RESEARCH BRIEF

Risk of Retinopathy of Prematurity in Small for Gestational Age Premature Infants

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Objectives: To evaluate the incidence, risk factors and severity of retinopathy of prematurity in neonatal intensive care unit and to evaluate its relationship with gestational age.

Methods: Cohort study of neonates with gestational age ≤32 weeks or birthweight ≤1500g.

Results: Of the 495 neonates screened, 43 (8.7%) infants were small for gestational age; the frequency of severe retinopathy of prematurity was 5.8%. Sepsis and being small for gestational age were independent risk factors for severe retinopathy of prematurity.

Conclusions: Clinicians should be aware of the presence of presence of retinopathy of prematurity when caring for protein small for gestational age infants.

Keywords: *Intrauterine growth retardation, Prematurity, Retina*.

Retinopathy of prematurity (ROP) is a major cause of preventable blindness in children all over the world [1]. Although the etiology of ROP is multifactorial, low birth weight (BW) and low gestational age (GA) are recognised as the most important risk factors [2]. Small for gestational age (SGA) infants have a greater risk for mortality and morbidity than appropriate for gestational age (AGA) infants [3,4]. The influence of being SGA on the retinopathy of prematurity is controversial with some studies reporting higher risk [4-6]. We aimed to evaluate the incidence, risk factors and severity of ROP and the relationship between SGA and retinopathy.

METHODS

In this prospective study, preterm infants born with birth weight ≤1500 g or gestational age ≤32 weeks at Etlik Zubeyde Haním Women's Health Teaching and Research Hospital, Ankara, Turkey, between January 2011 and January 2013 were recruited. Infants with lethal congenital anomalies, those who died or were lost to follow-up before development of threshold ROP/full vascularization of the retina were also excluded.

The first eye examination was performed at 4 weeks of chronologic age for infants born at ≥27 weeks or at 31 weeks of postmenstrual age for infants born at 22 to 26 weeks. Severe ROP was defined as that needing treatment. The criteria for treatment were: zone I any stage of ROP with plus disease or zone I stage 3 without plus and zone 2 stage 2 or 3 with plus disease (Type 1 ROP) as defined by Early Treatment for Retinopathy of Prematurity Cooperative Group [7]. Staging of ROP was recorded according to the International classification of ROP [8].

SGA was defined as birth weight below 10th percentile according to intrauterine growth charts of Usher and McClean [9]. The data recorded for each neonate included maternal, perinatal and postnatal characteristics.

Statistical analyses were conducted using the SPSS version 17.0 (SPSS Inc., Chicago, IL).

RESULTS

During the study period, complete clinical and eye examination data were available for 495 patients. Mean (SD) BW and GA for the cohort was 1266.8 (278.3) g (range 600-1690g) and 29.3 (2.1) weeks (range 23-33 weeks), respectively. Any stage of ROP was detected in 140 babies (28.2%), and severe ROP occurred in 29 (5.8%) babies. During the study period, 43 (8.7%) infants admitted to our NICU were SGA.

Risk factors for severe ROP were analyzed in patients ≤32 weeks GA or ≤1500 g BW (*n*=495) (***Table* I**). Amongst morbidity variables examined, all were found significantly more frequent in the neonates with severe ROP.

In the logistic regression model, presence of sepsis (Adjusted OR 3.8, 95% (I 1.6-9.1; *P* =0.002) and being SGA were (Adjusted OR 3.0, 95% (I 1.0-9.3; *P* =0.049) independent risk factors for severe ROP

TABLE I CHARACTERISTICS AND RISK FACTORS FOR SEVERE ROP IN THE STUDY SUBJECTS

	No ROP+mild ROP (n=466)	*Severe ROP (n=29)*	*PValue*
Gestational age (wks)	29.47 (1.98)	27.10 (2.14)	<0.001
Birth weight (g)	1289.9 (276.3)	965.3 (244.7)	<0.001
Sex (F/M)	232/234	14/15	0.875
Delivery(C/S/VD)	369/97	22/9	0.670
Small for gestational age	38 (8.2%)	5 (17.2%)	0.096
Multiple gestation	142 (30.5%)	8 (27.6%)	0.743
In vitro fertilization	46 (9.9%)	5 (17.2%)	0.206
Resuscitation at birth	124 (26.6%)	18 (62.1%)	<0.001
5 minute APGAR score	8 6	<0.001	
Maternal age (y)	28.1 (5.7)	29.1 (7.0)	0.665
Antenatal steroids	255 (54.7%)	18 (62.1%)	0.440
Preeclampsia	102 (21.9%)	6 (20.7%)	0.875
PPROM	78 (16.7%)	2 (6.9%)	0.201
Chorioamnionitis	27 (5.8%)	4 (13.8%)	0.101
Gestational diabetes mellitus	20 (4.3%)	0	0.622
Days on mechanical ventilation	1.1 (3.0)	8.1 (12.7)	<0.001
Days on nasal CPAP	2.5 (3.8)	9.6 (7.5)	<0.001
Days on supplemantal O_2	10.6 (15.8)	31.1 (31.4)	<0.001
Respiratory distress syndrome	201 (43.1%)	23 (79.3%)	<0.001
Patent ductus arteriosus	71 (15.2%)	11(37.9%)	0.004
Sepsis	63 (13.5%)	14 (48.3%)	<0.001
Intra-ventricular hemorrhage	25 (5.4%)	5 (17.2%)	<0.001
Necrotizing enterocolitis	4	3 (10.3%)	0.005
≥2 transfusions	58 (12.4%)	14 (48.3%)	<0.001
Duration of TPN infusion (d)	16.1 (9.7)	23.8 (15.9)	<0.001
Time to regain birth weight (d)	11.03 (5.04)	13.97 (9.39)	<0.001

PPROM: preterm premature rupture of membranes; Values in Mean (SD) or No. (%).

DISCUSSION

In the present study, the incidence of any stage of ROP was 28.2% and severe ROP was 5.8% in babies ≤1500 g birth weight or ≤32 weeks gestational age. Sepsis and being SGA were independently related with the presence of severe ROP.

The observed association of low GA or BW with ROP is in agreement with the most of the other studies [2,10]. Recent studies showed ROP incidence is higher in SGA infants than AGA infants [4,5,11]. Factors that may be responsible for the increased risk of severe ROP and the rapidity of its development in SGA babies include chronic uterine hypoxia, abnormal growth factor levels, antioxidant deficiency, and free oxygen radicals in utero [3,12,13].

Allegaert, *et al*. [5] from a tertiary neonatal intensive care unit in Belgium reported SGA infants were 3.7 times more likely to develop threshold ROP than their AGA peers. On the other hand, a cohort from Brazil reported that being SGA was not a significant risk factor for any stage of ROP or severe ROP [14].

The incidence of fetal growth restriction varies among populations and increases with decreasing gestational age. The limitations of our study include a small sample size and absence of AGA controls. In conclusion, preterm SGA infants are at higher risk of developing severe ROP. Clinicians should be aware of the presence of this morbidity when caring for preterm SGA infants.

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WHAT THIS STUDY ADDS?

- Preterm SGA infants are more likely to develop severe ROP.

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