Original Article

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Platelet Counts and Indices Are Altered in Pre-Eclampsia

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ABSTRACT

Background: Endothelial damage and activation of platelets leading to their increased consumption and increase inproduction of young platelets by bone marrow is one of the common pathophysiology of pre-eclampsia. Thus, fall in platelet count and altered platelet Indices may have diagnostic as well as prognostic value in pre-eclampsia.AIM: To evaluate platelet count and platelet indices between pre-eclamptic and normotensive women and to assess their association with severity of pre-eclampsia.

Methods: Platelet counts and indices were estimated in 30 normotensive and 30 PE women at20-24 weeks pregnancy and were repeated after every4 weeks.

Results: Mean platelet counts, platelet volume, platelet distribution width, and platelet large cell ratio between pre-eclampsia and normotensive women were significantly altered in PE women and were associated with severity of PE.This alteration of platelet count and indices occurred even before the rise of BP.

Conclusion: All the platelet indices were found to be reliable markers of PE and were found to be increased much earlier than BP. MPV had the maximum sensitivity (96.7%) and specificity (93.3%) and was the most reliable biomarker.

Keywords: *Pre-eclampsia, Thrombocytopenia, Platelet Indices, MPV, Platelet Distribution Width, P-LCR*

Introduction

Incidence of pre-eclampsia is about 5-8%. Pre-eclampsia (PE) is a pregnancy specific multisystem disease of unknown etiology and there is a constant search for better markers to predict and prognosticate the disease. Though the exact pathogenesis of PE is unknown, placental vascular under-perfusion, maternal endothelial damage and increased vascular permeability are thought to contribute to the pathophysiology of the disease. The injured endothelium leads to activation of platelets. The activated platelets contact the coagulation system and lead to increase consumption and compensatory bone marrow production of young platelets which are larger in size resulting in increased platelet indices such as MPV (mean platelet volume), PDW (platelet distribution width) and P-LCR (platelet large cell ratio). Increase consumption during low grade intravascular coagulation leads to a lower platelet count (PC) in PE.

It is likely that platelet count and indices may have both diagnostic as well as prognostic values in pre-eclampsia. Changes in these markers can be observed at an earlier stage than rise of BP and are directly proportional to progressive rise in blood pressure. Moreover, quantification of these platelet indices on automated analyzer is cost effective, simple and rapid method for assessment of severity of pre-eclampsia. Therefore, in this study, we have compared platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (P-LCR) in women who developed pre-eclamptic pregnancies with those who remained normotensive, to establish the role of platelet count and indices to predict pre-eclampsia and its severity,

Aim and Objectives

To evaluate and compare platelet counts and platelet indices (mean platelet volume, platelet distribution width, and platelet large cell ratio) between pre-eclamptic women and normotensive women.

To evaluate association of platelet counts and indices with severity of pre-eclampsia.

Material and Methods

It was a case control study conducted in the Deptt. of Obst. Gynae at Hindu Rao Hospital and associated NDMC Medical College, Delhi, India. Thirty normotensive women (control group) and 30 women with PE (study group) were enrolled at 20-24 weeks as per the inclusion and exclusion criteria and considered for the study. The study was approved by institutional ethical committee.

Inclusion Criteria: Control group - normotensive women

Study group - pre-eclamptic women [1]

Exclusion Criteria: Pregnant women with anemia, hemorrhage or bleeding disorder, gestational diabetes, hepatic/renal/cardiovascular disorder, abruption, DIC, multiple pregnancy, IUD, eclampsia, women on anti-coagulants

Detailed history including demographic details was recorded. Examination included general physical examination, systemic examination and obstetric examination. BP was recorded. All routine antenatal investigations, platelet counts and indices were estimated in 2cc venous blood sample collected in EDTA tube using automated hematology analyzer SYSMEX KX 21 at the time of enrolment. BP measurement and urine examination for proteinuria, platelet counts and indices were repeated at every 4-weekly visit. All the data was recorded in a pre-designed performa and was analyzed statistically using software SPSS 20. P value < 0.05 was taken as significant.

Results

Mean age was comparable in both the groups. Primipara women were significantly more in study group. Mean BMI, baseline mean systolic and diastolic BP were significantly high in study group. All initial lab parameters (except serum bilirubin) were significantly raised in the PE group (Table1).

Though significant increase of systolic and diastolic BP was observed from 28 weeks till term in the study group compared to controls, but preeclamptic range of BP was seen from 32 weeks of gestation onwards in the study group (Table 2). Mean platelet count was found to be significantly low and all the platelet indices were found to be significantly high in the PE group at all gestational ages (Table 3,4) and in severe PE (Table 5). Though all the platelet indices had a quite high sensitivity and specificity, yet mean platelet volume had the highest AUC with maximum sensitivity and specificity for predicting PE (Table 6).

Table 1: Baseline data and Lab Investigations.

Parameter	Study group (n=30)	Control group (n=30)	P value
Age mean years	25.13±3.79	24.66±3.34	0.164
Mean BMI kg/m^2	21. 896±2 2.7	19.58 ± 3.3	0.005
Mean systolic BP mm Hg	109.38±0.707	145.98±10.65	0.0001
Mean diastolic BP mm Hg	72.59±6.49	91.74±6.01	0.0004
S. Bilirubin mg/dL	0.22±0.17	0.19±0.90	0.344
SGOT units/L	32.57±6.01	22.67±5.95	0.0002
SGPT units/L	36.57±6.37	24.13±3.99	0.0005
Alkaline phosphatase IU/L	223.50±37.77	169.63±69.84	0.001
S. creatinine mg/dL	0.97±0.26	0.83±0.05	0.006
Blood urea mg/dL	30.70±7.03	27.43±5.33	0.048
S. uric acid mg/dL	6.4±1.31	4.3±1.32	0.009

P value <0.05 is significant

Table 2: Mean Blood Pressure according to gestational period.

Gestational age	Study group	Control group	P value
24-28 weeks Systolic (mmHg) Diastolic (mmHg)	(N=30) 114.60±16.78 76.40±9.86	(N=30) 108.20 ± 10.28 75.8 ± 7.58	 0.08 0.792
28.1 -32 weeks Systolic (mmHg) Diastolic (mmHg)	(N=29) 127.03 ±11.66 84.90 ± 8.22	(N=30) 106.4 ±10.51 73.27 ± 9.90	 0.0001 0.0001
32.1-36 weeks Systolic (mmHg) Diastolic (mmHg)	(N=29) 141.03± 14.08 96.90± 7.34	(N=30) 108.73± 10.58 72.20 ± 9.15	 0.0001 0.0001
36.1-40 weeks Systolic(mmHg) Diastolic (mmHg)	(N=25) 162.00 ±18.15) 107.28 ± 5.97	(N=30) 113.87 ±12.06 73.80 ± 10.22	 0.0001 0.0001

P value <0.05 is significant

Table 3: Mean Platelet counts and indices.

Parameter	Study group	Control group	P value
Platelet count mean 10^3/cu. mm	166.66±31.67	216.56±19.42	0.001
MPV (fl)	10.98±1.06	8.71±0.34	0.0001
Mean PDW (fl)	15.14±2.19	12.11±0.69	0.0001
Mean P-LCR	25.29±4.73	16.56±4.12	0.0001

P value <0.05 is significant

Table 4: Mean Platelet count and indices according to gestational age.

Gestation age	Parameter	Study group	Control group	P value
24-28 weeks		N=30	N=30	
	Platelet count (10^3/cu. mm)	195.30±34.77	221.27 ± 31.15	0.0035
	MPV (fl)	9.29 ± 1.201	8.55 ± 0.594	0.003
	Mean PDW (fl)	13.46 ± 2.35	11.46 ± 1.03	0.0001
	Mean P-LCR	19.97 ± 4.954	16.99± 2.87	0.005
28-32 weeks		N=29	N=30	
	Platelet count (10^3/cu. mm)	187.59±25.52	211.97±19.70	0.0001
	MPV (fl)	10.652 ± 1.412	8.713 ± 0.731	0.0001
	Mean PDW (fl)	14.21 ± 1.42	11.93 ± 1.13	0.0001
	Mean P-LCR	21.886 ± 4.84	17.83±2.15	0.0001
32-36 weeks		N=29	N=30	
	Platelet count (10^3/cu. mm)	164.03±37.14	216.50 ± 32.38	0.0001
	MPV (fl)	11.310 ± 1.453	8.783 ± 0.893	0.0001
	Mean PDW (fl)	15.21 ± 1.55	12.35 ±1.055	0.0001
	Mean P-LCR	27.83 ± 5.731	19.63 ± 1.13	0.0001
36-40 weeks		N=25	N=25	
	Platelet count	124.40±35.88	216.63± 22.32	0.0001
	MPV (fl)	12.724 ± 1.141	8.853 ± 0.693	0.0001
	Mean PDW (fl)	17.012 ± 2.82	12.73 ± 1.22	0.0001
	Mean P-LCR	31.292 ± 5.423	19.95 ±1.608	0.0001

Table 5: Association of platelet counts and indices with severity of PE.

Parameter	Mild PE (n=23)	Severe PE (n=7)	P value
Platelet counts mean (10^3/cu. mm)	176.49±21.2	134.36±40.08	0.001
MPV (fl)	10.62±0.86	12.14±0.86	0.0003
PDW mean (fl)	14.38±0.98	17.60±3.21	0.0002
P-LCR mean	23.90±3.58	29.85±5.46	0.002

P value <0.05 is significant

Table 6: AUC, sensitivity and specificity of platelet indices to predict PE.

Platelet indices	Cut off value	AUC	Sensitivity	Specificity
MPV (fl)	9.3	0.993	96.70 %	93.30 %
PDW mean (fl)	13.17	0.984	93.40 %	93.30 %
P-LCR mean	20.43	0.928	86.70 %	83.30 %

Discussion

In this study we have analyzed platelet counts and platelet indices in normotensive women (n=30) and in women who developed pre-eclampsia (n=30), enrolled at 20-24 weeks gestation. These parameters were repeated at every 4 weeks till term /delivery.

A significant increase in systolic and diastolic blood pressure was noticed from 28- 32 weeks of gestation (Table 2). Though the rise of BP of PE range (≥140/90 mm of Hg) was observed much later ie. at 32 weeks and onwards, yet, significant decrease in platelet count and increase in platelet indices were seen much earlier ie. at 24-28 weeks of gestational age (Table 2,4) or 6-8 weeks before rise in blood pressure. These changes in platelet count and indices remained significant at all gestational ages (Table 4). Thus, these parameters can be considered an earlier marker of developing pre-eclampsia and can be used for prediction of PE.

Thrombocytopenia is the most common hematological abnormality observed in preeclampsia and it may be due to consumption of platelets during abnormal activation of the coagulation system. A significant low platelet count (p value 0.001) was observed in our study in women with pre-eclampsia (mean 166.66 ± 31.67) compared to normotensive women (mean 216.56 ± 19.42) (Table 3). Analysis of platelet counts according to gestational period revealed a significant decrease of platelets from 24 weeks onwards in PE group compared to normotensive group (Table 4). Similar results in PE women about platelet counts were obtained by Gupta A et al, Al Sheeha et al, Gupta A et al, Annam V et al, in their studies [2-5] We also, observed a significant thrombocytopenia in severe pre-eclampsia women compared to those with mild (Table 5), which was in corroboration with studies by Gupta A et al, Gupta A et al, Somya et al [2,4,6]. However, Ceyhan and coworkers, found no significant difference between the platelet count in pre-eclamptic and normotensive pregnant control women [7].

Thrombocytopenia occurs in up to 50% of women with preeclampsia, and its severity parallels that of the underlying preeclampsia [8]. PC emerges as a good candidate for severe PE diagnosis [8]. These severe preeclamptic women had significantly higher MPV, but only some develop thrombocytopenia. This might be explained by a quick platelet turnover in PE, which is the result of continuous platelet consumption in the peripheral blood followed by continuous production in the bone marrow [9]. Importantly, thrombocytopenia may occasionally precede other manifestations of preeclampsia, and thus preeclampsia must be considered in the differential diagnosis of isolated thrombocytopenia developing in the late second or third trimester [8], though gestational thrombocytopenia, also known as incidental thrombocytopenia of pregnancy, is the most common cause of thrombocytopenia in pregnant women, accounting for approximately 75% of all cases [8]. Thus, platelet count, though an important parameter in PE, cannot be used alone as a definitive marker of pre-eclampsia.

Amongst all the platelet indices, MPV was found to have maximum sensitivity (96.7%) and specificity (93.3%) and maximum AUC of 0.993 compared to other platelet indices (Table 6) which corroborates observations by Tesfey et al [10]. As in our study, various other studies have also shown MPV to be a promising biomarker for differentiating pre-eclampsia and normotensive pregnancy [10,11,12], which remained significantly high at all gestational ages [13], similar to our study.

Ceyhan et al, AlSheeha et al and Altinbas et al found no significant difference between MPV in preeclamptic and normotensive pregnant control women [7,3,14] in contrast to our study where MPV was found to be the most reliable marker in preeclampsia.

PDW was found to be the 2ndmost reliable biomarker for pre-eclampsia with AUC of 0.984, sensitivity of 93.4%, and specificity equal to MPV (93.3%) in our study. Even in nonthrombocytopenic PE, PDW has been considered a very important parameter, and a reflection of ongoing platelet activation [15]. Thalor et al, Sitotaw C, Karateke et al also found a significant high MPV, PDW, P-LCR in PE women and rise of these indices correlated positively with mean blood pressure [16,17,18]. Thus, evaluation of these parameters as supportive clinical markers in the assessment of severity of pre-eclampsia may assist its management.

Regarding severity of pre-eclampsia, a significant low platelet count and significant increase in platelet indices were seen in women who developed severe pre-eclampsia compared to those who had mild pre-eclampsia at all gestational ages in our study. Therefore, platelet count and platelet indices can be used as prognostic markers to assess the severity of preeclampsia. Estimation of these indices are cost-effective and easily available and can be done during routine blood investigations.

Conclusion

In our study, all the platelet indices were found to be reliable markers of PE, which were found to be increased much earlier than the onset of hypertension emphasizing their utility in prediction and early diagnosis of PE. MPV was the most reliable biomarker and PDW was found to be the

2nd reliable biomarker for pre-eclampsia. Also, a significant association of rise in all the platelet indices in severe PE than in mild can be helpful to prognosticate the disease. Evaluation of these markers can be done easily and should be included in the work-up of at risk women for predicting /early diagnosing PE and for predicting its severity, thus predicting its prognosis. Thus, platelet indices are useful markers for early diagnosis and risk stratification for optimum feto-maternal outcome in a PE woman.

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Competing Interests
None

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