ORIGINAL RESEARCH PAPER

Paediatrics

KEY WORDS: Retinopathy of prematurity, low birth weight, Oxygen therapy

INCIDENCE AND RISK FACTORS FOR RETINOPATHY OF PREMATURITY IN A LEVEL 3 NICU OF A TEACHING INSTITUTE IN MAHARASHTRA.

Dr. Shivam Jannawar Postgraduate Resident, Paediatrics, PCMC'S PGI, YCMH, Pimpri, Pune-18.

Dr. Suryakant Mundlod Associate Professor Paediatrics, PCMC'S PGI, YCMH, Pimpri, Pune- 18.

Dr. Deepali Ambike* Professor and head Paediatrics, PCMC'S PGI, YCMH, Pimpri, Pune-18. *Corresponding Author

Dr. Himanshu Gohatre Postgraduate Resident, Paediatrics, PCMC PGI, YCMH, Pune-13

ABSTRACT

Background: Retinopathy of prematurity (ROP) is a serious complication seen in premature babies post treatment which can lead to blindness unless and until it is recognized and treated early. **Objective:** The objective was to estimate the incidence of ROP in preterm infants in Neonatal Intensive Care Unit (NICU) and to identify the risk factors which predispose to ROP. **Materials and Methods**: ROP prospective screening survey was performed enrolling all premature babies admitted to the NICU for a period of six months, with a gestational age of 34 weeks or less at birth and a birth weight of 2000gm or less. Those with a BW>2000g or GA>34 weeks with an unstable clinical course were included in the study as per recent IAP guidelines. **Results:** The incidence of ROP in our study was 18.6%. Among babies with gestational age less than 34 weeks had ROP incidence 31.1 %. No ROP was found in infants those who had weight of ≥ 2000g. Maximum babies had stage 2 ROP; only 1 baby had stage 1 ROP and all regressed spontaneously. Two babies had stage 3 ROP and required laser ablative therapy. Pearson Chi-Square test showed that there was a significant relationship between the occurrence of ROP and gestational age (P = 0.015) and low birth weight (P = 042) and number of days the baby was exposed to oxygen (p=0.0324). **Conclusion:** The incidence of ROP in our study was 18.6%. Low gestational age, low birth weight, oxygen therapy, were significant risk factors for ROP. Screening for early identification of retinal damage done soon after birth is important to prevent this blindness.

INTRODUCTION:

Retinopathy of prematurity (ROP) is a disease of the developing immature blood vessels in the retina of baby born prematurely and caused by toxicity of oxygen. Retinal blood vessels in premature babies are abnormal which makes them friable and fragile. This causes leakage or bleeding, leading to retinal detachment which is the major cause of blindness in ROP. As in various retinopathies like proliferative diabetic retinopathy and sickle cell retinopathy, oxygen plays an important role in ROP as well. There is inverse correlation between Incidence of ROP with gestational age and birth weight. If oxygen concentrations are in an excess, it can cause vasoconstriction of retina. Oxygen saturation is a controllable factor, which if kept low can prohibit the development and advancement of ROP.[1]

Studies done in most western regions shows that incidence of ROP ranges from 21 to 65.8%.[1,2] Whereas according to studies done in India, the incidence of ROP is from 38- 51.9% in babies with low birth weight.[3,4] In baby with birth weight less than 900 grams, the ROP incidence has increased and it is now a very big cause of neonatal blindness which can be avoided.[5] In new-borns born at less than 25 weeks, the incidence is found to be as high as 80-100%.[6] According to these risk factors screening of infants born less than 34 weeks gestation or 2000 grams is advised with adequate follow up.[7,8] In India, ROP is one of the main reasons of childhood blindness. Vision 2020 was introduced in 1999, in which five priority areas were set and childhood blindness was one of them.[9]

Several risk factors such as low BW (4, 6, 8,) low gestational age GA (4, 6, 8) high oxygen saturation [6] mechanical ventilation [5,6] phototherapy [8] intraventricular hemorrhage IVH [6,7] anaemia [6], blood transfusion [6] have been associated with the development of ROP.

We planned this study to determine the incidence and risk factors of ROP in premature, ELBW and extremely low GA (ELGA) infants as per recent IAP guideline admitted in NICU in our hospital which is a tertiary referral teaching institute.

MATERIALS AND METHODS:

Inclusion Criteria:-

1) All babies with birth weight less than 2000 gms and gestational age less than 34 weeks were included in the study.
2) Those with a BW>2000 g or GA>34 weeks with an unstable clinical course were included in the study as per recent IAP guidelines.

Exclusion Criteria:-

1) Infants with chromosomal abnormalities, congenital anomalies, inborn errors of metabolism
2) Those premature infants who were discharged prior to first screening and missed or did not complete all screening sessions were also excluded.

Study type and duration: This was a hospital-based prospective study conducted in the NICU of a tertiary care teaching hospital from March 2022 to December 2022.
Sample size: A total of 91 babies were screened for ROP.

Ethical clearance was obtained from the Institutional ethics committee on 15th January 2022 vide letter no. YCMH/7/APP/688/2022

ROP is a National Screening programme, still informed consent was taken.

Detailed history and discharge card record was taken from parents including gestational age, birth weight, number of day's baby was on oxygen, mechanical ventilation, sepsis, surfactant therapy, anaemia, frequent blood transfusions, and documentation was done in the pre-validated proforma.

All infants meeting the screening criteria were scheduled to have their first examination at between 20 to 30 days of life. The pupils of the babies were dilated using tropicamide 0.5% and phenylephrine 2.5% (after dilution). Topical anaesthetic (paracaine) was instilled in eyes and then paediatric wire speculum was applied. Indirect ophthalmoscope was used for fundus examination and the grading for severity (stages) and location (zones) was done. The babies were called for follow up as per the severity of ROP.

International Classification of ROP guidelines were used to record the stages of the disease, its location by zone and signs of plus disease.

The International Committee for the Classification of ROP has classified it using the following criteria:

1. The severity of the ROP
2. The zone in the retina where ROP is found
3. The extent of the ROP
4. Whether the retinal blood vessels are dilated and/or tortuous (pre-plus or plus disease)
5. Whether aggressive posterior ROP is present

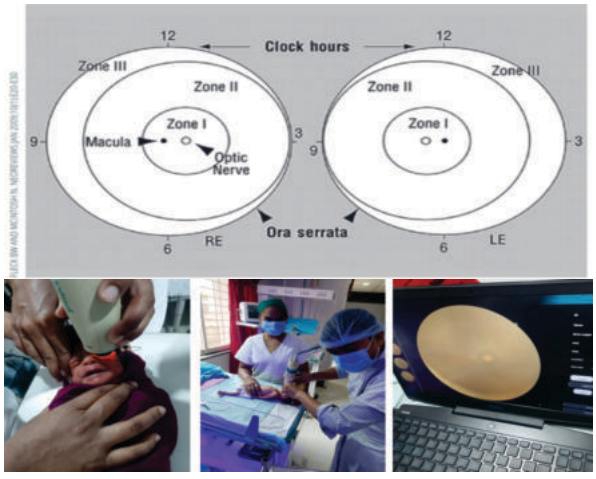
The severity of the ROP can develop when the immature retinal blood vessels have not reached the edge of the retina, known as the ora serrata.

- Stage 1 ROP: Demarcation line. A whitish line is visible between the normally vascularised retina and the peripheral retina in which there are no blood vessels.
- Stage 2 ROP: Visible ridge. The demarcation line develops into a ridge, with height and width, between the vascular retina and peripheral retina.
- Stage 3 ROP: Blood vessels in the ridge. Blood vessels grow and multiply (proliferate) and are visible in the ridge.
- Stage 4 ROP: Sub-total retinal detachment. Vitreoretinal surgery may be indicated.
- Stage 5 ROP: Total retinal detachment. No treatment is usually possible.

The three zones of ROP were classified as

- Zone I is the small circle of retina around the optic disc. The radius of the circle is twice the distance from the macula to the centre of the optic disc.
- Zone II is the ring-shaped section of the retina surrounding zone I, which extends to the ora serrata on the nasal side.
- Zone III is a crescent-shaped area of temporal retina. The zones in the retina where ROP is found

In plus disease, retinal arterioles and venules near the optic disc are dilated and tortuous. In pre-plus disease the changes are less pronounced, or may not affect all the blood vessels.



Images showing procedure of ROP in the NICU by Ophthalmologist team.

Ophthalmic examinations were continued till full retinal vascularization and maximum stage of ROP was reported for each infant. As our NICU was not having ROP treatment facility those who required treatment were transferred to other facilities where ROP treatment is available.

Statistical Analysis: -Data was entered in Excel and analysed using appropriate tests of statistical significance (chi square test).

RESULTS:-

In our study the incidence was 18.6%, 17 out of 91 babies admitted in NICU showed ROP changes.

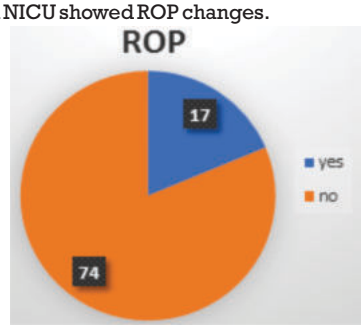


Figure 1: Incidence of ROP

Maximum babies had stage 2 ROP with 14 out of 17 babies, which regressed spontaneously. Only one baby had stage 1 ROP, regressed spontaneously. Only two babies had stage 3 ROP. Both of them required surgical intervention in the form of NdYAG laser surgery

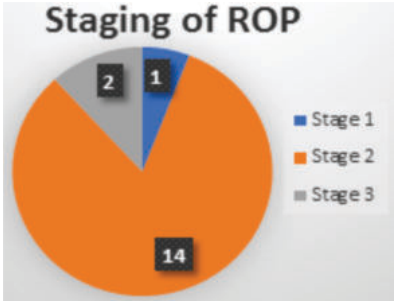


Figure 2: Staging of ROP

International Classification of ROP guidelines were used to record the stages of the disease, its location by zone and sign of plus disease. In our study; ROP in zone 3 region was more prevalent.

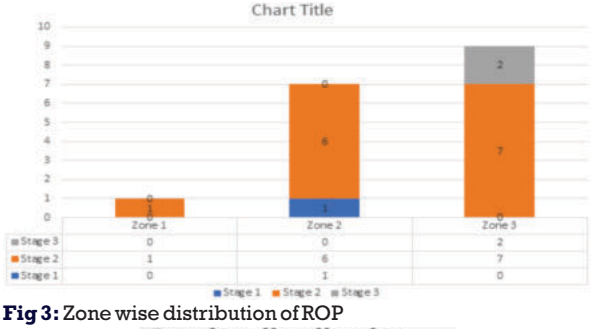


Fig 3: Zone wise distribution of ROP

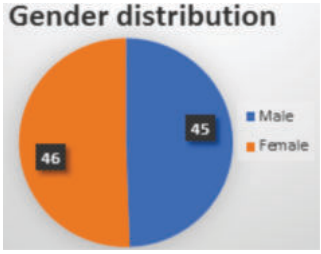


Fig 4: Gender wise distribution.

There is significant association observed between ROP and Gestational Age, with P value of 0.015. All babies with ROP had gestational age less than 34 weeks. None of the baby with >34week gestation developed ROP. We also found that there is inverse relation with Gestational Age as 2 babies with less than 28 weeks had stage 3 ROP

There is significant association observed between ROP and Gestational Age, with P value of 0.015. All babies with ROP had gestational age less than 34 weeks. None of the baby with >34week gestation developed ROP. We also found that there is inverse relation with Gestational Age as 2 babies with less than 28 weeks had stage 3 ROP

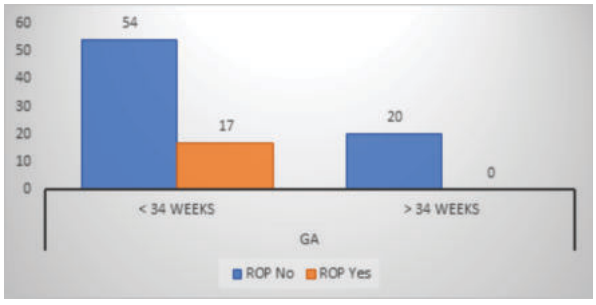


Fig 5: -Depicts the incidence of ROP as per the Gestational age

There is significant association observed between ROP and Birth Weight with P value of 0.04.There is inverse relation between ROP and Birth weight5 out of 12 babies with <1kg birth weight developed ROP(41%) 12 out of 74 babies with 1 to 2 kg birth weight developed ROP(16%)No babies with >2kg birth weight developed ROP

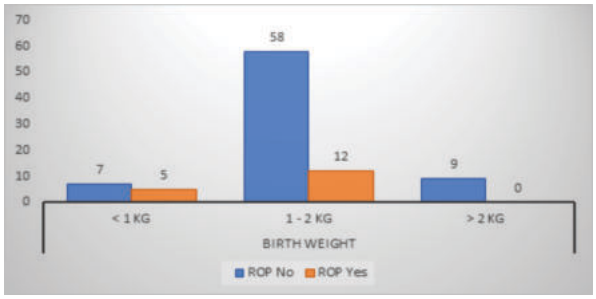


Fig 6: -Depicts the incidence of ROP as per the birth weight

There is significant association observed between ROP and O_2Day with P value of 0.032.

There is direct correlation between number of days babies exposed with oxygen and further development of ROP.None of the babies developed ROP when they did not receive any kind of oxygen support. 14% babies (10 out of 67) developed ROP when received oxygen for less than 10 days. 36% babies (7 out of 19) developed ROP when received oxygen for more than 10 days.

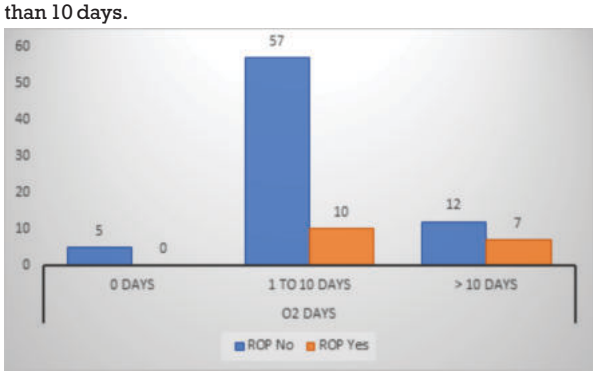


Fig 7: - Depicts the incidence of ROP as per numbers of days of exposure to oxygen.

There is no significant association observed between ROP and Mode of Delivery with P value of 0.65.

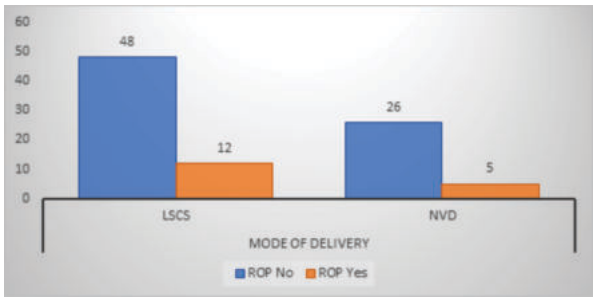


Fig 8: ROP and Mode of delivery

There is no significant association observed between ROP and Blood Transfusions with P value of 0.95.

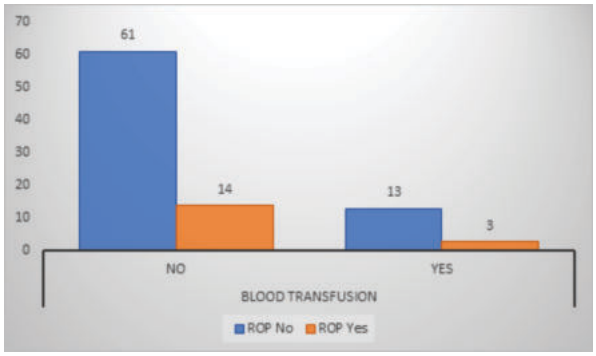


Fig 9: -Depicts the incidence of ROP as per number of blood transfusion

There is no significant association observed between ROP and Photo Therapy with P value of 0.49.

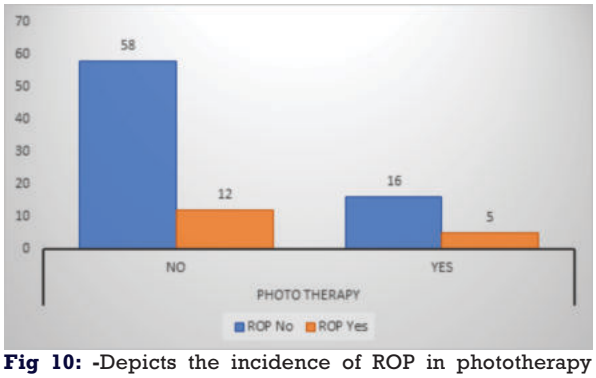


Fig 10: -Depicts the incidence of ROP in phototherapy received babies

DISCUSSION:

Short gestation and ELBW have been identified as the most important risk factors responsible for ROP [2]. In our study we enrolled 91 babies who were delivered before 34 weeks of gestation and had birth weight of less than 2000 gms and those with a BW>2000g or GA>34 weeks with an unstable clinical course were included in the study. We also studied the risk factors which are associated with the disease. In our study, the incidence was 18.6%, 17 out of 91 babies admitted in NICU showed ROP changes

There are many screening criteria described by different authors. Maheshwari, et al.[11] screened all babies weighing <1500g with a gestational age <35 weeks. Gupta, et al.[10] screened all babies ≤1500g and/or gestational age ≤35 weeks. Vinekar,et al.[12] suggested that the condition in developing countries is different. Larger and gestationally older babies are more likely to develop ROP compared to their counterparts in Western countries. Hence, the application of Western screening guidelines for developing

countries has been questioned in a study by Jalali, et al.[13]. As a higher cut off limit, they recommended screening babies born at<34 weeks gestation and/or birthweight <2000g in the presence of unstable course GA > 34 and weight >2000g were also included, in order to prevent any missing infant with threshold ROP as per recent IAP guideline, as instead of used <30 weeks criteria, as per American Academy of Paediatrics .[14]

Our study showed significant risk of ROP as the Gestational age decreases. With incidence of 100 % among babies with gestational age less than 28 weeks, 31.1 % among babies with gestational age less than 34 weeks, and no incidence found after gestational age of 34 weeks. Risk factors contributing to it may be more exposure of oxygen, mechanical ventilation, and immature retina in lower gestational age babies. Similar finding was found in a study done by Aggarwal et al. showed significant correlation between ROP and gestational age, with increase in incidence in babies with gestational age less than 30 weeks.[15] Maximum incidence of ROP was in gestational age group of 30.59 +- 1.52 weeks in a study done by Anuja Sathar et al.[16]

About 71.4 % (5 out of 07 babies) showed changes of ROP in babies with birth weight less than 1000 gram. 20.2% (12 out of 58 babies) showed changes of ROP in babies with birth weight 1kg to 2kg. no ROP was seen in babies with weight more than 2 kg. Similar finding were seen in study done by Ashish A. Ahuja et al. 65.1% in less than 1 kg and 18.3% in babies with weight in between 1 to 2 kg.[17]

Our study showed significant correlation between number of days babies received oxygen and incidence of ROP with p value of 0.0324. Most common mode of oxygen delivery was CPAP. Duration of oxygen therapy was found to be statistically significant when given for more than 10 days. Out of 19 babies who received oxygen for more than 10 days 7 babies had findings of ROP (36.8%). Babies which received oxygen less than 10 days, incidence was found to be 14.9 %, (10 out of 67 babies). Study done by Anuja sathar et al. showed similar finding with statistically significant ROP findings in babies with oxygen delivery for more than 7 days [16]

Out of 91 babies, 60 were delivered by LSCS. With 12 babies encountering with ROP but as P value was more than 0.05, it was not statistically significant. So, in our study mode of delivery was not a risk factor for ROP. Study done by Sucheta Kaul et al. showed similar finding with no statistically significance in mode of delivery and ROP.[18] Study done by Rania M.R. Bassiouny et al. got significant correlation between mode of delivery like caesarean section and ROP. [19]

Out of 91 babies, 16 babies received blood transfusion. Only 3 out of 16 babies who received blood transfusion acquired ROP with p value of 0.99. Hence, we could not find significant correlation between blood transfusion and ROP. 91% (115/126) of infants who developed severe ROP received blood transfusion in a study conducted by Christopher Lust et al[20] Maintaining higher amount of HbF may be beneficial to avoid ROP. Blood transfusion markedly reduces the foetal haemoglobin (HbF) concentration, may predispose babies to ROP, observed by CJ Stutchfield et al. in their study .[21]

There was no significant association observed between ROP and phototherapy in our study but Study done by Mikaniki Ebrahim et al.[22] had significant association between phototherapy and ROP with OR = 2.405, $P = 0.038$.

CONCLUSION:

ROP is a very important and preventable cause of blindness in babies with low birth weight, low gestational age, and unmonitored oxygen administration. Screening for early identification of retinal damage done soon after birth by an ophthalmologist is important to prevent this blindness. As observed screening guidelines and protocols are lacking in developing nations like India. The burden of this disease is bound to rise due to increased advances in the field of neonatology if screening protocols are not implemented stringently. The introduction of Retcam-assisted screening in developing economies facilitates screening and follow-up of the rural population and remote places where availability of an ophthalmologist is difficult. Team work by ophthalmologists, pediatricians and obstetricians is essential to prevent blindness due to ROP

Disclosure:
The authors report no conflicts of interest in this work.
Funding: None

Acknowledgement: We wholeheartedly acknowledge Dept of Ophthalmology, ROP Team from H.V Desai Eye Hospital, Hadapsar, Pune for their support in the ROP Screening of our Neonates.

REFERENCES:-

1. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol. 2005; 123(7):991–9.
2. Gergly A, Gerinec K. Retinopathy of prematurity- epidemics, incidence, prevalence, blindness. Bratisl Lec Listy. 2010; 111(9):514–7.
3. Singh M. Miscellaneous conditions: Retinopathy of prematurity 7th ed. In: Care of the newborn. vol. 2010. 7th Ed
4. Chaudhari S, Patwardhan V, Vaidya U, Kadam S, Kamat A. Retinopathy of prematurity in a tertiary care center - incidence, risk factors and outcome. Indian Pediatr. 2009; 46(3):219–24.
5. Fielder AR, Shaw DE, Robinson J, Ng YK. Natural history of retinopathy of prematurity: A prospective study. Eye. 1992; 6(3):233– 42.
6. Darlow BA. Incidence of retinopathy of prematurity in New Zealand. Arch Dis Child. 1998; 63(9):1083–6.
7. Palmer EA, Flynn JT, Hardy RJ, Phleps DL, Phillips CL, Schaffer DB, et al. Incidence and early course of retinopathy of prematurity. Ophthalmology. 1991; 98(4):84–96.
8. Maurya RP. Retinopathy of prematurity: An update. Ind J Clin Exp Ophthalmol. 2018; 4(1):1–1
9. Gopal L, Sharma T, Ramchandran S, Shanmugasundaram R, V A. Retinopathy of prematurity. A study. Indian J Ophthalmic. 1995; 43:50–61.
10. Gupta VP, Dhaliwal U, Sharma R, Gupta P, Rohtagi J. Retinopathy of prematurity – risk factors. Indian J Pediatr 2004; 71: 887- 892
11. Maheshwasri R, Kumar H, Paul VK, Singh M, Deorari AK, Tiwari AK. Incidence and risk factors of retinopathy of prematurity in a tertiary newborn unit in New Delhi. Natl Med J India 1996; 92: 211- 214.
12. Vinekar A, Dogra M, 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 center in a developing country. Indian J Ophthalmol 2007; 55: 331-336.
13. 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.
14. Screening examination of premature infants for retinopathy of prematurity. Section on Ophthalmology, American Academy of Pediatrics. American Academy of Ophthalmology. Pediatrics 2006; 117: 572-576
15. Aggarwal R, Deorari AK, Azad RV, Kumar H, Talwar D, Sethi A, Paul VK. Changing profile of retinopathy of prematurity. J Trop Pediatr. 2002 Aug; 48(4):239-42. doi: 10.1093/tropej/48.4.239. PMID: 12200987.
16. Kaul, Sucheta & Magdum, Renu & Mohan, Madhuvanthi & Motwani, Divya & Singh, Chirag & Kotecha, Megha. (2021). Prevalence and risk factors of retinopathy of prematurity inWestern Maharashtra. Indian Journal of Clinical and Experimental Ophthalmology. 7. 224-228. 10.18231/j.ijceo.2021.046.
17. Anuja Sathar, Shanavas A., P.S. Girijadevi, Jasmin L.B., Sobha Kumar S., Rajamohanan K. Pillai. Risk factors of retinopathy of prematurity in a tertiary care hospital in South India. Clinical Epidemiology and Global Health, Volume 6, Issue 1, 2018, Pages 44-49, ISSN 2213-3984, https://doi.org/10.1016/j.cegh.2017.02.002.
18. Ahuja AA, V Reddy YC, Adenuga OO, Kewlani D, Ravindran M, Ramakrishnan R. Risk factors for retinopathy of prematurity in a district in South India: A prospective cohort study. Oman J Ophthalmol. 2018 Jan-Apr; 11(1):33-37. doi: 10.4103/ojo.OJO_97_2016. PMID: 29563692; PMCID: PMC5848345.
19. Bassiouny, RaniaM.R. & Ellakkany, RasheedS & Aboelkhair, SamyA & Mohsen, TarekA & Othman, IhabS. (2017). Incidence and risk factors of retinopathy of prematurity in neonatal intensive care units: Mansoura, Egypt. Journal of the Egyptian Ophthalmological Society. 110. 71. 10.4103/ejos.ejos_25_17.
20. Lust C, Vesoulis Z, Jackups R Jr, Liao S, Rao R, Mathur AM. Early red cell transfusion is associated with development of severe retinopathy of prematurity. J Perinatol. 2019 Mar; 39(3):393-400. doi: 10.1038/s41372-018-0274-9. Epub 2018 Nov 20. PMID: 30459388; PMCID: PMC6391181.
21. Stutchfield CJ, Jain A, Odd D, Williams C, Markham R. Foetal haemoglobin, blood transfusion, and retinopathy of prematurity in very preterm infants: a pilot prospective cohort study. Eye (Lond). 2017 Oct; 31(10):1451-1455. doi: 10.1038/eye.2017.76. Epub 2017 May. PMID: 28548651; PMCID: PMC5639193.
22. Mikaniki Ebrahim, Rasolinejad Seyed Ahmad & Mikaniki Mohammad (2010) Incidence and Risk Factors of Retinopathy of Prematurity in Babol, North of Iran, Ophthalmic Epidemiology, 17:3, 166-170, DOI: 10.3109/09286581003734860