

COMPARITIVE STUDY OF COAGULATION PROFILE IN TERM NORMOTENSIVE, PREECLAMPSIA AND ECLAMPSIA

Dr Meghna Das¹, Dr. Purashree Sarma², Dr. Smita Das³, Dr Neha Beria^{4*}

¹ Assistant Professor, Department of Obstetrics and Gynaecology, GMCH, Guwahati

² Assistant Professor, Department of Obstetrics and Gynaecology, GMCH, Guwahati

³ Associate Professor, Department of Haematology, GMCH, Guwahati

⁴ Post Graduate Trainee, GMCH, Guwahati

***Corresponding Author:**

Email: nehaberia93@gmail.com

ABSTRACT

Aim: The determination of the abnormalities of the platelet and coagulation factors occurring in patients of pre-eclampsia and eclampsia, by comparing parameters with normotensive pregnancies at term.

Design: Prospective study design among antenatal patients attending department of Obstetrics and Gynaecology in Gauhati Medical College and Hospital from 1st June, 2020 to 31st May, 2021.

Materials and Methods: 200 patients were included in the study, out of which 100 normotensive pregnant females at term gestation were taken as controls, 100 pre-eclampsia and eclampsia term pregnancies were taken as cases.

Coagulation factors such as platelet count, PT, aPTT, BT, CT, D- dimer was evaluated in both the groups and compared using statistical analytic tests.

Results: Patients in the pre-eclampsia and eclampsia groups had an increasing trend in bleeding time within normal limits but decreasing platelet count, indicating a functional deficiency in platelets in the study population. The study group's PT and aPTT were also longer than the control group's. This indicates that the research population is hypercoagulable. D-dimer levels are significantly higher in patients with pre-eclampsia and eclampsia than in the control group (p value <0.001), indicating increased plasminogen activator activity in the study group, increasing the availability of plasmin, which degrades fibrin deposits in d-dimer, causing intravascular coagulation.

Conclusion: In all patients with severe eclampsia and pre-eclampsia who may develop DIC, combining platelet count with aPTT is useful for detecting an early ongoing coagulopathy. Coagulation tests are a simple, inexpensive, and easily accessible method for early diagnosis.

INTRODUCTION

The hypertensive disorders of pregnancy are one of the most common complications of pregnancy. It complicates around 5-10% of pregnancy.¹ The history of hypertensive disorders of pregnancy can be traced back to the 400 BC. Around 400 BC, Hippocrates was first to describe that headache accompanied by heaviness and convulsions during pregnancy. Along with haemorrhage and infection, it forms a member of the deadly triad and is the most common cause of maternal and perinatal morbidity and mortality. World health organization estimates that annually 50,000 to 75,000 pregnant women die due to the complications of preeclampsia making it one of the leading causes of death in pregnancy.² The basic pathology of pregnancy induced hypertension is endothelial dysfunction, poor placentation and vasospasm of vessels along with alterations of the haematological profile, of which thrombocytopenia is the most common.³ Profound changes in the coagulation and fibrinolytic system occur during normal pregnancy causing a hypercoagulable state.⁴ There is increase in many coagulant factors such as (I, VII,

VIII, IX, X) and markers of thrombin generation. The mean platelet count decreases by 10% and platelet activation is enhanced. In preeclampsia and eclampsia, this physiological activation of coagulation is exaggerated and includes excessive platelet activation, increased fibrin degradation products and intervillous fibrin deposition in the placenta. Due to repeated activation of the coagulation cascade because of the constant endothelial damage being experienced, as the placenta attempts to provide for the foetus, the excess produced fibrin is seen as thrombotic microangiopathies. Platelet plays an important role in pathogenesis of Preeclampsia. The platelets are normally present in the blood stream in an inactive state but they can activate immediately when they come in contact with damaged or activated endothelial wall. Increased consumption of platelet causes thrombocytopenia which is an important sign of severe Preeclampsia. In some cases, it may lead to DIC (Disseminated Intravascular Coagulation) and HELLP (Haemolysis, Elevated Liver enzymes, Low Platelet count) syndrome. There is also reduction of fibrinogen, antithrombin III and plasminogen level in the blood. In preeclampsia, there is endothelial dysfunction which will lead to altered level of fibrinogen, activated partial thromboplastin time (APTT), prothrombin time (PT), fibrin degradation products (FDP) and D-Dimers.⁵⁻⁸ The mean values of APTT and FDPs are higher in preeclamptic patient but the mean values of prothrombin time and fibrinogen level have no significant difference.⁷ The underlying coagulation abnormality increases the risk of bleeding complications, especially during delivery leading to postpartum hemorrhage, which is the leading cause of maternal mortality. Early assessment of severity of PIH is necessary to prevent complications like HELLP (Hemolysis, Elevated Liver enzymes, Low Platelet count) syndrome, DIC and cerebrovascular complications.⁴

MATERIALS AND METHODS

This is a Prospective study design among 100 pre-eclampsia and eclampsia women at term gestation and 100 normotensive term pregnancies attending department of Obstetrics and Gynaecology in Gauhati Medical College and Hospital. The study was conducted during the period of 1 year w.e.f. 1st June, 2020 to 31st May, 2021. All patients were followed up until delivery and early postpartum period and their babies were followed up till hospital stay. The study was explained to the participants and after obtaining consent either from the patient directly or from their close relative, the data was collected.

INCLUSION CRITERIA

1. Pregnant women at 37-42 weeks gestation with pre-eclampsia and eclampsia.
2. Normotensive pregnant women at 37-42 weeks gestation.

EXCLUSION CRITERIA

Pregnant women

1. With known bleeding disorders. (eg. ITP, VWD)
2. On anticoagulant therapy.
3. With abruptio placentae
4. With IUFD
5. With established DIC.
6. History of Deep Vein Thrombosis

The coagulation parameters used to assess platelet function were platelet count and bleeding time. Clotting time, prothrombin time, activated partial thromboplastin time were used to assess the coagulation system and D-dimer was used to assess the fibrinolytic system. Bar diagram and Pie-Chart were used to describe the descriptive statistics. Chi square test is used to evaluate association between categorical variables. Data were checked for normality using Kolmogorov-Smirnova and Shapiro-Wilk test. Independent T test is used to compare mean difference between two or ANOVA is used for more than two groups depending on fulfilment of normality assumption for continuous variables. For non-normal data Mann whitney test & Kushkar Wallis test is used. All data were analyzed using SPSS version 21. A p value less than 0.05 is considered as statistically significant at 5% level of significance.

RESULTS

	Platelet count (lac/cum m)	BT (sec)	CT (sec)	PT (sec)	aPTT (sec)	D-dimer (ngm/ml)
Contol(n=100)	2.93±0.76	152.97±26.02	305.2±67.35	10.96±1.44	28.80±4.28	1326.38±121.13
Pre-eclampsia(n=71)	2.15±0.49	181.48±22.7	301.87±56.73	13.14±0.48	29.89±0.99	1589.41±270.61
Eclampsia(n=29)	1.47±0.52	226.24±18.65	305.55±59.82	14.27±0.49	32.01±0.73	2362.45±617.32
P value	<0.001	<0.001	0.968	<0.001	<0.001	<0.001

Out of total of 200 cases included in the study, 100 were control and 100 were study of which 71 were pre-eclampsia and 29 were eclampsia. Most of the patients in the study and control group was of 20 to 24 years of age and most of the patient included in the study were primigavidas.

Majority of the population in the study belonged to lower middle class. Clinical features like headache, visual disturbance and epigastric pain increased with the increase in severity of the disease. The mean platelet count decreased significantly with increase in severity of the disease. The mean bleeding time was also significantly prolonged with in severity but was within normal limit. There was no statistical association in clotting time in both the groups. The p value of <0.001 shows significant association between prolonged prothrombin time and aPTT with increase in severity of the disease. There was a increase in d-dimer values from control to pre-eclampsia and eclampsia indicating increased fibrinolytic activity.

DISCUSSION

PIH and pre-eclampsia are complex disease processes which may affect maternal cardiovascular, haematological, renal, neurological and hepatic system. Hematological abnormalities such as thrombocytopenia and decrease in plasma clotting factors may develop in pre-eclampsia and eclampsia patients. Subtle changes consistent with DIC are potentially dangerous. Thus, coagulation profile should be done in these patients with evidence of DIC and HELLP syndrome.

In our study, incidence of pre-eclampsia and eclampsia was found to be 35% in age group <20years, 40% in 20-24years, 22% in 25-29 years and 3% in >30 years (p value- <0.001).

A positive association between lower maternal age and the prevalence of PIH has been shown in both White and non- White American subjects.⁹A prospective study from India (2016) reported a higher incidence of PIH in young first-time mothers, aged 12 to 19 and 13 to 19 years, respectively.¹⁰

In the present study, the incidence of pre-eclampsia and eclampsia was higher in primigravidas (66%) as compared to multigravidas (34%). In a study, E JasovicSiveska et al (2011) found that the incidence of PIH was higher in nulliparous (61.2%).¹¹

In our present study it was found that 33% pre-eclampsia and eclampsia patients belonged to lower socioeconomic status, 42% belonged to lower middle class, 16% belonged to upper middle class, and 9% belonged to upper class. (p value- <0.001).

Kolluru V et al (2016) found that 76% of PIH patients belonged to lower class, 23% belonged to middle class, 1% belonged to upper class.¹² So the findings of present study were comparable to above studies.

When coagulation parameters were assessed in patients of pre eclampsia and eclampsia with increasing severity of disease, there was statistically significant decrease in platelet count. In a study by S Mohapatra et al, shows the mean platelet count in eclampsia (1.21 ± 0.49) decreased as compared to pre-eclampsia (1.82 ± 0.45).¹³ In our study platelet count in eclampsia (1.47 ± 0.52) as compared to pre-eclampsia (2.15 ± 0.49) and controls (2.93 ± 0.76).

Kelton et al¹⁴ showed that thrombocytopenia in pre-eclampsia was frequently associated with prolonged bleeding time. This is also supported by another study done by Ivankovic M et al¹⁰⁰ which reported the association of pre-eclampsia with thrombocytopenia and prolonged bleeding time. In our study also, BT showed an increasing trend from normal control to eclampsia patients but was in normal range.

In our present study, the prothrombin time increased from control to pre-eclampsia and eclampsia group which is comparable with a study conducted by M. Nadeem S K et al² where the prothrombin time was 14.52 sec in pre-eclampsia patient and 13.60 sec in control group. In a study by Osmanagaoglu MA et al in the Karadeniz Technical University, Trabzon, Turkey, the prothrombin time was nearly identical in all the 3 groups. The plasma thrombocyte counts were significantly lower in severe pre-eclamptic women than in normotensive women. There was no significant difference in the prothrombin time value in all groups.¹⁵

A study by Priyanka C et al¹⁶ found that aPTT in control group was 29.31 ± 3.39 sec, in preeclampsia group it was 30.80 ± 1.62 and 32.84 ± 2.01 in eclampsia group which was highly significant. Similar findings were seen in our present study where aPTT was prolonged in eclampsia patients than pre-eclampsia and control patients which was highly significant (p- <0.001)

In a study by Lei H et al (2014)¹⁷, it was seen that the value of d-dimer had increased in the pre-eclampsia group (1037.7 ± 1381.8) as compared to control group (687.1 ± 592.5). A similar finding was observed in a study by Z Tacoosian et al (2007)¹⁸ where the d-dimer was 322.26 ± 117.65 in control group and increased in cases of pre- eclampsia (721.43 ± 401.13). In a study by Kucukgoz G U et al¹⁰⁴ reported that d-dimer levels were significantly higher in study group than in the control group and it was also significantly higher in patients with severe pre-eclampsia than mild pre-eclampsia.

In our present study, 36% of cases underwent vaginal delivery, 64% had caesarean delivery. Uddin A W et al in their study found that 49.2% underwent vaginal delivery, and 50.8% had caesarean delivery.¹⁹ Higher rate of caesarean section in our study is attributed to the fact that our institution is a tertiary centre where most of the patients were referred.

In the present study, 36% of babies with pre-eclampsia and eclampsia had NICU admission which is comparable to studies by Kolluru V et al¹² and Puneeta M et al²⁰ who had 42.3% and 49.20% NICU admissions.

CONCLUSION

The etiology of hypertensive disorders of pregnancy, one of the most common medical complication of pregnancy, is yet unknown. Coagulation abnormalities are one of the common maternal problems that accompanies with pre-eclampsia and eclampsia. We may conclude that if thrombocytopenia or aPTT and PT prolongation are discovered in a patient with severe pre-eclampsia, an ongoing coagulopathy should be suspected and assessed clinically.

Finding the best screening procedure necessitates much investigation. For a definitive diagnosis and therapy of coagulation failure in eclampsia and preeclampsia patients, various parameters such as INR, Thrombin Time, Euglobulin clot lysis time, Fibrinogen levels should be employed.

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