Original Research Article

Prevalence of early onset neonatal septicemia in babies born to mother with pre-eclampsia

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Abstract

Context: Pregnancy induced hypertension (PIH) is one of the important risk factor for preterm delivery. Neutropenia and thrombocytopenia are well recognized neonatal sequelae to maternal hypertension in pregnancy. Preeclampsia-associated neutropenia is a risk factor for an increased incidence of infection in preterm neonates. **Methods & material:** 87 neonates born to mother with preeclampsia were included with aim to find prevalence of EOS and their haematological profile. Diagnostic work up includes complete blood count, CRP, blood culture and sensitivity (C/S) and other relevant investigations according to cases. **Result:** Out of 87 neonates, 7 neonates had EOS (8%) with blood culture proven bacterial sepsis, Klebsiella pneumonia (57.14%) was commonest organism isolated followed by E. Coli (28.57%) and Enterococci (14.28%). About 32 (36.76%) mothers had severe hypertension and 55(68.22%) mothers had mild to moderate preeclampsia. About 60(68.79%) neonates were born preterm. 40 (45%) neonates had neutropenia. 38 (43.65%) babies had thrombo-cytopenia. All 7 septic babies had neutropenia and thrombocytopenia. **Conclusion:** Early onset septicemia is more common in babies born to mother with preeclampsia due to associated Prematurity, Neutropenia and Thrombocytopenia. Hence preventive measures should focus on recognition of these high risk neonates with prompt laboratory screening for sepsis and early institution of empirical antibiotics based on local data.

Keywords: Preeclampsia, Prematurity, Neutropenia, Early onset sepsis

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]. Pre-eclampsia is a multi-system disorder of the mother that affects the fetus because of utero-placental insufficiency. In consequence these children are at risk for intra-uterine growth restriction and may be delivered prematurely[2].

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]. Neutropenia and thrombocytopenia are well recognized neonatal sequel to maternal hypertension in pregnancy. Neutropenia hasbeen reported to occur in 50% of infants born to mothers with hypertension compared to 4% in babies born after a normal pregnancy [4]. Neutropenia is a common hematologic disorder in the newborn intensive care unit, particularly in preterm neonates. Although its cause varies, a significant proportion of the episodes are associated with pregnancy complicated by preeclampsia [5].

Pre-eclampsia-associated neutropenia is a risk factor for an increased incidence of infection in neonates born to mothers with pre-eclampsia. Preeclampsia associated neutrophil function disorders also contribute to the high incidence of infection in neutropenic infants [6].

The risk of early onset septicemia is more in neutropenic babies than in non-neutropenic babies of pre-eclamptic mothers [4,6]. Considering pre-eclampsia as a risk factor for early onset neonatal septicemia in babies born to mother with pre-eclampsia early

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detection and timely intervention can decline death rate because of sepsis. Sowith the aim to find prevalence of early onset septicaemia and to know haematological profile in newborns born to mothers with pre-eclampsia this study was planned.

Material and Methods

Study design and setting: This was aprospective observational study carried out in neonatal unit in Indira Gandhi Government Medical College and Hospital in central India.

Sample calculation: 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. Considering the prevalence of 6% of EOS in neonates born to mothers with preeclampsia from previous studies (R), absolute allowable error of 8% and normal deviate of 5% the minimum required sample size (n) was 87.

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

Exclusion criteria: Neonates with Congenital malformation, Severe birth asphyxia, 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 enrolment details regarding antenatal history including mother age, parity, blood pressure records, antihypertensive drugs taken and hospitalization during antenatal period were noted. Gestational age, mode of delivery, birth weight, perinatal complications and details of NICU admission, physical examination were done for each neonate.

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 only 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 hyper-tension): Blood pressure 140/90 to <160/110 mm of hg[8]. Neutropenia means Absolute neutrophil count <1800/mm3 as per Manroe chart for term and Mouzinhos chart for preterm neonates [9,10].

Thrombo-cytopenia considered as platelet count <1.5 lac/mm3. Early onset sepsis (EOS): Defined as neonatal sepsis which occurred within 3 days (72 hours) of birth [7].

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, 27(31.03%) neonates were born full term and 60(68.9%) neonates were born preterm. The rate of lower segment caesarean section was high (69%) as compared to normal vaginal delivery (31%). Out of 87 neonates, 7 neonates of total cases fulfilled the criteria for early onset septicaemia hence prevalence rate of EOS was 8%. 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 hypertension22 (40%) neonates born to them had neutropenia. (Table 1).

Amongst 40 neutropenic neonates, 7(17.5%) neonates had developed culture positive sepsis (Table 2)

Association of early onset septicemia and neutropenia with gestational age shown in Table no. 3, 33 (37.93%) neonates were born <32 wks gestation, 23(26.43%) neonates were between 32- <34 wks gestation and 21(24.13%) neonates were

born between 34-<36 wksgestation, 10(11.49%) neonates born > 36 wks. 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 34-36 wks and 3(7.5%) neonates were >36 wks gestation.

Neonates with septicaemia, 4 (57.14%) neonates were <32 wks gestation, 2(28.57%) neonates were between 32-<34 wks and 1(14.28%) neonate was between 34-36 wks. 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). 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 4). Common indication for admission was respiratory distress (63.21%).

Amongst the 7 septicemic neonates,commonest organism isolated was Klebsiella pneumoniae in blood culture of 4 (57.14%) neonates followed by E-coli (28.57%) and Enterococci (14.28%).

Out of 87 neonates, 38 (43.67%) neonates had neutropenia as well as thrombocytopenia. All septic neonates were thrombocytopenic (Table 5). Mortality rate in this study was 1.14% due to severe septicemia.

Table-1: 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-2: 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.

Table-3: Early onset septisemia and neutropenia as per gestational age.

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 -36 WKS	21(24.13%)	6(15)	1(14.28%)	
> 36 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-<36 weeks and 10 (11.49%0 neonates were > 36 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-4: Neutropenic and septicemic neonates according WT

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. 4 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-5: Association between thrombocytopenia and neutropaenia.

	Thrombocytopenic Neonates	Non Thrombocytopenic Neonates	Total	P value
Neutropenic neonates	38	2	**40**	**0.0000001**
Non neutropenic neonates	0	47	47	Chi Square -79.28
Total(87)	38	49	87	

In above table it is seen that out of 40 neutropenic babies 38 babies (95%) found thrombocytopenia and both these factor thrombocytopenia and neutropenia related to 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 prevalence of early onset septicemia in neonates born to pre-eclamptic mother was 8%. S. Bhaumik et al found risk of early onset neonatal septicaemia in babies born to mother with preeclampsia is 6.7% [7]. Doron MW et alin his study found sepsis in 6% neonates [6]. Procianoy RS et al [12] in his study of sepsis and neutropenia in very low birth weight babies found similar incidence of early onset sepsis in neonates born to mothers in preeclampsia group 4.6% and in non preeclampsia group 4.2%.

In present study the rate of lower segment caesarean section and preterm delivery rate were high (68.96%). Similar results were found in study done by Sikha Maria Siromani et al[13](63.01%), Nadkarni etal[11] (44.3%) and Sibai et al[14]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].

Inpresentstudy 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 [15]. Carl H. Bakers et al found incidence of neutropenia in 50% neonates born to pre-eclamptic mothers [16]. Similar results found by Doron MW et al [6]. It is a transient haematological alteration, lasting days to weeks, related to the severity of pregnancy induced hypertension. Neutropenia mainly affects the smaller and younger neonates and may be associated with an increased risk of nosocomial infections [15].

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 althat 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 [16].

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 [17]. 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 [18]**.**

In this study average gestational age was 33 wks (32-34 weeks) 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 alfound 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 [19]. Similar results found in various studies [13,15,20,24].

Common manifestation at the time admission was respiratory distress found in this study. Respiratory distress stays one of the majorproblem among these neonates. Mother's illnesses, especially hypertension are very strong risk factor for RD in preterm babies [21].

In present study,7 neonates had early onset septicaemia. Organism isolated were K. Pneumonia, E.coli and Enterococcus.

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 resultsfound 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% [22].

Similar results were also found in studies by SH Fraser et al and Prekshya L Prakash et althat 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 [4,23].

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 no. of interventional surgical deliveries amongst preeclamptic mothers.

Abnormal hematological finding like neutropenia and thrombocytopenia occurs in newborns born to mother with pre-eclampsia. Babies of pre-eclamptic mothers have relatively more risk of developing early onset septicemia than those of normal mothers. In neonates of pre-eclamptic mothers, neutropenia tends to increase with decreasing gestational age.

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 identification of early signs of clinical sepsis with prompt laboratory screening for sepsis and early institution of empirical antibiotic treatmentcan avoid morbidity and mortality in babies of pre-eclamptic mother.

What this study adds to existing knowledge: The effect of maternal pre-eclampsia on fetal outcome has been a subject of concern for a long time. Two decades back an association between pre-eclampsia and neonatal neutropenia was recognized. In the recent past the main focus of workers is to study the risk of sepsis amongst the neonates of pre-eclamptic mothers particularly among those with neutropenia.

So considering preeclampsia as a risk factor for early onset septicaemia in babies born to mother with preeclampsia early detection and timely intervention can decline death rate because of sepsis.

So we need to find indigenous data in our institute to know about incidence and prevalence of EOS and their causative organisms also to know other risk factors for development of EOS.

So we can make policy in our institute for management of these high risk neonates so that moratality and morbidity can decrease in our institute.

Contributions by Authors: Data collection done by Dr Santosh Daberao and Dr Bhagyashree Tirpude.

Analysis and manuscript preparation done by Dr Bhagy shree Tirpude. All research work had been done under the guidance of Dr Dipak Madavi.

Abbreviations: EOS (Early onset sepsis)

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