

A CASE-CONTROL STUDY ABOUT HEMATOLOGICAL PROFILE AND MORBIDITY OF NEWBORNS AT BIRTH, BORN TO MOTHERS WITH HYPERTENSION IN PREGNANCY.

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Abstract

Background: Hypertensive disorders of pregnancy complicate about 8% of all gestations. Hypertensive disorders are responsible for significant maternal and perinatal morbidity and mortality.

AIMS: To determine the hematological parameters and morbidity in neonates born to mothers with gestational hypertension, pre-eclampsia or eclampsia syndrome and in neonates born to normotensive mothers without any maternal complications or medical illness with special reference to platelet count and neutrophil count.

Methods and Material: The study was a prospective study conducted on neonates born to pregnant women complicated with gestational hypertension, pre-eclampsia or eclampsia syndrome and neonates born to normotensive mothers recruited at Neonatal Intensive Care Unit and Post natal wards who were delivered at Ananta Hospital and AIMS & RC, Rajsamand (Raj.) from October 2018 to September 2019 and the hematological parameters of these babies were studied.

Results: In our study we observed that the mean value of platelet count were significantly lower in study group compared to control group which was highly Statistical significant ($p < 0.001$). The mean value of PT, aPTT, Bleeding Time and Clotting time were significantly higher in study group, as compared to control group. The statistical analytic differences were highly significant in all parameters i.e. PT, aPTT, Bleeding Time and Clotting time ($P < 0.001$).

Conclusion: To conclude early hematological screening of babies are recommended to facilitate early detection and management of serious neonatal complications describes above, to decrease morbidity and improved growth, development and survival.

Keywords: Pre-eclampsia, Eclampsia, Gestational Hypertension, Newborns.

Introduction:

Hypertensive disorders of pregnancy complicate about 8% of all gestations¹. Hypertensive disorders are responsible for significant maternal and perinatal morbidity and mortality. Intracranial hemorrhage is the commonest cause of death associated with hypertension².

Fetal growth restriction and pregnancy-induced hypertension (PIH; preeclampsia or transient hypertension) complicate a significant proportion of all pregnancies and predict later cardiovascular disease³. Earlier studies have reported intergenerational recurrence of low birth weight⁴, as well as preeclampsia⁵.

Pregnancy-induced hypertension is the general classification for hypertension diseases during

pregnancy, which include pregnancy-induced hypertension (without proteinuria), pre-eclampsia (with proteinuria), and eclampsia (pre-eclampsia with convulsions). This disease is responsible for high maternal and perinatal morbidity and mortality rates, and is one of the main public health problems⁶.

The classification of hypertensive disorders complicating pregnancy by the Working Group of the National high blood pressure education program [NHBPEP] (2000) is shown in table. There are four types of hypertensive disease⁷.

1. Gestational hypertension (formerly pregnancy-induced hyper-tension that included transient hypertension).
2. Pre-eclampsia and Eclampsia syndrome

3. Pre-eclampsia superimposed on chronic hypertension.

4. Chronic hypertension.

Pre-eclampsia is currently believed to be a two stage disease⁷ with shallow cytotrophoblastic invasion of maternal spiral arterioles initially resulting in placental insufficiency. Acute or chronic uteroplacental insufficiency results in antepartum or intrapartum anoxia that may lead to fetal death, IUGR and /or preterm delivery. Prematurity is the most important factor responsible for increased perinatal morbidity and mortality. Neonatal complications occurring in babies of pre-eclamptic mothers closely related to the severity of hypertension and proteinuria.

Pre-eclampsia is known to be associated with adaptive changes in the fetal circulation and placentally derived factors implicated in the pathogenesis of the maternal manifestations of disease are known to contribute to the development of neonatal thrombocytopenia and growth restriction. Severe hypertension causes a marked imbalance in the haemostatic system of the mother and the neonate.

Aims and Objectives

- To determine the hematological parameters in neonates born to mothers with gestational hypertension, pre-eclampsia or eclampsia syndrome and in neonates born to normotensive mothers without any maternal complications or medical illness with special reference to platelet count and neutrophil count.
- To determine morbidity of newborns born to mother with gestational hypertension, pre-eclampsia and eclampsia.

Material and Methods

A prospective study conducted on 50 neonates born to pregnant women complicated with gestational hypertension, pre-eclampsia or eclampsia syndrome and 50 neonates born to normotensive mothers recruited at Neonatal Intensive Care Unit and Post natal wards who were delivered at ANANTA HOSPITAL and AIMS & RC, Rajsamand (Raj.) from October 2018 to September 2019.

In this study were included two groups:-The case group included 50 neonates born to mothers with gestational hypertension, pre-eclampsia or eclampsia with the following criteria-

(a) Inclusion criteria- includes neonates born to pregnant women with gestational hypertension, pre-eclampsia and eclampsia syndrome.

(b) Exclusion criteria

1) Babies born to mothers when pregnancy is complicated by any other risk factors for increase in maternal or fetal morbidity and mortality such as :

- a. Rh incompatibility
- b. Diabetes Mellitus
- c. Any other medical illness such as severe anemia, chronic hypertension, renal disease, heart disease, connective tissue disease and those who received drugs like aspirin which were likely to cause change in hematological profile were excluded from the study.

2) Babies born to mothers with hypertension diagnosed before 20 weeks of gestation.

3) Babies born with congenital malformations.

The control group

In this group 50 full term apparently healthy newborns born to normotensive mothers without maternal complications were included and matched for gestation with the study group.

All neonates included in the study were had the following questionnaire and through clinical examination.

- 1) Detailed maternal history like age, parity, immunization status, gestational age, onset of symptoms, blood pressure value and presence of seizures and proteinuria were noted.
- 2) Details of labour, mode of delivery, presence of complications if any during labour were also recorded.
- 3) Details of baby like: name, sex, date of birth, time of birth, APGAR scores were noted. Gestational age was assessed by New Ballard's scoring system.
- 4) Thorough clinical examination of the neonates was done.
- 5) Blood samples were collected at birth from the neonates and sent for:

- Hemoglobin (Hb), Total count (TC), Differential count (DC), Platelet count
- Red cell indices :Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC)

- Peripheral blood smear examination , nucleated Red blood cell (RBC's) count, Reticulocyte count, band cell, I/T ratio, absolute neutrophil count (ANC)
- Coagulation parameters which include Prothrombin time (PT) and Activated partial thromboplastin time (aPTT), Bleeding time (BT), Clotting time (CT).

Two ml of cord blood anti coagulated with EDTA was collected from these babies and various hematological parameters were studied:

Hb, TC, DC, Platelet count and the red cell indices were estimated using automated cell counter method. Peripheral blood smear and nucleated RBC's examined using the smear stained with Leishmenn's stain. Reticulocyte count estimated using the peripheral smear stained with supravital stain. PT and aPTT is estimated using 3.2% Trisodium citrate anticoagulant in 1:9 ratio i.e. 0.2 ml anticoagulant and 1.8 ml blood. Bleeding time estimated using Duke's method and clotting time estimated using Lee and White's method.

All investigations were done at the clinical pathology and hematology laboratory at Ananta Hospital. The consultant pathologists and laboratory technicians performing the tests were masked to the identity of the neonate.

6) All data were tabulated and statistically analyzed. Sensitivity, specificity, positive predictive value, negative predictive value of both the groups was assessed and compared using suitable statistical tests.

7) Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson's correlation has been used to show the relationship between the mothers and the babies' values.

Statistical software SPSS version 10.0 was used for the analysis of the data, Harvard Graphic Version 4.0 software was used for generate graphs.

Results

The mean value of platelet count were significantly lower in study group compared to control group which was highly Statistical significant ($p < 0.001$).

The mean value of PT, aPTT, Bleeding Time and Clotting time were significantly higher in study group, as compared to control group. The statistical analytic differences were highly significant in all parameters i.e. PT, aPTT, Bleeding Time and Clotting time ($P < 0.001$).

Mean value of TLC and ANC were significantly lower in study group as compared to control group which was highly Statistical significant ($P < 0.001$).

Mean value of hemoglobin was non-significant ($p > 0.05$) while mean value of Reticulocyte count, Band Cell, I/T Ratio, nRBC Counts were significantly higher in Study group as compared to Control group ($p < 0.001$).

Out of total 50 cases, CRP was positive in only 16 cases and out of them 3, 12 and 1 belonged to GHTN, Pre Eclampsia and Eclampsia respectively and the difference was found insignificant while out of total 50 cases, E. Coli was found in blood culture only 2 cases and they belonged to pre-eclampsia and the difference was also found insignificant ($p > 0.05$).

Out of total 5 gestational hypertensive cases, 1 each had NNH and, NNS with RDS while 2 cases had NNS with NNH while 3 cases were normal. Out of total 42 pre-eclampsia cases, 5 cases had NNS with NNH, 4 each cases had NNS and NNH, 4 cases had NNS with RDS, 3 cases had NNH, 2 cases had MAS while 1 each case had HIE-II and TTN while 26 cases were normal. Out of total 3 eclampsia cases 1 each case belonged to NNH, NNS with RDS and normal respectively. That means total morbidity were 44% in study group.

Percentage of SGA baby in case and control group had 38% & 10% which was highly significant ($P < 0.001$).

Table 1: Statistical analysis of Platelet count in both groups

Investigations	Groups				t-value	P-value
	Study		Control			
	Mean	SD	Mean	SD		
Platelet Count (lakh/ mm ³)	1.19	0.40	2.66	1.09	8.959	<0.001

Table 2: Statistical analysis of Coagulation profile in both groups

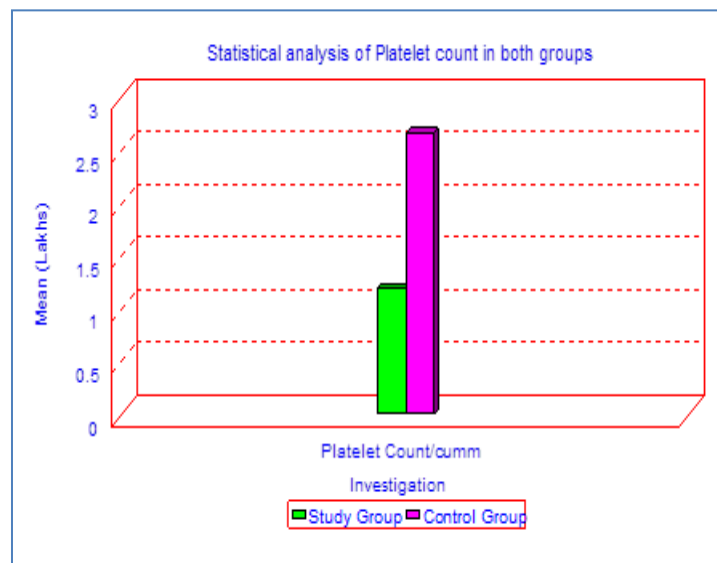
Investigations	Groups				t-value	P-value
	Study		Control			
	Mean	SD	Mean	SD		
PT (sec)	23.86	1.60	14.50	0.91	35.957	<0.001
aPTT(sec)	66.12	2.63	25.62	1.14	99.833	<0.001
Bleeding Time(min)	5.08	0.52	2.56	0.63	21.830	<0.001
Clotting Time (min)	6.17	0.60	2.28	0.63	31.711	<0.001

Table 3: Statistical analysis of Hematological profile in both groups

Hematological Parameters	Groups				t-value	P-value
	Study		Control			
	Mean	SD	Mean	SD		
Total Leukocyte Counts (Thousands/mm ³)	10.08	5.24	13.79	3.95	3.990	<0.001
Absolute Neutrophil Counts (thousands/mm ³)	6.49	2.65	8.67	3.24	3.673	<0.001

Table 4: Distribution of cases according to diagnosis in study group

Newborn Diagnosis	Mother Diagnosis						Total (n=50)	
	Gestational (n=5)		HTN (n=42)		Eclampsia (n=3)		No.	%
	No.	%	No.	%	No.	%		
Hypoxic Ischemic Encephalopathy-II	0	-	1	2.4	0	-	1	2.0
Meconium Aspiration Syndrome	0	-	2	4.8	0	-	2	4.0
Neonatal Hyperbilirubinemia	1	20.0	3	7.1	1	33.3	5	10.0
Neonatal Septicemia with Respiratory Distress Syndrome	1	20.0	4	9.5	1	33.3	6	12.0
Neonatal Septicemia with Neonatal Hyperbilirubinemia	2	40.0	5	11.9	0	-	7	14.0
Transient Tachypnoea of Newborn	0	-	1	2.4	0	-	1	2.0
Normal	1	20.0	26	61.9	1	33.3	28	56.0
Total	5	100	42	100	3	100	50	100

**Graph 1:**

Discussion

Hypertensive disorders are one of the most common obstetric complications in pregnancy. These disorders provide great challenges for obstetricians and neonatologists because they are associated with a number of adverse maternal outcomes and short and long term neonatal complications. Gestational hypertension, preeclampsia and eclampsia syndrome have important implications for the mother and her baby, suggesting that it is not a simple gestational disorder but a clinical syndrome involving important maternal and fetal vascular alterations that can persist and cause diseases in later life⁸.

The mean value of platelet count were significantly lower in study group as compared to control group which was highly Statistical significant ($P < 0.001$).

We observed, the mean platelet count were 1.19lakh/mm³ in study group as compared to control group 2.66 lakh/mm³ which is highly significant ($p < 0.001$)

Rote et al⁹, observed that PIH can be complicated by maternal or fetal thrombocytopenia, or both. In order to investigate possible immunologic causes of these thrombocytopenias, platelet-associated IgG (PAIgG) and IgM (PAIgM) were measured in mothers with PIH and in their infants. Presence of Platelet-associated IgM on fetal platelets, evidence of a fetal autoimmune reaction in pregnancy induced hypertension. A study by Romero et al¹⁰, thrombocytopenia (platelet count less than 100,000/mm³) was found in 11.6% of all patients with PIH. Thrombocytopenia was also associated with a higher incidence of preterm delivery and intrauterine growth retardation.

The mean value of PT, aPTT, Bleeding Time and Clotting time were significantly higher in study group, as compared to control group. The statistical analytic differences were highly significant in all parameters i.e. PT, aPTT, Bleeding Time and Clotting time ($P < 0.001$).

Agarwal et al¹¹ in which, the values of Prothrombin Time, Partial Thromboplastin Time with Kaolin, Thrombin Time, Fibrinogen Degradation Products were significantly raised and Fibrinogen and Platelet count were reduced significantly in both term and preterm test groups as compared to controls. Agarwal et al¹², who found that significant correlation existed between decreasing gestational age and alterations in all coagulation parameters. Higher

incidence of prematurity, hyper-bilirubinaemia and significant prolongation in prothrombin time (PT), partial thromboplastin time with kaolin (PTTK) and thrombin time (TT) values were observed with increasing severity of grade of gestational hypertension.

The mean of TLC and ANC were 10.08 & 6.49 thousand/mm³ in study group compared to 13.79 & 8.67 thousand/mm³ in control group respectively, which was highly significant. ($p < 0.001$).

A study by Mouzinho et al¹³ reported that 40% to 50% of neonates studied developed neonatal neutropenia, ($p < 0.01$) It is a transient hematologic 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 infection.

Our study results was similar to another study by Patricia et al²¹ which showed that infants born to mothers with gestational hypertension, pre-eclampsia, or eclampsia syndrome were associated with leucopenia, absolute neutropenia and thrombocytopenia.

Mean value of hemoglobin was non-significant ($P > 0.05$) while mean value of Reticulocyte count, Band Cell, I/T Ratio, nRBC Counts were significant and Statistically higher in Study group as compared to Control group ($p < 0.001$).

We observed the mean Hb value were 16.92 gm% in study group compared to control group 17.38%, which is insignificant (p value < 0.417).

Sivakumar et al¹⁴, mean Hb value 17.98 gm% in study group compared to control group 17.33%, which is insignificant (p value > 0.05)

Sunil Kumar et al 2013, mean Hb value 14.83 gm% in study group compared to control group 15.22 gm%, which is insignificant (p value > 0.05).

In study group out of total 50 deliveries 16 had their C-reactive protein positive while 34 had negative CRP while in control group only 3 cases had their CRP positive. This difference was found statistically significant (OR-0.136; 95% CI 0.037-0.503; $p < 0.01$).

Tsoa et al¹⁵ observed that C-reactive protein (CRP) was detecting inflammation, which was significantly increased in infant of preeclamptic mother.

Mosayeb et al¹⁶ had also found sepsis about that, Positive cultures including blood, urine and CSF were observed in 16.6%, 11.9% and 7.1% of infants respectively. They were almost all preterm neonates. There was concerned about the possible relationship between infant of hypertensive mother and sepsis.

Out of total 5 gestational hypertensive cases, 1 each had NNH and, NNS with RDS while 2 cases had NNS with NNH while 3 cases were normal. Out of total 42 pre-eclampsia cases, 5 cases had NNS with NNH, 4 each cases had NNS and NNH, 4 cases had NNS with RDS, 3 cases had NNH, 2 cases had MAS while 1 each case had HIE-II and TTN while 26 cases were normal. Out of total 3 eclampsia cases 1 each case belonged to NNH, NNS with RDS and normal respectively. That means total morbidity were 44% in study group.

Out of 50 Study group 13 (26%) babies had neonatal septicaemia in which 4 (8%) babies developed Necrotizing entero-colitis and also another 4(8%) babies developed bleeding (IVH-3cases in preeclampsia and rest 1belonged to eclampsia) and without any mortality while NNH had 11(22%), RDS had (6)12%, MAS had 2(4%), HIE-II had(1)2% and TTN had 1(2%).

Eeltink et al¹⁷ observed in which 44.7% of cases had jaundice as compared to control group while current study had 22% hyperbilirubinemia.

It was different from study by Sivakumar et al³⁰ based on morbidity and mortality, in which 5 (10%) babies born to mothers with PIH developed neonatal sepsis, of which 2 (4%) developed Necrotizing enterocolitis and 3(6%) died.

Our results similar to Sivakumar et al¹⁴, based on morbidity in control group, in which also none of the control babies had any complications and were discharged on day 2 of life.

Conclusion

The results of the study revealed that newborn, born to mothers specially with gestational hypertension, pre-eclampsia and eclampsia were more prone for development of prematurity (34%), small for gestational age (38%), leucopenia, neutropenia, thrombocytopenia with deranged coagulation profile, increased C-reactive protein (32%), reticulocyte count, band cell, I/T ratio and circulating nucleated RBCs during the early neonatal period and these babies were more prone to increased morbidity like sepsis(26%), jaundice(22%), Respiratory Distress

Syndrome (12%), bleeding tendencies(8%), Meconium aspiration syndrome(4%),HIE-II(2%)and TTN(2%). Early hematological screening of these babies is recommended to facilitate early detection and management of serious neonatal complications describes above, to decrease morbidity and improved growth, development and survival.

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