



**ORIGINAL RESEARCH PAPER**

**Ophthalmology**

**ROLE OF ANTENATAL BETAMETHASONE IN PREMATURE BABIES AND ITS EFFECT ON RETINOPATHY OF PREMATURITY**

**KEY WORDS:** ROP, risk factors of ROP, Antenatal betamethasone.

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**ABSTRACT**

**Background:** advances in medical science has increase the overall survival rate of human being. this applies to neonates who born before their complete development in womb and their increased survival rate lead to increase occurrence rate of retinopathy of prematurity (ROP). In the struggle of their survival many measures done and one of which is injection of betamethasone to pregnant mother at the time of their premature delivery to develop their lungs and to reduce mortality.

**Materials and Methods:** this is a prospective observational study carried out for 12 months duration. Mother who has been given antenatal betamethasone were included after their consent. Total 54 infants  $\leq$  32 weeks gestation at birth and babies born at 32 to 34 weeks who were exposed to oxygen support in NICU and babies having birth weight  $<$  1750gms were screened at one month of post-natal age. Infants pupils were dilated with short acting standard drops and indirect ophthalmoscopic examination was done, the grading of eyes was being done using International classification of ROP (ICROP). Zone I and zone II with any stage is considered as severe ROP including plus disease. Data were analysed by t-test for quantitative data and 2 test for qualitative data.

**Results:** Out of 54 babies examined over one year, 23 were diagnosed with ROP (any stage) incidence was 42.59%. out of 23 babies stage I ROP was in 33.33%, stage II ROP in 3.70% and stage III in 5.55% and severe ROP that required treatment was 5.55%. Low birth weight was important risk factor .Low gestational age was also a significant risk factor of ROP (p 0.04). Gender was not found as a risk factor for ROP. All babies were prevented from sight threatening complication by timely screening and treatment. Antenatal betamethasone did not show any significant effect on ROP.

**INTRODUCTION:**

ROP is a potentially avoidable cause of total blindness in infants who are born premature. It is a major cause of blindness in children in middle-income countries . It gives lifelong impact to their parents with increasing economical burden and magnitude of blindness.

The control of blindness in children is given a high priority in INDIA as well as by the World Health Organization's (WHO's) VISION 2020 — The Right to Sight Program.<sup>1</sup> Retinopathy of prematurity (ROP) is a disease affecting the retina of infants born Its key pathologic change retinal neovascularization, has several features in common with the other proliferative retinopathies such as sickle cell retinopathy, diabetes mellitus and vascular occlusions. Each of these proliferative retinal vascular disorders appears to be associated with local ischemia and the subsequent development of neovascularization. AS advances in diagnosis and treatment occurs and premature infants are surviving at earlier gestational ages, ROP continues to be a significant problem. Retinopathy of prematurity (ROP) is an avoidable cause of blindness in children if timely screened. ROP occurs due to neovascularisation that occur sin retinal periphery leading to retinal detachment. Predisposing factors for the development of ROP are oxygen therapy, blood transfusion, sepsis and apnoea.

Antenatal steroids play a role in prevention of various comorbidities associated with prematurity like respiratory distress syndrome (RDS), intraventricular haemorrhage<sup>2</sup> but their effect on ROP is still not well defined. Some western studies have shown the effect of antenatal steroids to be protective for severe ROP forms<sup>3,4,5</sup>, but some failed to find any effect on ROP severity<sup>6,7</sup>

**Aims and objectives:**

**Aim:**

Aim of the study is to find effects of antenatal betamethasone

on ROP in Indian babies ( $<$ 32 weeks of gestation) .

**Objectives:**

- To know the incidence of ROP
- To evaluate the effect of antenatal betamethasone on ROP
- Disease burden of ROP at a tertiary care hospital.

**MATERIAL AND METHOD:**

After the ethical committee permission, a prospective observational study carried out for 12 months duration. (2015-2016). Mother who has been given antenatal betamethasone were included with their consent other criteria's for selection are as follows:

**Inclusion criteria**

- All premature new born babies ( $\leq$ 32 weeks of gestation) coming for ROP screening to Dept. of Ophthalmology.
- Low birth weight babies less than 1.750 kg. born at  $>$ 32 weeks of gestation
- All indoor premature babies irrespective of betamethasone given to mother who were given oxygen between 32-34 weeks.

**Exclusion criteria**

- Babies with media opacities (e.g. PHPV, retinoblastoma, congenital cataract, Corneal opacity) in whom retinal examination could not be possible
- Babies whose parents do not give consent to be included in the study.

In this study screening guidelines given by royal college of ophthalmology was followed as standard guideline for screening<sup>8</sup>

All the preterm babies were screened after one month of their birth ( $\leq$ 32 weeks) .Those who were less than 28 weeks and less than 1.2 kgs were screened 2 weeks of their birth.

Detailed history (birth weight, intrauterine period, manner of delivery, birth asphyxia, hospital stay, ventilator support, blood transfusion etc.) was taken and parents' consent was taken.

Babies were examined after pupillary dilatation using phenylephrine hydrochloride 5% and tropicamide 0.8% eye drops at age of 4 weeks after instilling a topical anaesthetic drop like Proparacaine (0.5%). The retina was examined by an indirect ophthalmoscopy using 20D lens by trained retinal surgeon. The ora serrata was visualised using scleral depression.

If patient were found to have ROP, they were followed up at 7 days or 15 days according to their location and extent till normal vascularization reaches the ora serrata and no signs of worsening. The patients with zone II with stage II or stage III ROP were given diode laser photocoagulation to prevent further progression.

**Classification use for grading of ROP: (ICROP)<sup>9</sup> (INTERNATIONALLY ACCEPTED TO GRADE ROP)**

**Zone I:** (Posterior pole or inner zone): The distance of zone I are defined as twice the disc fovea distance in all directions from the optic disc

**Zone II:** Extends from the edge of zone I peripherally to a point tangential to the nasal ora serrata.

**Zone III:** It is a residual temporal crescent of retina anterior to zone 2.

**Extent:** The extent of the disease is coded by the number of clock hours with ROP. The extent of the disease is further described as contiguous clock hours of ROP or non-contiguous clock hours.

**Staging:**

**Stage 1:** Demarcation line.

**Stage 2:** Ridge

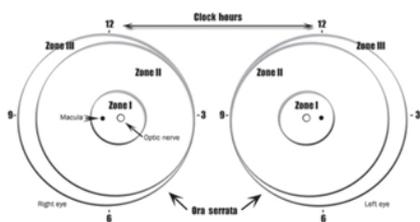
**Stage 3:** Ridge with extra- retinal fibro vascular Proliferation (Mild/Moderate/Severe)

**Stage 4:** Subtotal retinal detachment

A. Not involving macula

B. Involving macula

**Stage 5:** Total retinal detachment



**DISCUSSION AND RESULTS:**

In our study out of 54 premature babies examined 28 babies were male and 26 babies were females. ROP was found in 23 babies (any stage) out of which 13 were male and 10 were female babies. 18 cases were having zone III. Out of 54 babies 36 babies were born at less than 32 weeks of Gestational age and 18 babies were born between 32 to 34 weeks. Mean gestational age was 32.4 weeks with standard deviation of ± 1.38 and rate of occurrence of ROP was 42.59% which is near to other studies done by Charan et al.<sup>11</sup>

**Table 1. Incidence of ROP**

	No. of babies	Incidence
ROP diagnosed	23	42.59%
No ROP	31	
Total	54	

In India, with the development of neonatal care units, survival rate has increased. This premature babies are at risk of developing retinopathy of prematurity (ROP). Abdel HA et al.<sup>12</sup> did ROP prospective screening survey and also found that timely screening and periodic examination and early intervention prevent the sight loss.

**Table 2 Birth weight and incidence of ROP**

Birth weight	ROP diagnosed (any stage)	No ROP	Total	Incidence
≤1.25 kg	8	6	14	14.81%
1.26 to 1.5 kg	13	22	35	24.07%
>1.5 kg	2	5	7	3.70%

Here in our study p value is <0.01 that indicate that birth weight less than 1500 gms. is a risk factor for development of ROP. Here number of diagnosed ROP is highest in babies of birth weight 1.26 to 1.5 kg. This is because babies with birth weight less than 1.25 kg do not survive.

Charan et al.<sup>11</sup> conducted a study, to identify the occurrence of ROP in a prospective manner, they also found that babies with lower birth weights and lower gestation age at birth had a significantly higher incidence of ROP. Various studies done by Good WV, Hardy RJ et al.<sup>14</sup>, Ahmed MA, Duncan M, Kent A, et al.<sup>15</sup> and CRYO-ROP study<sup>13</sup> also shows the similar results.

**Table 3. Birth weight in severe ROP vs normal babies**

	No. of babies	Mean birth weight (kg)	SD
ROP babies who required treatment	3	1.01	0.338083
No ROP	31	1.44	0.257294

Here p value is 0.01090 that suggests lower birth weight increases risk and severity of ROP.

Out of 31 babies in No ROP group 15 were male and 16 females while in ROP group 13 male and 10 females and p value is 0.5541 that suggests there is no significant relation between gender and occurrence of ROP. Alajbegovic-Halimic, Jasmina et al.<sup>16</sup> also found no significance in gender. Lundgren P, Kistner A, Andersson EM et al.<sup>17</sup> concluded low birth weight and gender are main risk factor.

**Table 4. Gestational age and occurrence of ROP**

ROP (YES/NO)	No. of babies	MEAN GA (weeks)	SD
YES	23	32	1.705606
NO	31	32.77419	0.990275

Here p value is 0.0407 shows statistically noteworthy association with development of ROP and Low gestational age.

Alajbegovic-Halimic, Jasmina et al.<sup>18</sup>, Lundgren P, Kistner A, Andersson EM et al.<sup>19</sup>

Shah VA, Yeo CL, Ling YL, et al.<sup>20</sup>, Dhaliwal et al.<sup>21</sup> also showed that lower the gestational age higher the chances of ROP.

**Analysis of ROP zones and stages:**

In this study, maximum (87%) of ROP diagnosed were in zone III, 13% were in zone II and none of them was in zone I and maximum of ROP were in stage I(78%), 9% were in stage II and 13% were in stage III.



Ahmed MA, Duncan M, Kent A, et al.<sup>15</sup> reviewed low prevalence of ROP with birth weight more than 1250gms and gestational age more than 30 weeks. (2.0%).

Abdel HA et al.<sup>12</sup> also noted ROP in stage 1,2, and 3 with plus disease and also done laser ablation for stage 3 plus disease.

**Effect of antenatal betamethasone:**

Antenatal betamethasone was given 12 mg 12 hours apart in two doses to mothers

**Table 5. Comparison of Antenatal betamethasone and occurrence of ROP**

Antenatal betamethasone	No. Of babies	Babies developing ROP
Yes	27	11
No	27	12
Total	54	23

Here p value is 0.7832 that suggests no beneficial effect of antenatal betamethasone in ROP.

The National Institutes of Health (NIH) Consensus Development Conference recommends treatment regimens of two doses of 12 mg of betamethasone given intramuscularly 24 hours apart. As an alternate therapy four doses of 6 mg of dexamethasone given intramuscularly 12 hours apart between 24 and 34 weeks of gestation in pregnancies who are at risk for preterm delivery.<sup>22</sup> any of one can be chosen. (standard protocol)

Maini B, Chellani H et al.<sup>23</sup> showed that antenatal betamethasone show significance improvement in ROP severity, C Papagaroufalis, G Pollalis et al.<sup>24</sup> concluded antenatal betamethasone may directly reduce the incidence of severe ROP in VLBW infants, Chen-YuChen, Kuo-Gon Wang et al.<sup>25</sup> found no significant differences between antenatal betamethasone and dexamethasone.

**Table 6. Outcome of antenatal betamethasone on severity of ROP**

	No. of babies	Antenatal betamethasone given	Antenatal betamethasone not given
ROP babies who required treatment	3	2	1
No ROP	31	16	15

On analysis of effect of betamethasone p value is 0.9141 that suggests in this study that antenatal betamethasone was not beneficial against severe ROP. ROP diagnosed babies were followed up according to severity of ROP. 18 babies were called at 2 weeks and 13 were normal in first visit while 5 babies regresses at two weeks. 2 patients were called at weekly basis and turn to be normal after 3 weeks. among all diagnosed babies 3 babies require laser which shows complete regression in subsequent follow up. Preslan MW<sup>26</sup> also demonstrated regression after laser photocoagulation and preserved the sight.

In this study all diagnosed patients were savaged by timely screening and treatment. Mentioned The choice of treatment for ROP has shifted from cryo to diode laser photocoagulation. Few clinical studies showing that laser photocoagulation is superior to cryo.<sup>25,26,27,28.</sup>

**CONCLUSIONS: PREVENTION IS BETTER THAN CURE**

This study concludes that Low birth weight and low gestational age are acting as an individual risk factor . Antenatal betamethasone did not play any role in prevention and severity of ROP. More studies are recommended. Early detection by early screening and treatment of all premature babies prevent them from development of retinal detachment

and prevalence of potential childhood blindness.

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