RESEARCH PAPER

Profile of Retinopathy of Prematurity in Outborn and Inborn Babies at a Tertiary Eye Care Hospital

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Objective: To study the profile of retinopathy of prematurity (ROP) among outborn and inborn babies at a tertiary-care centre. **Methodology**: In a prospective observational study from 2015-2016, outborn and inborn babies eligible for ROP screening were evaluated for ROP profile and treatment results. **Results**: 532 outborns and 38 inborns had ROP. Respiratory distress, sepsis and apnea were present in 81.3%, 51.5% and 36.2% of outborns with ROP and 68.4%, 39.4% and 36.8% of inborns with ROP. Type 1 ROP was noted in 49.2% eyes of outborns with ROP and 36.8% eyes of inborns with ROP. Type 1 ROP regressed with laser in 97.3% and 100% eyes of outborn and inborn with ROP, respectively. Stage 4, 5 and sequelae were noted in 5.2%, 22.8% and 4.6% eyes of outborns with ROP, respectively, but none in inborns. **Conclusions:** Quality neonatal care and timely screening ensured lesser ROP-related morbidity in inborns as compared to outborns.

Keywords: *Blindness, Referral, Screening, Surgery*.

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Improved neonatal care of preterm babies has led to a reduction in mortality, but due to unrestricted use of supplemental oxygen there is a significant increase in retinopathy of prematurity (ROP), the so-called third epidemic in middle income countries [1].

The quality of neonatal care, neonatologist-ophthalmologist coordination, timely ROP screening and management may prevent advanced ROP, with recent studies showing lower rates of ROP ranging from 20% to 30% [2-4]. This study was conducted to determine the difference in ROP profile of inborn and outborn babies with respect to risk factors, diagnosis at presentation, treatment given and outcomes.

METHODS

The study was conducted at our tertiary eye-care centre and Neonatal intensive care unit (NICU) associated with the same hospital, from May, 2015 to May, 2016. The study was approved from the Institutional review board and adhered to the Declaration of Helsinki guidelines. Informed written consent was taken from the parents to participate in the study.

We studied the risk factors for ROP, demographics and screening referrals of ROP from the discharge summary or by interviewing the caregivers. Records were requested from the NICU, if unavailable. Outborn babies (referred from other health facilities to our centre) were screened for ROP as per the National Neonatology Forum (NNF) of India guidelines (<1750g; <34 week or 1750-2000 g or 34-36 week in babies with co-morbidities) [5], and inborn babies (born at level 3 nursery of our hospital) were screened as per our hospital NICU protocol (<1500g; <32 week or 1500-2000 g or 32-34 week with co-morbidities).

The babies were examined with indirect ophthalmoscope and Retcam wide field imaging system. Diagnosis at presentation was documented as per International classification of ROP (ICROP), 2005 [6]. The treatment was given as per early treatment of ROP (ETROP) guidelines [7]. As per these guidelines, type 1 ROP includes (*a*) Zone 1 any stage with plus disease; and (*b*) Zone 1 stage 3 without plus disease and (*c*) Zone 2 stage 2/3 with plus disease; and requires intervention. Type 2 ROP includes (*a*) Zone 1 stage 1/2 without plus disease, and (*b*) Zone 2 stage 3 without plus disease; and requires observation [7]. Advanced ROP cases such as stage 4 and 5 ROP underwent surgical management.

The data were entered in a predesigned proforma and analyzed using SPSS Version 23 (SPSS Inc. Chicago, IL, USA). Due to variability in baseline characteristics, risk factors were evaluated separately for ROP cases in outborns and inborn babies. The categorical risk factors were subjected to the Pearson chi-square test for

comparison between the groups.

RESULTS

A total of 722 outborn babies were referred among which 532 (73.6%) babies had ROP; 22.6% (*n*=38) of 168 inborn babies screened in NICU developed ROP.

The mean (SD) birthweight [1354.8 (376.3) g *vs* 1122.2 (271.2) g; *P*=0.0002] and gestational age [30.7 (2.7) week *vs* 29.6 (2) week; *P*=0.014] were higher/similar between outborn and inborn babies with ROP, respectively. Respiratory distress syndrome (RDS), sepsis, and apnea of prematurity (AOP) were the most commonly associated risk factors in both inborn and outborn ROP babies (***Table* I**).

Among the outborn group, type 2 ROP or less was seen in 192 (18%) eyes which spontaneously regressed on follow up. All the eyes with type 1 ROP (524 eyes, 49.2%) regressed following interventions like laser and anti-VEGF therapy. Out of 76 inborn eyes, 48 eyes (63.1%) were type 2 ROP or less and 28 eyes (36.8%) were type 1 ROP, which required only laser therapy and regressed (***Table* II**).

Median age for referral of outborns was 39 (range 29 to 316) weeks. Only 66.9% (*n*=483/722) babies had been advised ROP screening among outborns, out of which 219 (30.3%) were screened late. All inborn babies were advised timely ROP screening within 4 weeks by the pediatricians and were screened timely by the ophthalmologists.

DISCUSSION

The proportion of ROP was 22.6% with no case of severe/advanced ROP amongst the inborn babies. However, a much higher prevalence of ROP was found among outborn babies with a high proportion of advanced ROP due to the large number of referrals to our center.

Respiratory distress syndrome (RDS), sepsis and apnea of prematurity (AOP) were the main risk factors found in both the groups. These risk factors likely increase the chances of neonatal mortality, long NICU stay and high oxygen exposure, which increases the risk for severe ROP [8]. Although, a safe level of oxygen supplementation has not yet been defined, in our NICU we target a arterial oxygen saturation between 90-95% to avoid hyperoxia.

In our study, we saw a spectrum of ROP from milder forms to severe/advanced forms like type 1 ROP and stage 4 requiring immediate intervention (laser or anti-VEGF drugs or surgery). In our study, most outborn (97.3%) and inborn (100%) babies who underwent laser therapy as per ETROP guidelines had regressed ROP after the procedure. Anti-VEGF drug (Bevacizumab) was used in selected cases of zone I disease with informed parental consent. Though multiple studies have been done on efficacy of anti-VEGF agents in ROP, its safety profile has still not been fully established [9]. Operated stage 4 cases had good anatomical outcome while the outcomes were poor in stage 5 cases wherever surgery was attempted. Cases with sequalae were not operated in view of limited further visual potential. Though advanced ROP and its sequelae were not seen among the inborn babies due to timely treatment, a large number (32.7%) of outborn babies had advanced ROP or its sequelae. This clearly shows the importance of pediatrician-ophthalmologist coordination, early ROP screening and appropriate treatment to halt the progression of the disease to severe forms. Sicker babies who are not able to be screened and treated in peripheral cities are referred to tertiary eye care centres at a later stage and hence the ratio of severe cases among outborn and inborn babies is more [10].

Table I Neonatal Systemic Risk Factors in Babies Diagnosed With Retinopathy of Prematurity (*N*=570)

Risk factors	*Outborn babies with ROP (n=532)*	*Inborn babies with ROP (n=38)*
RDS	433 (81.3)	26 (68.4)
Sepsis	274 (51.5)	14 (36.8)
AOP	193 (36.2)	15 (39.4)
PDA	40 (7.5)	8 (21)
NEC	39 (7.3)	5 (13.1)
HIE	22 (4.1)	4 (10.5)
Seizures	20 (3.7)	3 (7.8)
TTN	11 (2.0)	14 (36.8)

All values in no. (%). RDS: Respiratory distress syndrome, TTN: Transient tachypnea of newborn, AOP: Apnea of prematurity, PDA: Patent ductus arteriosus, HIE: Hypoxic ischemic encephalopathy, NEC: Necrotizing enterocolitis.

Table II Profile of Retinopathy of Prematurity in Outborn and Inborn Babies (*N*=570)

Outcomes/treatment	*Outborn babies (n=1064 eyes)*	*Inborn babies (n =76 eyes)*
Type 2 ROP/Follow up	192 (18)	48 (63.1)
Type I ROP		
Laser	510 (47.9)	28 (36.8)
Laser plus anti-VEGF	14 (1.3)	0
Stage 4 ROP/Surgery	56 (5.2)	0
Stage 5 ROP		
Surgery attempted	88 (8.2)	0
Surgery not attempted	155 (14.5)	0
ROP sequalae	49 (4.6)	0

All values in no. (%); ROP: Retinopathy of prematurity; VEGF: Vascular endothelial growth factor.

WHAT THIS STUDY ADDS?

Inborn babies with appropriate neonatal care and timely screening/management of ROP did not develop or progress to severe/advanced stages of ROP, unlike outborn babies.

We found that 33.1% babies were never advised screening and 30.3% were screened late for ROP, showing the lack of awareness and structured protocol for ROP screening and referral in many centers. A pilot survey in Northern India showed that 34% of pedia-tricians never referred babies for ROP screening from their NICU and only 14.5% of pediatricians were following international guidelines for ROP [11]. Similar results were shown in another study conducted in stage 5 ROP where none of the babies were referred by their pediatricians for ROP screening [12]. Another study showed that the lack of awareness and compromise in screening and manage-ment leads to large number of stage 5 ROP cases being referred to tertiary eye care centres [13].

The major limitation of this study is the study design, which makes comparison between inborn and outborn cases difficult due to the missing information in outborn babies and their selective referral with higher stages of ROP. Since our center is a tertiary care referral facility, a larger number of babies are referred for advanced management which could account for a higher number of advanced ROP seen in the outborn group. A large multi-centre country wide study may be able to better estimate the true incidence and causal relationship between the risk factors leading to advanced ROP.

Superior NICU care and management practices can prevent development of ROP and reduce disease severity [14]. Health planners need to address the urgent need to establish effective ROP screening and treatment services as well as develop good neonatal services across the country.

Ethical clearance: Institutional Ethical Committee, AIIMS, New Delhi; No. IESC/T-01/21.01.2015, RT-18, dated April 1, 2015.
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