Original Article

Retinopathy of prematurity: Postnatal weight gain and risk factors profile; a hospital-based study from a tertiary care center

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ABSTRACT

Background: Premature infants often develop blindness in one or both eyes due to disparity in retinal growth. This condition is termed as retinopathy of prematurity (ROP). **Aim:** The aim of the study is to study the postnatal weight gain pattern of preterm infants (Age < 32 weeks) and risk factors of ROP in a tertiary care center and to validate the lower birth weight and gestational age (GA) for ROP. **Methods:** Hospital-based study on 110 preterm neonates admitted in the neonatal intensive care unit (NICU) who fulfilled the criteria for ROP screening. On screening, 55 neonates were identified to have ROP and 55 neonates identified to have no ROP. The profiles of ROP and risk factors were documented according to the International Classification for ROP recommendations. The data were analyzed for GA, birth weight, and risk factors predisposing to ROP. **Results:** A total of 110 preterm neonates were screened, out of which, 55 had ROP. The mean GA ($P = 0.002$), Apnea ($P = 0.001$), ventilation ($P = 0.001$), and surfactant ($P = 0.001$) were observed a significant difference. Further, a significant difference in weight gain pattern in the two groups ($P < 0.05$) was also observed. The group without ROP had a better weight gain pattern than the group with ROP. **Conclusion:** Our study revealed prematurity, low birth weight, and birth weight increasing patterns were found to be strong predictors of ROP. GA, apnea, ventilation, and surfactant were found to be statistically significant factors associated with ROP.

Key words: Retinopathy of Prematurity, Prematurity, Birth weight, Gestational age

Retinopathy of prematurity (ROP) is a complex disease which cause blindness in one or both eyes of premature infants due to the disorganized growth of retinal blood vessels [1]. Several investigators have identified several risk factors for ROP, such as low birth weight, hypoxia, duration of oxygen supplementation, respiratory distress syndrome, twin pregnancy, anemia, blood transfusions, sepsis, intraventricular hemorrhage, hypotension, hypothermia, maternal factors, and prenatal and perinatal factors [2,3]. Among these, birth weight and gestational age (GA) are the two major risk factors to screen the disease [4]. After preterm birth, the loss of placental supply of nutrients and reduction of infant growth factors (IGF) are the major reasons to develop ROP [5]. ROP is a leading cause of preventable childhood blindness with over 3,00,000 neonates affected with the incidence of 24%–47% worldwide [6]. Among these, one-fourth of the blind children live in India. The WHO suggests that India and other middle-income countries are suffering from the 'third epidemic' of this disease [7]. In India, the incidence of ROP varies in different geographical regions: 22.3% in Pune, Maharashtra [8], 16% in Shimla, Himachal Pradesh [9], 24.1% in Vadodara, Gujarat [10], 44% in Kalyani, West Bengal [11], 21.3% in Srinagar [12], 73.6% in New Delhi [13], 33.2% in Eastern India [14].

According to the American Academy of Pediatrics (AAP), neonates with birth weight<1500g or GA≤30 weeks should undergo retinal screening [15]. However, in India, the GA of infants are not always known or accurate. Even babies with body weight>1600 g and GA>32 weeks also fall prey to develop ROP and sometimes severe ROP [16]. In India, due to lack of proper screening guidelines, and other unknown etiologies for ROP, often contradictory reports are obtained. However, there is a paucity of population-based-ROP in these larger neonates. Further, there are no studies in our country aiming to validate the post-natal weight gain pattern to predict the development of severe ROP. The present study aimed to find the postnatal weight gain, record the profile of ROP, and to identify the risk factors associated with the development of ROP in our population.

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MATERIALS AND METHODS

A total of 110 preterm infants were included. All infants underwent screening for ROP, had their weight measured every week,

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and recorded for the survival to the final ophthalmologic ROP assessment. Based on the ROP screening, the included infants were divided into two groups: Infants with ROP (55 preterm infants) and infants without ROP (55 preterm infants). Neonates with GA at delivery < 23 or >31+6 weeks, incomplete weight entry, no final ROP outcome, and preterm infants who were discharged or died before 4 weeks of life were excluded from the study. GA <32 weeks and/or a birth weight (BW) ≤1500 g who stayed in NICU for minimum period of 4 weeks and had been screened for ROP were included for this study. Ethical clearance was obtained from the institutional ethics committee and informed consent was collected from all the guardians and/or the parents of the participants prior to the study. Infant's demographics, GA, gender and birth weight, other probable risk factors for the development of ROP such as oxygen exposure (ventilation), blood transfusions, surfactant, and apnea were documented. Each weekly weight had been entered into the WINROP algorithm measured at exactly 1st, 2nd, 3rd, and 4th week of postnatal age.

Infants who were eligible for ROP examination, according to the American Academy Pediatrics and National Neonatology Forum guidelines [17], were examined by ophthalmologists and categorized following the International Classification of ROP. All the babies were followed up till the time of the first ROP screening or WINROP alarm or till the retina was fully vascularized, whichever was later.

All the quantitative variables such as BW, GA, and mean weight gain are expressed in mean±standard deviation (SD). Mean weight gain in both cohorts was estimated and tested for statistical significance through Friedman test. Chi-square test was used to predict the association between the other risk factors and the development of ROP. Multiple logistic regressions were used to find the independent risk factors for the development of ROP. Mann-Whitney test was used to test the statistical significance of the difference in the median duration of total parenteral nutrition (TPN) and median age of reaching full feeds in the two groups. All the statistical analysis was done using the SPSS v.16 software.

RESULTS

ROP screening was carried out for a total of 110 infants of which, 55 had ROP and the remaining 55 did not have ROP. The clinical characteristics of study participants between the infants with/without ROP group were documented in Table 1. The mean GA, apnea, ventilation, and surfactant were observed to have a significant difference between the with/without ROP groups studied. However, the other studied risk factors for ROP such as mean BW, blood transfusion, and continuous positive airway pressure (CPAP) were not found to have a significant difference between the studied groups (Table 1).

The BW and weight gain at different weeks were documented in Table 2. There was a significant difference was observed between the groups for BW and weight loss of infants in the first week after birth. Furthermore, the mean weight gain in those without ROP was found to be significantly higher as compared to those with ROP.

The TPN and age to full feeds between with ROP and without ROP were documented in Table 3.

The longitudinal postnatal weight gain pattern in the two groups is presented in Fig. 1. There was a significant difference in weight gain pattern between the two groups ($p<0.05$). The group without ROP had a better weight gain pattern than the group with ROP.

DISCUSSION

In India, several studies on ROP were conducted. However, the screening method and incidence rate of ROP varies widely throughout the country. A study conducted by Nitin Kumar *et al*., [9] based in Shimla, Himachal Pradesh screened 50 babies; the mean BW of the ROP babies was 1043 g while that of non-ROP babies was 1334 gms. Lower BW was significantly associated with increased incidence ($p=0.007$) and severity ($p=0.017$) of ROP. The mean GA of the ROP babies was 30.63 weeks while that of non- ROP babies was 32.1 weeks. Similarly, another study from

Table 1: Clinical characteristics of study participants between the infants with/without ROP group

Risk factors	Infants with ROP n=55	Infants without ROP n=55	p value*
Mean gestational age (weeks)	29.35	31.27	0.002
Mean birth weight (gms)	1122	1276	0.602
Apnea; number (percentage)	24 (44%)	12 (22%)	<0.01
Blood transfusion; number (percentage)	34 (76%)	11 (23%)	0.12
Ventilation; number (percentage)	39 (71%)	15 (29%)	0.001
CPAP; number (percentage)	20 (76%)	15 (23%)	0.119
Surfactant; number (percentage)	34 (62%)	9 (16%)	<0.01

CPAP: Continuous positive airway pressure, *p value obtained from Chi square test. ROP: Retinopathy of prematurity

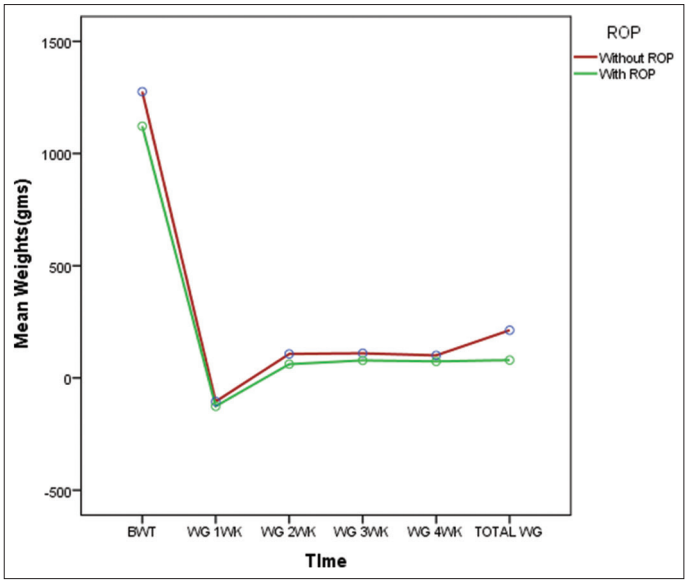

Figure 1: Postnatal weight gain pattern in the ROP and non-ROP groups

Table 2: Weight gain association between the infants with/without ROP at different weeks

Characteristics	Birth weight (g)	Weight gain (g) at the end of				Mean weight gain (g)
		Week 1	Week 2	Week 3	Week 4	
With ROP						
Mean	1122.18	-126.22	61.49	78.18	73.45	79.27
SD	187.03	79.57	69.18	65.80	55.11	137.63
Without ROP						
Mean	1275.91	-105.45	106.91	109.82	100.55	212.55
SD	192.30	68.30	49.81	57.26	48.43	96.67
p value*	<0.000	<0.038	<0.000	<0.001	<0.005	<0.000

ROP: Retinopathy of prematurity, SD: Standard deviation, p value*: Probability value obtained from Friedman test

Table 3: The duration of TPN and age of reaching full feeds in the two groups with and without ROP

Characteristics	With ROP median (range)	Without ROP median (range)	p value*
TPN (days)	0 (0-27)	10 (0-25)	<0.01
Age at full feeds (days)	28 (3-54)	17 (7-42)	0.001

ROP: Retinopathy of prematurity, p value*: Probability value obtained from Mann-Whitney test; TPN: Total parenteral nutrition

Gujarat found a significant difference between mean BW of ROP positive cases (1622.38±612.89). Further, the GA of ROP positive versus negative cases was also observed to have a significant difference (p<0.001) (10). A study from Srinagar was also found the mean GA of patients who developed ROP was 29.0±2.52 weeks and who did not develop ROP was 32.7±3.08. The mean weight of ROP positive group was 1.36±0.255 kg and ROP negative group was 1.67±0.227 kg [12]. Furthermore, studies from the Indian sub-continent such as in Pune, Maharashtra [8], Kalyani, West Bengal [11], Srinagar [12], New Delhi [13], and in Eastern India [14], also reported similar kind of results. In accordance with these previous reports, our study also found a significant difference of GA between the ROP and non-ROP group. However, the mean BW of infants were not significantly different.

In our study, low BW was found to be significantly correlated with the incidence of ROP, which is in agreement with the other studies conducted internationally such as in neonates from Oman [18], Egypt [19], Iran [20], Southeastern Turkey [21], Singapore [22], USA [23], Australia, and New Zealand [24]. Several risk factors have been reported to predispose to the development of ROP [25,26]. In our study, apnea, ventilation, and surfactant were found to be the significant risk factors in accord with other studies from India. Chaudhari *et al*., found that apnea and septicemia are the risk factors for ROP [8]. Vinekar, *et al*. [16] also found that septicemia was a significant risk factor. Aggarwal *et al*., [27] found apnea, clinical sepsis, and male sex to be significant risk factors. In our study, we found that the surfactant was significant risk factor for ROP in accord with the study by Seiberth, *et al*. [28]. In contrast, the study from pune, India by Chaudhari *et al*., did not find any significant association for surfactant [8]. Chauhan *et al*. [12] found that blood transfusion is a significant risk factor, whereas our study and the study by Nitin kumar *et al*. [9] did not find any such association.

Several studies revealed that poor postnatal weight gain is a predictor of the severe development of ROP [29-31]. However, studies have measured the weight analysis using the relative weight gain (g/kg/d) through 6 weeks, correlating the low weight gain and risk for the ROP development by WINROP and PINT-ROP methods [31-33]. In previous studies concerning with low BW standard deviation score (BWSDS) as a risk factor for ROP, infants were grouped differently and results have been inconclusive [24,34-36]. However, Qui *et al*. [37] reported that the impact of small GA as a risk factor for severe ROP varies for infants born ≤26, 27–28, 29–30, or 31–32 weeks GA. On the other hand, these studies did not correlate the development and severity of ROP. Consequently, differences among study results concerning low BWSDS as a risk factor for ROP may depend on the infants' GA at birth. Similarly, in our study also the postnatal weight gain was correlated with ROP. However, we have collected nutritional data to point out a particular nutrients function with the development of ROP. The highest number of preterm deliveries with burden of ROP was found in India compared to the other countries in the world [38]. Timely screening for ROP and proper treatments following the international guidelines could help in reducing the burden of ROP in India. However, the current study was conducted with a small sample size and thus may not represent all premature infants. Moreover, there was lack of nutritional data to correlate with ROP and severity. To find the proper screening, treatment, and method of screening and to know the exact incidence and risk factors involved for ROP, it is recommended to include larger sample size along with multicentric collaboration for the Indian geographic region.

CONCLUSION

The current study found a significant association of ROP with the GA, apnea, ventilation, surfactant, weight gain at different week follow-up, and TPN and age at full feed. Further, it can be concluded that there exists a correlation between the longitudinal postnatal weight gain pattern of preterm infants <32 weeks and the incidence of severe ROP. It can also be concluded that slowing postnatal weight gains is an independent predictor of the development of ROP and postnatal weight gain analysis can help to identify infants at high risk for developing treatable ROP, as well as identify those not at risk. However, studies with a larger

number of samples along with multicentric study will further confirm our results.

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