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Original Research Article

A Prospective Observational Study Assessing Outcome in Neonates Born to Mother with Pre-Eclampsia

Sunil Kumar Singh[1], Anil Kumar[2]

[1]Senior Resident, Department of Pediatrics, GMCH, Bettiah, Bihar, India
[2]Professor and HOD, Department of Pediatrics, GMCH, Bettiah, Bihar, India

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Corresponding Author: Dr. Sunil Kumar Singh
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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 prospective observational study carried out in neonatal unit. 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 ≥ 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 Enterocolities.

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 hematolog3e1ric 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 ≥140 mm Hg or a diastolic blood pressure of ≥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 ≥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 prospective observational study carried out in neonatal unit in GMCH, Bettiah, 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. [15] Severe hypertension: Blood pressure ≥ 160/110 mm of hg. [16] Mild to moderate hypertension (Nonsevere hypertension): Blood pressure 140/90 to <160/110 mm of hg. [16] 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 [19] Neutropenia means Absolute neutrophil count <1800/mm3 as per Manroe chart for term and Mouzinhos chart for preterm neonates. [17,18] Thrombocytopenia considered as platelet count <1.5 lac/mm3 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. [15] 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	
Total	**100**	**45**	**10**	

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
Total	**100**	**45**	**10**

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 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.

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
Total	**100**	**48**	**52**

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	Absent 41	48	0.0032
Non neutropenic 0	52	52	
Total	**92**	**100**	

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.1 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 ≥ 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 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 pre-eclampsia, 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. P value 0.0032 was significant, it means neutropenia was associated factor for sepsis. However David A Paul et al [28] 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 extrauterine 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.

References

1. Odegård RA, Vatten LJ, Nilsen ST, Salvesen KA, Austgulen R. Preeclampsia and fetal growth. Obstet Gynecol. 2000 Dec;96(6):950-5.
2. American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy Hypertension in Pregnancy.
3. Odendaal HJ, Pattinson RC, Bam R, Grove D, Kotze TJVW. Aggressive or expectant management for patients with severe preeclampsia between 28-34 weeks' gestation: a randomized controlled trial. Obstetrics and Gynecology. 1990;76(6):1070–1075.
4. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstetrics and Gynecology. 2003;102(1):181–19 2.
5. Berg CJ, Chang J, Callaghan WM, Whitehead SJ. Pregnancy-related mortality in the United States, 1991–1997. Obstetrics and Gynecology. 2003;101(2):289–296.
6. Duley L. Pre-eclampsia and the hypertensive disorders of pregnancy. British Medical Bulletin. 2003; 67:161–176.
7. Khedun SM, Moodley J, Naicker T, Maharaj B. Drug management of hypertensive disorders of pregnancy. Pharmacology and Therapeutics. 1997;74(2):221–258.
8. Sibai BM, Mercer BM, Schiff E, Friedman SA. Aggressive Versus expectant management of severe preeclampsia at 28 to 32 weeks' gestatian: a randomized controlled trial. American Journal of Obstetrics and Gynecology. 1994; 171(3):818–822.
9. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: current concepts. American Journal of Obstetrics and Gynecology. 1998;179(5):1359–1375.
10. Friedman SA, Schiff E, Kao L, Sibai BM. Neonatal outcome after preterm delivery for preeclampsia. American Journal of Obstetrics and Gynecology. 1995;172(6):1785–1792.
11. Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium: the role of antiangiogenic factors and implications for later cardiovascular disease. Circulation. 2011 Jun 21;123(24):2856-69.
12. Oddie S, Tuffnell DJ, McGuire W. Antenatal magnesium sulfate: Neuro-protection for preterm infants. Arch Dis Child Fetal Neonatal Ed. 2015 Nov;100(6):F553-7.
13. Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009 Jan 2 1;(1):CD004661.
14. Ngene NC, Moodley J. Role of angiogenic factors in the pathogenesis and management of pre-eclampsia. Int J Gynaecol Obstet. 2018 Apr;141(1):5-13.
15. Bhaumik S, Ghosh S, Haldar K.K, Mitra P.K, Manna B. Risk of early onset Neonatal septicemia in babies born to mother with pre-eclampsia. Indian Paediatrics. Jul 2000:37(7): 775-9.
16. DC Dutta, Textbook of obstetrics, 9 th edition, 2018
17. Mouzinho A, Rosenfeld CR, Sanchez PJ, Risser R. Revised reference ranges for circulating neutrophils in very low-birth-weight neonates. Pediatrics 1994; 94:76-82.
18. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I: Reference values for neutrophilic cells. J Pediatr 1979; 95: 89-98
19. Perrone S, Tataranno ML, Negro S, Cornacchione S, Longini M, Proietti F, Soubasi V, Benders MJ, Van Bel F, Buonocore G. May oxidative stress biomarkers in cord blood predict the occurrence of necrotizing enterocolitis in preterm infants?. The Journal of Maternal-Fetal & Neonatal Medicine. 2012 Apr 1;25 (sup1):128-31.
20. Muti M, Tshimanga M, Notion GT, Bangure D, Chonzi P. Prevalence of pregnancy induced hypertension and pregnancy outcomes among women seeking maternity services in Harare, Zimbabwe. BMC cardiovascular disorders. 2015 Dec; 15:1-8.
21. Sivakumar S, Vishnu Bhat B, Badhe BA. Effect of pregnancy induced hypertension on mothers and their babies. The Indian Journal of Pediatrics. 2007 Jul; 74:623-5.
22. Regina S. Pregnancy induced hypertension and the neonatal outcome. Actapul. Enferm Jan/ March. 2008;21.
23. Siromani SM, Varahala AM, Gopu S, Chidugull SK. Neonatal Outcome In Pregnancy Induced Hypertensive Mothers—A Tertiary Care Centre Experience. IOSR Journal of Dental and Medical Sciences. 2015;14(11):23-7.
24. Nash PL, Gillespie K, Devaskar UP. Effect of early onset bacterial sepsis or pregnancy induced hypertension (PIH) on neonatal white blood cell and platelet counts in infants less than 1,200 grams. Journal of Maternal-Fetal Medicine. 1993 Jan 1;2(1):1-4.
25. Chang EY, Menard MK, Vermillion ST, Hulsey T, Ebeling M. The association between hyaline membrane disease and preeclampsia. American journal of obstetrics and gynecology. 2004 Oct 1;191(4):1414-7.
26. Bashiri A, Zmora E, Sheiner E, Hershkovitz R, Shoham-Vardi I, Mazor M. Maternal hyperten-

sive disorders are an independent risk factor for the development of necrotizing enterocolitis in very low birth weight infants. Fetal diagnosis and therapy. 2003 Oct 23;18(6):404-7.
27. Backes CH, Markham K, Moorehead P, Cordero L, Nankervis CA, Giannone PJ. Maternal preeclampsia and neonatal outcomes. Journal of pregnancy. 2011 Apr 4;2011.
28. Paul DA, Leef KH, Sciscione A, Tuttle D, Stefano JL. Neonatal Neutropenia Associated With Preeclampsia Does Not Increase the Risk for Culture Proven Sepsis† 1462. Pediatric Research. 1998 Apr;43(4):250-.
29. Tian T, Wang L, Ye R, Liu J, Ren A. Maternal hypertension, preeclampsia, and risk of neonatal respiratory disorders in a large-prospective cohort study. Pregnancy Hypertens. 2020 Jan; 19:131-137.
30. Levy M, Mor L, Kovo M, Schreiber L, Marfogel T, Bar J, Weiner E. Histologic Chorioamnionitis in Pregnancies Complicated by Preeclampsia and the Effect on Neonatal Outcomes. Reprod Sci. 2021 Jul;28(7):2029-2035.