EVALUATION OF COAGULATION INDICES IN PREECLAMPSIA AND ECLAMPSIA

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ABSTRACT

BACKGROUND

The study was undertaken to compare the coagulation profiles of preeclampsia and eclampsia women with those of age matched women with normal pregnancies and to determine the accuracy of platelet count as a simple, cost effective screening test to assess the potential severity of complications associated with PIH.

METHODS

Total 176 cases with 88 PIH (Pregnancy Induced Hypertension) cases and 88 healthy age and parity matched pregnant women were included in the study. Coagulation parameters- Total Platelet Count (TPC), PT (Prothrombin Time) and aPTT (Activated Partial Thromboplastic Time) were performed by automatic analysers.

RESULTS

In preeclampsia and eclampsia, decrease in platelet count (1.69±0.53 lacs/cumm) compared to the control group was statistically significant (p= 0.000) and increase in PT (12.5 ± 1.17 sec) and aPTT (30.5 ± 2.29 sec) were significant (p<0.05).

CONCLUSIONS

Platelet count is inversely proportional to severity of PIH and the risk of coagulopathy increases with worsening thrombocytopenia. There are no cases with normal platelet count where PT or aPTT were prolonged. Platelet count is a simple, low cost and rapid routine screening test for coagulopathy in PIH.

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BACKGROUND

Hypertensive disorders are the most common medical complications of pregnancy and are important causes of maternal and perinatal morbidity and mortality affecting 7-15% of all pregnancies. It is associated with 16% of all maternal mortality and 20% of all perinatal mortality in India.[1,2] Due to low socioeconomic status, apathetic attitude, poor health education and lack of regular antenatal supervision, the incidence of preeclampsia is more in developing countries like India.[3]

Preeclampsia is characterized by the new onset of hypertension (≥140 mm of Hg systolic or ≥90 mm of Hg diastolic) after 20 weeks' gestation; associated with proteinuria (spot urine protein/creatinine ≥ 30 mg/mmol (0.3 mg/mg) or ≥300 mg/day or at least 1 g/L ('2+') on dipstick testing)). Severe preeclampsia is preeclampsia with severe hypertension with diastolic blood pressure ≥110 mm of Hg, systolic blood pressure ≥ 160 mm of Hg and/or with symptoms, and/or biochemical and/ or haematological impairment. Eclampsia is defined as the presence of new-onset grand-mal seizures in a woman with preeclampsia, after excluding the presence of other causes of seizures.[4] There is no effective treatment for preeclampsia and eclampsia, in addition to the termination of pregnancy.

Normal pregnancy is a procoagulant state, characterized by an increase in many procoagulant factors and markers of thrombin generation. In preeclampsia, 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. Also, this causes consumption of platelets and clotting factors, thereby reducing the total platelet count and increasing PT and aPTT in preeclamptic women and, in some cases leading to DIC (Disseminated Intravascular Coagulation) and HELLP (Haemolysis, Elevated Liver enzymes, Low Platelet count) syndrome.[5]

This study was therefore undertaken to compare the coagulation profiles of preeclamptic and eclamptic women with those of age matched women with normal pregnancies and to determine the accuracy of platelet count as a simple, cost effective screening test to assess the potential severity of complications associated with PIH.

METHODS

A prospective comparative study comprising of 176 cases with 88 PIH cases and 88 healthy age and parity matched

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pregnant women from Obstetrics and Gynaecology Department was conducted in the Department of Pathology, M.K.C.G. Medical College, Berhampur during a period of two years from 2015 to 2017.

Control Group

Comprised of healthy age and parity matched pregnant women with normal blood pressure and absent proteinuria.

Study Group

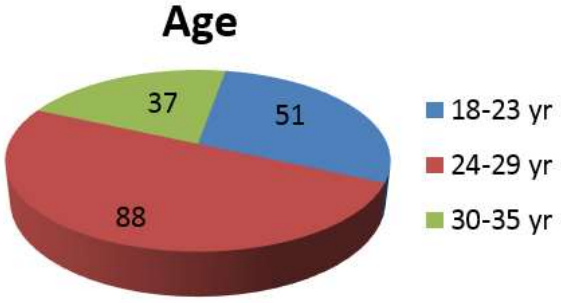
Comprised of diagnosed cases of preeclampsia and eclampsia. The preeclamptic women were selected based on criteria with blood pressure ≥140/90 mm of Hg with proteinuria ≥ 1 gm/litre or >2+ measured by dipstick. Cases were categorized into Mild (140-159/90-109 mm of Hg) and Severe (≥160/110 mm of Hg) on the basis of blood pressure based upon classification of American College of Obstetrician and Gynaecologist (ACOG). Cases of new-onset seizures in a woman with preeclampsia, after excluding the presence of other causes of seizures categorized as eclampsia.

Women with previous history of hypertension, diabetes mellitus, recurrent miscarriages, previous hepatic or renal disease, multiple foetuses, Idiopathic Thrombocytopenic Purpura (ITP) or any bleeding diathesis, immunosuppression or history of illicit drug use were excluded from the study.

Platelet count was done by using Sysmex XT 2000i automated blood cell counter and, PT and aPTT were done on automated coagulation analyser Sysmex CA 600 Series. Statistical analysis was done using Chi-square test, Kruskal Wallis test and Mann-Whitney test. As variables are not normally distributed, Kruskal Wallis test and Mann-Whitney test were used. The tests were applied using IBM SPSS version 16.0 software.

RESULTS

A total of 176 pregnant females were included in the study, out of which 88 were controls and 88 were in study group.



Graph 1

In present study, maximum numbers of cases were in the age group of 24 to 29 years. Most patients in normotensive pregnant control group and patients with PIH were in age group of 18 to 29 years.

PIH was more common in primigravida. As compared to mild and severe preeclampsia, eclampsia was more common in primigravida.

In the present study, maximum women were in the gestational age group of 33-40 weeks. PIH cases had significantly lesser duration of pregnancy. Gestational age at the time of admission varied from 32 weeks till term.

	Control Group	Study Group	p Value
SBP	120.2±11.4	161.9±16.6	0.000
DBP	75.4±4.6	103.2±7.31	0.000
TPC	2.14±0.46	1.69±0.53	0.000
PT	12.21±0.62	12.5±1.17	0.05
aPTT	30±1.52	30.5±2.29	0.05

Table 1. Comparison of SBP, DBP, Platelet Count, PT and aPTT Between Control & Study Groups

SBP- Systolic Blood Pressure, **DBP-** Diastolic Blood Pressure.

In the present study, both mean values of systolic and diastolic blood pressure were highly significant (p=0.000). Decrease in platelet count is statistically significant (p=0.000). There is statistically significant increase in PT (p<0.05) and aPTT (p<0.05) when compared between study and control group using Mann-Whitney test.

In the present study, mean values of platelet gradually decrease with increasing grade of severity. Mean values of PT and aPTT fall in normal reference range in all groups, but when compared with increasing grade of severity it shows gradual increase. Decrease in platelet count is statistically significant (p=0.000). There is statistically significant increase in PT (p=0.000) and aPTT (p=0.000) when compared between study and individual group using Kruskal Wallis test.

In the present study, no cases had prolonged PT or aPTT in control group and mild preeclampsia. Among study group, 12 cases had prolongation of PT and 03 cases had prolongation of aPTT.

TPC (lac/cu mm)	PT		aPTT	
	Normal (76)	Prolonged (12)	Normal (85)	Prolonged (03)
< 1.0	06	09	12	03
1.0-1.5	11	03	14	0
>1.5	59	0	59	0
	χ^2 = 35.3 p value = 0.000 (significant)		χ^2 = 11.1 p value = 0.004 (significant)	

Table 2. Correlation of Platelet Count with PT and aPTT

In the present study, PT was prolonged only when platelet count was <1.5 lac/cumm and aPTT was prolonged when platelet count was <1 lac/cumm. However, 06 cases (40%) with platelet count of <1 lac/cumm had normal PT. Similarly, 12 cases (80%) with platelet count <1 lac/cumm had normal aPTT. This signifies that with increase in severity, there occurs prolongation of PT and aPTT. 3 cases with prolonged aPTT also had prolonged PT along with

	Control	MPE	SPE	E	p Value
TPC	2.14±0.46	1.93±0.39	1.45±0.51	0.95±0.37	0.000
PT	12.21±0.62	12.19±0.58	12.93±1.46	13.88±1.61	0.000
aPTT	30±1.52	29.97±1.3	31.23±2.52	32.25±4.39	0.000

Table 3. Comparison of Platelet Count, PT & aPTT between Control and Study Subgroups

MPE- Mild Preeclampsia, **SPE-** Severe Preeclampsia, **E-** Eclampsia

thrombocytopenia. Overall 33% cases of PIH showed thrombocytopenia, 13% had prolonged PT and 3% had prolonged APTT.

DISCUSSION

In the present study, maximum numbers of cases were between 18 to 29 years of age which is comparable with the studies of Priyadarshini G et al,[6] Nirmala T et al[7] and Lakshmi CV et al.[8] PIH occurring in younger age in these studies signify to the early age of marriage and first pregnancy in developing countries like India.

The findings of the present study (56%) and many other studies such as Chaudhary S et al[9] (64%), Leduce et al[10] (65%) and Naaz A et al[11] (60%) also confirm that PIH is more prevalent in primgravidae. Increased incidence of eclampsia in primipara in the present study was in agreement with several studies such as Dube et al[12] and Lopez-Llera et al.[13]

In the present study, the mean duration of pregnancy was significantly higher in control group, which means most of them were full term deliveries, whereas the duration of pregnancy was reduced in test group in patients with PIH which is comparable with the studies of Vinodhini R et al.[14] This indicates that many cases with PIH, especially those with severe preeclampsia and eclampsia, do not reach full term and that early delivery is the prompt treatment of the disease for preventing complications.

Coming to the clinical parameters, the mean systolic /diastolic blood pressure in mild preeclampsia, severe preeclampsia and eclamptic patients was 150/96 mm of Hg, 178/110 mm of Hg and 186/112 mm of Hg respectively. When compared to the SBP/DBP in normal pregnancies (120/74 mm of Hg), the difference was statistically significant (p- 0.000). These values were in concordance with several other studies such as Lopez-Llera et al,[14] Chaware S A et al[15] and Metz et al.[16] Proteinuria is an important indicator of severity because it usually develops late in the course of the disease. Proteinuria in women in the present study correlates well with other authors such as Chaware S A et al[15] and Shetty J et al.[17]

In the present study, there is significant increase in percentage of patients with low platelet count with increase in severity of disease. The low platelet count was attributed to immunologically mediated destruction, platelet aggregation and consumption, which appear to be due to endothelial damage. Platelet activation may lead to increased generation of thromboxane A2 and serotonin release, in turn increase vasoconstriction and platelet aggregation. The present study correlates well with the study by Chaudhary S et al,[9] Chavan et al[18] and Jambhulkar et al.[19]

In the present study, mean platelet count show statistically significant difference (p-0.000) between study and control groups which correlates well with other authors such as Chaudhary S et al[9] and Sameer MA et al.[20]

Studies	MPE	SPE	E
Lakshmi CV[8]	2.1±0.5	0.8±0.3	0.7±0.3
Chauhan P[21]	1.73±0.25	1.45±0.24	1.21±0.22
Mohapatra S[22]	2.23±0.19	1.82±0.45	1.21±0.49
Sarkar PD[23]	1.98±0.41	1.47±0.31	-
Mirza AB[24]	1.81±0.52	1.05±0.64	-
Chaudhary S[9]	2.35±0.54	1.24±0.73	0.86±0.45
Present Study	1.93±0.39	1.45±0.51	0.95±0.37

Table 4. Comparison of Platelet Count with Other Studies

Table 3 shows that even though there is not much decrease in platelet count between control group and mild preeclampsia group, there is significant (p- 0.000) decrease in platelet count with increase in severity of disease. Several studies have also shown similar findings such as Chaudhary S et al,[9] Chaware S A et al,[15] Awolola OO et al,[25] and Sharma UK et al.[26]

Comparing the degree of thrombocytopenia in various severity of pregnancy induced hypertension in the present study, as the severity of PIH increases; not only the number of cases with thrombocytopenia increase but also the platelet counts are decreasing which correlates well with other authors such as Priyanka P et al[27] and Chaware S A et al.[15] The much higher occurrence of thrombocytopenia among sever preeclampsia and eclampsia patients in the present study can be explained by the poor socioeconomic status of the patients, leading to lack of antenatal check-ups and late presentation of women with PIH to the hospital only after developing severe systemic symptoms.

In the present study, no cases had prolonged PT in control as well as mild preeclampsia groups but severe preeclampsia and eclampsia group had prolonged PT which correlates with other studies such as Chaudhary S et al[9] and Lakshmi CV et al.[8] The mean prothrombin time in control and mild preeclampsia were very similar but was significantly increased ($p < 0.05$) in severe preeclampsia and eclampsia groups in the present study which can be correlated with the study conducted by Priyadarshini G et al[6] and Chaware S A et al.[15] The presence of higher number of cases with prolonged PT can be explained by the higher proportion of patients with thrombocytopenia, since it's now widely accepted that endothelial damage leading to platelet activation and aggregation is the driving force behind the pathophysiology of preeclampsia.

In the present study, no prolongation of aPTT among mild preeclampsia but severe preeclampsia and eclampsia group had prolonged aPTT which correlated well with the study by Chaudhary S et al,[10] Chaware S A et al[15] and Lakshmi CV et al.[8] The mean aPTT in control and mild preeclampsia were very similar but was also significantly increased ($p<0.05$) in severe preeclampsia and eclampsia groups in the present study. Similar findings were documented by Jambhulkar et al,[19] Priyadarshini G et al,[6] Chaware S A et al[15] and Chaudhary S et al.[9]

Studies	TPC	PT	aPTT
Priyadarshini G[6]	< 0.001	< 0.05	< 0.001
Naaz A[11]	< 0.01	< 0.001	< 0.0001
Chauhan P[21]	< 0.001	> 0.05	> 0.05
Chaudhary S[9]	< 0.001	< 0.001	< 0.001
Present Study	0.000	< 0.05	< 0.05

Table 5. Comparison between the study and control groups based on the three coagulation parameters and correlation with other studies.

The present study shows concordance with several other studies in showing significant correlation between study and control groups in all parameters but Chauhan P et al[21] found only platelet count to be of significant difference. This indicates that while evaluating the coagulation profile of patients with PIH, platelet count is a more reliable indicator.

In the present study, evaluating the coagulation parameters (PT and aPTT) in relation to platelet count, it was observed that prolongation of PT or aPTT was never seen with normal platelet count. Thus, prolongation of PT and aPTT was significantly correlated with degree of thrombocytopenia with p value of <0.05 in present study. Similar findings were documented by Leduce L et al,[10] Sharma K et al,[26] Priyadarshini G et al,[6] Nirmala T et al,[7] S Mohapatra S et al,[22] Metz J et al[16] and FitzGerald MP et al.[28] This suggests that increasing severity causes more deterioration of PT and aPTT profile.

The development of coagulopathy in preeclampsia appears to occur early, progressing over the course of the disease to involve with varying degrees, the coagulation parameters, especially in those with early onset disease. Thrombocytopenia was predictive of the risk of coagulopathy in this study. Biochemical coagulopathy was unlikely at platelet count above 1 lac/µl. The finding that only participants with low platelet count were found to have biochemical coagulopathy has previously been documented by authors such as Priyadarshini G et al,[6] Nirmala T et al[7] and Chaudhary S et al[9] and Leduce L et al.[10] It has been postulated that lower platelet count is associated with abnormal activation of coagulation system and is believed to reflect increased platelet consumption.

However, majority of cases with low platelet count had normal PT and aPTT.

CONCLUSIONS

Normal pregnancy is a procoagulant state which is aggravated in PIH because of the constant endothelial damage that causes repeated activation of the coagulation cascade leading to consumption of platelets and coagulation factors. Platelet count is inversely proportional to severity of PIH and the risk of coagulopathy increases with worsening thrombocytopenia. There are no cases with normal platelet count where PT or aPTT were prolonged. Platelet count is a simple, low cost and rapid routine screening test for coagulopathy in PIH and also accurate in assessing the potential severity of complications associated with PIH. The study gives a guideline for investigation to be done in cases of PIH which can alert the obstetrician, of the severity of the disease so that appropriate and timely management can be initiated. Severe preeclampsia and eclampsia can be associated with normal platelet counts; therefore, present study shows that platelet count alone cannot be relied upon to assess the severity of PIH.

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