ASSESSMENT OF COAGULATION PROFILE AND ITS CORRELATION WITH SEVERITY OF PREECLAMPSIA IN WOMEN OF ODISHA- A COMPARATIVE CROSS-SECTIONAL STUDY

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ABSTRACT: Background: Preeclampsia is an idiopathic multisystem disorder. It is associated with alteration of haematological profile of which thrombocytopenia is the most common which may be accompanied by a clinically evident consumptive coagulopathy or may be the sole abnormality seen. **Objective:** The aim of the study is to compare the coagulation parameters in the patients with preeclampsia and normal pregnant women. **Material and methods** The study comprised of 100 pregnant women with preeclampsia in age group 18-35years. 100 healthy age matched pregnant women served as controls. Coagulation parameters done were total platelet count (TPC), prothrombin time (PT) activated partial thromboplastin time (aPTT), bleeding time (BT), coagulation time (CT) .The parameters were compared by using Student's t-test. **Result: I**n preeclamptic women, mean age group is 25.52 ± 4.38 years. A significant decline in platelet count ($p<0.001$), increase in PT ($p<0.05$), aPTT ($p<0.001$), BT (<0.001) and CT($p<0.05$) was seen in preeclampsia as compared to normal pregnancy. With severe fall in platelet count in preeclamptic subjects prolongation of aPTT is more pronounced than PT. **Conclusion:** it is concluded from the study that total platelet count estimation can be taken as an early and rapid procedure for screening preeclampsia cases at admission followed by serial platelet counts while monitoring coagulation indices.

Key words: thrombocytopenia, preeclampsia, coagulation, bleeding time, prothrombin time

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INTRODUCTION

Preeclampsia, the most common of hypertensive disorders of pregnancy is an idiopathic multisystem disorder affecting 2 – 10% of all pregnancies.[1, 2]

It is the major cause of maternal mortality and substantial cause of neonatal morbidity and mortality. 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]

According to the criteria of the International Society of the Study of Hypertension in pregnancy, the preferred definition is a diagnosis of pregnancy-induced hypertension (diastolic blood pressure =90 mm Hg) occurring after week 20 of gestation with proteinuria (either =300 mg protein per day or an urinary protein/creatinine ratio =30 mg/mmol).[4]

The basic pathology of preeclampsia is endothelial dysfunction, poor placentation and vasospasm of vessels along with alteration of haematological profile of which thrombocytopenia is the most common. [5, 6]

Thrombocytopenia may be accompanied by a clinically evident consumptive coagulopathy or may be the sole abnormality seen. The present study is designed to compare the coagulation parameters in patients with preeclampsia and normal pregnant women and to determine the relationship between total platelet count and severity of preeclampsia along with changes in coagulation parameters.

MATERIAL AND METHODS

The present cross-sectional study was carried out in the Department of Physiology, along with collaboration of Department of Obstetrics and Gynaecology, Department of Haematology and Department of Biochemistry of S.C.B. Medical College, Cuttack from the period of March 2013 to June 2014.

The study includes 100 preeclampsia patients from the outdoor, indoor and labour room of

Department of Obstetrics and Gynaecology and 100 normal pregnant women within age group of 18-35 years. The healthy pregnant women were selected from antenatal outdoor of Obstetrics and Gynaecology department of S.C.B. Medical College and Hospital, Cuttack at random. It was believed that, in the healthy individuals, the socio economic strata of the community had been adequately represented.

Exclusion Criteria:

Women with previous history of hypertension, diabetes mellitus, history of recurrent miscarriages, previous hepatic or renal disease, multiple foetuses, idiopathic thrombocytopenic purpura (ITP) or any other bleeding diathesis, immunosuppressant or history of illicit drug use were excluded from the study

The preeclamptic women were selected based on the following criteria:

Pregnant women with blood pressure over the baseline ≥ 140 /90 mm of Hg with proteinuria ≥ 0.3 gm / l or >1 + measured by dipstick.

Cases were categorized into Mild (140-159 /90-109 mm Hg) and severe (≥160 /110) on the basis of blood pressure based upon classification of American College of Obstetrician & Gynaecologist (ACOG). [2]

After taking informed written consent from each subject and approval of institution ethical committee, detailed history was recorded regarding gravida, parity, history of diabetes mellitus, hypertension and other obstetrics and gynaecological complications. Ultrasonography was done in all cases to confirm the gestational age and to exclude any obstetrical and gynaecological complications

Complete clinical examination was done at the start of experiment. The anthropometric parameters like height and weight of subject were measured. Blood pressure was measured with patients in supine position and resting comfortably on her right hand at 30 degrees to the horizontal with the sphygmomanometer cuff at the level of the heart.

Experimentation and collection of data

Blood was collected from all the enrolled patients who were not given any therapy for preeclampsia for the assessment of coagulation profile

Coagulation Parameters done are –

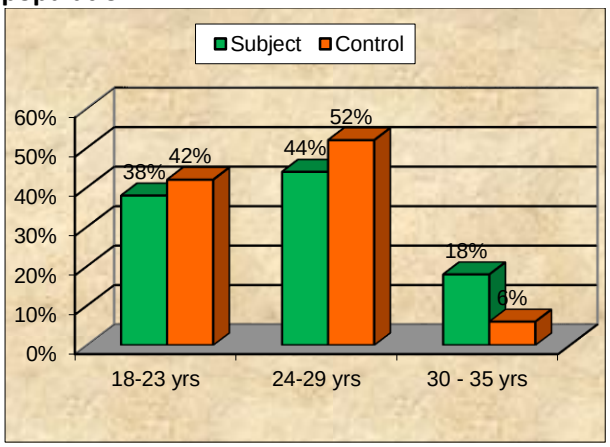
- Total Platelet count (TPC) – Direct method using Rees-Ecker fluid.
- Prothrombin Time (PT) – Automated coagulation analyzer – Thromborel S. reagent.
- Activated partial thromboplastin time (aPTT) – Automated coagulation analyzer – Dade Action FSL activated PTT analyzer.
- Bleeding time (BT) – Duke's Method.
- Coagulation time (CT) – Capillary tube method of Wright.

Statistical analysis of data

All data were expressed as Mean ± SD. Statistical analysis was done using unpaired students t test. A level of p value <0.05 was used to indicate statistical significance in all analyses. Data was analysed using SPSS version 19.

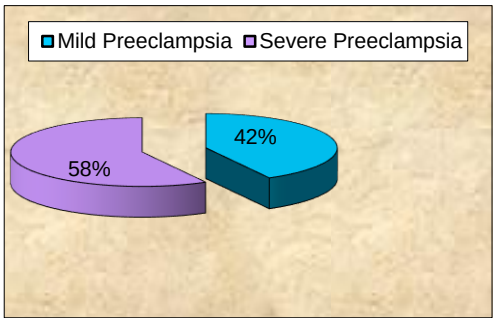
RESULTS

Figure1: Age distribution in the study population.



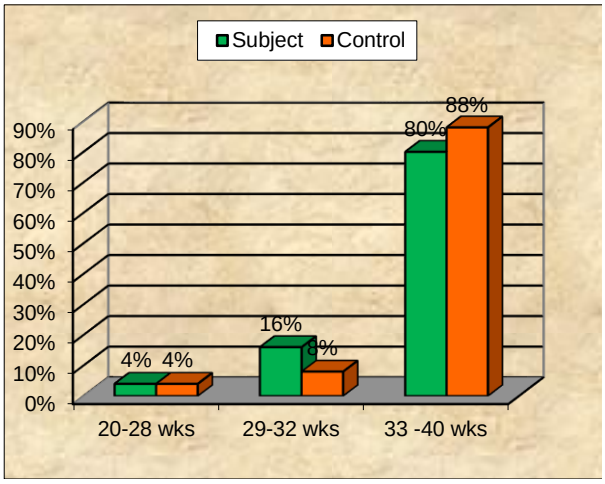
In normal pregnancy the mean age is 24.72 ± 3.53 years and in preeclampsia, mean age group is 25.52 ± 4.38 years, with a statistically insignificant difference. Maximum numbers of cases are in the age group of 24-29 years.

Figure 2: Distribution of cases



Out of 100 cases of preeclampsia, 42 cases have mild preeclampsia and 58 cases with severe preeclampsia.

Figure 3: Gestational age among subjects and control



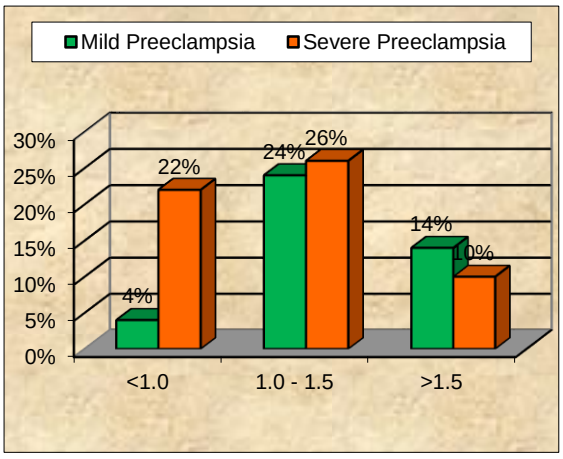
Maximum women in this study are in the gestational age group of 33-40 weeks, 88% cases in normal pregnancy and 80% cases in preeclampsia with mean gestational age of 36.08±3.12 weeks and 36.1±3.61 weeks respectively

Table 1: Abnormalities of coagulation tests in preeclampsia compared with normal pregnancy

Parameters	Preeclampsia	Normal Pregnancy	P. Value
TPC(lac/mm^3)	1.23 ± 0.416	2.41 ± 0.450	< 0.001
PT(sec)	15.27 ± 3.47	13.72 ± 1.97	<0.05
aPTT(sec)	34.20 ± 11.46	22.16 ± 4.70	<0.001
BT(min)	5.03 ± 1.52	3.65 ± 0.9	<0.001
CT(min)	4.81±1.19	4.37±0.85	<0.05

The mean total platelet count in normal pregnancy is 2.41 ± 0.450 lacs/mm^3 and in preeclampsia 1.23±0.416 lacs/mm^3.There is statistically significant increase in PT($p<0.05$), aPTT($p<0.001$), BT(<0.001) and CT($p<0.05$) in preeclampsia as compared to normal pregnancy.

Figure 4: Distribution of cases based on severity of preeclampsia and estimated platelet count.



In the study group, 13(26%)cases have platelet count below 1 lac/mm3, out of which 2(4%)cases have mild preeclampsia and 11(22%)cases are of severe preeclampsia.

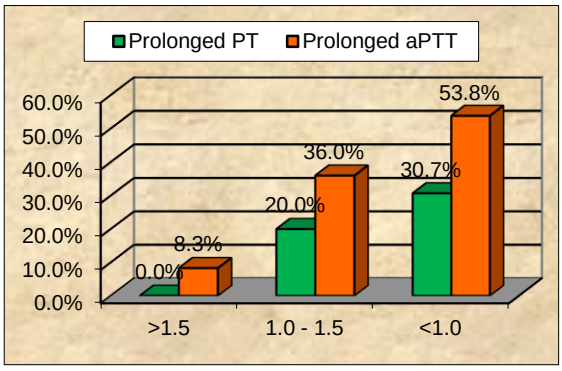
25(50%)cases have platelet count between 1 lac – 1.5 lacs /mm3. Platelet count above 1.5 lacs /mm3 are found in only 12(24%) cases; 7(14%)cases having mild preeclampsia and 5(10%)cases severe preeclampsia.

Table 2: Distribution of cases in relation to total platelet count and severity of preeclampsia

G.Age (in weeks)	Cases	TPC(in lacs/mm^3)		
		<1 No. of Cases	1-1.5 No. of Cases	>1.5 No. of cases
20-28	Mild		1 (2%)	
	Severe			1 (2%)
29-32	Mild		2 (4%)	2 (4%)
	Severe	2 (4%)	2 (4%)	
33-40	Mild	2 (4%)	9 (18%)	5 (10%)
	Severe	9 (18%)	11 (22%)	4 (8%)

Severe preeclampsia is present in 4% cases at 29-32 weeks of gestation and increases to 18% at 33 – 40 weeks of gestation with platelet count <1 lac /mm^3.

Figure 5: Coagulation abnormalities in subjects depending on platelet count.



Prothrombin time is found to be prolonged in 9(18%) cases and activated partial thromboplastin time is prolonged in 17(34%) cases. Out of 13 cases having platelet count below 1 lac/mm^3,4 (30.7%)cases have prolonged PT and 7(53.8%) cases with prolonged aPTT.

DISCUSSION

The findings of the present study confirm that preeclampsia is more prevalent in primigravida and most of the cases presented for treatment at an advanced stage of disease. Younger age of occurrence of preeclampsia in this study testifies the early age of marriage and pregnancy in this country compared to western countries. In this study both the normal pregnant women serving as control and preeclampsia patients are in the same gestational age group. Similar findings were documented in various studies.[7-]

The present study documents significant reduction of platelet count, prolongation of bleeding time ($p<0.001$), prothrombin time($p<0.05$)and activated partial thromboplastin time($p<0.001$)in preeclampsia as compared to normal pregnancy. Similar findings were documented in various studies. The low platelet level was attributed to immunologically mediated destruction, platelet aggregation and consumption whereas prolonged BT & PTT and increased level of fibrin degradation products(FDP) were due to reduced synthesis of coagulation factors due to liver dysfunction.[10-13]

Thrombocytopenia is reported frequently in severe preeclampsia which has also been reported in various studies. There is progressive fall of mean platelet count with the increasing severity of disease.[14, 15]

In the present study ,severe preeclampsia is present in 4% cases at 29-32 weeks of gestation and increases to 18% at 33 – 40 weeks of gestation with platelet count <1 lac /mm^3 which is attributed to increased platelet activation, enhanced aggregation, destruction which appear to be due to endothelial damage.[16,17]

Platelet activation may lead to increased generation of thromboxane A_2 and serotonin release, in turn increase vasoconstriction and platelet aggregation.

In the present study we documented increased prolongation of aPTT when total platelet count is very low(<1lac/mm^3)Similar findings were documented by several studies. Leduce et al and S. Mohapatra et al in their study claimed that no subject had an abnormal prolonged PT or aPTT in the absence of thrombocytopenia.[14, 18]

Jambhulkar S et al documented that platelet count and partial thromboplastin time have predictive value in detecting disseminated intravascular coagulation (DIC) in preeclampsia and these parameters show more abnormal results with increasing severity of preeclampsia. Bleeding time, coagulation time & prothrombin time were normal but partial thromboplastin time was significantly prolonged. [19]

However, Prieto JA et al observed that there was no correlation between the level of thrombocytopenia and the levels of PT & PTT.[20]

Jahromi N et al stated in their study that the mean value of platelet count was lower ($p<0.001$) and the mean value of aPTT was higher($p<0.05$) in preeclamptic patients. However, the mean value of PT showed no statistical difference between two groups ($p>0.05$).There was significant correlation between thrombocytopenia and prolonged aPTT which led to conclusion that the measurements of aPTT seems to be important for early diagnosis of coagulation abnormalities in patients with severe preeclampsia who have normal platelet count.[21]

Similar to the present study , Mc Donagh RJ et al documented platelet count to be very specific for predicting a prolonged bleeding time. There was a significant negative correlation between TPC and BT ($r = -0.45$, 95% CI – 0.26 to 0.60 $P <0.0001$.).[22]

However, Rodgers RPC et al suggested that earlier bleeding time was used to assess platelet count in pregnancy with thrombocytopenia but now it is rarely used because of its disadvantages i.e it is invasive, unreliable, highly operator dependent and is also insensitive, especially to mild platelet defects and not a good predictor of bleeding risk. [23]

So, it is concluded from the study that total platelet count estimation can be taken as an early and rapid procedure for screening preeclampsia cases at admission followed by serial platelet counts while monitoring coagulation indices. Evaluation of PT and aPTT should be kept reserved and added only if the platelet count falls below 1 lac/mm^3.An ongoing coagulopathy should be suspected if thrombocytopenia along with prolongation of PT and aPTT is found and the treatment should be started at the earliest.

However, more research is required in this field to find an ideal screening method for early identification of preeclampsia and prediction of its severity. This would open up new possibilities for early diagnosis and effective management of preeclampsia cases.

Limitations & future scope of the study

Sample size is less. Broad spectrum, multicentric studies are strongly recommended

Competing Interests

Authors don't have any competing interest.

AUTHORS' CONTRIBUTION

Girija Priyadarshini and Rama Raman Mohanty designed the study, performed the experiment, interpreted the data, drafted the manuscript and revised it. Final manuscript was approved by all authors.

REFERENCES

1. World Health Organization. *Make Every Mother and Child Count. World Health Report, 2005.* Geneva, Switzerland: World Health Organization; 2005.
2. American College of Obstetricians and Gynecologists Committee on Practice Bulletins–Obstetrics. ACOG practice bulletin: diagnosis and management of pre-eclampsia and eclampsia: number 33, January 2002. *Obstetric Gynecol.* 2002; 99:159 –167.
3. Villar K, Say L, Gu¨lmezoglu AM, Merialdi M, Lindheimer MD, Betran AP, Piaggio G. Eclampsia and pre-eclampsia: a health problem for 2000 years. In: Critchley H, MacLean AB, Poston L, Walker JJ, eds. *Preeclampsia*. London: RCOG Press; 2003; 189–207.

4. Brown MA, Lindheimer MD, de Swiet M, van Assche A, Moutquin JM. The classification and diagnosis of the hypertensive disorders of pregnancy: statement from the International Society for the Study of Hypertension in Pregnancy (ISSHP). *Hypertens Pregnancy.* 2001; 20: IX-XIV.
5. Redman CWG, Sargent IL. Pre-eclampsia, the placenta and the maternal systemic inflammatory response -a review. *Placenta.* 2003; 24:S21–S27.
6. Levine RJ, Maynard SE, Qian C, Lim KH, England LJ, Yu KF, Schisterman EF, Thadhani R, Sachs BP, Epstein FH, Sibai BM, Sukhatme VP, Karumanchi SA. Circulating angiogenic factors and the risk of preeclampsia. *N Engl J Med*. 2004; 350:672–683.
7. Yusuf Ustun, Yaprak Engin Ustun, Ozlem Ozturk, Ibrahim Alanday, Halil yaman. Ischemia modified albumin as an oxidative stress marker in preeclampsia. Journal of maternal – fetal and neonatal medicine 2010; Early Online : 1-4.
8. Mc Donald, Mauricean, Miles. Am J. Perinatology ; 4 : 130-147.
9. Mc Gilivary, Some observations on the incidence of preclampsia B.J. Obst. Gynaeco. Br. Emp; 65;536-539.
10. Sharma SK, Philip J, Whitten CW, Padakandla UB, Landers DF. Assessment of changes in coagulation in parturients with preeclampsia using thromboelastography. *Anesthesiology* 1999; 90:385-90.
11. Redman CW, Bonnar J, Beilin L – Early platelet consumption in preeclampisa. Br. J. Med; 1: 467-An increased platelet aggregation rate has been reported in preclampisa
12. Stubbs TM, Lazarchick J, et al : Plasma fibrinonectin level in preelampsia : A Possible marker for vascular endothelial damage. Am J. Obstet Gynecol ; 150 : 885-7.
13. Whighem KAE, Howie P.W, Drummond AHB, Prentice CRM – Abnormal platelet function in preeclampsia. Br. J. Obstet Y Gynaecol ; 85 : 28-32.
14. Leduc L, Wheeler JM, Kirshon B, Mitchell PS Cotton DB : Coagulation Profile in Severe preeclampsia. Obstet Gynecol 1992; 79 : 14-8.
15. Weinstein L. Syndrome of hemolysis, elevated liver enzyme, low platelet count; a severe consequence of hypertension in pregnancy. *Am J Obstet and Gynaecol* ; 142: 159.
16. Konijnenberg A, Stokkes EW, Vander Post JA, et al: Extensive platelet activation in preeclampsia compared with normal pregnancy. Enhanced expression of cell adhesion molecules. Am. J. Obstet Gynecol 176: 461, 1997.
17. Bellegeer VC, Spitz B, De Baene LA, et al : Platelet activation and vascular damage in gestational hypertension. Am J. Obstet Gynecol 166 : 629, 1992 .
18. S. Mohapatra, B. B. Pradhan, U. K. Satpathy, A Mohanty AND J. R. Pattanaik. platelet estimation: Its prognostic value in pregnancy-induced hypertension Indian J Physiol Pharmacol 2007; 51 (2) : 160–164.
19. Jambhulkar S, Shrikhande A, Shrivastava R, Deshmukh K. Coagulation profile in pregnancy induced hypertension. Indian Journal of Hematology & blood transfusion, 2001Mar; 19(1):3-5.
20. Prieto JA, Mastrobettista JM, Blanco JD Coagulation studies in patiens with marked thrombocytopenia due to severe preecmplasia. Am J Perinatol 1995 May; 12 (3) 220-2.
21. B.Namavar Jahromi, S H Rafiee: Coagulation factors in severe preeclampsia.ICRMJ 2009;11(3):321-32
22. McDonagh RJ, Ray JG, Burrows RF, Burrows EA, Vermeulen MJ. Platelet count may predict abnormal bleeding time among pregnant women with hypertension and preeclampsia. Can J Anaesth. 2001 Jun;48(6):563-9.
23. Rodgers RPC, Levine J A critical reappraisal of the bleeding time.Seminars in thrombosis & hemostasis.16:1-20

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