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ORIGINAL ARTICLE

Serum Arginine Level and Platelet Volume in Prediction of Preeclampsia

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Abstract

Background: ***In the second trimester, approximately ten percent of first-time mothers will experience the very common pregnancy condition known as pre-eclampsia. Serious, potentially harmful effects on both mother and child are associated with the disorder.***

Objective: ***To evaluate the predictive role of serum arginine level and platelet volume in the prediction of preeclampsia.***

Patients and Methods: ***Outpatient gynecology and obstetrics clinics at Al Azhar University Hospitals were the sites of this prospective observational study, which is a type of comparative case-control research. One hundred pregnant women participated in our study. Pregnancies involving pre-eclampsia (n = 50) were included in Group A of the participants. Hypotensive pregnancies (n = 50) made comprised Group B. Six to twelve months was the time frame of the study.***

Results: ***The L-arginine was found to be an excellent predictive test where the area under the curve (AUC) equaled 0.960 ± 0.017 (95% CI, 0.927; 0.992), and the P value was .050 (statistically significant). At a cut-off point of 71 μM, the test was found to have a sensitivity of 94% and a specificity of 86%; a receiver operating characteristic (ROC) analysis was carried out to demonstrate the predictive value of MPV (mean Platelet Volume) & L-arginine.***

Conclusion: ***Pregnancies complicated with pre-eclampsia had higher MPV and lower levels of serum L-arginine. The MPV was found to be a good predictor of PE. L-arginine was found to be an excellent predictor of PE.***

Keywords: Pre-eclampsia; mean Platelet Volume; Serum Arginine

1. Introduction

Pre-eclampsia occurs in the second part of pregnancy and affects approximately ten percent of first-time mothers. Mother and child are both put at risk by the condition's severe effects. Hypertension, proteinuria, premature birth, and growth retardation are symptoms of this condition. While our understanding of the pathophysiology is limited, there is evidence that platelets play a crucial role.[1]

The patient was previously normotensive until 20 weeks pregnant, when she developed hypertension defined as two readings of blood pressure (BP) more than 140 mm Hg or 90 mm Hg, taken at least 4 hours apart. In a woman who was previously normotensive, preeclampsia develops after 20 weeks of pregnancy when hypertension and proteinuria or end-organ failure first appear. Generalized tonic-clonic convulsions in a pregnant woman who has preeclampsia and no other known cause or history of the condition are known as epileptic seizures. Preeclampsia, a complex illness involving several factors and systems, is identified by the observation of elevated blood pressure and the presence of protein in the urine after the 20th week of pregnancy. It is categorized as either moderate or severe based on the existence, absence, and severity of the symptoms or indicators. Preeclampsia, a condition that occurs in 5%–8% of all pregnancies, significantly contributes to higher rates of maternal death and morbidity.[2]

Although the exact mechanisms by which preeclampsia develops remain a mystery, platelets are known to have a significant pathophysiological role in the condition. In pregnancies afflicted with severe preeclampsia (SPE), the platelet count seems to drop; nevertheless, there are contradictory findings about the mean platelet volume (MPV) in earlier studies. Preeclamptic pregnancies have conflicting findings on the MPV; some find it to be greater, and others find it to be much lower.[3]

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In addition, reports indicate that the MPV has little effect on preeclampsia. Because of its pathophysiological function, the MPV may alter in preeclampsia; it may also be associated with preeclampsia severity and the week of gestation. Finding out whether MPV's effect on clinical use differs in instances of isolated SPE was the driving force for this research. This publication aims to assist readers better understand the contradicting findings of past studies.[4]

Lithium arginine is a component of nitric oxide (NO). One of the most efficient agents for dilating blood arteries is endothelial nitric oxide synthase (eNOS), which converts L-arginine to NO in endothelial cells. No controls the adherence of white blood cells and the aggregation of platelets. Preeclampsia symptoms may begin with alterations in the L-arginine-NO signaling pathway.[5]

Preeclampsia risk factors including blood arginine level and platelet volume were the focus of this investigation.

2. Patients and methods

This is a comparative case-control study that is a prospective observational study with 100 women who were chosen from Al Azhar University Hospitals' out-patient obstetrics and gynecology clinics between June 2021 and August 2022. Samples were gathered in a methodical and random manner. All patients provided written informed consent, which was authorized by the local ethics committee. Group (A) [case group] consisted of 50 pregnant women with pre-eclampsia complications, while group (B) [control group] consisted of 50 normal pregnant women. All cases were split into these two groups.

Inclusion criteria: were a singleton pregnancy in women between the ages of 18 and 40, a single healthy fetus, gestational age beyond 20 weeks, and a complex preeclamptic pregnancy.

Exclusion criteria: Premature membrane rupture, polyhydramniosis, diabetes mellitus, anemia, cardiovascular disease, fetal abnormalities, anemia, renal disease, and collagen vascular disease.

Methods

All cases underwent an informed consent process, comprehensive medical history assessment, and determination of gestational age using the last menstrual cycle, as well as the findings of any first-trimester ultrasound exams, complete physical examination, and general examination. Upon admission, all cases underwent complete blood counts (CBC) utilizing a commercially available analyzer. By means of the CBC, white blood cells, lymphocyte percentage, and MPV were quantified in the absence of any therapeutic intervention, including steroid use. For accurate MPV detection, blood sampling and MPV analysis were performed within one hour and with simultaneous administration in both groups. Levels of human arginine were detected by enzyme-linked immunosorbent assay kit (MAK370) according to the manufacturer's protocols (MerkKGaAcompany, Germany). The ability of MPV value and arginine level in all pre-eclamptic women There was an examination of the control group using the receiver operating characteristic (ROC) curve and their corresponding areas under the curves (AUC) with confidence intervals of ninety-five percent. All data were recorded, analyzed, and compared.

Sample collection

The study group and control group each had 2.5 ml of venous blood drawn once by vein puncture using a sterile disposable syringe. The blood was then transferred into containers that had been commercially prepared with a concentration of EDTA.

Hematological Analysis

Blood samples taken in EDTA tubes were well mixed to avoid clumping and clot formation when evaluating hematological parameters. The hematological auto analyzer SF300, made by the Japanese company Sysmex, will measure the samples within two hours of blood collection.

Principle of Hematological Analyzer: Direct Current Detection Technique

The blood samples were drawn, measured to a certain volume, and diluted according to the given ratio before being introduced into each transducer. The aperture was a small opening in the transducer chamber. Electrodes, through which direct current flowed, lined up on either side of the hole. As a result of the blood cells in the diluted sample passing through the aperture, the electrodes saw a change in direct current resistance. Electric pulses were used to monitor changes in platelet size as a function of direct current resistance. By measuring the diameter of the pulse, we were able to compute the platelet count and create a histogram of blood size.

Platelets Discriminator

The microcomputer automatically found the ideal placement of the PLT lower discriminator (LD) in the 2–6 fl range, while the optimal location of the upper discriminator (UD) was found in the 12–30 fl range. PLT was determined by tallying the particles between the lower and upper discriminators.

Mean Platelet Volume (MPV)

We used the following formula to determine MPV: Formula: MPV (fl) = PCT (%) × 1000 / PLT (103/μl). In this case, platelet-crit or platelet volume ratio (PCT) (%) denotes the value of weight in relation to platelet frequency.

Ethical Considerations

After being briefed on the study's purpose,

methodology, and any relevant objectives, all participants gave their informed permission. The research methods had no negative side effects on either the participants or the service itself. The primary investigators took every precaution to ensure the confidentiality of the individuals' data. The investigators covered all expenses; therefore, there was no additional cost for the participants.

Sample size

$$\left(\frac{Z_{a/2} + Z_B}{P_1 - P_2}\right)^2 (p_1q_1 + p_2q_2)$$

Takazawa & Morita[6]

n = sample size

Z a/2 (The critical value that divides the central 95% of the Z distribution)

ZB (The critical value that divides the central 20% of the Z distribution)

p1 = prevalence in case group

p2 = prevalence in control group.

q = 1-p

The sample size for this investigation was determined using the following assumptions, which were based on a study conducted by Osmanagaoglu et al.,7 Epi Info STATCALC: - An 80% power and a 95% two-sided confidence level. & an odds ratio of 1.115 was obtained with a 5% error. 46 was the ultimate maximum sample size obtained from the Epi-Info output. In order to account for any instances that may drop out during follow-up, the sample size was raised to 50 cases. As a result, there will be 50 subjects in the case group (the patients) and 50 subjects in the control group (the total being 100 subjects).

Statistical analysis

The collected data were coded, processed, and analyzed using the SPSS program (Version 25) for Windows. Descriptive statistics were calculated to include means, standard deviations, medians, ranges, and percentages.

3. Results

Table 1. Baseline Demographic Data (n=100)

	GROUP A (N=50)	GROUPB (N=50)	P-VALUE
MATERNAL AGE (YEARS)	32.2+4.2	31.1+4.0	.066
MATERNAL BMI (KG/M2)	32.7+4.1	26.4+4.8	.068
GRAVIDITY	2.7+1.5	3.3+1.7	.080
MULTIGRAVIDA	35(70)	37(74)	
PARITY	1.6+1.4	2.2+1.6	.088
NULLIPARA	12(24)	11(22)	

Table 1 compared the baseline characteristics of enrolled patients in each group, including maternal age, BMI, gravidity, parity and showed no statistically significant variance was detected among groups concerning gravidity or parity.

Table 2. Laboratory Data (n = 100)

	Group A (n = 50)		Group B (n = 50)		P value
PLATELET INDICES	Mean	SD	Mean	SD	
PLT $X10^3$/MCL	286.4	72.86	266.5	69.9	.166
PTC (%)	0.23	0.01	0.24	0.01	.588
PWD (%)	16.5	5.0	15.5	5.30	.352
MPV (FL)	9.5	1.2	8.2	1.4	.228
PLT/MPV	30.3	8.6	33.8	12.4	.042
PTC/MPV	0.024	0.004	0.029	0.007	.036
SERUM L-ARGININE (MM)	47.9	12.5	78.1	9.8	.028

As demonstrated in Table 2, a statistically significant variance was noted among groups regarding MPV & L-arginine, where pregnancies complicated with pre-eclampsia had higher MPV and lower levels of serum L-arginine (Independent sample t test, P = .001).

Table 3. Predictive Value of MPV and L-arginine (n = 100)

	CUT-OFF	*SENSITIVITY*	*SPECIFICITY*	*AUC*	*P VALUE*	*CONFIDENCE INTERVAL*	
						Lower Limit	*Upper Limit*
MPV	*8.45*	*74%*	*54%*	*0.748*	*.000*	*0.653*	*0.842*
L-ARGININE	*71*	*94%*	*86%*	*0.960*	*.000*	*0.927*	*0.992*

As shown in Table 3, ROC analysis was carried out to demonstrate the predictive value of MPV & L-arginine. The MPV was found to be a good predictive test where area under the curve (AUC) equalled 0.748 ± 0.048 (95% CI, 0.653; 0.842), and P value was .001 (statistically significant). At a cut-off point of 8.45 fL, the test was noted to have a sensitivity of 74% & a specificity of 54%.

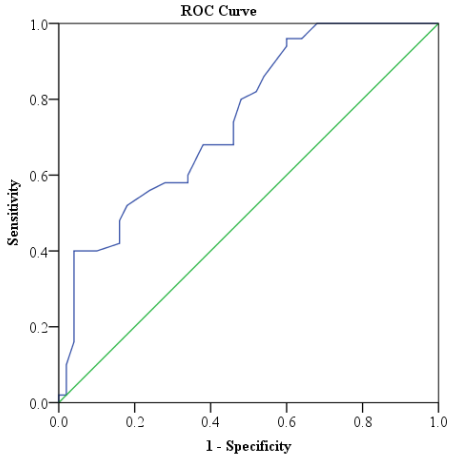

Figure 1. ROC curve of MPV

The L-arginine was found to be an excellent predictive test where area under the curve (AUC) equalled 0.960 ± 0.017 (95% CI, 0.927; 0.992), and P value was .050(statistically significant). At a cut-off point of 71 µM, the test was noted to have a sensitivity of 94% & a specificity of 86%.

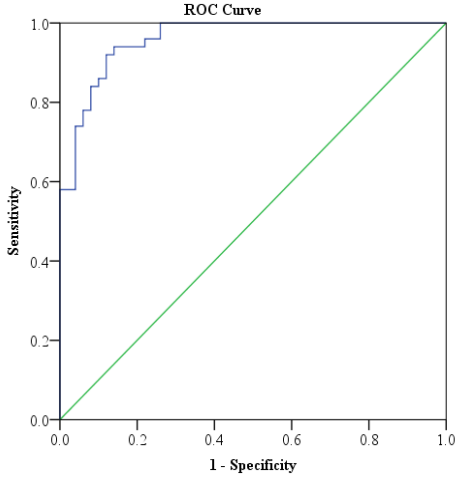

Figure 2. ROC curve of L-arginine

4. Discussion

The current investigation revealed that the MPV was found to be a good predictive test, with an area under the curve (AUC) equal to 0.748 ± 0.048 in predicting preeclampsia. At a cut-off point of 8.45 fL, the test was found to have a sensitivity of 74% and a specificity of 54%.

Thrombocytopenia, the most common coagulation problem in pre-eclampsia, is thought to arise when the damaged endothelium activates platelets, leading to an increased consumption of platelets. This might explain why MPV levels are higher in PE cases .[8]

The presence of thrombotic microangiopathy throughout the second and third trimesters of pregnancy is typically observed in pre-eclampsia, the most prevalent cause of thrombocytopenia. The result is an increase in MPV due to the bone marrow's production of big platelets and the subsequent increase in platelet consumption and destruction.[9]

Alkholy et al. endorsed our findings and stated that, with a P-value < 0.001, there is a progressive rise in MPV from normotensive pregnant females (8.5 ± 0.75 fl) to patients with moderate preeclampsia (9.82 ± 0.68 fl) & severe preeclampsia cases (11.07 ± 1.08 fl). According to an ROC curve study, MPV can distinguish mild PE from severe PE at a cut-off value of ≥ 10.4 fl with a sensitivity of 82% and specificity of 92%, and it can distinguish normotensive pregnant women from mild PE at a cut-off value of ≥ 9.3 fl with a sensitivity of 90% & specificity of 92%.[10]

Nooh et al. found that mean platelet volume (MPV) increased with the progression of PE, which agrees with our results. The best cut-off for predicting the development of PE was determined to be MPV > 9.5 fL based on ROC curve analysis of changes in MPV value between twenty-four and twenty-eight weeks of pregnancy. In terms of predicting the development of PE, this cut-off level had an AUC of 0.940, a sensitivity of 92.6%, and a specificity of 87.0%. More than eight times as many women were at risk of developing PE if their MPV at twenty-four- and twenty-eight-weeks' gestation was greater than 9.5 fL. Additionally, MPV was found to correlate positively with MAP in women with PE, and a rise in MPV was directly correlated with an increase in MAP. These results recommend that MPV may be a moderate indicator of the severity of hypertension.[11]

Our findings concurred with research performed by Hassan et al., which noted that. In contrast, MPV was significantly higher in the patient group than in the control group; platelet count was significantly lower in the patient group. Platelet count and MPV are predictors of PE; in univariate analysis, MPV is significantly correlated with PE. PE development was correlated with higher MPV.[12]

Similarly, Certain platelet activation indicators, particularly p-selectin MPV, were significantly elevated when comparing both groups of females in the meet study by Jakobsen et al., but others were not. Overall, the meta-analysis showed that MPV was considerably greater in preeclamptic women than in non-preeclamptic females.[13]

Also, according toKashanian et al., pre-eclamptic women had significantly higher MPV during the first trimester (10.2 ± 1.06 fl VS 9.68 ± 1.09 fl) than normotensive women. Additionally, pre-eclamptic women had higher MPV in the third trimester of pregnancy (10.16 ± 1.23 fl vs. 9.62 ± 1.12 fl) than normotensives. The predictive value of MPV during the first and third trimesters of pregnancy was shown to have a low area under the curve (ROC) of 0.64, indicating that this test is not very effective for predicting pre-eclampsia.[14]

In addition, Bawore et al. stated that MPV PDW

was significantly greater in the preeclampsia group than in the control group. The value of MPV amongst preeclamptic females was 9.25 (8–12.5), and its value between normotensive pregnant females was 8(6.9–9.3) fl. MPV can differentiate normotensive pregnant women from preeclamptic pregnant females at a cut-off value ≥of 8.55fl with a sensitivity of 86.6 percent, a specificity of 89.2 percent, PPV of 88.9 percent, and NPV of 86.94 percent.[15]

4. Conclusion

Pregnancies complicated by pre-eclampsia had higher MPV and lower levels of serum L-arginine. MPV was noted to be a good predictor of PE, and L-arginine was found to be an excellent predictor.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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