

## A Clinico-Epidemiological Assessment of the Outcome of Neonates Born to Mothers with Pre-Eclampsia

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### Abstract

**Aim:** The aim of the present study was to assess the outcome in neonates born to mother with pre-eclampsia.

**Methods:** This was a retrospective study carried out in neonatal unit in department of Pediatrics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India for one year. 100 Neonates born to mother with history of pre-eclampsia between and admitted in NICU were taken in to study after informed written parent consent.

**Results:** 39 (39%) neonates of < 32 weeks, 25 (25%) neonates between 32-< 34 weeks, 24 (24%) neonates between 34-<37 weeks and 12 (12%) neonates were  $\geq$  37 weeks gestation. The percentage of neutropenia and septicemia was less as gestational age advances in neonates. It was statistically significant with p value 0.007 which was statistically significant. It is also seen that as the gestational age decreases more is chance of having neutropenia and septicemia in babies. 34 (34%) neonates were between 1.5- 2.5kg birth weight, 32 (32%) neonates were between 1-<1.5kg birth weight, 24 (24%) neonates had birth weight <1kg. Out of 40 neutropenic neonates, 20 neonates had birth weight between 1-<1.5kg, 16 neonates were < 1kg birth weight and 9 neonates had birth between 1.5-2.5kg. Similarly out of total septicemic neonates 5 neonates had birth weight between 1-<1.5 kg, 3 neonates were <1kg birth weight and 2 neonates between 1.5-2.5kg birth weight. The common perinatal outcome was RDS (46%) followed by IUGR babies 32%, birth asphyxia in 12% neonates, NEC was seen in 10% , 8% neonates had culture positive sepsis. 40 mothers has severe hypertension and 22 neonates born to them were having neutropenia, similarly 60 mothers with mild to moderate hypertension and 26 neonates born to them had neutropenia.

**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 factors for preterm and low birth weight babies. There is higher number of interventional surgical deliveries amongst preeclamptic mothers. Perinatal outcome of babies born to mother with preeclampsia are RDS, IUGR, Sepsis, NEC, birth asphyxia.

**Keywords:** Pre-eclampsia, Prematurity, RDS, IUGR, Sepsis, necrotising enterocolitis

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### Introduction

Preeclampsia is defined as hypertension in pregnancy after the gestational age of 20 weeks associated with proteinuria (>300 mg/day), multiple organ dysfunction (renal, hepatic, neurological, and hematologic involvement), or uteroplacental dysfunction potentially causing intrauterine growth restriction (IUGR). [1] According to ACOG (American College of Obstetricians and Gynecologists), gestational hypertension is defined as hypertension with a systolic blood pressure of  $\geq$ 140 mm Hg or a diastolic blood pressure of  $\geq$ 90 mm Hg or both without proteinuria that develops after 20 weeks of gestation with a return to normal blood pressure after delivery. 2 Severe hypertension

is defined by a systolic blood pressure of >160 mm Hg or a diastolic blood pressure of  $\geq$ 110 mm Hg or both. [2]

While preeclampsia complicates 6%–10% of all pregnancies in the United States, the incidence is believed to be even higher in underdeveloped countries. [3,4] Recent evidence suggests that preeclampsia accounts for approximately 15.9% of all maternal deaths in the United States and is a major cause of perinatal morbidity and death. [5,6] Therefore, physicians must carefully weigh the risks to both mother and fetus in management decisions. To that end, optimal treatment strategies have not

been fully defined, leaving physicians with incomplete data to guide their patient care practices. [7,8] 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. [9,10]

Depending on the time of occurrence of the disease, there is an early form (onset before 34 weeks) and a late form (onset after 34 weeks of gestation). The early form of the disease is rarer, but with a higher incidence of neonatal complications and perinatal death. In the early form of the disease, abnormal placentation occurs, with the abnormal development of spiral arteries that remain with a narrow lumen, causing placental perfusion disorders as well as the release of inflammatory cytokines and proangiogenic factors that will trigger an endothelial response. This will generate the clinical picture and IUGR. [11] In the late form of the disease, vascular abnormalities are limited and much reduced compared to the early form. As a result, neonatal complications in this type of preeclampsia are rare or non-existent. [12-14]

The aim of the present study was to assess the outcome in neonates born to mother with pre-eclampsia.

### Materials and Methods

This was a retrospective study carried out in neonatal unit in department of Pediatrics, Shri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India for one year. 100 Neonates born to mother with history of pre-eclampsia between 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.

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.<sup>15</sup> Severe hypertension: Blood pressure  $\geq$  160/110 mm of hg.<sup>16</sup> Mild to moderate hypertension (Nonsevere hypertension): Blood pressure 140/90 to <160/110 mm of hg.<sup>16</sup> 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<sup>19</sup> Neutropenia means Absolute neutrophil count <1800/mm<sup>3</sup> as per Manroe chart for term and Mouzinhos chart for preterm neonates.<sup>17,18</sup> Thrombocytopenia considered as platelet count <1.5 lac/mm<sup>3</sup> Sepsis: Defined as microbial recovery from blood or any other biologic material culture 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.<sup>15</sup> Late onset sepsis (LOS): It usually presents after 72 hours of age.

### Results

**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	39	22	5	0.007
32 WKS – < 34 WKS	25	14	3	
34 - <37 WKS	24	6	2	
≥ 37 WKS	12	3	0	
<b>TOTAL</b>	<b>100</b>	<b>45</b>	<b>10</b>	

39 (39%) neonates of < 32 weeks, 25 (25%) neonates between 32-< 34 weeks, 24 (24%) neonates between 34-<37 weeks and 12 (12%) 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 0.007 which was statistically significant. 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	N	Neonates With Neutropenia	Early Onset Neonatal Septicemia
< 1 KG	24	16	3
1 TO < 1.5 KG	32	20	5
1.5 TO 2.5KG	34	9	2
>2.5 KG	10	0	0
<b>TOTAL</b>	<b>100</b>	<b>45</b>	<b>10</b>

34 (34%) neonates were between 1.5- 2.5kg birth weight, 32 (32%) neonates were between 1-<1.5kg birth weight, 24 (24%) neonates had birth weight <1kg. Out of 40 neutropenic neonates, 20 neonates had birth weight between 1-<1.5kg, 16 neonates were < 1kg birth weight and 9 neonates had birth

between 1.5-2.5kg. Similarly out of total septicemic neonates 5 neonates had birth weight between 1-<1.5 kg, 3 neonates were <1kg birth weight and 2 neonates between 1.5-2.5kg birth weight.

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

Perinatal Outcome	N	%
Respiratory distress Syndrome (RDS)	46	46
Intrauterine growth retardation(IUGR)	32	32
Birth Asphyxia	12	12
Culture proven Sepsis	8	8
Necrotising Enterocolitis(NEC)	10	10

The common perinatal outcome was RDS (46%) followed by IUGR babies 32%, birth asphyxia in 12% neonates, NEC was seen in 10% , 8% neonates had culture positive sepsis.

**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	40	22	18
With mild to moderate hypertension	60	26	34
<b>Total</b>	<b>100</b>	<b>48</b>	<b>52</b>

40 mothers has severe hypertension and 22 neonates born to them were having neutropenia, similarly 60 mothers with mild to moderate hypertension and 26 neonates born to them had neutropenia.

**Table 5: Association between neutropenia and sepsis**

Culture	Positive sepsis	Total	P value
Present Neutropenic neonates	7	48	0.0032
Non neutropenic	0	52	
<b>Total</b>	<b>8</b>	<b>100</b>	

Out of total 48 neutropenic neonates, 8 neonates developed sepsis and none of the non neutropenic neonates found to have sepsis. P value 0.0032 was significant, it means neutropenia was associated factor for sepsis.

### Discussion

Pregnancy induced hypertension (PIH) is one of the most common cause of both maternal and neonatal morbidity, affecting about 5-8% of pregnant women. Preeclampsia is a multisystem, highly variable disorder unique to pregnancy and a leading cause of maternal and fetal/neonatal morbidity and mortality. [20] 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. [21,22]

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. [22] Other perinatal complications include low birth weight, intrauterine foetal death (IUFD), intrauterine growth restriction (IUGR), asphyxia, respiratory distress, sepsis, stillbirths and neonatal deaths. [23] 39 (39%) neonates of < 32 weeks, 25 (25%) neonates between 32-< 34 weeks, 24 (24%) neonates between 34-<37 weeks and 12 (12%) neonates were  $\geq$  37 weeks gestation. The percentage of neutropenia and septicemia was less as gestational age advances in neonates. It was statistically significant with p value 0.007 which was statistically significant. It is also seen that as the gestational age decreases more is chance of having neutropenia and septicemia in babies. 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. [24]

34 (34%) neonates were between 1.5- 2.5kg birth weight, 32 (32%) neonates were between 1-<1.5kg birth weight, 24 (24%) neonates had birth weight <1kg. Out of 40 neutropenic neonates, 20 neonates had birth weight between 1-<1.5kg, 16 neonates were < 1kg birth weight and 9 neonates had birth weight between 1.5-2.5kg. Similarly out of total septicaemic neonates 5 neonates had birth weight between 1-<1.5 kg, 3 neonates were <1kg birth weight and 2 neonates between 1.5-2.5kg birth weight. Chang et al [25] 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 [26] reported an association between maternal hypertensive disorders and NEC in very-low-birth-weight infants.

Backes CH et al [27] states that infants with neutropenia had mothers with more severe preeclampsia, were born more premature, weigh less and more likely small for gestational age. The common perinatal outcome was RDS (46%) followed by IUGR babies 32%, birth asphyxia in 12% neonates, NEC was seen in 10% , 8% neonates had culture positive sepsis. 40 mothers has severe hypertension and 22 neonates born to them were having neutropenia, similarly 60 mothers with mild to moderate hypertension and 26 neonates born to them had neutropenia. Out of total 48 neutropenic neonates, 8 neonates developed sepsis and none of the non neutropenic neonates found to have sepsis. [28] P value 0.0032 was significant, it means neutropenia was associated factor for sepsis. However David A Paul et al<sup>28</sup> in their study states that neonatal neutropenia associated with preeclampsia does not increase the risk for culture proven sepsis. After birth, the association and severity of some diseases were monitored, as well as the frequency of some therapies in the group of neonates exposed to hypertension compared to those unexposed. Asphyxia at birth had a similar incidence in the two groups. Maternal preeclampsia did not influence the immediate transition of the newborns. The birth occurred in the preeclampsia group before severe fetal impairment developed, with an impact on adaptation to birth and on the transition to extra uterine life. Thus, it can be extrapolated that termination of pregnancy by cesarean section was adequate for the newborns of the case group. Tian et al [29] reported a low Apgar score more often in the case of newborns from mothers with pregnancy hypertension and preeclampsia, and the risk had an increasing trend with the progress of maternal hypertension than in the non-exposed population. Maternal hypertension and preeclampsia increase the risk of a low Apgar score. [29,30]

### 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 factors for preterm and low birth weight babies. There is higher number 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 the 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. 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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