



Incidence and Risk Factors of Retinopathy of Prematurity in Khatam Al-Anbia Ophthalmology Hospital in Mashhad City

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ARTICLE INFO

Article history:

Received 01 July 2019

Received in revised form 09 August 2019

Accepted 23 August 2019

Available online 01 September 2019

Keywords:

Retinopathy of prematurity

Risk factor

Screening

ABSTRACT

Background and aim: Retinopathy of prematurity (ROP) is a complex disease initiated by abnormal retinal vascularization in premature infants. ROP causes more than 10% of childhood blindness in developed countries and a preventable disease with determining its risk factors. Then it's necessary to resolve the incidence rate and risk factors of ROP in our area.

Materials and methods: In a retrospective study, all premature infants referred to the ROP clinic of Khatam Al-Anbia Ophthalmology hospital (April 2015- Sept 2016) recorded. Chi-Square Test analyzed qualitative data and quantitative data analyzed by T-test and ANOVA.

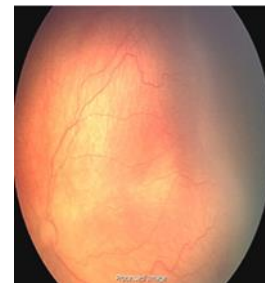
Results: Among 1247 premature infants there were 553, (44%) different stages of ROP. Data analysis showed a significant relationship between ROP and low birth weight (P value<0.0001), prematurity (P value<0.0001), NICU admission (P value<0.0001), oxygen therapy (P value<0.0001), multiple pregnancy (P value=0.049), surfactant therapy (P value=0.03). Gender (P value=0.52), gravid (P value=0.46) and type of delivery (P value=0.8) didn't have significant relationship to ROP.

Conclusion: Among 1247 infants referred to Khatam Al-Anbia hospital, there were 553 (44%) different stages of ROP. According to the study, there is a significant relationship between ROP and variables such as low gestational age, low birth weight, NICU admission, receiving surfactant, and multiple pregnancies. There is no meaningful relationship between ROP and the gender, type of delivery, and gravid.

1. Introduction

Retinopathy of premature infants characterized by abnormal development of retinal vessels in premature infants.^[1] This disease is Vasoproliferative retinopathy due to abnormal vascular regeneration.^[2] The sooner the condition is known and treated, the treatment's outcome will be fewer complaints.^[3] Retinopathy in premature infants is progressive, but its early stages can improve on its own over time. The lack of vessels in the precocious retinal part causes the growth factor in the ischemic regions and eventually, the growth of the vessels in the area. In this disease, the vascular velocity of the avascular regions of the retina impaired. It grows in the border between the normal retina and the avascular of the blood vessels to the vitreous cavity.^[4] Retinopathy rates vary considerably between developed and developing countries and are dependent on neonatal care, active screening, and therapeutic programs in that area.^[5] Due to improved neonatal care, the

premature newborns' survival rates and the prevalence of retinopathy in preterm infants increased in Iran.^[6] The retinopathy of premature infants divided into stages by stage. The word "zero steps" is used when the retinal arteries have no pathological changes. Of course, this stage has no place in the international classification. Stages 1 to 3 are used when there is a border between the normal and vascular retina and avascular retina, and stages 4 and 5 are referred to as degrees of retinal detachment.



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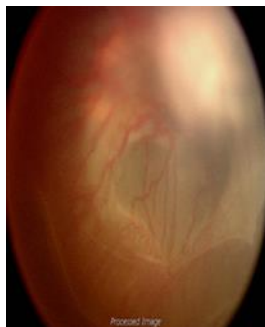
<http://doi.org/10.30485/ijstdms.2019.192413.1008>



Stage 2



Stage 3



Stage 4



Stage 5

The retinal vascularization generally performed from the optical disk to the out borders, and at the nasal side, about 36 weeks of gestation and temporal side for about 40 weeks completed. In the 4th to 5th month of gestational age, mesenchymal precursor cells grow from the neural layer to the outside of the optic disc region. The mesenchymal cells of the endothelial cells create retinal capillaries to form a capillary system. Some of the capillaries enlarged, and arterioles and Venuses are formed, and an apoptotic series also occurs for reconstructions. Local or systemic tissue factors contributing to the progression or reversal of ROP are still not fully understood. Again, predictably, ROP is a transient disease in many lactating babies, and in 85%

of cases, there is self-improvement. The initial sign of self-improvement is the formation of a clear area behind the shunt. It characterized by the creation of direct vessels that overlap the shunt and bring the feeding vessels to the regions without retinal vessels. The following conditions may be associated with improved retinopathy in premature infants:

- Myopia and astigmatism
- Strabismus
- Cataracts
- Glaucoma

Screening involves at least two fundoscopic examinations used for indirect observation and recommended in all newborns weighing less than 1500 gr or gestational age below 30 weeks. Testing is also recommended for several babies weighing between 1500- 2000 gr or more than 30 weeks old, diagnosed high-risk by pediatricians. After each assessment, the follow-up intervals are adjusted depending on the severity of the disease. If the severity of the illness is more, the shorter ranges of the follow-up are needed. Prevention of retinopathy begins at the same time as preventing the birth of a premature baby with good care before, during, and after delivery. It is essential to avoid the birth of premature infants and low birth weight. Premature neonates are more likely to develop ROP, especially with diseases such as sepsis, blood transfusion, and slow-weight weight gaining the risk of developing the disease^[4, 6]

2. Materials and methods

The data from this study were collected from the approval of the proposal on 2015/11/23 to the end of February 2017 at the ROP clinic of Khatam-Al-Anbia Hospital in Mashhad. During this process, all records of the ROP section of Khatam-Al-Anbia Hospital in Mashhad, which refers to the section, have been reviewed from 2015/03/31 to 2016/09/21. This retrospective and a cross-sectional study conducted between April 2015 and September 2016. The incidence and risk factors affecting ROP evaluated, and no intervention has performed in the diagnostic and therapeutic process of the patients.

• Entry Criteria: Patients referred to the ROP clinic at Khatam-Al-Anbia Ophthalmology Hospital during the interval mentioned with the congenital disability complaint who were examined by Ret Cam Fundus Photogrammetry and indirect ophthalmoscopy.

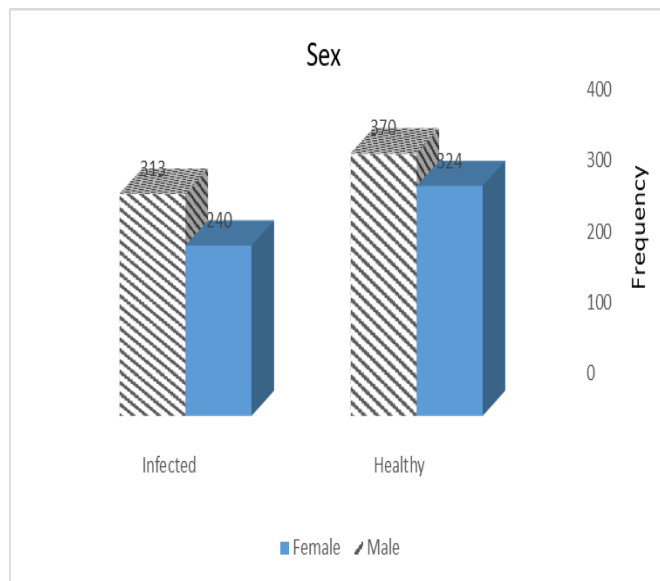
• Exit criteria: Incomplete recorded data, co-morbidity of retina, non-complete follow-up

Required information such as pregnancy age, patient weight, the prevalence of systemic factors, and patient weighing profiles was extracted from the clinic records and analyzed using statistical methods. Compare the qualitative data, the Chi-Square tests used, although to analyze the quantitative data between groups and within the groups at different time intervals with the base state ANOVA, the T-test was used. Of about 2000 records, all records counted, and 1247 records were extracted and analyzed statistically. The process of reviewing the records was kept in the archives of the hospital's ROP section, observing ethical standards and maintaining patient information confidentiality. This study conducted on the title "the onset and risk factors of retinopathy in premature infants at Khatam-Al-Anbia Hospital Mashhad, April-September 2015" with a code of 940537. The study conducted in the Department of Ophthalmology of Mashhad University of Medical Sciences.

3. Results

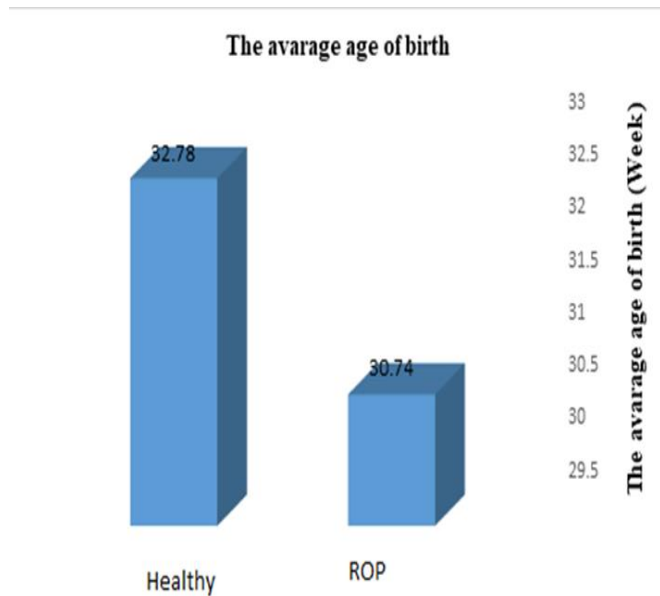
In this study, about 2000 cases studied, and 1247 premature infants entered the project. Of these, 553 (44.3%) infants were infected with retinopathy, and 694 (55.7%) were healthy infants. Of the 553 infants infected, 2 (0.3%) newborns had reached the disease's threshold stage.

Fig1. Frequency of Sex.



From 564 female newborns, 324 (57%) premature infants afflicted retinopathy, but 240 (43%) were healthy infants and from 683 male newborns, 370 (54%) were infected, and 313 (46%) were healthy infants. Based on the Chi-Square test, there is no significant difference in retinopathy incidence between male and female groups (P-value = 0.52).

Fig2. Mean age of birth.



Based on Fig 2, Compared to the age of birth in two groups with retinopathy and non-infected, the mean age of birth in the affected group was 30.74 weeks with SD 2.32 non-affected group 32.78 weeks with a standard deviation of 2.04 weeks. Based on the T-test, there is a significant relationship between low birth weight and infant retinopathy (p <0.0001).

According to Table 1, In comparison, the mean weight in the retinopathy group was 1478 g with a standard error of 17.8 g and in the whole group 1765 g with a standard error of 17.2 g. Based on the T-test, there was a significant correlation between low birth weight and the prevalence of retinopathy in premature infants (P-value <0.0001).

Table 1. Comparison of birth weight in two groups of patients infected with retinopathy and healthy premature infants.

Birth weight (g)	Mean	Standard error	Domain
Infected	1478	17.8	3220
Healthy	1765	17.2	2650

According to Table 2, the average daily oxygen therapy days in premature infants were 14.64 ± 16.8 days, and in non-infected infants, they were 5.65 ± 8.7 days. According to the Chi-Square test, there was a significant difference between the mean days of oxygen intake and retinopathy (p-value < 0.0001). A large number of cases of incomplete oxygen reception considered missing data.

Table 2. Comparison of the average days of oxygen therapy in both infected with retinopathy and healthy premature infants.

Oxygen Therapy (Day)	Average	Standard deviation	Range
Infected	14.64	16.8	102
Healthy	5.65	8.7	56

According to Table 3, in this study, 164 (30%) infected infants and 212 (30%) healthy infants were born in the natural method, and 387 (70%) affected infants and 478 (70%) healthy infants carried by a cesarean method. According to the Chi-Square test, there is no significant difference between the two groups in terms of delivery type (P-value = 0.8).

Table 3. Comparison of the type of delivery in the two groups of infected with retinopathy and healthy premature infants.

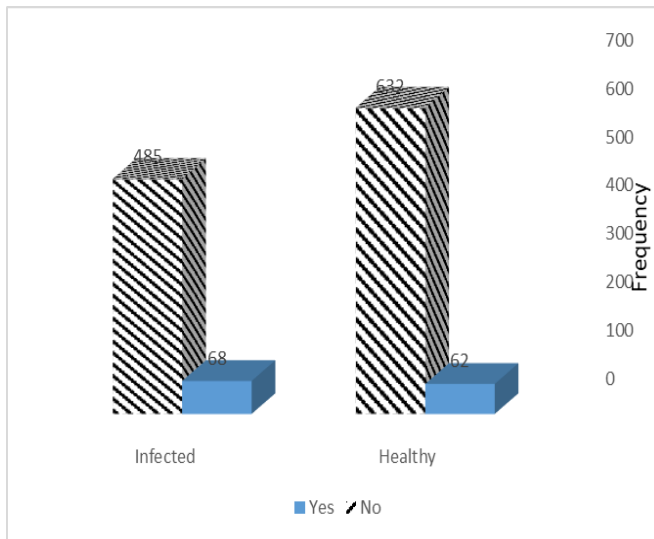
Type of Delivery	Infected	Healthy
Cesarean	164(30%)	212(30%)
Natural	387(70%)	478(70%)

The other result showed that compared to the two groups in terms of NICU admission, the group with retinopathy was 22.5 ± 14 days old, and the non-affected group was 13.21 ± 10.7 days. Based on the T-test, there is a significant difference between the mean days of admission to NICU in both the affected and non-diabetic patients with retinopathy (P-value <0.0001). In Table 4, they were comparing two groups in terms of gravidity of the mother, 249 (45.5%) infants with retinopathy, and 309 (45%). Healthy infants were the result of first pregnancy 297 (54.5%) infants and 375 (55%) healthy infants, resulting from a second pregnancy or more of a mother. According to the Chi-Square test, there is no significant relationship between pregnancy rate and disease (P-value = 0.46).

Table 4. Comparison of maternal gravidity in two groups of infected with retinopathy and healthy premature infants.

Gravidity	Healthy	Infected
First Pregnancy	309(45%)	249(45.5%)
Second or more Pregnancy	375(55%)	297(54.5%)

In comparison to the type of pregnancy, 348 (63%) infants with retinopathy and 469 (67.5%) of healthy infants found infertile. 205 (37%) with retinopathy and 225 (32.5%) were healthy infants. There is a significant relationship between the type of pregnancy and retinopathy in premature infants (P-value = 0.049) by the Chi-Square test.

Fig 3. Surfactant Therapy.

Compared to the two groups, 68 (12.3%) patients with retinopathy and 62 (8.9%) of the healthy newborns received surfactant therapy. 485 (87.7%) with retinopathy and 632 (91.1%) healthy infants did not receive surfactant. In the study, based on the Chi-Square test, there is a significant relationship between receiving surfactant and preterm infants' retinopathy (P -value = 0.03).

4. Discussion

In this study, 2000 referral neonates included 1247 cases, of which 553 were infants with retinopathy (44%) and 694 healthy infants (56%). The prevalence of retinopathy in neonates was 43% (240) in girls and 46% (313) in boys. Based on the study between retinopathy and variables such as low gestational age, low birth weight, oxygen therapy, low mean weight gain in a week, NICU admission, receiving surfactant, pregnancy type, there is a meaningful relationship. Still, there is no meaningful relationship between the incidence of retinopathy and gender variables, the type of delivery, and the mother's gravidity, 2 (0.3%) infants reached the stage of the disease threshold. Mansouri et al. in 2014 in Sanandaj studied 47 premature infants. The overall prevalence of retinopathy in this study was 10.6%, reported 16% in girls and 4.5% in boys, and 23.5% of newborn infants needed mechanical ventilation.¹⁷ Our study was conducted on a high sample size (1247) that examined various variables of retinopathy. In our study, the incidence of retinopathy in both groups was 43% in girls and 46% in boys. In 2013, Stevenson's study found that lower SPO₂ levels are associated with a reduction in the risk of retinopathy, but significantly increases mortality.¹⁸ In the present study, there is a significant relationship between the number of oxygen receiving days and retinopathy. Also, by comparing the two groups of newborns receiving and not receiving oxygen, there was a significant increase in retinopathy in infants who received oxygen. The data recorded in the files of this center was limited to the number of days of oxygen therapy, and the SPO₂ interval not recorded. In a 2012 screening center in southern Iran, Farid and et al. studied retinopathy screening for premature infants. The incidence of retinopathy in premature infants was 37.2% in the population referred to as the center. The main risk factors for the development of retinopathy in premature infants were low gestational age and low birth weight. Also, there was no significant relationship between sex, multinational factors, and pregnancy methods with the incidence of disease.¹⁹ In our study, several techniques and methods of pregnancy had a significant relationship with the prevalence of the disease,

but gender was not significantly related to disease incidence. The main risk factors in our study were low birth weight and oxygen consumption.

5. Conclusion

The prevalence of retinopathy in 44% of premature infants represents a high incidence of disease in this population. According to a study, there is a meaningful relation between retinopathy and variables such as low gestational age, low birth weight, oxygen consumption, low weekly weights, NICU admission, receiving surfactant. Still, there is no meaningful relationship between the incidence of retinopathy and sex variables, the type of delivery, and the gravidity of the mother.

Conflict of Interest

The authors declared that there is no conflict of interest.

Acknowledgments

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Bayat-Mokhtari M, Pishva N, Attarzadeh A, Hosseini H, Pourarian S. Incidence and Risk Factors of Retinopathy of Prematurity among Preterm Infants in Shiraz/Iran. Iranian journal of pediatrics. 2010;20(3):303-7.
2. Gilbert C. Retinopathy of prematurity--the "second lull"? The British journal of ophthalmology. 2001; 85(9):1017-9.
3. Gibson DL, Sheps SB, Schechter MT, Wiggins S, McCormick AQ. Retinopathy of prematurity: a new epidemic? Pediatrics. 1989; 83(4):486-92.
4. Raab EL, Aaby AA, Bloom JN, Edmond JC, Lueder GT, Olitsky SE, et al. Pediatric Ophthalmology and Strabismus. Weiss JS, editor: American Academy of Ophthalmology; 2012-2013.
5. Gilbert C. Characteristics of Infants With Severe Retinopathy of Prematurity in Countries With Low, Moderate, and High Levels of Development: Implications for Screening Programs. Pediatrics. 2005;115(5):e518-e25.
6. Ghaseminejad AK, Niknafs P. Distribution of Retinopathy of Prematurity and Its Risk Factors. Iranian journal of pediatrics.2011; 21(2):209-14.
7. Mansouri M, Hemmatpour S, Sedighiani F, Ghamari D, Chavoshi D. Factors associated with retinopathy of prematurity in hospitalized preterm infants in Sanandaj, Iran. Electronic Physician. Sept 2016;8(9):2931-2934.
8. Stenson BJ. Oxygen targets for preterm infants. Neonatology.2013; 103(4):341-5.
9. Afarid M, Hosseini H, Abtahi B. Screening for retinopathy of prematurity in South of Iran. Middle East African Journal of Ophthalmology. 2012;19(3):277-81.