A STUDY ON CHANGES IN PLATELET COUNT AND PLATELET INDICES IN PATIENTS WITH PREECLAMPSIA AND ECLAMPSIA: A CASE CONTROL STUDY

Cardiology

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ABSTRACT

Preeclampsia is a hypertensive pregnancy specific multisystem disorder. It requires prompt intervention that may include observation in tertiary care setting and termination of pregnancy either by inducing labour or by caesarian section. To study the variation of platelet counts, platelet indices in preeclampsia and eclampsia Department of Pathology and Gynaecology & Obstetrics Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences from January 2017 to June 2018. **Group I:** Women affected with convulsion and having signs of preeclampsia during pregnancy or within seven days after delivery after ruling out epilepsy or any other convulsive disorder were treated as eclamptic women. **Group II:** Women having BP > 140/90 mmHg and significant proteinuria (>300mg/24hrs) and or edema are treated as preeclampsia. **Group III:** Normotensive women having pregnancy >20 weeks were considered as control group. Total sample size was 66 pregnant women. 22 patients are taken from each group. The platelet indices e.g. MPV, PDW and also PLCR are in consistent relationship with PIH. The higher their values, the greater severity of PIH, from preeclampsia to eclampsia. The estimation of platelet count and indices offer early, simple, rapid assessments of the disease for its severity and the risk of complications. Therefore these tests may be considered as screening tests to be routinely performed in antenatal workup of women with PIH.

KEYWORDS

Platelet Count, Platelet Indices, Preeclampsia And Eclampsia

INTRODUCTION

Everyday approximately 830 women die from preventable causes related to pregnancy and childbirth. 99% of all maternal death occurs in developing countries. Maternal mortality ratio in developing countries in 2015 is 239 per 100,000 live births versus 12 per 100,000 live births in developed countries. Younger and adolescents face higher risk of complication and death as a result of pregnancy than other women. Maternal mortality ratio for our country is 130 per 100,000 live births from 2014-2016 as per WHO¹.

The major complications that account for nearly 75% of all maternal deaths are severe bleeding (mostly postpartum bleeding), infection (usually after child birth), high blood pressure during pregnancy (preeclampsia and eclampsia), complication from delivery and unsafe abortion.

Hypertensive disorders of pregnancy occur in about 10% of all pregnant women around the world. Preeclampsia affects 3-5% of pregnancies. Along with preeclampsia, other diseases which are included in the group of hypertensive disorders of pregnancy are eclampsia, gestational hypertension and chronic hypertension. In Asia and Africa, nearly one tenth of all maternal deaths are associated with hypertensive disorders of pregnancy. In India, the incidence of preeclampsia is reported to be 8-10% among the pregnant women².

According to a study, the prevalence of hypertensive disorders of pregnancy is 7.8%, with preeclampsia is 5.4% of the study population in India³.

Preeclampsia is a syndrome that chiefly includes the development of new-onset hypertension in the second half of pregnancy. Although often accompanied by new-onset proteinuria, preeclampsia can be associated with many other signs and symptoms, including visual disturbances, headaches, epigastric pain, and the rapid development of edema⁴.

There are many placenta derived biomarkers regarding early diagnosis of preeclampsia like, the antiangiogenic proteins sFLT1 (Soluble fms-like tyrosine kinase), or soluble vascular endothelial growth factor

receptor 1 (VEGF) and sENG (Soluble Endoglin) as well as proangiogenic proteins PlGF or PGF (Placental growth factor). But as they are not easily accessible and cost effective they are not used routinely in developing countries^{5,6}.

Platelet plays an important role in pathogenesis of Preeclampsia. The platelets are normally present in the blood stream in an inactive state but they can activate immediately when they come in contact with damaged or activated endothelial wall. Platelet sizes correlate with platelet activity. Larger platelets are metabolically more active and have higher potential for thrombotic activity as compared with smaller one. Increased consumption of platelet causes thrombocytopenia which is an important sign of severe Preeclampsia. Thrombocytopenia occurs up to 50% of women with Preeclampsia. The platelet decreased average of 10% during third trimester due to haemodilution. Many studies suggest that when platelets are activated they become larger in size which cause increased platelet indices.

Circulating platelets are exposed to the soluble factors such as lipid mediators, cytokines and chemokines released by activated leukocytes and endothelial cells as they course through inflamed vasculature. Accumulation of these mediators elicits an activation response that is characterized by the degranulation of platelet granules.

Therefore, it may be a valuable marker for development of PE. Furthermore, it has been suggested that PDW & P-LCR can be a practical tool to evaluate consumptive coagulopathy⁷.

AIMS AND OBJECTIVES

- To study the variation of platelet counts, platelet indices in preeclampsia and eclampsia
- To study the platelet indices in normal pregnant women > 20 weeks gestation
- To compare the platelet indices, platelet counts between normal and hypertensive pregnant patients.
- To associate the variation in platelet indices with different forms of pregnancy induced hypertension.

METHOD & MATERIALS:

Study Setting: Department of Pathology and Gynaecology &

Obstetrics Ramakrishna Mission Seva Pratisthan, Vivekananda Institute of Medical Sciences from January 2017 to June 2018.

Group I: Women affected with convulsion and having signs of preeclampsia during pregnancy or within seven days after delivery after ruling out epilepsy or any other convulsive disorder were treated as eclamptic women.

Group II: Women having BP > 140/90 mmhg and significant proteinuria (>300mg/24hrs) and or edema are treated as preeclampsia.

Group III: Normotensive women having pregnancy >20weeks were considered as control group.

Total sample size was 66 pregnant women. 22 patients are taken from each group.

f) Inclusion Criteria:

- Pregnant women >20weeks of gestation having BP >140/90 mmhg and significant proteinuria (>300mg/24hr) and or oedema.
- Pregnant women >20weeks of gestation with eclamptic convulsion.
- Uncomplicated pregnancy >20 wks of gestation.

g) Exclusion Criteria: Pregnancy with following diseases history

- Coagulation disorder
- Epilepsy
- Hypertension
- Diabetes Mellitus
- Chronic liver/ kidney disease
- Anaemia/Haemoglobinopathy
- Any drug intake history that affects platelet functions.

RESULT

In our study ANOVA-test showed that there was no significant difference in mean ages of the patients of the three groups ($p=0.399$). Thus the patients of the three groups were matched for their ages. $2\chi=3.66$; $p=0.45$ NS- Not Significant Corrected Chi-square () test showed that there was no significant association between parity and the patients of the three groups ($p=0.45$). Thus the patients of the three groups were comparable for their parity. ANOVA-test showed that there was no significant difference in mean period of gestation of the patients of the three groups ($p=0.221$). Thus the patients of the three groups were comparable for period of gestation.

ANOVA-test showed that there was significant difference in mean SBP of the patients of the three groups ($p<0.0001$). As per the Turkey's Critical Difference (CD) ($CD_1=6.98$) the mean SBP of the patients of Group-I followed by the patients of Group-II were significantly higher than that of the patients of Group-III ($p<0.0001$). ANOVA-test showed that there was significant difference in mean DBP of the patients of the three groups ($p<0.0001$).

Our study showed that as per the Turkey's Critical Difference (CD) ($CD_1=6.98$) the mean DBP of the patients of Group-I followed by the patients of Group-II were significantly higher than that of the patients of Group-III ($p<0.0001$). ANOVA-test showed that there was significant difference in mean platelet count of the patients of the three groups ($p<0.0001$). As per the Turkey's Critical Difference (CD) ($CD_1=12454.41$) the mean platelet count of the patients of Group-I followed by the patients of Group-II were significantly lower than that of the patients of Group-III ($p<0.0001$). ANOVA-test showed that there was significant difference in mean MPV of the patients of the three groups ($p<0.0001$). As per the Turkey's Critical Difference (CD) ($CD_1=0.28$) the mean MPV of the patients of Group-I followed by the patients of Group-II were significantly higher than that of the patients of Group-III ($p<0.0001$). ANOVA-test showed that there was significant difference in mean PDW of the patients of the three groups ($p<0.0001$).

It was found that as per the Turkey's Critical Difference (CD) ($CD_1=1.39$) the mean PDW of the patients of Group-I followed by the patients of Group-II were significantly higher than that of the patients of Group-III ($p<0.0001$). ANOVA-test showed that there was significant difference in mean PLCR of the patients of the three groups ($p<0.0001$). As per the Turkey's Critical Difference (CD) ($CD_1=2.04$) the mean PLCR of the patients of Group-I followed by the patients of Group-II were significantly higher than that of the patients of Group-

III ($p<0.0001$). $=108.81$; $p<0.0001$ S- Significant Corrected Chi-square () test showed that there was significant association between urine protein and the patients of the three groups ($p<0.0001$).

In our study the test of proportion showed that the proportion of patients with proteinuria was significantly higher in Group-I followed by Group-II were significantly higher than that of Group-III. $=94.54$; $p<0.0001$ S- Significant Corrected Chi-square () test showed that there was significant association between edema and patients of the patients of the three groups ($p<0.0001$). Test of proportion showed that the proportion of patients with edema was higher in Group-I and Group-II which was significantly higher than that of Group-III. $=32.60$; $p<0.0001$ S- Significant Corrected Chi-square () test showed that there was significant association between Platelet Count and the patients of the three groups ($p<0.0001$). Test of proportion showed that the proportion of patients with platelet count below the normal was higher in Group-I and Group-II which was significantly higher than that of Group-III. $=17.79$; $p<0.0001$ S- Significant Corrected Chi-square () test showed that there was significant association between MPV and the patients of the three groups ($p<0.0001$).

Our study showed that proportion of patients with abnormal MPV was significantly higher in Group-I followed by Group-II than that of Group-III. $=14.75$; $p=0.0052$ S- Significant Corrected Chi-square () test showed that there was significant association between PDW and the patients of the three groups ($p=0.0052$). Proportion of patients with abnormal PDW was significantly higher in Group-I followed by Group-II than that of Group-III. $=36.54.41$; $p<0.0001$ S- Significant Corrected Chi-square () test showed that there was significant association between PLCR and the patients of the three groups ($p<0.0001$). Test of proportion showed that the proportion of patients with PLCR above the normal limit was higher in Group-I and Group-II which was significantly higher than that of Group-III. From ROC the area under curve (AUC) showed that the cut-off value for eclampsia were : MPV= 11.74 PDW = 14.81 PLCR= 42.68 From ROC the area under curve (AUC) showed that the cut-off value for pre-eclampsia were : MPV= 11.52 PDW = 12.88 PLCR= 38.65

DISCUSSION

- Controls (Normotensive) as well as cases (Preeclampsia & eclampsia group) taken as study population are comparable for age, parity and gestational age.
- Mean Systolic BP for Preeclampsia and Eclampsia groups are 152.36 & 160.64 respectively.
- Mean Diastolic BP for Preeclampsia and Eclampsia groups are 91.91 & 95.91 respectively.
- Corrected Chi-square test shows significant association ($p<0.0001$) between urine protein and patients of all three groups
- Corrected Chi-square test shows significant association ($p<0.0001$) between edema and patients of all three groups
- Mean Platelet count for normotensive pregnancy, preeclampsia and eclampsia is 223681.82, 147363.64, 120863.64 respectively showing significant statistical difference ($p<0.0001$). Our study shows 86.4 % of preeclampsia and 100% of eclampsia has thrombocytopenia.
- Mean MPV for normotensive pregnancy, preeclampsia and eclampsia is 10.36, 11.58, 12.90 respectively showing significant statistical difference ($p<0.0001$). Increased MPV is seen more in eclampsia (90.90%) and preeclampsia (81.8%) patients than normal pregnant women (36.4%).
- Mean PDW for normotensive pregnancy, preeclampsia and eclampsia is 10.78, 13.52, 15.00 respectively showing significant statistical difference ($p<0.0001$). Similarly increased PDW is observed more in eclampsia (100%) and preeclampsia (95.5%) patients than normal pregnant women (63.6 %).
- Mean PLCR for normotensive pregnancy, preeclampsia and eclampsia is 27.48, 36.53, 39.44 respectively showing significant statistical difference ($p<0.0001$). Increased PLCR is also seen in eclampsia (100%) and preeclampsia (81.8%) patients than normal pregnant women (18.2%).
- From ROC the area under curve shows the cut-off values of platelet indices (MPV, PDW, PLCR) for preeclampsia and eclampsia groups. Cut off value are as follows

	Eclampsia	Preeclampsia
MPV	11.74	11.52
PDW	14.81	12.88
PLCR	42.68	38.65

Present study is prospective institution based case – control study, in which comparative observation is made in three groups of study populations, which include 66 subjects, out of which 22 subjects are normotensive pregnancies (Group III) taken as control, another two groups each includes 22 from preeclampsia (Group II) and eclampsia (Group I) subjects taken as case.

The patients of all the three groups are matched for ages. In our study mean age of patients is 27 years which is close to Onisai et al study (mean age of PIH is 29 years) and Prakash J et al study (mean age for PIH is 26 years)^{8,9}.

Present study has controls as well as cases are of 3rd trimester of pregnancy and all are comparable for period of gestation.

Metz et al¹⁰ had 71% of their primiparae in sub group of gestational hypertension. The other studies have not specified about that. With regard to the primiparae subgroup among cases, our study have lesser participants in comparison to the study performed by Metz et al¹⁰ (63.63% VS 71%)

The observation that primiparae being more affected by PIH as compared to the multiparae subjects had been highlighted by Davidson Philips¹¹ and Dubey¹² et al. The present study has a concordant observation with that of the aforesaid studies.

In our study mean platelet count in preeclampsia 1.47 lakh per mm³ which is comparable to studies by Mahapatra et al¹³ and Vrunda et al¹⁴ showing 1.4 lakh and 1.82 lakh per mm³ respectively. Mean platelet count in eclampsia is 1.2 lakh per mm³ in our study which is agreeable with Vrunda¹⁴ et al and Mahapatra et al¹³ who observed platelet count 1.30 lakh and 1.30 lakh per mm³ respectively.

Platelet Count	Mahapatra et al ¹³	Vrunda et al ¹⁴	Present Study
Normotensive(lakh/mm ³)	2.38	2.2	2.23
Preeclampsia(lakh/mm ³)	1.4	1.82	1.47
Eclampsia(lakh/mm ³)	1.3	1.3	1.20

In present study we observe an increase in MPV and PDW values from normotensive pregnant women to preeclampsia and eclampsia patients which correlates with other studies.

In our study mean MPV is 11.58±1.01 and 12.9±1.60 for preeclampsia and eclampsia which is comparable with Mondal et al¹⁵ study showing mean MPV 11.5±0.86 and 12.16±1.05 for preeclampsia and eclampsia respectively. However the values are less in a study by Annam et al (10.3, 11.0 respectively)¹⁶.

MPV Mondal et al¹⁵ Annam et al¹⁶ Present Study

MPV	Mondal et al ¹⁵	Annam et al ¹⁶	Present Study
Preeclampsia	11.5	10.3	11.58
Eclampsia	12.16	11.0	12.9

With regard to PDW, the values for the preeclampsia and eclampsia group are comparatively lower in present study in respect to other studies i.e. Annam et al¹⁶ & Mondal et al¹⁵.

PDW	Mondal et al ¹⁵	Annam et al ¹⁶	Present Study
Preeclampsia	14.99	15.51	13.5
Eclampsia	17.0	16.78	15.3

In our study we found an increasing trend of PLCR among patients with PIH. The mean PLCR values are 27.48, 36.53 and 39.44 among normotensive, preeclampsia and eclampsia groups respectively. This observation corroborates with the findings in the study conducted by Mondal et al¹⁵ (25.62, 36.42, 40.24 normotensive, preeclampsia and eclampsia groups respectively) and others^{17,18}.

PLCR	Mondal et al ¹⁵	Present study
Preeclampsia	36.42	36.53
Eclampsia	40.24	39.44

Vagadati et al (2010) explained that larger platelets create increased MPV, PDW & PLCR¹⁹. Kaito et al²⁰ also explained hyper destruction of platelet increases MPV, PDW, & PLCR. They also stated that increased PLCR indicates increased bone marrow activity. Our study corroborate with aforesaid studies.

CONCLUSION

- There is an inverse relationship between the severity of PIH and platelet count which suggest that the depleted platelet counts are consistently associated with preeclampsia and eclampsia and the

risk of consumptive coagulopathy

- The platelet indices e.g. MPV, PDW and also PLCR are in consistent relationship with PIH. The higher their values, the greater severity of PIH, from preeclampsia to eclampsia.
- There is definite statistical difference in values of platelet count, platelet indices in PIH groups when compared with that of normotensive pregnant women from which we deduce the Cut off value of platelet indices for preeclamptic and eclamptic women.

The estimation of platelet count and indices offer early, simple, rapid assessments of the disease for its severity and the risk of complications. Therefore these tests may be considered as screening tests to be routinely performed in antenatal workup of women with PIH.

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