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Original Research Article

Baby weight gain parameters as predictive factors for progression of retinopathy of prematurity

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ABSTRACT

Purpose: To study whether postnatal weight gain pattern can be a predictor of severe ROP.
Materials and Methods: We conducted a prospective observational study**.** Birth weight and weight gain was recorded at 2 weeks,4 weeks and 6 weeks for all premature babies undergoing screening for ROP in our ROP clinic and NICU. The weight gain data was collected for those who developed any grade of ROP- these babies were followed up for spontaneous regression or given laser treatment for Type 1 ROP. Type 1 ROP which required treatment was termed as Severe ROP. The weight gain parameters analysed were absolute weight gain at 2,4 and 6 weeks and weight gain proportion
Results: We included 94 babies were included in the study. Out of 94, in 73 babies spontaneous ROP regressed was noted and 21 developed severe ROP. Mean birth weight in treated babies and non-treated babies were 909.29 ± 210.88 grams and 1107 ± 375.00 grams respectively. Absolute weight at 2,4 and 6 weeks were significantly low in severe ROP. Weight gain proportion at completed 2,4,6 weeks of life showed that at 4 weeks it was significantly (p 0.025) low in severe ROP. Weight gain per week at 4 and 6 weeks was low in Type I ROP babies (P 0.006 and 0.016 respectively)
Conclusion: In conclusion, this study found that postnatal weight gain is a significant factor that can predict the progression of ROP and those babies having a lower weight gain proportion in first 6 weeks should be followed up very closely for ROP progression.

1. Introduction

Retinopathy of prematurity (ROP) is vascular disorder of immature retina which is a significant contributor for worldwide childhood blindness.[1,2] With advancement in perinatal care, chances of survival of preterm babies have significantly improved, but so has the incidence of this condition.[3] This put additional burden on screening programs that traditionally rely on two major factors; (1) Gestational age (2) Birth weight.

Socio-economic status of population at risk has an impact on incidence of ROP. In developed countries, ROP occurs almost exclusively among most premature infants and the incidence of ROP is considerably lower than in developing countries. On the other hand, in developing countries like India the average birth weight and gestational age vary considerably, with very broad ranges.[4]

In literature, new screening models have come up suggesting that poor postnatal weight gain can be a good predictor of ROP. Premature birth is associated with depleted plasma concentrations of insulin-like growth factor (IGF1). Low circulating levels of this anabolic hormone and poor weight gain have been linked to the development of ROP and other diseases.[5,6] Postnatal weight gain can thus serve as a surrogate marker of IGF1 levels.[7] Some studies have reported correlation between severity of ROP and poor

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post natal weight gain by 4-6 weeks.

We have conducted this study to evaluate whether post-natal weight gain pattern can be a predictor of severe ROP in Indian population.

2. Aim

1. To study the relationship between postnatal weight gain parameters and development of severe ROP.
2. To develop a prediction model or cut-off value based on postnatal weight gain for prediction of development of severe ROP.

3. Materials and Methods

In our hospital all neonates who met the criteria for screening guidelines for Retinopathy of prematurity were screened for ROP[1] and their weight was recorded during the follow ups. Among the screened babies, those who developed any stage of ROP were included in our study. They were followed up weekly or two weekly depending upon the clinical findings. Those who progressed to Type I ROP (ETROP)[1] were given treatment.

Postnatal weight parameters recorded were:

1. Absolute weight measured at 2,4,6 weeks of life
2. Weight gain at 2,4,6 weeks of life
   Defined as: Baby's weight at completed 'x' weeks of life - birth weight.
3. Weight gain proportion measured at completed 2, 4, 6 weeks of life in relation to birth weight.
   It was calculated as: [baby's weight measured at 'x' weeks of life - the birth weight] / birth weight
4. Relative weight gain in gm/kg/day for each baby at 2, 4 and 6 weeks of post natal life.
   It was calculated as [weight at 'x' weeks - birth weight] / [birth weight (in kg) x chronological age (in days)]

These factors evaluated in each case to find out their relationship in progression of ROP.

Statistical analysis was performed using IBM SPSS version 20.0 software. Numerical variables were presented using mean and standard deviation. Independent sample t test was used to study the statistical significance of the comparison of all numerical risk factors between groups in the case of normality and Mann Whitney test in the case of non-normality. ROC curve was used to find an ideal cut-off for weight and relative weight gain with respect to severe ROP. Diagnostic measures such as sensitivity, specificity, PVP, PVN and Accuracy were calculated. A p value < 0.05 was considered to be statistically significant

4. Results

Of the 698 babies screened for ROP, 94 babies developed any stage of ROP and enrolled in the study. Among the 94 babies with Retinopathy of prematurity who were included in the study for analysis, 21 (22.3 %) babies progressed into Type I ROP (ETROP) and 73 (77.7%) regressed spontaneously without any treatment (Type II).

Our study group population consisted of 54 (57.4%) boy babies and 40 (42.6%) girl babies and the gestational age ranged from 23 weeks to 36 weeks with a mean of 29.34 (±2.76). Birth weight in all studied newborns ranged from 370 grams to 2270 grams, with a mean of 1063.29 grams (±354.02).

In our study incidence of ROP was found to be 13.4% among all the screened neonates (n=698) from which 10.4% resolved spontaneously and 3 % progressed to severe ROP.

Patients with ROP requiring treatment had significantly lower birth weight of 909.29 gm (±210.88, p=0.011) and gestational age of 27.29 (±2.41) weeks, p<0.001) compared with those spontaneously resolved. (Table 1)

Absolute weight measurements in severe ROP babies was 821.19 (± 204.14) at 2 weeks, 963.19 (± 239.85) at 4 weeks, 1179.3 (± 335.72) at 6 weeks. These were significantly low when compared with mild ROP babies (Table 2)

Weight gain at 2, 4, and 6 weeks were also calculated and we found weight gain at 4 weeks (p=0.006) and 6 weeks (p=0.016) had statistically significant difference between mild and severe ROP babies.(Table 2)

Weight gain proportion in relation with birth weight also calculated for 2, 4, and 6 weeks and at 4 weeks it showed a statistically significant (p=0.025) difference between those who resolved spontaneously and those who underwent treatment.(Table 2)

Relative weight gain in gm/kg/day was again calculated for these babies at 2,4 and 6 weeks and at 4 weeks it was very low among treated babies with a significant statistical difference .(p=0.025) (Table 2)

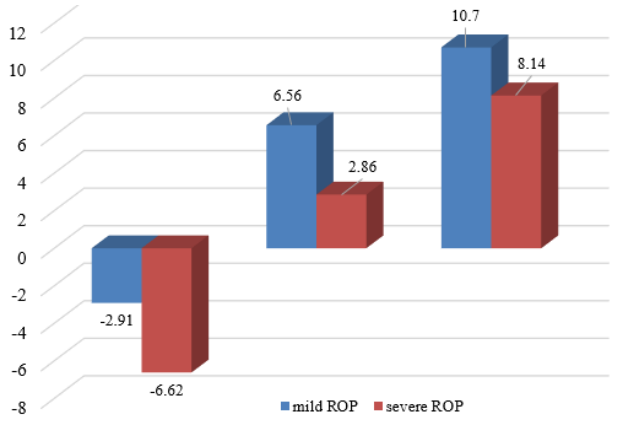

Fig. 1: Comparison of relative weight gain at 2,4 and 6 weeks among two groups

Receiver operating curve analysis was done with relative weight gain (gm/kg/day) and the area under the curve for

Table 1: Comparison of birth weight and gestational age among two groups

Risk factors	Mild ROP (n=73) Mean (SD)	Severe ROP (n=21) Mean (SD)	p value
Birth weight	1107.59 (375.00)	909.29 (210.88)	0.011
Gestational age	29.93 (2.53)	27.29 (2.42)	<0.001

Table 2: Comparison of all weight parameters in two groups

	Mild ROP (n=73)	Severe ROP (n=21)	p value
Weight at 2 weeks	1061.66 (± 365.36)	821.19 (± 204.14)	0.001
Weight at 4 weeks	1293.56 (± 1183.00)	963.19 (± 239.85)	<0.001
Weight at 6 weeks	1574.32 (± 550.04)	1179.3 (± 335.72)	<0.001
Weight at 40 completed weeks	2132.84 (± 659.54)	1179.3 (± 335.72)	0.476
Weight gain at 2 weeks	-45.93 (±86.14)	-88.09 (±90.05)	0.139
Weight gain at 4 weeks	186.00 (± 222.53)	53.90 (±194.9)	0.006
Weight gain at 6 weeks	466.73 (± 339.21)	270.00 (± 337.78)	0.016
Weight gain proportion at 2 weeks	-4.09 % (±.080)	-9.34 % (±.101)	0.070
Weight gain proportion at 4 weeks	18.3 %(±0.24)	8.01 % (±0.252)	0.025
Weight gain proportion at 6 weeks	44.9 % (±0.332)	34.2 % (±0.46)	0.076
Relative weight gain at 2 weeks	-2.91 (± 7.24)	-6.62 (± 5.78)	0.070
Relative weight gain at 4 weeks	6.56 (± 8.62)	2.86 (±9.00)	0.025
Relative weight gain at 6 weeks	10.70 (±7.93)	8.14 (±11.01)	0.076

relative weight gain at 4 weeks was 0.661 (95% confidence interval: 0.515-0.808, p=0.025). We selected a cut - off of 2.80 gm/kg/day weight gain to predict severe ROP and we found that 83.3 % of babies with a relative weight gain more than 2.8 gm/kg/day resolved spontaneously without taking any treatment while only 59.1% of babies with relative weight gain less than 2.8gm/kg/day resolved spontaneously and this was statistically significant with a p value of 0.17 and the Odds ratio corresponding to this was 0.321(Table 3).

Receiver operating curve analysis for weight at 4 and 6 weeks were done. Area under the curve was maximum for weight at 4 weeks (0.761, 95% confidence interval 0.651-0.871, p=0.000 and at 6 weeks it was 0.730 (95% CI 0.651-0.618, p = 0.01). So a cut off weight of 1010 gm at 4 weeks predict ROP progression to treatment requiring stage and we found only 6% of babies with a weight more than 1010gms at 4 weeks progressed to severe ROP while 39.5% of babies less than1010 gms progressed to severe/ treatment requiring ROP. This was statistically significant with a p value 0.001 and the Odds ratio corresponding to this was 0.184 (Table 3).

At 6 weeks we took the cut off value as 1302 gm to predict severity of ROP, and 86.8% of babies with a weight more than1302 gms at the end of 6 weeks of postnatal life resolved spontaneously without taking any treatment and only 65.9% of babies with weight <less than 1302gms resolved spontaneously. This was statistically significant with p value 0.016 and the Odds ratio corresponding to this was 0.293 (Table 3).

5. Discussion

Incidence of ROP varies widely depending on the population screened for ROP and ranges from 29% to 68% in developed country and 38-51% in India and incidence of ROP in our study was 13.4%.

Incidence of spontaneous regression of ROP was 86.6% in all babies screened. Among the babies with ROP included in our study 77.7% resolved spontaneously without any treatment. This was comparable with other studies.[2,3]

Gestational age and Birth weight were associated with the increased severity of ROP with a statistical significant p value.

Our study on 94 babies with ROP showed that in addition to birth weight, the postnatal weight gain pattern was different for babies with severe ROP and mild ROP and could be used as predictive factor for development of severe ROP. Several studies have looked into these parameters separately but we have analysed all the postnatal weight gain parameters to formulate a possible prediction model for severe ROP.

Wallace et al[4] in a multiple regression model showed that poor postnatal weight gain in the first six weeks of life is an independent risk factor for stage 3 or more ROP. Our study measured weight at 2, 4 and 6 weeks of postnatal life and we found weight gain at the end of 4 weeks and 6 weeks was very low in severe ROP babies, and was statistically significant.

Allegaert et al[5] in 2003 in a prospective case control study concluded that small for GA preterm newborns and those with intrauterine growth restriction had an increased risk of developing ROP threshold disease. Absolute weight gain at 2 weeks and 6 weeks were significant in their studies. In contrast, the relative WG (grams/kg/day) was

Table 3: Predictive cut-off values for weight parameters from ROC analysis.

Variable	Predictive cut-off value	Sensitivity	Specificity	Odds ratio
Relative weight gain	2.8 gm/kg/day	82.19%	42.86%	0.321
Weight at 4 weeks	1010 gm	68.49 %	71.43 %	0.184
Weight at 6 weeks	1302 gm	63.01%	66.67%	0.293

not significantly different in the group with ROP and in the control group. Our study calculated relative weight gain (gm/kg/day) for 2, 4 and 6 weeks and was found to be low at 4 weeks in babies who were treated and this showed a significant statistical result. Also, the absolute weight gain at 4 and 6 weeks was significantly different in the two groups in our study and statistically significant

Filho et al[6] through a prospective cohort study in 2008 showed that weight gain proportion lower than 51.2% according to the ROC curve, was an independent risk factor for severe ROP development. Weight gain proportion at 4 weeks was low in our severe ROP group and was statistically significant whereas at 6 weeks it was low in severe ROP babies, but was not significant statistically.

The comparison of these studies with our study is shown in Table 4.

We tried to get a cutoff predictive value for weight gain below which a baby would be high risk for severe ROP. Ayedimir et al[7] in 2011 in a prospective study analyzed the relative weight gain in ROP babies and revealed a cut off of 9.1g/kg/day weight gain in the first 4 weeks of life using ROC analysis. We found a cut off in our population as a weight gain less than at least 2.80 gm/kg/day by 4 weeks of postnatal life to have more chance of developing into severe or treatment requiring ROP, with a sensitivity and specificity of 61.6% and 61.9% respectively using ROC analysis.

Thus, the weight gain pattern over the first 6 weeks in a baby is a very good indicator of the severity of ROP the baby develops later. We can see this clearly in these graphs. This is the weight gain pattern of a baby with severe ROP comparing the mean birth weight of 909 gms with the expected weight gain of a preterm baby with almost the same birth weight.[8]

Here we can clearly see the poor weight gain of the severe ROP baby with mean birth weight of 909 gm when compared with the actual weight gain required for a preterm baby of same birth weight. In the initial 2 weeks there is a drop in weight but later the weight gain is increasing, but does not meet the required rate. On the other hand, the weight gain pattern over the first 6 weeks in a baby with mild ROP was recorded by comparing the mean birth weight of 1107 gms with the expected weight gain of a preterm baby with almost the same birth weight.[8]

Here we can see the babies with mild ROP shows low weight gain but maintains a parallel relation with expected growth rate, with uniform increase in weight over 6 weeks.

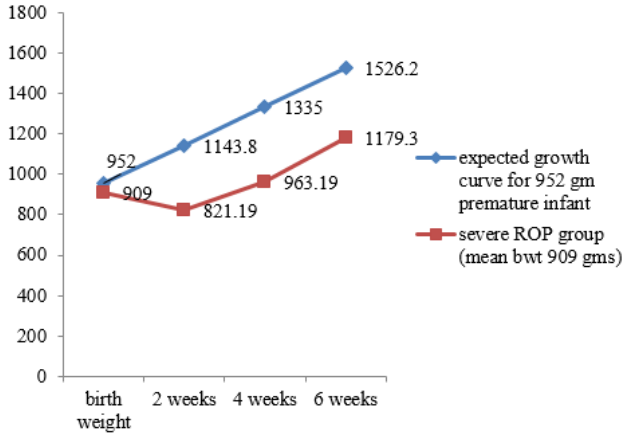

Fig. 2: Graph showing Weight gain in the first 6 weeks of life in infants with severe ROP compared with expected weight gain of a preterm baby with almost same birth weight.

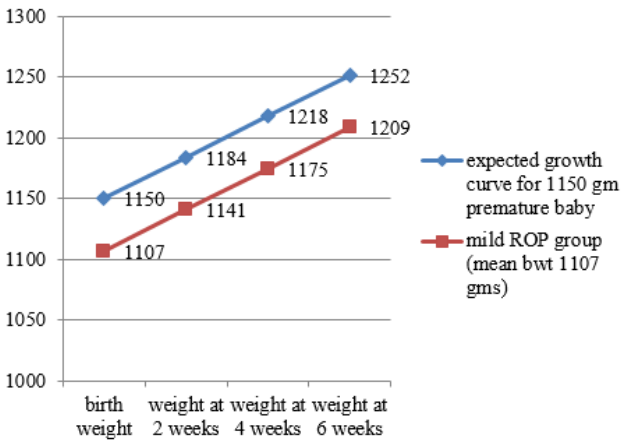

Fig. 3: Graph showing weight gain in the first 6 weeks of life in infants with mild ROP compared with expected weight gain of a preterm baby with almost same birth weight.

6. Conclusion

The main aim of our study was to find out the relationship of postnatal weight gain to the progression of ROP.

The incidence of ROP was found to be 13.4 % among all the screened neonates (n=698) from which 10.4% resolved spontaneously and 3 % progressed to severe ROP.

Birth weight and Gestational age was found to be very low in severe ROP babies demonstrating a statistical significance.

Table 4: Comparison of our study with other international studies

Studies	BW	GA	Absolute wt 2,4,6 weeks	Weight gain 2,4,6 weeks	Weight gain proportion 2,4,6 weeks	Relative weight gain 2,4,6 weeks	Sample size
Our study	Significant	Significant	2,4,6 weeks	4,6 weeks	4 weeks	4 weeks	94
Wallace et al	Significant	NS	NS	NS	NS	6 weeks	111
Allagaert et al	Significant	NS	2,4,6 weeks	4,6 weeks		NS	59
Filho et al	Significant	Significant	6 weeks	6 weeks	6 weeks	NS	317
O Aydemir et al	Significant	Significant				2,4 weeks	300
Rui Hong et al	Significant						56

Other antenatal and postnatal factors that were studied didn't show a statistical significance.

From our study we found that postnatal weight gain measured at 2 weekly intervals was significantly low in severe ROP babies.

Analysing the postnatal weight gain parameters we were able to find a cut off value above which, if the baby fails to attain, may results in progression into Type I or treatment requiring ROP.

That is, if the baby has a relative weight gain less than 2.80 gm/kg/day by 4 weeks they have more chance of developing severe or treatment requiring ROP.

Also if the baby has not attained a weight of at least 1010 gm by 4 weeks, they have high chance of progressing into severe ROP.

From this study we conclude that the postnatal weight gain is a significant risk factor for the development of severe ROP. This simple measurement can be used as a non-invasive tool for the Ophthalmologist and Neonatologist to predict the progression of ROP.

7. Source of Funding

None.

8. Conflict of interest

The authors declare that there are no potential conflicts of interest for the authorship and publication of the article.

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