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Original Research Article

Study of coagulation profile and platelet indices in pregnancy induced hypertension with special reference to preeclamptic and eclamptic patients

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ABSTRACT

Background: Hypertensive disorders of pregnancy affect about 10% of all pregnant women around the world. A variety of haematological abnormalities may occur in women with Pregnancy Induced Hypertension (PIH), thrombocytopenia being the most common. There is also a definite exaggeration of the hypercoagulable state during PIH. A strong relationship exists between the two most important causes of maternal mortality and morbidity worldwide: Preeclampsia and Post-partum hemorrhage. The aim of this study was to find out the changes that occur in the coagulation profile and platelet indices in PIH as compared to that in normal pregnancy and if they can be used as a reliable indicator of the onset and severity of Preeclampsia and eclampsia.
Methods: This was a hospital based analytical prospective study carried out in R. G. Kar Medical College, between January 2017 to June 2018 on 120 patients with PIH. The study parameters included Platelet count, Platelet Distribution Width (PDW), Mean Platelet Volume (MPV), Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT).
Results: The results showed significant decrease in platelet count in preeclampsia and eclampsia patients when compared to normotensive patients. Also, there was significant increase in MPV and PDW in preeclamptic and eclamptic patients. Coagulation profile showed increased PT and APTT both in preeclamptic and eclamptic patients with eclamptic patients having significantly higher APTT than other groups.
Conclusions: Thus, authors came to the conclusion that platelet indices and coagulation profile can be used as a reliable early indicator of onset and severity of preeclampsia and eclampsia.

Keywords: Coagulation, Eclampsia, Preeclampsia, Platelet

INTRODUCTION

Hypertensive disorders of pregnancy affect about 10% of all pregnant women around the world.[1,2] The prevalence of PIH in India ranges from 5% to 8%. Hypertensive disorders of pregnancy are an important cause of severe acute morbidity, long term disability and death among mothers and babies. Though most of these conditions can be prevented or identified and treated early by good antenatal care; the situation is still not very bright in India. A variety of hematological abnormalities may occur in women with PIH. Out of all hematological changes that occur in preeclampsia and eclampsia, thrombocytopenia is the most common abnormality found. There is also a definite exaggeration of the hypercoagulable state of pregnancy during Pregnancy Induced Hypertension (PIH). Faulty coagulation of blood can be a cause of hemorrhages. There is a strong relationship between the two most important causes of maternal mortality and morbidity worldwide:

Preeclampsia and Postpartum haemorrhage.[3] Currently, there is no screening test that would help in identifying which pregnancy will be associated with PIH or assess its severity.[4] This study was to find out the changes that occur in the coagulation profile and platelet indices in Pregnancy induced hypertension as compared to that in normal pregnancy. The study was done to see if platelet indices and coagulation profile can be used as a reliable indicator of the onset and severity of Pre-eclampsia and eclampsia.

METHODS

This was an Analytical, Prospective study carried out in Department of Pathology in collaboration with Department of Gynecology and Obstetrics of R.G.Kar Medical College and Hospital(a tertiary care hospital in eastern India). Period of study was Eighteen months (January 2017- June2018).

Definition of study population

Pregnant women coming to the Gynaecology and Obstetrics department of RG Kar medical college and hospital who were diagnosed as cases of Pregnancy induced hypertension on routine ante natal checkup and were admitted to the labor and maternity wards of RG Kar Medical College and hospital over a period of one and a half years from January 2017 to June 2018.

Inclusion criteria

- Gestational Hypertension: Systolic BP>=140 mmHg or diastolic BP>=90 mmHg for first time after mid pregnancy with no proteinuria and BP returned to normal before 12 weeks post-partum.
- Mild/Non-Severe Pre-eclampsia: Systolic blood pressure between 140-160 mm Hg Diastolic blood pressure between 90-110 mm Hg, Proteinuria 1+.
- Severe Pre-eclampsia: Systolic blood pressure>160 mm Hg, Diastolic blood pressure >110 mm Hg, plus one or more of the following criteria: proteinuria >=1+, headache, visual disturbances, upper abdominal pain, oliguria (<400 ml/24 hours), serum creatinine elevated >1.2 mg/dl, thrombocytopenia (platelet<100,000/mm3), marked elevation of serum transaminase AST or ALT, fetal growth restriction and pulmonary edema.
- Eclampsia: In a woman with preeclampsia, a convulsion that cannot be attributed to another cause.[6]

Exclusion criteria

- Patients with Pre-existing medical disorders like Diabetes Mellitus, Renal disease, coagulopathies, chronic hypertension and hepatitis, Placental abruption or previa, Sepsis, Oral Contraceptive use history, ITP, HELLP syndrome, Severe trauma History.

Sample design

Cases were selected by systematic random sampling, as per inclusion and exclusion criteria.

Controls

Normotensive pregnant women not associated with any other complications.

Study technique

After getting approval from the ethics committee, authors proceeded as follows-patients coming to the Gynecology and Obstetrics department of RG KAR Medical College for routine ante natal checkup were first diagnosed as cases of pregnancy induced hypertension. They were included on the basis of inclusion criteria and review of their records was done.

After that blood samples were drawn by clean aseptic venepuncture using 23 G needle and were collected in EDTA vials and 3.2% Sodium Citrate vials with prior consent. Platelet indices and coagulation profile was measured using Horiba ABX Micro ES 60 automated cell counter and Sysmex CA 50 coagulation analyzer respectively in Department of Pathology RG Kar Medical College and Hospital. All blood samples were analysed between 1 hour to 3 hours after blood collection to avoid time dependent compounding factor on MPV and PDW. Normotensive pregnant women without any complications were tested for the same parameters. Results were tabulated. Correlation studies were done to correlate the parameters with the onset and severity of PIH.

Statistical analysis

Data was analysed using SPSS version 16. Shapiro Wilk test was done to test if the data was normally distributed for each parameter tested. If the data was normally distributed for a particular parameter, ANOVA test and Post hoc Gabriel test was done to compare between groups. If the data was not normally distributed for a particular parameter, Kruskal Wallis test and Dunn's Pairwise test was done to compare between groups.

RESULTS

Mean Age of all selected cases were 25.60±5.27 years with range from 18 to 42 years. Mean age was slightly higher in gestational hypertension group than severe preeclampsia group, but the difference was not statistically significant (p>0.05) according to the Kruskal Wallis Test (Non-parametric K independent sample test).

Table 1: Mean value of parameters in different groups of patients.

Mean value of parameters					
Diagnosis	**Platelet Count (/cmm)**	**MPV (fl)**	**PDW (%)**	**Prothrombin Time(sec)**	**Activated partial thromboplastin time(sec)**
Gestational hypertension	243166.7±62039.73	9.82±1.15	14.42±1.50	14.73±1.48	27.74±2.40
Mild preeclampsia	181541.7±37946.16	10.32±0.88	15.41±2.62	14.81±1.02	29.73±2.77
Severe preeclampsia	170291.7±67813.35	11.21±1.36	18.71±2.57	15.75±1.61	31.29±3.71
Eclampsia	128291.7±45271.62	12.97±1.49	20.6±2.01	16.73±3.14	40.41±6.59
Control	260000±52372.41	8.20±0.87	12.5±1.00	13.8±1.10	26.66±2.44

Comparison of Platelet Count in each group

The Platelet Count in Mild Preeclampsia group (181541.7±37946.16 /cmm), Severe Preeclampsia group (170291.7±67813.35 /cmm) and Eclampsia group (128291.7±45271.62 /cmm) were significantly lower than the control group (260000±52372.41 /cmm). Anova test revealed that the differences in platelet count between the groups was statistically significant ($p<0.05$). So, post hoc tests were carried out to see difference in platelet counts between which specific groups was statistically significant.

The Post hoc Gabriel test revealed that the differences in platelet count between Eclampsia and control, Severe Preeclampsia and control as well as Mild Preeclampsia and control group was statistically significant ($p<0.05$). This means that platelet counts were significantly lower in cases of preeclampsia and eclampsia than normotensive patients.

Comparison of Mean Platelet Volume (MPV) in each group

The Mean Platelet Volume in Mild Preeclampsia group (10.32±0.88 fl), Severe Preeclampsia group (11.21±1.36 fl) and Eclampsia group (12.97±1.49 fl) were significantly higher than the control group (8.20±0.87 fl). Kruskal Wallis Test revealed that difference of MPV between any of the two groups is statistically significant ($p<0.05$). To find out difference of MPV between which two groups are statistically significant, Pairwise Comparison tests were done.

Dunn's Pairwise test revealed that difference in MPV between mild preeclampsia and control group, severe preeclampsia and control group, eclampsia and control group, gestational hypertension and eclampsia group as well as mild preeclampsia and eclampsia group is statistically highly significant, i.e. $p<0.001$.

Comparison of Platelet Distribution Width (PDW) in each group

The Platelet Distribution Width in Mild Preeclampsia group (15.41±2.62%), Severe Preeclampsia group (18.717±2.57%) and Eclampsia group (20.6±2.01%) were significantly higher than the control group (12.5±1.00%). Kruskal Wallis Test revealed that difference of PDW between any of the two groups is statistically significant ($p<0.05$).

To find out difference of PDW between which two groups are statistically significant, Pairwise Comparison tests were done. It revealed that difference in PDW between severe preeclampsia and control group, eclampsia and control group, gestational hypertension and severe preeclampsia group, gestational hypertension and eclampsia group as well as mild preeclampsia and eclampsia group is statistically highly significant, i.e. $p<0.001$. This shows that there is a correlation between the PDW and severity of hypertension with mild preeclamptic, severe preeclamptic and eclamptic patients having significantly higher PDW.

Comparison of Prothrombin Time (PT) in each group

The Prothrombin Time in Severe Preeclampsia group (15.7±1.6 sec) and Eclampsia group (16.7±3.1 sec) were significantly higher than the control group (13.8±1.1 sec). Kruskal Wallis Test revealed that difference of PT between any of the two groups is statistically significant ($p<0.05$). To find out difference of PT between which two groups are statistically significant, pairwise comparison tests were done.

It showed that difference in PT between severe preeclampsia and control group as well as between eclampsia and control group is statistically highly significant, i.e. $p<0.001$. Difference in PT between other groups is not statistically significant, i.e. $p>0.05$. This shows that there is a correlation between the Prothrombin Time and severity of hypertension with severe preeclamptic and eclamptic patients having significantly higher PT than normotensive patients.

Comparison of Activated Partial Thromboplastin Time (aPTT) in each group

The Activated Partial Thromboplastin Time in Mild Preeclampsia group (29.7±2.7 sec), Severe Preeclampsia

group (31.2±3.7 sec) and Eclampsia group (40.4±6.5 sec) were significantly higher than the control group (26.6±2.4 sec). Kruskal Wallis Test revealed that difference of aPTT between any of the two groups is statistically significant ($p<0.05$). To find out difference of aPTT between which two groups are statistically significant, pairwise comparison tests were done.

It revealed difference in aPTT between eclampsia and control group, gestational hypertension and eclampsia group, as well as between mild preeclampsia and eclampsia group is statistically highly significant, i.e. $p<0.001$. This shows that there is a correlation between the aPTT and severity of hypertension with severe preeclamptic and eclamptic patients having significantly higher aPTT.

DISCUSSION

Platelet count

The study showed significantly reduced platelet count in mild preeclampsia, severe preeclampsia and eclampsia patients in comparison to control group with statistically significant correlation. In fact, platelet count was significantly reduced in eclamptic and severe preeclamptic patients even when compared to gestational hypertension patients with statistically significant correlation. But there was no significant difference in platelet count between gestational hypertension and control group. This shows that with the onset of preeclampsia platelet count begins to reduce with severe preeclampsia and eclampsia patients having markedly reduced platelet counts. Thus, with increasing severity of preeclampsia and eclampsia, platelet counts continue to fall significantly.

In a Study conducted by Mohapathra S, platelet numbers were found to be 2.38 lacs/mm^3±0.33 in control group, 2.23 lacs/mm^3±0.19 in mild PIH, 1.82 lakhs/mm^3±0.45 in pre-eclampsia and 1.21 lacs/ mm^3±0.49 in eclampsia.[7] They indicated that there was an inverse relationship between the severity of PIH and platelet numbers. So, they concluded that platelet estimation is useful as a rapid method of assessment in PIH even in rural hospital settings. Their findings corroborated with the findings in this study.

Chauhan P found that in pre-eclampsia and eclampsia, decrease in platelet count (157.18±56.66 lacs/cumm) was highly significant ($p<0.001$).[8] This finding corroborated with this study.

Mean platelet volume and platelet distribution width

The study showed increase in mean platelet volume and PDW in gestational hypertension, mild preeclampsia, severe preeclampsia and eclampsia patients when compared to normotensive pregnant women with statistically significant correlation. Mean platelet volume and PDW was also significantly higher in eclamptic patients when compared to gestational hypertension and mild preeclampsia patients. This shows that there is significant increase in mean platelet volume and PDW with the onset of PIH and consequently with preeclamptic and eclamptic patients having a statistically significant higher MPV and PDW than mild hypertensive groups.

Vijaya C found that the platelet counts were lower while mean platelet volume, platelet distribution width were increased in preeclampsia and eclampsia as compared to control group.[9] They concluded that there was an association between platelet indices and severity of preeclampsia. Hence the estimation of platelet indices can be considered as an early, simple and rapid procedure in the assessment of severity of preeclampsia and eclampsia which can be used as a prognostic marker. Their findings corroborated well with this study.

In the study conducted by Annam the mean platelet volume and platelet distribution width were increased in pre-eclampsia and eclampsia as compared to control group.[10] They found a relationship between platelet indices and severity of pre-eclampsia. Their findings were consistent with the findings in this study.

Prothrombin time and activated partial thromboplastin time

In this study, prothrombin time was increased in severe preeclamptic and eclamptic patients when compared to control group and it was statistically significant. But increase in prothrombin time in gestational hypertension and mild preeclampsia group was not statistically significant when compared to control group.

The study also showed significantly prolonged APTT in mild preeclampsia, severe preeclampsia and eclampsia patients when compared to control group with statistically significant correlation. Not only that there was also statistically significant increase in APTT in eclamptic patients when it was compared with other subgroups of PIH.

In the study conducted by Lakshmi CV, it was seen that prothrombin time and activated partial thromboplastin time were prolonged in severe preeclampsia and eclampsia.[11] The results corroborated with this study. In the study conducted by Uppam Kr. Sharma there was statistically significant increase in aPTT with increase in the severity of PIH. This was in concordance with this study.[12]

Joshi SR conducted a study where they found that severe pre-eclampsia and eclampsia were characterized by thrombocytopenia and coagulation abnormalities particularly prolongation of APTT.[13] Their findings were in concordance with the findings in this study.

Line Leduce conducted a study where they concluded that when monitoring intrapartum coagulation indices in preeclampsia, one can safely follow only the platelet

count at admission and subsequently, reserving PT and aPTT and fibrinogen levels for those cases complicated by counts less than 100,000/microL.[14] Their conclusion did not corroborate with the findings in this study as authors found PT and aPTT to be equally important as Platelet count in monitoring intrapartum coagulation indices in preeclampsia even in cases with platelet count more than100,000 /microL.

CONCLUSION

From the study of platelet indices, it may be concluded that decrease in platelet count starts from PIH and it is significantly reduced in preeclampsia and eclampsia patients when compared to normotensive patients with eclamptic patients having thrombocytopenia (platelet count <150000/cmm). Also, there is significant increase in mean platelet volume and platelet distribution width in preeclamptic and eclamptic patients. Study of Coagulation profile showed coagulation abnormalities in preeclampsia and eclampsia patients who have significantly higher prothrombin time and Activated Partial Thromboplastin Time than control groups. Thus, authors come to the conclusion that platelet indices and coagulation profile can be used as a reliable early indicator of onset and severity of preeclampsia and eclampsia. These are routine tests which can be performed in every government hospital and can help to reduce the maternal and fetal morbidity and mortality associated with pregnancy induced hypertension.

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