Prospective Study on Prevalence of Retinopathy of Prematurity in Ganjam District

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ABSTRACT

BACKGROUND

Retinopathy of prematurity (ROP) also known as retrolental fibroplasia is a vasoproliferative retinopathy which affects the retinal blood vessels in developing state. ROP is one of the major causes of preventable blindness in children. It usually occurs in very low birth weight premature infants. Its presentation varies from complete regression in some, to leaving long term sequelae in others. Our aim was to find the prevalence of ROP in Ganjam district, Odisha.

METHODS

A prospective study was undertaken in M.K.C.G. Medical College and Hospital along with Christian Hospital and City Hospital, Berhampur, from 01/10/2016 to 30/09/2018. Babies fulfilling the inclusion criteria were screened after 3rd week of life or post-conceptional age of 31 - 33 weeks whichever was at a later date, and followed till 45 weeks of gestation according to stage. The babies were screened by indirect ophthalmoscopy and 28 D lens with the help of infant speculum and scleral depressor after instilling topical anaesthetic 2 % proparacaine. The pupil was dilated with 0.4 % tropicamide and 2.5 % phenylephrine. Analysis of qualitative data was done by chi-square test.

RESULTS

Out of 123 babies examined, 26 were lost to follow up and 19 out of 97 babies (19.58 %) developed ROP (inclusive of all stages). Low birth weight, low gestational age, duration of oxygen exposure > 2 days, exchange transfusion, septicaemia with positive CRP value were found to be significant risk factors in development of ROP. Hyperbilirubinemia, gender and multiple gestation were found to be insignificant in the development of ROP.

CONCLUSIONS

Timely screening, regular follow-up, early detection and intervention are the best ways to reduce the prevalence of ROP. Neonatal intensive care unit (NICU) should follow strict guidelines for screening of new-borns. Proper counselling and motivation of parents for regular screening of at-risk infants are the need of the hour.

KEYWORDS

Retinopathy of Prematurity, Low Birth Weight, Low Gestational Age, Oxygen Exposure, Exchange Transfusion

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BACKGROUND

Retinopathy of prematurity also known as retrolental fibroplasia is a vasoproliferative retinopathy that affects developing retinal blood vessels in very low birth weight premature infants (< 1500 gms).[1] It was first described by Terry in 1942. Campbell first theorised the relation of ROP to introduction of oxygen in the newborn. This was confirmed by Patz. Premature retina exposed to high concentration of oxygen, followed by abrupt withdrawal, easily undergoes uncontrolled vasculo-fibrotic proliferation and eventually results in retinal detachment.[2] It begins to develop between 32 to 34 weeks after conception, regardless of gestational age at delivery and has two distinct phases.[3] During the first acute phase, the normal vasculogenesis of the retina is disturbed by the relative hyperoxia of the extrauterine environment. This causes vaso-obliteration and non-vascularisation of some areas of anterior retina.[4] The subsequent hypoxia causes a second chronic phase, characterised by the proliferation of vascular and glial cells, arteriovenous shunt formation, occasionally leading to involution or permanent cicatricial changes and visual impairment.[5,6] The key pathological change is local ischemia with subsequent peripheral retinal neovascularisation. This may regress completely or leave sequelae like myopia, strabismus, anisometropia, amblyopia, glaucoma and cataract.[7] Visual impairment or blindness can be caused due to severe forms. It can affect normal motor, language, conceptual and social development of the child. It can also cause financial burden to society in advanced stages.

Today it is well known that along with oxygen therapy many other risk factors play a causative role in the pathogenesis of ROP.[8,9] Other causes are multiple gestation, anaemia requiring blood transfusion, sepsis, hyperbilirubinemia, hyaline membrane disease, respiratory distress syndrome, exchange transfusion, intraventricular haemorrhage etc.[7,10,11]

In India with the development of neonatal intensive care units, premature infants with extremely low birth weights are surviving and are at highest risk of developing ROP.[12] Timing is one important factor that makes the treatment successful in ROP, because the disease can advance very quickly and delayed treatment reduces the chances of success.[13] As there are very few studies on the prevalence of retinopathy of prematurity in Orissa, this study was performed to study the prevalence and risk factors for ROP so that these data will help to plan strategies to prevent blindness as a result of ROP.

METHODS

A prospective cross-sectional observational study was done in the Department of Ophthalmology, Maharaja Krishna Chandra Gajapati Medical College and Hospital, Berhampur, along with Christian Hospital and City Hospital from October 2016 to September 2018. Neonates born at or before 34 weeks of gestation, birth weight ≤ 1750 gms admitted in neonatal intensive care unit were included in the study along with neonates born after 34 weeks' gestation or birth weights between 1.751 Kg & 2 Kg if they had any unstable neonatal course with risk factors like ventilation, oxygen requirement, use of surfactant, septicaemia, hyperbilirubinemia, intraventricular haemorrhage, patent ductus arteriosus, exchange transfusion, apnoea and use of blood products or after paediatrician's advice. Neonates > 34 weeks of gestation with a stable neonatal course, children with major congenital malformation, chromosomal aberration and any fatal disease were excluded from the study. Infants who were having unilateral or bilateral retinal or choroidal disease (excluding ROP) or media opacity obstructing the fundal view or those infants who were highly dependent on oxygen and could not be removed from the incubator for examination were also excluded from study.

The hospital ethical committee provided the ethical clearance. Parents were informed about the study and their consent was taken. History of all enrolled neonates was taken which included a detailed birth history, number of days of oxygen exposure, any significant positive investigations (C reactive protein), history of any blood transfusion, hyperbilirubinemia etc. Unstable neonates were screened in neonatal care unit & stable / discharged infants were screened in the outpatient department of ophthalmology.

The examination of the infants was done by indirect ophthalmoscopy with scleral indentation with the help of infant speculum and a 28 D lens. The infant was well clothed and wrapped and was fed and burped an hour before evaluation. A quick flashlight examination of the adnexa and anterior segment was done before instilling the dilating drops.

Drops used for dilation included 0.4 % tropicamide and 2.5 % phenylephrine. The dilating drops were freshly prepared by diluting the available adult dosage drops with tear substitute. Two or three instillations of each of these drops, five minutes apart were usually sufficient to dilate pupils in 10 – 15 minutes. Spilled eye drops were cleaned. One drop of local anaesthetic 0.5 % proparacaine was instilled just before the examination.

The first screening was done between 21 – 30 days after birth or at post-conceptional age of 31 - 33 weeks whichever was found to be at a later date. ROP was graded into stages and zones as per the International Classification for ROP. Follow up was done as per the findings of first examination. If the initial examination showed no changes of ROP, the infant was followed up at an interval of 2 – 3 weeks until the vessels reached the ora serrata or till 45 weeks of gestation. If changes of ROP were noted on initial examination the infant was followed up according to the severity of ROP.

Data was collected in proforma which included name and age of mother, gestational age, birth weight and gender of infant, mode of delivery and place of delivery, delivery was eventful / uneventful, twin / singleton pregnancy, number of days in NICU and reason for stay in NICU, duration of oxygen given, significant positive finding like C-reactive protein (CRP), hyperbilirubinemia, sepsis, exchange transfusion, administration of antibiotic, date of 1st, 2nd, 3rd screening of ROP and their finding and post-conceptional age at the time of screening.

Inclusion Criteria

Babies born ≤ 34 weeks of gestational age and or birth weight ≤ 1750 gms weight, preterm infants with birth weights between 1.750 gms - 2 Kg or gestational age 34 - 36 weeks with risk factors.

Exclusion Criteria

Children with major congenital anomaly with suspected chromosomal aberration, any other retinal or choroidal disease, media opacity obstructing fundal view, refusal of consent by parents / guardian

Statistical Analysis

Numerical data like birth weight, gestational age at birth etc. were presented as mean scores and chi-square test was used to evaluate the statistical significance of the risk factors between two groups. Entire data was calculated on 95 % CI. A P value < 0.05 was considered significant.

RESULTS

A total of 123 infants who satisfied the inclusion criteria were enrolled in our study. Initial and follow up screening was conducted. However, only 97 infants could be followed up and completed the study. 26 infants were lost to follow up. Thus, our study showed a drop-out rate of 21.14 %.

The weight of infants studied ranged from 850 – 1980 gms with a mean weight of 1430.93 gms with a SD of ± 270.26 gms. Among the 97 infants enrolled 9 (9.3 %) were ≤ 1000 gms, 73 (75.25 %) were between 1000 – 1750 gms and 15 (15.46 %) were > 1750 gms. The gestational age of infants studied had a range from 26 – 36 weeks. The mean of the gestational age was 31.89 weeks with a standard deviation of 2.46 weeks. Among the 97 infants studied 29 (29.9 %) were ≤ 30 weeks, 54 (55.67 %) were between 30 – 34 weeks and 14 (14.43 %) were > 34 weeks.

Out of 97 infants who were studied, 19 infants were reported with some stage of ROP after the completion of the study. Our study thus reported the prevalence of ROP to be 19.58 %. Among these 19 infants, 2 (10.52 %) were in stage 2 ROP, 1 (5.26 %) in stage 3 ROP, 1 (5.26 %) was in stage 4 ROP, 15 (78.94 %) were in regressing stage.

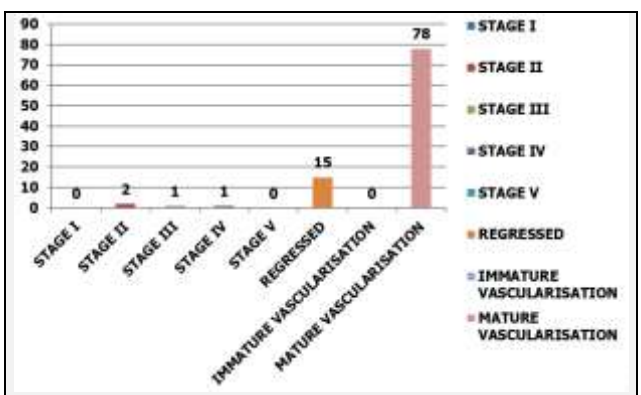

Figure 1. Prevalence of ROP

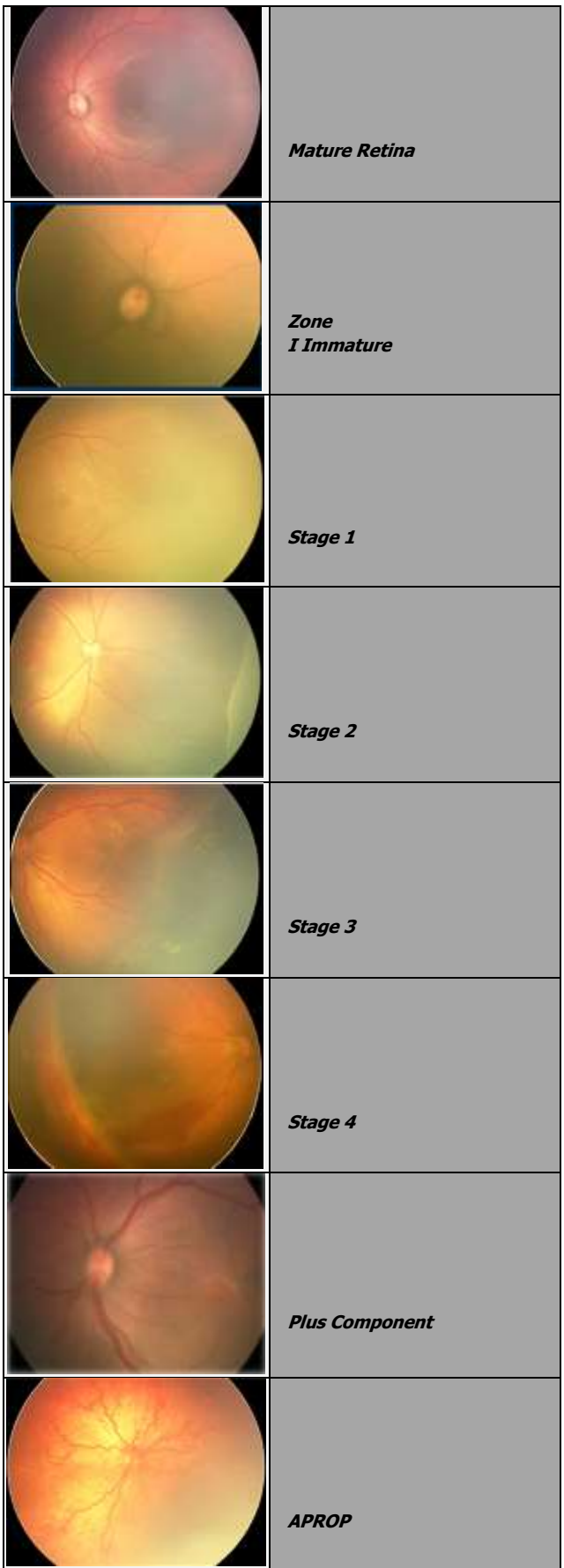

Figure 2. Fundus Changes in ROP

In our study all the 19 (100 %) infants who developed ROP had the birth weight ≤ 1750 gms as compared to 63 of 78 (80.76 %) infants who did not develop ROP. The

difference was statistically significant with (P value = 0.038). The mean birth weight of infants who developed ROP was 1218.158 gms with a SD of ± 223.74 gms as compared to 1482.756 gms with a SD of ± 255.864 gms in infants who did not develop ROP.

100 % of the infants who developed ROP were ≤ 34 weeks of gestation as compared to 82.05 % of the infants who did not develop ROP. The difference in terms of development of ROP in the 2 groups is significant with (P value = 0.046). The gestation age of infants who developed ROP had a mean of 30.947 weeks with a SD of ± 2.146 weeks as compared to 32.128 weeks with a SD of ± 2.48 weeks in infants who did not develop ROP.

Risk Factors	ROP + Group Yes	ROP + Group No	ROP + Group Yes	ROP + Group No	P Value
Birth Weight (< 1750 gms)	19	0	63	15	0.038, SIG
Gestational Age (< 34 Weeks)	19	0	64	14	0.046, SIG
Oxygen Exposure (> 2 Days)	15	4	39	39	0.023, SIG
Septicemia (CRP+)	11	8	23	55	0.02 SIG
Exchange Transfusion	11	8	2	76	< 0.001, SIG
Multiple Gestation	2	17	21	57	0.318, NS
Hyperbilirubinemia	3	16	9	69	0.614, NS

Table 1. Risk Factors of ROP. (SIG – Significant, NS – Not Significant 0)

Out of 97 infants who completed the study, number of male infants was 57 and 40 were females. Out of 19 infants who developed ROP in our study, 14 were males and 5 were females. We did not find any significant correlation between gender and development of ROP (P value = 0.141).

Among the 97 infants screened in our study, 54 were exposed to oxygen more than 2 days, of whom 15 (27.78 %) developed ROP as compared to 4 (9.3 %) of 43 infants who were exposed to oxygen for less than 2 days. Statistically this difference of duration of oxygen exposure in infants who developed retinopathy and who didn't develop ROP was significant (P value = 0.023).

34 of the 97 infants screened in our study were diagnosed with septicaemia and C reactive protein levels positive. 32.35 % of these infants developed ROP as compared to 12.69 % of the infants who were not diagnosed with septicaemia and CRP levels negative. Statistically this difference was found to be significant (P value = 0.02).

We found that 84.61 % of the infants who received exchange transfusion developed ROP as compared to 9.52 % of the infants who did not receive blood transfusion and this difference was found highly significant (P value < 0.001).

23 infants of 97 were of multiple gestation. Among them, only 2 (10.52 %) had ROP as compared to 17 (22.97 %) who were of singleton pregnancy. In our study there was no statistical significance between development of ROP and multiple gestation (P value = 0.318).

DISCUSSION

Our study thus reported the prevalence of ROP to be 19.58 % which is comparable to various studies conducted all over the world. Hakeem AH et al. (2012) reported a prevalence of 19.2 %.[14] K Lathiesh Kumar et al. (2017) found the prevalence of 19.2 %.[15] Milad Azami et al. (2017) reported the prevalence of 23.5 %.[16] A recent study carried out by Snigdha Sen et al. (2018) reported the prevalence to be 22.58 %.[17]

A statistically significant association was found between development of ROP in infants with birth weight ≤ 1750 gms (P value being 0.038). The birth weight of infants who developed ROP had a mean of 1218.158 gms with a SD of ± 223.74 gms as compared to 1482.756 gms with a SD of ± 255.864 gms in infants who did not develop ROP. This significant association between birth weight and ROP reported here was comparable to several other studies. Recent studies conducted by Gholam Hossein Yaghoubi et al. (2017),[18] Milad Azami et al. (2017),[16] Oscar Onyango et al. (2018)[19] & Snigdha Sen et al. (2018)[17] have also found low birth weight to be an independent risk factor for developing ROP.

With a P value of 0.046 a significant risk association between development of ROP and gestational age ≤ 34 weeks was reported in our study. The mean gestation age of infants who developed ROP was 30.947 weeks with a SD of ± 2.146 weeks as compared to 32.128 weeks with a SD of 2.48 weeks in infants who did not develop ROP. Studies conducted by Hakeem AH et al. (2012),[14] Ilham M Omer et al. (2014),[20] Bodhraj Dhawan et al. (2016),[21] Gholam Hossein Yaghoubi et al. (2017)[18], K Lathiesh Kumar et al. (2017),[15] Milad Azami et al. (2017),[16] Oscar Onyango et al. (2018)[19] & Snigdha Sen et al. (2018)[17] have also found low gestational age to be an independent risk factor for developing ROP.

A significant correlation between duration of oxygen exposure > 2 days and retinopathy of prematurity in infant was found with a P value of 0.023. Thus, longer duration and unmonitored oxygen exposure is a risk factor for ROP. Studies conducted by Kumar P et al. (2011),[22] Hakeem AH et al. (2012),[14] Ilham M Omer et al. (2014),[20] Bodhraj Dhawan et al. (2016),[21] K Lathiesh Kumar et al. (2017),[15] Milad Azami et al. (2017)[16] & Snigdha Sen et al. (2018)[17] have also found duration of oxygen exposure to be an independent risk factor for developing ROP.

There was no significant correlation between gender and the development of ROP (P value = 0.141). There are no studies till date that found gender and development of ROP to be associated significantly.

Infants diagnosed with sepsis along with C Reactive Protein levels + were also found to be significantly associated with development of ROP with a P value of 0.02. Recent studies conducted by Reza Saeidi et al. (2009)[23], Kumar P et al. (2011),[22] Hakeem AH et al. (2012)[14], Ilham M Omer et al. (2014)[20], Samatha Shetty et al. (2015)[24], Milad Azami et al. (2017)[16] & Snigdha Sen et al. (2018)[17] have also found sepsis as a significant risk factor for developing ROP.

Exchange transfusion was also found to be a highly significant risk factor for developing ROP with a P value of < 0.001. Studies conducted by Hakeem AH et al. (2012),[14] Ilham M Omer et al. (2014),[20] K Lathiesh Kumar et al. (2017),[15] Milad Azami et al. (2017),[16] Oscar Onyango et al. (2018)[19] & Snigdha Sen et al. (2018)[17] have also found exchange transfusions to be an independent risk factor for developing ROP.

No significant association between siblings of multiple gestation and development of ROP was found (P value = 0.318). Rohit Charan et al. (1995) also didn't find any significant relation between multiple birth and development of ROP.[25] This is in contrast with study carried out by Sood V et al. (2012) in which multiple gestation was confirmed as an independent risk factor for ROP. Sicker the twin infant more the chances of developing ROP than the other sibling.[26] Snigdha Sen et al. (2018)[17] also found twin delivery to be independent risk factor for ROP.

There was no significant association between hyperbilirubinemia and development of retinopathy (P value = 0.614) in our study. This is in contrast with study carried out by Samatha Shetty et al. (2015) who found hyperbilirubinemia to be significantly associated with development of ROP.[24]

CONCLUSIONS

The prevalence of retinopathy of prematurity was found to be 19.58 % in our study. Along with prematurity and low birth weight, duration of oxygen exposure, exchange transfusion and septicaemia were found to be significant risk factors. Multiple gestation and hyperbilirubinemia were not found to have any significant association with development of retinopathy. One of the leading causes of blindness among children is ROP. Timely screening, regular follow-up, early detection and intervention are the best ways to reduce the prevalence. NICU in association with ophthalmologist should follow strict guidelines for screening of newborns under their care. Proper counselling and motivation of parents for regular screening of at-risk infants are the need of the hour.

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REFERENCES

[1] Kanski JJ. Clinical Ophthalmology. 7th edn. Elsevier Saunders 2011: p. 573-576.
[2] Ryan SJ. Retina. Chap – 144. 4th edn. Elsevier Ltd., 2006: p. 2463-2477.
[3] Flynn JT. The premature retina: a model for the in vivo study of molecular genetics? Eye 1992;6(Pt 2):161-165.
[4] Kushner BJ, Essner D, Cohen IJ, et al. Retrolental fibroplasia. II. Pathologic correlation. Arch Ophthalmol 1977;95(1):29-38.
[5] Chan-Ling T, Tout S, Hollander H, et al. Vascular changes and their mechanisms in the feline model of retinopathy of prematurity. Invest Ophthalmol Vis Sci 1992;33(7):2128-2147.
[6] Chan-Ling T, Gock B, Stone J. The effect of oxygen on vasoformative cell division. Evidence that 'physiological hypoxia' is the stimulus for normal retinal vasculogenesis. Invest Ophthalmol Vis Sci 1995;36(7):1201-1214.
[7] Jalali S, Anand R, Kumar H, et al. Programme planning and screening strategy in retinopathy of prematurity. Indian J Ophthalmol 2003;51(1):89-99.
[8] Hammer ME, Mullen PW, Fergusson JG, et al. Logistic analysis of risk factors in acute retinopathy of prematurity. Am J Ophthalmol 1986;102(1):1-6.
[9] Seiberth V, Linderkamp O. Risk factors in prematurity of retinopathy. A multivariate statistical analysis. Ophthalmologica 2000;214(2):131-135.
[10] Karhanch R, Mousavi SZ, Riazi-Esfahani M, et al. Incidence and risk factors of retinopathy of prematurity in a tertiary care eye hospital in Tehran. Br J Ophthalmol 2008;92(11):1446-1449.
[11] Rao KA, Purkayastha J, Hazarika M, et al. Analysis of prenatal and postnatal risk factors of retinopathy of prematurity in a tertiary care hospital in South India. Indian J Ophthalmol 2013;61(11):640-644.
[12] Park JE, Park K. Preventive medicine in obstetrics, paediatrics and geriatrics. In: Park JE, Park K, eds. Park's Textbook of Preventive and Social Medicine. New Delhi, Banarasidas Bahnot 1991: p. 306-320.
[13] Fanroff AA, Martin RJ. Neonatal-perinal medicine. 7th edn. St. Louis: Mosby 2002: p. 676-745.
[14] Hakeem AH, Mohamed GB, Othman MF. Retinopathy of prematurity: a study of prevalence and risk factors. Middle East Afr J Ophthalmol 2012;19(3):289-294.
[15] Kumar LK, Seeealar ATA, Kamalarathnam CN. Retinopathy of prematurity in a tertiary care centre: a study of prevalence, risk factors and outcomes. Indian J Child Health 2017;4(3):390-393.
[16] Azami M, Jaafari Z, Rahmati S, et al. Prevalence and risk factors of retinopathy of prematurity in Iran: a systematic review and meta-analysis. BMC Ophthalmol 2018;18(1):83. https://doi.org/10.1186/s12886-018-0732-3
[17] Sen S, Kumar P, Saharan N, et al. To study the prevalence and risk factors of retinopathy of prematurity at a tertiary care centre in Agra. International Journal of Science and Research (IJSR) 2018;7(2):350-353.
[18] Yaghoubi GH, Heydari B, Faal G, et al. Prevalence and risk factors of retinopathy of prematurity (ROP) in preterm infants in ophthalmology clinic of Birjand University of Medical Science from 2014 to 2016. Journal of Surgery and Trauma 2017;5(3 and 4):62-66.
[19] Onyango O, Sitati S, Amolo L, et al. Retinopathy of prematurity in Kenya: prevalence and risk factors in a hospital with advanced neonatal care. The Pan African Medical Journal 2018; 29:152.
[20] Omer IM, Hassan HA. The prevalence and risk factors of retinopathy of prematurity among preterm babies admitted to Soba Neonatal Intensive Care Unit. Sudanese Journal of Pediatrics 2014;14(2):17-21.
[21] Dhawan B, Khandewal R, Gupta K. Retinopathy of prematurity – prevalence and high-risk characteristics in a rural tertiary care hospital in central India. Indian Journal of Neonatal Medicine and Research 2016;4(3):PO5-PO5.

[22] Kumar P, Sankar MJ, Deorari A, et al. Risk factors for severe ROP in preterm low birth weight neonates. Indian J Pediatr 2011;78(7):812-816.
[23] Saedi R, Hashemzadeh A, Ahmadi S. Prevalence and predisposing factors of retinopathy of prematurity in very low birth weight infants discharged from NICU. Iran J Pediatr 2009;19(1):59-63.
[24] Shetty S, Shetty J, Amin H, et al. The incidence, risk factors and outcome of retinopathy of prematurity at a tertiary care centre in South India. IOSR-JDMS 2015;14(6):77-83.
[25] Charan R, Dogra MR, Gupta A, et al. The incidence of retinopathy of prematurity in a neonatal care unit. Ophthalmology 1995;43(3):123-126.
[26] Sood V, Chellani H, Arya S, et al. Changing spectrums of retinopathy of prematurity (ROP) and variations among siblings of multiple gestation. Indian J Pediatr 2012;79(7):905-910.