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Original Research Article

Pre-eclampsia and platelet indices: a cross sectional study

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ABSTRACT

Background: Pre-eclampsia is a complex disease process originating at the maternal- fetal interface that affects multiple organ systems. The exact pathophysiology of preeclampsia is not known but it is considered to be associated with endothelial cell dysfunction, increased inflammatory responses and hypercoagulability. The receptors located on platelets are activated in pre-eclampsia by several proteases plus the vasoconstriction associated with preeclampsia leads to platelet activation which can be evaluated by platelet indices like platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and palteletcrit (PCT). The objective of this study was to compare the platelet count and platelet indices- MPV, PDW, and PCT in patients with pre-eclampsia and normotensive pregnant women.
Methods: A cross sectional study which included a total of 204 patients divided into two groups (102 pre-eclampsia and 102 control. The patients were compared for platelet count and platelet indices like MPV, PDW and PCT.
Results: The platelet count (PC) was decreased in pre-eclampsia group as compared to control group with statistically significant difference in means between the two groups ($p<0.05$). The MPV and PDW also showed significant difference between the two groups ($p<0.05$) with preeclampsia group having increased MPV and PDW values. The PCT value was lower in pre-eclampsia group as compared to control group but it did not reach statistically significant level.
Conclusions: In pre-eclampsia patients while as MPV and PDW showed increased value as compared to control group and the difference between the two had statistical significance, platelet count was lower in them and had statistical significance when compared to control group. Therefore these platelet indices and platelet count can be used to predict and prevent complications arising from preeclampsia.

Keywords: Mean platelet volume, Platelet distribution width, Plalteletcrit

INTRODUCTION

Pre-eclampsia (PE) typically affects 2-5% of pregnant women and is one of the primary causes of maternal and perinatal morbidity and mortality, especially when the condition is of early onset.[1,2] In the past half century, the incidence of pre-eclampsia and maternal mortality has reduced significantly in developed countries. However, in developing countries, the incidence rates of pre-eclampsia and maternal mortality are still very high.[3]

Hypertension is at the center of the syndrome and is often, but not always, accompanied by proteinuria. Severe forms of pre-eclampsia can be complicated by renal, cardiac, pulmonary, hepatic, and neurological dysfunction; hematologic disturbances; fetal growth restriction;

stillbirth; and maternal death.[4,5] Pre-eclampsia (PE) is a multi-system disorder of human pregnancy, whose etiology remains poorly understood.[6]

The predisposition to endothelial dysfunction is thought to play a crucial part. This may cause abnormal activation of the haemostatic and/or inflammatory systems. Indeed, maternal endothelial cell disorder can explain many of the clinical aspects associated with PE. For example, hypertension is probably due to endothelial disruption or uncontrolled vascular tone, fluid retention is a consequence of increased endothelial permeability, and clotting dysfunction results from increased blood borne pro-coagulant-microparticles.[7,8] Activation of blood coagulation produces proteases that not only interact with coagulation protein but also with specific cell receptors involved in inflammatory responses.

Binding of coagulation proteases (such as thrombin and/or tissue factor) or anticoagulant proteins (e. g., APC) to protease activated receptors (PARs) may affect cytokine production or inflammatory cell apoptosis.[9,10] These receptors are localised on the vasculature on endothelial cells, mononuclear cells, platelets, fibroblasts and smooth muscle cells.[11] In addition, superoxide produced due to pro-inflammatory effects in pre-eclampsia causes vasoconstriction, either directly through contracting smooth muscle or indirectly by inactivating nitric oxide and reducing the release of prostacyclin .Vasoconstriction is associated with slow blood flux and platelet activation.[12,13]

Several indices are used to measure platelet activation and function these include platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT). These indices can be followed and used to predict pre-eclampsia as they are readily available.[14] The current study was a step in this regard to establish role of platelet indices in predicting pre-eclampsia.

METHODS

Study population

A cross sectional study of 204 patients was conducted at the LD hospital (obstetrics and gynaecology section)- a tertiary care hospital associated with GMC Srinagar from January 2022 to June 2022.

After relevant history and consent the subjects were included in the study. Blood samples were taken under aseptic conditions and evaluated for platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT).

The following formula was used to calculate the sample size.

$$N = \frac{Z^2 P(1-P)}{d^2}$$

where N is the sample size, Z is the statistic corresponding to level of confidence (95%), p is the prevalence of pre-eclampsia and d is the precision.

Inclusion criteria

Pregnant female patients of >20 years of age with singleton normal pregnancy with normal blood pressure who consented for were grouped as control group (n=102), while as the pre-eclampsia consisted of female pregnant patients >20 years of age with features suggestive of pre-eclampsia (n=102).

The subjects were classified as pre-eclampsia if they had de novo hypertension of ≥140/90 mmHg after 20 weeks gestation accompanied by proteinuria and/or evidence of maternal acute kidney injury, liver dysfunction, neurological or cerebral features like headache, visual disturbances, haemolysis or thrombocytopenia, and/or fetal growth restriction.

Exclusion criteria

Exclusion criteria consisted of multiple pregnancy, chronic hypertension, diabetes mellitus, women with cardiovascular diseases, chronic liver disease, patients taking steroids or diuretics, gestational trophoblastic diseases. Chronic inflammatory diseases like SLE, rheumatoid arthritis, ITP etc.

Statistical analysis

Data was compiled in MS Office Excel and analyzed with SPSS 26 software. Continuous data were presented by minimum, maximum, arithmetic mean and standard deviation. Comparison of means of clinical characteristics between groups was performed by independent sample t-test. Results with p value of <0.05 were considered statistically significant.

RESULTS

A total of 204 patients divided among pre-eclampsia (P) (N=102) group and equal number of women with normotensive pregnancy were taken as control group (C) (n=102). The mean age (M) of pre-eclampsia group was 29.27 years with standard deviation (SD) of 3.45 with most in the 26-30 years age group (65%) (Figure 1) while as that of control group was 29.01 with SD of 3.37. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) in pre-eclampsia group was 160.62 mmHg (SD=15.74) and 100.67 mmHg (SD of 10.27) respectively (Figure 3) while as in control group SBP was 120.62 mmHg (SD=11.13) and DBP 74.78 mmHg (SD=6.21). Mean parity of pre-eclampsia group was 2.63 (SD=1.59) while that of control group was 2.24 (SD=1.09).

The mean gestational age of pre-eclampsia group was 34.02 weeks (SD=3.49) (Figure 2) with most in the 33-36

weeks duration of gestational age, while that of control group was 34.66 (SD=3.61) weeks.

Most of the patients in pre-eclampsia group had systolic blood pressure (SBP) >140-150 mmHg range (40%) while about 20% patients had >170 mmHg among them 3 patients had systolic blood pressure >190 mmHg.

An independent samples t-test was conducted to compare the platelet count, MPV, PDW and PCT of pre-eclampsia and control group. There was statistically significant difference in the platelet count in pre-eclampsia group (M=174.12, SD=56.59) and control group (M=200.93, SD=88.76); t (202)=-2.57, p=0.011 (Table 2 and 3).

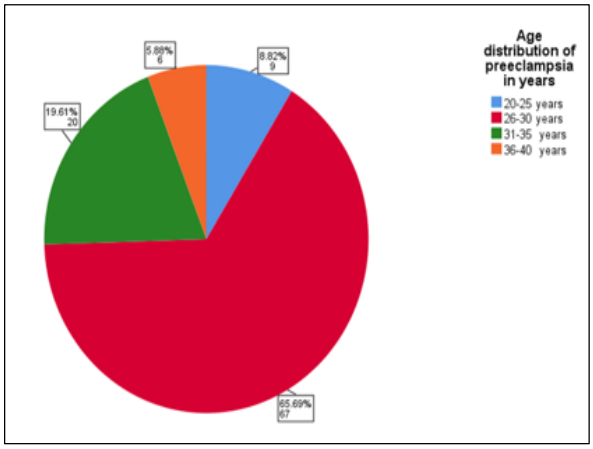

Figure 1: Age distribution of pre-eclampsia patients.

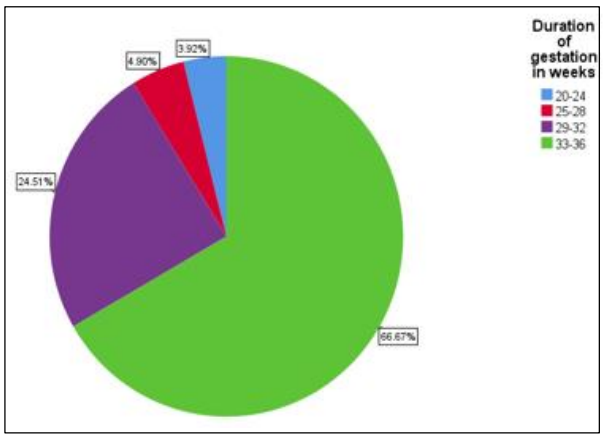

Figure 2: Duration of gestation in weeks of pre-eclampsia patients enrolled in the study.

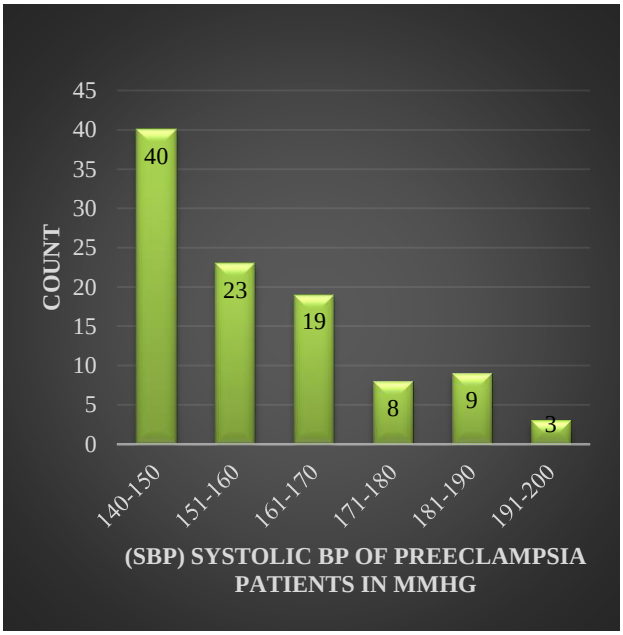

Figure 3: Systolic blood pressure in (mmHg) of patients in the preeclampsia group.

The platelet count was on lower side in pre-eclampsia as compared to control group (174.12×103/µl) vs (200.93×103/µl) respectively. There was statistically significant difference when independent samples t-test was used to compare the mean platelet volume (MPV in fl) in pre-eclampsia group (M=11.01, SD=0.85) and control group (M=10.64, SD=1.17); t (202)=2.58, p=0.011 (Table 4 and 5).

The MPV was elevated in case of pre-eclampsia group when compared to control normotensive group (11.01 fl vs 10.64 fl).

There was also statistically significant difference when independent samples t-test was used to compare the platelet distribution width (PDW) in pre-eclampsia group (M=15.80%, SD=2.50) and control group (M=15.03%, SD=2.93); t (202)=2.030, p=0.044 (<0.05) (Table 6 and 7).

The PDW was higher in case of pre-eclampsia group as compared to normotensive control group. There was no statistically significant difference when independent samples t-test was used to compare the PCT in pre-eclampsia group (M=0.21, SD=0.12) and control group (M=0.22, SD=0.11).

Table 1: Demographic and clinical characteristics of pre-eclampsia (n=102) and control (n=102) group.

Variables	N	Minimum	Maximum	Mean	SD
Age of control group (C)	102	21	38	29.01	3.37
Age of pre-eclampsia (P)	102	20	40	29.27	3.45
SBP control (C)	102	100.00	168.00	120.30	11.13
DBP control (C)	102	60.00	89.00	74.78	6.21
SBP preeclampsia (P)	102	140	200	160.62	15.74
DBP pre-eclampsia (P)	102	85	130	100.67	10.27

Continued.

Variables	N	Minimum	Maximum	Mean	SD
Parity of control (C)	102	1	6	2.24	1.09
Parity of pre-eclampsia(P)	102	1	9	2.63	1.59
Gestational age of C in weeks	102	20.00	36.00	34.66	3.61
Gestational age of P in weeks	102	20	36	34.02	3.49

Note: P-Pre-eclampsia; C- control; SBP=systolic blood pressure, DBP=diastolic blood pressure.

Table 2: Mean and standard deviation of platelet count of preeclampsia and control group.

	Groups	N	Mean	SD	Standard error mean
Platelet count ($\times10^3$/µl)	**Pre-eclampsia**	102	174.12	56.59	5.60
	Control	102	200.93	88.76	8.78

Table 3: Independent samples test for platelet count of preeclampsia and control group.

Variables		Levene's test for equality of variances		t-test for equality of means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% CI of the difference	
									Lower	Upper
Platelet count ($\times10^3$/µl)	Equal variances assumed	14.447	0.00	-2.572	202	0.011*	-26.80	10.42	-47.35	-6.25
	Equal variances not assumed			-2.572	171.47	0.011*	-26.80	10.42	-47.37	-6.22

Note: *-P=0.011.

Table 4: Mean and standard deviation of mean platelet volume of preeclampsia and control group.

	Groups	N	Mean	SD	Standard error mean
MPV (fl)	**Pre-eclampsia**	102	11.01	0.85	0.084
	Control	102	10.64	1.17	0.117

Table 5: Independent samples test for MPV of pre-eclampsia and control group.

Variables		Levene's test for equality of variances		t-test for equality of means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% CI of the difference	
									Lower	Upper
MPV	Equal variances assumed	9.617	0.002	2.580	202	0.011*	0.372	0.144	0.088	0.656
	Equal variances not assumed			2.580	183.92	0.011*	0.372	0.144	0.087	0.656

Note: *-P=0.011.

Table 6: Mean and standard deviation of PDW of pre-eclampsia and control group.

	Groups	N	Mean	SD	Standard error mean
PDW (%)	**Pre-eclampsia**	102	15.80	2.50	0.248
	Control	102	15.03	2.93	0.291

Table 7: Independent samples test for PDW of pre-eclampsia and control group.

Variables		Levene's test for equality of variances		t-test for equality of means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% CI of the difference	
									Lower	Upper
PDW	Equal variances assumed	3.397	0.067	2.030	202	0.044*	0.775	0.382	0.022	1.529
	Equal variances not assumed			2.030	196.942	0.044*	0.775	0.382	0.022	1.529

Note: *-P=0.044.

Table 8: Mean and standard deviation of PCT of pre-eclampsia and control group.

	Groups	N	Mean	SD	Standard error mean
PCT (%)	**Pre-eclampsia**	102	0.21	0.12	0.012
	Control	102	0.22	0.11	0.011

Table 9: Independent samples test for PCT of pre-eclampsia and control group.

Variables		Levene's test for equality of variances		t-test for equality of means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean difference	Standard error difference	95% CI of the difference	
									Lower	Upper
PCT	Equal variances assumed	0.273	0.602	-0.596	202	0.552	-0.010	0.016	-0.042	0.022
	Equal variances not assumed			-0.596	200.858	0.552	-0.010	0.016	-0.042	0.022

Note: *-P=0.044.

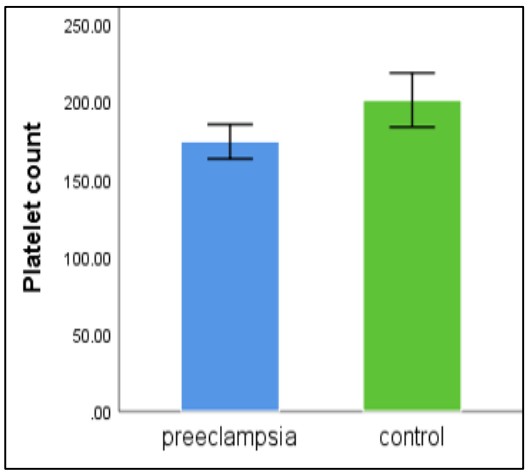

Figure 4: Box and Whisker plot for platelet count (×10³/µl) of pre-eclampsia and control group.

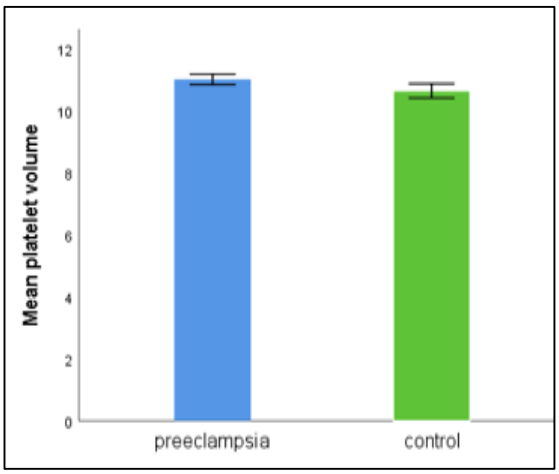

Figure 5: Box and Whisker plot for MPV (fl) of pre-eclampsia and control group.

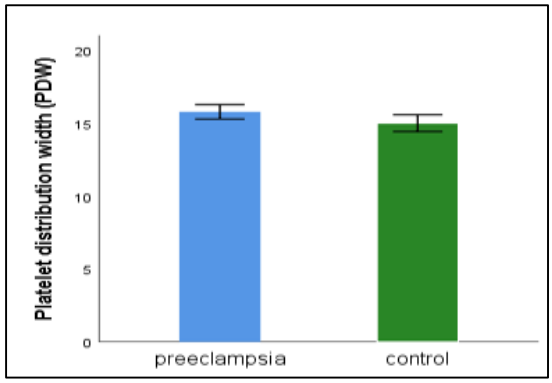

Figure 6: Box and Whisker plot for PDW (%) of pre-eclampsia and control group.

DISCUSSION

Pre-eclampsia (PE) is a multi-system disorder of human pregnancy, whose etiology remains poorly understood.[6] It is characterized by abnormal vascular response to placentation that is associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of the coagulation system and endothelial cell dysfunction.[15] Activation of blood coagulation produces proteases that interact with several cells involved in inflammatory response including platelets.[11] In addition vasoconstriction produced due to pro inflammatory response leads to platelet activation.[12] The current study was done to study the platelet count, MPV, PDW and PCT in pre-eclampsia.

In our study maximum number of patients with pre-eclampsia were having gestational age between 33-36 weeks and was in agreement with previous study by Lisonkova et al where rates of early-onset and late-onset disease were 0.3% and 2.7%, respectively.[16]

According to the pathophysiology of pre-eclampsia, endothelial activation leads to increased platelet aggregation which in turn is responsible for decrease in the platelet count. In the present study, there is a statistically significant difference in means of platelet count among pre-eclampsia and normotensive control group (M=174.12, SD=56.59) vs control group (M=200.93, SD=88.76) with lesser platelet count seen in preeclamptics; (Table 2 and 3). Similar results were observed by Dogan et al and Freitas et al.[17,18] In our study the mean MPV value showed statistically significant increase in pre-eclampsia patients as compared to control. The results were in agreement with other studies by Dogan et al and Freitas et al.[17,18]

The comparison of PDW value in pre-eclampsia group showed significant increase as compared to control with $p<0.05$ which were similar to conclusions drawn by studies of Freitas et al.[18] Karateke et al and Yang et al.[19,20] The increased PDW can be explained by increased platelet turnover which supports the idea that platelet survival time is reduced resulting in increased destruction of platelets.

The PCT in our study showed a mild reduction in pre-eclampsia however the difference in pre-eclampsia and controls did not achieve statistically significant levels with $p>0.05$.

Hence in our study platelet indices of platelet count, MPV and PDW can be used for prediction of pre-eclampsia, though PCT showed mild decrease in pre-eclampsia women but it did not reach statistical significance. These indices are simple laboratory parameters and easy to check and follow in antenatal period to prevent grave complications arising from pre-eclampsia.

Limitation of the study was the sample size was small, further studies with larger sample size will be beneficial in establishing the role of these economical and easily available hematological indices to add weight to or negate the results derived from this study.

CONCLUSION

The current study lends credence to study easily available platelet indices of PC, MPV and PDW in risk evaluation of pre-eclampsia, however further prospective studies with increased number of patients.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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