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Role of Mean Platelet Volume in Prediction of Preeclampsia

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ABSTRACT

Background: preeclampsia (PE) is a pregnancy-specific multisystem disorder that is characterized by development of hypertension and proteinuria with or without body edema after twenty weeks of gestation, resolving by 6-12 weeks postpartum in previous normotensive women.

Objectives: comparing complete blood count (CBC) parameters especially Mean platelet volume (MPV), in pre-eclamptic and normal pregnant women in the third trimester of pregnancy and to evaluate whether this parameter have a prognostic significance in determining the severity of preeclampsia.

Methods: The study was conducted at alhussein university hospital. It included 150 pregnant women. They were assigned to 2 groups: 1st group: 34 pregnant women with preeclampsia, and 2nd group: 116 normal pregnant women free of any medical disorders

Results: The current study showed no statistically significant difference between PE compred to normal pregnancy (with p-value >0.05 NS).

Conclusions: we have found that MPV values do not have any determining effect on the presence of preeclampsia.

Recommendation: The results of this study recommend that MPV has no prognostic significance in determining preeclampsia, although large-scale clinical studies and longitudinal study of platelet size changes through gestations are still awaited and fixing methods and methods used for automated blood count.

Keywords: Preeclampsia, Mean Platelet Volume.

INTRODUCTION

Preeclampsia is a pregnancy-specific multisystem disorder that is characterized by development of hypertension and proteinuria with or without body edema after twenty weeks of gestation, resolving by 6-12 weeks postpartum in previous normotensive women [(1)].

It occurs in about 5% to 10% of all pregnancies and resulting substantial maternal and fetal morbidity and mortality [(2)].

Many organs may be affected as, liver, kidney, placenta, brain, hematopoietic, and coagulation system [(3)].

Frequency and severity of preeclampsia increased in women with chronic hypertension. The overlap of signs makes it more difficult to diagnose preeclampsia among women with chronic hypertension; one should maintain a high index of suspicion, and over diagnosis is preferable and unavoidable [(4)].

A good diagnostic test for preeclampsia would be especially useful in this setting. Conditions that make the diagnosis of preeclampsia superimposed upon chronic hypertension highly likely are as follows: New-onset proteinuria (0.3 g of protein in a 24-hour urine collection) after 20 weeks' gestation. Any of the following in a woman with hypertension and protienuria before 20 weeks' gestation: Sudden increase in proteinuria. Sudden increase in blood pressure in cases in which hypertension was previously well controlled. Thrombocytopenia (platelet count of less than 100,000 cells per cubic millimeter). Increase in alanine aminotransferase (ALT) or aspartate

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aminotransferase (AST) to abnormal levels [5].

The goal of researchers for many decades was safe, reliable, and cost-effective screening tests for prediction of preeclampsia, aiming to improve maternal and fetal outcome, despite the fact that the only effective treatment is delivery because pathologic changes caused by preeclampsia are reversible once pregnancy has ended [6].

Some recent studies show a predictive effect of increased mean platelet volume (MPV) in pregnant patients who have gestational hypertension and they developed preeclampsia later on in the third trimester of pregnancy. Mean platelet volume is measurement of the mean volume of the platelets present in blood typically included in blood tests. Since the average platelet volume is larger when body is producing increased number of platelets, MPV test results can be used to make inferences about platelets production in bone marrow. Abnormally high MPV values associated with thrombocytopenia [7].

In preeclampsia there is a decrease in the platelet count, a decreased life span, and increased MPV [8].

Conflicting results have been published regarding platelet number and volume changes during normal pregnancy and preeclampsia. Some researchers found no difference in platelets count and MPV values between preeclamptics and controls [9], whereas others demonstrated lower platelet count and higher MPV in preeclamptics, referring these changes to increased platelets consumption in preeclampsia [10].

The major reason for the discrepancy between these results may be the method of measurement of MPV [11].

In addition, it is known that different systems used in measurement of MPV can yield different results up to 40%. This can explain the differences between studies but results still remain solid since all the measurements were done with the same anticoagulant and with the same system [9].

AIM OF THE WORK

This study aims to assessment Mean platelet volume (MPV), in pregnant women in the third trimester of pregnancy and to evaluate whether this parameter have a prognostic significance in determining preeclampsia.

PATIENTS AND METHODS

Study design:

A prospective cohort study was performed.

Participation:

150 pregnant women in their third trimester (≥ 28 weeks gestation) were selected to participate in the study, they were assigned to 2 groups: ***1st group:*** 34 pregnant women with preeclampsia, ***2nd group:*** 116 normal pregnant women free of any medical disorders.

Detailed history and clinical assessment including blood pressure and laboratory assessment including CBC, liver enzymes and urinary protein (Dip stick) were done.

This study was done at Al Hussein University Hospital at December 2017 to February 2018. **The study was approved by the Ethics Board of Al-Azhar University.**

Selection criteria:

Inclusion criteria: Age between 18-45 years old, Primigravida or multipara, Gestational age (28 – 40) weeks' gestation, Single viable intrauterine pregnancies.

Exclusion criteria: Women with preeclampsia or gestational hypertension at 28weeks gestation. Multifetal pregnancy, Women with other medical disorders, congenital fetal malformation, Meconium stained liquor, Rhesus isoimmunization (Coombs positive), Smoking, Other causes of thrombocytopenia as ITP – TTP – HUS – SLE.

Method protocol:

All pregnant women who met inclusion criteria were subjected to: History taking, general, abdominal and gynecological examinations were performed.

Physical examination: Vital signs: blood pressure, heart rate, temperature, respiratory rate measurement were performed. Systemic examination of heart, lungs, abdomen, lower limbs, and neurological examination were done. Obstetric and gynecological examinations were done.

Determination of gestational age: By using the date of last menstrual period, which is confirmed by ultrasonographic findings.

A complete laboratory investigation for preeclampsia will be done, i.e.: A complete blood picture with platelet count. Liver functions test. Renal function test. Dip stick urine protein collection.

Investigations: Sampling: 3ml of venous blood sample were obtained and put on test tube containing EDTA **(Ethylenediaminetetraacetic acid**) as anticoagulant to perform **CBC** (complete blood count) using automated cell counter (**Light impedence 3-parameters cell counter)**, **Diagon D-cell 60,** (mean platelet volume one of parameters of CBC).

Follow up:

Pregnant women examined at (28+0) weeks gestation, blood pressure measured, lab investigations done and all of them are recorded.

Routine ANC performed blood pressure and lab investigation recorded as weekly till (36+0) weeks then weekly till delivery. Just elevation of blood pressure, presence of albumin in urine, lower limb edema or, alteration in kidney or liver functions was detected, preeclampsia diagnosed.

Outcome:

Women included in this study classified into two groups:

Group (1): 34 women developed P.E.T.

Group (2): 116 women not developed P.E.T.

Reference range of MPV is (7.4-10.4 fl.) ***(12)*.**

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

Independent-samples t-test of significance was used when comparing between two means.

Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.

Pearson's correlation coefficient (r) test was used for correlating data.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

Probability (P-value): P-value <0.05 was considered significant. P-value <0.001 was considered as highly significant. P-value >0.05 was considered insignificant.

RESULTS

Table (1): All parameters descriptive of the all study.

	Total (N=150)
Age (years)	18-45 [28.92±5.67]
GA (wks)	28-40 [38.13±2.29]
Parity	
P0	60 (40.0%)
P1	39 (26.0%)
P2	28 (18.7%)
P3	17 (11.3%)
P4	2 (1.3%)
P5	3 (2.0%)
P7	1 (0.7%)
Systolic	90-150 [139.95±11.73]
Diastolic	60-150 [89.56±9.52]
Alb.	
0	116 (77.3%)
1	10 (6.7%)
2	9 (6.0%)
3	14 (9.3%)
4	1 (0.7%)
Hb	7.5-13.3 [11.16±1.28]
HT	20-46.5 [36.79±4.74]
Platelet count	142-400 [238.10±68.11]
MPV pre	3.5-31 [7.48±4.13]
MPV post	4.6-39 [9.95±5.03]
AST	10-95 [35.06±11.63]
ALT	7-65 [29.21±11.93]
Creatinine	0.5-4 [0.90±0.30]

Data were expressed as mean± standard deviation (SD) and number (%)

Table (2): Comparison between among groups regarding BP.

BP	Groups	Mean	±SD	Min.	Max.	t-test	
						t	p-value
Systolic	Preeclampsia	160.32	13.36	135	150	19.451	<0.001**
	Control	119.58	10.10	90	130		
Diastolic	Preeclampsia	102.13	10.30	90	150	15.020	<0.001**
	Control	76.98	8.73	60	90		

This table shows statistically significant difference between groups regarding BP, using Independent Sample t-test, with p-value <0.001 HS.

Table (3): Comparison between among groups regarding Alb.

Alb	Preeclampsia		Control	
	No.	%	No.	%
0	0	0.0%	116	100.00
1	10	29.4%	0	0.00
2	9	26.5%	0	0.00
3	14	41.2%	0	0.00
4	1	2.9%	0	0.00
Total	34	100.0%	116	100.00
x2	52.914			
p-value	<0.001**			

This table shows statistically significant difference between groups regarding Alb. using Chi-square test, with p-value <0.001 HS.

Table (4): Comparison between among groups regarding Platelet count.

Groups	Platelet count				t-test	
	Mean	±SD	Min.	Max.	t	p-value
Preeclampsia	221.62	72.86	142.00	348.00	2.668	0.008*
Control	254.57	63.36	150.00	400.00		

This table shows statistically significant difference between groups regarding platelet count, using Independent Sample t-test, with p-value <0.05 S.

Table (5): Comparison between among groups regarding Mean platelet volume.

Groups	MPV				t-test	
	Mean	±SD	Min.	Max.	t	p-value
Pre						
Preeclampsia	5.95	3.29	3.5	18	3.816	0.016*
Control	9.01	4.96	5.8	31		
Post						
Preeclampsia	9.70	4.01	4.6	23.0	1.974	0.324
Control	10.19	6.05	7.1	39.0		

This table shows statistically significant difference between groups regarding pre MPV, using Independent Sample t-test, with p-value <0.05 S.

DISCUSSION

Preeclampsia (PE) develops in 4–5% of human pregnancies. It is characterized by an elevated blood pressure and proteinuria and develops after 20 weeks of gestational age. It is the main cause of maternal and perinatal morbidity and mortality, low birth weight and intrauterine growth restriction [(13)].

Studies have shown that markers of endothelial activation or platelet aggregation have an active role in preeclampsia [(14)].

Evidence of increased platelet activation in vivo in normal pregnancies compared to healthy non-pregnant women has been published earlier. Since preeclampsia is primarily characterized by endothelial damage, uncontrolled intravascular platelet activation and enhanced platelet consumption are expected outcomes of this condition [(15)].

In this study, cases were selected ranging from 28 to 40 weeks gestation. The mean age of cases studied for preeclampsia and control were (30.44±6.11), (27.39±5.22) respectively.

Regarding elevated blood pressure (systolic & diastolic), highly significant statistical correlation between preeclampsia group and control has been detected (p-value=<0.001). It agree with ***Poon and Nicolaides*** [(16)] as reported, hypertension was only secondary sign as it was an early indication of the disease.

Albuminuria was involved and highly statistically significant difference was resulted (p-value=<0.001). It agree with ***Airoldi and Weinstein*** [(17)] that discussed preeclampsia was the leading diagnosis must be excluded in all women with albuminuria.

There was significant statistical association among preeclamptic group and control recordedin this study (p-value=0.008).

In current research, MPV was measured in pregnant women at the start of the third trimester and at the time of termination for preeclamptic group, and by comparison, no statistically significant difference between groups (preeclampsia & control) regarding MPV detected, using ANOVA-test, with (p-value >0.05 NS). it

correlates with ***Ceyhan et al.*** [9], in their study was carried out with 56 pre-eclamptic pregnant women [29.54±6.02 years; mean±SD]. For the control group, 43 healthy pregnant women participated in the study (28.65±4.84 years; mean±SD). There was no statistically significant difference according to CBC, platelet count and MPV when pre-eclamptic patients were compared with controls. As a result, no prognostic significance of CBC, platelet count and MPV on the presence of pre-eclamptic condition was observed.

Conflicting results have been published regarding platelet number and volume changes in preeclampsia.

Some researchers ***Makuyana et al.*** [18] found no difference in PLTs count and MPV values between preeclamptics and controls, whereas others [10,19] demonstrated lower PLT count and higher MPV in preeclamptics, referring these changes to increased platelet consumption in preeclampsia.

It should be noted that the major reason for the discrepancy between these studies is probably the method of MPV measurements must be noted. It is known that different anticoagulation substances used in measurement of MPV can yield different results up to 40% [9]. This can explain the differences between studies but the result of our study still remain solid since all measurements were done with the same anticoagulant and same system.

Fay et al. [20] found that there was a decrease in platelet count throughout the normal pregnancy reaching to nadir around 30 weeks and suggested that the decrease was due to plasma dilution and increased consumption. The MPV is increased during pregnancy indicating a younger platelet population.

Redman [21] found that the platelet count decreased in early evolution of preeclampsia, and suggested that it could be predictor of preeclampsia. Beta thromboglobin (BTG) is found in alpha granules of platelets. An increase BTG has been reported to precede the clinical development of preeclampsia by four weeks.

In this study, it shows no statistically significant difference between groups (preeclampsia & control) regarding MPV, using ANOVA-test, with p-value >0.05 NS.

Our study significantly correlates with ***Ceyhan et al.*** [9], in their study was carried out with 56 pre-eclamptic pregnant women [29.54±6.02 years; mean±SD]. For the control group, 43 healthy pregnant women participated in the study (28.65±4.84 years; mean±SD). There was no statistically significant difference according to CBC, platelet count and MPV when pre-eclamptic patients were compared with controls. As a result, we observed no prognostic significance of CBC, platelet count and MPV on the presence of pre-eclamptic condition.

In our case, as far as platelet count is concerned, there are significant differences between healthy pregnant women and pre-eclamptic pregnant women.

Makuyana et al. [18] observed no significant difference in the hematological parameters, haemoglobin, WBC, red blood cell, mean cell volume and platelet count in 38 preeclamptic and 72 normal women. Our study agree with except there was significant difference in platelet count.

Neiger et al. [22] have reported that the platelet counts in 67 pre-eclamptic women were lower when compared with 71 control cases.

Jaremo et al. [10] have declared that pre-eclamptic cases involve lower platelet numbers and higher MPV values. In our study, we haven't observed any difference in MPV values.

Boriboonhirunsarn et al. [23] have suggested that high values in MPV are useful in differentiating severe preeclamptic cases from normal pregnancy. In our study, no differences have been detected in terms of MPV values between pre-eclamptic cases and normal pregnancies taken as the control group

Von Dadelszen et al. [24] have expressed that MPV/ platelet count ratio

reflects platelet consumption and could be used as an indicator of poor maternal progress in preeclamptic cases. Yet, ***Calvert et al.*** [25] have stated that platelet number and MPV are not the determinants of clinical progress in their study involving 336 women. But we found no difference between MPV/platelet rates. The MPV varies with time in EDTA-anticoagulated samples. EDTA-induced platelet shape changes result in a progressive increase in MPV with impedance technology. The effect of EDTA on MPV with optical analysis is less well-documented but appears to be unpredictable, decreasing in many patient samples and increasing in others. It is possible to claim that the differences between all these study results are related to the differences in the use of anticoagulant. Yet, there is another point one should not underestimate. Using EDTA as anticoagulant in general hospital practic for CBC measurements and different technologies, give different results.

CONCLUSION

MPV values do not have any determining effect on the presence of preeclampsia.

RECOMMENDATION

The results of this study recommend that MPV has no prognostic significance in determining the preeclampsia. Although large- scale clinical studies and longitudinal study of platelet size changes through gestations are still awaited and fixing methods and methods used for automated blood count.

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