ORIGINAL ARTICLE

Comparison of platelet count, platelet indices and coagulation profile in preeclampsia and normal pregnancy

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ABSTRACT

Aim: To compare platelet count, platelet volume indices (MPV and PDW) and coagulation profile in preeclampsia and normal pregnancy.

Method: This comparative cross sectional study was performed at King Edward Medical University, Lahore and its affiliated hospitals. Study was conducted for six months after approval of synopsis.The patients fulfilling inclusion and exclusion criteria were enrolled after informed consent. Venous blood sample was properly taken in dipotassium EDTA (Ethylene diamine tetra acetic acid) vacutainer for platelet count and platelet volume indices. In sodium citrate vial the sample was taken from both groups (i.e.; normal pregnant woman and preeclamptic patients) for PT, APTT, FDPs, D-Dimers and fibrinogen level and tested within six hours of collection to minimize variations due to sample aging. Improperly collected samples (hemolysed and clotted samples) were discarded. Samples were stored at room temperature.

Results: The mean age of patients with preeclampsia was 26.19±5.02 years and with normal pregnancy was 25.17±5.68 years. The mean platelets count in preeclampsia and normotensive pregnant female was 219.43±100.58 and 254.43±70.35 respectively. The mean platelet volume in preeclampsia and normotensive pregnant female was 9.78±0.96 and 9.34±1.30 respectively. The mean platelet distribution width (PDW) in preeclampsia and normotensive pregnant female was 12.43 ±3.45 and 11.98±3.45 respectively. The mean prothrombin time (PT) in preeclampsia and normotensive pregnancy was 14.52±3.16 and 13.60±1.75 respectively. The mean Activated partial thromboplastin time (APTT) in preeclampsia and normotensive pregnancy was 38.67±18.52 and 35.31±11.88 respectively. The mean Fibrinogen level in preeclampsia and normotensive pregnant female was 247.79±392.10 and 261.93±57.89 respectively. Among women with preeclampsia, the FDP of 35 (83.3%) women was <10 and of 7 (16.7%) was >10 whereas, among women with normal pregnancy group, all females (100%) had FDP <10.

Conclusions:Current study shows that the hematological parameters such as platelet count, Mean platelet volume (MPV), Platelet Distribution Width (PDW), fibrinogen, FDPs and D-Dimers were differing in women with preeclampsia compared to normal pregnancy but were not statistically significant.

Key words: Coagulation profile, Preeclampsia, Pregnancy

INTRODUCTION

Preeclampsia is diagnosed by blood pressure of > 140/90 mmHg on two different occasions more than 4 hours apart with more than 300 mg of protein in 24 hours urine collection after 20th week of gestation in a previously normotensive woman and resolving completely after 6th postpartum week.[1] About 5-7% of primigravida and 1-3% of multiparous women are complicated by preeclampsia.[2] World health organization estimates that annually 50,000 to 75,000 pregnant women die due to the complications of preeclampsia making it the leading cause of death in pregnancy.[3]Maternal complicationsof preeclampsia include multi-organ failure, seizures, stroke, adult respiratory distress syndrome, renal failure, pulmonary edema, disseminated intravascular coagulation and HELPP (hemolysis, elevated liver enzyme and low platelet count) syndrome. Neonatal complications include intra uterine growth retardation maturity and death. [4] In obstetrics, nowadays major challenge is the early detection of high risk patient in order to reduce the prevalence of disease. [5] Exact mechanism of preeclampsia is still not understood[6]. It is proposed that in preeclampsia there is impaired invasion of trophoblasts causing spiral artery atherosis leading to multi-organ dysfunction due to local and systemic immunological processes, endothelial cell damage and platelet activation. [7] Platelet activation can be demonstrated by raised levels of 3-thromboglobulin p-selectin (CD62) and Scd40l, increased platelet volume and turnover[8]. Platelets are important in normal homeostasis and mean platelet volume (MPV) indicate their function.[9] As their size gets bigger, more dense granules are present in them increasing their potency. Raised mean platelet volume is documented in Diabetes Mellitus (DM), congestive cardiac failure and in acute and chronic inflammation[10,11] but there is conflicting evidence that MPV is raised in preeclampsia[12].

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[13-16]. The mean valuesof APTT and FDPs are higher in preeclamptic patient but the mean values of prothrombin time and fibrinogen level have no significant difference[15].

Purpose of this study was to find out any significant difference in platelet count, platelet indices and coagulation profile in normal pregnancy and preeclampsia. If such a difference appears in the study, it may be used to develop additional diagnostic criteria for preeclampsia. As these investigations are widely available in Pakistan, they could

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actually increase early detection of preeclampsia and prevention of complication. In Pakistan most of population lives in rural areas with no proper medical facilities and secondly73.6% of population is below poverty line when 2 dollar criteria[17] is used who cannot afford expensive investigation.

MATERIAL AND METHODS

Study design: Comparative cross sectional study.
Sampling technique: Non-probability purposive sampling
Inclusion criteria: All pregnant women more than 20th week of gestation and pregnant female blood pressure of > 140/90mmhg on two different occasions more than 4 hours apart with more than 300 mg of protein in 24 hour urine collection who are already diagnosed.
Exclusion criteria: Patient's having any red blood cell or platelet disorder or any other hematological disorder was identified by complete blood count and subsequent peripheral blood film if needed.

1. Patients having hypertension due to other causes (Secondary hypertension) on history.
2. Patients having renal failure or any malignancy identified by history and other investigations if needed
3. Patients having other causes of thrombocytopenia identified by history and other investigations if required.
4. Patients on anti-platelet drugs identified by history.

RESULTS

Table 1: Comparison of platelet count (× 10^9) in both study groups

	Study groups	n	Mean	S.D	p-value
platelet count(× 10^9/L)	Preeclampsia	42	219.43	100.58	0.68
	Normal Pregnancy	42	254.43	70.35	

Table-2: Comparison of thrombocytopenia with study groups

platelet count(× $10^{9)/L}$	Preeclampsia	Normal pregnancy	Total
Decreased	12 (28.6%)	1 (2.4%)	13(15.5%)
Normal Range	30 (71.4%)	41 (97.6%)	71(84.5%)
Total	42 (100%)	42 (100%)	84 (100%)

Chi-square = 11.01 p-Value=0.001

Table-3: Comparison of Mean Platelet volume (fl) in both study groups

MPV (fl)	Study groups	N	Mean	S.D	p-Value
	Preeclampsia	42	9.78	0.96	0.082
	Normal pregnancy	42	9.34	1.30	

Table-4: Comparison of Mean Platelet volume (fl) with study groups

MPV (fl)	Preeclampsia	Normal pregnancy	Total
Increased	0 (0%)	1 (2.4%)	1 (1.2%)
Decreased	42 (100%)	41(97.6%)	71 (98%)
Total	42(100%)	42 (100%)	84 (100%)

Chi-square= 1.01 p-Value=0.314

Table-5: Comparison of mean platelet distribution width (fl) in both study groups

	Study groups	n	Mean	S.D	p-Value
PDW (fl)	Preeclampsia	42	12.43	3.45	0.173
	Normal Pregnancy	42	11.98	4.98	

Table-6: Comparison of mean platelet distribution width (fl) with study groups

PDW (fl)	Preeclampsia	Normal pregnancy	Total
Increased	3 (7.1%)	3 (7.1%)	6 (7.1%)
Decreased	39 (92.9%)	39 (92.9%)	78 (92.9%)
Total	42 (100%)	42 (100%)	84 (100%)

Chi-square= Not applicable p-value= not applicable

Table-7: Comparison of Prothrombin Time (PT) in both study groups

Prothrombin Time (PT) sec	Study groups	N	Mean	S.D	p-value
	Preeclampsia	42	14.52	3.16	0.10
	Normal pregnancy	42	13.60	1.75	

Table-8: Comparison of Prothrombin Time (PT) with study groups

PT (sec)	Preeclampsia	Normal Pregnancy	Total
Increased	5 (11.9%)	1 (2.4%)	6 (7.1%)
Normal Range	37 (88.1)	41 (97.6%)	78 (92.9%)
Total	42 (100%)	42 (100%)	84(100%)

Chi-square= 2.87 p-value= 0.090

Table-9: Comparison of activated partial thromboplastin time (APTT) in both study groups

	Study groups	N	Mean	S.D	p-value
APTT (sec)	Preeclampsia	42	38.67	18.52	0.325
	Normal pregnancy	42	35.31	11.88	

Table-10: Comparison of Activated partial thromboplastin time (APTT) with study groups

APTT (sec)	Preeclampsia	Normal pregnancy	Total
Increased	8 (19%)	1 (2.4%)	9 (10.7%)
Normal Range	34 (81%)	41 (97.6%)	75(89.3%)
Total	42 (100%)	42 (100%)	84 (100%)

Chi-square= 6.098 p-value= 0.014

Table-11: Comparison of fibrinogen levels in both study groups

	Study groups	N	Mean	S.D	P value
Fibrinogen level (mg/dl)	Preeclampsia	42	247.79	92.10	0.402
	Normal pregnancy	42	261.93	57.89	

Table-12: Comparison of decreased fibrinogen level with study groups

Fibrinogen (mg/dl)	Preeclampsia	Normal pregnancy	Total
Decreased	5 (11.9%)	1 (2.4%)	6 (7.1%)
Increased	37 (88.1%)	41 (97.6%)	78(92.9%)
Total	42 (100%)	42 (100%)	84(100%)

Chi-square= 2.87 p-value= 0.090

Table-13: Comparison of FDP in both study groups

FDP (mg/dl)	Study groups		Total
	Preeclampsia	Normal pregnancy	
<10	35(83.3%)	42(100.0%)	77(91.7%)
>10	716.7%	0%	78.3%
Total	42(100%)	42(100%)	84(100%)

Chi-square test= 7.63 p-value= 0.006

Table-14: Comparison of D-Dimers in both study groups

D-Dimers (mg/dl)	Study groups		Total
	Preeclampsia	Normal pregnancy	
< 0.5	35	42	77
	83.3%	100.0%	91.7%
≥ 0.5	7	0	7
	16.7%	0%	8.3%
Total	42	42	84
	100.0%	100.0%	100.0%

Chi-square= 7.63 p-value= 0.006

DISCUSSION

Among the leading cause of maternal mortality, pre-eclampsia and eclampsia are at the top. However, no data is available on their occurrence at national level. Discharge survey from one public sector hospital during 1979 to 1986 reports that 26 per 1000 births were complicated by eclampsia. Over the study period, frequency of mild pre-eclampsia stood constant while of severe pre-eclampsia raised sharply and that of eclampsia was reduced by 36%. This study showed that the strongest risk factor for

development of both pre-eclampsia and eclampsia is age of mother <20 years and> 40 years[18].

When there is increase in blood pressure for the first time after 20 weeks pregnancy and returns to normal after delivery is termed as pregnancy induced hypertension (PIH). During pre-eclampsia and eclampsia, multiple hematological changes occur in the body of which thrombocytopenia is the most common. Prothrombin time (PT) and activated partial thromboplastin time (APTT) tens to increase. Hematological changes due to pre-eclampsia and eclampsia tends to effect 6-8% of all pregnancies. Primigravida with age less than 20 years are more affected. During pregnancy the mother undergoes various anatomical and physiological changes which not only occur in the genital system but all the organ system of the body in order to adopt for the increased nutritional demands of the growing fetus [19].

Hypertension is the most common condition requiring medical attention during pregnancy and is the leading cause at morbidity and mortality of child and mother. It accounts for about quarter of all hospital admission in the antenatal period and complicates approximately 15% of all pregnancies. Pre-eclampsia is the leading cause of maternal mortality in pregnancy induce hypertension [20]. Due to high risk associated with this condition we compared platelet count, platelet volume indices (MPV and PDW), prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen level, fibrin degradation products (FDP's) and D-Dimer level in normal pregnancy and pre-eclampsia to study the hematological changes with this condition.

In our study, the mean age of patients with preeclampsia was 26.19 + 5.02 years and with normal pregnancy was 25.17± 5.68 years. The mean age of two groups was statistically same (p-value= 0.384). The mean weight of patients with preeclampsia was 67.55± 5.59 kg and with normal pregnancy was 65.00± 7.48 kg. The mean height of patients with preeclampsia was 1.55± 0.04 m and with normal pregnancy was 1.54± 0.04m. The mean BMI of patients with preeclampsia was 28.23± 2.46 and with normal pregnancy was 27.42± 3.29. The mean weight, height and BMI were all statistically same in both study groups (p-values = 0.081, 0.38 and 0.204 respectively.

In a study conducted by lie Han et. Al, platelet indices and blood coagulation parameters were studied to predict the onset and severity of preeclampsia. 173 pregnant females were enrolled in this retrospective case control study. The study participants were divided into 3 groups. Group 1 include 53 female with mild preeclampsia. Group II contains 41 patients with severe preeclampsia and group III contains 79 normal pregnant females. This study showed no statistical difference in age and body mass index (BMI) in all the three groups which was similar to our results. The mean age in normal pregnancy was 2.67± 2.3 years in mild preeclampsia was 27.2± 1.9 years and in severe preeclampsia was 27.5± 1.6 years. The mean BMI in normal pregnancy group was 23.4± 1.2, in mild preeclampsia was 23.8± 0.8 and in severe preeclampsia was 22.3± 0.9[21].

Further in this study, it was observed that PT and APTT were shortened in late pregnancy as compared to early pregnancy. PT decreases from 9.9 ± 0.5 sec in early pregnancy to 9.6 ± 0.5 sec in late pregnancy while APTT was reduced from 29.0±2.5 sec in early pregnancy to 27.7±2.4 sec in late pregnancy (p-<0.05). However, no difference was observed in fibrinogen level and thrombin time with the progression of gestational stage (p > 0.05). Platelet count is significantly reduced in third trimester, from 185.7±47.2 × 10^9/ L in first trimester to 164.9±51.1 × 10^9/ L in third trimester (p< 0.05) but the mean platelet volume (MPV) is increased from 9.5±1.1 fl in early pregnancy to 10.4±1.4fl in late pregnancy (p<0.05). No significant variation was found in mean platelet distribution width (PDW) in early and late pregnancy (p>0.05). This study found that in normal pregnancy the coagulation parameters like PT, APTT and TT decrease significantly in late pregnancy, whereas fibrinogen level increases in late pregnancy[21].

We also measured all these parameters and found descriptively notable, however, not statically significant difference. The mean platelet counts was 219.43+ 100.58 x 10^9 /L in women with pre-eclampsia and 254.43+70.35 x 10^9 /L in women with normal pregnancy. The mean platelet volume was 9.78 + 0.96 fl in patients with pre-eclampsia and 9.34 + 1.30 fl in women having normal pregnancy. The mean platelet distribution width (PDW) was 12.43+3.45 fl in patients with pre-eclampsia and 11.98+4.98 fl women having normal pregnancy. The mean prothrombin time (PT) was 14.52+3.16 sec in patients with pre-eclampsia and 13.60+1.75 sec in women having normal pregnancy. The mean activated partial thromboplastic time (APTT) was 38.67+18.52 sec in patients with pre-eclampsia and 35.31 + 11.88 sec in women having normal pregnancy.

Another study that compared the hematological parameters among patients with healthy pregnancy as control vs patient with pregnancy induced hypertension and found statistically significant differences among the two study groups in terms of hemoglobin, total leucocyte, count (TLC), platelet count, serum globulin, PT and APTT. This study correlated the severity of pre-eclampsia with platelet count, Pt and APTT. [19]

Haliloglu, et. Al, prospectively investigated sixty-eight pregnant females to study the relationship between serum homocysteine level and changes in hemostatic system in pregnancy & post-partum period. They analyzed hemoglobin level, total leukocyte count (TLC), platelet count, prothrombin time (PT), activated partial thromboplastic time (APTT), fibrinogen level, D-Dimers, vitamin B-12, folate level, homocystine level in pregnancy and post-partum period. Negative correlation was found between serum-homocystine level and D-Dimer level, (r= -0.57, P<0.0001). In the third trimester, D-Dimer level was highest (1046.62 + 322.01 mg / ml) while homocystine level was lowest (9.45 + 1.23 mmol/L). Whereas in the fourth week postpartum, D-Dimer level returned to normal (238.27 + 198.59 ng / ml). They concluded that this inverse proportion between D-Dimer and homocystine level may be part of compensatory mechanism to establish hemostatic balance during pregnancy [22].

We also observed in our study that among women with pre-eclampsia, D-Dimer of 35 (83.3%) women was <0.5 and of 7 (16.7%) was > 0.5, whereas, among women with normal pregnancy group, 42(100%) has D-Dimer of <0.5. The mean fibrinogen level was 247.79 + 92.10 in

patients with pre-eclampsia and 261.93 + 57.89 in women having normal pregnancy.

Among women with pre-eclampsia, the FDP of 35 (83.3%) women was < 10 and 7(16.7%) was > 10, whereas, among women with normal pregnancy group (42(100%) had FDP<10.

In a study conducted by Sartori M T et.al, fibrinolytic parameters and inhibin-A along with routine clinical test were performed in normal pregnant females and patients of pregnancy induce hypertension and pre-eclampsia. Results of this study were very close to ours. This study divided participants into three groups. Group I contains 68 females with normal pregnancy, Group II contains 21 females with pregnancy induced hypertension and Group III contains 35 females with pre-eclampsia. There was no statically significant difference between the three groups in terms of mean age, ethnicity, parity or cardiovascular risk factors [23].

Mean BMI in patients of pregnancy induced hypertension was higher that the females with normal pregnancy of pre-eclampsia. However the other clotting tests, patient with pre-eclampsia showed no statistically significant difference. All these results are compatible with our study.

CONCULSION

The early diagnosis of pre-eclampsia remains to be a critical problem that may not only cause complications during pregnancy but also plays role in maternal and fetal outcome. Current study shows that the hematology parameters such as platelet count, PT, APTT, fibrinogen level, FDPs and D-Dimer were notably differing except MPV and PDW in women with pre-eclampsia compared to normal pregnancy but were not statistically significant, it was may be due to the severity of our cases, we could achieve significant result if we take severe pre-eclampsia. Further work is thus suggested including more parameters and possibilities.

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