The Egyptian Journal of Hospital Medicine (July 2019) Vol. 76 (1), Page 3204-3210

Comparative Study of Mean Platelet Volume in Preeclampsia versus Normal Pregnancy in 3rd Trimester

Ibrahim Ahmed Oun, Abdallah Khaleel Ahmed, Mohamed Khedr and Mohamed Aly Abdelmonem Ragab *
Department of Obstetrics and Gynecology, Faculty of Medicine - Alazhar University
***Corresponding author:** Mohamed Aly Abdelmonem Ragab, **Mobile:** (+20)01001255778

ABSTRACT

Background: Preeclampsia is a pregnancy-specific multisystem disease that is characterized by development of hypertension and proteinuria after 20 weeks of gestation, resolving by 6-12 weeks postpartum in previous normotensive women. The pursuit of safe, reliable, and cost-effective screening tests for prediction of preeclampsia has been the goal of researchers for many decades, with the aim of improving maternal and fetal outcome, despite the fact that the only current effective treatment remains delivery of fetus and placenta. **Objective:** The aim of this study is to compare 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 presence of preeclampsia.

Patients and methods: This study was done at Kafr Elsheikh General Hospital from January 2018 to December 2018. 80 pregnant women in their third trimester (from 31weeks gestation to completed 37 weeks gestation) were selected to participate in the study. **Result:** We found in our study that CBC, and MPV values do not have any determining effect on the presence of preeclampsia but the platelet count showed difference. In the literature, papers that include conflicting results especially on MPV values are available, yet this fact is most probably due to the differences between the methods and/or equipment used.

Conclusion: Our study found that MPV values do not have any determining effect on the presence of preeclampsia.

Keyword: MPV, Preeclampsia, Pregnancy in 3rd trimester.

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 results in substantial maternal and fetal morbidity and mortality [(2)].

Although the etiology of preeclampsia is still unclear, recent hypothesis have been proposed that the current most accepted hypothesis is abnormal placentation leading to placental ischemia [(3)].

Preeclampsia is a syndrome that involves many organs, liver, kidney, placenta, brain, hematopoietic, and coagulation system [(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: A) New-onset proteinuria (0.3 g of protein in a 24-hour urine collection) after 20 weeks' gestation. B) Any of the following in a woman with hypertension and proteinuria 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 aminotransferase (AST) to abnormal levels [(1)].

The pursuit of safe, reliable, and cost-effective screening tests for prediction of preeclampsia was the goal of researchers for many decades, with the aim of improving 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 [(5)].

In preeclampsia there is a decrease in the platelet count and life span, and increased MPV [(6)].

Conflicting results were 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 [(7)], whereas others demonstrated lower platelet count and higher MPV in preeclamptics, referring these changes to increased platelets consumption in preeclampsia [(8)].

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 [(7)].

AIM OF THE WORK

The aim of this study is to compare mean platelet volume (MPV) in pre-eclamptic and normal pregnant women in the third trimester of pregnancy, and to evaluate whether this parameter has a prognostic significance in determining the presence of preeclampsia.

SUBJECTS AND METHODS

Study design: A case control study was performed.

Participation: 80 pregnant women in their third trimester (from 31 weeks gestation to completed 37 weeks gestation) were selected to participate in the study, they were assigned to 2 groups:

Received:1/4/2019
Accepted:30/4/2019

- 1st group: 40 pregnant women with preeclampsia (blood pressure more than or equal 150/100 and proteinuria more than or equal 3 gm/24 h. urine collection with or without body edema)
- 2nd group: 40 pregnant women free of any medical disorders.

This study was done at Kafr Elsheikh General Hospital from January 2018 to December 2018. A written consent was taken from all the patients to participate in the study. Also, **An approval of the study was obtained from Al-Azhar University academic and ethical committee.**

Inclusion criteria:

1) Age between 18-40 years old.
2) Primigravida.
3) Gestational age from 31 weeks gestation to completed 37 weeks gestation.

Exclusion criteria :

1) Women with other medical disorders (e.g. Diabetes mellitus, heart disease, atherosclerosis, systemic lupus erythematosus)
2) Rhesus isoimmunization (Coombs positive).
3) HCV.
4) Other causes of thrombocytopenia as ITP – TTP – HUS – SLE .
5) Premature rupture of membrane.

Method:

All pregnant women who met inclusion criteria were subjected to: History taking including past history of any diseases especially HTN, obstetric history and menstrual history especially LMP. General, abdominal and obstetric examinations were performed.

- **Physical examination:**

- Vital signs: blood pressure, heart rate, temperature and respiratory rate were performed.
- Systemic examination of heart, lungs, abdomen, lower limbs, and neurological examination.
- Obstetric examination : FL , FG , FHS.

Blood pressure was measured with the woman comfortably seated, legs uncrossed and her back and arm supported. The lower end of the cuff 2.5 cm above the antecubital fossa. She should be relaxed and not talking. The SBP was initially determined by palpation and then by auscultation. SBP was recorded then DBP. The average blood pressure from each patient was obtained from three consecutive readings at 2-3 min intervals.

- **Determination of gestational age**

By using the date of last menstrual period, which is confirmed by ultrasonographic findings and clinically by fundal level and fundal height.

- **A complete laboratory investigations were done, i.e.**

1) Complete blood picture including MPV
2) Liver function tests (SGOT, SGPT, serum albumin)
3) Kidney function tests (blood urea, serum creatinine)
4) Dip stick urine protein collection

Urinary protein :

+1 means (300 mg to 2000 mg / 24 hr urine collection)
+2 means (2000 mg to 3000 mg /24 hr urine collection)
+3 means (more than 3000 mg / 24 hr urine collection)

-Sampling: 3 ml 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 impedance 3-parameters cell counter)**, **Sysmex.**

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative date 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 qualitative parameters.
- Pearson's correlation coefficient (r) test was used to assess the degree of association between two sets of variables
- 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:

– P-value <0.05 was considered significant.
– P-value <0.001 was considered as highly significant.
– P-value >0.05 was considered insignificant.

RESULTS

The present work is a cross sectional case-control study that included 40 preeclamptic pregnant women and 40 normal pregnant women recruited from Kafr El-Shekh General Hospital from January 2018 to December 2018.

Table (1): Comparison between groups regarding age.

Age (years)	Preeclampsia (n=40)	Control (n=40)	p-value
Range	18-40	18-40	>0.05
Mean±SD	29.37±6.03	28.86±4.89	

This table shows no statistically significant difference between groups according to age (years).

Table (2): Comparison between groups regarding BP.

Blood pressure (mmHg)	Preeclampsia (n=40)	Control (n=40)	p-value
Systolic			
At GA 31wks	165.18±7.89	110.50±8.64	<0.001**
At GA 34wks	160.62±7.50	109.40±8.20	<0.001**
At GA 37wks	155.44±7.12	108.31±7.79	<0.001**
Diastolic			
At GA 31wks	108.96±7.52	71.14±7.46	<0.001**
At GA 34wks	102.61±7.15	70.43±7.08	<0.001**
At GA 37wks	98.53±6.79	69.72±6.73	<0.001**

**p-value <0.001 HS

This table shows highly statistically significant difference between groups according to blood pressure (mmHg).

Table (3): Comparison between groups regarding urinary Protein.

	Urinary Protein	Preeclampsia (n=40)	Control (n=40)	p-value
At GA 31wks	0	0 (0.0%)	32 (80%)	<0.001**
	1	4 (10.0%)	8 (20%)	
	2	24 (60.0%)	0 (0%)	
	3	12 (30.0%)	0 (0%)	
At GA 34wks	0	0 (0.0%)	30 (750%)	<0.001**
	1	4 (10.0%)	10 (25%)	
	2	25 (62.5%)	0 (0%)	
	3	11 (27.5%)	0 (0%)	
At GA 37wks	0	0 (0.0%)	28 (70%)	<0.001**
	1	5 (12.5%)	12 (30%)	
	2	26 (65.0%)	0 (0%)	
	3	9 (22.5%)	0 (0%)	

**p-value <0.001 HS; This table shows highly statistically significant difference between groups according to urinary protein.

Table (4): Comparison between groups regarding Hb.(mg/dl)

Hb.	Preeclampsia (n=40)	Control (n=40)	p-value
At GA 31wks			
Mean±SD	9.43±0.82	9.61±1.03	Insig.
At GA 34wks			
Mean±SD	9.86±0.88	9.99±1.10	Insig.
At GA 37wks			
Mean±SD	10.32±0.95	10.42±1.19	Insig.

This table shows no statistically significant difference between groups according to Hb.

Table (5): Comparison between groups regarding platelet count.

Platelet count	Preeclampsia (n=40)	Control (n=40)	p-value
At GA 31wks			
Range	160.76-380.93	167.08-445.54	<0.001**
Mean±SD	211.06±83.44	261.65±64.73	
At GA 34wks			
Range	140.01-362.79	159.12-424.32	<0.001**
Mean±SD	197.26±77.98	244.54±60.50	
At GA 37wks			
Range	119.66-348.84	153.00-408.00	<0.001**
Mean±SD	186.67±74.98	232.13±58.17	

**p-value <0.001 HS;This table shows highly statistically significant difference between groups according to platelet count.

Table (6): Correlation study between MPV and the other studied parameters in preeclampsia, using Pearson correlation coefficient test.

Parameter	MPV					
	At GA 31 wks		At GA 34 wks		At GA 37 wks	
	r	p-value	r	p-value	r	p-value
Age (year)	0.385	0.038*	0.306	0.032*	0.385	0.027*
Systolic	0.072	0.753	0.057	0.627	0.072	0.546
Diastolic	0.359	0.043*	0.285	0.044*	0.359	0.038*
Alb	-0.233	0.226	-0.185	0.188	-0.233	0.164
Hb (g/L)	0.287	0.129	0.228	0.107	0.287	0.093
HT (%)	0.123	0.548	0.098	0.456	0.123	0.397
Platelet count (104/µL)	-0.413	0.025*	-0.328	0.021*	-0.413	0.018*
AST (U/L 37°C)	0.188	0.334	0.150	0.278	0.188	0.242
ALT (U/L 37°C)	0.201	0.300	0.160	0.250	0.201	0.218
Creatinine (mg/dL)	0.125	0.542	0.099	0.452	0.125	0.393

r: Pearson Correlation Coefficient;

Positive correlation and significant between MPV with age, diastolic and platelet count through GA 31 wks, GA 34 wks and GA 37 wks.

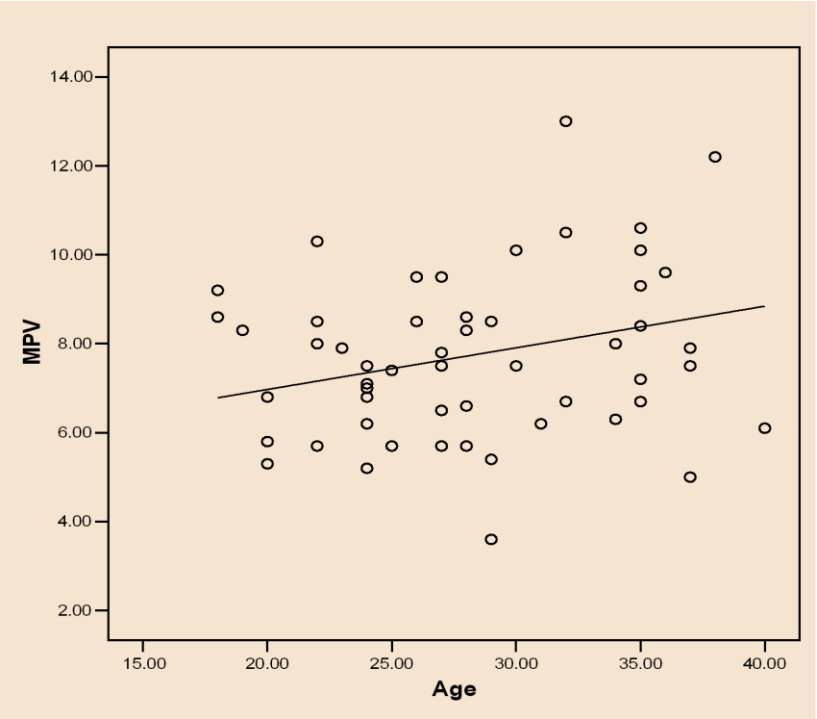

Fig. (2): Positive significant correlation between age and MPV in severe group.

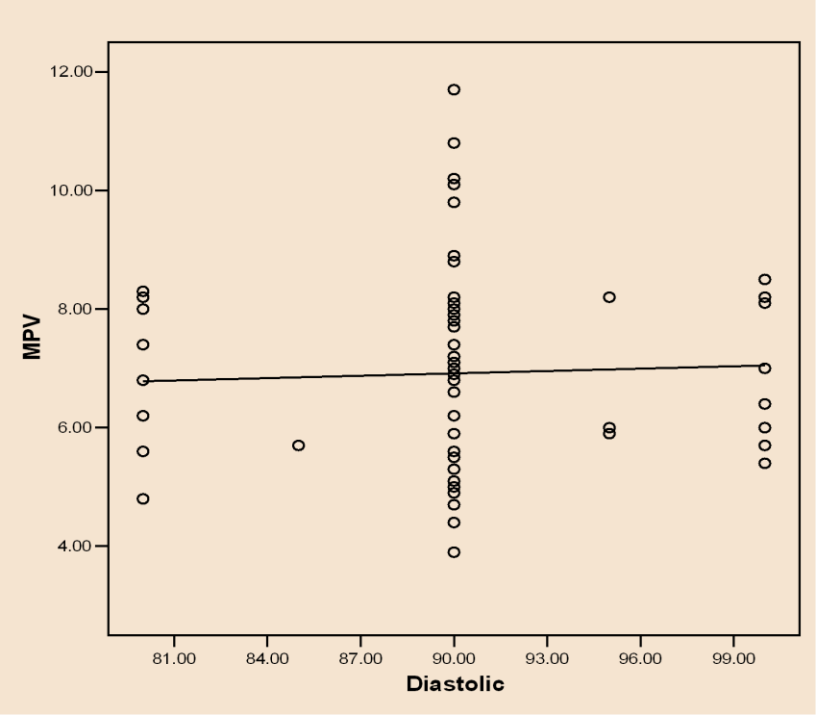

Fig. (3): Positive significant correlation between diastolic and MPV in severe group.

.

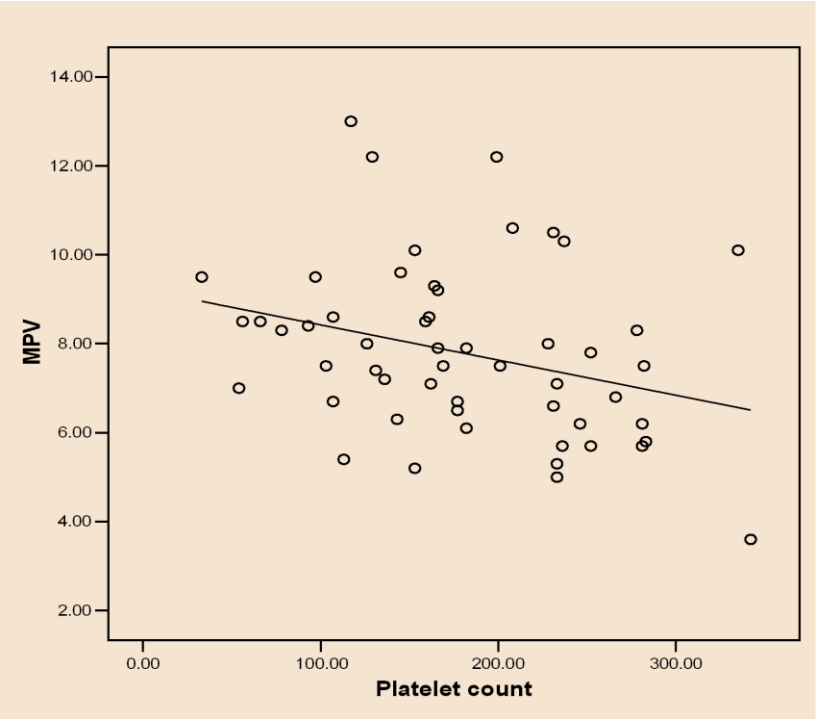

Fig. (4): Negative significant correlation between platelet count and MPV in severe group.

Table (7): Correlation Study between MPV and the other studied parameters in control using Pearson correlation coefficient test.

Parameter	MPV					
	At GA 31wks		At GA 34wks		At GA 37wks	
	r	p-value	r	p-value	r	p-value
Age (year)	0.206	0.085	0.216	0.089	0.211	0.087
Systolic	0.161	0.139	0.169	0.146	0.165	0.142
Diastolic	0.198	0.113	0.208	0.119	0.203	0.116
Alb	0.159	0.148	0.167	0.155	0.163	0.152
Hb (g/L)	0.211	0.111	0.222	0.117	0.216	0.114
HT (%)	0.215	0.071	0.226	0.075	0.220	0.073
Platelet count (104/µL)	0.102	0.175	0.107	0.184	0.105	0.179
AST (U/L 37°C)	0.121	0.151	0.127	0.159	0.124	0.155
ALT (U/L 37°C)	0.166	0.116	0.174	0.122	0.170	0.119
Creatinine (mg/dL)	0.171	0.123	0.180	0.129	0.175	0.126

r: Pearson Correlation Coefficient

No correlation and significant between MPV with other studied parameters in control group.

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. PE can result in eclampsia when convulsions develop or manifest as the hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome. Both eclampsia and HELLP syndrome are known to be associated with severe complications such as cerebral hemorrhage, lung edema, renal insufficiency and liver hemorrhage [(9)].

Some researchers as **Makuyana *et al.*** [(10)] **and Marshall *et al.*** [(11)] found no difference in PLTs count and MPV values between preeclamptics and controls, whereas others **Jaremo *et al.*** [(8)] **Redman**[(12)]**, and Ahmed *et al.*** [(13)] 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. It is known that different anticoagulation substances used in measurement of MPV can yield different results up to

40% [7]. This can explain the differences between studies but the result of our study still remains solid since all measurements were done with the same anticoagulant and same system.

Redman[12] found that the platelet count decreased in early evolution of preeclampsia, and suggested that it could be predictor of preeclampsia. Beta thromboglobulin (BTG) is found in alpha granules of platelets. An increase BTG has been reported to precede the clinical development of preeclampsia by four weeks.

The current study was a case control study that was conducted in order to establish a reference data representing the value of measurement of mean platelet volume (MPV) to evaluate whether this parameter has a prognostic significance in determining the severity of preeclampsia and compare these levels with those in normotensive pregnant women in the third trimester of pregnancy.

Our study correlates with **Ceyhan *et al.* [7].** 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 and severely pre-eclamptic patients were compared with controls. As a result, we observed no prognostic significance of CBC, platelet count and MPV on the presence and/or severity of pre-eclamptic condition.

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

Makuyana *et al.* [10] observed no significant difference in the hematological parameters, hemoglobin, WBC, red blood cell, mean cell volume and platelet count in 38 preeclamptic and 72 normal women. These results are similar to the results we obtained in our study except there was significant difference in platelet count.

Neiger *et al.* [14] reported that the platelet counts in 67 pre-eclamptic women were lower when compared with 71 control cases. **Jaremo *et al.*** [8] 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.

Fischer *et al.*[15] suggested that high values in MPV are useful in differentiating severe preeclamptic cases from normal pregnancy. In our study, no differences were seen in terms of MPV values between severe pre-eclamptic cases and normal pregnancies taken as the control group. **Duse *et al.*** [16] expressed that MPV/platelet count ratio reflects platelet consumption and could be used as an indicator of poor maternal progress in preeclamptic cases. Yet, **Diacovo *et al.*** [17] stated that platelet number and MPV are not the determinants of clinical progress in their study involving 336 women. MPV is measured by clinical hematology analyzers using sodium citrate as the anticoagulant. Measurement in EDTA can be unreliable as MPV increases significantly in a time-dependent manner [18].

In our study 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. In general hospital practice, in CBC measurements, generally EDTA is used as anticoagulant. Furthermore, different technologies for measuring the MPV give different results. For example, Beckman–Coulter systems employ impedance technology and derive the MPV from the fitted lognormal platelet curve. Bayer instruments use laser-based light scatter measurements at two angles; the platelet histogram is derived from measurements of high angle light scatter, and the MPV is calculated as the mode of the measured platelet volumes. Studies comparing results from these instruments showed MPV differences of up to 40%. As a result, we have found in our study that CBC, and MPV values do not have any determining effect on the presence of preeclampsia but the platelet count showed difference. In the literature, papers that include conflicting results especially on MPV values are available, yet this fact is most probably due to the differences between the methods and/or equipment used.

CONCLUSION

As a result, we have found in our study 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 occurrence of preeclampsia. So the use of MPV should not be used as a prognostic factor for determination of preeclampsia.

REFERENCES

1. **Sibai BM, Caritis S and Hauth J (2003)**: What we have learned about preeclampsia. Semin Perinatol., 27:239-246.
2. **Cunningham FG, Gant NE, Leveno KJ *et al.* (2005)**: Hypertensive disorders in pregnancy. In Williams Obstetrics, 22nd ed., New York, Mcgraw- Hill.
3. **Chun Lam, Lim KH and Karumanchi SA (2005)**: Circulating angiogenic factors in pathogenesis and prediction of preeclampsia. Hypertension, 46 (5): 1077-85.
4. **Anderson GD and Sibai BM (1996):** Hypertension in pregnancy, in Gabbe S, Niebyl J, Simpson J (eds): Obstetrics Normal and Problem Pregnancies. New York, NY, Churchill Livingstone.
5. **Caughy, AB, Stotland NE and Washington E (2005) :** Maternal ethnicity, Paternal ethnicity, Parental ethnic discordance : Predictors of preeclampsia. Obstet Gynecol., 16: 106-156.
6. **Nadar S and Lip GY (2004)**: Platelet activation in the hypertensive disorders of pregnancy. Expert Opin Investig Drugs, 13 (5):523–9.

7. **Ceyhan T, Beyan C, Baster I *et al.* (2006)**: The effect of preeclampsia on complete blood count, platelet count and mean platelet volume. Ann Hematol., 85:320- 322.
8. **Jaremo P, Lindahl TL, Lennmarken C *et al.* (2000):** The use of platelet density and volume measurements to estimate the severity of preeclampsia. Eur J Clin Invest., 30:1113-1118.
9. **O'Connell S, Impeduglia T, Hessler K *et al.* (2008)**: Autologous platelet – rich fibrin matrix as cell therapy in healing of chronic lower-extremity ulcers. Wound Rep Reg., 16:749-756.
10. **Makuyana D, Mahomed K, Shukusho FD *et al.* (2002):** Liver and Kidney function tests in normal and preeclamptic gestation. A comparison with non geststional reference values. Cent Afr J Med., 48:55-59.
11. **Marshall A, Lichman W, Enrest B *et al.* (2005)**: Williams hematology, mean platelet volume reference range, clinical evaluation of patient. https://accessmedicine.mhmedical.com/content.aspx?bookid=358&sectionid=39835823
12. **Redman CW (1999):** Platelets and beginning of preeclampsia. N Engl J Med., 323:478-480.
13. **Ahmed Y, Van Iddeking B, Paul C *et al.* (1993):** Retrospective analysis of platelet numbers and volumes in normal pregnancy and in preeclampsia. Br J Obstet Gynaecol., 100:216-220.
14. **Neiger R, Contag SA and Coustan DR (1992)**: Preeclampsia effect on platelet count. AmJ Perinatol., 9:378-380.
15. **Fischer T, Schneider MP, Schobel HP *et al.* (2000)**: Vascular reactivity in patients with preeclampsia and HELLP syndrome. Am J Obstet Gynecol., 183 (6) :1489-94.
16. **Duse LM, Carvalho MG and Getliffe K (2007):** Increased circulating thrombomodulin levels in preeclampsia. Clin Chim Acta., 5 (10):1016-1023.
17. **Diacovo TG (1996):** Platelet – mediated lymphocyte delivery to high endothelial venules. Science, 273: 252-255.
18. **Bath PM and Butterworth RJ (1996) :** Platelet size : measurement, physiology and vascular disease. Blood Coagul Fibrinolysis, 7:157-1661.