Severe Retinopathy of Prematurity in Babies Having Birth Weight >1500 Grams in a Tertiary Care Centre in Southern Odisha

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ABSTRACT

BACKGROUND

Retinopathy of prematurity, earlier known as retrolental fibroplasia, continues to be a major cause of preventable blindness in children. Increase in the incidence of ROP even in heavier babies, reminds us of the first epidemic of 1940s. Early detection and timely management can reduce the burden of ROP blindness to a large extent. We wanted to detect ROP in babies weighing more than 1500 grams at birth and analyse the risk factors associated with the same.

METHODS

This is a retrospective analysis (2 years) of 286 eyes (143 babies) with ROP. Qualitative data was analysed with the chi-square test. p Value <0.05 was considered as significant.

RESULTS

The mean birth weight was 1566.43 gms. (range 1500 gms. to 2000 g) and the mean period of gestation was 33.6 weeks (range 30 to 36). 286 eyes of 143 babies were evaluated, out of which 56 babies had signs of ROP. 6 babies needed urgent intervention and underwent laser ablative therapy and anti-VEGF. Multiple blood transfusions (p value =0.03), septicaemia (p value=0.0011) and oxygen supply (p value=0.029) showed significant correlation with the development of ROP

CONCLUSIONS

Customized screening guidelines are needed for developing countries. Stringent screening at the SNCU analysing the risk factors is required to battle the menace of ROP.

KEYWORDS

Developing Countries, Birth Weight, Retinopathy of Prematurity, Risk Factors, Screening

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BACKGROUND

Retinopathy of prematurity, earlier known as retrolental fibroplasia, continues to be a major cause of preventable blindness in children.[1] The increase in the incidence of ROP even in heavier babies, reminds us of the first epidemic of 1940s.[2] Early detection and timely management can reduce the burden of ROP blindness to a large extent. The 2019 American Academy of Paediatrics recommends screening of infants <1500 gms. or a GA <30 weeks as well as at risk infants outside these criteria.[3] But in our country, we have to incorporate a guideline which will ensure that not even a single case will be missed. Our study aims to alter the western criteria and emphasizes the need of a customized criteria for our nation,[4] which is home to 2 lakh at risk ROP babies every year.[5] We wanted to evaluate the incidence of ROP in babies having birthweight >1500 Grams and determine the risk factors causing ROP in babies >1500 grams at birth.

METHODS

The study was a retrospective, observational clinical case series conducted at MKCG, MCH, Odisha (Departments of Ophthalmology and Paediatrics). We retrospectively analysed the records of babies diagnosed to have ROP during our regular screening at SNCU, between June 2017 and May 2019. This cohort was derived from the babies diagnosed with ROP at our institution and having a birth weight more than 1500 that came to be about 143 babies out of 631 who had been screened.

Inclusion Criteria

- Birth weight >1500 grams.
- GA <36 weeks.
- Complete documentation of hospital records including period of gestation, birth weight and details regarding neonatal illnesses and their course.
- Documentation and categorization according to the International Classification of ROP (ICROP)[6]

Exclusion Criteria

- Babies with other ocular morbidities or craniofacial anomalies.
- Babies less than 1500 grams.

The data of babies were reviewed for the date of birth, birth weight, period of gestation, oxygen exposure, neonatal illness and records of treatment received at the Special Newborn Care Unit (SNCU). Risk factors looked for included septicaemia, multiple blood transfusions, unmonitored oxygen supply and prolonged hospital stay. All infants whose birth weights were ≤2000 gms. and/or whose gestational age at birth was ≤36 weeks were routinely screened. Infants outside these criteria were also screened if the attending neonatologist sought a referral for this purpose based on the stormy postnatal course. The initial examination was carried out around 21st day after birth or between a post-conceptual age of 31 to 33 weeks, whichever came earlier. The frequency of subsequent examinations depended on the findings at the initial presentation. Ocular examination was carried out at the SNCU for all the babies and ROP was graded into different zones and stages. Data was correlated with the risk factors and analysed.

Statistical Analysis

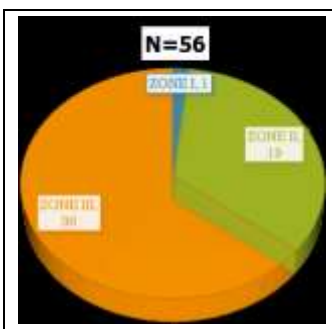
Data were tabulated and categorical variables such as the presence or absence of a neonatal risk factor were tested for statistical significance using the Chi-square test. Quantitative data such as gestational age and birth weight was expressed in the form of continuous variables. p value of less than 0.05 was considered as significant.

RESULTS

During the period between June 2017 and May 2019, 631 infants were screened, out of which 143 were >1500 grams fulfilling the inclusion criteria. Among the heavier babies, 56 (39.1%) babies were diagnosed with ROP. The male: female ratio was 1.15:1, which didn't show any statistical significance (p>0.05). The birth weight ranged from 1500 to 2000 gms. with a mean of 1566.43 gms. (±286). The mean period of gestation was 33.6 weeks (±1.8, range 28 to 36). The demographic details of babies in this group has been summarized in Table 1.

	n = 56
Gender M:F	1.15:1 (30/26)
Gestational Age	
30-32 weeks	20
32-34 weeks	19
34-36 weeks	17
Birthweight	
1500-1750 grams	42
1750-2000 grams	14

Table 1. Demographic Profile



Pie Diagram 1. Zones of ROP

According to involvement of zones, 36 (64.28%) babies were in zone III, 19 (33.92%) in Zone II and 1 (1.78%) baby had Zone I disease. (Pie Diagram 1). Out of 36 babies having Zone III disease, 19 (52.77%) had Stage 1 ROP, 15 (41.67%) had Stage 2 ROP, while 2 (5.55%) had Stage 3 plus which needed immediate treatment. Zone II disease was noted in 19 babies, out of which 9 (47.37%) had Stage 1 ROP, 6 (31.58%) were having Stage 2 ROP, while 4 (21.05%) had Stage 3 plus which needed urgent treatment.

The profile of the 6 babies who warranted immediate management revealed multiple risk factors associated such as multiple blood transfusion, septicaemia, prolonged oxygen supply and long duration of hospitalization. One baby was a case of bronchopulmonary dysplasia who was oxygen dependent and was under unmonitored oxygen supply. (Chart 1)

- Case 1
  - ZII Stage 3 with plus.
  - H/O prolonged oxygen support (15 days).
- Case 2
  - ZII Stage 3 with plus.
  - Multiple blood transfusions, prolonged hospitalization, supplemental oxygen for 17 days.
- Case 3
  - ZII Stage 3 with plus.
  - Septicaemia, multiple blood transfusions.
- Case 4
  - ZII Stage 3 with plus.
  - Supplemental oxygen for 13 days.
- Case 5
  - ZIII Stage 3 with plus.
  - Bronchopulmonary dysplasia.
  - Prolonged hospital stay, supplemental oxygen for 21 days.
- Case 6
  - ZIII Stage 3 with plus.
  - Septicaemia, multiple blood transfusions.
  - Prolonged oxygen supply for 18 days.

On the basis of univariate analysis, 3 risk factors were found to be significant. These were blood transfusion (p value =0.003), septicaemia (p value=0.0011) and unmonitored oxygen supply (p value=0.029). Using the American screening guidelines (birthweight <1500 grams), 56 babies (8.87%) of the total screened would have been missed. Of these, 6 (10.71%) babies had ROP requiring immediate management, whom could have been ignored. Twelve eyes (6 babies) were treated using either anti VEGF (4 eyes) or laser photocoagulation (8 eyes). The laser used was 532 green laser (532 Iris Green Laser, Oculight GL, Iris Medical Inc. USA). Four eyes (2 babies) treated with laser needed supplement treatment.

DISCUSSION

Our data reveals that ROP requiring treatment is not uncommon in babies > 1500 gms. birth weight in our setting. Almost a decade ago, from North India, Charan et al.[7] reported an occurrence of any stage ROP of 47.2% in babies outside the western criteria. Of these babies, 26.1% were greater than 1250 gms. at birth. In another study, Dogra et al[8] reported that 30.7% of babies with threshold ROP treated with cryotherapy were > 1250 gms. and 15.3% were >1500 gms. at birth. Deshpande et al[9] reported 21.7% infants with threshold ROP having birth weight > 1500 gms. in southern India. Fielder[10] commented that 54% of the infants requiring treatment for ROP in Lithuania had birth weight >1500 g. The revised screening criteria recommended by the collaborative of neonatal care and ROP experts in India, London School of Hygiene and Tropical Medicine, led by the Indian Institute of Public Health – Public health Foundation of India and supported by the Queen Elizabeth Diamond Jubilee Trust takes these considerations into regard.[11]

The birth weight of our group ranged from 1500 to 2000 gms. (mean 1566.43 gms.). The period of gestation of the babies in our study varied from 28 to 36 weeks (mean 33.6 weeks). There are only limited reports of ROP in infants from the developed countries with birth weights >1250 gms.[12-21] In these reports, severe ROP was either not found in heavier babies[17,19] or was observed rarely.[14,16,20] Our center, which is a tertiary referral center for ROP, had a problem with the central line of oxygen which may have affected the study. We saw 6 babies needing immediate intervention and their profile revealed that they had been exposed to unmonitored oxygen supply, prolonged hospitalization, multiple blood transfusions and septicaemia. One of the babies had bronchopulmonary dysplasia which made the baby oxygen dependent and had to undergo oxygen supplementation without saturation monitoring. We tried to find out the risk factors associated with the occurrence of ROP in babies outside the conventional western criteria.

Blood transfusion emerged as one of the risk factors causing the occurrence of ROP (p value =0.03). 32 (57.1%) babies of the ROP group had history of blood transfusion, while only 28 (32.1%) of non ROP group had been transfused. Shohat et al (1983) had found multiple blood transfusion to be significantly associated with ROP.[22] On univariate analysis, Swarna Rekha et al. (1996) observed that blood transfusion increases the risk of ROP.[23] Vinekar et al (2007) concluded that risk for threshold or worse disease had an association with exchange transfusion (p= 0.003).[24] Chawla D (2008) also found frequent blood transfusions to be a significant factor for developing ROP.[25] Kumar P et al. (2011) showed a similar association with packed cell transfusion[26]. Recent studies conducted by Hakeem AH et al. (2012),[27] Ilham M Omer et al. (2014),[28] K Lathiesh Kumar et al. (2017),[29] Milad Azami et al. (2017),[30] Oscar Onyango et al. (2018)[31] & Snigdha Sen et al. (2018)[32] have also found blood transfusion to be a significant risk factor for developing ROP. Septicaemia also correlated well with ROP (p value =0.0011).32 (57.1%) babies of ROP group had CRP positive, while only[25] (29.88%) had septicaemia in the non ROP group. A similar association was observed by Gupta VP (2004)[33] & Chawla D (2008)[25] who found sepsis to be a significant risk factor. Sudha Chaudhari et al. (2009) also found sepsis as a significant risk factor with a p value <0.001[34]. Recent studies conducted by Reza Saeidi et al. (2009),[35] Kumar P et al. (2011),[26] Hakeem AH et al. (2012),[27] Ilham M. Omer et al. (2014),[28] Samatha Shetty et

al. (2015),[36] Milad Azami et al. (2017)[30] & Snigdha Sen et al. (2018)[32] have also found sepsis as a significant risk factor for developing ROP. Unmonitored oxygen supplementation also showed a significant association with ROP (p value =0.029).[30] (55.36%) babies of ROP group had history of oxygen support without proper saturation monitoring, while 32 (36.78%) babies of the non ROP group had the same history. Statistically this difference was found to be significant (p value =0.023). Various studies having similar results have been conducted in the past.

Prendiville A et al. (1988) found hyperoxia with an oxygen tension more than 12 kilo pascals to be independent risk factor associated with the development of ROP.[37] Flynn JT (1992) concluded that there was positive correlation between incidence and severity of ROP and continuous oxygen levels of more than or equal to 80 mmHg.[38] Gopal L et al. (1995) concluded that oxygen exposure increases the development of ROP with 51.5% babies exposed to oxygen developing ROP[39] Swarna Rekha et al. (1996) found that duration of oxygen therapy was significant risk factor of development of ROP.[23] Sudha Chaudhari et al. (2009) observed that oxygen therapy was a significant risk factor for ROP with a p value of 0.03135. Recent studies conducted by Kumar P et al. (2011),[26] Hakeem AH et al. (2012),[27] Ilham M Omer et al. (2014)29, K Lathiesh Kumar et. al. (2017),[29] Milad Azami et al. (2017)[30] & Snigdha Sen et al. (2018)[32] have also found duration of oxygen therapy to be an independent risk factor for developing ROP. The modification of existing guidelines, however, needs more prospective, multicentric studies before such recommendations can be advocated. The limitations of our study lies in its retrospective nature and the incomplete analysis of babies less than 1500 grams. Various risk factors such as maternal disease, antenatal factors and genetic mutations in these infants responsible for diseases mimicking ROP have not been taken into consideration.

CONCLUSIONS

ROP manifesting in babies >1500 grams at birth can be attributed to the improved neonatal survival, supplemental oxygen therapy, multiple blood transfusions and septicaemia. Customized criteria are required for developing countries since a total of 56 babies would have been missed if western guidelines were followed. 6 babies could undergo timely treatment who could add to the burden of blindness. An efficient collaboration between neonatologist, ophthalmologist and the primary caregivers is a must to battle the menace of ROP.

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