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A study on the incidence of retinopathy of prematurity in small and appropriate for gestational age babies

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Abstract

Background: Retinopathy of prematurity is a significant contributor to the magnitude of preventable childhood blindness in developing countries. Its initially low incidence in India is now increasing as a result of improved screening procedures and higher preterm infant survival rates. The incidence of Retinopathy of prematurity and its risk factors must therefore be studied in detail to plan effective preventive measures.

Methodology: This prospective analytical study was done in the Ophthalmology department of Coimbatore medical college hospital from January 2022- December 2022. 200 babies who fulfilled the inclusion criteria (birth weight < 2000 grams, gestational age <34 weeks and gestational age between 34 to 36 weeks but with risk factors) were selected and divided into two categories - appropriate for gestational age and small for gestational age. Incidence, systemic risk factors and severity of Retinopathy of prematurity in both groups were analyzed.

Results: The overall incidence of Retinopathy of prematurity in the screened population was 32%. Small for Gestational Age was found to be significant risk factor for developing the disease. More mature babies being affected in this group when compared to their appropriate for gestational age peers. The risk factors for the disease were found to be almost similar in both

groups. Significant risk factors were multiple pregnancy, oxygen supplementation, apnea and sepsis.

Conclusion: Small for gestational age infants are at greater risk of developing Retinopathy of prematurity. So, these babies must be provided special attention in regard to supplemental oxygen use, aseptic precautions while handling, vigorous screening for early detection and prompt treatment upon diagnosis.

Keywords: Retinopathy of prematurity, incidence, small for gestation.

Introduction

Retinopathy of prematurity (ROP), a Vaso proliferative condition that affects preterm babies, can range from an innocuous presentation that doesn't cause any vision loss to an advanced disease that causes permanent blindness.[1] presently India is witnessing its third epidemic of rop-induced blindness.[2]

The initially low incidence of rop in India is now increasing as a result of improved screening procedures and higher preterm infant survival rates, lack of equipment such as oxygen-blenders and pulse oximeters necessary for safe use of supplemental oxygen in premature babies, lack of routine screening protocol for rop in rural areas, lack of trained personnel for rop screening, and lack of ophthalmologists to promptly initiate treatment when infants develop severe rop.

Apart from low birth weight and low gestational age, rop development is influenced by a number of variables like respiratory distress syndrome, apnea, unregulated oxygen use, chronic lung disease, foetal hemorrhage, sepsis, blood transfusion, patent ductus arteriosus, multiple pregnancy etc.

Sga also forms a part of the extensive list of risk factors mentioned above, according to studies. The occurrence of rop in small and appropriate for gestational age preterm newborns must therefore be compared and analyzed.

Aims and objectives

This study aims to compare the risk factors, incidence and severity of rop in small and appropriate for gestation babies.

Review of literature

In a study done in north Kerala, Ratheesh et al they observed that the incidence of rop is higher in sga babies compared to aga babies.

A study in central Maharashtra by Thakre et al concluded that the incidence of rop was higher in sga infants compared to aga infants. However, there was no difference in the risk factors and severity of rop between the two groups.

Kavurt et al. (28.2% incidence of rop in sga) and raj et al. (40% incidence of rop in sga) have also observed sga as a significant risk factor for the development of rop.[5]

Dhaliwal et al. Have also observed sga as a significant risk factor for the development of rop in their study.[6]

A systematic review[7] concluded that sga is a strong risk factor for the development of any stage as well as rop needing treatment.

Lundgren et al. [8,9] observed that infants born more mature but are growth restricted are more prone to develop rop.

Methods and materials

This prospective analytical study was done in the ophthalmology department of Coimbatore medical college hospital from January 2022- December 2022(12 months). 200 babies who fulfilled the inclusion criteria were included in the study. The study was approved by the institutional ethics committee and adhered to the guidelines of the declaration of Helsinki. Informed

consent was obtained from parents of all neonates included in the study.

Inclusion criteria

- Birth weight less than 2000 grams
- Gestational age less than 34 weeks
- Gestational age between 34 to 36 weeks but with risk factors such as cardio-respiratory support, prolonged oxygen therapy, respiratory distress syndrome, chronic lung disease, fetal hemorrhage, blood transfusion, neonatal sepsis, exchange transfusion, intraventricular hemorrhage, apnea.

Exclusion criteria

- Babies born at >34 weeks of gestational age and >2000 grams without risk factors.
- Patients/guardians not willing to enrol for study.

Methodology

The newborns were examined at 4 weeks after birth for the first screening or at 3 weeks after delivery if they were < 1200 grams or <28 weeks gestation. Following dilatation with 0.4% tropicamide with 2.5% phenylephrine eye-drops, the study population was examined for rop using an indirect ophthalmoscope and 20d lens under topical anesthesia monitoring vital signs.

All the preterm neonates included in the study were divided into two categories — appropriate for gestational age (aga) and small for gestational age (sga) using fenton's criteria [10]

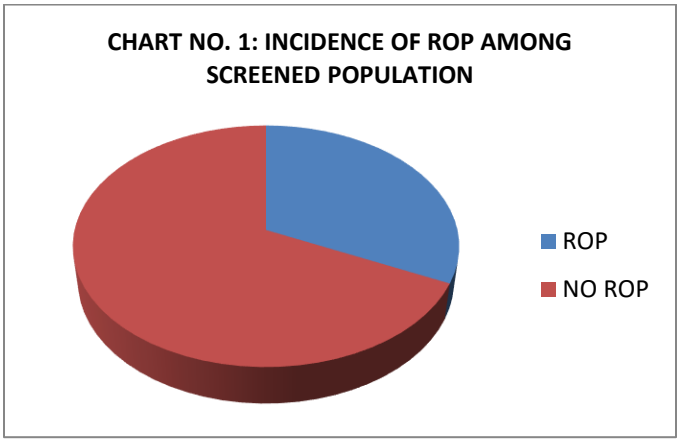
Systemic risk factors and ocular examination findings were documented.

Anterior segment problems if any, like rubeosis iridis, corneal abnormalities, secondary glaucoma, and cataractous lens were noted. Rop was categorized in accordance with the revised international classification of retinopathy of prematurity. Regular screening was continued at frequent intervals until the retina was entirely vascularized, rop has fully regressed, or till there were no warning signals for risk of vision loss.

All babies diagnosed with type 1 rop were treated as per early treatment of rop protocol (etrop), while those with aggressive posterior rop (aprop) were treated with intravitreal anti-vegf agents after taking informed consent. Collected data was compiled in an ms excel sheet. The collected data were analyzed with statistical packages for social science v.20 (spss). Quantitative data are represented in the form of mean and standard deviation. Odds ratio, univariate analysis, and chi-square test were applied to analyse the significant association between risk factors and rop development. P-value was checked at a 5% level of significance.

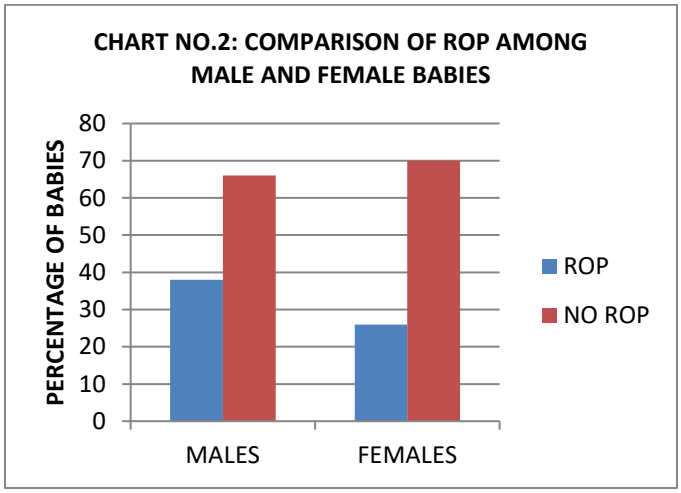
Results

200 preterm neonates met the screening criteria in the study. The incidence of rop was found to be 32% (64 out of 200) in the study population.

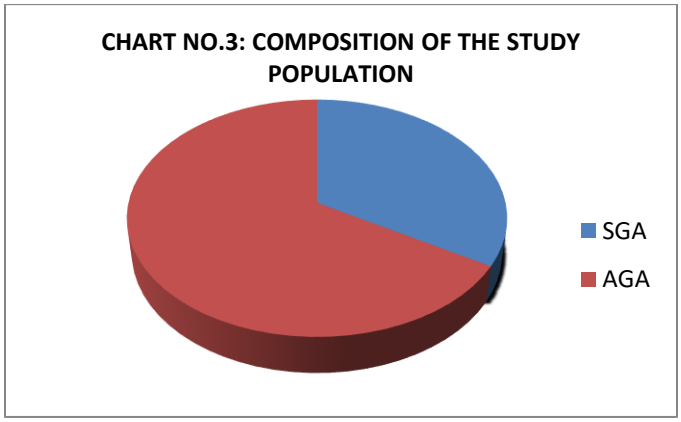


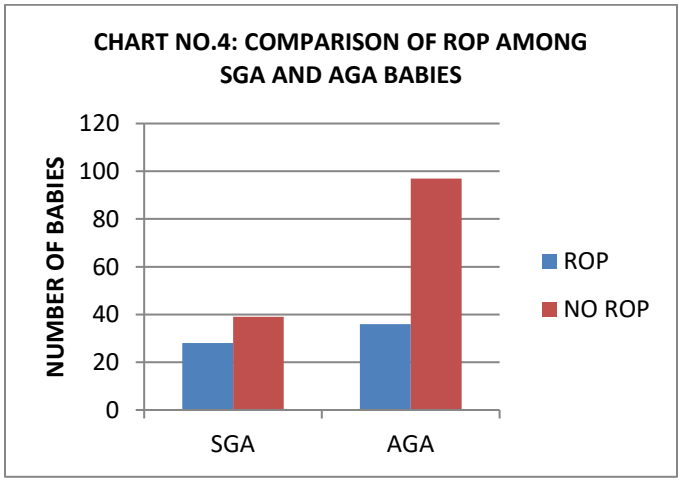
Among the study population, males comprised 52% and females 48%.

38 male babies (36.5%) and 26 female babies (27.1%) developed ROP. There was no statistically significant association between male and female gender for the occurrence of ROP. (P value 0.152113, X2: 2.0509)



Among the 200 babies, 67(33.5%) were SGA and 133(66.5%) were AGA infants. The incidence of ROP in the SGA group was 41% (28 out of 67) and in the AGA group was 27.1% (36 out of 133). This was statistically significant (p = 0.035; result significant at p < 0.05) .





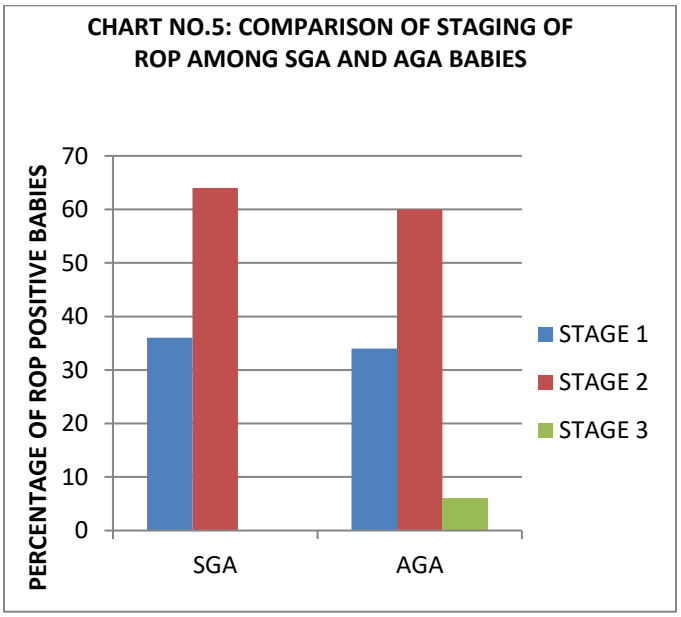
Out of 64 neonates who developed Retinopathy of prematurity,23, 39 and 2 babies were in stage 1, stage 2 and stage 3 respectively. Stage 2 was the most common out of all stages. Plus, disease was noted in 2 SGA babies and APROP in 1AGA baby.

Of the 28 ROP positive SGA infants, 10(36%) and 18(64%) babies developed Stage 1 and 2 ROP respectively.

Table 1: Comparison of Staging of Rop Among Sga and Aga Babies

	STAGE 1	STAGE2	STAGE3
SGA	10(36%)	18(64%)	0
AGA	13(36%)	21(59%)	2(5%)

Of the 36 ROP positive AGA infants, 13(36%),21(59%) and 2(5%) babies developed Stage 1, 2 and 3 ROP respectively.

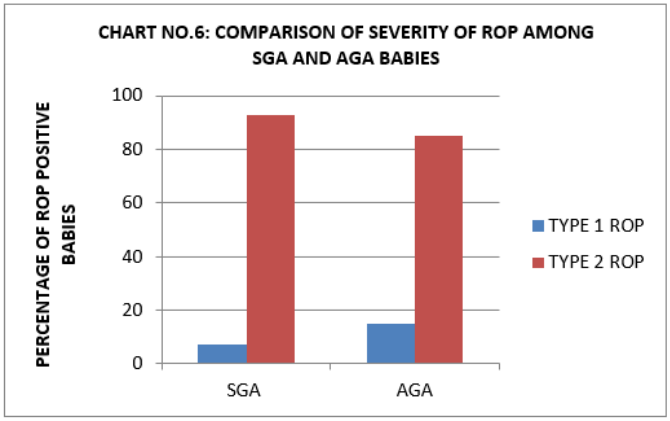


While in zone wise distribution, out of 64 cases of ROP, 4 (6.3%) cases were in zone 1, 28(43.8%) cases were in zone 2, 32(50%) cases were in zone 3. Maximum incidence of ROP was seen in zone 3.

ROP was classified according to ETROP guidelines. There were no cases of threshold ROP. Pre-threshold ROP cases were divided into Type1 and 2 as follows:

Table 2: Comparison of Severity of Rop Among Sga and Aga Babies

	Type 1 Rop	Type 2 Rop
SGA	2(7%)	26(93%)
AGA	6(15%)	30(85%)

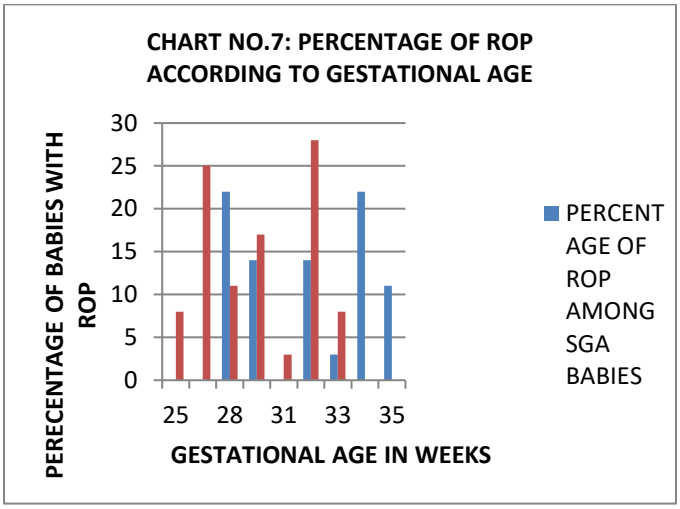


Type 1 ROP was seen in 8/64 babies. The incidence of type 1 ROP in SGA and AGA groups was 7% and 15%, respectively, with 2/28 babies in the SGA group and 6/36 babies in the AGA group having treatable ROP. But this was not statistically significant (p value 0.4485).

Retinopathy of prematurity was observed in babies with higher gestational age (32.57 weeks; p = 0.008) in the SGA group as compared to the AGA group where it was babies with lesser gestational age (29.4 weeks; p = 0.006)

Table 3: Incidence of Retinopathy of Prematurity (Rop) According To Gestational Age In Sga And Aga Babies

Gestational Age [weeks]	No. of ROP positive babies in the specified Gestational Age	Mean GA	T-value	P-value
SGA				
28	6(22%)	32.57	2.446911851	0.00896758
30	4(14%)			
32	4(14%)			
33	1(3%)			
34	6(22%)			
35	3(11%)			
36	4(14%)			
AGA				
25	3(8%)	29.43	2.446911851	0.00630462
27	9(25%)			
28	4(11%)			
30	6(17%)			
31	1(3%)			
32	10(28%)			
33	3(8%)			

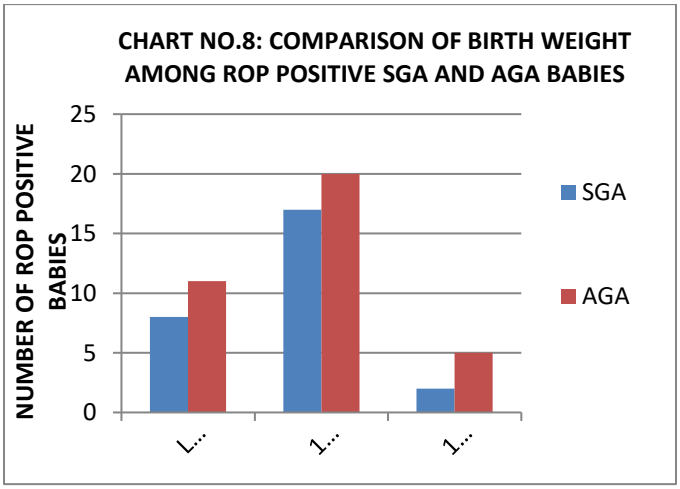


The mean birth weight was lower amongst ROP positive infants (1081 grams in the SGA group and 1180 grams in the AGA group) when compared to ROP negative babies (1332 g in the SGA group and 1507 g in the AGA group) in both groups. Though the mean birth weight was more in ROP positive AGA group it was not statistically significant.

Table 4: Comparison of birth weight among ROP positive SGA and aga babies

Birth Weight [grams]	Number ROP positive babies with the specified birth weight	Number of ROP negative babies with the specified birth weight	Mean birth weight of ROP positive babies[grams]	Mean birth weight of ROP negative babies[grams]
SGA				
Less than 1000gms	8	4	1081.6	1332.62
1000-	17	19		

1500gms				
1500-2000gms	2	10		
More than 2000gms	-	6		
AGA				
Less than 1000gms	11	18	1180.83	1507.89
1000-1500gms	20	34		
1500-2000gms	5	38		
More than 2000gms	-	7		



On univariate analysis, the risk factors for ROP in both the SGA and AGA groups were almost similar. Risk factors like multiple pregnancy, oxygen supplementation, apnea and sepsis were found to be significant in both groups.

Table 5: Risk Factor Analysis Among Sga and Aga Babies

Sn.	Risk Factors	SGA babies		AGA babies	
		ROP positive	p value	ROP positive	p value
	Multiple pregnancy	9/28	0.04	12/36	0.043
	Respiratory distress	8/28	0.03	4/36	0.06
	Oxygen supplementation	10/28	0.007	6/36	0.01
	Apnea	4/28	0.04	9/36	0.03
	Sepsis	8/28	0.03	12/36	0.04
	Fetal distress	2/28	0.06	5/36	0.06
	Anaemia	6/28	0.04	4/36	0.09
	Blood transfusion	6/28	0.07	6/36	0.10
	Thrombocytopenia	4/28	0.06	3/36	0.07

Discussion

The overall incidence of ROP in the screened population was 32%. This was in agreement with the results of many Indian studies, wherein the incidence of ROP varied—46%, 47%, 21.7%, 21%, and 22.3% in studies conducted by Charan et al[11], Rekha et al[12] , Gupta et al[13] and Dutta et al.[14]

Males and females were almost equally affected.

There was a statistically significant difference in the incidence of ROP in the SGA group (41%) when compared to the AGA group(27.1%) . Thus being Small for Gestational Age was found to be significant risk factor for developing ROP. This was in agreement with the study done in North Kerala,by Ratheesh et al[3] where they observed that the incidence of ROP is higher in SGA babies compared to AGA babies.

Another study in Central Maharashtra by Thakre et al[4] concluded that the incidence of ROP was higher in SGA infants compared to AGA infants. Kavurt et al. (28.2% incidence of ROP in SGA) and Raj et al. (40% incidence of ROP in SGA) have also observed SGA as a significant risk factor for the development of ROP.[5] Chronic uterine hypoxia, abnormally high oxygen free radicals and deficient antioxidants are some of the factors that may contribute to the severity and the rapidity of ROP progression in SGA infants[18]. These babies are typically sicker, necessitating a longer stay in the intensive care units and sometimes more oxygen

support. Additionally, they have reduced levels of insulin-like growth factor 1 (IGF1), which is a crucial element in the pathophysiology of ROP.

The incidence of type 1 ROP in SGA and AGA groups was 7% and 15%, respectively. While the incidence of ROP was more in the SGA group, the AGA group developed severe ROP. But this could not be proved statistically and hence cannot be extrapolated into population studies. In their study, Thakre et al also concluded that there was no difference in the severity of ROP between the two groups.

Allegaert, et al. [16] 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 [17].

In the SGA group, more mature babies (Mean gestational age- 32.57 weeks) developed ROP when compared to their AGA peers only where less mature babies got affected. (Mean gestational age- 29.4 weeks). Lundgren et al. [(8,9)] in their study also observed that infants born more mature but are growth restricted are more prone to develop ROP.

The mean birth weight was lower amongst ROP positive babies in both groups when compared to the ROP negative babies.

The risk factors for ROP were found to be almost similar in the SGA and AGA groups. Significant risk factors were multiple pregnancy, oxygen supplementation, apnea and sepsis. These findings corroborate with the above-mentioned studies

The limitations of our study include a small sample size and lack of appropriate age matched controls.

SUMMARY AND CONCLUSION

In conclusion, preterm SGA infants are at greater risk of developing ROP. However, the risk factors and the severity of ROP were found to be almost similar between the two groups. Thus, SGA being a high risk group, can be provided better care like giving them monitored oxygen therapy, maintaining strict aseptic precautions while handling them, and stressing on their postnatal weight gain as all these measures have already been proved helpful to prevent ROP.

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