e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15 (12); 633-638

Original Research Article

Association of Gestational Age and Birth Weight with Retinopathy of Prematurity: A Prospective Clinical Study

Sini P S[1], Vijayamma N[2], Manjit P S[3]

[1]Resident, Department of Ophthalmology, Government Medical College, Kottayam, Kerala, India, 686008

[2]Professor, Department of Ophthalmology, Government Medical College, Kottayam, Kerala, India, 686008

[3]Associate Professor (CAP), Department of Ophthalmology, Government Medical College, Kottayam, Kerala, India, 686006

Received: 25-09-2023 / Revised: 28-10-2023 / Accepted: 30-11-2023

Corresponding author: Dr. Manjit P S

Conflict of interest: Nil

Abstract:

Background: Retinopathy of prematurity (ROP) is a condition that mostly affects premature newborns. It encompasses a range of symptoms, from modest and temporary alterations in the retina that resolve on their own, to severe and progressive growth of abnormal blood vessels, scarring, detachment of the retina, and eventual blindness. India accounts for 20% of global childhood blindness. In addition to congenital cataract, congenital glaucoma, and ocular traumas, Retinopathy of Prematurity (ROP) is becoming recognized as a significant contributor to childhood blindness in India.

Aim and Objectives: The enhancement of neonatal care has led to an increase in the survival rates of preterm babies. However, as a consequence, there has been a rise in the number of infants affected with retinopathy of prematurity (ROP). This study quantified the incidence of retinopathy of prematurity (ROP) and examined the correlation between gestational age and birth weight with the development of ROP.

Research Methodology: A prospective research conducted in a hospital setting.

Setting: Study conducted at the Ophthalmology department of the Government Medical College and Hospital in Kottayam, Kerala, India, from March 2012 until August 2013.

Material and Methods: Seventy-two premature newborns were screened for retinopathy of prematurity between March 2012 and August 2013. This was done after obtaining approval from the institutional ethics committee and obtaining consent in writing from the parents.

Outcome measures: The primary outcome measure utilised was the cumulative incidence of ROP, whereas the secondary outcome measure focused on the association between gestational age and birth weight with ROP.

Results: Out of the 72 newborns included in the study's sample, 28 of them had Retinopathy of Prematurity (ROP) in either one or both of their eyes. The total incidence rate of ROP in the population under study was 38.88%. Significant differences were seen in the average gestational age (29.55±1.79 weeks) and average birth weight (1030.12±175.08 grams) between the ROP group and the control group (Without ROP) (32.31±1.83 weeks) and (1371.37±309.64 grams), respectively ($P < 0.0001$ and $P=0.0005$, respectively).

Conclusion: In the population examined, researchers found a notable prevalence of ROP in this study (38.88%). Furthermore, an early gestational age and a low birth weight have a statistically significant influence on the advancement of ROP in its active state. Minimizing future postnatal risk factors relies on receiving excellent prenatal and postnatal care, along with following to stringent ROP screening criteria. Timely identification and treatment of ROP are crucial for optimizing visual outcomes. Collaboration between ophthalmologists and neonatologists is crucial for prompt screening and consistent monitoring in order to alleviate the prevalence of blindness caused by retinopathy of prematurity (ROP).

Keywords: Birth weight; Gestational age; Preterm infants; ROP; Risk factors; Screening.

Introduction

Retinopathy of prematurity (ROP) is a condition characterised by the abnormal development of retinal arteries due to inadequate blood supply to the retinal tissue caused by excessive oxygen levels. This leads to the down regulation of VEGF and the death of endothelial cells. VEGF is necessary for the endothelium, as per this approach. The closure of growing capillaries leads to the ischemia and hypoxia of developing retinal tissue. Neovascularisation occurs as a result of the

increased expression of Vascular Endothelial Growth Factor (VEGF) in this process. [1-3].

Retinopathy of prematurity (ROP) is a potentially preventable cause of blindness in children, especially in middle-income nations and Asian cities. [4-7] The survival rates have risen, resulting in a higher likelihood of severe ROP development that necessitates treatment in these infants. [5-8] ROP is a multifaceted condition that has an inverse relationship with both gestational age and birth weight. [4,5] The most significant and frequently observed risk variables are a short gestational age and a low birth weight. [4,9,10] The relationship between low birth weight and low gestational age is strongly associated, although the specific impact on the development of ROP and the relative influence of each component remain uncertain. Birth weight is often seen as an indicator of growth quality and has a significant correlation with the survival rate of infants. [11] Gestational age, however, is used to determine the level of health condition, specifically the level of maturity.

Ophthalmologists and neonatologists can conduct thorough screening, make accurate diagnoses, and prevent the progression of the condition by identifying risk factors that hinder the development of ROP and understanding where it originated.

Aim and Objectives:

This study determined the mean incidence rate of ROP and evaluated the correlation between gestational age as well as birth weight with retinopathy of prematurity.

Material and Methods:

At this hospital-based study, 72 preterm infants were evaluated for retinopathy of prematurity (ROP) at the ophthalmology department of a government hospital and medical college in Kottayam, Kerala, India. From March 2012 until August 2013, the study was carried out.

The research obtained approval from the Ethical Committee (IEC No. 45/2012/GMCK) and obtained a written consent from the parents after providing them with comprehensive information.

Inclusion criteria:

The research included preterm babies who satisfied any of the following criteria:

1. Infants with a gestational age (GA) of less than or equal to 32 weeks or a birth weight (BW) of less than or equal to 1500 grams.
2. Infants with a GA between 32 and 37 weeks or a BW greater than 1500 grams, who also have any of the following risk factors: respiratory distress syndrome, oxygen therapy, septicaemia, blood components transfusion, multiple pregnancies, PIH, anaemia, IVH etc.

Exclusion criteria:

1. Infants that died or were lost to follow-up before the retina fully vascularised or before retinopathy of prematurity (ROP) began to manifest during the research period.
2. Infants who are seen for the first time either before or after the research period.
3. Reluctant to provide consent.

Following the administration of one drop of 0.8% tropicamide eye drops and one drop of 1% phenylephrine eye drops, a total of three times in each of the eyes, with a 15-minute interval between each administration, fundoscopy was performed utilising an indirect ophthalmoscope equipped with a 20 diopter convex lens. A highly trained ophthalmologist, specialising in the identification and treatment of retinal diseases in children, performed the examination.

The initial assessment took place when the infants were around 4 to 6 weeks old. The retinal vascularisation and the existence of any retinopathy of prematurity (ROP) were observed. Infants with incomplete vascularisation of the retina were scheduled for weekly or biweekly follow-up tests, depending on the extent of vascularisation in the zone. Using the 'International Classification of Retinopathy of Prematurity' as a reference, each patient was given a stage according to the eye with the worst ROP symptoms during the follow-up exam. [12]. Individuals who developed retinopathy of prematurity (ROP) were thereafter monitored on a weekly or biweekly basis, or even sooner, to evaluate the advancement or reversal of ROP. Individuals who satisfied the requirements for treatment were directed to a more advanced facility for their care. Subsequent tests were conducted until full vascularisation of the retina in both eyes of the newborns was achieved.

Statistical Analysis:

The statistical analysis was conducted using the SPSS software, version 21.0 for Windows, developed by SPSS Inc. in Chicago, IL, USA. The examination of univariate data for unpaired samples was performed using statistical tests such as the Independent-Sample t-test, Mann-Whitney U-test, $\chi 2$-test, or Fisher's exact test. A Pearson correlation analysis was employed to assess the link between the gestational age and birth weight. The McNemar test and paired t-test were used to conduct univariate paired comparisons between the bigger newborn and the smaller infant from the same twin pair. The chi-squared test was employed for the examination of count data. All P-values presented are two-sided, and P-values less than 0.05 were deemed statistically significant.

Results: Among the 72 newborns examined in the research, 28 infants experienced the development

of various stages of retinopathy of prematurity (ROP) in either one or both eyes. Therefore, the study population had an incidence rate of ROP of 38.88%. [Figure 1]

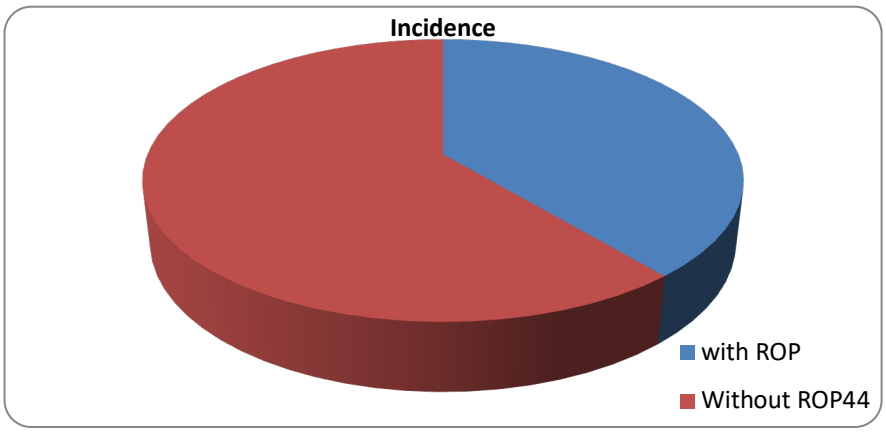

Figure 1: Pie diagram showing ROP distribution

In the ROP group 67.8% infants were males and 32.1% were females. The study found no statistically significant correlation between ROP and gender (P= 0.264). **(Table 1)**

Table 1: Correlation of gender with ROP

Gender	Male	Female	Total	Odd Ratio	95% CL	P-Value
With ROP	19	9	28	0.569	0.212 to 1.531	0.264

Table 2: T-test and statistics GA and BW of the study population

Parameters	Gestational age at birth	Birth weight
Mean	31.23	1238.6528
Standard deviation	2.24989	312.70826
Standard error mean	0.26515	36.85302
T	117.781	33.611
Df	71	71
P value	0	0
95% CL	30.7013-31.7587	1165.1699-1312.1356

Table 3: Distribution of gestational age at birth and ROP

Gestational Age	ROP	No ROP	Total	Treatment requiring ROP
≤ 26 weeks	2	0	2	2
26-27 weeks	0	0	0	0
27-28 weeks	4	1	5	2
28-29 weeks	2	0	2	0
29-30 weeks	7	4	11	3
30-31 weeks	8	8	16	0
31-32 weeks	4	8	12	0
32-33 weeks	1	8	9	0
>33 weeks	0	15	15	0
Total	**28**	**44**	**72**	**7**

A statistically significant difference was found in the average gestational age between the ROP group (29.55±1.79 weeks) and the control group (32.31±1.83 weeks), which did not develop ROP **(P < 0.0001).** Out of the 28 infants who developed ROP, 27 (96.42%) infants had a gestational age ≤32 weeks. Hence gestational age ≤32 weeks are significantly associated with the development of ROP. (OR 29.571 95% CL3.6878 to 237.1272, P=0.0014) (Table 4)

Table 4: Analysis of Gestational Age (GA) and Birth Weight (BW) distribution

Parameter (Mean±SD)	ROP (n=28)	No ROP (n=44)	P-Value
Gestational Age (weeks)	29.55±1.79	32.31±1.83	<0.0001
Birth Weight (grams)	1030.12±175.08	1371.37±309.64	<0.0001

A statistically significant difference was found in the mean birth weight between the ROP group (1030.11±175.07 grams) and the control group (1371.36±309.63 grams, no ROP) **(P < 0.0001).** Out of the 28 infants with ROP 25 infants 89.28% had a birth weight of ≤1250g. Hence birth weight ≤1250g is significantly associated with ROP (OR 10.9649 95% CL 2.8771to 41.7888, **P=0.0005) (Table 4 & 5)**

Table 5: Distribution of birth weight and ROP

Birth weight (grams)	ROP	No ROP	Total	Treatment requiring ROP
≤750	2	0	2	2
751-1000	10	4	14	3
1001-1250	13	15	28	2
≥1251	3	25	28	0
Total	**28**	**44**	**72**	**7**

Discussion

Based on the findings of the bulk of studies [13–14], the prevalence of ROP in low birth weight infants in India is within the range of 38 to 51.9%. However, because of variations in the criteria used to determine inclusion and the lack of a universally accepted screening criterion for ROP, there have been reported occurrences as low as 21.7% [15] and as high as 71.1% [16]. Several studies on retinopathy of prematurity (ROP) have examined newborns with a gestational age of 32 weeks or less, or a birth weight (BW) of less than 1500 g [17, 18].

However, we expanded the range of participants in this analysis to include newborns weighing more than 1500 g or delivered at or after 323 weeks of gestation, who exhibited identifiable risk factors. Despite India being a developing nation, the prevalence of ROP in our setting has increased to a level comparable to developed countries [19]. This implies that immaturity and low birth weight are likely the most significant factors linked to the development of ROP. If these circumstances are not addressed, the incidence rate of ROP may continue to increase. Alternatively, these results may indicate the increasing prevalence of neonatal care in countries like India, as the occurrence of ROP and the number of individuals at risk for developing ROP depends on the presence, ease of access, and standard of neonatal treatment. The current study found that the incidence of therapy requiring retinopathy of prematurity (ROP) was 9.7%. This is analogous to prior inquiries. In 2004, Larson et al [20] conducted a community-based study and determined that the incidence of ROP requiring treatment was 12.3%.

Our analysis found no statistically significant correlation between ROP and gender. This was primarily in conformity with the findings of Shah et al [21]. Darlow et al. [9] discovered a significant association between male gender and ROP.

The results of our investigation showed a statistically significant link between shorter gestation periods and low birth weight and the development of ROP. Multiple studies have demonstrated that the gestational age at which a baby is born with low birth weight is the primary factor associated with the development of retinopathy of prematurity (ROP) [22-25].

Limitations of the study:

Due to the research being done at a tertiary care centre, a greater number of infants who were at higher risk were assessed. This may have contributed to a high prevalence of ROP. Due to the predominance of newborns referred from the Neonatal Intensive Care Unit (NICU), the sample group in our study does not fully represent the whole population. Therefore, it was not feasible to estimate the prevalence for the entire population by extrapolation. Another significant bias in current studies is the exclusion of newborns that cannot be followed up. We suggest doing a comparative study with a greater number of participants, considering preterm infants who are not admitted to the Neonatal Intensive Care Unit (NICU). This would help address some of the limitations of the current study.

Conclusion

Within the analysed population, researchers found a notable prevalence of ROP in this study (38.89%). Additionally, an early gestational age and a low birth weight have a statistically significant influence on the advancement of ROP in its active state. Minimising future post-natal risk factors relies on receiving appropriate prenatal and postnatal care, as well as following to rigorous ROP screening criteria. Timely identification and treatment of ROP are crucial for optimising visual outcomes. Collaboration between ophthalmologists

and neonatologists is essential to ensure prompt screening and consistent monitoring, hence mitigating the prevalence of blindness caused by retinopathy of prematurity (ROP).

Recommendations:

Our screening recommendations are based on two criteria:

1. Gestational age at delivery of 33 weeks or less, and a birth weight of 1400gms or less.
2. Premature infants who were born after 33 weeks of gestational age and have a birth weight of more than 1400 grams may be eligible for inclusion if they have a history of respiratory distress syndrome or have been exposed to therapeutic oxygen for an extended period of time.

In order to ensure that all eligible children are tested and monitored, it is recommended to do the initial ROP screening prior to the infant's discharge from the hospital, if feasible. Alternatively, an appointment for screening should be scheduled before the infant's discharge.

References

1. Beharry KD, Valencia GB, Lazzaro DR, Aranda JV. Pharmacologic interventions for the prevention and treatment of retinopathy of prematurity. Semin Perinatol. 2016; 40:189–202.
2. Celebi AR, Petricli IS, Hekimoglu E, Demirel N, Bas AY. The incidence and risk factors of severe retinopathy of prematurity in extremely low birth weight infants in Turkey. Med Sci Monit. 2014; 20:1647–1653.
3. Lee TC, Chiang MF. Pediatric Retinal Vascular Diseases. In: Schachat AP, Wilkinson CP, Hinton DR, Sadda SR, Wiedemann P, editors. Ryan's Retina. 6. New York: Elsevier; 2018. pp. 1246–1267.
4. Gilbert C. Retinopathy of prematurity: a global perspective of epidemics, population of babies at risk and implication for control. Early Hum Dev. 2008; 84(2):77–82.
5. Todd DA, Wright A, Smith J, NICUS Group Severe retinopathy of prematurity in infants <30 weeks' gestation in New South Wales and the Australian Capital Territory from 1992 to 2002. Arch Dis Child Fetal Neonatal Ed. 2007; 92(4):251–254.
6. Kong M, Shin DH, Kim SJ, Ham DI, Kang SW, Chang YS, Park WS. Retinopathy of prematurity in infants born before 25 weeks gestation in a Korean single neonatal intensive care unit: incidence, natural history and risk factors. J Korean Med Sci. 2012; 27(12):1556–1562.
7. Hagadorn JI, Richardson DK, Schmid CH, Cole CH. Cumulative illness severity and progression from moderate to severe retinopathy of prematurity. J Perinatol. 2007; 27(8):502–509.
8. Isaza G, Arora S. Incidence and severity of retinopathy of prematurity in extremely premature infants. Can J Ophthalmol. 2012; 47(3):296–300.
9. Darlow BA, Hutchinson JL, Henderson-Smart DJ, Donoghue DA, Simpson JM, Evans NJ, Australian and New Zealand Neonatal Network Prenatal risk factors for severe retinopathy of prematurity among very preterm infants of the Australian and New Zealand Neonatal Network. Pediatrics. 2005; 115(4):990–996.
10. Sarikabadayi YU, Aydemir O, Ozen ZT, Aydemir C, Tok L, Oquz SS, Erdeve O, Uras N, Dilmen U. Screening for retinopathy of prematurity in a large tertiary neonatal intensive care unit in Turkey: frequency and risk factors. Ophthalmic Epidemiol. 2011; 18(6):269–274.
11. Dhaliwal CA, Fleck BW, Wright E, Graham C, McIntosh N. Retinopathy of prematurity in small-for-gestational age infants compared with those of appropriate size for gestational age. Arch Dis Child Fetal Neonatal Ed. 2009; 94(3):193–195.
12. Gole GA, et al. The international classification of retinopathy of prematurity revisited. Arch Ophthalmol. 2005; 123:991–999.
13. Gopal L, Sharma T, Ramchandran S, Shanmugasundaram R, Asha V. Retinopathy of prematurity. A study. Indian J Ophthalmol 1995; 43:50-61.
14. Varughese S, Jain S, Gupta N, Singh S, Tyagi V, Puliyel JM. Magnitude of the problem of retinopathy of prematurity. Experience in a large maternity unit with a medium size level-3 nursery. Indian J Ophthalmol 2001; 49:187-88.
15. Gupta VP, Dhaliwal U, Sharma R. Retinopathy of prematurity-risk factors. Indian J Pediatr 2004; 71:887–92.
16. Anand Vinekar, Mangat R Dogra,Tiakumzuk Sangtam, Anil Narang, Amod Gupta. Retinopathy of prematurity in Asian Indian babies weighing greater than 1250grams at birth: Ten year data from a tertiary care center in a developing country. Indian J Ophthalmol 2007 Sep-Oct; 55(5): 331–336.
17. Fortes Filho JB, Valiatti FB, Eckert GU, Costa MC, Silveira RC, Procianoy RS. Is being small for gestational age a risk factor for retinopathy of prematurity? A study with 345 very low birth weight preterm infants. J Pediatr (Rio J). 2009; 85:48–54.
18. Goncalves E, Nasser LS, Martelli DR, Alkmim IR, Mourao TV, Caldeira AP, et al. Incidence and risk factors for retinopathy of prematurity

in a Brazilian reference service. Sao Paulo Med J. 2014; 132:85–91.
19. Gilbert, C, et al. Characteristics of Infants With Severe Retinopathy of Prematurity in Countries With Low, Moderate, and High Levels of Development: Implications for Screening Programs. Pediatrics2005; 115 (5), e518-25.
20. Larson E, Holmstrom G. screening for retinopathy of prematurity: evaluation and modification of guidelines. Br J Ophthalmol 2002; 86:1399-1402
21. Shah VA, Yeo CL, Ling YL. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. Ann Acad Med Singapore. 2005; 34:169–78
22. Kinsey, V E, Jacobus, J T, and Hemphill, F M. Retrolental Fibroplasia: Cooperative Study of Retrolental Fibroplasia and the Use of Oxygen. Arch Ophthalmol1956;56 (4), 481-543
23. Lanman, J T, Guy, L P, and Dancis, J. Retrolental fibroplasia and oxygen therapy. J Am Med Assoc 1954; 155 (3), 223-6
24. Patz, A, Hoeck, L E, and De La Cruz, E. Studies on the effect of high oxygen administration in retrolental fibroplasia. Am J Ophthalmol 1952; 35 (9), 1248-53.
25. Arroe M, Peitersen B. Retinopathy of prematurity: review of seven year period in a Danish neonatal intensive care unit. Acta Paediatr 1994; 83:501-5.