Evaluation of Platelet Count and Platelet Indices and Their Significance in Pre-Eclampsia

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Abstract: Preeclampsia is a common medical complication of pregnancy. It is one of the leading cause of maternal and foetal morbidity and mortality. Several studies have demonstrated the relationship between platelet indices and preeclampsia with variable results. To evaluate the relationship between platelet count and platelet indices and their significance in preeclampsia. To study the platelet count and indices in preeclampsia and compare to normal pregnant women and to study their role in diagnosis of severity of preeclampsia. This study was a prospective case control study done over a period of two years in a tertiary care Hospital and Research centre, Pune. Study comprised of 200 pregnant women of which 100 were normotensive and 100 had preeclampsia (mild to moderate grade:89, severe grade:11). Blood samples were analysed for platelet count and indices in both groups and results were compared. Platelet count decreased and platelet indices like Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Platelet Large Cell Ratio (P-LCR) were significantly increased in preeclampsia as compared to normotensive women. Platelet count decreased and platelet indices increased in severe grade of preeclampsia as compared to mild-moderate grade however there was no statistical significant difference. Platelet count and indices can be used for early detection of preeclampsia. Rise in platelet indices suggests increased severity of preeclampsia which alerts physician for close management of the patient.
Keywords: Preeclampsia, Platelet indices, Platelet count, Hypertension.

INTRODUCTION

Hypertensive disorders are common in pregnancies. This along with haemorrhage and infection significantly increases the maternal morbidity and mortality [1]. Preeclampsia is characterised by hypertension with blood pressure >140/90 mm of Hg, proteinuria > 0.3 gm/dl, oedema and other symptoms. It may begin as early as twentieth week of gestation and last for 6 weeks after delivery [2]. Preeclampsia affects approximately 6-8% of pregnancies [3]. Preeclampsia disorder has higher incidence among nulliparous women [4]. It is commonly responsible for thrombocytopenia occurring in 2nd and 3rd trimesters. Around 20-50 % of women with preeclampsia develops thrombocytopenia. Occasionally thrombocytopenia is the only manifestation of severity of preeclampsia [5]. It is a multisystem disease. Alteration in coagulation, fibrinolysis, platelet and vascular endothelial function are believed to play an important role in the pathogenesis of preeclampsia. Pathogenesis of preeclampsia is complex. There is interaction of numerous genetic, immunologic and environmental factors. The first stage is asymptomatic. It is characterised by abnormal placental development

during the first trimester which further leads to placental insufficiency and release of excessive amount of placental material (two endogenous antiangiogenic proteins of placental origin–circulating soluble FMS like tyrosine kinase and soluble endoglin) into maternal circulation. Second stage is symptomatic, where pregnant woman develops characteristic hypertension, renal dysfunction, significant proteinuria and thrombocytopenia [6]. In preeclampsia there is abnormal platelet endothelium interaction with excessive platelet consumption. Storage of platelet in the areas with endothelial damage is the cause of thrombocytopenia [7]. The degree of thrombocytopenia increases with severity of disease. Lower the platelet count, associated with increase in incidence of maternal foetal morbidity and mortality [8]. Platelet count and platelet indices like mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR) are valuable markers for thromboembolic disease. There are multiple studies on platelet count and MPV in the preeclampsia with varied results [9]. Very little is known about the newer platelet indices like PDW and PLCR. Considering the role of platelets during course of disease as well as alteration in coagulation, we aimed to evaluate various parameters of platelets and their role in severity of preeclampsia and establish the statistical significance of the results including newer indices.

MATERIALS AND METHODS

A case control study was conducted in the department of Pathology, Dr. D. Y. Patil Medical College over a period of 18 months. The ethical committee approval was taken and informed consent was obtained from all participants. The study was conducted on 100 cases of pregnant women diagnosed with preeclampsia and 100 cases of normotensive pregnant women. Preeclamptic group was further divided into mild to moderate and severe grade.

Inclusion criteria's were as follows:
- Normal Pregnant Females. (Healthy normotensive women with a singleton gestation and a normal obstetric history)
- Pregnancy with mild to moderate preeclampsia (B.P.>140/90 mm Hg on more than two readings taken 6 hr apart after 20 weeks gestation with proteinuria > 0.3 g/24hr)
- Pregnancy with severe preeclampsia (B.P.>160/110 mm Hg, severe proteinuria >2g/24hr with manifestations of multiple organ damage, for example, headache, pulmonary oedema, oliguria or even foetal growth restriction)

Women with HB level <10 g/dl, pre-existing renal disease, insulin dependent diabetes, asthma requiring steroid treatment, chronic hepatitis, patients on anticoagulant drug, and diagnosed cases of known thrombocytopenia like ITP (Idiopathic thrombocytopenic purpura) and HELLP syndrome were excluded from study.

Detailed medical and gynaecological history was taken. Blood pressure was recorded and urine routine was done. 3 ml of venous blood was collected in EDTA vacutainer tube under aseptic precautions. Sample was tested for complete blood count including Hb, RBC and RBC indices, total and differential WBC, platelet count and platelet indices (MPV, PDW, P-LCR) with fully automated Sysmex haematology analyzer. MPV denotes the average volume of platelets. PDW represents the degree of heterogeneity of the platelets and PLCR implies the fraction of platelets which are larger in size. In normal subjects, MPV has inverse, nonlinear relation with platelet count while platelet volume heterogeneity i.e. PDW has a direct, nonlinear relation with MPV. The statistical tests used on our samples were mean, standard deviation, chi square, unpaired t –test. The p-value < 0.05 was accepted as significant.

RESULTS

A total of 100 clinically diagnosed patients of preeclampsia were enrolled for the present study. This study group was divided in mild to moderate i.e. non severe type and severe preeclampsia respectively. Results were compared with normal 100 healthy pregnant women who were taken as control.

In our study, maximum numbers of pregnant women were in the age group of 21-25 years in both control group (n=41) and study group (mild to moderate grade of preeclampsia n=39). In severe preeclampsia group, maximum patients were in the age group of 26-30 years (n=4). The mean age of control group was 25.98±4.24 years ranging from 19 to 37 years. The mean age of the study group was 26.11±4.21 years with range of 19 to 36 years. In this study they were equally distributed.

The mean gestation age in control group was 34.34±2.95 and in study group was 34.29±3.06. There was no significant difference between the mean gestation age in the control and study group.

There were 53 primigravida and 47 multigravida cases in study group. Primigravida had more risk of developing preeclampsia than multigravida. But p value was not statistically significant in our study.

The mean systolic blood pressure in control group, mild to moderate eclampsia and severe eclampsia group were 124.44+/- 7.93, 146.17+/- 3.29, 164.18+/-1.89 mm of Hg respectively. The mean diastolic blood pressure in control group, mild to moderate eclampsia and severe eclampsia group were

78.24+/-4, 94.02+/- 2.91, 94.02+/-2.59 mm of Hg respectively.

Comparison of platelet count and platelet indices in control group and study group is shown in Table 1. In preeclampsia there was decrease in platelet count as compared to normotensive pregnant women but it was not statistically significant. However, platelet indices increased in preeclampsia as compared to normal pregnant women and it showed statistically significant relationship.

Comparison of platelet indices based on severity of preeclampsia in study group is shown in Table 2. In severe grade, the mean platelet count was on lower side than mild to moderate grade, however, it was not statistically significant. Though platelet indices like MPV, PDW and PLCR are on higher side in severe grade of preeclampsia as compared to mild to moderate grade, it was also statistically insignificant.

Table-1: Comparison of platelet count and platelet indices in control group and study group

Parameter	Control Group A (n=100)		Study Group B (n=100)		P Value
	Mean	SD	Mean	SD	
PLT count in lakh/mm^3	1.89	0.52	1.73	0.67	0.072
MPV (fl)	8.62	1.38	10.98	1.99	<0.0001
PDW	14.53	1.71	15.88	2.88	<0.0001
PLCR (%)	21.19	5.84	35.08	13.02	<0.0001

Table-2: Platelet parameters according to the severity of preeclampsia

Parameter	Severity of preeclampsia				P Value
	Mild to moderate (n=89)		Severe (n=11)		
	Mean	SD	Mean	SD	
PLT count in lakh/mm^3	1.75	0.67	1.65	0.71	0.64
MPV (fl)	10.87	2.05	11.92	1.08	0.098
PDW (fl)	15.71	2.98	17.19	1.26	0.11
PLCR (%)	34.56	13.42	39.34	8.40	0.25

DISCUSSION

The present prospective study included two groups of pregnant women: the first group included 100 pregnant women with normal blood pressure and second group included 100 pregnant women with preeclampsia (mild to moderate preeclampsia 89 cases and severe preeclampsia 11 cases). In our study the maximum numbers of cases were in age group between 19 to 36 years, with mean age of control group was 25.98±4.24 and study group was 26.11±4.21. Annam et al study also revealed the mean age of 24.57±3.46. This age group is the most common age group for marriage and pregnancy in India. Maternal age more than 35 years is a risk factor for preeclampsia [3].

In the study conducted by Dogru HY *et al*. the mean age was 26.75±5.51 years and mean gestation age was 34.38±1.68 weeks [10]. Our study showed mean gestational age of cases and controls as 34.29±3.06 and 34.34±2.95 weeks respectively.

Dadhich S *et al.* found that 53.84 % of the primgravida develop preeclampsia [11]. In our study 53% of the cases were primigravida. Primigravida have more risk of developing preeclampsia than multigravida [11]. The findings of this study were similar to our study. The association between primiparity and preeclampsia is so widely accepted that it is at the core of several pathophysiological theories. It has been proposed that preeclampsia is consequences of a maternal immune reaction against paternal antigens expressed in the placenta and that reaction might result in defective trophoblastic invasion and subsequent placental dysfunction. The lower risk of preeclampsia among multiparous women has been attributed to desensitization after exposure to paternal antigens in the placenta during previous pregnancies [12].

Our study revealed that there was definite decrease in platelet count in preeclampsia as compared to normotensive group along with statistically significant increase in platelet indices (MPV, PDW, P-LCR). According to severity grading the platelet count was on lower side and platelet indices are on higher side in severe preeclampsia as compared to mild to moderate grade preeclampsia, however it was not statistically significant. The study conducted by various authors Wael ahmed kamel ammar *et al*.[13], Mohapatra *et al*.[7], Annam *et al*. [3], Dogru H. Y. *et al*. [10], Freitas LG *et al*.[14] showed that there was decrease in platelet count in preeclampsia as compared to normal pregnant women. They also found that there was decrease in platelet count in severe grade as compared to mild to moderate grade of preeclampsia.

Santos *et al*.[15], Maryam Zangeneh *et al*.[16], Ceyan T *et al*.[17] observed that there was no statistical significant difference in platelet count between preeclampsia cases and normal pregnant women.

Hemoconcentration is the hallmark of the preeclampsia. This results from generalised vasoconstriction that follows endothelial activation and leakage of plasma into interstitial space because of increased permeability. The certain factors originated from the placenta are secreted into maternal circulation that provokes endothelial cell activation and dysfunction in preeclampsia. The injured endothelium activates the coagulation system that leads to increased consumption of platelets. This leads to increase in platelet aggregation resulting in decreasing in platelet count [3].

The present study revealed gradual increase in MPV from normal pregnant women to mild to moderate and severe preeclampsia. There was statistically significant increase in MPV between cases and controls. However, the rise in MPV was statistically insignificant according to severity of preeclampsia. Few studies have shown significant increases in MPV with severity of preeclampsia. We had low sample size of severe grade preeclampsia which may be the reason for above finding.

There is hyper destruction of platelets in preeclampsia due to shorter platelet half-life leading to release of younger and larger platelets from the megakaryocytes of bone marrow into the peripheral blood in response to thrombocytopenia [5]. This leads to increases in MPV.

PDW and PLCR are the recent platelet indices obtained by cell counter. Few studies in the literature have found that there is increase in these indices in preeclampsia and also with increase in severity [7, 14]. Other studies have reported no statistical significance in PDW in preeclampsia [16]. The present study revealed statistically significant increase in PDW and PLCR in preeclampsia as compared to control group however this was insignificant with increase in severity of preeclampsia. The platelet changes the shape from discoid to spherical during activation resulting in rise in platelet indices like PDW and PLCR which reflects increase in platelet turnover showing larger, younger platelets and normal platelets expressing variation in the size of platelets[3,18,19].

PLCR is calculated in automated blood analyzers using formula PLCC/PLT COUNT where PLCC are the platelet larger than 12 fl and 30 fl. Increase marrow activity releases of younger platelets which are larger resulting in increase in PLCR in preeclampsia.

Increase in MPV, PDW, PLCR may form basis for prediction of severity of preeclampsia in pregnancy which may be related to be associated with bad pregnancy outcome both on mother as well as foetus. We did not have records on the outcome of pregnancy of these cases which was the limitation of our study.

CONCLUSION

Our study revealed that there is significant decrease in platelet count and increase in the platelet indices like MPV, PDW, P-LCR in preeclampsia women as compared to normal pregnant women. According to severity of the disease, platelet counts are on lower side and platelet indices are on higher side but are found to be statistically insignificant. Preeclampsia is the major cause of maternal and perinatal morbidity. We feel that simple, rapid test like hemogram with focus on platelet count and platelet indices can help in early detection of preeclampsia and can also be useful in assessing the severity of preeclampsia.

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