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The Incidence, Risk Factors and Outcome of Retinopathy of Prematurity at a Tertiary Care Centre in South India

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Abstract: *Retinopathy of prematurity (ROP) is a retinal disease that principally affects preterm neonates. It is recognized as the leading cause of preventable blindness and visual impairment in paediatric population, the major brunt of the disease affecting relatively immature newborns. An increase in survival of very young preterm infants, due to the advances in neonatology, have subjected them to the risk of developing ROP.*
This study has been undertaken to determine the incidence of ROP, its association with various clinical and social risk factors and also to study the vasculogenesis and outcome of the ROP positive cases detected in the course of screening.

Materials and Methods: *94 preterm neonates with gestational age less than 36 completed weeks and weighing less than 2000 grams at birth, being born or admitted at Justice K. S. Hegde Charitable Hospital, Mangalore, were included in the study. Dilated fundus examination of these neonates was done at 31 weeks post conceptional age or 3 – 4 weeks chronological age, whichever is earlier. Follow up fundus examinations were carried out as per the fundus findings.*

Results: *Out of the 94 neonates screened, 12 cases (12.76%) had ROP; in which 6.38% were in stage 1 and 6.38% were in stage 2. 66.66% of the ROP positive cases were below 34 weeks gestational age. All the neonates weighing 1500 grams or less were found to develop ROP. Longer duration of hospital stay, higher duration of NICU stay, sepsis, hyperbilirubinemia, hypocalcemia, previous preterm delivery were some of the factors found to be significantly associated with ROP in this study. Max pO_2 with a mean of 97.4% in ROP positive cases was also found to be statistically significant.*

Conclusion: *Most of the positive cases were below 34 weeks of gestational age and weighed less than 1500grams at birth. Thus the need for a routine screening programme for the detection of Retinopathy of prematurity in preterm and sick neonates is indispensible in our clinical setting.*

Keywords: *Retinopathy of prematurity, ROP, Preterm neonates, low birth weight, gestational age.*

I. Introduction

Retinopathy of Prematurity (ROP) is a retinal disease that affects prematurely born neonates. Premature retina exposed to high oxygen concentration, followed by abrupt withdrawal, easily undergoes uncontrolled vasculo-fibrotic proliferation and eventually results in retinal detachment.[1,2] Complications of ROP, in the absence of retinal detachment, include myopia, strabismus, anisometropia, amblyopia, glaucoma and cataract.[3]

It is recognized as the leading cause of preventable blindness and visual impairment in paediatric population[1,5] especially its severe form affecting relatively immature infants[6] and infants weighing less than 1250 grams in developing countries.[5] Advances in neonatology have led to an increase in survival of very young premature infants and subjected them to the risk of developing ROP.[2,4] Thus, screening guidelines pose important legal and economic issues for the clinician.

A number of risk factors have been put forward as playing a role in development of ROP like multiple gestation, anemia, blood transfusion, oxygen administered, hyperbilirubinaemia, sepsis, respiratory distress syndrome, hyaline membrane disease, exchange transfusion, intraventricular haemorrhage and so on.[3,6,7] Early identification of risk factors and timely screening provides an opportunity for effective treatment. Various studies have been carried out previously on ROP. This study is being performed to assess the incidence of ROP, to establish its relationship between various risk factors and outcome in our clinical scenario. This study aims (i) To determine the incidence of ROP in neonates of gestational age less than 36 completed weeks; weighing less than 2000 grams at birth; (ii) To determine its association with various clinical and social risk factors; (iii) To study the vasculogenesis and assess the outcome of positive cases detected in the course of screening.

II. Materials And Methods

This study was conducted in the Department of Ophthalmology of Justice K.S. Hegde Charitable Hospital.Approval for the study protocol and clearance were obtained from the Ethical Review Committee of the institute. A total of 94 preterm neonates born or admitted in the hospital between October 2012 and September 2014 have been taken as subjects for the study. All neonates of gestational age less than 36 completed wks and birth weight less than 2000 grams were included in the study.

All preterm infants weighing less than 2000grams were examined at 31 weeks post-conceptional age or 3-4 weeks chronological age, whichever is earlier, by Indirect Ophthalmoscopy, after dilating the pupils using half strength of combination of tropicamide 1% and phenylephrine 5% eyedrops.A sterile lid speculum is inserted and fundus visualized with a 20D lens. Fundus examination is repeated every 2 weeks until vascularisation has progressed to zone 3 and the risk of ROP has passed. If ROP is present, fundus examination was done as and when required.All infants were followed up till their retinal vascularization was complete.

Statistical Methods:

Chi-Square test with Odds ratio for categorical data and Logistic Regression to determine the strength of association have been used in the study.

III. Results

The following were the results obtained for the **94** neonates that were screened:

Table 1: Incidence of ROP (out of 94 neonates screened):

	Number of ROP cases	Incidence (%)
Stage 1	6	6.38
Stage 2	4	4.26
Stage 2 Plus	2	2.12
Total	12	12.76

Table 2: Sex distribution:

	Male	Female
ROP +ve	6	6
ROP -ve	42	40

Table 3: Gestational age and ROP:

	GA 30-32weeks	GA 32-34weeks	GA 34-36weeks
ROP +ve	4	4	4
ROP -ve	6	36	40

Table 4: Birth weight (in grams) and ROP:

	750-1000	1001-1500	1501-2000
ROP +ve	2	8	2
ROP –ve	0	0	82
Total	2	8	84

Table 5: PIH and ROP:

	Present	Absent
ROP +ve	4	8
ROP –ve	22	60

$X^2 = 0.2213$, $p = 0.638$; not statistically significant

Table 6: Previous preterm delivery and ROP:

	Present	Absent
ROP +ve	2	10
ROP –ve	2	80

$X^2 = 5.201$, $p = 0.023$; **statistically significant**

Table 7: Hyaline Membrane Disease and ROP:

	Present	Absent
ROP +ve	4	8
ROP –ve	32	50

p value = 0.827, statistically not significant. Odds ratio: 1.154, **association likely**

Table 8: Sepsis and ROP:

	Present	Absent
ROP +ve	4	8
ROP –ve	36	46

p value = 0.489, statistically not significant. Odds ratio: 1.565, **association likely**

Table 9: Congenital pneumonia and ROP:

	Present	Absent
ROP +ve	4	8
ROP –ve	12	70

p value = 0.107, statistically not significant. Odds ratio: 0.343, association unlikely

Table 10: Feed intolerance/ Necrotizing enterocolitis and ROP:

NEC	Present	Absent
ROP +ve	2	10
ROP -ve	4	78

p value = 0.119, statistically not significant. Odds ratio: 0.256, association unlikely

Table 11: Hypoglycemia and ROP:

	Present	Absent
ROP +ve	6	6
ROP -ve	26	56

p value = 0.671, statistically not significant. Odds ratio: 0.766, association unlikely

Table 12: Hypocalcemia and ROP:

	Present	Absent
ROP +ve	4	8
ROP -ve	24	58

p value = 0.698, statistically not significant. Odds ratio: 1.316, **association likely**

Table 13: Hyperbilirubinemia and ROP:

	Present	Absent
ROP +ve	8	4
ROP -ve	66	16

p value = 0.736, statistically not significant. Odds ratio: 1.275, **association likely**

Table 14: Thrombocytopenia and ROP:

	Present	Absent
ROP +ve	4	8
ROP –ve	18	64

p value = 0.384, statistically not significant. Odds ratio: 0.563; association unlikely

Table 15: Oxygen supplemement and ROP:

	Given	Not given
ROP +ve	10	2
ROP –ve	74	8

p value = 0.095, not statistically significant

Table 16: Phototherapy and ROP:

	Given	Not given
ROP +ve	8	4
ROP –ve	66	16

p value = 0.581, not statistically significant. Odds ratio: 1.489; **association likely**

Table 17: Blood transfusion and ROP:

	Given	Not given
ROP +ve	2	10
ROP -ve	6	76

p value = 0.278, not statistically significant

Table 18: Group statistics:

GROUP		N	Mean	SD	t
Duration of stay (d)	ROP + ROP –	12 82	24.000 17.037	11.732 7.862	2.676 p=0.009
Gestational age	ROP + ROP –	12 82	33.783 34.172	1.415 1.228	1.004 p= 0.136
Birth weight	ROP + ROP –	12 82	1443.333 1759.756	365.795 203.470	4.470 p<0.01
NICU Stay (d)	ROP + ROP –	12 82	18.583 10.207	15.353 5.590	3.631 p<0.01
Maternal age (yrs)	ROP + ROP –	12 82	29.167 29.073	3.243 5.003	0.063 p=0.95
Max pO_2	ROP + ROP –	12 82	97.429 99.212	3.780 1.152	2.685 **p=0.01**
Oxygen supplement (d)	ROP + ROP –	12 82	9.300 10.530	3.529 5.139	0.729 p=0.468

p value <0.05 is significant

Fig.1: Incidence Of Rop

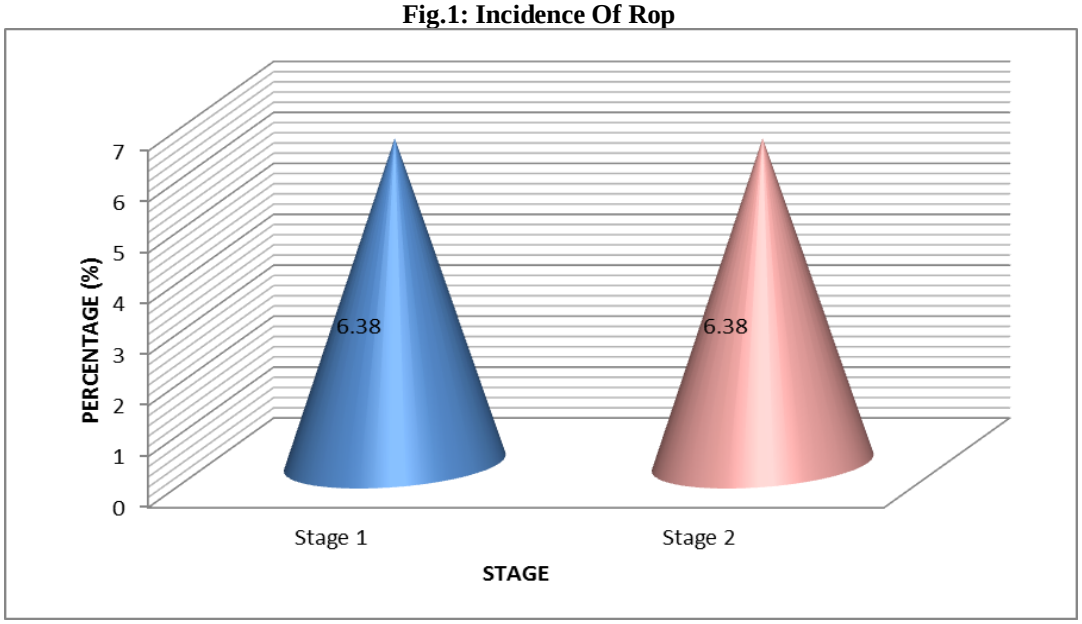


Fig.2: Gestational Age And Rop

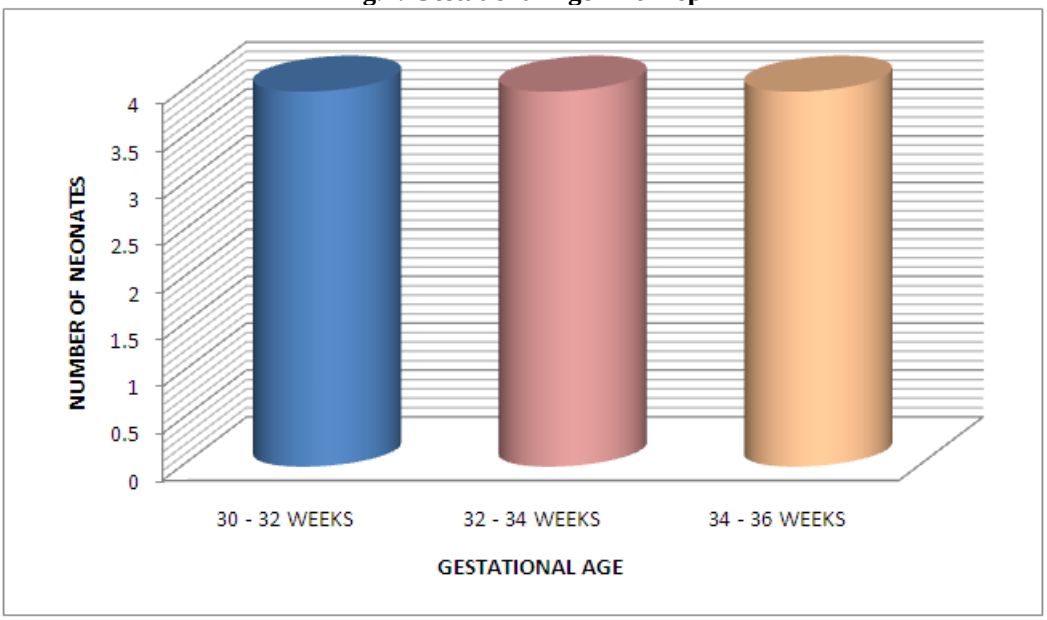


Fig.3: Birth Weight And Rop

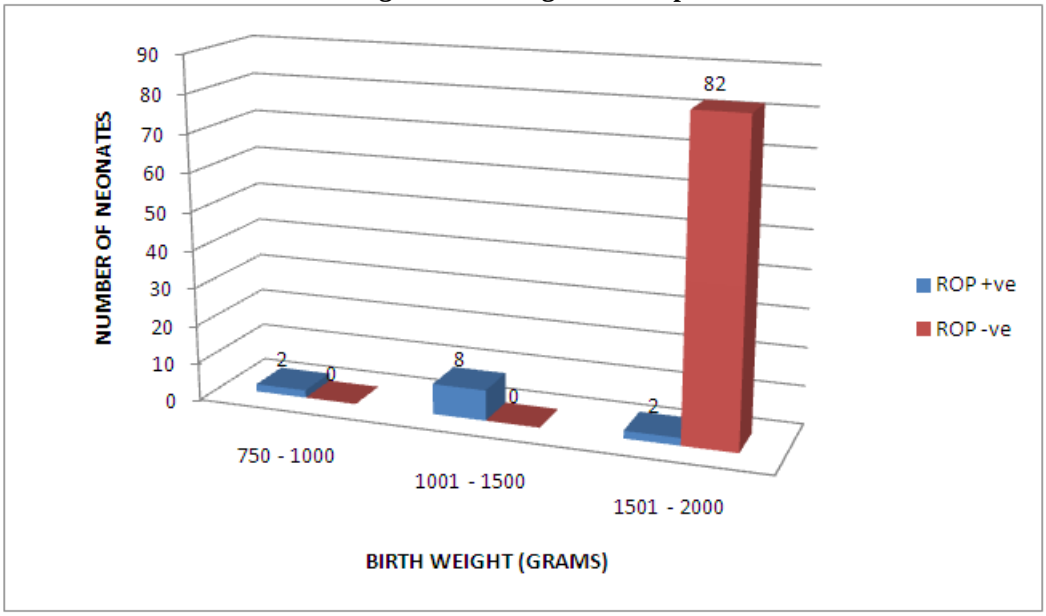
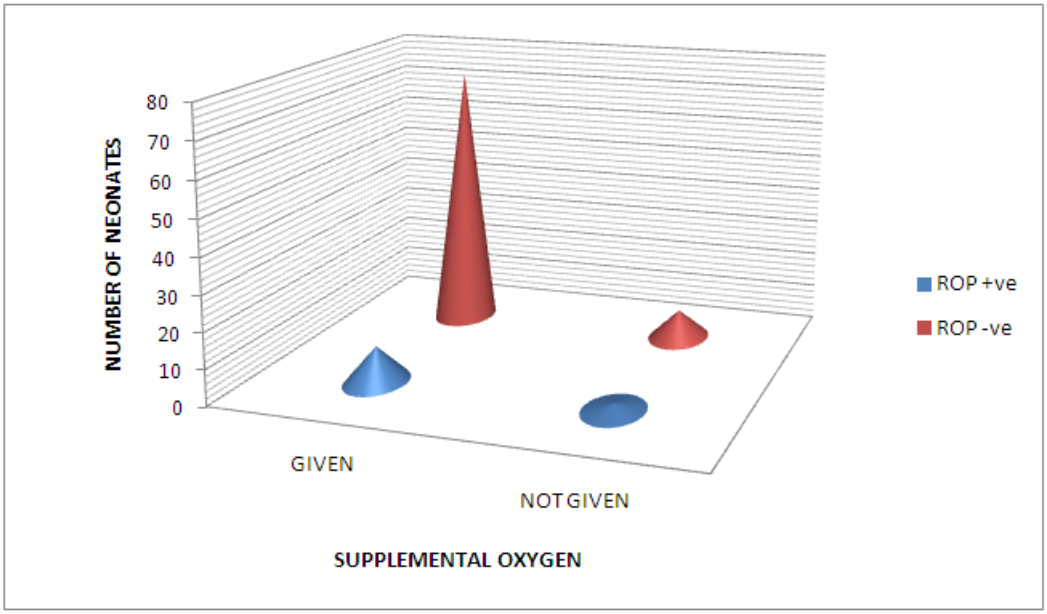


Fig.4: Supplemental Oxygen And Rop



IV. Discussion

Out of the 94 neonates screened, 46 were male (48.9%) and 48 were female (51.1%). Among the neonates who developed ROP, 6 were male (50%) and 6 were female (50%). No statistically significant correlation could be found.

The total incidence of ROP was found to be 12.76%. Out of the 12 neonates with ROP, 50% of the cases i.e., 6 were in stage 1 and 6 were in stage 2 of the disease, each accounting for 6.38% of the total cases screened. 2 of the Stage 2 cases had Plus disease.

In stage 1, 33.33% of the cases regressed spontaneously and 66.66% were lost to follow up. Whereas out of the stage 2 cases, two of which had Plus disease, accounting for 33.33%, were treated and 33.33% underwent spontaneous regression. The rest were lost to follow up. Thus, about one third of the cases who were followed up were found to have resolved spontaneously.

Of the 10 neonates that fell in the 30 – 32 weeks gestational age group, 40 neonates in the 32 – 34 weeks GA group and 44 in 34 – 36 weeks GA group, 4 (4.26%) neonates in each group had ROP. It was seen that the relative percentage of neonates who had ROP was higher in the younger age group, being 40% in the 30 – 32 weeks GA group, 10% in the 32 – 34 weeks GA group and 9.09% in the 34 – 36 weeks GA group. In a

report[84] on the current incidence of ROP in neonates (22-36 weeks GA), the incidence was found to be 21.3% for any stage and 4.6% for stage 3 ROP or greater and no ROP was noted in infants more than 32 weeks GA. The lower incidence of ROP in our study is probably due to the higher gestational age group of neonates screened. Low birth weight is one of the major risk factors for the development of ROP. In our study, out of the 94 neonates screened, all the neonates with birth weight less than 1500 grams, and 2 out of the 84 neonates weighing between 1501 and 2000 grams developed ROP. A statistically significant correlation was found between ROP and birth weight in our study on performing the chi square test. Majority of the cases weighed between 1000 to 1500 grams at birth. The percentage of neonates having ROP in the gestational age group of 30-32 weeks is 40%, in 32-34 weeks is 10% and in 34-36 weeks is 9.09%.

Also, the multicenter trial of cryotherapy showed that lower the birth weight, greater the risk of developing ROP, especially birth weights less than 750 grams.

Several other factors associated with ROP like supplemental oxygen, apnoea, hyaline membrane disease, septicemia, anemia, respiratory distress syndrome, hypoxic ischemic encephalopathy, hemolytic disease of the newborn, hyperbilirubinemia, phototherapy, hypoglycemia polycythemia, thrombocytopenia, maternal risk factors like pregnancy induced hypertension (PIH), diabetes mellitus, anaemia, heart disease, infections and so on were also considered in the study. Factors that were found to have a likely association with ROP are sepsis, hypocalcemia, hyperbilirubinemia, previous preterm delivery and MaxpO_2.

The average duration of hospital stay in ROP cases was 24 days, compared to 17 days in ROP negative cases, which was statistically significant. Similarly the length of stay in NICU was also statistically significant, the mean being 18.5 days in ROP cases. Low birth weight was another factor that showed positive association with ROP. Max pO_2 with a mean of 97.4% in ROP positive cases was also found to be statistically significant. None of the other above mentioned factors showed any statistically significant correlation with the development of ROP. Out of the 12 ROP positive cases, 4 neonates were one of the twins from multiple pregnancies. Two of the neonates were initially stage 0 and subsequently found to have developed stage 1 ROP on first follow up visit of 2 weeks. Both the cases were lost to follow up thereafter. The other 2 neonates were in stage 2 on first screening examination, both weighing less than 900 grams at birth. Follow up examination of both cases were done after 1 week. The cases failed to come for subsequent examination as per advice and were reviewed only after about 8 weeks time. But, the ROP regressed in both cases and retina was fully vascularized.

2 of the cases weighing less than 1500 grams at birth were found in stage 1 and on follow up screening 2 weeks later, they were found to be in stage 2 ROP. Both the cases were lost to follow up.

2 neonates with birth weight below 2000 grams with stage 0 on initial examination, were found to have developed stage 1 ROP during follow up after 2 weeks. The cases were lost to follow up. Another 2 cases weighing below 2000 grams at birth were found in stage 1 and subsequently the ROP regressed in 2 weeks duration, as seen on their first follow up.

2 cases with birth weight of 1500 grams with incomplete retinal vascularization and mild congestion on initial screening, showed stage 2 Plus ROP on their first follow up after 1 week. The cases were referred outside for indirect ophthalmoscope laser photocoagulation. The cases were subsequently followed up weekly for 2 weeks and then after 3 months. Confluent laser marks were seen, with no further disease progress.

4 of the neonates without ROP showed single, small, superficial retinal hemorrhage in zone 2 of one eye. The hemorrhages resolved on subsequent follow up.

A major drawback of our study is that many of the patients were lost to follow up, of which, many had incompletely vascularized retina. There is a possibility that these neonates might develop ROP in case normal complete retinal vascularization does not take place. This could be one of the reasons of low incidence of ROP in our study. Another point to be noted is that there is no standard means of accurately measuring the amount of oxygen that is administered to the neonates. Though in this study a positive correlation has not been found between oxygen supplementation and ROP, a precise method of assessing the amount of oxygen exposure would be of help for further study. Another limitation of the study is that we have included only the neonates fulfilling both criteria of gestational age below 36 weeks and 2000 grams. By doing this, we might have missed a few cases of low birth weight term infants who could be susceptible to development of ROP.

V. Conclusion

A greater risk of developing ROP was seen in neonates with birth weight of less than 1500 grams. Longer duration of hospital stay, higher duration of NICU stay, sepsis, hyperbilirubinemia, hypocalcemia, previous preterm delivery were some of the other factors we found to be significantly associated with ROP in our study.

Thus, the need for a routine screening programme for the detection of Retinopathy of prematurity in preterm and sick neonates is indispensible in our clinical setting. This also brings to light the need for parental education about the need for a regular follow up involving a simple, non-invasive examination which will enable timely detection and save the child's vision.

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References

[1]. Stephen J Ryan. Retina. 4th edition 2006
[2]. Charan R, Dogra M R, Gupta A, Narang A. The incidence of retinopathy of prematurity in a neonatal care unit. Indian J Ophthalmol 1995;43:123-6
[3]. Jalali S, Anand R, Kumar H, Dogra MR, Azad R, Gopal L. Programme planning and screening strategy in Retinopathy of prematurity. Indian J Ophthalmol 2003; 51:89-99
[4]. Gopal L, Sharma T, Ramachandran S, Shanmugasundaram R, Asha V. Retinopathy of prematurity: A study. Indian J Ophthalmol 1995;43:59-61
[5]. Vinekar A, Dogra MR, Sangtam T, Narang A, Gupta A. Retinopathy of prematurity in Asian Indian babies weighing greater than 1250 grams at birth: Ten year data from a tertiary care centre in a developing country. Indian J Ophthalmol 2007;55:331-6
[6]. R Karkhaneh, S Z Mousavi, M Riazi-Esfahani, S AEbrahimzadeh, R Roohipoor, M Kadivar, L Ghalichi, S F Mohammadi, M R Mansouri. Incidence and risk factors of retinopathy of prematurity in a tertiary eye hospital in Tehran. Br J Ophthalmol 2008;92:1446-1449
[7]. Krishna A Rao, JayashreePurkayastha, ManaliHazarika, Raghuvamsi Chaitra, K MithunAdith. Analysis of prenatal and postnatal risk factors of retinopathy of prematurity in a tertiary care hospital in South India. Indian J Ophthalmol 2007; 55: 329-330
[8]. Campbell K. Intensive oxygen therapy as a possible cause of retrolental fibroplasias. Med J Aust 1951; 2: 48-50
[9]. EM Lad, TC Nguyen, JM Morton, DM Moshfeghi. Retinopathy of prematurity in the United States. Br J Ophthalmol2008;92:320-325
[10]. Muhammed, Jafri WH, Nizami AM, Shomrani AI, Al-Dabaan A, Rashid K. Retinopathy of prematurity: Are we missing any infants with retinopathy of prematurity. Br J Ophthalmol2012;96:1052-1055
[11]. Austeng D, Kallen KBM, Ewald UW, WallinA, Holmstrom GE. Treatment for retinopathy of prematurity in infants born before 27 weeks of gestation in Sweden. Br J Ophthalmol 2010;94:1136-1139
[12]. Gopal L,SharmaT,Ramachandran S et al.Retinopathy of Prematurity-a study .Ind J Ophthalmol 43:59-62,199
[13]. Ashton N:1970;Retinal angiogenesis in the human embryo"Br.Med Bull 1970,26:103-106
[14]. Ashton N et al:effect of oxygen on developing retinal vesssels with particular reference to the problem of retrolental fibroplasias.Br J Ophthal 38:397-432,1954
[15]. Axer-SiegalR,SnirM,MalayanA,etal.Retinopathy of Prematurity and Surfactant treatment ,J PaediatrOphthalmol Strabismus 1996,33:171-4
[16]. Tasman W. Late complications of retrolental fibroplasias. Ophthalmology 1979; 86: 1724-1740
[17]. Flynn JT, Bancalari E et al: Retinopathy of prematurity. Diagnosis, severity and natural history. Ophthalmology 1987: 94: 620-9
[18]. Paysse EA, Lindsey JL, Coats DK, Contant CF Jr.,Steinkuller PG: Therapeutic outcomes of cryotherapy versus transpupillary diode laser photocoagulation for threshold retinopathy of prematurity. J AAPOS 1999 Aug; 3;4: 234-40
[19]. Maguire AM, Trese MT: Lens sparing vitreoretinal surgery in infants. Arch Ophthalmol 110: 284, 1992
[20]. Ashton N,WardB,SerpellG.Role of oxygen in the genesis of retrolentalfibroplasias.Apreliminary report. Br J Ophthalmol 1953;37:513-20
[21]. MaheshwariR,KumarH,PaulVK,SinghM,DeoraAK,TiwariHK.Incidence and risk factors of retinopathy of prematurity in a tertiary care newborn unit in New Delhi Natl.Med J India 1996;Sep-Oct:9(5):211-4
[22]. Yanovitch TL, Siatkowski RM, McCaffree MA, Corff KE. Retinopathy of prematurity in infants with birth weight more than 1250 grams-Incidence, severity and screening guideline cost-analysis. J AAPOS 2006;10:128-34
[23]. Vedantham V. Retinopathy of prematurity screening in the Indian population: It's time to set out own guidelines!. Indian J Ophthalmol 2007 sep oct;55(5)
[24]. Jalali S, Anand R, Kumar H, Dogra MR, Azad RV, Gopal L. Programme planning and screening strategy in retinopathy of prematurity. Indian J Ophthalmol 2003;51: 89-99
[25]. Fatih MM, Serdar US. Treatment of retinopathy of prematurity: a review of conventional and promising new therapeutic options. Int J Ophthalmol 2013;6(2):228-236.