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A Study of Clinical Profile of Retinal Diseases in Premature Infants

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Abstract: ***Purpose: Retinal diseases in premature infants, particularly retinopathy of prematurity (ROP), are significant causes of childhood blindness worldwide. The prevalence and severity of these conditions are influenced by various factors, including gestational age, birth weight, and neonatal care quality. This study aims to analyze the clinical profile of retinal diseases in premature infants visiting or admitted to the Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand. Methods: The present observational study was conducted in the Department of Ophthalmology, Himalayan Institute of Medical Sciences (HIMS), Swami Rama Himalayan University, Dehradun over a period of 12 months. Preterm neonates attending ophthalmology or pediatric outpatient department or admitted in neonatal intensive care unit of Himalayan hospital were included in the study. Premature infants born before 37 weeks of gestation were screened for retinal diseases using indirect ophthalmoscopy. Data on gestational age, birth weight, oxygen therapy, and other relevant clinical parameters was collected. Results: Of the total 101 patients studied, 62 (61.4%) had retinal disease. Males had significantly higher proportion of retinal disease 42 (67.7%) as compared to females 20 (32.2%). P value 0.012. The incidence of ROP was found to be 62 (61.4%). Significant risk factors for the development of retinal diseases included low gestational age, birth asphyxia, ventilator support, oxygen administration and delivew by cesarean section. Conclusion: The study highlights the need for early screening and intervention for retinal diseases in premature infants, particularly those with identified risk factors.***

Keywords: Retinopathy of Prematurity, Retinal Diseases, Premature Infants, Neonatal Care

1. Introduction

Retinal diseases are an emerging cause of visual impairment in the developing world and are an important cause of ocular Inorbidity globally. There are many retinal disorders that can affect the infants and children (1). Of all retinal diseases, ROP stands out as a prominent concern. The incidence and severity of ROP conelate with the degree of prematurity and low birth weight, making it a critical issue in neonatal care (2).

Ophthalmic challenges following preterm birth are numerous, and overall extremely low birth weight (<1000 g) infants are three times more likely to have a visual acuity of less than 1.0 (logMAR) than those born at term. In India, approximately, 1 in 1000 children is blind, and the incidence of ROP is repolted between 24% and 47% (3). Globally, ROP is estimated to affect more than 50, 000 infants annually and in India, every year, 500 children are estimated to become blind from ROP.

Retinal diseases may be congenital or acquired. Early detection and prompt treatment is essential for preventing visual impairment. The purpose of this study aims to evaluate retinal diseases in premature infants, study systemic associations with retinal diseases and identify risk factors (4).

2. Materials and Methods

The present observational study was conducted in the Department of Ophthalmology, Himalayan Institute of Medical Sciences (HIMS), Swami Rama Himalayan University, Dehradun over a period of 1 year from May 2022 to April 2023. Pretenn neonates attending ophthalmology or pediatric outpatient department or admitted in neonatal intensive care unit of Himalayan Hospital were included in the study.

A total of 101 neonates born before 37 weeks of gestation were included in the study. Neonates with congenitally deformed globe and poor media clarity were excluded. A well informed written consent was taken from the parents for dilated fundus evaluation. Neonates were kept fasting for I hour prior to fundus evaluation. Pupils were dilated with eye drop tropacimade (0.8%) + phenylephrine (5%) diluted with eye drop polyvinyl alcohol and povidone I: I, 1 drop 3 times at 10 minute interval. Special warmers were kept available to keep the child warm. Pulse oximeter was connected and topical proparacaine (0.5%) was used for anaesthetic effect. A sterile set of infant wire speculum was applied and fundus was examined with the help of a binocular indirect ophthalmoscope and +20D biconvex lens. A pediatric scleral

depressor was used for examination of 360^0 peripheral retina upto ora senata.

3. Statistical Analysis

Entry, interpretation and analysis of the data was carried in Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 22.0. Data was summarized using mean, standard deviation and range for continuous variables and percentage for categorical variables. Systemic association with retinal diseases was tested. Comparison between groups was done using t - test for continuous variables and chi - square test for categorical variables. Univariate regression was done. P - values less than 0.05 was considered as statistically significant

4. Results

In the current study 101 preterm infants were included. Of this 65 (64.4%) were males and 36 (35.6%) were females. The male: female ratio was found to be I 8:1 (Table I) Mean gestational age - 30 weeks 6 days (Table 2) and mean birth weight was 1617 grams. Of the total 101 preterms studied, 62 ($61.4^0/0$) had retinal disease. Males had significantly higher proportion of retinal disease 42 (67.7%) as compared to females 20 (32.2%) (p - value — 0.012) .

Thirty (29.7%) preterms were delivered through normal vaginal delivery (NVD) out of which only 4 (3.9%) preterms had retinal disease. Seventy one (70.29%) preterms were delivered through LSCS and 58 (57.4%) developed retinal diseases. Pretenns delivered through caesarian section had significantly higher proportion of retinal disease 58 (57.4%) as compared to ones delivered via NVD, 4 (3.9%) (p - value =0.012) .

Of total 24 (23.8%) neonates who had history of blood transfusion, 19 (30.6%) had retinal disease whereas, 43 (69.4%) neonates had retinal disease without any history of transfusion. (p > 0.05). No significant association of retinal disease in preterm neonates with blood transfusion was observed (p=0.122). Of total 16 (15.8%) neonates who had hist01Y of surfactant use, 13 (21.0%) had retinal disease whereas, 49 (79.0%) neonates had retinal disease without any history of surfactant use. No significant association was found between retinal disease in preterm neonates with surfactant use (p=0.119).

Out of 62 preterms, retinal disease was found in 12 (19.4%) preterms with GA less than 28 weeks, 31 (50%) preterms with GA between 28 and 32 weeks, and 19 (30.6%) preterms with GA 33 - 36 weeks. (Table2). Retinal disease was found to be significantly higher in GA group of 28 - 32 weeks. (p - value=0.019)

Out of 62 preterms with retinal disease, 34 (54.83%) were on oxygen support (510 days). There was significant increase in the incidence of retinal disease with increase in the number of days on oxygen support (p = 0.020). (Table 3) Significant association of retinal disease in preterm neonates with birth asphyxia was observed. A total of 30 (29.7%) preterms who had history' of birth asphyxia, 23 (37.1%) had retinal disease whereas, 39 (62.9%) preterms had retinal disease without any history of birth asphyxia (p=O.044). (Table 4)

A total of 74 (73.3%) preterms had history of ventilation support, out of which 51 (82.3%) had retinal disease. Twenty three (59.0%) preterms had retinal disease without any history of ventilator support (p=0.010). (Table 5)

Our study showed no significant association of retinal disease with birth weight. (p - value=0.696). Of all the preterms with retinal diseases, 5 were of extremely low birth weight (568 - 999g), 21 were very low birth weight (10001500g) and 36 were low birth weight (1501 - 2000g).

ROP was found in 60 preterms out of which 2 preterms were diagnosed with aggressive ROP (AROP), Zone Il Stage I were found in 27 preterms, Zone Il Stage Il in 26 preterms, Zone Il Stage Ill in 4 preterms and Zone Ill Stage Ill in I preterm. Ninteen preterms had immature retina with no ROP. One preterm had vitreous hemorrhage and one had retinal hemorrhage.

As per extent, ROP was seen more in Zone Il and Zone Ill, and as per staging, Stage I and Stage Il.

Univariate analysis showed that significant risk factors for the development of retinal diseases included low gestational age. birth asphyxia, ventilator support, oxygen administration and delivery by cesarean section.

5. Discussion

Screening of retinal diseases is essential in all high risk preterms, which is almost not possible in developing countries like India with poor resources in peripheral areas. Early screening and treatment of retinal diseases among high risk preterms is essential.

Understanding the clinical profile, including the incidence, risk factors and progression patterns of retinal diseases is essential for developing effective screening protocols, preventive measures, therapeutic interventions. This research aims to fill gaps in knowledge regarding retinal disease in premature infants, ultimately leading to improved outcomes and quality of life for the fragile cohort.

The study showed that of the total 10 Ipreterms studied 62 had retinal diseases of which 42 were males showing that males had significantly higher proportion of retinal diseases. Similar results were found in a study conducted by Ying GS, et al. where total number of participants were 979 out of which 523 were males and 456 were females. Number of males developing retinal disease was 92 which was significantly higher than that of females (5). Darlow BA, et al showed similar results (6). The Cryotherapy for ROP (CRYO - ROP) study and New York cohort study found no difference in the proportion of retinal disease by gender (7).

Of the total 101 preterms studied, 30 were delivered through non vaginal delivery of which only 4 had retinal disease. Rest preterms delivered by LSCS were 71 of which 58 developed retinal diseases showing that preterms delivered through LSCS had significantly higher proportion of retinal diseases.

Several studies have studied the association of mode of delivery and retinal disease, with conflicting results, including studies showing increased risk for retinal disease with vaginal birth, increased risk with Caesarean section, and no associations. Wikstrand MH, et al. found a strong conelation of retinal disease with LSCS (8). Darlow BA et al showed that preterms delivered by vaginal delivery had more incidence of retinal disease (6).

Of the 101 neonates, 62 had retinal disease and only 19 had undergone blood transfusion and our study showed no clinical significant association with the same. Abdel HA, et al showed that preterms with multiple blood transfusions had a clinically significant association with retinal diseases. They found that of the total 33 cases of retinal diseases, three cases showed retinal disease with one time blood transfusion and 9 had retinal disease with multiple blood transfusions (9). Ebrahim M et al found similar results supporting association of blood transfusion and retinal diseases (10).

In our study, we found that 16 preterms received surfactant therapy out of which 13 had retinal diseases, 49 preterms had retinal disease without any history of surfactant use (p value 0.119). It has been reported that surfactant might reduce the incidence of retinal diseases by shortening the weaning period of the infant from mechanical ventilation due to improved pulmonary stability. A statistically significant correlation between surfactant treatment and the risk of ROP occurrence was found by Ved GP et al in which ROP was diagnosed in 70.8% of the babies who received surfactant treatment, while only 33.5% of the rest developed retinopathy (l I).

Our study showed that low gestational age caries a risk of developing retinal diseases. Prevalence of retinal disease was significantly higher in gestational age of 28 - 32 weeks and <28 weeks of gestation. A lower GA was associated with a higher incidence of severe retinal disease. Markestad et al found that no infant with GA >25 weeks developed retinal disease (12).

Ashton and Patzel et al found that exposure to >50% oxygen increased the incidence of retinal diseases compared to a curtailed - oxygen group (13). In our study, we found that there was significant increase in the incidence of retinal disease with increase in number of days on oxygen support (p - value=O.02). Kim et al, in their study which included 979 infants, revealed that the need for respiratory support including mechanical ventilation and high - frequency oscillatory ventilation was an independent risk factor for development of retinal disease (14).

A study by Hwang JH, studying 2386 preterm infants found mechanical ventilation as a significant risk factor in the development of retinal diseases with a p value < 0.001 (15). In our study we found that majority of preterms who had retinal diseases had exposure to mechanical ventilation and therefore stands out as a major risk factor. (p - value =0.01).

6. Conclusion

Retinopathy of prematurity was the most common retinal disease found in preterms in our study.0ther retinal diseases found in our study were premature retina, vitreous hemorrhage and retinal hemorrhage. Significant risk factors for the development of retinal diseases included low gestational age, birth asphyxia, ventilator support, oxygen administration and delivery by cesarean section. Timely screening of preterms particularly with risk factors and intervention can reduce burden of childhood blindness to a great extent.

7. Limitations of Study

1) The study was limited only to a tertiary care center and peripheral areas could not be covered.
2) The study included a small sample size.

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Table I: Gender wise distribution of retinal disease

Gender	Retinal disease		Total
	Present	Absent	
Female	20 3 (2.2)	16 (41.0)	36
Male	42 (67.7)	23 (58.9)	65
Total	62	39	101
P value	0.012		

Table 2: Association of retinal disease with Gestational A e

Gestational Age	Retinal disease		Total
	Present	Absent	
< 28 weeks	12 (19.4)	5 (12.8)	17 (16.8)
< 28- 32 weeks	31 (50.0)	11 (28.2)	42 (41.6)
33- 36 weeks	19 (30.6)	23 (59.0)	42 (41.6)
Total	62	39	101
P value	0.019		

Table 3: Association of retinal disease with oxygen therapy

No. of days on oxygen support	Retinal disease		Total
	Present	Absent	
0 - 5 days	18 (29.0)	28 (71.8)	46 (45.5)
5 - 10 days	34 (54.8)	9 (23.1)	43 (42.6)
10 - 15 days	2 (3.2)	0	2 (2.0)
15 - 20 days	5 (8.1)		5 (4.9)
20 - 25 days	1 (1.6)	1 (2.6)	2 (2.0)
25 - 30 days	1 (1.6)	1 (2.6)	2 (2.0)
30 - 35 days	1 (1.6)		1 (1.0)
Total	62	39	101
P value	0.02		

Table 4: Association of retinal disease with birth as h Xia

Birth Asphyxia	Retinal disease		Total
	Present	Absent	
Yes	23 (37.1)	7 (17.9)	30 (29.7)
No	39 (62.9)	32 (82.1)	71 (70.3)
Total	62	39	101 (100)
P value	0.044		

Table 5: Association of retinal disease with ventilation

Ventilation	Retinal disease		Total
	Present	Absent	
Yes	51 (82.3)	23 (59.0)	74 (73.3)
No	11 (17.7)	16 (41.0)	27 (26.7)
Total	62	39	101 (100)
P value	0.010		

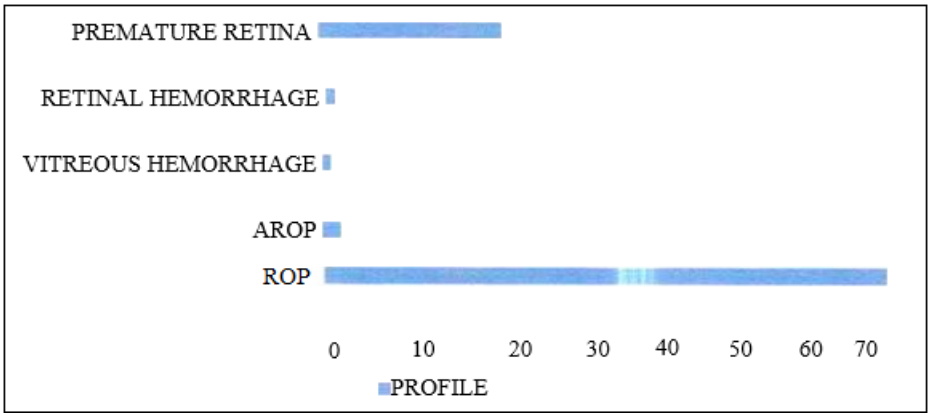

Figure 1: Profile of Retinal Diseases