROP to a large extent.

Methodology

This cross-sectional observational study was conducted at medical retina department of Chittagong Eye Infirmary and Training Complex from December 2019 to November 2020 with appropriate ethical and institutional approval. Informed written consents were taken from the parents of those babies who were referred from different government and nongovernment centres with history of prematurity (≤ 37 weeks) and low birth weight (≤ 2.5 kg) . Patient examination was done by ophthalmologist trained on ROP. Pupil was dilated using topical mydriatic drops (1% tropicamide and 2.5% phenylephrine) and was instilled twice in both eyes 10 min apart, at least 30 min before examination with indirect ophthalmoscope. The ROP stage and plus disease were defined on the basis of revised international classification scheme (ICROP)[11].

Revised ICROP Stages:

Stage 1 : Demarcation line

Stage 2 : Ridge

Stage 3 : Extra retinal fibrovascular proliferation. Proliferation was further divided into mild, moderate and severe.

Stage 4 : Partial retinal detachment.
4a) Extrafoveal 4b) Foveal

Stage 5 : Total retinal detachment

Plus disease: Increased venous dilatation and arteriolar tortuosity of posterior vasculature, with increasing iris engorgement, pupillary rigidity and vitreous haze were defined under the more active ROP, "plus disease". At least two quadrant involvements of the signs were required to define the disease as plus disease.

Aggressive posterior ROP: A rapidly progressive, ill-defined form of ROP. It is characterized by severe dilatation and tortuosity of the vessels which is out of proportion to the peripheral retinopathy. The disease is limited to the posterior pole in zone 1 or posterior zone 2 and usually does not progress through the classic stages 1-3 of ROP.

The Early treatment of ROP (ETROP) guidelines were used to categorize-Type 1 and Type 2[12].

Type 1 ROP-

(a) Zone 1 any stage with plus disease; and

(b) Zone 1 stage 3 without plus disease an

(c) Zone 2 stage 2/3 with plus disease; requires intervention.

Type 2 ROP-

(a) Zone 1 stage 1/2 without plus disease, and

(b) Zone 2 stage 3 without plus disease; requires observation.

Data were collected for each baby regarding gestational age at birth, birth weight, no of pregnancy, the stage of ROP, the affected zone, and presence of suspected risk factor like oxygen therapy, presence of common problems of prematurity and stay of infant in the Intensive Care Unit of the Neonatology Department. Data regarding demographics and risk factors for ROP were collected from referral note or interviewing caregiver. The data were entered in a predesigned proforma and analysed using SPSS 16.

Result

428 eyes of 214 infant were screened from December 2019 to November 2020. Mean gestational age for total screened infant was 33.86 ± 2.43 weeks and mean birth weight for the same was 1590 ± 0.36 gram. Out of 428 eyes, incidence of ROP of different stages was 25.47 % (n=109). Rest of them had normal retinal vascularization.

With prematurity and low birth weight there was increased incidence of ROP. Among the screened 33 infants of gestational age below 32 weeks, ROP was found in 36.36% (n=24), whereas 23.48% (n=85) had ROP in rest of 181 with gestational age between 32 to 37weeks.Frequency of different stages of ROP by gestational age in weeks is shown in Table 01.

Table-01: Frequency of ROP with Gestational Age

Different Stages	*<32 weeks*	*32- 37 weeks*	*Total*
Stage 1	*5*	*38*	*43*
Stage 2	*5*	*19*	*24*
Stage 3	*8*	*21*	*29*
Stage 4	*Nil*	*Nil*	*Nil*
Stage 5	*2*	*Nil*	*2*
*APROP **	*4*	*7*	*11*
No ROP	*34*	*285*	*319*

**APROP = Aggressive Posterior Retinopathy of Prematurity*

75 infants had birth weight<1500 gm and among them 59 eyes (39.33%) had developed ROP. Frequency found decreases with increased birth weight. (Table 02)

Table-02: Frequency of ROP with birth weight

Different Stages	<1.5 kg	1.5-2 kg	2-2.5 kg	Total
Stage 1	24	15	4	43
Stage 2	14	10	nil	24
Stage 3	15	14	nil	29
Stage 4	Nil	Nil	nil	Nil
Stage 5	2	Nil	nil	2
APROP	4	7	nil	11
No ROP	86	208	25	319

Data regarding suspected risk factors were obtained from patient referral note or interviewing caregiver included twin birth, oxygen therapy, sepsis, respiratory distress syndrome and blood transfusion. Association of risk factors with ROP is shown in Table 03.

Table-03: Risk factors associates with ROP

Characteristics	Number	ROP % (Eyes)
Multiple birth	23	58.70%
Oxygen inhalation	188	98.16%
Sepsis	135	88.99%
RDS	10	3.60%
Blood transfusion	1	0%

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We categorize the diagnosed ROP case into type 1, type 2 to decide further management. In our study we found 5.37% Type 1 ROP, 19.63% Type 2 ROP, (Fig:1). Type 1 cases were given treatment with anti-VEGF or Laser or both. Type 2 cases were followed up and managed subsequently.

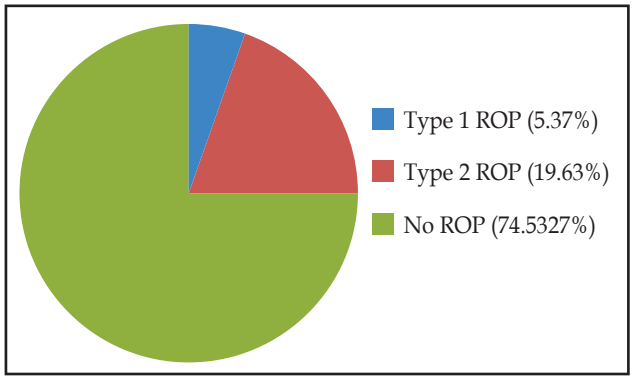

Figure-01: Different ROP Category

Discussion

Retinopathy of prematurity is a debilitating disease which if left untreated can cause permanent vision loss. It has become a major health problem in developing countries. This increase in rate of ROP in developing countries may be due to increased rate of preterm birth due to increased rate of teenage pregnancy, and in developing countries large portion of women are admitted in health care facility for delivery as a result premature infants are admitted in NICU[7].

In our study the incidence of ROP was 25.47%. A study done on ROP and its risk factors at Bangabandhu Sheikh Mujib Medical University also showed 23.7% incidence which match with our study[13]. Finding is also similar with other studies that deal with ROP and risk factor[14,15]. But incidence of 31% and 40% found in two recent study done in Bangladesh[8,16]. Developed countries follow American and British guidelines for screening which recommend that all infants born weighing ≤ 1500 gm or present at ≤ 30 weeks gestational age and selected infants with birth weight of 1500–2000 gm or gestational age >32 weeks who experience an unstable course requiring cardio-respiratory support should also be screened. But these criteria cannot be followed in the perspective of developing country. Because here infants with larger birth weight and gestational age also develop ROP in comparison to developed country. Jalali et al have recommended cut off limit of screening babies born at ≤ 37 weeks and/or birth weight 2000gm in the presence of a systemic illness in order to prevent missing any infant with threshold ROP[18]. In our study, we screened of babies up to birth weight 2.5kg and gestational age at birth up to 37 weeks and got ROP in larger babies group too. So, if we followed the guideline of screening for developed countries many ROP case would have remain undiagnosed. Trpadhi et. al. also reported ROP in larger babies in his case series for ROP in larger and near term babies[19].

We found inverse relationship of ROP with birth weight and gestational age. As birth weight and gestational age decreased the incidence of ROP increased. This findings are consistent with the study finding of James Rommer D et al and Warad C et al[20,21].

Our data suggest that multiple gestation, oxygen inhalation, sepsis and respiratory distress syndrome had association with development of ROP.

Hyperoxia–vasocessation and Hypoxia-vasoproliferation play the role in the pathogenesis of ROP. Widely fluctuating arterial oxygen plays an important role in this pathogenesis[22]. 58.70% of multiple birth and 98.16% oxygen inhaled infant developed ROP in our study. Khalesi N et al found multiple birth and oxygen therapy as risk factor[23]. 88.99% baby that had sepsis developed ROP. Sepsis was identified as independent risk factor for ROP development by Kavurt S et al[24]. Similar to our study Gupta et al also found ROP in babies respiratory distress syndrome[25]. Though we evaluate association of the risk factors with ROP, we could not estimate individual significance as there was overlapping of risk factors.

Limitation

The limitation of our study is its short duration and limited information about risk factors , like no information about flow and duration of oxygen therapy , cause of NICU admission etc. So we could not properly evaluate the association risk factors with development of ROP.

Conclusion

With the improvement in survival rate of preterm infants, ROP is emerging as a major cause of childhood blindness. Early detection and treatment can prevent the blindness from ROP which is only possible by screening at proper time. So a well established screening and motivational program should be initiated in

collaboration with gynecologists, neonatologists and ophthalmologists so that no prematurely born babies miss the opportunity of screening and prevent blindness.

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