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Association between Changes of Blood Indices, Ultrasound Parameters and the Severity of Preeclampsia

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ABSTRACT

Background: Preeclampsia (PE) affects 2 to 8% of pregnancies with its enormous effect on maternal and newborn morbidity. Placental dysfunction and placental hypoxia are thought to have systemic inflammation, and endothelial dysfunction leading to increased neutrophil numbers and thrombocyte activation through different immunological mechanisms.

Objective: Appraisal the changes occur in both platelet, white blood cell indices and ultrasound with preeclampsia.

Patients and methods: case control observational study conducted in Menoufia University Hospital started on May 2020, ended by May 2021. The study included 120 patients divided to group (A) 70 pregnant participants with PE and group (B) 50 healthy pregnant participants. Venous blood sample was obtained and ultrasound examination for each women was done.

Results: this study resulted in significant difference between both groups regarding the WBC indices (TLC, ANC, ALC), platelets indices (PLT, MPV and PDW) and US parameters including the placental site and umbilical artery Doppler (S/D and RI) (p-value < 0.05). Lateral placenta was presented in 25 cases of PE. There was statistical difference in TLC, ALC, ANC and PLT in women with PE had lateral placenta than same group with other sites of placenta.

Conclusions: Blood indices **(**PLT, WBC) have been recognized as possible markers for predicting preeclampsia. Especially if they are associated with lateral placenta.

Keywords: Platelet indices, Preeclampsia and lateral placenta.

INTRODUCTION

Pregnancy-induced hypertension represented the second cause of maternal death (9%–26%), coming after hemorrhagic disease[(1)]. Preeclampsia defined as new onset of hypertension and proteinuria after 20 weeks of pregnancy which affect 5–8% of pregnancies leading to more than 500 000 fetal deaths and 70 000 maternal deaths each year[(2)].

The pathological cause of preeclampsia is unclear but many theories about the endothelial dysfunction and hemostatic changes due to underlying genetics and the epigenetics factors[(3)]. There is a request for a low-cost test and markers for early diagnosis and prognosis of PE, essentially in underdeveloped nations particularly in community health clinics where wide range of clinical presentations and early identification remains a challenge[(4)].

The leukocyte activation due to interactions of platelets with different cell types (endothelial, dendritic, T-lymphocytes, neutrophils and mononuclear phagocytes) makes and exaggerates the inflammation in the arterial wall[(5)].

Platelet indices represent unpretentious performed procedure in the clinical laboratory mainly in resource-limited hospitals. Different parameters are used to evaluate platelet activity like, platelet count (PLT), mean platelet volume (MPV), and platelet distribution width (PDW) [(6)].

Impaired placental perfusion in PE and its adverse outcome can be predicted by ultrasound Doppler analysis. Umbilical artery Doppler is the simple one included in the evaluation but no complete data about the most frequently altered Doppler parameters[(7)].

Lateral placenta and its association with women developed PE was estimated in different studies depending on the theories that in lateral placenta, the uterine artery close to the placenta has lower resistance than the opposite one, so the uteroplacental blood flow have unequal contribution from both uterine arteries. This is not found in case of central placenta by ultrasound[(8)].

The aim of the present study was to appraisal the changes occur in both platelet, white blood cell indices and ultrasound with preeclampsia.

PATIENTS AND METHODS

An observational study applied at Menoufia University Hospital, Egypt started on May 2020 and completed on May 2021.

Each participant included in the study was pregnant woman attended the hospital at third trimester. 70 pregnant women (group A) were diagnosed with preeclampsia by hypertension (systolic blood pressure >140 mmHg or diastolic blood pressure > 90 mmHg) after 20 weeks of gestation in addition to proteinuria (presence of 300 mg or more of protein in 24 h urine sample or ++ on dipstick). Preeclampsia cases were considered mild or severe according to the diastolic blood pressure of <110 or >110 mmHg[(9)]. About 50 Healthy pregnant women (group B) attended the hospital at same time were added as control.

Pregnant patients with obstetric history of habitual miscarriage, pre-term labor, intrauterine growth restriction, gestational diabetes or pre-gestational DM, chronic hypertension, renal or liver disorders, disseminated intravascular coagulation,

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symptomatic infections, autoimmune disorders like lupus, drugs change PLT count such as heparin, corticosteroid, were excluded.

For each patient in the control or case group, demographic data as patient age, gravidity and body mass index (BMI) were documented. The blood pressure (BP) was measured by a mercury sphygmomanometer then recorded and patients with PE were classified and diagnosed as mild or severe[9].

Venous blood sample, about 3 ml was taken into ethylene diamine tetraacetic acid (EDTA) tubes and mixed well. complete blood picture was done using Sysmex KX-21 automatized hematology analyzer (Sysmex Corporation, Kobe, Hyogo, Japan) measuring platelet indices (PLT, MPV, PDW) and WBC indices (TLC, ALC, ANC).

An initial obstetric ultrasound scan was achieved using Solo Compact ® computerized ultrasound system (from International biomedical engineering. Egypt, in Menoufia University, Obstetrics and Gynecology Dep.) scanner machine to record fetal biometry and placental location.

Doppler study was done using transabdominal pulsed, curved array 3.5–5.0 MHZ transducer. The umbilical artery Doppler was carried out at a free loop of the cord and the velocimetry was recorded. Automatic tracing of the waveforms was done to demonstrate the Doppler parameters. RI and the systolic-diastolic ratio (S/D) were documented[10].

Sample size: based on previous studies [5, 6, 7] two tailed sample size calculation rendered 120 participants for case control study (∞ 0.05, power 0.85) the calculation was done using GPower 3 Software.

Ethical consent:

The trial was registered with local ethics committee of the Faculty of Medicine, Menoufia University (Registration number: 11/2019 OBSGN 27-11). Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. **(**Armonk, NY: IBM Corp**).** The Kolmogorov-Smirnov test was used to verify the normality of distribution of variables. Categorical variables were presented as frequency and percentage and were compared by Chi-square test (Fisher or Monte Carlo). Quantitative data were presented as median, range, mean and standard deviation (SD) and were compared by Student t-test was for normally distributed quantitative variables and Mann Whitney test for not normally distributed quantitative variables. P value < 0.05 was considered significant.

RESULTS

Characteristics of the studied participants:

There was no statistically difference observed between the healthy women and PE women regarding age, number of pregnancies (gravidity) and BMI. There was significant difference between the studied groups regarding SBP and DBP, which increased with preeclampsia. Proteinuria, measured by complete urine analysis was 0 in normal healthy women and range from trace to ++++ in PE women. Unfortunately, 4 pregnant women had severe PE complicated with intrauterine fetal death so umbilical artery Doppler analysis was done for 66 women (Table 1).

Table (1): Descriptive demographic data of the two studied groups

Variable	PE group (A) (n=70)	Healthy group(B) (n=50)	p- value
Age (years)			
Median (Range)	29 (17 – 41)	28 (18 – 41)	
Mean ± SD	28.3 ± 6	28.6 ± 6.3	0.815
Gravidity			
0	2 (2.9%)	0 (0%)	
1	22 (31.4%)	16 (32%)	0.587
2	16 (22.9%)	17 (34%)	
3	21 (30%)	12 (24%)	
>3	9 (12.9%)	5 (10%)	
Median (Range)	2 (0 – 5)	3 (1 – 5)	
Mean ± SD.	2.2 ± 1.2	2.1 ± 1	0.709
BMI(Kg/M^2) Median (Range) Mean ± SD	10 (20.6–30.8) 25.1±5.16	11(21–31) 24.60±4.71	0.841
Systolic (mmHg) Median Mean ± SD.	160 (140 – 200) 158.7 ± 15.9	120 (100 – 135) 119.4 ± 9.6	<0.001*
Diastolic (mmHg) Median (Range) Mean ± SD.	100 (85 – 130) 103.6 ± 11.1	70 (50 – 85) 70.8 ± 7.7	<0.001*
Protein in urine	28 (40%)	–	
+	11 (15.7%)	–	
++	15 (21.4%)	–	–
+++	10 (14.3%)	–	
++++	6 (8.6%)	–	
Trace			
Severity of PE	38 (54.3%)	–	
Mild	32 (45.7%)	–	–
Severe			

*: Statistically significant

Blood indices changes associated with PE:

Regarding the WBC indices, both white blood cell count (TLC) and absolute neutrophilic count (ANC) had shown significant elevation in women with PE in comparison to healthy group. While ALC was significantly decreased in PE group than the healthy group (Table 2).

Platelet indices changes associated with PE:

Platelet count (PLT) was significantly lower in PE group than the healthy group. Otherwise mean platelet volume (MPV) and platelet distribution width (PDW) were significantly higher in PE group than healthy group. Furthermore, umbilical artery Doppler in healthy pregnant women, who did not develop PE had lower mean umbilical RI than in women who developed PE RI. The same was for umbilical S/D ratio. Lateral placenta was observed in 25 PE women compared to 6 women in healthy group. This showed significant differences between both groups (Table 2).

Table (2): Comparison between the two studied groups regarding the WBC indices, platelet indices and US parameters

Variable	PE group (n=70) Mean ± SD	Healthy group (n=50) Mean ± SD	p- value
WBC ($10^3/\mu L$)	12.1 ± 2.8	9.4 ± 1.7	<0.001*
ANC ($10^3/\mu L$)	8.7 ± 2	5.9 ± 1	<0.001*
ALC ($10^3/\mu L$)	2 ± 0.4	2.2 ± 0.5	0.005*
PLT($10^3/\mu L$)	180.8 ± 6.3	276.5 ± 6.5	<0.001*
MPV (fL)	9.6 ± 0.8	9.2 ± 0.5	0.003*
PDW (fL)	14.4 ± 1.9	12.3 ± 1.2	<0.001*
Placental site Anterior Posterior Fundal Lateral Fundal and posterior Fundal and anterior	 14 (20%) 10 (14.3%) 13 (18.6%) 25 (35.7%) 4 (5.7%) 4 (5.7%)	 11 (22%) 12 (24%) 12 (24%) 6 (12%) 4 (8%) 5 (10%)	 0.790 0.175 0.470 0.003* p=0.718 p=0.488
Umbilical Doppler	**(n=66)**	**(n=50)**	
S/D	2.6 ± 0.4	2.2 ± 0.2	<0.001*
RI	0.7 ± 0.1	0.6 ± 0.1	<0.001*

*: Statistically significant

Regarding the changes in WBC indices and platelets indices in women with PE with lateral placenta localized by US; we found significant elevation in both TLC and ANC with statistical difference. However PLT and ALC showed significant decline (Table 3).

Table (3): Relation between lateral placenta with WBC indices and platelet indices in PE group (A**)**

Variable	Lateral placenta		p
	No (n=45) Mean ± SD.	Yes (n=25) Mean ± SD	
TLC ($10^3/\mu L$)	11.4 ± 2.5	13.4 ± 3	0.004*
ANC($10^3/\mu L$)	8.3 ± 1.9	9.4 ± 1.9	0.026*
ALC ($10^3/\mu L$)	2.1 ± 0.4	1.8 ± 0.3	0.002*
PLT($10^3/\mu L$)	193.3 ± 5.2	158.1 ± 5.7	0.011*
MPV(fL)	9.4 ± 0.8	9.8 ± 0.7	0.062
PDW(fL)	14.2 ± 1.9	14.9 ± 2	0.167

*: Statistically significant

DISCUSSION

A lot of researcher's effort is done trying to define the pathology and etiology of PE in addition to available tests for the clinical diagnosis. Systemic maternal inflammatory response and endothelial cell dysfunction recently have been suggested to be the cause of PE[(11)].

This study was designed to demonstrate the changes in WBC indices and platelet indices, which occur in pregnant women who develop PE in addition to the changes in umbilical Doppler parameters and placental site, aiming to suggest some available tests for clinical diagnosis and prediction.

In this study, no significant difference related to age, gravidity and parity between patients who had PE and healthy pregnant women but SBP and DBP were significantly high in pregnant women with PE than healthy women. This was documented by **Liu *et al.*[(12)] and Bawore *et al.* [(13)]** in their studies.

Significant elevation in WBC and neutrophil in women with PE than healthy women was established by our results. This also reported by other researchers in their different studies[(13-16)]. All of these studies proposed that PE had inflammatory process leading to leukocytosis with elevation of WBC and neutrophil count. In contrast to **AlSheeha *et al.*[(17)]** who found that there was no significant difference in WBC between healthy pregnant women and pregnant women developed PE.

Our study agrees with **Liu *et al.* [(12)], Bawore *et al.* [(13)] and Alisi *et al.* [(14)]** who reported that ALC was significantly reduced in PE group compared to the control group. This suggests that, abnormal activation of the immune system may play a role in the etiology and pathogenesis of PE. But, the result is different from a study done by **Canzoneri *et al.* [(5)]** as they didn't find difference in ALC between PE group and the control group.

According to this study, platelet count (PLT) were lower in the PE group while, both MPV and PDW were significantly greater. Many researcher's results [(13, 18, 19)] were in agreement with our findings. This explained the

PLT consumption due to the increase in the vascular reaction and activity in addition to the PLT activation after the effect on the placental endothelium due to preeclampsia. In contrast to our findings, another studies concluded that there were no changes in PLT and occurrence of PE [6, 17, 20, 21].

PE is a condition associated with endothelial damage with consumption of platelets resulted in increase the platelets destruction and their turnover. All of that leading to increase the MPV and PDW in PE women. A lot of studies were in agreement with our results [18, 22, 23], but unfortunately, other investigators [17, 24] have established inconsistency with our findings.

Previous researches reported different findings on the Doppler parameter as predictor of PE. Regarding to our findings, there was significant elevation in the S/D ratio and RI of the umbilical Doppler among PE cases compared to healthy women. This was also promoted by **Mallikarjunappa *et al.* [25] and Li *et al.* [26]** who observed significant difference RI in the umbilical artery in women with PE. Also, **Ademola [27]** who studied with his colleagues the changes in both uterine and umbilical artery Doppler indices in the third trimester among the Nigerian pregnant women who had PE in comparison with healthy pregnant women, they concluded that there were significant elevation in both S/D ratio and RI level in patients with PE than healthy women like our study concluded.

Pregnant women with lateral placental site may be associated with increased incidence of PE. This was promoted by different recent researches [8, 28, 29] and our results reinforce also this.

Limitations of the study:

Further prospective trials are required following pregnant female from the first trimesters to pick up the beginning of WBC indices and platelets indices changes. Also addition of uterine artery Doppler at second trimester and correlation of it with blood indices changes may add predictive information about PE development.

CONCLUSIONS

Complete blood picture parameters such as WBC, ANC, ALC, MPV and PDW may be considered as predictors factor for PE especially if associated with lateral placental site and abnormal umbilical Doppler parameters.

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Data Availability Statement: The data presented in this study are available upon request from the corresponding author.
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