Blood Coagulation Parameters and Platelet Indices Change in Normal and Preeclamptic Pregnant Women, 2022

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Abstract

Background: The hypercoagulable state of preeclamptic women can cause multiple organ dysfunction, systematic metabolic disorders, and even endanger the lives of the mother and fetus. As a result, the onset and clinical severity of preeclampsia are well predicted by the coagulative and fibrinolytic status**.**

Aim: The current study aimed to explore the variation in laboratory markers of the coagulation-fibrinolytic system and evaluate their potential value in predicting the severity of preeclampsia for early intervention.

Patients and methods: A case-control study was conducted in Salahadeen General Hospital /Gynecology and Obstetrics department during the period from the 1st of January to the 30th of June 2022. A convenient sampling method was adopted to enrol 100 pregnant women in the current study and included two groups: The case group (consisted of 50 pregnant women who presented with preeclampsia) and the control group (consisted of 50 healthy pregnant women who were matched with the case group regarding the age. A P-value < 0.05 considered statistically significant

Results: According to the results of the current study, the means of prothrombin time, activated partial thromboplastin time, and International Normalized Ratio were significantly higher in the case group than in the control group. The platelet count and plateletcrit were significantly lower in the case group compared to the control group (P-values were 0.001 and 0.002, respectively).

In conclusion, the platelet indices can also be used in the prediction and early diagnosis of preeclampsia and as markers for the severity of preeclampsia. The coagulation parameters including prothrombin time, activated partial thromboplastin time, and International Normalized Ratio were significantly elevated in pregnant women with preeclampsia and can be used in the diagnosis, assessment of the severity, and follow-up.

Keywords: Blood Coagulation, Platelet Indices, Pregnancy, Preeclampesia.

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INTRODUCTION

Preeclampsia (PE), in particular, is one of the most feared complications of pregnancy. Hypertensive disorders of pregnancy are particularly difficult because the pathology and its therapeutic management simultaneously affect mother and fetus, sometimes putting their well-being at odds with each other[(1)]. It is a multi-system disorder characterized by the new onset of hypertension and proteinuria and/or end-organ dysfunction after 20 weeks in a patient who was previously noted to be normotensive[(2)]. The last decade has seen great advancement in the study of PE as evidenced by the discovery of a wide array of novel biomarkers that allow early diagnosis of the disease and prediction of the outcome after a half-century of struggling to understand the molecular basis of the disease[(3)]. According to World Health Organization (WHO), the overall global incidence of PE of 2.61% and accounts for 3–4% of all adverse effects of pregnancy[(4)]. With the greatest morbidity and mortality, PE is responsible for over 70 000 maternal deaths and 500 000 fetal deaths worldwide every year[(1)]. The incidence of PE is estimated to be seven times higher in developing countries as compared to developed countries[(5)]. In these countries, PE is a leading cause of maternal and fetal morbidity and mortality. It is responsible for about 16-18% of maternal perinatal deaths and up to 40% of fetal and neonatal deaths[(6)]. PE

manifests in a variety of ways, with early onset (prior to 34 weeks of gestation) being linked to a high rate of fetal growth restriction. While eclampsia and HELLP (haemolysis, elevated liver enzymes, and low platelets), which are examples of life-threatening crises that are more frequent in late gestation- and post-term manifestations of PE, are frequently associated with late-onset preeclampsia[7]. In addition, PE can lead to serious maternal complications such as eclampsia, stroke, and multiple organ failure. Importantly, it has been identified as among the most preventable causes of maternal morbidity and mortality[8]. The control of uteroplacental circulation and organ perfusion in pregnant women depends on the balance between coagulation and anticoagulation[9]. Women with preeclampsia are known to be more hypercoagulable than those who are pregnant normally. Early in the course of the disease in women with PE, blood coagulation is activated[10]. The extremely hypercoagulable state of women with PE may also result in systemic metabolic disorders, multiple organ dysfunction, and even endanger the lives of the mother and foetus. Consequently, the onset and clinical severity of PE can be accurately predicted by the coagulative and fibrinolytic status[9]. Obstetricians must determine whether a patient's coagulation status is normal or abnormal in order to predict preeclampsia and make subsequent treatment decisions. Many laboratories, however, only offer reference ranges for coagulation parameters in the population who are not pregnant. Therefore, it is crucial from a clinical standpoint to identify the variations in coagulation parameters between pregnant women who are healthy and those who have preeclampsia. Routine coagulation parameters usually include prothrombin time (PT), activated partial thromboplastin time (APTT), antithrombin (AT), platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT)[11]. These indices can be used as an early marker for the diagnosis of thromboembolic diseases because they are inexpensive and readily available as a result of being obtained from routine blood tests[12]. Consequently, early disease stages could then be considered for the primary preventative measures and targeted therapies[10]. The a**im of the study** was to explore the variation in laboratory markers of the coagulation-fibrinolytic system and evaluate their potential value in predicting the severity of PE for early intervention.

PATIENT AND METHODS

A case-control study was conducted in Salahadeen General Hospital /Gynecology and Obstetrics department during the period from the 1st of January to the 30th of June 2022. A convenient sampling method was adopted to enrol 100 pregnant women in the current study and included two groups:

- Case group: Consisted of 50 pregnant women who presented with PE.
- Control group: Consisted of 50 healthy pregnant women who were matched with the case group regarding age.

Exclusion criteria

- History of anticoagulant drug use, oral contraceptive, or smoking history
- Pre-existing renal disease, diabetes mellitus, and asthma require steroidal treatment, and chronic hepatitis (with or without hepatic dysfunction).
- History of severe trauma.
- Idiopathic thrombocytopenic purpura, hemolysis, elevated liver enzymes, HELLP syndrome, gestational thrombocytopenia, or any haematological diseases.
- Pregnant women with placental abruption or previa, sepsis, stillborn, or heavy vaginal bleeding.

Data collection

The data was collected through a standardized questionnaire prepared by the researcher after a review of many similar articles with revision by the supervisor. The questionnaire is divided into three parts:

Part one: Medical and obstetrical history, including age, gestational age, parity, and abortions.

Part two: Examination, including blood pressure (systolic blood pressure (SBP) and diastolic blood pressure (DBP)), weight, and height.

According to the weight and height, the BMI was calculated according to the formula:

BMI= weight (Kg) / **(**height (m)**)**^{2}[45]

Part three: Including the results of the investigation:

- Liver function tests included Alanine transaminase (AST) and Alanine transaminase (ALT)
- Platelets indices, included PC, PDW, MPV, and PCT.
- Coagulation parameters included prothrombin time PT, ApTT, and International Normalized Ratio (INR).

RESULTS

A total of 100 pregnant women were enrolled in the current study. There was no significant difference between the study groups regarding age (P-value<0.05), as shown in table 1.

Table 1: Age distribution according to the study groups

Age (years)	Groups		P-value
	Case N (%)	Control N (%)	
≤19	14 (28.0)	13 (26.0)	0.898
20-29	25 (50.0)	23 (46.0)	
30-39	8 (16.0)	11 (22.0)	
≥40	3 (6.0)	3 (6.0)	

Significant differences were obtained between the study groups regarding parity and abortion (P-values were 0.010 and 0.014, respectively), as shown in table 2.

Table 2: Distribution of the age and body mass index according to the study groups

Obstetrical history		Groups		P-value
		Case Mean (±SD)	Control Mean (±SD)	
Gestational age (weeks)		34.9 (3.3)	34.3 (3.4)	0.600*
		Case N (%)	Control N (%)	
Parity	0-3	33 (66.0)	18 (36.0)	**0.010****
	4-6	15 (30.0)	27 (54.0)	
	≥7	2 (4.0)	5 (10.0)	
Abortion	1	31 (62.0)	25 (50.0)	**0.014****
	2	11 (22.0)	20 (40.0)	
	3	2 (4.0)	5 (10.0)	
	4	6 (12.0)	0 (0.0)	

A significant difference was obtained between the study groups regarding BMI, as shown in figure 1.

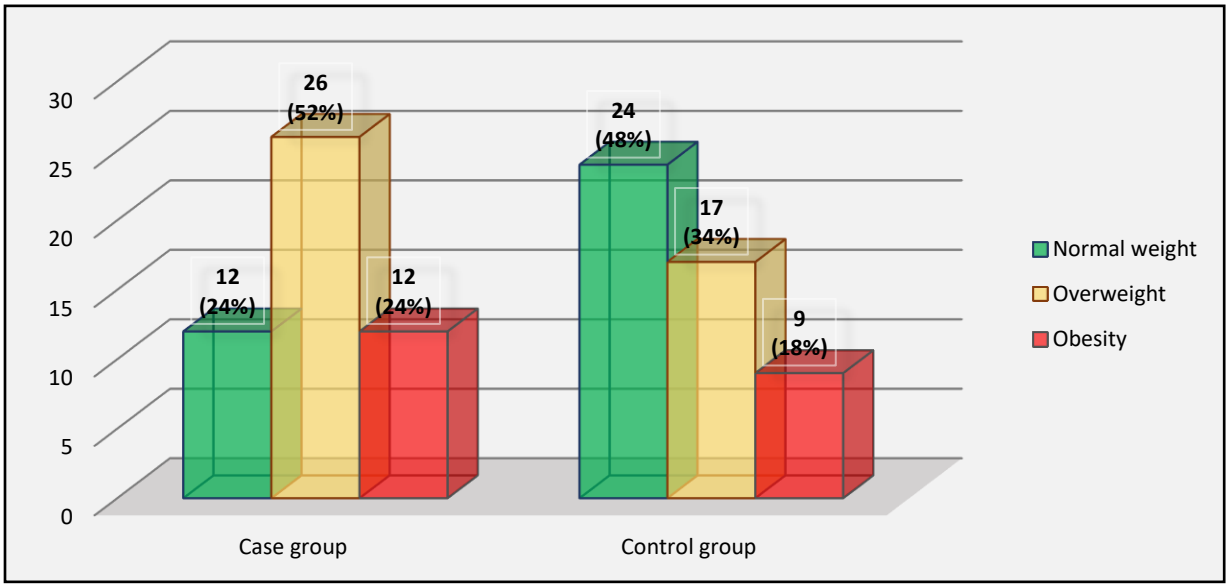

Figure 1: Distribution of the body mass index according to the study groups

The SBP and DBP were significantly higher in the case group than in the control group (P-value<0.001), as shown in table 3.

Table 3: Distribution of blood pressure according to the study groups

Blood pressure and liver function test	Groups		P-value
	Control Mean (±SD)	Cases Mean (±SD)	
Systolic blood pressure (mmHg)	158.5 (±10.3)	115.1 (±5.1)	**0.001**
Diastolic blood pressure (mmHg)	105.4 (±8.2)	78.0 (±13.1)	**0.001**
Aspartate transaminase (IU/L)	21.4 (±2.3)	20.0 (±2.3)	**0.001**
Alanine transaminase (IU/L)	30.3 (±9.9)	21.5 (±4.4)	**0.001**

The means of PT, APTT, and INR were significantly higher in the case group than in the control group (P-values were 0.001, 0.048, and 0.001, respectively). As shown in table 4.

Table 4: Distribution of coagulation parameters according to the study groups

Coagulation parameters	Groups		P-value
	Case Mean (±SD)	Control Mean (±SD)	
Prothrombin time (seconds)	12.5 (±1.3)	11.1 (±1.2)	**0.001**
Partial thromboplastin time (seconds)	27.7 (±3.3)	26.1 (±4.4)	**0.048**
International normalized ratio	1.23 (±0.16)	0.97 (±0.1)	**0.001**

SD (Standard Deviation).

The platelet count and PCT were significantly lower in the case group compared to the control group (P-values were 0.001 and 0.002, respectively). While the PDW and MPV were significantly higher in the case group compared to the control group (P-values were 0.001 for both). As shown in table 5.

Table 5: Distribution of the platelet indices according to the study groups

Platelets indices	Groups		P-value
	Case Mean (±SD)	Control Mean (±SD)	
Platelets count (x 109/L)	133.6 (±53.3)	244.6 (±51.9)	**0.001**
Platelet distribution width (%)	15.8 (±3.2)	13.4 (±3.0)	**0.001**
Mean platelet volume (fL)	10.5 (±1.2)	9.9 (±1.5)	**0.001**

Within the case group, there was a significant positive correlation between the APTT with SBP, DBP, AST, and ALT. At the same time, the PT and INR had a significant positive correlation with SBP, DBP, and ALT (Table 6).

Table 6: Correlation between the coagulation parameters and body mass index, blood pressure, and liver function test

		PT	APTT	INR
SBP	Pearson Correlation	0.558	0.662	0.598
	Significancy	**0.001**	**0.000**	**0.001**
DBP	Pearson Correlation	0.423	0.453	0.480
	Significancy	**0.001**	**0.001**	**0.001**
AST	Pearson Correlation	0.180	0.297	0.174
	Significancy	0.072	**0.036**	0.083
ALT	Pearson Correlation	0.412	0.289	0.155
	Significancy	**0.001**	**0.042**	**0.001**

Within the case group, there was a significant positive correlation between the platelets count and SBP, DBP, AST, and ALT (Table 4.6).

Table 4.7: Correlation between the platelets indices and body mass index, blood pressure, and liver function test

Blood pressure and liver function test		Platelets count	PDW	MPV	PCT
SBP	Pearson Correlation	-0.590-	0.455	0.356	0.165
	Significancy	**0.001**	**0.001**	**0.011**	0.253
DBP	Pearson Correlation	-0.420-	0.381	0.327	0.340
	Significancy	**0.002**	**0.006**	**0.021**	0.016
AST	Pearson Correlation	-0.402-	0.243	0.120	0.200
	Significancy	**0.004**	0.090	0.120	0.163
ALT	Pearson Correlation	-0.394-	0.132	0.113	0.023
	Significancy	**0.005**	0.360	0.435	0.874

DISCUSSION

In recent days, there has been a significant improvement in the management of PE patients, which has led to a decrease in mortality and morbidity caused by PE. However, the challenge lies in its early diagnosis, when there are no apparent clinical signs. Therefore, early intervention could be initiated and maternal mortality and morbidity could be reduced substantially, even in developing countries[11]. The first finding of the current study was that the prevalence of PE was significantly associated with increased gravidity and the number of abortions. In agreement, Yuval et al. concluded that nulliparity is a risk factor for preeclampsia as the nulliparous pregnant women had higher circulating Soluble fms-Like Tyrosine Kinase (sFlt1) levels and sFlt1/ Placental Growth Factor (PlGF) ratios than multiparous pregnancies, suggesting an association with an angiogenic imbalance[12].In the current study, there was a significant association between the incidence of PE and increased weight. The same finding was obtained by another study that was done by Lisa et al.[13]. In agreement with these results, Patricio et al. obtained a significant association between obesity and overweight with the presence of preeclampsia[14]. The mean of SBP and DBP were significantly higher in the case group than in the control group. In comparison, the same findings were obtained by Ekun et al who conducted a cross-sectional study and enrolled 49 preeclamptic women and 50 normotensive healthy pregnant women, the SBP was 172 mmHg and DBP was 112 mmHg among pregnant women with PE compared to SBP of 113 and DBP of 72 among healthy pregnant women[15]. Another study was done by Murat et al and included 36 cases with mild preeclampsia, 36 cases with severe preeclampsia and 33 cases of normotensive pregnancy concluded a significant difference in the SBP and DBP between healthy pregnant women, those with mild to moderate, and those with severe PE[16].

There was a significant difference between the study groups regarding the AST and ALT, the means of the AST and ALT were higher in the case group. The same results were obtained by another case-control study that was done in Iraq by Lamyaa et al. and included 130 pregnant women (40 with severe preeclampsia, 40 with non-severe preeclampsia, and 50 with normal pregnancy as a control group)[17]. A cross-sectional study among 100 pregnant women after 20 weeks of gestation was conducted by Munazza et al and concluded that the liver function tests particularly AST and ALT levels were significantly increased among pregnant women with preeclampsia compared to healthy pregnant women[18]. In concordance with these results, a study was done in Iran by Kasraeian et al and included 450 women with preeclampsia revealed a significant increase in the level of AST and ALT in patients with severe PE compared to those with mild PE[19]. Another study that was done by Rajoria et al and enrolled 250 women of more than 20 weeks gestation concluded that liver involvement is common in PE and eclampsia and the derangement of parameters of liver function test can be taken as predictors of the disease[20].An important finding of the

current study was a significant deceased in the platelet count and PCT in the case group compared to the control group. While the MPV and PDW were significantly elevated in the case group compared to the control group. The same findings were obtained by another study that was done by Nitesh et al.[21]. While Muzaffer et al. revealed that the platelet count, PCT, and PDW were significantly lower in pregnant women with significant elevation of the MPV[22]. Another study was done in Turkey by Kazım Uckan and Hanım Guler Sahin and enrolled 120 women revealed an insignificant decrease in platelet count for pregnant women with PE comparing healthy pregnant[23]. In the Kingdom of Saudi Arabia, a study conducted there by AlSheeha et al. and included 120 participants revealed a significant decrease in platelet count in the preeclampsia group (including mild and severe PE) compared to the control group[24]. There was a significant negative association between the platelet count with SBP and DBP and a significant positive association between the PDW and MPV with SBP and DBP. The same results were obtained in another study that was done in India by Shilpa[25].In agreement with the current study, the MPV and PDW showed a significant correlation with increased blood pressure in another study that was done by Nitesh et al[26].A significant negative correlation was obtained between the platelet count with AST and ALT, while no significant correlation was reported between the live function test and other platelet indices. In comparison, other studies revealed that the platelet count was significantly associated with the severity of PE[27,28]. In the current study, the mean of APTT was significantly higher in the case group than in the control group, while no significant differences were obtained regarding PT and INR.

CONCLUSION

1. The platelet indices can also be used in the prediction and early diagnosis of preeclampsia and as markers for the severity of preeclampsia.
2. The coagulation parameters including APTT, PT, and INR were significantly elevated in pregnant women with preeclampsia and can be used in the diagnosis, assessment of the severity, and follow-up.

RECOMMENDATIONS

1. Platelet indices and coagulation parameters should be done in routine investigations for patients with preeclampsia.
2. Other studies should be done in the upcoming period including a larger sample to identify factors that impact the platelets indices and coagulation parameters.

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