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Analysis of Incidence and Risk Factors for Retinopathy of Prematurity among Preterm Neonates in a Tertiary Care Neonatal Unit.

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ABSTRACT

Advances in neonatology has achieved several milestones in reducing the morbidity and mortality among high risk newborns. Preterm care is one such major domain where expanding knowledge and technology has ensured a higher survival chance. Reduced mortality comes but with a greater co incidence of diseases exclusive in preterm neonates like Retinopathy of prematurity, anaemia of prematurity, bronchopulmonary displasia etc. In our study we have made an attempt to identify the incidence and risk factors in preterm neonates associated with the development of ROP.100 preterm neonates who satisfied the inclusion criteria of birth weight ≤1750 grams and ≤34 weeks GA with or without risk factors and birth weight between 1750-2000 grams and 34-36 weeks GA with additional risk factors for ROP were screened in the Neonatal intensive care unit. Out of the 100 babies screened, only 21 babies developed ROP. Lower birth weight and gestational age were significantly associated with the incidence of ROP. Other risk factors that were found to be of statistical significance were oxygen administration, RDS, sepsis, shock and phototherapy by Chi Square analysis. Using multivariate analysis, shock, gestational age and APH were found to be significant factors.

Keywords: retinopathy of prematurity, risk factors, screening, treatment

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INTRODUCTION

Retinopathy of prematurity (ROP), previously known as 'retrolental fibroplasia' because of its end stage appearance is a developmental vaso proliferative disorder that occurs in the retina of preterm infants with incomplete vascular proliferation. Incidence of ROP in India is reported to vary between 38 – 51.9%.[1-3] Out of the approximate 26 million annual live births in India, approximately 8.7 % of newborns are < 2000 grams in weight.[4]

There are about 45 million blind people in India out of which nearly 30 % are in Asia. Of the total blindness, childhood blindness accounts for 4%. India shares 20% of world's childhood blindness.[5] ROP affects 3,00,000 infants worldwide. The incidence of ROP in developing countries like India is reported to be around 24 – 47% among high risk preterms.[6]It is important not only in terms of economic burden but also in its severe social implication, which is very long in terms of blind years.

As regards our country, we are sitting at the summit of two volcanoes – one where all the latest state of the art health care facilities are available and the other, where even the basic health care is unavailable. ROP is known to grow in both these situations. Among the preventable causes of blindness in India, ROP figures very high in the agenda. Low birth weight and gestational age were found to be the most significant risk factor associated with ROP.

With neonatal units being equipped with state of the art technical support and well trained health care providers to provide quality care to the preterm neonates, ROP incidence is on the rise. By recognition of risk factors, early detection and timely intervention, blindness due to ROP is preventable.

Purpose of this study is to know the incidence of ROP and to correlate it with maternal and neonatal risk factors.

MATERIALS AND METHODOLOGY

Inclusion Criteria [7]

Preterm low birth weight babies admitted to NICU at CMCH with

- Gestational age < / = 34 weeks
- Birth weight < / = 1750 gms
- Gestational age between 34 – 36 weeks with risk factors for ROP
- Birth weight between 1750 – 2000 gms with risk factors for ROP

Exclusion Criteria

- Preterm babies who die before reaching the age for screening
- Babies who did not complete the follow up protocol
- Babies with major congenital anomalies / chromosomal anomalies

Study Design

Longitudinal study with short follow up done from October 2012 to September 2013. Data was collected by interviewing parents, from hospital records and by examination of the neonate. Sample size was 100. Variables studied were gestational age, postconceptional age, sex, birth weight, oxygen administration and modes, presence of RDS, surfactant administration, sepsis, shock, anaemia, phototherapy, blood transfusion, exchange transfusion, maternal history of PIH and APH.

Statistical Methods Used

The data are reported as mean ± SD or as median, depending on their distribution. Differences in the quantitative variables between groups were assessed by means of unpaired t test. Comparison between

groups were made by non parametric Mann-Whitney test. Chi square test was used to analyze categorical variables and multivariate analysis was done to test dependent variables. P value of < 0.05 using a two tailed test was taken as statistically significant. All data were analyzed using SPSS software, version 16.0 for windows.

Definition of Risk Factors

Respiratory Distress Syndrome [8]

- Premature infant with clinical signs soon after birth including tachypnoea, retractions, alar nasal flaring, grunting, cyanosis
- X ray evidence : low volume lungs, diffuse reticulo nodular pattern, air bronchogram, white out lung

Apnoea [9]

Cessation of respiration for > 20 seconds or cessation of respiration of any duration when accompanied by bradycardia (< 100 bpm) and/ or cyanosis

Sepsis

- Clinical sepsis : lethargy, refusal feeds, apnoea, hypoglycemia, sclerema, seizures, respiratory distress, altered nasogastric tube aspirate, abdominal distension, shock etc
- Laboratory evidence : positive sepsis screen, culture positive sepsis, thrombocytopenia

Shock

- Pallor in the absence of bleeding, skin mottling, cold and cyanosed extremities, capillary refilling time > 3 seconds, absent peripheral pulses, tachycardia, narrow pulse pressure, fall in mean arterial pressure

Anaemia [10]

- Hematocrit < 40% in ventilated babies, <30% in babies requiring CPAP and <20% in babies breathing room air is taken as anaemia.

Blood Transfusion

- Transfusion of packed cells, platelets, fresh frozen plasma or whole blood

Procedure

After obtaining oral informed consent from the parents, neonate is screened in the NICU using an indirect ophthalmoscope. Baby is preferably fed one hour prior to examination in order to avoid vomiting and aspiration. Pupils are dilated using a combination of cyclopentolate 0.5 % and phenylephrine 2.5 % drops two to three times about 10 – 15 minutes apart. Excess eye drops must be wiped off to avoid systemic absorption. The changes in the retina were graded according to the International Committee for Classification of Retinopathy of Prematurity (ICROP) guidelines 2005.[11](table 1)

Timing of Screening [7]

- First retinal examination is performed not later than 4 weeks postnatal age in infants born > 28 weeks of gestation or 31 weeks of age whichever is later. (table 3)
- Infants born < 28 weeks of gestation and birth weight < 1200 grams are examined at 2 – 3 weeks of postnatal age

Follow Up Protocol [12]

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If no ROP was detected at initial examination, the infants were re-evaluated once every 2 weeks until vascularization is complete. If ROP was detected, the examinations were performed weekly for stage 1-2 disease and more frequently for stage 3 disease, till the disease started resolving or progressed to threshold stage. Babies showing evidence of regression were followed up till vascularization was complete.

RESULTS

Results obtained by Chi Square analysis are shown in table 2. Multivariate analysis is shown in table 3.

Table 1: Classification of ROP

Location	Zone I	Circle with optic nerve in centre and a radius of twice the distance between optic nerve and macula
	Zone II	From edge of Zone 1 to nasal oraserrata nasally and equator temporally
	Zone III	Lateral most cresent shaped area from Zone II to oraserrata temporally
Severity	Stage 1	Presence of thin white demarcation line between the vascular and avascular retina
	Stage 2	The line becomes prominent to become a ridge with length and width
	Stage 3	Presence of extra retinal fibrovascular proliferation arising from the ridge extending into the vitreous
	Stage 4	Partial retinal detachment: not involving the macula (4A) or involving the macula (4B)
	Stage 5	Complete retinal detachment
Plus disease		Presence of dilatation and tortuosity of posterior retinal vessels; associated with vitreous haze and papillary rigidity
Extent		Extent of involvement of retina expressed as clock hours

Table 3: Multivariate Analysis

								95% C.I.for EXP(B)	
		B	S.E.	Wald	Df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	SH(1)	2.480	.777	10.185	1	.001	11.943	2.604	54.777
	Constant	.611	.285	4.596	1	.032	1.842		
Step 2[b]	SH(1)	2.789	.830	11.301	1	.001	16.264	3.199	82.679
	APH(1)	1.513	.684	4.888	1	.027	4.539	1.187	17.351
	Constant	-.626	.635	.974	1	.324	.534		
Step 3[c]	CGA			6.015	2	.049			
	CGA(1)	2.038	.852	5.714	1	.017	7.673	1.443	40.787
	CGA(2)	.982	1.231	.637	1	.425	2.671	.239	29.796
	SH(1)	3.280	1.006	10.634	1	.001	26.565	3.700	190.704
	APH(1)	1.909	.718	7.060	1	.008	6.746	1.650	27.581
	Constant	-2.632	1.074	6.008	1	.014	.072		

a. Variable(s) entered on step 1: SH.
b. Variable(s) entered on step 2: APH.
c. Variable(s) entered on step 3: CGA.

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	ROP PRESENT	ROP ABSENT	P value	ODDS RATIO	CONFIDENCE INTERVAL	
					Low 95% CI	Hi 95% CI
SEX						
Male	43%	57%	0.249(ns)			
Female	57%	43%				
GESTATIONAL AGE						
<30 weeks	24%	8%				
30-34 weeks	67%	72%	0.023(s)			
34 weeks	10%	20%				
BIRTH WEIGHT						
<1000 grams	14%	5%				
1001 - 1500 grams	48%	57%	0.007(s)			
>1501 grams	38%	38%				
OXYGEN						
Bubble CPAP	57%	58%				
Mechanical ventilation	43%	19%	0.013(ns)			
Not given	0%	23%				
RDS						
Present	90%	47%	0.0003(s)	10.784(OR)	2.353	49.432
Absent	10%	53%		7.464(RR)	1.836	30.345
SURFACTANT						
Present	67%	33%	0.005(s)	4.077(OR)	1.468	11.323
Absent	33%	67%		3.000(RR)	1.329	6.773
APNOEA						
Present	33%	22%	0.0259(s)	1.824(OR)	0.636	5.232
Absent	67%	78%		1.583(RR)	0.724	3.463
SEPSIS						
Present	81%	54%	0.027(s)	3.558(OR)	0.997	13.844
Absent	19%	46%		2.833(RR)	0.998	9.640
SHOCK						
Present	90%	44%	0.0002(s)	11.943(OR)	2.604	54.777
Absent	10%	56%		8.093(RR)	1.990	32.914
ANAEMIA						
Present	14%	4%	0.072(ns)	4.222(OR)	0.786	22.672
Absent	86%	96%		2.611(RR)	1.060	6.432
PHOTOTHERAPY						
Present	90%	67%	0.034(s)	4.660(OR)	1.008	21.538
Absent	10%	33%		3.694(RR)	0.920	14.834
BLOOD TRANSFUSION						
Present	62%	44%	0.151(ns)	2.043(OR)	0.691	6.145
Absent	38%	56%		1.760(RR)	0.746	4.343
EXCHANGE TRANSFUSION						
Present	29%	13%	0.077(ns)	2.760(OR)	0.869	8.768
Absent	71%	87%		2.100(RR)	0.961	4.587
PIH						
Present	62%	54%	0.539(ns)	1.360(OR)	0.508	3.646
Absent	38%	46%		1.2779RR)	0.581	2.806
APH						
Present	33%	16%	0.086(ns)	2.538(OR)	0.858	7.511
Absent	67%	84%		2.000(RR)	0.932	4.292

Table 2

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DISCUSSION

The present study reflects the problem of ROP in a tertiary care neonatal unit. Incidence of ROP in the present study is 21%. Out of the 21 babies, only one baby developed ROP requiring surgery and remaining 20 babies developed ROP not requiring surgery (includes both regressing ROP and ROP requiring follow up). Birth weight of ROP babies ranged from 930 – 1750 grams (mean 1363.81±251.41) while that of non ROP babies ranged from 900 – 1900 grams (mean 1396.33±277.42). Lower birth weight was significantly associated with the incidence of ROP ($p = 0.007$). Incidence of ROP was 20 % among babies ≤1500 grams.Incidence of ROP in babies < 34 weeks was found to be 23%. Lower gestational age was found to significantly associated ($p =0.023$) with development of ROP. Gestational age, birth weight, oxygen, respiratory distress syndrome, surfactant, sepsis, shock and phototherapy were found to be significantly associated with ROP by Chi Square analysis. Shock, gestational age and antepartum hemorrhage were found to be significant through multivariate analysis. These results show that ROP incidence is influenced by almost every illness and treatment carried out in the preterm neonate. Effective management of ROP requires a team effort by a pediatrician, ophthalmologist and the NICU staff. Thus implementing an intelligent screening policy in every NICU will help to reduce effectively one of the preventable causes of childhood blindness.

CONCLUSION

Regular screening program that includes all preterm neonates satisfying the screening guidelines should be followed strictly. Along with regular screening, effective control of administration of oxygen, monitoring of oxygen saturation, management of RDS, following strict asepsis and prompt recognition and management of shock with fluids and inotropes and careful administration of phototherapy based on the bilirubin normogram must be followed.

REFERENCES

[1] Charan R,Dogra MR,Gupta A,Narang A. Indian J Ophthalmol 1995;43:123-26.
[2] Gopal L, Sharma T, Ramchandran S, Shanmugasundaram R, Asha V. Indian J Ophthalmol 1995; 43:50-61.
[3] Varughese S, Jain S, Gupta N, Singh S, Tyagi V, Puliyel JM. Indian J Ophthalmol 2001:49:187-88.
[4] National Neonatalogy Forum of India. National Neonatal Perinatal Database. Report for 2003-2003. New Delhi 2005.
[5] Global Initiative for the elimination of Avoidable Blindness Action Plan. 2006-2007.
[6] Seyedeh Khatami et al. Iran J Pediatr 2008;18(2) :137-142.
[7] Retinopathy of Prematurity. Clinical practice guidelines. National neonatology forum. October 2010 ; 253-55
[8] John P Cloharty. Respiratory distress syndrome. Manual of Neonatal Care. 7th Edition; 406-407
[9] John P Cloharty. Apnea. Manual of Neonatal Care. 7th Edition; 397
[10] Janie M Rennie. Rennie and Roberton's Textbook of Neonatology, 5th edition. Chapter 30
[11] Arch Ophthalmol 2005;123:991–999
[12] American Academy of Pediatrics, Screening examination of premature infants for Retinopathy of Prematurity. Pediatrics; 117: 572-576