Original Article

Role of platelet count and mean platelet volume and red cell distribution width in the prediction of preeclampsia in early pregnancy

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Abstract

Introduction: Mean platelet volume (MPV), platelet count (PC), and red cell distribution width (RDW) are various blood indices that play important role in preeclampsia. **This study aimed** to evaluate the role of MPV, RDW, and PC for the prediction of preeclampsia in the early second trimester of pregnancy and to observe its correlation with disease severity. **Material and Methods:** A prospective case-control study was conducted for 1 year in the Department of Obstetrics and Gynecology. A total of 543 healthy pregnant women were recruited, after obtaining informed consent and ethical clearance and followed till 6 weeks postpartum, 43 were lost to follow-up. Out of 500 women, nonsevere preeclampsia (NSPE) occurred in 16 women and severe preeclampsia (SPE) in 34 women. Around 51 healthy normotensive pregnant women were recruited after systematic randomization from the same cohort, who had not developed the disease, served as controls. NSPE and SPE were defined as per ACOG 2013b guideline. MPV, RDW, and PC were measured two times by the Siemens Advia analyzer; the first samples were withdrawn at the time of enrolment and the next sample was taken after the development of the disease, and both samples were analyzed. **Results:** MPV was increased with the severity of preeclampsia, diagnostic accuracy was 69.4%, at a cutoff value of ≥9.05 fl and MPV discriminated controls and NSPE with 50.0% sensitivity and 82.4% specificity. To discriminate between controls and SPE, diagnostic accuracy was 74.6% at a cutoff value of ≥9.05 fl, with a sensitivity of 50%. For control versus SPE, MPCs at the cutoff value of ≥2.085 lac/mm^3 had sensitivity 52.9% and specificity 66.7%, and diagnostic accuracy 61.2%. For RDW NSPE, at a cutoff value of ≥11.5%, it discriminated against controls and NSPE with 85.3% sensitivity and 49.0% specificity. **Conclusion:** NSPE, MPV, RDW, and PCs had good discriminatory value with the severity of the disease.

Keywords: Preeclampsia, prediction, mean platelet volume, red cell distribution width

Introduction

Preeclampsia is a major cause of maternal and neonatal morbidity and mortality worldwide, hence to improve the outcome in preeclampsia, early prediction of the disease is necessary to identify high-risk women.

The incidence of hypertensive disorder of pregnancy (HDP) in India is 5.38%[1] while the incidence of preeclampsia and eclampsia ranges from 5–15% and 1.5%, respectively.[2] Maternal and perinatal deaths have been reported in 5.5% and 37.5% of deliveries, respectively.[3] HDP comprises preeclampsia and eclampsia. Platelet count (PC), mean platelet volume (MPV),

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lymphocyte, and red cell distribution width (RDW) all are inflammatory markers, and almost every physician has routinely advised complete blood count in women having minor illnesses during pregnancy, which could be readily obtained on laboratory evaluation of blood samples. Association of preeclampsia with inflammation makes use of these parameters for prediction of disease severity. These blood indices are potentially a low cost and good predictive tool in the assessment of preeclampsia in a clinical setting. Though the previous studies show an association between hematological parameters and preeclampsia, this association between the severity of disease and hematological parameters in women having preeclampsia still requires further exploration.

The word "low-grade inflammation" is the condition, characterized by a slight increase in immune cell count, the rise of acute-phase reactant, and pro-inflammatory protein levels in healthy individuals before the evidence of disease.[4,5] Identification of systemic inflammation can be possible by the use of a variety of biochemical and hematological markers. Recent studies indicating the measuring blood cell subtype ratio, such as the neutrophil to lymphocyte (NLR) and platelet to lymphocyte (PLR) ratios, might provide prognostic and diagnostic clues to those diseases related to chronic low-grade inflammation.[4,6] Other platelet indices, including MPV and PC are other noninvasive biomarkers that can be tested easily and at low cost to predict the disease and assess the severity of the disease.[7] Measuring blood cell subtype ratios, such as RDW, MPV, PC might provide prognostic and diagnostic clues to diseases. It is thought that HDP is a state of low-grade inflammation. Thus this study was carried out to establish the role of various blood indices MPV, PC, and RDW for prediction of preeclampsia in the early second trimester (13–20 weeks) of pregnancy and also to observe its correlation with disease severity.

Material and Methods

This prospective case-control study was carried out at the Department of Obstetrics and Gynecology in collaboration with the Department of Medicine for 1 year. After taking informed written consent, a total of 543 pregnant women were recruited who had attended the antenatal OPD of Queen Mary's hospital at 13–20 weeks of gestation. This study was approved by the institutional ethics committee (Ref. Code- 75th ECM II-CB Thesis/P27, No. 9115/Ethical / R. Cell-15 dated 02.01.2016). Women who were not willing to take part in the study, multifetal pregnancy, ruptured membrane, chronic hypertension, diabetes mellitus, chronic liver disease, chronic kidney disease, collagen vascular diseases, major fetal anomaly, cardiovascular disease, history of smoking, and alcoholism were excluded from the study. A total of 43 pregnant women were lost to follow-up, so excluded from the analysis. Nearly 500 pregnant women were followed till 6 weeks postpartum. Out of 500 women, 16 women developed severe preeclampsia (SPE) (Group 3), 34 women developed nonsevere preeclampsia (NSPE) (Group 2), and 51 were healthy normotensive pregnant women (Group 1) from the same recruited group of women after systematic randomization were considered as controls. The diagnosis of NSPE and SPE was defined as per the American College of Obstetricians and Gynecologists (ACOG) 2013b guidelines. In our study, various hematological parameters, MPV, RDW, and PC were measured twice with the use of a fully automated three-stage analyzer, Siemens Advia; first at the time of recruitment at 13–20 weeks of gestation and the second time after the development of disease (preeclampsia and eclampsia).

Modified ACOG 2013b, diagnostic criteria for NSPE is defined as BP >140/90 mmHg after 20 weeks of pregnancy in previously normotensive women with proteinuria ≥300 mg/24 h or protein/creatinine ratio ≥0.3 with mildly elevated liver enzymes.

SPE is defined as BP >160/110 mmHg with PCs <100,000/μL, creatinine >1.1 mg/dL, or doubling of baseline, serum glutamic oxaloacetic transaminase/serum glutamic pyruvic transaminase (SGOT/SGPT) levels twice than normal with headaches, visual disturbances, and when this preeclampsia is associated with convulsions then it is called eclampsia.

Statistical analysis

All statistical analyses were done on the retrieved data in SPSS, version 17 software (Statistical Program for Social Sciences). The variables were stated as mean ± standard deviation. For comparison of these data between the patient and controls group, analysis of variance test (ANOVA tests) was used and *P* value <0.05 was considered as statistically significant. Assessment of diagnostic accuracy was done by receiver operating characteristic curve analysis (ROC).

Results

The demographic profile of these women (three groups) at the presentation was similar except for body mass index (BMI). The mean BMI of Group 3 was significantly ($P < 0.024$) different and higher (-25.13 ± 0.96) than Group 1 (22.10 ± 0.52) [Table 1].

Most of the parameters showed an increasing trend with increasing severity of the disease i.e., levels of clinical and biochemical parameters were highest in SPE as compared to NSPE and lowest in controls [Table 2].

The ROC curve analysis showed a significant diagnostic accuracy of MPV at 69.4% and at a cutoff value of ≥9.05 fl, with (AUC = 0.643, $P = 0.002$) it discriminated the controls and NSPE cases with 50.0% sensitivity and 82.4% specificity 0.641, positive predictive value (65.4%) and negative predictive value (71.2%) [Figure 1].

Further ROC analysis of MPV showed significant diagnostic accuracy (74.6%) at (AUC = 0.636, $P = 0.009$) when evaluated between controls and SPE, at a cutoff value of ≥9.05 fl, it discriminated the two groups with a sensitivity of 50% and

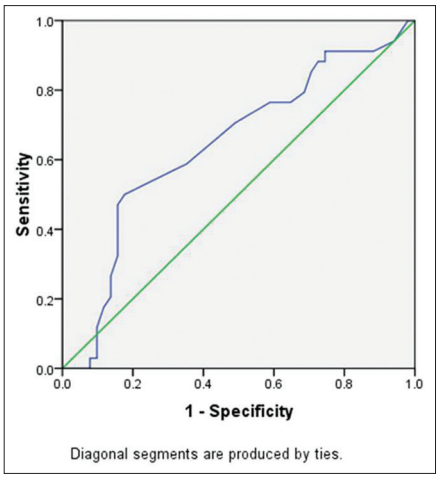

Figure 1: Receiver operating curve (ROC) of MPV. (Group 1 vs Group 2). *(At a cutoff value of ≥9.05 fl mean platelet volume had sensitivity 50% and 82.4% specificity at 95% CI and area under curves 0.641, and diagnostic accuracy 69.4%, controls vs nonsevere preeclampsia)*

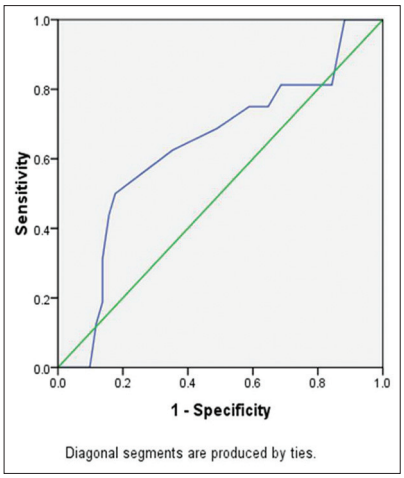

Figure 2: ROC curve analysis of MPV (Group 1 vs Group 3). *(At a cutoff value of ≥9.05 fl mean platelet volume had sensitivity 50% and 82.4% specificity at 95% CI and area under curves 0.636, and diagnostic accuracy 74.6%, controls vs severe preeclampsia)*

Table 1: Demographic characteristics (Mean±SD) of three groups

Demographic characteristics	Group 1 (*n*=51) (%)	Group 2 (*n*=34) (%)	Group 3 (*n*=16) (%)	F/χ^2	*P*
Age (years)	25.90±0.57	25.56±0.58	25.13±0.97	0.27	0.765
BMI (kg/m²)	22.10±0.52	23.06±0.69	25.13±0.96	3.86	0.024
SES:					
Upper	3 (5.9)	2 (5.9)	1 (6.3)	0.67	0.955
Middle	33 (64.7)	23 (67.6)	9 (56.3)		
Lower	15 (29.4)	9 (26.5)	6 (37.5)		
Parity:					
PRIMI	20 (39.2)	21 (61.8)	11 (68.8)	10.58	0.227
GRAVIDA 2	13 (25.5)	7 (20.6)	1 (6.3)		
GRAVIDA 3	11 (21.6)	5 (14.7)	1 (6.3)		
GRAVIDA 4	5 (9.8)	1 (2.9)	2 (12.5)		
GRAVIDA 5	2 (3.9)	0 (0.0)	1 (6.3)		

specificity of 82.4%, positive predictive value (47.1%) and negative predictive value (84.0%) [Figure 2].

As per ROC curve analysis PCs had significant diagnostic accuracy, 61.2% with (AUC = 0.564, *P* = 0.072) and at a cutoff value of ≥2.0855 lac/mm3, it discriminated the controls and NSPE cases with 52.9% sensitivity and 66.7% specificity, positive predictive value (51.4%) and negative predictive value (68.0%) [Figure 3].

Further platelets count also showed significant diagnostic accuracy (62.7%) (AUC = 0.520, *P* = 0.229) when evaluated between controls and SPE at a cutoff value of ≥2.085 it discriminated the two groups with a sensitivity of 50% and specificity of 66.7%, positive predictive value (32.4%) and negative predictive value (81.0%) [Figure 4].

The ROC curve analysis showed RDW, at a cut-off value of ≥11.5%, (AUC = 0.751, *P* = 0.001) it discriminated the controls and NSPE cases with 85.3% sensitivity and 49.0% specificity [Figure 5].

When evaluated between NSPE and SPE, at a cut-off value of ≥12.8 (AUC = 0.808, *P* = 0.009), RDW discriminated the two groups with a sensitivity of 93.8% and specificity of 44.1% [Figure 6].

Discussion

HDP is the most common complication of pregnancy. Reported maternal and perinatal mortality in HDP is 5.5% and 37.5% of total deliveries, respectively.[3] The incidence of preeclampsia is 5% of all pregnancies and it is a multisystem disorder accompanied by proteinuria.[8] It is a major contributor to maternal and neonatal morbidity and mortality. It can complicate up to 10% of pregnancies in developing countries.[9]

The exact pathophysiology of preeclampsia is unknown but it is thought that generalized endothelial dysfunction with the systemic inflammatory response (SIRS) is the final common pathway that leads to maternal signs of preeclampsia.[10] The evidence suggests that the placenta is the causal factor for the development of this disorder. There are many pro-angiogenic and antiangiogenic substances involved in placental vascular development.[11] Various authors have described the role of these substances for diagnosis of preeclampsia and results are encouraging, yet till date, no marker has been proven highly efficacious for the same.

In our study, most of the women were primigravida; 39.2% in the control group, 61.8% in NSPE, and 68.8% in SPE. In similar reports by Levine *et al.*, 80.8% preeclampsia women and 79.2% controls were primigravidas.[12]

In our study, the gestational age range of the three groups was similar at enrolment. EL-Said *et al.* (21.73 ± 1.55 weeks

Table 2: Clinical parameter levels (Mean±SD) of three groups at recruitment

Clinical parameter	Group 1 (*n*=51) (%)	Group 2 (*n*=34) (%)	Group 3 (*n*=16) (%)	F/χ^2	*P*
SBP (mmHg)	117.63±1.36	117.38±1.48	117.25±2.01	0.01	0.986
DBP (mmHg)	80.24±1.15	80.68±1.19	80.19±2.26	0.04	0.964
Hb (mg/dL)	10.85±0.14	10.65±0.15	10.46±0.26	1.09	0.340
N1	71.08±0.86	77.38±1.70	89.31±3.39	25.72	<0.001
L1	24.33±0.71	23.94±0.78	22.00±1.10	1.45	0.240
Platelet count (lac/mm^3)	2.06±0.08	1.95±0.11	1.81±0.14	0.96	0.388
MPV (fl)	8.89±0.18	9.14±0.17	9.37±0.22	1.15	0.322
RDW (%)	12.96±0.51	14.73±0.80	15.05±0.46	3.11	0.049

SBP - Systolic Blood Pressure, Diastolic Blood Pressure, Hb - hemoglobin, HDP - Hypertensive disorders of pregnancy, N - Neutrophil, L - Lymphocyte, MPV - Mean platelet volume, RDW - Red cells distribution width

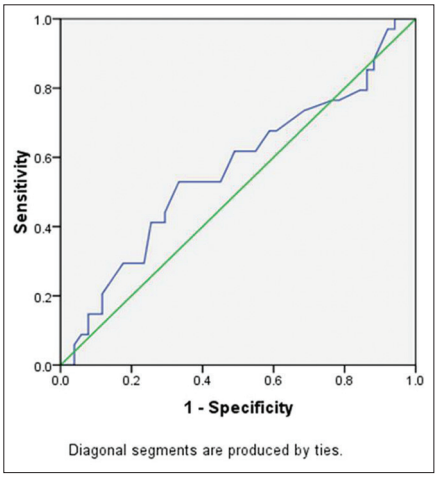

Figure 3: Receiver operative curve (ROC) of platelets count (Group 1 vs Group 2). *(At a cutoff value of ≥2.085 lac/mm^3 mean platelet count had sensitivity 52.9% and 66.7% specificity at 95% CI and area under curves 0.564, and diagnostic accuracy 61.2%, controls vs severe preeclampsia)*

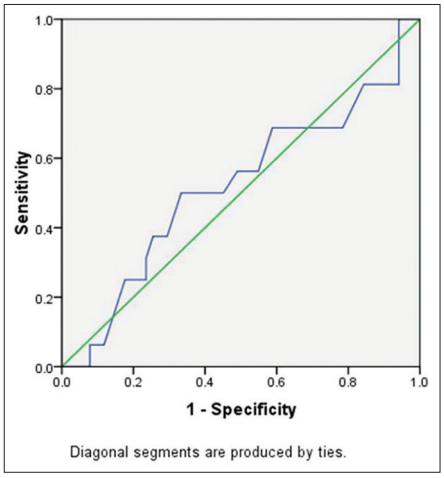

Figure 4: ROC curve of platelets count (Group 1 vs Group 3). *(At a cutoff value of ≥2.085 lac/mm^3 mean platelet count had sensitivity 50% and 66.7% specificity at 95% CI and area under curves 0.520, and diagnostic accuracy 62.7%, controls vs severe preeclampsia)*

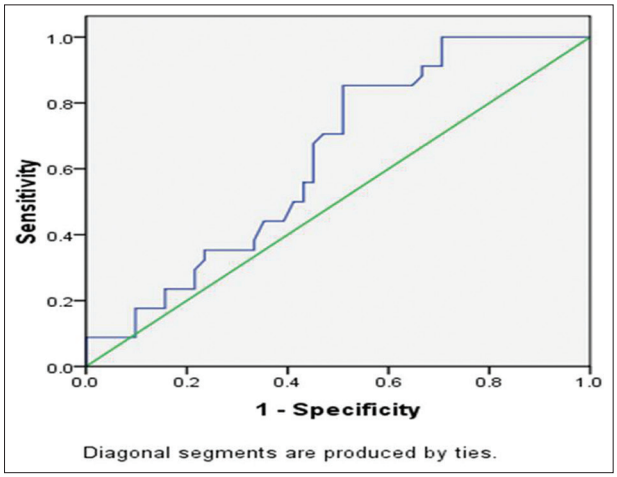

Figure 5: ROC Curve of RDW (Group 1 vs Group 2). *(At a cutoff value of ≥11.5% Red cell distribution width (RDW) had sensitivity 85.3% and 49.0% specificity at 95% CI and area under curves 0.751, controls vs severe preeclampsia)*

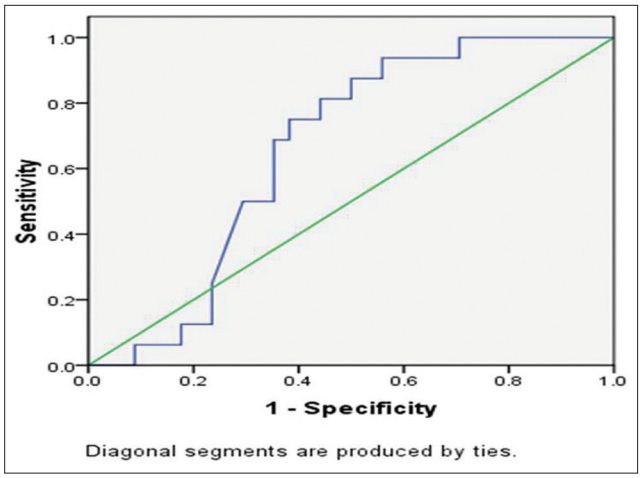

Figure 6: ROC Curve of RDW (Group 2 vs Group 3). *(At a cutoff value of ≥12.8% Red cell distribution width (RDW) had sensitivity 93.8% and 44.1% specificity at 95% CI and area under curves 0.808 nonsevere preeclampsia vs severe preeclampsia)*

Vs 21.97 ± 1.77 weeks) and Gaber *et al.* (15.4 ± 1.03 weeks vs 15.6 ± 1.5 weeks) reported almost similar gestation age between cases and controls.[13,14]

Increased platelet volume resulted in increased activity of the platelets because dense granules more in number present over large size platelets, these are metabolically and enzymatically

more active as compared to small size platelets.[15] In our study, the specificity of MPV was better than the mean PC. So it can be used for discrimination of preeclampsia from the controls.

In our study, PC decreased significantly in NSPE and SPE when women developed the disease as compared to their control value ($P < 0.01$). Elhawary *et al.* found a significant difference in PCs between controls ($190.333 \pm 13.819 \times 10^3$) and preeclampsia group ($167.667 \pm 38.539 \times 10^3$) ($P = 0.014$).[9] Various studies reported increased MPV and decreased PCs in hypertension and preeclampsia.[16,17] One meta-analysis reported significantly increased MPV in women with preeclampsia as compared to women without preeclampsia.[18] Another author reported significantly increased MPV in SPE as compared to NSPE.[19] A recent study reported that increased MPV is associated with the development of severe hypertension.[20]

In the current study increased MPV and decreased PC might be due to the rapid turnover of the platelets. One study reported no significant difference in MPV and PC in hypertensive pregnant women as compared to normotensive.[21] Makuyana *et al.* reported no significant difference concerning hematological parameters.[22]

A recent study done by Duan *et al.* reported no significant difference in PCs and MPV with the presence of preeclampsia or with the severity of preeclampsia.[23] In our study, in preeclampsia patients, RDW had a significant difference from controls, and our findings matched with one meta-analysis which concluded that the RDW level is higher in SPE as compared to NSPE.[24] In our study, RDW predicts NSPE and SPE with 85.3% and 93.8% sensitivity, specificity 49%, and 44.1%, respectively. Thus we can say it might be used for the prediction of poor prognosis in preeclampsia.

Though there are several mechanisms responsible for the development of preeclampsia, the important one is the inflammatory process which might increase RDW levels through iron metabolism impairment, and this might be responsible for disruption of response to erythropoietin, and which further results in shortening of the life of RBC. This might explain the increasing RDW in preeclampsia.[25]

In preeclampsia endothelial damage probably responsible for abnormalities within the coagulation system, this might enhance the platelet activity which could be responsible for pathogenesis. MPV and PDW increased with the progression of the disease. When the author compared these indices with the severity of disease significant elevation was observed with SPE as compared to mild preeclampsia.[26] In our study, RDW values were higher in pregnant patients who later developed preeclampsia. RDW can be used for screening purposes because it has low specificity and high sensitivity. MPV at a cutoff value of ≥9.05 fl discriminated between controls versus non-SPE and severe versus NSPE and its specificity is better in both conditions.

Conclusion

The diagnostic accuracy of MPV, PCs, and RDW is quite good. The above laboratory markers might be useful in the prediction of preeclampsia. MPV, RDW, and PCs are fast and low cost easily available test at every primary health center, so they can be used routinely in every pregnant woman.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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