www.jmscr.igmpublication.org

ISSN (e)-2347-176x ISSN (p) 2455-0450

crossrefDOI: https://dx.doi.org/10.18535/jmscr/v7i1.99

IGM Publication

Journal Of Medical Science And Clinical Research

An Official Publication Of IGM Publication

Research Article

Study of Coagulation Profile and Platelet Counts in Pre Eclamptic and Eclamptic Patients

Authors

Priyamvada Singhal[1], Vishal Agrawal[2*], Narayan Ingole[3], Nitin Gangane[4]

[1]Department of Pathology, Subharti Medical College, Meerut, U.P, India

[2]Health care imaging centre, 43, Shivaji road (Opp. Shankar Ashram), Meerut, U.P, India

[3]Department of Pathology, Mahatma Gandhi Institute of Medical Sciences, Sewagram, Wardha, Maharashtra, India

[4]Department of Pathology, Mahatma Gandhi Institute of medical sciences, Sewagram, Wardha, Maharashtra, India

*Corresponding Author

Vishal Agrawal

Email: *docvishalagrawal@hotmail.com*, Phone no. +918605728404

Abstract

Objectives: *We conducted this prospective case-control study in rural population based medical institute of central India. The aim of the study was to assess and analyze the coagulation profile (PT, aPTT, fibrinogen and fibrin degradation product [FDP] levels) and platelet counts in 3rd trimester normotensive, pre-eclamptic and eclamptic pregnant women.*

Methods: *In all subjects (cases and controls) 2 ml of blood sample was collected in EDTA and tri-sodium citrate bulbs for platelet counts and coagulation profile respectively.*

Results: *The mean PT and aPTT were significantly high in cases and mean fibrinogen level was significantly low in cases as compared to controls. FDP was significantly increased in cases as compared to non-detectable level in the controls. Thrombocytopenia was observed in 45% of cases. No any correlation between level of platelet count and abnormal coagulation test results (PT, aPTT, fibrinogen and FDP) were found.*

Conclusion: *We found in our study that platelet count and above coagulation tests should be performed in cases of pre eclampsia and eclampsia to identify severity of disease and to prevent development of complications.*

Keywords: *pre eclampsia, eclampsia, platelet count, coagulation tests.*

Introduction

Normal pregnancy is associated with impressive changes in the haemostatic mechanism to maintain placental function during pregnancy and to prevent excessive bleeding during delivery. The combined changes of increased coagulation factors and suppression of fibrinolytic activity leads to hypercoagulable state or prothrombotic state.[1,2]

During pregnancy the concentrations of coagulation factors VII, VIII, IX, X, XII and the von Willebrand factor rise significantly, accompanied by a relevant increase in the concentration of plasma fibrinogen. Plasma fibrinolytic activity is reduced during pregnancy due to liberation of plasminogen activator inhibitor from placenta.[2]

Pre-eclampsia (PE) is a disease of pregnancy resulting from a maternal physiological response to abnormal placentation. It is a multisystem disorder affecting approximately 2-7% of all pregnancies and is a significant cause of maternal and fetal morbidity and mortality. It usually occurs in the last trimester of pregnancy and more commonly in primiparous. It is characterised by widespread maternal endothelial dysfunction presenting clinically with hypertension, edema and proteinuria.

The onset of convulsion in a woman with pre-eclampsia that cannot be attributed to other causes is termed as eclampsia.

The systemic endothelial dysfunction in pre-eclampsia results in hypercoagulable state. Many haemostatic abnormalities have been reported in association with hypertensive disorder of pregnancy. Thrombocytopenia is the most common of this.[3,4] Reduced platelet counts in patients of mild and severe pregnancy induced hypertension(PIH) and very low counts in eclampsia was reported by many authors.[5] The degree of thrombocytopenia increases with the severity of disease.[4,6] The measurement of aPTT seems to be important for early detection of coagulation abnormalities in patients with severe pre-eclampsia who have normal platelet counts.[7] Low fibrinogen levels and increase in fibrin split products (D-dimer) has also been observed with increasing severity of pre-eclampsia.[8,9]

Several studies identified imbalance between coagulation and fibrinolysis in pre eclampsia which could be due to alterations of endothelial cells and fibrin deposition in microvasculature which lead to enhanced activation of the coagulation cascade and impaired fibrinolysis associated with multiple organ dysfunctions.[10-12]

Early assessment of severity of pre eclampsia and eclampsia is necessary to prevent complications and increased maternal and fetal morbidity and mortality. Therefore, the present study was done at rural population based medical institute to analyze the significance of various coagulation parameters and platelet counts in assessing severity of pre-eclampsia and eclampsia to prevent further complications.

Material and Methods

The present study was a prospective case-control study carried out in the haematology division of the Department of Pathology, in a rural population based medical institute over a period of 2 years. The study was approved by Research ethical committee of the institute. The blood samples for the study were obtained from the pregnant women in 3rd trimester of gestation admitted in obstetric wards. The patients of pre-eclampsia and eclampsia served as the cases whereas the uncomplicated normotensive age and gestation matched pregnant women served as controls.

Inclusion criteria

Pregnant women between 28 to 40 weeks of gestation with pre-eclampsia and eclampsia with having minimum criteria of -

(1) BP ≥140/90 mm Hg after 20 weeks of gestation.

(2) Proteinuria ≥ 300mg/24hrs or ≥1+ with dipstick.

Exclusion criteria

Pregnant women with known bleeding disorders, liver disease, abruptio placentae, intrauterine fetal death, trauma, any associated inflammatory disease or sepsis, any associated malignancy, in labor and on anticoagulant therapy.

All the cases were grouped into mild preeclampsia, severe pre eclampsia and eclampsia, The severity of pre eclampsia is graded into two categories. (Table 1)

Table 1: Grading of pre eclampsia

Abnormality	Mild	Severe
Diastolic Blood Pressure	<110 mm Hg	≥110 mm Hg
Systolic Blood Pressure	<160 mm Hg	≥160 mm Hg
Proteinuria	≤2+	≥3+
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper Abdominal Pain	Absent	Present
Oliguria	Absent	Present
Serum Creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
SerumTransaminase level	Minimal	Marked
Fetal Growth Retardation	Absent	Obvious
Pulmonary Edema	Absent	Present

Methods

In all the subjects, informed consent was obtained and the venous blood samples were collected as under-

(1) 2 ml EDTA (0.25mg/ml) bulb for complete blood count including platelet count.

(2) 2 ml in 3.2% tri-sodium citrate bulb maintaining ratio of blood and anticoagulant as 9:1 (1.8ml blood and 0.2 ml anticoagulant).

For platelet counts, the blood sample in EDTA bulb was run on Beckman coulter make (18 parameters) automated blood cell counter within 2 hours of collection of sample

For coagulation testes, the citrate blood sample was immediately centrifuged at 3000 rpm for 15 minutes and the supernatant plasma was transferred to a clean polystyrene tube. This plasma sample was used for studying Prothrombin time (PT), Activated partial thromboplastin time (aPTT), Fibrinogen levels and Fibrin degradation products (FDP) levels. These tests were carried out within 3 hours of collection of blood sample.

For PT & aPTT the semi-automated coagulometer, for quantitative estimation of fibrinogen the 'FIBROQUANT' test kit and for qualitative and semiquantitative estimation of FDP test 'TULIP XL FDP' kit were used.

Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were considered abnormal if they were >15 seconds and >35 seconds respectively. Fibrinogen was considered low if it was <250 gm/dl and FDP was considered elevated if it was detected as ≥200ng/ml. Thrombocytopenia was defined as platelet count $<150 \times 10^9$/L.

The data thus obtained was tabulated and statistical analysis were performed by student's unpaired t-test, multiple comparison Tukey test, one way ANOVA test, Chi square test and Fisher's exact test. Statistical significance was considered at $p<0.05$.

Results

We have studied coagulation profile (PT, aPTT, Fibrinogen and FDP levels) and platelet count in total 80 cases of pre eclampsia and eclampsia in 3rd trimester of pregnancy. It included 21 (26.25%) cases of mild pre eclampsia, 28 (35%) cases of severe pre eclampsia and 31 (38.75%) cases of eclampsia. Similarly 80 normotensive age and gestation matched pregnant women in 3rd trimester were also studied as controls. The mean age of the cases was 24.68±3.67 years. Maximum 68 (85%) cases were between 20-29 years of age.

The mean gestational age observed in cases was 33.85±4.10 weeks. 61.25% of the cases were primiparous.

Table 2: Mean prothrombin time (PT) and Activated partial thromboplastin time (aPTT) in cases and controls.

Sr. No.	Diagnosis	No. of patients	PT (sec)		aPTT (sec)	
			Range	Range	Mean ±SD	Mean ±SD
1	Cases	80	10.8-24.5	25.6-70.1	34.88±6.37	14.30±1.77
	a. Mild PE	21	11.5-15.2	26.0-36.0	31.46±2.38	13.31±0.68
	b. Severe PE	28	11.7-24.5	25.6-46.1	34.77±5.48	14.55±2.31
	c. Eclampsia	31	10.8-18.0	27.8-70.1	37.29±7.88	14.76±1.50
2	Controls	80	10.2-13.9	26.9-34.0	31.11±1.55	12.71±0.83

On comparing, the mean PT and aPTT were found to be increased in cases as compared to that in the controls and this difference was found to be statistically significant. In subgroups of cases, the PT and aPTT were found to increase gradually with progression of disease from mild pre eclampsia to severe pre eclampsia to eclampsia.(Table 2)

Of the total 80 cases, abnormal prothrombin time results >15 seconds found in 25% cases and abnormal aPTT results >35 seconds in 38.75% cases of pre eclampsia and eclampsia.

Table 3: Mean fibrinogen levels and FDP levels in cases and controls

Sr. No.	Diagnosis	No. of patients	Fibrinogen (mg/dl)		FDP (ng/ml)	
			Range	Mean ±SD	Range	Mean ±SD
1	Cases	80	100-350	221.56±63.93	0-600	177.50±198.71
	a. Mild PE	21	160-350	269.05±45.60	0-200	9.52±43.64
	b. Severe PE	28	120-330	215.18±59.99	0-600	200.00±188.56
	c. Eclampsia	31	100-300	195.16±61.64	0-600	270.97±203.62
2	Controls	80	240-390	285.75±28.05	0	0

The mean fibrinogen level observed in cases of pre eclampsia and eclampsia was found to be significantly decreased than that in the controls. In subgroups of cases, there was gradual decrease of fibrinogen level with progression of disease. Compared to that in the controls, the decreased fibrinogen level in mild pre eclampsia was insignificant but in severe pre eclampsia and eclampsia this decreased fibrinogen level was statistically significant. Similarly amongst the subgroups of cases, the decrease in fibrinogen level in severe pre eclampsia and eclampsia as compared to that in mild pre eclampsia were statistically significant. (Table 3)

The mean fibrin degradation products (FDP) levels observed in cases was significantly increased compared to the non detectable level in the controls. (Table 3) It was seen in 40(50%) cases. In subgroups of cases only one (4.7%) case showed elevated FDP in mild pre eclampsia, whereas in severe pre eclampsia and eclampsia 60.71% cases and 70.96% cases respectively showed detectable FDP levels.

Table 4: Mean platelet counts in cases and controls

Sr. No.	Diagnosis	No. of patients	Platelet count (x 10^9/L)	
			Range	Mean ±SD
1	Cases	80	16-430	174.30±87.56
	a. Mild PE	21	97-386	214.9±80.87
	b. Severe PE	28	16-430	177.96±100.88
	c. Eclampsia	31	21.2-285	143.49±67.23
2	Controls	80	80-414	224.19±69.81

The mean platelet count in cases was found to be significantly lower than that in the controls. In subgroups of cases there was gradual decrease in mean platelet count with progression of disease. (Table 4)

In this study, cases and controls were also distributed according to the levels of platelet count into three categories as normal (>150 x 10^9/L), low (100-150 x 10^9/L), and very low (<100 x 10^9/L) platelet counts. The present study observed that there was increased frequency in thrombocytopenia cases with progression of disease. (Table 5)

Table 5: Distribution of cases and controls according to the level of platelet counts

Sr. No.	Diagnosis	Platelet Count (x 10^9/L)			
		>150	100-150	<100	Total
1	Cases No. (%)	44 (55)	22 (27.5)	14 (17.5)	80 (100)
	a. Mild PE	16	4	1	21
	b. Severe PE	15	7	6	28
	c. Eclampsia	13	11	7	31
2	Controls No. (%)	68 (85)	10 (12.5)	2 (2.5)	80 (100)

We also assessed, if there is any correlation between the level of platelet count with the simultaneous abnormal coagulation test results. (Table 6).

Table 6: Coagulation abnormalities of patients with pre eclampsia and eclampsia according to their platelet counts

Platelet counts	No. of cases	Prolonged PT(>15secs) No. (%)	Prolonged aPTT(>35secs) No. (%)	Low Fibrinogen (<250mg/dl) No. (%)	Elevated FDP(≥200ng/ml) No. (%)
<100	14	5(35.71)	10 (71.42)	10 (71.42)	7 (50)
100-150	22	4(18.18)	6 (27.27)	14 (63.63)	14 (63.63)
>150	44	11(25)	15 (34.09)	23 (52.27)	19 (43.18)
p value	-	0.49,NS	0.092,NS	0.38,NS	0.29,NS

Thus the abnormal coagulation test results of PT, aPTT, fibrinogen and FDP were also observed in patients with even normal platelet counts. Statistically there was no any correlation between level of platelet count and abnormal coagulation test results.

Discussion

In the present study, we compared the coagulation profile (PT, aPTT, levels of fibrinogen and FDP) and platelet counts in 80 cases of pre eclampsia and eclampsia in 3rd trimester of pregnancy with that in 80 normotensive age and gestation matched pregnant women as controls.

The mean age of the cases was 24.68±3.67 years. Maximum 68(85%) cases were between 20-29 years of age. Priyadarshini and Mohanty (2014)[13] also found maximum cases between 21-30 yrs of age, similar to the present findings. Younger age of occurrence of pre eclampsia and eclampsia testifies the early age of marriage and pregnancy in our country as compared to western countries.[13]

Different studies have reported the frequency of abnormal PT and aPTT in patients with pre eclampsia and eclampsia to be between 0% and 50%.[3,9] In our study also, the abnormal prothrombin time results were observed in 20 of the 80 (25%) cases with prothrombin time >15 seconds and abnormal aPTT results were observed in 31 of the 80 (38.75%) cases with aPTT >35 seconds in cases of pre eclampsia and eclampsia, similar to the findings of other studies.

The aPTT and PT reflects the function of endogenous and exogenous coagulation pathways respectively. Normal late pregnancy shows a physiological hypercoagulable state with decreased levels of aPTT, PT and TT and increased levels of fibrinogen compared to early pregnancy. This result may be caused by platelet consumption and aggregation followed by a secondary regeneration.[14] However with the

onset of preeclampsia, in particular severe pre eclampsia, there may develop complex disorders in exogenous and endogenous coagulation pathways which may relate to increased PT and aPTT in these conditions. As pre eclampsia and eclampsia syndrome is considered as a multisystem inflammatory disorder[14] and as the diagnostic criteria involve elevated serum transaminase levels suggesting increased certainty of pre eclampsia[15], it indicates hepatic insult in pre eclamptic syndrome. The liver damage is usually associated with increased prothrombin time level and this is likely to be the mechanism for increased prothrombin time in cases of pre eclampsia and eclampsia.

Similarly the significant prolongation of aPTT in severe pre eclampsia occurs due to activation and consumption of coagulation factors[1,16] especially factor VIII.[2]

The significant decrease in mean fibrinogen level in cases of pre eclampsia and eclampsia as compared to that in the controls have also been observed by Srivastava et al (1995)[8], Acmaz et al (2008)[3], Jahromi and Rafiee (2009)[7] and Dave et al (2014)[17], similar to the present findings.

The changing levels of fibrinogen in pre eclampsia were explained by various authors as under-

(1) Preeclampsia is a systemic inflammation and fibrinogen being an acute phase reactant, is increased in response to inflammation.[3]

(2) In healthy pregnant women, fibrinogen levels are increased by inflammation. However, since compensatory coagulation and fibrinolysis become exaggerated in preeclampsia, consumption coagulopathy occurs and fibrinogen levels are returned to normal values.[3]

(3) In pre eclampsia patients, the coagulation-fibrinolytic system is thought to be one of the most seriously affected systems by maternal inflammatory reactions and immune dysfunction.[16]

Srivastava et al (1995)[8], Jahromi and Rafiee (2009)[7] and Dave et al (2014)[17] also found significantly higher levels of FDP in cases as compared to controls, similar to the present findings.

D-dimer (FDP) is a specific degradation product resulting from the hydrolysis of the fibrin monomer and is considered to be an indirect marker for thrombosis and fibrinolytic activity. The maternal D-dimer concentration in normal pregnancy increases progressively from conception to delivery.[16] The findings of Heilmann et al (2007)[12], Han et al (2014)[16] and that of present study showed higher D-dimer concentrations in pregnant women with pre eclampsia, especially in women with severe pre eclampsia and eclampsia compared to normotensive women. D-dimer is involved in the dynamic balance between plasminogen activators [t-PA and Urokinase-type plasminogen activator (uPA)] and plasminogen activator inhibitor (PAI-1) in women with preeclampsia; therefore, D-dimer concentration can reflect the dynamic changes in both the super-hypercoagulable status and the activated fibrinolytic state in pre eclampsia patients.[16]

The gradually reduced platelet counts in patients of mild pre eclampsia to severe pre eclampsia to eclampsia were comparable to those reported in other studies. (Table 7).

Table 7: Comparison of platelet counts in different studies

Sr.No	Studies (year)	Platelet counts (x 10^9/L)			
		Control	Mild PE	Severe PE	Eclampsia
1.	Srivastava et al (1995)[8]	194.4	179.7	164.2	152.6
2.	Jambhulkar et al (2001)[18]	238	230	170	151
3.	Vrunda and Shaila (2004)[6]	220	200	140	130
4.	Present study	224.19±69.81	214.9±80.87	177.96±100.88	143.49±67.23

The mechanism of thrombocytopenia in pre eclampsia and eclampsia syndrome is variously explained as under

- It may be due to increased consumption of platelets with increased megakaryocytic activity to compensate it. Platelets adhere to areas of damaged vascular endothelium resulting in secondary destruction of platelets.[3,19]
- Platelets from severely preeclamptic patients showed less response than normal to a variety of aggregating agents suggesting that platelets may have undergone previous aggregation in the microcirculalion.[20]
- Recent studies have documented that increased plasma levels of sFlt1-soluble vascular endothelial cell growth factor (VEGF) receptor type 1, as well as endoglin, an endothelial cell-derived member of the tumor growth factor-² (TGF-²) receptor family, are present in patients intended to develop preeclampsia as early as the late first trimester. Increased levels of soluble fms-like tyrosine kinase-1(sFlt1) and endoglin mRNA is present in preeclamptic placentae,. sFlt1 binds and neutralizes VEGF and placental growth factor (PLGF), another important VEGF family member whose levels normally increase during pregnancy, whereas endoglin blocks the binding of TGF-² to endothelial cells. These types of pregnancies are also associated with qualitative alterations suggesting increased platelet turnover. There is a shortened platelet life span and increased number of megakaryocytes in the bone marrow, accompanied with an increased number of immature platelets seen in the peripheral blood. Many investigators believe that increased platelet consumption is due to disseminated intravascular coagulation while others suggest an immune mechanism.[3]

In the present study, the results of the distribution of cases and controls according to the levels of platelet count into three categories as normal (>150 x 10^9/L), low (100-150 x 10^9/L), and very low (<100 x 10^9/L) platelet counts are comparable with that of various authors showing decreasing platelet counts with increasing severity of disease.

The findings of various studies in cases and controls in respect to the normal, low and very low platelet counts are given below. (Table 8)

Table 8: Comparison between the normal, low and very low platelet counts in cases and controls in different studies

	Studies (Year)	>150 x 10^9/L (Normal)		100-150 x 10^9/L (Low)		<100 x 10^9/L (Very low)	
		Controls %	Cases %	Controls %	Cases %	Controls %	Cases %
1.	Vrunda and Shaila (2004)[6]	38	48	12	32	0	20
2.	Mohapatra et al (2007)[4]	100	53.3	0	27.7	0	18.8
3.	Present study	85	55	10	27.5	2	17.5

The findings of the present study are similar to that of Mohapatra et al (2007)[4] and Vrunda and Shaila (2004).[6]

The present study also assessed, if there is any correlation between level of platelet counts with simultaneous abnormalities of different coagulation test results. We found abnormal results of PT, aPTT, decreased fibrinogen level and increased FDP levels in very low, low and even normal range of platelet counts. However

statistically there was no any correlation between level of platelet count and abnormal coagulation tests results. (Table 6). Our results are in agreement with Jahromi and Rafiee (2009)[7] who commented that platelet count > 150 x 10^9/L can not assure the physician that no other significant coagulation abnormalities are present.

The deranged coagulation profile in patients of pre eclampsia and eclampsia ultimately affects maternal and fetal outcome.

Conclusion

We found in our study that platelet counts and various coagulation parameters (PT, aPTT, Fibrinogen, FDP) were important diagnostic tool to assess the severity of pre eclampsia and eclampsia to prevent further complications and to reduce maternal and fetal morbidity and mortality.

References

1. de Boer K, ten Cate JW, Sturk A, Borm JJ, Treffers PE. Enhanced thrombin generation in normal and hypertensive pregnancy. Am J Obstet Gynecol 1989 Jan;160(1):95-100.
2. Prisco D, Ciuti G, Falciani M. Hemostatic changes in normal pregnancy. Haematologica reports 2005;1(10):1-5.
3. Burrows RF, Hunter DJ, Andrew M, Kelton JG. A prospective study investigating the mechanism of thrombocytopenia in preeclampsia. Obstet Gynecol 1987 Sep;70(3 Pt 1):334-8.
4. Mohapatra S, Pradhan BB, Satpathy UK, Mohanty A, Pattnaik JR. Platelet estimation: its prognostic value in pregnancy induced hypertension. Indian J Physiol Pharmacol 2007 Apr-Jun;51(2):160-4.
5. Dube B, Bhattacharya S, Dube RK. Blood coagulation profile in Indian patients with pre-eclampsia and eclampsia. Br J Obstet Gynaecol 1975 Jan;82(1):35-9.
6. Vrunda JK, Shaila S. Lowered platelet count: A prognostic index in preeclampsia. J Obstet Gynaecol Ind 2004; 54(3):235-36.
7. Jahromi BN, Rafiee SH. Coagulation factors in severe preeclampsia. Iran Red Crescent Med J 2009;11(3):321-4.
8. Srivastava M, Bali S, Pandey J, Nayar V, Talib VH. Pregnancy induced hypertension and antithrombin-III. Indian J Pathol Microbiol 1995 Jul;38(3):257-60.
9. FitzGerald MP, Floro C, Siegel J, Hernandez E. Laboratory findings in hypertensive disorders of pregnancy. J Natl Med Assoc 1996 Dec;88(12):794-8.
10. Bonnar J, McNicol GP, Douglas AS. Coagulation and fibrinolytic systems in pre-eclampsia and eclampsia. Br Med J 1971; 2(5752): 12-16.
11. Wood SM, Burnett D, Picken AM, Farrell GW, Wolf P. Assessment of coagulation and fibrinolysis in pre-eclampsia. Br Med J 1974 Apr 20;2(5911):145-9.
12. Heilmann L, Rath W, Pollow K. Hemostatic abnormalities in patients with severe preeclampsia. Clin Appl Thromb Hemost 2007 Jul;13(3):285-91.
13. Priyadarshini G, Mohanty RR. Assessment of coagulation profile and its correlation with severity of preeclampsia in women of Odisha. A comparative cross-sectional study.. Int J Basic Appl Physiol 2014;3(1): 139-145.
14. Han L, Liu X, Li H, Zou J, Yang Z, Han J, et al. Blood coagulation parameters and platelet indices: Changes in normal and preeclamptic pregnancies and predictive values for preeclampsia. PLoS ONE 2014;9(12):e114488.
15. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY editors. Williams obstetrics. 2[3rd] ed. New York: Mcgraw- Hill; 2010. p. 706 -56.
16. Redman CW. Coagulation problems in human pregnancy. Postgrad Med J 1979 May;55(643):367-71.

17. Dave R, Agravat A, Dhruva G [1], Katara A. Comparative study of coagulation factors in Pre-eclampsia and normal pregnancy. Int J Sci Res April 2014. 3(4).
18. Jambhulkar S, Shrikhande A, Shrivastava R, Deshmukh K. Coagulation profile in pregnancy induced hypertension. Indian J Hematol Blood Transfus 2001 March; 19(1): 3-5.
19. O'Brien WF, Saba HI, Knuppel RA, Scerbo JC, Cohen GR. Alterations in platelet concentration and aggregation in normal pregnancy and preeclampsia. Am J Obstet Gynecol 1986 Sep;155(3):486-90.
20. Whigham KA, Howie PW, Drummond AH, Prentice CR. Abnormal platelet function in pre-eclampsia. Br J Obstet Gynaecol 1978 Jan;85(1):28-32.