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Original Article

Pathology Section

Haematological Parameters, Coagulation Profile and Serum Lactate Dehydrogenase in Women with Pregnancy Induced Hypertension versus Normotensive Pregnant Women: A Case-control Study

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ABSTRACT

Introduction: Pregnancy-Induced Hypertension (PIH) is the most common disorder of pregnancy, affecting approximately 5-7% of pregnancies and it is a significant cause of maternal and foetal morbidity and mortality. In a proportion of these patients, the risk to the mother can be substantial, including the possible development of Microangiopathic Haemolytic Anaemia (MAHA). Altered haemogram and coagulation abnormalities, such as anaemia, thrombocytopenia, the presence of schistocytes and deranged Prothrombin Time (PT) and activated Partial Thromboplastin Time (APTT) values, are hallmarks of these patients.

Aim: To compare haematological and coagulation parameters, as well as serum Lactate Dehydrogenase (LDH) levels, in normal pregnant women and those with PIH.

Materials and Methods: This was a case-control study in which 100 patients were analysed in a tertiary care centre attached to a University Medical College in western India over two years. Complete Blood Count (CBC) with peripheral blood smear, PT, aPTT and serum LDH were performed on patients with PIH (50) and normal pregnancies (50). The data were analysed using Statistical Package for the Social Sciences (SPSS) version 25.0 software. For qualitative data, various rates, ratios and percentages were calculated. Chi-square test was used to find associations between two or more attributes. For quantitative data, Mean±SD was calculated. The unpaired t-test was utilised to compare the two independent groups for the data variables. A p-value of <0.05 was considered significant.

Results: The platelet count was decreased in 48 out of 50 PIH patients (96%), while PT and aPTT were increased in all 50 patients with PIH. Serum LDH values were elevated in 16 patients with PIH (32%). The p-value was found to be <0.0001 in women with Preeclampsia (PE) and Eclampsia (E) compared to normal pregnant women for platelet count, PT, APTT and serum LDH. Only four PIH patients showed the presence of schistocytes on the peripheral smear.

Conclusion: Patients with PIH exhibited low platelet counts, high PT/APTT values and elevated serum LDH levels compared to normal pregnant patients. PIH and Disseminated Intravascular Coagulation (DIC) can present with overlapping features, such as thrombocytopenia and abnormal liver function tests, but they differ in clinical context and severity of coagulation abnormalities.

Keywords: Anaemia, Blood coagulation disorders, Complete blood count, Preeclampsia, Schistocytes

INTRODUCTION

Thrombotic Microangiopathies (TMAs) are associated with microangiopathic haemolytic anaemia and thrombocytopenia, resulting in microvascular thrombosis and end-organ damage. In pregnancy, this may be the result of pregnancy-related TMAs such as preeclampsia and Haemolysis, Elevated Liver enzymes and Low Platelets (HELLP) [1]. Hypertensive disorders are a common pregnancy complication that puts women and their foetuses at higher risk of further complications as well as long-term consequences. Gestational hypertension/PIH is defined as blood pressure of ≥140 mmHg systolic or 90 mmHg diastolic on two separate occasions at least four hours apart after 20 weeks of gestation. Preeclampsia is classically defined as gestational hypertension accompanied by new-onset proteinuria, while eclampsia is preeclampsia with convulsions [2].

Preeclampsia and eclampsia are unique among hypertensive disorders in terms of their effects on maternal and neonatal health. Preventing acute and chronic consequences for both the mother and the foetus requires early detection of pregnant women at risk of developing preeclampsia and eclampsia [3]. Preeclampsia/eclampsia can cause a variety of haematological changes, the most common of which is thrombocytopenia, caused by increased consumption during low-grade intravascular coagulation [4]. The more ominous complications seen in severe preeclampsia/eclampsia include thrombocytopenia, consumption coagulopathy and the triad of HELLP [5].

Various haematological changes are observed, including numerical and functional platelet abnormalities (thrombocytopenia), changes in haemoglobin values and erythrocyte parameters and an increase in the procoagulant state during normal pregnancy [4]. Coagulation studies are not routinely performed but are recommended for patients who have additional complications such as abruptio placentae, severe bleeding, thrombocytopenia, or severe liver dysfunction [6]. HELLP syndrome is one of the more severe forms of preeclampsia, as it has been linked to higher rates of maternal morbidity and mortality. The most common measure of haemolysis in HELLP is LDH, an enzyme found in abundance in Red Blood Cells (RBCS) [7]. Although various diagnostic criteria have been proposed, many clinicians use the following criteria to make the diagnosis: LDH

elevated to 600 U/L or more, Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) elevated to more than twice the upper limit of normal and platelet count < 100,000/µL [8]. As a result, LDH can be used as a biochemical marker because it reflects disease severity, complications and foetal outcomes.

The present study aimed to find differences in blood counts, peripheral smears, coagulation profiles and serum LDH values in patients with PIH compared to normal pregnant women. The objectives of the study were to analyse various haematological parameters in patients with PIH and normal pregnancy, to compare these findings between the PIH group and normal pregnant women and to assess the utility of these findings for early detection and prevention of complications.

MATERIALS AND METHODS

This case-control study was conducted over a period of two years i.e. from 1st September 2019 to 31st August 2021 in the Department of Pathology at a tertiary care centre attached to University Medical College in Pune, Western India. The Institutional Ethics Committee (IEC) number for this study was BVDUMC/IEC/74E. A total of 100 patients were included in this study. 50 patients had preeclampsia/eclampsia and the remaining fifty were normal pregnant patients.

Inclusion criteria: Patients diagnosed with PIH (preeclampsia/eclampsia) were evaluated along with an equal number of normal pregnant females were included in the study.

Exclusion criteria: Patients diagnosed with essential hypertension, sepsis, malnutrition, valvular heart diseases and those on anticoagulants were excluded from the study.

The required history and clinical details were collected from the medical records department Complete haemogram with peripheral blood smear, PT, aPTT and serum LDH were performed on these patients. The samples for the study were obtained from patients in the Obstetrics and Gynecology (OBGY) outpatient department and ward. Peripheral blood samples were collected and evaluated. EDTA vacutainers were used for CBC and peripheral blood smears. CBC was performed on the LH750/DxH800 fully automated hematology analyser. A 3.2% tri-sodium citrate vacutainer was used for coagulation tests, which were performed on the ACL Top300 analyser. A plain vacutainer was employed for serum LDH and the test was performed on the fully automated Abbott Alinity and Architect analyser. There were no anticipated risk factors involved in this study, except for those arising due to the natural progression of the disease.

STATISTICAL ANALYSIS

The data were analysed using SPSS version 25.0 software. The results were presented in tabular and graphical formats. Various rates, ratios and percentages were calculated. The Chi-square test was used to find associations between two or more attributes for qualitative data variables. Mean±SD was calculated and the unpaired t-test was used to compare the two independent groups for quantitative data variables. A p-value of < 0.05 was considered significant.

RESULTS

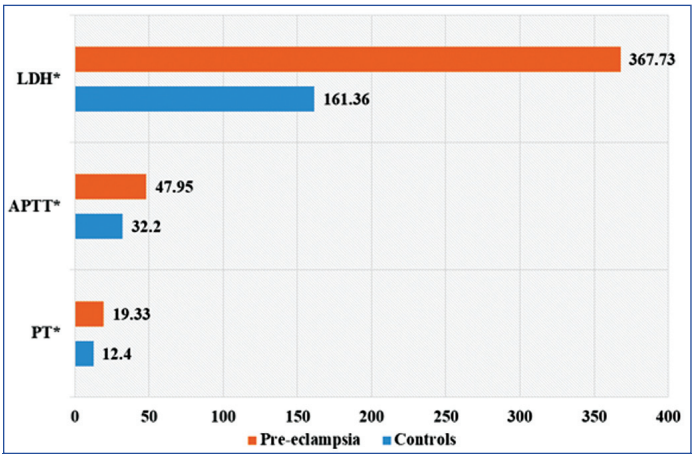
The mean ages of the women in each group were 24.72±2.65 years and 25.02±3.17 years, respectively, with no significant difference (p-value=0.6052) in the mean ages between the groups.

The haematological parameters, including haemoglobin, Mean Corpuscular Volume (MCV), RBC count, platelet count, coagulation parameters (namely PT and APTT) and the biochemical parameter serum LDH were measured. The mean±SD values of age, haematological, coagulation and biochemical parameters in all study groups are presented in [Table/Fig-1].

Variables	Controls (n=50) Mean±SD	PE/E (n=50) Mean±SD	p-value (Unpaired t-test)
Age (years)	24.72±2.65	25.02±3.17	0.6052
Haemoglobin (g/dL)	11.4±1.12	11.16±1.39	0.3413
MCV (fL)	83.8±6.08	83.16±6.64	0.6112
RBC count (millions/cu.mm)	3.74±0.42	3.71±0.49	0.7247
Platelet count (lacs/cu.mm)	273510±80037.8	102902±23804.4	<0.0001*
PT (seconds)	12.40±1.40	19.33±1.15	<0.0001*
aPTT (seconds)	32.2±3.19	47.95±2.11	<0.0001*
LDH	161.36±49.69	367.73±82.22	<0.0001*

[Table/Fig-1]: Comparison of haematological and coagulation markers in Pre-Eclampsia (PE) women with normal pregnant women.
Platelet count, PT, APTT and LDH values showed significant variation in Pre-Eclampsia (PE)/Eclampsia (E) patients

There was no significant difference in the means of age, haemoglobin, MCV and RBC count reported between the groups. The platelet count was decreased (Mean 102,902/µL) in 48 out of 50 PIH patients (96%) compared to controls, with the count being normal in two patients. Meanwhile, PT (mean 19.33 seconds) and aPTT (mean 47.95 seconds) were increased in all 50 patients with PIH. Serum LDH values (mean 367.73 IU/L) were elevated in 16 patients with PIH (32%) and were normal in 34 patients. The p-value was found to be significant (p-value <0.0001) in women with preeclampsia and eclampsia compared to normal pregnant women for platelet count, PT, APTT and serum LDH. The association between coagulation parameters and LDH is presented in [Table/Fig-2].



[Table/Fig-2]: Shows significant increase in LDH activity along with increase in PT and APTT in patients of Pre-Eclampsia (PE)/Eclampsia (E).

The distribution of patients according to RBC morphology was compared between the groups using the Chi-square test; however, there was no significant difference (p-value=0.5388) in RBC morphology (i.e., normochromic normocytic vs. microcytic hypochromic) between the study groups. The distribution of patients based on the presence or absence of schistocytes was also compared using the Chi-square test. Although four patients showed the presence of schistocytes, the distribution of patients did not differ significantly (p-value=0.1176) between the study groups [Table/Fig-3].

	Schistocytes			p-value
	No n (%)	Yes n (%)	Total	
PE/E	46 (92.16)	4 (7.84)	50	0.1176
Controls	50 (100)	0	50	

[Table/Fig-3]: Association of schistocytes between the study groups.
Chi-square test was used

DISCUSSION

Hypertensive disorders complicate 5-10% of all pregnancies and are a leading cause of maternal and foetal death and morbidity. In India, the incidence of preeclampsia and eclampsia is reported to be 8-10% among pregnant women. According to a study, the prevalence of hypertensive disorders of pregnancy was 7.8%, with preeclampsia occurring in 5.4% of the study population in India [9].

The present study aimed to compare haematological and coagulation parameters, along with serum LDH values, in normal pregnant women and PIH patients. A total of 100 pregnant women were recruited for the present study, with 50 each in the PIH and control groups. The mean ages of the women in each group were 24.72±2.65 and 25.02±3.17 years, respectively, with no significant difference noted. The mean and standard deviation of the age of onset reported by Bhutani N et al., were similar with those of the current study, with 28.32 years in the control group and 28.64 years in the cases [4].

In the present study, there was no significant difference in the means of haemoglobin, MCV and RBC count reported between the PIH and normal pregnant women, while the platelet count significantly decreased in the PIH group compared to controls. In a study by Mtali YS et al., haemoglobin along with red cell indices, including MCV, MCH and MCHC, were slightly lower in the PIH group than in the normotensive group [9]. The blood smear may show the presence of schistocytes in cases of PIH [10]. Hernández JD et al., observed a pronounced increase in abnormal erythrocytes in women with PIH. Their study found haematological findings associated with eclampsia included thrombocytopenia, evidence of haemolysis and clinically insignificant DIC. Women with preeclampsia and eclampsia were reported to have schistocytes, which are characteristic of microangiopathic haemolysis [11]. Present study observed the presence of schistocytes in four cases of PIH, but this was statistically insignificant (p-value=0.1176) in terms of RBC morphology and the presence or absence of schistocytes between the study groups. Although the result of this study regarding schistocytes among the two groups is not statistically significant, this finding is crucial for diagnosing MAHA.

Thrombocytopenia is the most common haemostatic abnormality and its detection is important as it is one of the preventable factors contributing to some cases of life-threatening cerebral and hepatic haemorrhage [5]. Similar to the present study, Bhutani N et al., reported a platelet count of 2.71 lacs/µL in the control group compared to 1.52 lacs/µL in the PIH group; the difference in the mean was significant. They also reported significant differences in platelet volume and platelet distribution width [4]. The mean platelet count reported by Jhajharia N and Verma M, was significantly lower in the PIH group, consistent with the present study [12].

In the present study, the values of PT and aPTT were significantly increased in the PIH group compared to controls. The results of the present study for PT and aPTT were similar to the study by Bhutani N et al., [4] The values of PT and aPTT in the control and PIH groups were 12.4 seconds; 19.33 seconds and 32.2 seconds; 47.95 seconds, respectively. The difference in the means of both parameters was statistically significant [4]. Shetty J et al., studied coagulation profiles of patients with platelet counts below 1.5 lacs/µL and found that both PT and aPTT were prolonged in PIH [5]. Sharma UK et al., reported a significant positive association between PT and aPTT and the severity of PIH [13].

Due to repeated activation of the coagulation cascade as a result of the constant endothelial damage experienced while the placenta attempts to provide for the foetus, the excess fibrin produced is observed as TMA. This process also causes the consumption of platelets and clotting factors, thereby reducing the total platelet count and increasing PT and aPTT in preeclamptic women, which may, in some cases, lead to DIC and the HELLP syndrome [14].

It is known that elevated LDH levels are associated with adverse maternal and neonatal outcomes in hypertension and PIH, independent of HELLP syndrome. Levels of LDH >400 U/L have been shown to be associated with preeclampsia [15]. The present study reported significantly increased activity of the LDH enzyme in women with PIH compared to normal pregnant women. Bhave N and Shah PK, reported significantly higher LDH levels in pregnant women with severe forms of hypertensive disorders and those who had poor maternal and perinatal outcomes [16].

LDH is a cytoplasmic enzyme found in many tissues and cells. It is an enzyme of the glycolytic pathway that catalyses the conversion of L-lactate to pyruvate using Nicotinamide Adenine Dinucleotide (NAD+) as a hydrogen acceptor [17,18]. LDH is an intracellular enzyme whose levels rise in PE patients due to cellular death. As a result, serum LDH levels can be used to assess the severity of the disease in this group of women by determining the extent of cellular death [19]. Hypoxia boosts glycolysis and raises LDH activity in PE. Studies have shown that LDH activity and gene expression are higher in preeclampsia placentas than in normal pregnancies. Hypoxia increases lactate production by enhancing LDH isoenzyme activity in trophoblasts. Elevated LDH levels are indicative of cellular damage and dysfunction [18].

Patients with preeclampsia/eclampsia more commonly exhibit thrombocytopenia along with increased PT/aPTT and elevated serum LDH values compared to normotensive patients.

Limitation(s)

This study was conducted with a limited number of patients. To further assess and validate the role of various markers, similar studies involving larger cohorts are recommended.

CONCLUSION(S)

Patients with PIH were found to have low platelet counts, high PT/aPTT values and elevated serum LDH levels in comparison to normal pregnant patients. A few of the PIH patients also exhibited the presence of schistocytes on their peripheral smear, which is a marker of MAHA. PIH and DIC can present with overlapping features such as thrombocytopenia and abnormal liver function tests, but they differ in clinical context and severity of coagulation abnormalities. PIH, including PE and HELLP syndrome, typically presents after 20 weeks of gestation with hypertension and proteinuria, while DIC is a secondary complication triggered by severe obstetric events like placental abruption or sepsis. DIC is characterised by more profound coagulopathy, including markedly prolonged PT/APTT, low fibrinogen, elevated D-dimer and severe thrombocytopenia, whereas these changes are milder or absent in PIH.

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