A STUDY ON ASSOCIATION OF MATERNAL PREECLAMPSIA AND RETINOPATHY OF PREMATUREITY

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ABSTRACT

BACKGROUND

With improved neonatal care and better survival rate of premature babies, incidence of Retinopathy of Prematurity (ROP) in our country is on the increasing trend. As we know there are many foetal and maternal risk factors influencing the development of ROP, not all preterm babies develop ROP.

MATERIALS AND METHODS

The aim of this study is to determine the effect of maternal pre-eclampsia on development and severity of ROP among preterm babies delivered in our Govt. Rajaji Hospital; 200 babies with birth weight less than 1750 grams and less than 34 weeks of gestation were taken up for this prospective observational study. Babies of mothers with gestational hypertension, eclampsia, chronic hypertension, preeclampsia superimposed on chronic hypertension, babies with congenital anomalies and who expired before completion of ROP screening were excluded.

RESULTS

Among 140 babies of normotensive mothers and 60 babies of preeclampsia mothers, 43.6% and 45% had developed any stage of ROP respectively. Incidence of severe ROP in babies of normotensive mothers was 13.6%, whereas it was 3.3% in babies of preeclampsia mothers. Statistical analysis done using student's t-test, "P" value was found to be < 0.05.

CONCLUSION

We conclude that maternal preeclampsia is a protective factor for the development of severe ROP.

KEYWORDS

Preeclampsia, Prematurity Retinopathy, Gestational Hypertension.

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BACKGROUND

Retinopathy of Prematurity (ROP) is a disease characterised by abnormalities in the vascular development of retina in premature infants. With improved neonatal care and better survival rate of premature babies, incidence of ROP in our country is on the increasing trend. ROP incidence increases¹ with decreasing Gestational Age (GA) and Birth Weight (BW); however, not in all preterm babies. So, there might be other foetal and/or maternal risk factors influencing the development of ROP. These factors may protect or increase the probability of development of ROP.

Preeclampsia is one of the leading causes of maternal and foetal morbidities and mortalities with increased incidence of preterm deliveries. Angiogenic imbalance plays an important role in pathogenesis² of both preeclampsia and development of ROP. Thus, aim of our study is to determine the effect of maternal preeclampsia on both development and severity of ROP in our hospital.

MATERIALS AND METHODS

A prospective observational study was conducted at Ophthalmology Department and Neonatal Intensive Care Unit (NICU) of Government Rajaji Hospital, Madurai, in babies fulfilling eligibility criteria for a period of one year. Babies born less than 34 weeks gestation and BW less than 1750 grams were included for the study. Babies of mothers with gestational hypertension, eclampsia, chronic hypertension, preeclampsia superimposed on chronic hypertension, babies with congenital anomalies, babies expired before the completion of ROP screening were excluded from this study. Preeclampsia³ is defined as a diastolic blood pressure of greater than 90 mmHg accompanied by proteinuria of at least 1+ (30 mg per decilitre) in random urine sample after 20

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weeks of pregnancy. GA is calculated according to last menstrual period or first trimester ultrasonogram.

A total of 200 babies were included in our study, of which 140 were babies of normotensive mothers and 60 were babies of preeclampsia mothers. Informed and written consent was obtained from their parents or guardian before enrolment. Parameters recorded were Infant's birth weight, gestational age, duration of exposure to oxygen, mechanical ventilation, respiratory distress syndrome, septicaemia, multiple blood transfusions, multiple births, apnoeic episodes and intraventricular haemorrhage. The screening examination for ROP followed guidelines proposed by National Neonatology Forum.⁴ Ocular fundus examinations carried out using indirect ophthalmoscope and the findings were recorded and categorised according to revised International classification of ROP. Severe ROP is defined as presence of stage 3ROP, stage 4ROP, stage 5ROP plus disease or AP-ROP. Scheduled followup examinations were based on retinal findings and continued until complete vascularisation or regressing ROP was documented or until treated based on the ETROP guidelines.⁵ Babies were divided into two groups. Group 1: 140 babies of normotensive mothers and Group 2: 60 babies of preeclampsia mothers.

OBSERVATION AND RESULTS

There is no significant difference in risk factors of ROP such as GA, BW, oxygen therapy, mechanical ventilation, sepsis between two groups (Table 1). Among the 140 babies of normotensive mothers, 63 were males and 77 were females. Among the 60 babies of preeclampsia mothers, 24 were males and 36 were females. In babies of normotensive mothers 61 developed any stage of ROP with incidence being 43.6% and in babies of preeclampsia mothers 27 developed any stage of ROP with incidence being 45%. There is no statistical significance between these two groups in terms of overall incidence of ROP. The incidence of severe ROP are 13.3% and 3.3% in babies of normotensive and preeclampsia mothers respectively with statistically significant 'p' - value of < 0.05 with Odds ratio of 0.2196, 95% confidence interval being 0.0495 to 0.9747 (Table 2).

Our observation shows that parameters like GA, BW, oxygen therapy, mechanical ventilation and sepsis were comparable between the two groups. First incidence of no ROP and ROP then secondly incidence of severe ROP were calculated between the two groups. Statistical analysis done using student's t-test, and the Odds ratio and 95% confidence interval calculated to determine the magnitude of association between maternal preeclampsia and severe ROP.

Risk Factors	No. of Babies of Normotensive Mothers (n = 140)			No. of Babies of Preeclampsia Mothers (n = 60)		
	No ROP	ROP	Total	No ROP	ROP	Total
Gestational Age						
≤ 30 weeks	7	23	30	4	11	15
31 - 32 weeks	38	23	61	17	10	27
> 32 weeks	34	15	49	12	6	18
Birth Weight						
≤ 1000 grams	9	16	25	2	6	8
1001 - 1500 grams	33	35	68	19	18	37
> 1500 grams	37	10	47	12	3	15
O ₂ therapy	18	54	72	7	27	34
Mechanical ventilation	17	52	69	5	25	30
Sepsis	5	15	20	2	7	9

Table 1: Risk Factors for ROP

Risk Factors	No. of Babies of Normotensive Mothers (n = 140)					No. of Babies of Preeclampsia Mothers (n = 60)				
	No ROP (Nos)	No ROP (%)	ROP (Nos)	No ROP (%)	Total	No ROP (Nos)	No ROP (%)	ROP (Nos)	ROP (%)	Total
Gestational Age										
≤ 30 weeks	7	23.3	23	76.7	30	4	26.7	11	73.3	15
31 - 32 weeks	38	62.3	23	37.7	61	17	63	10	37	27
> 32 weeks	34	69.4	15	30.6	49	12	66.7	6	33.3	18
Birth Weight										
≤ 1000 grams	9	36	16	64	25	2	25	6	75	8
1001 - 1500 grams	33	48.5	35	51.5	68	19	51.4	18	48.6	37
> 1500 grams	37	78.7	10	21.3	47	12	80	3	20	15
O ₂ therapy	18	25	54	75	72	7	20.6	27	79.4	34
Mechanical ventilation	17	24.6	52	75.4	69	5	16.7	25	83.3	30
Sepsis	5	25	15	75	20	2	22.2	7	77.4	9

Table 2

DISCUSSION

Preeclampsia is one of the major obstetric problems with significant maternal and neonatal morbidities and mortalities. Hypoxia is common to both preeclampsia and ROP pathogenesis. Studies were published to determine the associations of maternal preeclampsia with ROP and the results are conflicting. Taiwan Premature Infant Developmental Collaborative Study Group⁶ concluded that although there was potential bias of a link between preeclampsia and ROP, our large population-based retrospective analysis found no association between these two diseases. A study done by Filho et al results revealed preeclampsia was protective for development of severe ROP and reduced the risk for any stage of ROP by 60% in early preterm infants. Seiberth et al showed that preeclampsia was significantly associated with a reduced risk of ROP. Holmstrom et al in a population-based study reported that preeclampsia was less common in the non-ROP group, but the difference was not statistically significant. However, our study showed no significant difference between overall incidences of ROP between two groups. Our study results showed that preeclampsia is associated with significantly lower risk of severe ROP. Neovascularisation in ROP is due to deregulated overproduction of VEGF. Anti-angiogenic factors like soluble Flt-1 and soluble endoglin is markedly elevated in maternal blood and plays an important role in pathogenesis of preeclampsia.⁷ Soluble FLT-1, a VEGF inhibitor binds to VEGF and prevents it from signalling through its receptors, which is supported by a study using murine model of proliferative retinopathy result showed that sFLT1 reduces the retinal neovascularisation by approximately 50%.

CONCLUSION

Relationship between ROP and maternal risk factors are poorly established at present. Our study concluded there is no statistically significant difference between these two groups in terms of overall incidence of ROP, whereas the incidence of severe ROP is 13.3% and 3.3% in babies of normotensive and preeclampsia mothers respectively with statistically significant 'p' - value of < 0.05.

Future Scope of Our Study

We do not know exact mechanism which protects babies from development of severe ROP. We hypothesize that factors

which protect the foetus from development of severe ROP include elevated anti-angiogenic factors in maternal blood may pass through the placenta to enter foetal circulation or anti-angiogenic factors in amniotic fluid may be absorbed through cornea into retina of the foetus or there may be genetic tendency of the foetus to produce more anti-angiogenic factors (sFlt1, sEng) in response to hypoxia,⁸ both in the placenta (foetal tissue) and the retina.

We need further studies analysing anti-angiogenic factors level in maternal blood, amniotic fluid, aqueous and vitreous of babies helping us in understanding the protective role of preeclampsia in development of severe ROP.

REFERENCES

1. Ghaseminejad A, Niknafs P. Distribution of Retinopathy of Prematurity and Its Risk Factors. *Iran J Pediatr* 2011;21(2):209-14.
2. Majed BH, Khalil RA. Molecular mechanisms regulating the vascular prostacyclin pathways and their adaptation during pregnancy and in the newborn. *Pharmacol Rev* 2012;64(3):540-82.
3. Zhong Y, Zhu F, Ding Y. Serum screening in first trimester to predict pre-eclampsia, small for gestational age and preterm delivery: systematic review and meta-analysis. *BMC Pregnancy Childbirth* 2015;15:191.
4. Chawla D, Agarwal R, Deorari A, et al. Retinopathy of prematurity. *Indian J Pediatr* 2012;79(4):501-9.
5. Good WV. Final results of the early treatment for retinopathy of prematurity (etrop) randomized trial. *Trans Am Ophthalmol Soc* 2004;102:233-50.
6. Hsin-Chung H, Hwai-I Y, Hung-Chieh C, et al. Preeclampsia and retinopathy of prematurity in very-low-birth-weight infants: a population-based study. *PLoS One* 2015;10(11):e0143248.
7. Cerdeira AS, Karumanchi SA. Angiogenic factors in preeclampsia and related disorders. *Cold Spring Harb Perspect Med* 2012;2(11):a006585.
8. Hartnett ME. Vascular endothelial growth factor antagonist therapy for retinopathy of prematurity. *Clin Perinatol* 2014;41(4):925-43.