Original Research Article

Outcome in neonates born to mother with pre-eclampsia

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Abstract

Context: Pregnancy induced hypertension (PIH) is a major cause of maternal, fetal and neonatal morbidity and mortality. Preterm birth is a common complication of hypertensive diseases in mothers. Other complications includes low birth weight, intrauterine fetal death, intrauterine growth restriction, asphyxia, Respiratory distress, Sepsis, Stillbirths and neonatal deaths. **Methods and Materials:** 87 neonates born to mother with pre-eclampsia were included in study and their demographic characteristics, neonatal morbidities and mortality were evaluated. **Results:** Out of 87 neonates, 77(88.5%) neonates were born preterm and half of them were extremely to very preterm, 31.03% neonates were IUGR. Other neonatal morbidities developed in these neonates were Respiratory distress syndrome (RDS)(45.9%), birth asphyxia(12.64%), necrotising enterocolities (NEC)(10.34%). Neutropenia found in 45.97% neonates and it is correlated to gestational age and birth weight. 17.5% neonates out of total neutropenic ones had culture positive sepsis. **Conclusion:** Pre-eclampsia was associated with increased caesarean delivery and preterm birth. Other perinatal morbidities found were IUGR, RDS, birth asphyxia, NEC, and Sepsis.

Key Words : Pre-eclampsia, Prematurity, RDS, IUGR, Sepsis, NEC.

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INTRODUCTION

Pregnancy induced hypertension (PIH) is one of the most common cause of both maternal and neonatal morbidity, affecting about 5-8% of pregnant women.[1] Preeclampsia is a multisystem, highly variable disorder unique to pregnancy and a leading cause of maternal and fetal/neonatal morbidity and mortality.[1] The increased incidence of perinatal morbidity and mortality seen in pregnancies complicated by preeclampsia, although complex and multifactorial, is primarily due to the need for premature delivery and uteroplacental insufficiency resulting in a compromise of blood flow to the fetus.[2,3] Preterm birth is a common complication of hypertensive disease, either due to the spontaneous labour or to the obstetric conduct of interrupting the pregnancy due to the compromised maternal-fetal health. Prematurity increases perinatal morbidity and mortality rates with possible immediate or late sequels.[3] Other perinatal complications include low birth weight, intrauterine foetal death (IUFD), intrauterine growth restriction (IUGR), asphyxia, respiratory distress, sepsis, stillbirths and neonatal deaths.[4] Neutropenia and thrombocytopenia are well recognized neonatal sequel to maternal hypertension in pregnancy. Neutropenia has been reported to occur in 50% of infants born to mothers with hypertension compared to 4% in babies born after a normal pregnancy.[5] Pre-eclampsia-associated neutropenia is a risk factor for an increased incidence of infection in neonates born to mothers with pre-eclampsia.[6]So with the aim to find various morbidity and mortality pattern in babies born to mother with preeclampsia so that we can delivers care to women with high risk pregnancies and offers specialized care in neonatology this study was planned.

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MATERIAL AND METHODS

Study design and setting: This was a prospective observational study carried out in neonatal unit in Indira Gandhi Government Medical College and Hospital in central India. 87 Neonates born to mother with history of pre-eclampsia between October 2016 to October 2017 and admitted in NICU were taken in to study after informed written parent consent.

Inclusion criteria: All neonates born to pre-eclamptic mothers in our hospital and admitted in our NICU for various complaints were included.

Exclusion criteria: Neonates with Congenital malformation, any illness to mother likely to cause changes in haematological profile like severe anemia, connective tissue disorders, diabetes and chronic hypertension and mothers with chorioamnitis, genital tract infections and prolonged rupture of membranes were excluded.

Ethical approval: This study was approved by institutional ethics committee.

Method of data collection: At the time of enrollment details regarding antenatal history including mother age, parity, blood pressure records, antihypertensive drugs taken and hospitalization during antenatal period were noted. The following variables were recorded: Mode of delivery, Apgar score (1min and 5min), Gestational age, birth weight, sex, presence of small for gestational age (SGA), Respiratory distress syndrome (RDS), Neonatal Sepsis, necrotising enterocolitis (NEC), Retinopathy of prematurity. Their haematological profile was estimated through CBC. Other investigations includes-Sepsis screen, Blood culture and sensitivity. Chest X-ray, Urine culture, cerebrospinal fluid (CSF) analysis and fungal culture were done wherever necessary. Neonates with blood culture positive sepsis were considered as having septicemia.

Statistical analysis: The data was analyzed using SPSS version 20.0. Pre-eclampsia**:** Pre-eclamptic mothers will be identified by finding hypertension (systolic BP >140 mm of Hg or diastolic BP>90 mm of Hg on two occasions) plus proteinuria and edema after 20th week in a previously normotensive and nonproteinuric woman [7]. Severe hypertension: Blood pressure ≥ 160/110 mm of hg [8].Mild to moderate hypertension (Nonsevere hypertension): Blood pressure 140/90 to <160/110 mm of hg[8]. Preterm Neonate: Preterm is defined as babies born alive before 37 weeks of gestation. Subcategories of Preterm birth: Extremely preterm (less than 28 weeks), Very Preterm (28 to < 32 weeks), Moderate to late preterm (32 to <37 weeks) SGA/IUGR **:** Neonate with birth weight or crown heel length for gestational age less than 10 th percentile for GA or <2SD below mean for infant's GA. Low birth weight: Birth weight 1500gms to <2500gms. Very low birth weight: Birth weight 1000gms to <1500gms. Extremely low birth weight: Birth weight <1000gms. RDS was described as clinical findings (tachypnea, retractions or nasal flaring, grunting respiration, and possible central cyanosis) and radiologic findings (reticular granular pattern or air bronchograms). NEC was categorized in conformity with the modified Bell's criteria [25] Neutropenia means Absolute neutrophil count <1800/mm3 as per Manroe chart for term and Mouzinhos chart for preterm neonates.[9,10] Thrombocytopenia considered as platelet count <1.5 lac/mm3 Sepsis: Defined as microbial recovery from blood or any other biologic material cul-ture in addition to the presence of a clinical or biological syndrome of sepsis. Early onset sepsis (EOS): Defined as neonatal sepsis which occurred within 3 days (72 hours) of birth [7]. Late onset sepsis(LOS): It usually presents after 72 hours of age.

RESULTS

Over the study period 87 neonates born to mothers with pre-eclampsia were included in the study. In this study, 32 mothers (36.78%) were having severe hypertension (BP >160/110 mm of hg) and remaining 55 (63.22%) had mild to moderate hypertension(BP between 140/90 to 160/110 mm of hg). Out of 87 neonates, 10 (11.49%) neonates were born full term and 77(88.5%) neonates were born preterm. The rate of lower segment caesarean section was high (69%) as compared to normal vaginal delivery (31%). Most common indications for lower segment caeserean sections was IUGR with fetal distress which is 27(45%) in no. out of 60 lower segment ceaserean section delivery followed by severe pre-eclampsia 17(28.35%) in mothers requiring termination of pregnancy 33 (37.93 %) neonates were extremely to very preterm (born < 32 wks gestation), 23(26.43 %) neonates were between 32- <34 wks gestation and 21(24.13 %) neonates were born between 34- <37 wks gestation, 10(11.49 %) neonates born ≤ 37 wks.(Table 1) Approximately one third neonates (36.78%) had a low birth weight (1.5-2.5kg), another one third (31.03%) neonates had very low birth weight (1-<1.5kg) and 20 (22.9%) neonates were extremely low birth weight(<1kg).(Table 2) Most common perinatal complication developed in babies born to pre-eclamptic mother was respiratory distress syndrome in 40(45.90%) neonates, 27(31.03%) neonates were born IUGR, birth asphyxia in 11(12.64%) neonates, NEC developed in 9(10.34%) neonates, culture positive sepsis developed in 7(8.04%) neonates.(Table 3) Out of 87 neonates, 40(45.97%) neonates had neutropenia. Of total mothers with severe hypertension, 18 (56.25%) neonates born to them had neutropenia and out of total mothers with mild

to moderate hypertension 22 (40%) neonates born to them had neutropenia.(Table 4) Of the total 40 neutropenic neonates, 19(47.5%) neonates were born <32 wks gestation, 12(26.43%) neonates were born between 32-<34 wks, 6(15%) neonates born between 34-<37 wks and 3(7.5%) neonates were ≥37 wks gestation.(Table 1) Out of total neutropenic neonates, 18(45%) neonates had very low birth weight and 13(32.5%) were having birth weight <1kg. Also the rate of septicaemia was high in very low birth weight neonates. (Table 2) Amongst 40 neutropenic neonates, 7(17.5%) neonates had developed culture positive sepsis. (Table 5) Out of 87 neonates, 38 (43.67%) neonates had neutropenia as well as thrombocytopenia. All septic neonates were thrombocytopenic.

Mortality rate in this study was 3.34% due to severe septicemia.

Table 1 : Distribution of neonates according to gestational age and relation with neutropenia and septicemia

GESTATIONAL AGE	TOTAL NUMBER	NEONATAL NEUTROPENIA	EARLY ONSET NEONATAL SEPTICEMIA	P value
< 32 WKS	33(37.93%)	19(47.5%)	4(57.14)	= 0.004
32 WKS – < 34 WKS	23(26.43%)	12(30%)	2(28.57%)	Chi-square= 13.06
34 - <37 WKS	21(24.13%)	6(15)	1(14.28%)	
≥ 37 WKS	10(11.49%)	3(7.5%)	0(0%)	
TOTAL	**87(100%)**	**40(100%**	**7(100%)**	

In above table we can see neonates of following gestational age, 33(37.93%) neonates of < 32 weeks, 23(26.43%) neonates between 32-< 34 weeks, 21(24.13%) neonates between 34-<37 weeks and 10 (11.49%) neonates were ≥ 37 weeks gestation. The percentage of neutropenia and septicemia was less as gestational age advances in neonates. It was statistically significant with p value 0.004 which is statasticaly significant with chi-squre 13.06. It is also seen that as the gestational age decreases more is chance of having neutropenia and septicemia in babies.

Table 2: Distribution of neonates according to weight and relation with neutropenia and septicemia

WT IN KGS	NUMBER OF NEONATES 87(100%)	NEONATES WITH NEUTROPENIA 40(100%)	EARLY ONSET NEONATAL SEPTICEMIA 7(100%)
< 1 KG	20(22.98%)	13(32.5%)	2(28.57%)
1 TO < 1.5 KG	27(31.03%)	18(45%)	4(57.14%)
1.5 TO 2.5KG	32(36.78%)	9(22.5%)	1(14.28%)
>2.5 KG	8(9.19%)	0(0%)	0(0%)
TOTAL	**87(100%)**	**40(100%)**	**7(100%)**

Table No. 2 shows that 32 (36.78%) neonates were between 1.5- 2.5kg birth weight, 27(31.03%) neonates were between 1-<1.5kg birth weight, 20(22.9%) neonates had birth weight <1kg. Out of 40 neutropenic neonates, 18 (45%) neonates had birth weight between 1-<1.5kg, 13(32.5%) neonates were < 1kg birth weight and 9(22.5%) neonates had birth between 1.5-2.5kg. Similarly out of total septicaemic neonates 4(57.14%) neonates had birth weight between 1-<1.5 kg, 2(28.57%) neonates were <1kg birth weight and 1(14.28%) neonate between 1.5-2.5kg birth weight.

Table 3: Perinatal outcome of neonates born to pre-eclamptic mothers

PERINATAL OUTCOME	NUMBERS OF NEONATES	PERCENTAGE (%)
Respiratory distress Syndrome (RDS)	40	45.9%
Intrauterine growth retardation(IUGR)	27	31.03%
Birth Ashyxia	11	12.64%
Culture proven Sepsis	7	8.04%
Necrotising Enterocolitis(NEC)	9	10.34%

Above table shows common perinatal outcome was RDS(45.9%) followed by IUGR babies 31.03%, birth asphyxia in 12.34% neonates, NEC was seen in 10.34% , 8.04% neonates had culture positive sepsis and mortality rate 3.34%.

Table 4: Neutropenic babies born to mother according to severity of hypertension

PRE-ECLAMPTIC MOTHERS	TOTAL NUMBER OF PRE ECLAMPTIC MOTHERS	NEUTROPENIC BABIES	NON NEUTROPENIC BABIES
WITH SEVERE HYPERTENSION	32 (100%)	18 (56.25%)	14 (43.75%)
WITH MILD TO MODERATE HYPERTENSION	55 (100%)	22 (40 %)	33 (60%)
TOTAL	**87**	**40**	**47**

In above table it is seen that, 32 mothers has severe hypertension and 18 (56.25%) neonates born to them were having neutropenia, similarly 55 mothers with mild to moderate hypertension and 22 (40%) neonates born to them had neutropenia.

Table 5: Association between neutropenia and sepsis

	CULTURE POSITIVE SEPSIS		TOTAL	P value
	PRESENT	ABSENT		
NEUTROPENIC NEONATES	7	33	40	0.0027
NON NEUTROPENIC NEONATES	0	47	47	Chi-square : 8.945
TOTAL	7	80	87	

Above table shows that out of total 40 neutropenic neonates, 7 (17.5%) neonates developed sepsis and none of the non neutropenic neonates found to have sepsis. P value 0.0027 was sugnificant, it means neutropenia is associated factor for sepsis.

DISCUSSION

Hypertensive disorders of pregnancy have been identified as a major worldwide health problem, associated with increased perinatal morbidity and mortality [11]. Studies have shown that hypertensive disorders of pregnancy predisposes women to acute or chronic uteroplacental insufficiency, there by having an effect on perinatal and neonatal outcome that may result in ante or intrapartum anoxia that may lead to fetal death, intrauterine growth retardation and/or preterm delivery [11]. In present study the rate of lower segment caesarean section and preterm delivery rate were high (68.96%) and (88.5%) respectively. Similar results were found in study done by Dr.Sikha Maria Siromani *et al* [4] (63.01%), Nadkarni *et al* [11] (44.3%) and Sibai *et al* [12] S. Shivkumar *et al* in his study stated that there was higher number of preterm, intrauterine growth restriction (IUGR) and small for gestational age (SGA) babies among the infants of hypertensive mothers[2]. In this study average gestational age was 33 wks (32-34 wks) and average birth weight was 1839 grams. Solange Regina *et al* in their study of pregnancy induced hypertension and neonatal outcome found DBP >110 mm of hg was associated with low birth weight and prematurity [3]. Less gestational age and low birth weight neonates were at more risk to developed neutropenia and septicemia. Patricia *et al* found that infants <1200g and <32 weeks gestation and born to mothers with gestational hypertension, preeclampsia, or eclampsia syndrome were associated with leukopenia, absolute neutropenia and thrombocytopenia [13]. Similar results found in various studies [4,14,15,16]. Common perinatal complication was respiratory distress found in this study. Respiratory distress stays one of the major problem among these neonates. Mother's illnesses, especially hypertension are very strong risk factor for RD in preterm babies [17]. Chang *et al*.[18] showed an increased risk of RDS in early preeclamptic premature infants. Necrotizing colitis is a serious reason of mortality and morbidity in preterm infants. Although the pathophysiology of NEC is multifactorial, prematurity, low birth weight, enteral feeding, and neonatal infection are obvious predisposing factors for the occurrence of NEC [19]. There are a variety of outcomes in the literature about preeclampsia and its relationship with NEC. Bashiri *et al*. reported an association between maternal hypertensive disorders and NEC in very-low-birth-weight infants [19].In present study 45.97% neonates born to mother with pre-eclampsia had neutropenia. Ziba Mosayebi *et al* in 2013 evaluated laboratory disorders in admitted neonates in NICU who were born to pre-eclamptic mothers found 37% cases with neutropenia [14]. Carl H. Bakers *et al* found incidence of neutropenia in 50% neonates born to pre-eclamptic mothers [20]. Similar results found by Doron MW *et al* [6].. Neutropenia mainly affects the smaller and younger neonates and may be associated with an increased risk of nosocomial infections [14]. In this study, out of total mothers with severe hypertension, 56.25% neonates developed neutropenia and 40 % neonates developed neutropenia which were born to mothers with mild to moderate hypertension. Similar result was found in study done by Bhaumik S *et al* that Neonatal neutropenia was about three-fold more when maternal hypertension was Severe (diastolic >110 mm of Hg) compared to moderate <110 mm of Hg) [7].Carl H Bakers *et al* states that infants with neutropenia had mothers with more severe pre-eclampsia, were born more premature, weigh less and more likely small for gestational age [20]. In present study amongst 40 neutropenic neonates 7 developed septicemia that was 17.5% (P <0.002). Doron MW *et al* found 6% neonates amongst neutropenic babies had developed sepsis [6]. Cadnapaphornchai M *et al* in his study shows increased nosocomial infection in neutropenic low birth weight (2000 grams or less) infants of hypertensive mothers [21]. However David A Paul *et al* in their study states that neonatal neutropenia associated with preeclampsia does not increase the risk for culture proven sepsis [22].In present study it was seen that 43.67% of neonates had thrombocytopenia and 95 % of neutropenic babies had associated thrombocytopenia. All septicemic babies found with thrombocytopenia (100%). So there is strong association between early onset septicemia and thrombocytopenia in babies born to mother with pre-eclampsia and it can be indirect indicator of sepsis to be used for accessing diagnosis and prognosis. Similar

results found in study done by Y.R. Bhatt and Carol S. Cherian, thrombocytopenia occurred in 36% of neonates born to mothers with pregnancy induced hypertension and was severe in 20% [23]. Similar results were also found in studies by SH Fraser *et al* and Prekshya L Prakash *et al* that babies of hypertensive mothers are more prone for development of leucopenia, neutropenia and thrombocytopenia during the early neonatal period, these babies should be closely monitored and managed in order to decrease the perinatal morbidity and mortality[5,24].

CONCLUSION

Pregnancy induced hypertension is one of the most common causes of both maternal and neonatal morbidity. The risk for delivering prematurely is high in babies born to mothers with pre-eclampsia. Pre-eclampsia is one of the causative factor for preterm and low birth weight babies. There is higher no. of interventional surgical deliveries amongst preeclamptic mothers. Perinatal outcome of babies born to mother with preeclampsia are RDS, IUGR, Sepsis, NEC, birth asphyxia. Abnormal hematological finding like neutropenia and thrombocytopenia are the frequent finding in this neonates. The risk of early onset sepsis is more in babies born to mothers with pre-eclampsia due to prematurity, low birth weight and associated neutropenia. These findings indicate that neonatal outcomes of preeclampsia were dependent on prematurity and were related to premature deliveries of preeclamptic women, not only preeclampsia itself. Therefore the management strategy for high risk neonates born to mother with pre-eclampsia should focus on multidisciplinary care approach and identification of early signs of clinical sepsis.

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