

# Association of Head Circumference, Gestational Age and Birth Weight with Severity of Retinopathy of Prematurity



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## ABSTRACT

**Purpose:** To determine relationship between head circumference, gestational age and birth weight with stage of Retinopathy of Prematurity (ROP).

**Study Design:** Descriptive observational.

**Place and Duration of Study:** Jinnah Postgraduate Medical Centre (JPMC), Karachi from January 2022 to June 2022.

**Methods:** Infants born at or before 32 weeks of gestation, birth weight of less than or equal to 1500 grams at birth were enrolled. Their head circumference, gestational age and birth weight was measured. Fundoscopy was done to find out ROP. Staging of ROP was recorded four weeks after birth. The severity of ROP was correlated with head circumference, gestational age and birth weight.

**Results:** Of the 82 infants with ROP, 44 (54%) were male and 38 (46%) were female. Mean gestational age was  $30 \pm 1.4$  weeks (range 27 – 32 weeks), mean birth weight was  $1275 \pm 155$  gram (range 800 – 1500), and mean Fronto Occipital Circumference (FOC) was  $29 \pm 1.6$  cm (range 25 – 32 cm). Degree (stage) of ROP was as follows; 14 (17.1%) infants had stage 1 disease, 24 (29.3%) had stage 2 disease, 28 (34.1%) had stage 3 disease, 13 (15.9%) had stage 4 disease and 3 (3.7%) had stage 5 disease. There was statistically significant association of gestational age, birth weight and head circumference (FOC) with the degree of ROP ( $P < 0.001$ ).

**Conclusion:** Head circumference, gestational age and birth weight had a significant association with degree of ROP ( $P < 0.001$ ).

**Key Words:** Retinopathy of Prematurity, Head, Gestational Age, Birth Weight.

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## INTRODUCTION

ROP is a retinal vascular disorder caused by interruption of the normal vascular growth of retina in a premature infant, resulting in abnormal vessel formation and if not tackled in time can lead to

blindness.<sup>1</sup> Its incidence is on the rise, due to advancements in healthcare, translating to improved chances of survival in newborns, especially preterm births with low birth weight.<sup>2-5</sup> This along with extended oxygen supplementation, forms the triad of the most common risk factors associated with ROP.<sup>6</sup>

Due to improvements in neonatal intensive care unit (ICU) and a drop in infant mortality rate, ROP is on the rise in Pakistan.<sup>7</sup> According to a study from Pakistan, ROP was seen in 32% of premature ( $\leq 32$  weeks) and low birth weight ( $\leq 1500$ g) children.<sup>8</sup> Given this high frequency, it has become prudent for

us to increase surveillance for ROP, and to give pediatricians and neonatologists easily available tools to screen and refer these newborns to ophthalmologists to prevent blindness in premature infants.

In this study, we tried to find an association between the stage of ROP and head circumference, gestational age and birth weight. All these parameters can be easily measured by neonatologist and pediatricians, so that they can promptly refer such cases to ophthalmologists.

## METHODS

In this study, 82 neonates were enrolled. Institutional Review Board (IRB) of Jinnah Postgraduate Medical Centre (JPMC), Karachi approved the study (F.2-81/2022-GENL/1593/JMPC) and written informed consent was taken from the parents of the newborns. Infants born at or before 32 weeks of gestation and birth weight of 1500 grams or less at birth were included. Children with comorbidities that limited us in getting the measurements or conditions that might result in errors in measurement were excluded. For example; hydrocephalus, microcephaly or any conspicuous congenital anomaly.

Sample size was calculated using 'openepi' sample size calculator with 95% confidence interval and absolute precision of 10%. A sample of 82 infants (actual sample size 72) was taken with 10-15% extra due to non-compliance). Neonates born between January 1<sup>st</sup> 2022 and June 30<sup>th</sup> 2022 were screened. The birth weight of these neonates was taken on a standard weighing machine in grams along with their head circumference (Fronto Occipital Circumference or FOC) in centimeters by a trained neonatal nurse. These neonates were referred to department of Ophthalmology at JPMC where ophthalmic examination of these neonates was performed four weeks after birth. In cases where the neonates were too sick to be brought to the department of Ophthalmology, they are accessed via indirect ophthalmoscopy in the neonatal ICU. The neonates were examined according to a routine protocol that consisted of dilated fundus examination. After pupillary dilation with 1% Tropicamide, 0.5% Proparacaine was instilled to anesthetize the eyes and retina was examined with the help of indirect ophthalmoscopy. Effort was made to make the entire process as gentle and pain free as possible. The eyes were opened with an eye speculum and examination was performed using scleral indenter. Information

regarding the severity of ROP was noted according to the International Classification of Retinopathy of Prematurity (ICROP).<sup>9</sup>

Statistical software SPSS version 19.0 was used for data analysis. The results were presented in the form of mean  $\pm$  SD for quantitative/continuous variables i.e. gestational age, birth weight and FOC. Number/percentages were calculated for qualitative/categorical variables i.e. grouping gestation age, birth weight and FOC. Pearson's Chi-square test was used for association of qualitative variables with degree of Retinopathy of Prematurity (ROP). P-value of  $<0.05$  was considered significant.

## RESULTS

Out of 82 infants, 44 (54%) were male and 38 (46%) were female. Gestational age ranged from 27 to 32 weeks with mean of  $30 \pm 1.4$  weeks. Mean birth weight was  $1275 \pm 155$  grams (range 800 – 1500) and mean FOC was  $29 \pm 1.6$  cm, (range 25 – 32 cm). Degree or stage of ROP was as follows; 14 (17.1%) had stage 1 disease, 24 (29.3%) had stage 2 disease, 28 (34.1%) had stage 3 disease, 13 (15.9%) had stage 4 disease and 3 (3.7%) had stage 5 disease. There was significant association of gestational age (Pearson Chi-Square, value 79.8), birth weight (Pearson Chi-Square, value 64.3) and head circumference (FOC) (Pearson Chi-Square, value 59.3) with the degree of ROP (stage I,II,III,IV,V) ( $P < 0.001$ ). Table 1 shows details.

## DISCUSSION

ROP is increasing in frequency in Pakistan and with the increase in its frequency, the responsibility of the medical staff that come into contact with the newborn also increases. If not tackled in time, it can be disastrous and can lead to blindness and a lifelong handicap child. The pediatricians and neonatologists have the responsibility of making sure that children born with the risk factors of ROP be screened and immediately referred to ophthalmologists.<sup>10</sup>

There can a multitude of risk factors for ROP but we specifically chose gestational age, birth weight and head circumference as they can be easily measured in any hospital setup and require no special training or apparatus to record values. The results of our study showed a significant relationship between these three risk factors and the severity of ROP in neonates with P-value of  $<0.001$ .

**Table 1:** Shows the relationship of gestational age, birth weight and head circumference with the degree of ROP.

	No. of Subjects	Degree of ROP					P-value
		Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	
<b>Gestational age</b>							
27-28 Weeks	10	-	-	1 (10.0%)	6 (60.0%)	3 (30.0%)	0.001
29-30 Weeks	29	-	3 (10.3%)	19 (65.5%)	7 (24.1%)	-	
31-32 Weeks	43	14 (32.6%)	21 (48.8%)	8 (18.6%)	-	-	
<b>Birth weight</b>							
<1200 grams	21	-	1 (4.8%)	6 (28.6%)	11(52.4%)	3 (14.3%)	0.001
1200-1300 grams	31	2 (6.5%)	9 (29.0%)	18 (50.1%)	2 (6.5%)	-	
1400-1500 grams	30	12 (40.0%)	14 (46.7%)	4 (13.3%)	-	-	
<b>Head circumference (FOC)</b>							
≤28 cm	31	-	2 (6.5%)	14 (45.2%)	12 (38.7%)	3 (9.7%)	0.001
29-30 cm	34	4 (11.8%)	16 (47.1%)	13 (38.2%)	1 (2.9%)	-	
31-32 cm	17	10 (58.8%)	6 (35.3%)	1 (5.9%)	-	-	

Our results share similar findings with a study conducted by Anudeep et al., which showed a very strong correlation of gestational age and birth weight of neonates with the severity of ROP.<sup>11</sup> They concluded that birth weight of ≤1700g and gestational age of ≤32 weeks was associated with a higher chance of development of ROP. Similar results were seen in studies by Zarei et al,<sup>12</sup> but they had selected extremely low birth weight (≤1000 g) and extremely premature (≤28 weeks gestational age) neonates in their study.<sup>12</sup> The results were however similar to ours. The same could be said about studies conducted by Khorshidifar et al,<sup>13</sup> Bortea et al,<sup>14</sup> and Ying et al,<sup>15</sup> where the researchers concluded that ROP was associated with low birth weight and low gestational age at birth among other risk factors.

Chang et al. divided the risk factors in two groups, first group included risk factors involved in the development of ROP and the second group included risk factors associated with progression of ROP.<sup>16</sup> They found that gestational age was related to both development and progression of ROP. Caberry et al, published a very concise review of 18 studies spanning over a decade and came to the conclusion that for every week decrease in gestational age the odds of developing ROP were 1.4 times, which increased to 1.8 times for every 100g decrease in birth weight.<sup>17</sup>

Gao et al, considered a rather uncommon screening criteria.<sup>18</sup> They included children up to 37 weeks of gestational age and birth weight up to 2500g. They then divided them in two groups, the first group included children between 35 and 37 weeks of gestation and weighing between 1750g and 2500g and the second group included the remaining neonates (with gestational age less than 35 weeks and birth weight less than 1750g). They found out that risk of

ROP was similar in both groups. They reported that 40 percent of ROP (Type 1 ROP) would be missed if we continued following the current screening guidelines. This study definitely gives us a new perspective as far as screening criteria is concerned.

Head circumference is one parameter, which we were able to find in only a few studies. One such study was conducted by Lofqvist et al. in which the researchers tried to find if there was any significant relation between postnatal head circumference and degree of retinopathy of prematurity.<sup>19</sup> They found that in prematurely born infants (< 28 weeks) immediately after birth, head growth retards until 30 to 32 weeks of post menstrual age and this coincides with the suppression of retinal vascular growth which is directly related to development and severity of ROP. However, the study did mention that this direct relation was valid only until the post menstrual age of 31 weeks. If, at this age the head circumference of the child was 2.5 standard deviation below normal then there was increased risk of developing ROP (of at least stage 3) by five times as compared to their counterparts with a greater head circumference.

Poor postnatal growth has been linked to worse ROP outcomes as poor weight gain in the postnatal period adversely affects retinal vascular proliferation. This is evident from a study conducted by Ingolfsland et al. where the researchers included hospitalized neonates with gestational age of less than 32 weeks and birth weight of less than 1500g.<sup>20</sup> They found that in the second half of their hospitalization, increase in the general body mass of the neonates with fat and/or fat free mass and an increase in the body fat percentage was directly linked to decreased chances of development of ≥stage 2 ROP. According to Bae et al. who included more than 3000 neonates between the

gestational age of 24 and 28 weeks and birth weights of <1500g postulated that ROP, which required treatment was essentially associated with poor head growth (decreased FOC) in the post-natal period.<sup>21</sup> However, they explicitly mentioned that ROP, that needed to be treated, in these children was not linked to their birth weight.

Limitation of the study was that we included only small birth weight babies of less than 1500 grams. Other studies including greater birth weight can be conducted keeping in view the local criteria of screening.

## CONCLUSION

Our study shows that the risk factors namely, head circumference, gestational age and birth weight have a direct relationship with the stage of ROP.

**Conflict of Interest:** Authors declared no conflict of interest.

**Ethical Approval:** The study was approved by the Institutional review board/Ethical review board (F.2-81/2022-GENL/1593/JPMC).

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### Authors' Designation and Contribution

Saad Jan; Postgraduate Trainee: *Literature Search, Data Acquisition, Manuscript Preparation.*

Muhammad Ali Tahir; Consultant Ophthalmologist: *Manuscript Editing, Manuscript Review.*

Arifa Farooq Ghazipura; Vitreoretinal Fellow: *Data Analysis, Statistical Analysis.*

Aziz - ur - Rehman Arain; Consultant Ophthalmologist: *Design.*

Alyscia Cheema; Head of Department: *Concepts, final review.*

