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RESEARCH ARTICLE

Role of Laboratory Investigations to Assess Maternal and Perinatal Outcome in Hypertensive Mothers

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ABSTRACT

Introduction: The aim of this study was to evaluate the relevance of routinely done laboratory parameters in women with hypertensive disorders in pregnancy.

Materials and methods: Hypertensive pregnant women were divided into two groups based on perinatal outcome as those with and without poor perinatal outcome. They were analyzed with various laboratory tests done at the time of diagnosis: Hematological parameters, such as hemoglobin, hematocrit, platelet count, total leukocyte count, and differential count; renal parameters, such as serum urea, creatinine, and uric acid; liver function tests; and serum lactate dehydrogenase (LDH). Coagulation parameters, such as prothrombin time, activated partial thromboplastin time, and international normalized ratio were compared between the two groups. Data were presented as mean ± standard deviation; α level of $p < 0.05$ was set as statistically significant.

Results: Among the various hematological parameters, platelet count showed statistically significant differences between hypertensives with and without perinatal mortality or morbidity ($p = 0.029$, $p = 0.029$ respectively). All renal parameters showed statistically significant differences ($p \leq 0.005$). Serum aspartate aminotransferase ($p = 0.034$) among the liver parameters and serum LDH ($p = 0.024$) showed statistically significant differences between the two groups. Coagulation parameters were abnormal among patients with thrombocytopenia.

Conclusion: Blood pressure alone is not sufficient in monitoring women with hypertensive disorders in pregnancy. Laboratory parameters that are cost-effective and routinely done in most laboratories are significant in assessing the severity of maternal disease and the perinatal outcome. It can hence, be used to monitor hypertensive women in pregnancy.

Keywords: Coagulation, Cohort study, Gestational hypertension, Platelet, Preeclampsia, Uric acid.

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INTRODUCTION

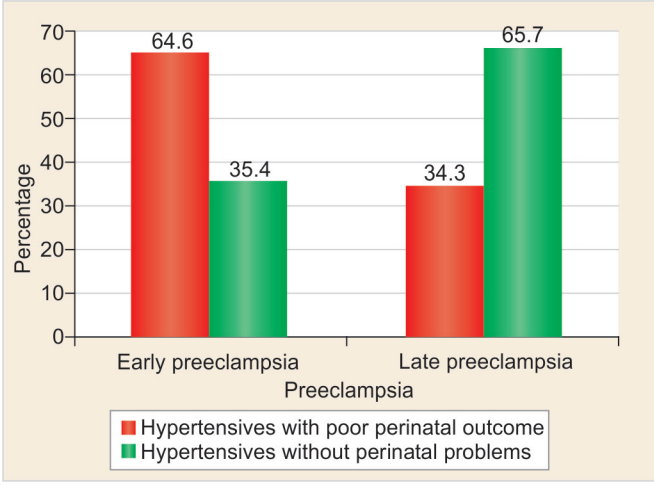
Hypertensive disorders in pregnancy affect 5 to 10% of all pregnancies.[1,2] It is considered to be a major cause of maternal and perinatal morbidity and mortality. An estimated 8.4 million pregnant women suffer from hypertensive disorders worldwide.[3] It is an unpredictable multiorgan disorder unique to human pregnancy.

The erratic onset and progression of the symptoms warrant the need for early detection. This study was undertaken to evaluate the relevance of routinely done laboratory parameters in women with hypertensive disorders in pregnancy.

MATERIALS AND METHODS

The present study was a prospective, single-center observational cohort study, carried out in the Department of Obstetrics and Gynecology in a tertiary care teaching hospital. The study was reviewed and approved by the Institutional Ethics Committee. Singleton pregnant women with blood pressure recording of 140/90 mm Hg or more after 20 weeks of gestation, diagnosed with gestational hypertension, preeclampsia, or eclampsia were included. A total of 100 women were considered as study subjects. At the time of diagnosis of hypertension, various parameters, such as age of the subject, parity index, blood pressure (systolic and diastolic) recording, and gestational age at which high blood pressure was initially detected were noted. Laboratory tests were done for these subjects at the time of initial high blood pressure recording: Hematological tests, such as hemoglobin, packed cell volume (PCV), platelet count, total leukocyte count, and differential count (neutrophil, lymphocyte); biochemical tests, such as serum urea, serum creatinine, serum uric acid, total bilirubin, direct bilirubin, serum aspartate aminotransferase (AST), serum alanine transaminase (ALT), serum alkaline phosphatase (ALP), and serum lactate dehydrogenase (LDH); coagulation tests,

such as prothrombin time, activated partial thromboplastin time, and international normalized ratio were done and the values were recorded. These women were closely monitored, and laboratory tests were repeated weekly. They were followed up till delivery, and the gestational age at which they delivered was noted. They were then divided into two groups based on the perinatal outcome. Hypertensive pregnant women with poor perinatal outcome, such as intrauterine growth restriction (IUGR) and intrauterine death (IUD) were considered as group A (n = 54), and those without IUGR and IUD were considered under group B (n = 46). Various laboratory parameters noted at the time of initial diagnosis were analyzed between the two groups.



Graph 1: Correlation of timing of preeclampsia with perinatal outcome

Statistical Analysis

- The observations were tabulated on Microsoft Excel and the results were analyzed using Statistical Package for the Social Sciences software version 16.0. *Chi-square test* and Student's *t*-test were used for detailed analysis.
- α level of $p < 0.05$ was set as statistically significant.

RESULTS

A total of 100 women diagnosed with hypertensive disorders in pregnancy were analyzed in the study. Among the total, 54 (54%) women had poor perinatal outcome and were allotted under group A and 46 (46%) had no perinatal problems and were allotted under group B.

Out of the total women (n = 100), 65 women (65%) were diagnosed with early-onset preeclampsia that occurred before 34 weeks of gestation and 35 (35%) women were found to have late-onset preeclampsia that occurred at or beyond 34 weeks of gestation. Among the women with early-onset preeclampsia (n = 65), 42 (64.6%) had poor perinatal outcome compared with 12 (34.3%) of 35 women with late-onset preeclampsia who had poor perinatal outcome as depicted in Graph 1.

Data were presented as mean ± standard deviation (SD). Baseline characteristics were compared between the two groups as shown in Table 1. Mean systolic and diastolic blood pressure in group with poor perinatal outcome (150.37 ± 7.82 and 96.66 ± 6.79 mm Hg respectively) was comparable with mean systolic and diastolic blood pressure in group with good perinatal outcome (149.52 ± 6.66 and 95.73 ± 5.63 mm Hg respectively). The difference was found to be insignificant at 5% probability level.

Average gestational age in weeks at which high blood pressure was initially noted at the time of diagnosis was significantly lower in hypertensive women with poor perinatal outcome (gestational age of 30.22 ± 4.24 weeks) compared with hypertensive women with good perinatal outcome (gestational age of 32.72 ± 4.18 weeks), which was proved to be statistically significant (p = 0.004).

Average gestational age in weeks at which delivery was conducted was significantly lower in group A (32.70 ± 3.40) than in group B (37.39 ± 1.97), with a p-value of 0.000. Group A consisted of only seven cases that went beyond 37 weeks of gestation as in comparison with

Table 1: Baseline characteristics

Parameters	*Poor perinatal outcome (n = 54) (mean±SD)*	*Good perinatal outcome (n = 46) (mean±SD)*	*p-value*
Age (years)	28.02 ± 3.47	28.63 ± 4.69	0.457
Primipara (number)	38	34	0.637
Multipara (number)	16	12	0.450
Systolic blood pressure (BP; mm Hg)	150.37 ± 7.82	149.52 ± 6.66	0.274
Diastolic blood pressure (mm Hg)	96.66 ± 6.79	95.73 ± 5.63	0.416
Gestational age at which initial high BP recorded (weeks)	30.22 ± 4.24	32.72 ± 4.18	0.004
Average gestational age at time of delivery (weeks)	32.70 ± 3.40	37.39 ± 1.97	0.000
Number of preterm delivery	47	7	0.000
• Iatrogenic	47	5	
• Spontaneous	0	2[a]	

[a]Preterm delivery was due to preterm premature rupture of the membranes in both the cases at 35 and 36 weeks of gestation

Table 2: Hematological parameters

Parameters	Poor perinatal outcome (n = 54) (mean±SD)	Good perinatal outcome (n = 46) (mean±SD)	p-value
Hemoglobin (g/dL)	11.82 ± 1.27	11.96 ± 1.11	0.560
Packed cell volume (%)	35.98 ± 3.75	36.28 ± 3.62	0.693
Platelet count (/µL)	195240.74 ± 54982.994	220652.17 ± 59329.66	0.029
Total leukocyte count (/µL)	13733.33 ± 3890.43	12680.43 ± 3003.08	0.138
Neutrophil (%)	75.66 ± 9.64	72.63 ± 6.89	0.072
Lymphocyte (%)	17.38 ± 7.51	19.15 ± 5.62	0.183

39 cases in group B (p = 0.000). Hence, there were 47 (87%) women with poor perinatal outcome that had preterm delivery and only 7 (15%) women with good perinatal outcome that underwent preterm delivery.

Among the hematological parameters (Table 2) observed between the two groups, platelet count was significantly (p = 0.029) lower in the group with poor perinatal outcome (195240.74 ± 54982.994/µL) as compared with the group with good perinatal outcome (220652.17 ± 59329.66/µL). There was no notable difference in other hematological parameters.

Table 3 shows the correlation of thrombocytopenia with the severity of perinatal outcome. At a platelet count less than 50,000/µL, 100% women had poor perinatal outcome, hence, suggesting poorer perinatal outcome among hypertensives with lower platelet count.

All the renal function parameters, such as serum urea, serum creatinine, and serum uric acid showed statistically significant differences between the two groups (p = 0.000, p = 0.005, and p = 0.000 respectively) as shown in Table 4. Serum urea in those with poor perinatal outcome was significantly increased (19.68 ± 3.21 mg/dL) compared with women with good perinatal outcome (11.76 ± 5.21 mg/dL). Serum creatinine in those with poor perinatal outcome was found to be 0.65 ± 0.20 mg/dL compared with 0.56 ± 0.10 mg/dL in those with good perinatal outcome. Similarly, serum uric acid was significantly raised in the group with poor perinatal outcome (5.71 ± 1.54 mg/dL) as compared with the group with good perinatal outcome (4.45 ± 1.17).

Among the liver function tests (Table 5) measured, serum AST was found to be significantly increased in the group with poor perinatal outcome (47.07 ± 75.23 IU/L) compared with the group with good perinatal outcome (23.84 ± 29.40 IU/L), with a p-value of 0.034. Serum LDH was significantly elevated in the group with poor

Table 3: Correlation of thrombocytopenia with severity of perinatal outcome

		Poor perinatal outcome		Good perinatal outcome		Total (n = 100;
Parameters	Platelet count (/µL)	n = 54	%	n = 46	%	% = 100)
Thrombocytopenia	≤50,000	2	100	0	0	2
	50,001–100,000	1	50	1	50	2
	100,001–150,000	6	60	4	40	10
Total with thrombocytopenia	<150,000	9	64	5	36	14
Normal platelet count	≥150,000	45	52	41	48	86

Table 4: Renal parameters

Parameters	Poor perinatal outcome (n = 54) (mean±SD)	Good perinatal outcome (n = 46) (mean±SD)	p-value
Serum urea (mg/dL)	19.68 ± 3.21	11.76 ± 5.21	0.000
Serum creatinine (mg/dL)	0.65 ± 0.20	0.56 ± 0.10	0.005
Serum uric acid (mg/dL)	5.71 ± 1.54	4.45 ± 1.17	0.000

Table 5: Liver parameters and serum LDH

Parameters	Poor perinatal outcome (n = 54) (mean±SD)	Good perinatal outcome (n = 46) (mean±SD)	p-value
Total bilirubin (mg/dL)	0.47 ± 0.79	0.35 ± 0.15	0.306
Direct bilirubin (mg/dL)	0.20 ± 0.40	0.12 ± 0.05	0.168
Serum AST (IU/L)	47.07 ± 75.23	23.84 ± 29.40	0.034
Serum ALT (IU/L)	41.90 ± 100.88	15.78 ± 16.82	0.066
Serum ALP (IU/L)	152.44 ± 77.12	151.78 ± 38.56	0.956
Serum LDH (IU/L)	320.31 ± 152.14	262.45 ± 96.38	0.024

Table 6: Effect of thrombocytopenia on maternal and perinatal outcome

	Hypertensive mothers with normal platelet count		*Hypertensive mothers with thrombocytopenia*	
	n	*%*	*n*	*%*
Maternal outcome				
Increased uric acid	17	19.8	6	42.9
Increased urea	59	68.6	11	78.6
Increased creatinine	5	5.8	2	14.3
Abnormal LFT	8	9.3	5	35.7
Increased LDH	1	1.2	4	28.6
Eclampsia	3	3.5	1	7.1
HELLP	0	0	2	14.2
Fundoscopy changes	2	2.3	1	7.1
Perinatal outcome				
IUGR	44	51.2	9	64.3
IUD	9	10.5	1	7.1
APGAR at 1 minute <9	29	35	7	50
APGAR at 5 minutes <9	11	12.7	3	21.4
NICU admission	44	51.2	10	71.4
Total	86	100	14	100

HELLP: Hemolysis, Elevated Liver enzymes, and Low Platelet count; NICU: Neonatal intensive care unit; APGAR: Activity pulse grimace appearance respiration

perinatal outcome (320.31 ± 152.14 IU/L) compared with the group with good perinatal outcome (262.45 ± 96.38 IU/L), with a p-value of 0.024. Differences among the other liver parameters were found to be insignificant at 5% probability level.

The two groups were further subdivided into hypertensive pregnant women with thrombocytopenia with a platelet count less than 150,000/μL and those with normal platelet count. A slight increase in coagulation parameters was noted among the patients with thrombocytopenia as compared with those with normal platelet count in both the groups. Prothrombin time was 15.23 ± 3.98 in hypertensive women with thrombocytopenia and poor perinatal outcome, whereas it was 14.16 ± 0.61 in hypertensive women with thrombocytopenia and good perinatal outcome. This variation was found to be significant statistically as evident by p-value of 0.046.

Table 6 shows adverse maternal and perinatal outcome in hypertensive pregnant women with thrombocytopenia when compared with women with normal platelet count.

DISCUSSION

Hypertensive disorders of pregnancy are responsible for a large proportion of perinatal deaths resulting from prematurity and IUGR.[4] Currently, there are no suitable and reliable indicators in monitoring the progression of the disease leading to poor perinatal outcome. Hence, we have evaluated in our study, the significance of measurement of various laboratory parameters in detecting those hypertensive women with poor perinatal outcome.

In our study, the blood pressure of hypertensive women with poor perinatal outcome and blood pressure of hypertensive women with good perinatal outcome did not vary. This is in agreement with the findings of Monteiro et al[1] who observed that the blood pressure of the study subjects with normal fetus did not vary compared with hypertensive mothers with IUGR and IUD of fetus.

Perinatal outcome was found to be poor if high blood pressure recordings were noted at an earlier gestational age. Average gestational age at which delivery was conducted was significantly lower in group A than group B. Group A consisted of only 7 cases that went beyond 37 weeks of gestation, suggesting that timing of the disease itself is an indicator of the disease severity and perinatal outcome.

Nevertheless, prognosis does not depend on blood pressure alone. Laboratory tests play a significant role. During the second trimester of pregnancy, normally there is an increase in the maternal plasma volume, but such hemodynamic changes do not occur in preeclampsia due to vasospasm and absence of hypervolemia, leading to a rise in the hematocrit value. Hemoconcentration leads to decreased placental circulation that plays a pathogenic role in the development of preeclampsia. This may, therefore, be considered as an indicator for detection of preeclampsia.[5] However, in the present study, hemoglobin and PCV did not differ significantly between the two groups; this is in agreement with two studies that reported hemoglobin and hematocrit to be poor indicators.[2,6] Conflicting results were observed in a study by Monteiro et al[1] who observed that hypertensive mothers with IUGR and IUD of fetus had significantly lower hemoglobin concentration and PCV compared with those mothers with normal fetus.

Thrombocytopenia is most frequently found in preeclampsia and is probably due to consumption of platelets during low-grade intravascular coagulation.[7] Platelet count showed statistically significant differences between the two groups in our study. Poor perinatal outcome was observed among the hypertensives with low platelet count. This is in accordance to the findings of Monteiro et al,[1] who observed that a decline in the platelet count was associated with severity of hypertensive disorder in pregnancy progressing to IUGR and IUD of the fetus. Other studies also showed that thrombocytopenia is directly proportional to severity of hypertension in pregnancy.[7,8] Hence, lower the platelet count, greater the maternal and perinatal morbidity and mortality.

In the development of preeclampsia, leukocyte activation plays a crucial role. It is a major component of

exaggerated inflammatory response in the maternal vascular system and leads to vascular injury by interacting with platelets and endothelial lining of blood vessels.[9] Some studies have shown increase in total count and differential count in hypertensive women compared with normotensives, but very few have evaluated its significance in hypertensive women with poor perinatal outcome.[1,10] In our study, total count and differential count showed no significant differences between the hypertensive women with poor perinatal outcome and hypertensive women without perinatal problems, which is in concordance to the results found by Monteiro et al.[1]

Hyperfiltration that occurs as a result of increased glomerular filtration rate and renal plasma flow in normal pregnancy leads to a reduction in serum urea, serum creatinine, and serum uric acid concentrations. In preeclampsia, due to vasospasm and glomerular endotheliosis, renal perfusion and glomerular filtration rate is reduced, which is responsible for elevated values.[6] Hyperuricemia in preeclampsia may be due to decreased renal tubular secretion or raised uric acid production caused by breakdown of trophoblasts, release of cytokines, and ischemia.[11] This can promote endothelial dysfunction, damage, and inflammation leading to oxidation, which is a characteristic feature of preeclampsia.

In the present study, all renal parameters (serum urea, serum creatinine, and serum uric acid) showed statistically significant differences between the two groups, with increased values in hypertensive women with poor perinatal outcome. Serum uric acid and serum urea were found to be more significant than serum creatinine in our study. Hawkins et al[2] concluded in their study that serum creatinine is not a sensitive marker and that hyperuricemia identifies hypertensive women at risk of adverse fetal outcome. Other research has also shown a positive relationship between hyperuricemia and adverse obstetric and perinatal outcome in hypertensive women.[12,13] Hence, renal parameters, especially serum uric acid, can be considered as reliable predictors of severity of preeclampsia. Contradictory findings were found in a study by Monteiro et al,[1] wherein serum uric acid level was comparable between hypertensive subjects with and without IUGR and IUD of fetus. Andrews et al[3] stated that uric acid is not useful to predict fetal complications.

In preeclampsia, hypervascularization and vasoconstriction of liver lead to modification of the cell membrane permeability and injury to the liver cells, which permits leakage of intracellular enzymes into the blood. Consequently, there is elevation of serum transaminases and LDH.[3,14] Among the liver parameters, serum AST and serum LDH showed statistically significant differences between the two groups in our study. A study by Paneri et al[14] also showed raised liver function tests in preeclamptics. Andrews et al[3] highlighted that LDH may prove useful as a selective predictive biochemical marker of preeclampsia and its severity.

In preeclampsia, vasoconstriction and platelet aggregation lead to systemic dysfunction. This further leads to activation of coagulation with consequent hypoxic damage to the endothelium. In our study, coagulation parameters were abnormal among patients with thrombocytopenia. Majority of the women with thrombocytopenia in our study had poor perinatal outcome. In a study by Meshram et al,[4] out of 32 patients with deranged coagulation profile, 30 (93.75%) had unfavorable fetal outcome.

The limitation of this study was that the blood pressure and various laboratory parameters noted at the time of initial diagnosis of hypertension only were analyzed. There was no further follow-up of the laboratory investigations.

CONCLUSION

Based on the findings of the study, it can be concluded that the timing of occurrence of the disease itself is an indicator of disease severity and perinatal outcome. Among hematological parameters, platelet count is the most suitable marker in monitoring hypertensive women during pregnancy. More poor perinatal outcome is seen in hypertensives with low platelet count. Abnormal renal parameters portend a poor perinatal outcome. Liver function tests and serum LDH are of significance in monitoring. Patients with deranged coagulation profile have unfavorable fetal outcome.

Hence, blood pressure alone is not sufficient in monitoring women with hypertensive disorders during pregnancy. Laboratory parameters that are cost-effective and routinely done in most laboratories are significant in assessing the severity of maternal disease and the perinatal outcome. It can, hence, be used to monitor hypertensive women in pregnancy.

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