Platelet Indices and Serum Uric Acid in Preeclampsia Prediction and its Severity in Primigravida

Ali Al-Shabrawy Ali, Hend Salah Abdo, Mohamed Al –Housseiny Alkodousy and Noha Moustafa Esmaeel

Obstetrics & Gynaecology Department, Faculty of Medicine, Zagazig University, Egypt.

**Corresponding author: Noha Moustafa Esmaeel,
Email:nohamostafaobgyn@gmail.com**

Abstract

Background: Preeclampsia (PE) is a multisystem disorder that complicates 5%–10% of pregnancies and constitutes a major source of morbidity and mortality worldwide. Primigravidae are high risk group for development of PE and are almost four times as likely to develop the disease with its adversematernal and fetal outcome. Our study aimed to evaluate the platelet indices and serum uric acid and their significance in prediction of preeclampsia and assessment of its severity. Patients and methods: this study was included 108 primigravida at gestatational age (24-28) weeks at the first visit and divided into: group (1): including 54 pregnant women with pregnancy induced hypertension (PIH) of varying severity; group (2): including 54 normotensive pregnant women. Full history taking, complete clinical examination and laboratory investigations including platelet indices (platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW) and serum uric acid was estimated. Results: Age was distributed as 27.07±3.44 and 27.0±3.45 respectively between Preeclampsia group and Control group without significant difference and GA at start of the study was 26.01±1.49 and 26.11±1.40 respectively with no significant difference. SBP and DBP were significantly higher among Preeclampsia group. There was no significant difference between cases or control. PLT was significantly higher among control at all times but MPV and PDW were significantly higher among cases at al times. Low APGAR1, preterm, CS delivery type and PPH were significantly associated with preeclampsia group. Conclusion: The estimation of platelet indices and serum uric acid can be considered as an early, economical and rapid procedure for assessment of Preeclampsia in pregnant women. Thus platelet indices can have a significant impact on maternal and perinatal outcome.

Keywords: Preeclampsia; Platelet Indices; Primigravida

INTRODUCTION:

Pre-eclampsia is a pregnancy-specific syndrome of unknown etiology, manifested by hypertension, proteinuria, edema and activation of coagulation cascade, which resolve rapidly following delivery. It is a late manifestation of a multifactorial, multisystem

disease, that is initiated very early in pregnancy **(1)**. The disease progresses from a pre-clinical stage, through symptomless clinical phase in the second half of pregnancy, to several possible crises of which are eclampsia, cerebral hemorrhage, retinal detachment, and disseminated intravascular coagulopathy **(2)**.

The incidence of preeclampsia is remarkably variable and the effect of parity was striking on the incidence of preeclampsia. The incidence of hypertensive disorders due to pregnancy in healthy nulliparous women has been carefully studied and that incidence of preeclampsia is 7.6 % **(3)**. The signs and symptoms of pre-eclampsia are usually apparent relatively late in pregnancy (late second to early third trimester). However the disorder results from abnormal interaction between fetal and maternal tissues much earlier in pregnancy, between 8-18 weeks gestation **(4)**.

The early diagnosis of pre-eclampsia remains one of the most important functions of antenatal care. More than 100 clinical, biophysical and biochemical tests have been recommended to predict the future development of the disease. Results of pooled data suggest that non-of these tests are sufficiently sensitive or specific for use as a screening test in clinical practice. So, there is an urgent need to identify a marker of early pre-eclampsia **(5)**.

The ideal test for prediction should be simple, easy to perform early in pregnancy and be reproducible and non-invasive with high sensitivity and a high positive predictive value. Several tests (clinical, biophysical and biochemical) have been reported in the world literature's to predict the future development of preeclampsia **(6)**.

Mean platelet volume (MPV) and platelet distribution width (PDW) are significantly higher in patients with preeclampsia compared to those with normal pregnancy.The physiological changes in pregnancy normally show decreasing platelet count with increasing gestational age. However in patients with pregnancy induced hypertension (PIH) the effect on platelets is increased significantly leading to manycomplications in mother and fetus. PIH continues to be a major cause of maternal mortality and morbidity, preterm deliveries and abruption **(7)**. Increased platelet activation and markers of activation antedate clinical diagnosis of preeclampsia by weeks to months. These findings led to know that endothelial cell injury or dysfunction might be an early pathophysiological event in the development of preeclampsia **(8)**.

The aim of this study is evaluation of platelet indices and serum uric acid and their significance in prediction of preeclampsia and assessment of its severity.

PATIENTS AND METHODS:

A Prospective Cohort study was included 108 Primigravid women and was carried out in obstetrics and gynecology outpatient clinic, Zagazig University hospital at

September 2019 to May 2020. Approval to conduct the study will be obtained from IRB, Zagazig university.

Inclusion criteria:
Primigravid women between 18-35 years of age with uncomplicated singleton pregnancy at a gestational age 24-28 week.

Exclusion criteria:
Multiparous women, twin pregnancy, gestational age less than 24 weeek, patients having medical disorders, intrauterine fetal death, women with significant history of hemorrhagic disorder and women with history of a known cause of hypertension prior to pregnancy or history of drug intake which would affect platelet count or bone marrow.

Pregnant women included in the study will be divided into 2 groups: Group 1: (cases) including 54 pregnant women with pregnancy induced hypertension (PIH) of varying severity (systolic blood pressure of 140 mm Hg and above or diastolic blood pressure of 90 mm Hg or above). Group 2: (controls)including 54 normotensive pregnant women.

Investigations:
Platelet indices (platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW) and serum uric acid was estimated. An ultrasonography and Doppler were performed to all women.

Primary assessment: early prediction of preeclampsia by a reliable, safe and cost-effective screening tests.

Secondary assessment: early intervention to decrease preeclampsia severity and decrease its adverse outcome.

All patients will be followed up till delivery. At each scheduled antenatal visit subsequently 29-31 weeks (visit 2), 32-34 weeks (visit 3), 35-37 weeks (visit 4) and 38w- delivery (visit 5) samples was drawn for platelet indices and serum uric acid with measurement of blood pressure, detection of urinary albumin, CBC, Serum uric acid ,obstetric abdominal ultrasonography and doppler.

Statistical analysis:
Data analyzed using SPSS version 20.0. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used as Chi square test (X2) and agreement by Kappa agreement. Differences between quantitative independent groups by t test, correlation by Pearson's correlation or Spearman's. P value was set at <0.05 for significant results &<0.001 for high significant result.

RESULTS:

The present study showed that age was distributed as 27.07±3.44 and 27.0±3.45 respectively between Preeclampsia group and Control group without significant difference and GA at start of the study was 26.01±1.49 and 26.11±1.40 respectively with no significant difference **(Table 1)**. SBP and DBP were significantly higher

among Preeclampsia group **(Figure 1)**. There was no significant difference between cases or control regard any parameters **(Table 2)**. PLT was significantly higher among control at all times but MPV and PDW were significantly higher among cases at al times **(Table 3)**. Low APGAR1, preterm, CS delivery type and PPH were significantly associated with preeclampsia group **(Table 4)**.

Table (1): Age and Gestational age distribution between groups

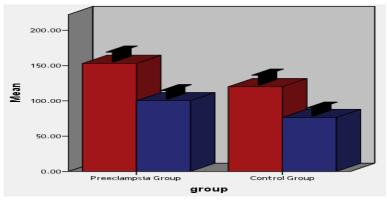|	Preeclampsia group	Control group	t	P
Age	27.07±3.44	27.0±3.45	0.112	0.911
GA	26.01±1.49	26.11±1.40	-0.331	0.741

Figure (1): SBP and DBP distribution between groups.

Table (2): HB and WBCs distribution at different times between studied groups

	Preeclampsia group	Control group	t	P
HB 1st	11.26±1.05	11.08±0.97	0.892	0.375
WBCs 1st	8.31±1.39	8.09±1.41	0.820	0.414
HB 2nd	11.03±1.03	11.18±0.95	-0.791	0.430
WBCs 2nd	7.31±1.39	7.95±1.41	-1.150	0.287
HB 3rd	10.92±0.93	11.13±0.94	-1.845	0.061
WBCs 3rd	6.55±1.47	7.41±1.42	-1.625	0.095
HB 4th	10.97±0.91	11.21±0.94	-1.248	0.215
WBCs 4th	5.93±1.62	6.67±1.68	-1.903	0.058

Table (3): PLT indices distribution at different times between studied groups:

	Preeclampsia group	Control group	t	P
PLT 1st	204.9±26.9	270.64±37.83	-10.404	0.00**
MPV 1st	11.52±1.14	10.21±1.04	6.179	0.00**
PDW 1st	15.11±1.33	12.61±1.44	9.330	0.00**
PLT 2nd	199.35±28.83	278.87±37.96	-12.258	0.00**
MPV 2nd	11.92±1.14	11.12±1.08	3.725	0.00**
PDW 2nd	15.41±1.33	12.41±1.44	11.196	0.00**
PLT 3rd	189.11±26.81	287.5±37.45	-15.696	0.00**
MPV 3rd	12.33±1.36	11.84±1.17	2.008	0.046*
PDW 3rd	15.94±1.27	12.29±1.45	13.886	0.00**
PLT 4th	186.64±26.77	287.61±41.93	-13.882	0.00**
MPV 4th	12.47±1.31	11.91±1.44	2.005	0.048*
PDW 4th	15.99±1.07	12.32±1.63	12.850	0.00**

Table 4: Maternal and baby outcome distribution between studied groups

			Preeclampsia group	Control group	t/ X^2	P
APGAR1			5.72±0.89	6.68±1.06	-4.993	0.00**
APGAR2			7.88±0.95	9.18±0.84	-1.723	0.088
Term	Preterm	N	9	4		
		%	17.6%	7.0%		
	Full-term	N	42	53	5.11	0.026*
		%	82.4%	93.0%		
Delivery	CS	N	41	30		
		%	80.4%	52.6%		
	VD	N	10	27	9.83	0.003*
		%	19.6%	47.4%		
PPH	No	N	40	53		
		%	78.5%	93.0%		
	Yes	N	11	4	5.84	0.022*
		%	21.5%	7.0%		
Stillbirth	No	N	51	57		
		%	100.0%	100.0%		
	Yes	N	0	0	0.0	1.00
		%	0.0%	0.0%		
NICU	No	N	41	51		
		%	80.4%	89.5%		

	Yes	**N**	**10**	**6**	**2.31**	**0.12**
		%	**19.6%**	**10.5%**		
IUGR	**No**	**N**	**47**	**55**		
		%	**92.2%**	**96.5%**		
	Yes	**N**	**4**	**2**	**2.07**	**0.15**
		%	**7.8%**	**3.5%**		
Total		**N**	**51**	**57**		
		%	**100.0%**	**100.0%**		

DISCUSSION:

A variety of biochemical and biophysical markers, based primarily on rationales implicated in the pathology and pathophysiology of hypertensive disorders due to pregnancy, have been proposed for the purpose of predicting the development of preeclampsia later in pregnancy. Investigators have attempted to identify early markers of faulty placentation, reduced placental perfusion, endothelial cell dysufnction, and activation of coagulation. Virtually all these attempts have resulted in testing strategies with low sensitivity for the prediction of preeclampsia **(1)**.

The present study was included 108 primigravida at gestatational age (24-28) weeks This study aims to observe the serial changes in various platelet indices and serum uric acid during the course of normal pregnancy ,compare them in hypertensive pregnancies and find the correlation of changes in platelet indices in hypertensive pregnancies with increasing severity of PE also to determine the potential value of platelet indices predicting the onset and severity of PE possibly for early intervention.

In the present study: Age was distribution as 27.07±3.44 and 27.0±3.45 respectively between Preeclampsia group and Control group without significant difference and GA at start of the study was 26.01±1.49 and 26.11±1.40 respectively with no significant difference. These in agreement with the study done by **Tesfa (9)** reported who characteristics of preeclamptic and normotensive pregnant women are presented . While a significant difference was not found among the mean ages of mild PE, severe PE and control groups (p>0.05), gestational age of preeclamptic patients was found to be lower than the normotensive pregnant women (p< 0.05). These are agreed with **Nair and Savitha (10)** compared the systolic and diastolic blood pressure of the groups and difference was statistically significant.

Our study showed no significant difference between preeclampsia group and control group regard any parameters through visits. These agree with **Nasiri (11)** stated the levels of hemoglobin can be used to predict preeclampsia and monitoring the pregnant women and its regular measure in 3 trimesters help us to identify women at risk for preeclampsia.

Our study showed PLT was significantly higher among control at all times but MPV and PDW were significantly higher among preeclampsia group at al times. These agree with **Sitotaw et al., (12)** reported 33mPE, 30sPE and 63 healthy pregnant

women revealed an increase in MPV, PDW, P-LCR with the advancement of PE. Whereas, PC decreased with the severity of the disease. Also, **Singh and Varma (13)** found a significant relationship between platelet indices and severity of PIH, increase in MPV and PDW and decrease in plateletcrit along with an increase in severity of PIH. Platelet indices estimation, especially PDW and plateletcrit, should be assessed to evaluate the severity of preeclampsia and eclampsia along with platelet count, instead of relying on platelet count alone, as normal platelet count does not rule out a severe disease. Serial detection of the PDW and plateletcrit throughout pregnancy can be used to assess the severity of the PE.

In accordance with the present study **Dadhich et al., (14)** evaluated the association between changes in platelet indices (plateletcount, MPV, PDW) and development of PE. Two hundred pregnantwomen at 20 to 24 weeks of gestation with singleton pregnancy andnormal blood pressure were enrolled. At monthly intervals CBC(complete blood count) was done from 20 to 24 weeks till 40 weeks and 7days after delivery. Platelet count decreased significantly in patients withPE compared to normal pregnant patients (19.4% vs 7.4%). MPV increased significantly in PE patients (44.5% vs 9.22%). Increase in PDW was observed significantly in patients with PE (47.19% vs 29.4%).

Also, **Al Sheeha et al., (15)** performed a case-control study via comparing platelet indices, platelet count (PC), (MPV), (PDW), and PC to MPV ratio in women with PE compared with healthy controls. Sixty PE women were the cases and an equal number of healthy pregnant women were the controls. Sixteen and 44 of the cases had severe and mild PE, respectively. There was no significant difference in PDW and MPV between the PE and control women. Both PC and PC to MPV ratios were significantly lower in the women with PE compared with the controls. There was no significant difference in the PC, PDW, MPV, and PC to MPV ratio when women with mild and severe PE were compared.

Our results showed uric acid was significantly higher among preeclampsia group at all times. These agree with **Meena et al., (16)** suggested preeclampsia is associated with rise in serum uric acid level, the higher the blood pressure in preeclampsia the higher the rise in serum uric acid level, increased gravidity is not associated with hyperuricemia, fetal outcome is worsen with rise in serum uric acid level.

Our results showed APGAR 1&2, preterm, CS mode, PPH , Stillbirth and baby mortality were significantly associated with severe cases. These are agreed with **Nair and Savitha (10)** concluded a significant increase in perinatal mortality in severe preeclamptic patients with hyperuricemia,more so in preterm group, compared to control group. The mean gestational age of delivery decreased significantly with increasing MSUA concentration in preeclamptic patients. Perinatal morbidity is significantly increased in preeclamptic patients with hyperuricemia compared to control group. Also, **Meena et al., (16)** reported fetal outcome is worsen with rise in

serum uric acid level, maternal outcome also worsen with rise in serum uric acid level. In spite of the many hidden facts about this disease improved perinatal outcome, maternal wellbeing can be achieved to a satisfactory level by establishing specialized referral centers fully equipped with facilities for proper neonatal and maternal handling, antenatally, during labour and and further follow up afterwards.

Conclusion:

The estimation of platelet indices and serum uric acid can be considered as an early, economical and rapid procedure for assessment of Preeclampsia in pregnant women. Thus platelet indices can have a significant impact on maternal and perinatal outcome.

No conflict of interest.

REFERENCES:

1- Savaj S, Vaziri N. An overview of recent advances in pathogenesis and diagnosis of preeclampsia. Iran J Kidney Dis. 2012;6:334–338.
2- Macdonald-Wallis C, Lawlor DA, Fraser A, May M, Nelson SM, Tilling K. Blood pressure change in normotensive, gestational hypertensive, preeclamptic, and essential hypertensive pregnancies. Hypertension. 2012; 59:1241–1248.
3- Xiong, Xu, William D, et al. History of abortion, preterm and term birth and risk of preeclampsia: A population-based study. Am Journal of Obstetric and Gynecology 2002;187(4):1013-18.
4- Diaz Sonia Hernandez, Toh Sengwee, et al. Risk of preeclampsiain first and subsequent pregnancies: A prospective cohort study. BMJ 2009;338:b2255.
5- Leduc Line, Wheeler, James M, et al. Coagulation profile in severe preeclampsia, Obstetrics and Gynecology 1992;79(1):14-18.
6- Joshi Kale Vrundra, Sapre Shaila. Lowered platelet count: Aprognostic index in preeclampsia. J Obstet Gynaecol Ind 2004;54(3):235-36.
7- Doğan, K., Guraslan, H., Senturk, M. B., Helvacioglu, C., İdil, S., & Ekin, M. (2015). Can platelet count and platelet indices predict the risk and the prognosis of preeclampsia?. Hypertension in pregnancy, 34(4), 434-442.
8- Vamseedhar Annam, Srinivasa K, Santhosh K Yatnatti, Suresh DR. Evaluation of platelet indices and platelet counts and their significance in preeclampsia and eclampsia. Int J Biol Med Res, 2011;2(1):425-28.
9- Tesfa, E., Nibret, E., Gizaw, S. T., Zenebe, Y., Mekonnen, Z., Assefa, S., ... & Munshea, A. (2020). Prevalence and determinants of hypertensive disorders of pregnancy in Ethiopia: a systematic review and meta-analysis. PloS one, 15(9), e0239048.
10- Nair, A., & Savitha, C. (2017). Estimation of serum uric acid as an indicator of severity of preeclampsia and perinatal outcome. The journal of obstetrics and gynecology of India, 67(2), 109-118.

11- **Nasiri M, Faghihzadeh S, Majd HA, Zayeri F, Kariman N and Ardebili NS (2015):** Longitudinal discriminant analysis of hemoglobin level for predicting preeclampsia. Iranian Red Crescent Medical Journal, 17(3):1-7.

12- Sitotaw, C., Asrie, F., & Melku, M. (2018). Evaluation of platelet and white cell parameters among pregnant women with Preeclampsia in Gondar, Northwest Ethiopia: A comparative cross-sectional study. Pregnancy hypertension, 13, 242-247.

13- Singh, A., & Varma, R. (2018). Role of platelet distribution width (PDW) and plateletcrit in the assessment of nonthrombocytopenic preeclampsia and eclampsia. The Journal of Obstetrics and Gynecology of India, 68(4), 289-293.

14- Dadhich, S., Agrawal, S., Soni, M., Choudhary, R., Jain, R., Sharma, S., & Saini, S. L. (2012). Predictive value of platelet indices in development of preeclampsia. J SAFOG, 4(1), 17-21.

15- AlSheeha MA, Alaboudi RS, Alghasham MA, Iqbal J and Adam I (2016): Platelet count and platelet indices in women with preeclampsia. Vascular Health and Risk Management, 12:477-480.

16- Meena, R., Pachori, P., & Chaudhary, S. (2019). Level of serum uric acid in patients with preeclampsia compared to controls and its relation to feto-maternal outcome.