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RETINOPATHY IN HIGH-RISK NEWBORNS IN TERTIARY CARE HOSPITAL IN WESTERN INDIA

Paediatrics

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ABSTRACT

Aim: To study various factors of retinopathy in high-risk newborns **Material & Method** All patients admitted in NICU/ high risk OPD with diagnosis of premature retinopathy. Fundus examination with direct ophthalmoscope, RETCAM the findings were noted and analysed to rule out various serious causes of retinopathy of prematurity in high risk newborns. **Results:** A total 100 patients of retinopathy of prematurity were examined in premature babies. A significant positive association of retinal changes and risk factors were analysed by taking p value, fishers exact test. In this study 38 neonates developed hyperbilirubinemia, 30 newborn had apnea, 18 had alidosis, 16 cases suffered from septicaemia, 9 newborn required blood or blood production with retinopathy in high risk newborns.

KEYWORDS

Infants, Laser, Retrolental fibroplasia, Retinopathy of Prematurity, risk factors

INTRODUCTION

Retinopathy of prematurity (ROP) is a disease of premature retina. It is recognised as an important cause of visual blindness since 1940. ROP, that was formerly referred as retrolental fibroplasia, was initially identified in the 1940s by Terry, who was the earliest to link the disorder to preterm delivery.[1]

ROP is a Vaso proliferative eye condition that mostly affects preterm babies. It affects normal motor skills, linguistic, mental, and social development, resulting in significant vision impairment and blindness at a huge financial cost to the society and the child's family. Premature newborns acquire prematurity retinopathy within a few weeks after giving birth. Amblyopia, Strabismus and Myopia are sequelae of regressive Retinopathy of Prematurity. In spite of modern medical treatment in the late stages of the illness, ROP remains a significant reason of visual impairment in infants in both the developed and developing nations.[2]

Laser photocoagulation and cryotherapy of the avascular retina were demonstrated to be somewhat successful in averting impaired vision in ROP newborns in the 1980s and 1990s, paving the way for major advancements in ROP treatment.

The study conducted by Deorari A K et al.,[3] in Delhi showed the incidence of ROP to be 20 % as compared to various western studies which varies from 21 to 65.8% by selection criteria.

ROP was linked to increased oxygen usage early after the condition was first described, as shown by observations in the nursery and animal investigations.[4,5] Premature newborns now get controlled supplementary oxygen to maintain appropriate oxygen levels in their blood. Despite the use of regulated oxygen, the incidence of newborns with ROP has grown, owing to the increasing continued existence of extremely low weight birth babies.[6,7] Currently, oxygen usage and the baby's gestational age/birth weight seem to be the two most important for ROP's risk factors, while new data show that increased $C_6H_{12}O_6$ may also perform an important part.[8]

MATERIAL AND METHODS

Type of Study: Prospective study
Period of Study : 2 years
Sample Size : 100 neonates.

Inclusion Criteria

Neonates with birth weight less than 2500 gms, gestational age less than 37 wks, exposure to oxygen therapy, respiratory distress syndrome, septicaemia (blood culture being positive), multiple blood transfusions, multiple births, apnoeic spells and intraventricular haemorrhage.

Detailed Procedure

The proforma was used to examine all of the newborns. The parents' informed agreement was obtained, and an examination was performed at the NICU/HIGH RISK OPD. The majority of the newborns were examined for the first time at four weeks of life or 33 weeks of gestational age, whichever came first. The second visit was place at 6 weeks, with a follow-up at 6 months as well as a final follow-up at 1 year. RETCAM was used to assess the patients. After receiving clearance from the Institutional Ethical Review committee, the research was carried out.

Standardization of Examination Techniques

The pupils of babies were dilated with cyclomydril for eye tests 0.2 percent cyclopentolate and 1.0 percent phenylephrine). Because of the unsatisfactory dilatation, 0.5 percent cyclopentolate and/or 2.5 percent phenylephrine were given if required. To view the peripheral retina, sterilized eyelids specula as well as scleral depressors were used as needed throughout the test. A hand-held lens was used in conjunction with a binocular indirect ophthalmoscope. Ophthalmologists also observed any other local sterility requirements. Because of concerns that topical anaesthetic drugs would cloud the cornea as well as impede vision of the retina, they were not used during exams. Infants were evaluated while being closely watched for symptoms of discomfort from the procedure. Infants who were unable to bear the examination were reassessed later or on a different day.

OBSERVATION & RESULTS

Table. No: 01 Gender Wise Distribution of Patients.

Gender	Number of patients	Percentage (%)
Male	49	49.0
Female	51	51.0
Total	100	100.0

Forty-nine male neonates were screened for ROP and 51 female neonates were screened for ROP out of total 100 neonates.

Table. No. 02: Distribution Of Patients With Respect To Number Of Days For O_2 Requirement.

O2 requirement days	Number of patients	Percentage (%)
< 3	9	9
3 – 5	44	44

6 – 9	40	40
≥ 10	7	7
Total	100	100

Nine neonates required oxygen for less than 3 days,43 neonates were requiring oxygen for 3-5 days,40 neonates were requiring oxygen for 6-9 days,7 neonates were requiring oxygen for more than 10 days.

Table. No. 03: Distribution Of Patients With Respect To Fio2 Level

FiO2	Number of patients	Percentage (%)
0.3 – 0.5	96	96.0
> 0.5	4	4.0
Total	100	100.0

Ninety-six neonates had required FiO_2 between 0.3-0.5, four neonates had required FiO_2 of more than 0.5.

Table. No. 04: Distribution Of Patients With Respect To Requirement Of Respiratory Therapy In Nicu

	Number of patients	Percentage (%)
Ventilator	2	2
CPAP	14	14
Nil	84	84
Total	100	100

Two neonates had required mechanical ventilation, fourteen neonates had required CPAP support.

Table. No. 05: Distribution Of Patients With Respect To Risk Factors And Rop

Risk factor	Number of patients	Percentage (%)
hyperbilirubinemia	38	38
Apnea	30	30
Acidosis	18	18
Required blood or blood products	9	9
Septicemia	16	16
Total	100	100

Out of 100 newborns, 9 newborns required blood or blood products, 38 neonates developed hyperbilirubinemia, 16 cases suffered from septicemia, 30 newborns had apnea and 18 had acidosis

Table. No. 06: Distribution Of Patients With Respect To Stage Of Rop Before Treatment And After Treatment.

Stage	Number of Patients	
	Visit 1	Visit 2
I	4	3
II	5	1
III	1	1
IV	1	1

Out of 11 newborns who developed RPO, 3 were male and 8 were female. Four neonates were diagnosed to have stage 1 ROP in visit 1 in which 3 of those neonates had stage 1 ROP on the next visit.5 neonates were diagnosed to have Stage 2 ROP on visit 1 following which only 1 developed ROP on next visit. One neonate had Stage 3 ROP on visit 1 as well as visit 2. One neonate was diagnosed to have Stage 4 ROP on visit 1 and visit 2.

Table. No. 07: Distribution Of Patients With Respect To Gestational Age And Occurrence Of Rop

Gestational age (weeks)	ROP		Total	p-value
	Present	Absent		
28 – 30	7	38	45	0.022
31 – 35	3	47	50	
> 35	1	3	5	

By using Fisher's exact test p-value < 0.05 therefore there is association between occurrence of ROP and gestational age (weeks).Seven neonates between 28-30 weeks had developed ROP out of 45 neonates of that gestational age.

Threeneonates of 31-35 wks gestational age had developed ROP. One neonate of gestational age of > 35 wks had developed ROP. Hence there is association between occurrence of ROP and gestational age.

Table. No. 08: Association Of Risk Factor With Rop

Risk factor		ROP		Total	P-value
		Present	Absent		
Hyperbilirubinemia	Present	6	32	38	0.32
	Absent	5	57	62	
Apnea	Present	4	26	30	0.72
	Absent	7	63	70	
Acidosis	Present	2	16	18	0.99
	Absent	9	73	82	
Septicemia	Present	6	10	16	0.002
	Absent	5	79	84	

Only two neonates (11%) had ROP out of the 18 neonates who had acidosis. Out of 82 neonates who did not have acidosis, 9 neonates (10.9%) had ROP. Six neonates had both hyperbilirubinemia as well as ROP out of 38 neonates who had hyperbilirubinemia. Five neonates had ROP but no hyperbilirubinemia. Four neonates had both apnea as well as ROP out of 30 neonates who had apnea. 7 neonates had ROP but no apnea. Six neonates had both ROP as well as septicaemia out of total 16 neonates, whereas 5 neonates had ROP but no septicaemia and 79 patients had no ROP and no septicaemia. Hence there was a significant association between occurrence of ROP and septicaemia. Whereas there was no association between occurrence of ROP with Hyperbilirubinemia, Apnea and Acidosis.

DISCUSSION

With advances in modern technology like ventilation, high frequency oscillation, use of surfactant, total parental nutrition, preterm, VLBW & extremely low birth weight babies are surviving hence it is important to have surveillance for retinopathy of prematurity.

Out of 100 babies screened 11 babies i.e. 11% developed some stage of ROP. The incidence of ROP is much less as compared to other Indian studies which is about 15.9%.[9,10]. Forty-nine male neonates were screened for ROP and 51 female neonates were screened for ROP out of total 100 neonates.

Many studies have been carried out throughout the world[11,12] suggesting this strong and important risk factor for the genesis of ROP of actual duration and FiO2 delivered to the baby during the course of hospital stay. Thus present study shows that oxygen requirement alone or the duration of oxygen therapy alone is not the only criteria for development of ROP and it is FiO_2 which has an association with ROP The EpiBel study group[9] has shown severe metabolic acidosis due to renal failure as an independent risk factor for ROP. In our study 18 babies out of 100 had acidosis (18%) due to various reasons like hypothermia, electrolyte disturbances, metabolic derangements, respiratory distress syndrome, dehydration, septicaemia.

It has been hypothesized[13] that adult haemoglobin being more capable of releasing oxygen to tissues causes tissue level hyperoxia. The hyperoxia in tissues leads to free oxygen radical release and reflex vasoconstriction leading to cascade of events which lead to ROP. In this study 9 babies received blood product/or exchange transfusion. Three out of 9 babies developed ROP and association was found to be insignificant. So we cannot support the observations made by other Indian studies.[14,15]

In our study 38 % babies among those who were screened had hyperbilirubinemia. None of the babies required exchange transfusions. All the neonates were managed by intensive phototherapy. Probably because of these strategies only 6 % babies with hyperbilirubinemia developed ROP and the association is not statistically significant. In majority of the studies in India[14,15] and abroad, exchange transfusion was an independent risk factor but nothing has been shown about hyperbilirubinemia.

Prematures are prone for apnea of prematurity, obstructive apneas and sepsis. Apnea leads to severe hypoxia, hypoxemia which leads to retinal vasoconstriction which further leads to genesis of ROP. Shohat et al[16] showed that apnea responding to bag and mask ventilation was significant in the development of ROP. Bag & mask ventilation with FiO2 (90%) leads to hyperoxia, thus generating ROP. Four neonates had both apnea as well as ROP out of 30 neonates who had apnea. Seven neonates had ROP but no apnea. Hence there is no association between occurrence of ROP and apnea in our study.

Premature babies often require respiratory support due to various reasons like hyaline membrane disease, septicaemia, birth asphyxia,

apnea of prematurity. Not only high FiO2 administered in ventilation is deleterious but also the duration or the length of O2 exposure in days, nosocomial sepsis has a role in the development of ROP. In our study we found FiO2 requirement of >0.5 was significant.

A study conducted by Vasileios showed that189 infants without congenital anomalies born at GA 24–32 weeks ROP was diagnosed in 24 (12.7%) (> grade 2: 6). interval (CI) 1.3–3.3, $p < 0.01$ and CLD, OR 10.2, CI 2.3–44, $p < 0.01$, respectively, independent of confounding factors. By estimating interaction on an additive scale, it was shown that the combined risk effect of GA and CLD was larger than the sum of the individual risk effects, implying synergistic effect. This study showed that lower the gestational age greater was the risk of developing ROP.[17] In the present study seven neonates between 28-30 weeks had developed ROP out of 45 neonates of that gestational age. Three neonates of 31-35 wks gestational age had developed ROP. One neonate of gestational age of > 35 wks had developed ROP. Hence there is association between occurrence of ROP and gestational age. In this study one neonate out of two of birth weight less than 1000 gms had ROP. Six neonates out of 76 neonates of birth weight between 1000-1500 gms had ROP and 4 neonates out of 12 of birth weight more than 1500 gms had ROP. Hence there is association between occurrence of ROP and low birth weight.

Premature infants with a history sepsis, mechanical ventilation, RDS, and PDA may be at a higher risk for progression of ROP despite diode laser treatment.[18] In our study six neonates had both ROP as well as septicaemia out of total 16 neonates with septicemia, Hence there was an association between occurrence of ROP and septicemia.

In our study 11 out of 100 babies had ROP. Babies who had Stage 1,2 and 3 ROP did not require treatment and the disease had regressed on its own. The baby who had stage 4 ROP had required vitrectomy surgery and had required aphakic glasses by 1 year of age. Early detection can prevent blindness.

All the babies who were diagnosed to have ROP were tested for outcome at 1 year of age. The outcome was assessed from clinical history, tested by visual fixation and fundoscopy. Babies who were diagnosed for stages 1, 2 and 3 had good visual outcome as assessed by good visual fixation and following of objects. The baby who was diagnosed with stage 4 had to use aphakic glasses. The drop out rate in our study was 1% which is comparable to 5 to 6% in other studies. [14,15] Those who did not have ROP, visual outcome was normal. This is compared to most of the studies from India and abroad.[15,19]

CONCLUSION

Low gestational age, low birth weight, septicemia, respiratory therapy in NICU and FiO2 concentration have role in the development of ROP in neonates. If oxygen therapy is meticulously utilised in terms of FiO2, duration and aim saturation of oxygen in blood, then the incidence of ROP may be altered.

We can train the health personnel, the nursing staff and the residents of NICU in order to increase the awareness of this avoidable disease. The disease can be prevented by giving optimal oxygen with pulse-ox and blood gas monitoring, documenting duration of oxygen therapy, maintenance of strict asepsis, judicious use of antibiotics and judicious use of blood product/blood transfusions.

The high preterm birth rate, suboptimal neonatal care which places more mature infants at risks. For the detection and treatment of ROP that threatens vision, high-quality programmes are required. By using a multidisciplinary approach, early detection of high-risk ROP due to numerous reasons can be avoided.

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