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Haematology

EVALUATION OF ROLE OF PLATELET INDICES IN PREDICTION Of PREECLAMPSIA

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ABSTRACT **Background:** Preeclampsia is a serious pregnancy complication marked by high blood pressure and potential organ damage. Early detection is crucial for preventing complications for both mother and baby. Platelet indices, a part of complete blood count (CBC), has emerged as potential tool in diagnosing and predicting preeclampsia. **Aim and Objectives:** Objectives were to evaluate role of platelet indices (platelet count, mean platelet volume, platelet distribution width, and plateletcrit, in predicting preeclampsia and its severity. **Methods:** Present prospective study included 160 normotensive pregnant women at 20-24 weeks and followed till delivery. Their blood samples were taken and analysed for Platelet indices. Those who developed hypertension were categorized into mild and severe PE and compared with normotensive patients. **Results-** It was observed that, platelet indices Platelet count and Plateletcrit were significantly lower, and Mean platelet volume and Platelet distribution width was significantly higher in PE group in comparison to normotensives. ROC curve analysis observed that MPV and PDW can predict PE cases with high accuracy while accuracy of PC to predict PE was low in our study. **Conclusion:** We conclude that Platelet indices, along with other can serve as efficient tool to predict preeclampsia cases with accuracy.

KEYWORDS : MPV, PDW, Preeclampsia, Platelet count.

INTRODUCTION:

Preeclampsia, a syndrome specific for pregnancy affecting multiple organs. It is characterised by hypertension and proteinuria after 20 weeks of pregnancy. But some women of preeclampsia syndrome lacks feature of proteinuria.

Hypertensive disorder has been observed in 5%-10% of all pregnancies. Preeclampsia is identified in 4-5% of all pregnancies world wide and 16% of maternal deaths are globally attributed to this disorder. [1,2]

The criteria (ACOG 2013) for diagnosis of preeclampsia in pregnancy are, BP more than 140/90 mmHg after, 20 weeks of pregnancy in previously healthy women, and proteinuria more than 300mg per day or urine protein to creatinine ratio ≥ 0.3 or persistent dipstick 1+ or Platelets <100,000/µL, Creatinine level>1.1mg/dL, two folds increase in serum transaminase and neurological symptoms (headache, visual disturbances and convulsions). [1]

Although, exact pathophysiology of pre-eclamptic disorder still remains unclear but, studies suggest, basic pathology is, extensive endothelial injury and vasospasm affecting blood vessels of almost all the organ system.[3]

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Besides this, activation of inflammatory system along with involvement of chemokines and cytokines play important role in preeclampsia (PE). For evaluation of inflammatory status in PE, several biomarkers and components of Complete Blood Count (CBC) were taken into consideration. Studies suggest, these markers are involved in inflammatory and thrombotic process, also, play important role in prognosis .[1,4]

Inadequate perfusion of placenta in preeclampsia causes, endothelial injury that leads to increased thrombocyte aggregation and consumption. This results in activation of coagulation system and simultaneously, enhancing bone marrow synthesis of immature, bigger platelets which reflect as decrease in platelet count and increase in Mean Platelet Volume (MPV) in peripheral circulation of mothers who are destined to develop preeclampsia. A decline in platelet count is noted during progression of disease indicating, worsening of preeclampsia.[5] These phenomenon explain platelet's relationship to preeclampsia. Measurement of platelet count and its functions are done by using various indices like PC, MPV, PDW and plateletcrit, also known as platelet indices.

Compared to conventional techniques, platelet indices may provide an earlier insight into preeclamptic processes since they represent changes in platelet activation, destruction, and production. Studies suggest abnormal platelet indices, particularly increased MPV and PDW, might be associated with preeclampsia development, even before significant blood pressure changes occur.[6] These indices, are affordable, simple to derive, and effective predictive tool in the assessment of preeclampsia.[7]

MATERIAL AND METHOD

A Prospective study conducted to evaluate and predict the role of platelet indices in preeclampsia. Antenatal women in between 20-24 weeks of gestation attending antenatal OPD who fulfilled inclusion criteria and after applying the exclusion criteria, were enrolled for the study.

INCLUSION CRITERIA:

- Pregnant woman in second trimester of pregnancy (20-24 weeks of gestation) with normal blood pressure values
- Singleton pregnancy.

EXCLUSION CRITERIA:

- Pregnant patients with underlying diseases like-- diabetes mellitus, chronic hypertension and known platelet disorders, anticoagulant use, haemolysis, haematological disease, chronic liver disease, chronic kidney disease, cardiovascular disease and collagen vascular disorders.
- Period of gestation less than 20 weeks or period of gestation more than 24 weeks.
- Cases with multiple gestations.

Convenient sampling method is used for the selection of cases, Antenatal women between 20-24 weeks fulfilling the inclusion criteria were enrolled for the study after taking written informed consent and clearance from the ethical committee. Subjects were followed every 6-8 weeks till delivery. On every visit required parameters were noted and blood samples were taken. Total 182 women were enrolled, 22 lost to follow up so study was done on 160 remaining subjects. At the end of study, patients were divided into normotensives, non-severe and severe preeclampsia on the basis of ACOG criterion. Information from pregnant women was collected by preformed questionnaire. Blood samples (2ml blood) were collected under aseptic precautions in fresh EDTA vials and for estimation of platelet indices by performing CBC. Haematological samples were processed on three-part automated haematology counter and result displayed on screen were recorded. Data were collected for neutrophil count, lymphocyte count and various platelet indices PC, MPV, PCT and PDW.

Statistical analysis of compiled data was done by using SPSS statistical software 23.0 Version in the Microsoft Excel 2007. Quantitative data were measured by using mean, standard deviation frequency and percentage. P value <0.05 is considered significant. The intergroup comparison was done using the One way ANOVA. The correlation was established using the Pearson Correlation Coefficient. ROC curve used for Sensitivity and Specificity. Shapiro–Wilk test was used to investigate the distribution of the data and Levene's test to explore the homogeneity of the variables.

RESULTS: 182 patients were selected from 220 antenatal women in 20-24 weeks, who attended obstetrics and gynaecology OPD in one year were screened. Among those, 22 cases were lost to follow up, 160 cases were taken for the study. Out of these, 142 were normotensive (88.75%), 14 non severe preeclampsia (8.75%) and 4 severe preeclampsia (2.50%). Incidence of preeclampsia was 11.75% in our study.

Study showed platelet count (Table 1) and plateletcrit (Table3) decreases significantly with increase in gestational age and severity among normotensive pregnant female non-severe preeclamptic and severe preeclamptic females when followed from 20 to 40 weeks (p value < 0.05) . While MPV(Table 2) and PDW(Table 4) values were increased significantly with gestational age and severity among all three groups .

ROC curve analysis observed Area under curve for platelet count is 0.501(for cut off value of 1.35), which is just above the cutoff point (Fig5a). This indicates that the PC can predict the preeclampsia cases but with less accuracy. AUC for MPV is 0.791(Fig 5b), which is high, this indicates that the MPV can predict the preeclampsia cases with high accuracy (high sensitivity90.50% and 47.70 specificity). AUC for PCT model is 0.368, which is low(Fig5c). This indicates that the PCT cannot predict the preeclampsia cases with accuracy. AUC for PDW is 0.773(Fig5d), which is high, this indicates that the PDW can predict the preeclampsia cases with high accuracy (sensitivity 85.7% and specificity 64.4%).

Table1 Intergroup comparison of platelet count at different weeks of gestation

PLATELET COUNT (lac / mm^3)								
	Normotensive		Non severe Preeclampsia		Severe Preeclampsia		F value	P value
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		
20-24 Weeks a1	2.203	0.096	1.63	0.043	1.27	0.043	392.631	0.001 (Sig)
28-32 Weeks a2	2.129	0.049	1.65	0.051	1.57	0.075	306.350	0.001 (Sig)
36- 40 Weeks a3	1.927	0.032	1.26	0.060	0.76	0.069	571.690	0.001 (Sig)
Difference between a1 –a3	0.276		0.310		0.512			
Overall Mean of all Gestational periods	2.088	0.592	1.51	0.0343	1.20	0.092		

Table 2 Intergroup comparison of MPV at different weeks of gestation

MEAN PLATELET VOLUME (MPV)(fl)								
	Normo tensive		Non-Severe Preeclampsia		Severe Preeclampsia		F value	P value
	Mean	Std dev	Mean	Std dev	Mean	Std Dev		
20-24 Weeks	10.733	1.187	11.55	0.615	12.78	0.613	8.625	0.001 (Sig)
28-32 Weeks	11.059	1.853	11.85	0.562	13.05	0.617	8.147	0.001 (Sig)
36-40 Weeks	11.374	1.321	12.90	0.513	14.87	0.615	26.393	0.001 (Sig)
Difference between a1 –a3	0.641		1.35		2.09			0.001 (Sig)
Overall Mean of all Gestational periods	11.055	1.4536	12.1	0.563	13.566	0.076		

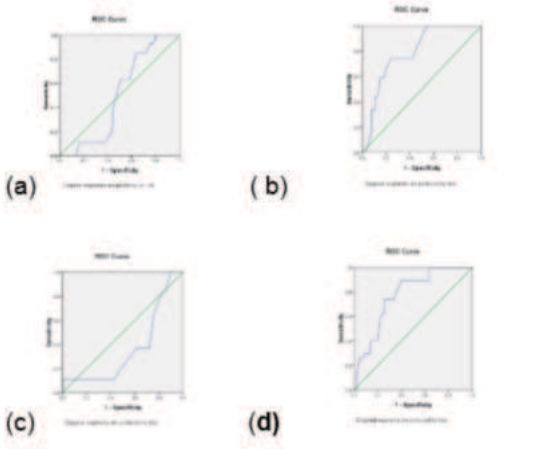
Table 3 Intergroup comparison of plateletcrit at different weeks of gestation.

PLATELETCRIT (PCT) (%)								
	Normotensive		Non severe Preeclampsia		Severe Preeclampsia		F value	P value
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		
20-24 Weeks	0.235	0.060	0.220	0.035	0.180	0.017	4.047	0.012 (Sig)
28-32 Weeks	0.222	0.048	0.205	0.025	0.160	0.005	3.606	0.037 (Sig)
36-40 Weeks	0.213	0.118	0.180	0.031	0.120	0.005	6.524	0.002 (Sig)
Difference between a1 -a3	0.022		0.040		0.060			
Overall Mean of all Gestational periods	0.223	0.075	0.201	0.030	0.153	0.009		

Table 4 Intergroup comparison of PDW at different week of gestation

PLATELET DISTRIBUTION WIDTH (PDW) (%)								
	Normotensive		Non-severe Preeclampsia		Severe Preeclampsia		F value	P value
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev		

20-24 Weeks	14.584	1.750	17.28	1.061	18.90	1.616	25.020	0.001 (Sig)
28-32 Weeks	15.508	2.268	16.21	1.083	17.15	0.057	33.606	0.001 (Sig)
36-40 Weeks	18.250	4.868	22.20	2.899	24.50	0.115	53.122	0.001 (Sig)
Difference between a1 -a3	3.66		4.92		5.60			
Overall Mean of all Gestational periods	16.114	2.962	18.563	1.681	20.18	0.596		



Table/Fig 5 Receiver Operating Characteristic Curve For (a) Platelet Count, (b) MPV, (c)Plateletcrit and (d)PDW

DISCUSSION :

Preeclampsia, or toxaemia of pregnancy one of the major health problems of the pregnancy, which is accountable for high rate of perinatal, maternal morbidity and mortality. Exact pathophysiology of preeclampsia is still not clear but several factors that play important role in its pathophysiology include abnormal trophoblastic invasion of placental vasculature which leads to ischaemic endothelial injury, resulting in increased platelet consumption as well as activation of coagulation system. The usefulness of different platelet indices was studied in previous studies, although reports in this respect are contradictory.

Total 182 selected patients were analysed, out of which 22 were lost to follow up; hence study done on 160 patients. Out of 160 patients, 18 developed preeclampsia giving incidence of preeclampsia 11.75%. Out of 18 preeclamptic patients,14 are of non-severe preeclampsia and 4 were of severe preeclampsia.

Incidence of preeclampsia in our study group was 11.75%, which is comparable to incidence of preeclampsia in hospital practice, which ranges from 5-15%. Dadhich et al[15] showed comparable rate of preeclampsia with incidence of 13% in 200 study population. Sachan et al[7] also showed incidence of 10% out of 500 study population.

Consistent decrease in PC values was statistically more significant in non-severe preeclampsia and severe preeclampsia patients. Significant decrease in PC is directly proportional to the severity and intensity of disease. Also, this decrease in PC preceded the significant rise in BP. These findings align with the known pathophysiology of preeclampsia, where platelet consumption increases due to increased vascular endothelial damage with the advancement of preeclampsia. Similar findings of significant decrease in PC in preeclampsia with increase in gestational age were observed in the study of Dadhich et al[15]. Han et al[14] also detected sharp reduction in PC with gestational age while Thalor et al[12] did not demonstrate any significant decrease in platelet count between preeclampsia and control group.

MPV increases as normal pregnancy advances from 20 to 40 weeks, but the increase is more significant with non-severe preeclampsia and severe preeclampsia with (P<.001). Mean platelet volume (MPV) was higher in patients with severe preeclampsia, suggesting increased platelet activation due to more consumption of platelets resulting in release of bigger and young platelets from bone marrow in circulation. On reviewing the literature, comparable findings were seen in study by Dadhich et al[15]. They also reported significant MPV increase as severity of preeclampsia increases (46.26% in mild preeclampsia and 51.02% in severe preeclampsia). In another study of Cintesun E et al[10] MPV was higher in control group than preeclampsia group.

Table 3 showed steady decrease in PCT with the advancement of pregnancy in severe and non-severe preeclampsia patients in comparison to normotensive patients. Significant differences were observed between the groups ($p < 0.001$ for all comparisons), suggesting that PCT levels may have diagnostic significance in distinguishing the severity of preeclampsia. Moreover these changes can be observed before significant rise in BP. Thalor et al[12] showed similar result with decrease in PCT in preeclampsia patients than control group. While study of Temur et al[9] and Han et al[14] showed no statistically significant difference in plateletcrit values between PE cases and control group.

PDW levels were significantly higher in severe preeclampsia compared to non-severe preeclampsia and normotensive patients across all gestational weeks , indicating that PDW levels increase with the severity of preeclampsia(Table 4). Increase in PDW indicates increased turnover of platelets resulting from increased destruction of platelets and this may be also because of increased bone marrow activity. Other studies Annam et al[16], and Salvi et al[8] showed similar results with increase in PDW with severe preeclampsia than mild preeclampsia and normotensive patients. While Han et al[14] found no significant difference in PDW among three groups , Temur et al[9] reported no statistically significant difference in PDW between PE cases and control group.

Present study also assessed of diagnostic accuracy of these indices were done by receiver operating characteristic curve analysis (ROC). Analysis shows that MPV and PDW can predict preeclampsia cases with high accuracy. PC can predict preeclampsia cases but with less accuracy. Plateletcrit showed low AUC, inability to predict PE cases.. Sachan et al[7], Reddy et al[11] and Han et al[14] also observed that platelet count and MPV are good predictor of preeclampsia.

Our study conclude that Platelet indices, PC, MPV, PDW, PCT along with clinical manifestations can serve as easy and reliable diagnostic, predictive as well as prognostic marker of preeclampsia. They are easily derived with routine CBC count, less invasive, quick and cost-effective biomarkers, which can detect patients who may develop preeclampsia and early intervention can be initiated.

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