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Original Article

Pathology Section

Platelet Indicies in Pre-eclampsia and Eclampsia

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ABSTRACT

Introduction: Activation of platelets due to defective placental trophoblastic invasion in the pathophysiology of pre-eclampsia and eclampsia is known. The changes in the platelet parameters and its relevance are discussed in this article.

Aim: To compare the changes of platelet parameters in patients diagnosed with pre-eclampsia and eclampsia versus the control group of pregnant women.

Materials and Methods: A random selection of 50 normal pregnant controls and 50 patients with pre-eclampsia or eclampsia were included in the study. The platelet indices that include platelet count, Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) of both the controls and cases were documented and compared using statistical analysis.

Results: The PDW is greater in the cases than controls and shows that there was a statistically significant difference between the values of the cases versus the controls. MPV was mildly increased and platelet count mildly decreased in cases versus controls. Platelet count and MPV did not show a statistical significant difference between the cases and controls.

Conclusion: The significant difference in the PDW and the increase in MPV can contribute to the pathophysiology of pre-eclampsia and eclampsia. The changes in these parameters can provide a cue towards early diagnosis or potential worsening of pre-eclampsia and eclampsia status. However, platelet count alone is not always a potential indicator in detecting pre-eclampsia and eclampsia. Assessing the PDW can also be beneficial as an indicator of pre-eclampsia and eclampsia.

Keywords: Mean platelet volume, Platelet count, Platelet distribution width

INTRODUCTION

Pre-eclampsia eclampsia syndrome has been a known deadly complication of pregnancies. Several mechanisms of injury are postulated with the pathophysiology of pre-eclampsia. Studies have suggested that placental vascular under perfusion, maternal endothelial damage and increased vascular permeability has been contributory to the pathophysiology of the disease [1]. The injured endothelium due to defective placental trophoblastic invasion leads to activation of platelets. Activation of platelets can cause changes in size, count and distribution [2]. Similar to myocardium, vascular under perfusion can be due to intrinsic factors like changes in blood constituents or extrinsic factors like thickening of placental capillaries. In this study, we assess the changes in platelets indices (platelet count, PDW and MPV) of pre-eclamptics and eclamptics in comparison with normal pregnant controls and to compare the hematological changes in patients diagnosed with pre-eclampsia and eclampsia with the control group.

MATERIALS AND METHODS

This is a cross-sectional study conducted from November 2012 to December 2014 in the Department of Pathology, PES Institute of Medical Sciences, Kuppam, Andhra Pradesh, India. The study was approved by the Institutional Scientific Review Committee which provided ethical clearance for the study. Fifty cases and 50 controls were collected randomly amounting to 100 as the sample size of total study.There were 39 cases of pre-eclampsia and 11 cases of eclampsia diagnosed. All patients above 18 years of age who have been diagnosed with pre-eclampsia and eclampsia according to the standard clinical criteria published by American College of Obstetrics and Gynaecology (2002) and admitted for follow-up and delivery were included [3]. All cases of gestational hypertension and pre-eclampsia super imposed on a known case of essential hypertension were excluded. Also, all pre-eclamptics with any co-existing unrelated but prognostically influencing medical, surgical or gestational conditions such as anaemia, insulin dependent diabetes mellitus, gestational diabetes, medications known to affect hematological parameters and infections like dengue and malaria were excluded.

On admission a complete blood profile of those identified as cases and controls were procured after an oral informed consent. About 3 mL of venous blood samples were collected into K3-EDTA anticoagulant vaccutainers and processed in

SYSMEX 1000i automated haematology analyzer. All the samples were collected and processed within 4 hours. The results were obtained within 4 hours complying with the pre fixed turn around time of the institution. A peripheral smear was performed and correlated with the values to rule to confounding factors of platelet clumps, anaemia, leucocytosis etc. Other non haematological preliminary data focussing on past history, smoking history, current medication history, previous use of oral contraceptive pills of the cases and controls were recorded on admission, coded and recorded into a master chart.

The platelet indices that include the total platelet count, MPV and PDW were recorded for both controls and cases. The platelet parameters and non platelet hematological parameters like hemoglobin, WBC count, etc., were recorded in a separate sheet.

STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) software package, version 16.0, was used to analyse the data obtained. The normality of variables has been checked using histograms and rule of thumb. Mean and standard deviations were used to describe the continuous variable. Categorical variables were represented using percentages. An independent Student's-t-test was used to analyse hematological data after checking the normality.

RESULTS

The number of patients with primigravida was as high as 56% with 44% of the cases being multigravida. The mean ages of the pre-eclampsia and eclampsia group ranged from 21 years to 24 years. The mean days of gestation range from 237 days in imminent eclampsia to 278 days in mild pre-eclampsia. The percentage of cases with mild pre-eclampsia, severe eclampsia, imminent eclampsia and eclampsia are 24%, 36%, 18% and 22% respectively. The comparison of the platelet indices in cases versus controls are elucidated in [Table/Fig-1].

The PDW has been found out to be less than <0.05 and is statistically significant. This implies that there is a difference between the PDW values of eclampsia and normal people.

Hematological Variables	Mean (SD) Group of Pre-eclampsia and Eclampsia Syndrome	Mean (SD) Normal Pregnant Controls	p-value
Platelets (10^9/L)	226.16 (99.72)	267.25 (127.16)	0.075
MPV (in fL)	10.67 (1.69)	10.35 (1.68)	0.348
PDW (in %)	13.42 (2.07)	11.86 (2.07)	<0.001

[Table/Fig-1]: Comparison of the platelet indices in cases versus controls.
*p<0.05 was considered as statistically significant

DISCUSSION

The changes in platelet indices that appear in pre-eclamptic pregnancy are divided into two major groups, numerical abnormalities which include the structural changes regarding size and distribution width which can be quantified numerically and functional platelet abnormalities. In this article we discuss the numerical abnormalities of the platelets and its functional impact on the pathophysiology of pre-eclampsia and eclampsia.

Thrombocytopenia can be associated with pre-eclampsia which is life threatening if it gets complicated with HELLP syndrome. Thromboxane A which is released by thrombocyte has known to play a major role in pre-eclamptic pathophysiology. There is also evidence of increase in the thromboxane/prostacyclin ratio. Thromboxane A increases invoking platelet aggregation and endothelial damage promoting platelet dysfunction and platelet consumption causing thrombocytopenia. Platelets are activated by P selectin, CD 63 and PECAM- platelet surface glycoprotein which also are markers of activation. Platelet activation is associated with increased endothelial dysfunction with micro thrombi formation causing end organ degenerative necrosis and placental infarction [4].

This is followed by the bone marrow responding to the decrease in platelets by release of younger platelets bearing increased MPV [5]. Increase in MPV is also associated altered Doppler velocimetric studies which are used in the prediction of pre-eclampsia [6].

Several studies have evaluated platelet indices in prognostication and understanding the pathogenesis of pre-eclampsia. Some studies like Vijaya C et al., concluded that it is considered as an early, economical and rapid method of assessing the severity of pregnancy induced hypertension cases [7]. Though, the mean platelet count of the present study was decreased in comparison to control subjects, it lacked statistical significance. A case control study by Ceyhan T et al., was done in which 56 pre-eclamptic women and 43 normotensive pregnant women were compared using MPV and platelet count, which could not find difference between the 2 groups for platelet count and MPV. The study also compared MPV and platelet count between two groups of severe pre-eclampsia and mild pre-eclampsia. Their study also could not show any differences for these two parameters between severe pre-eclampsia, mild pre-eclampsia and normotensives [8]. Freitas LG et al., reported that the platelet count was a good candidate for diagnosis of severe pre-eclampsia. However, the effect of platelet count on other types of pre-eclampsia was not discussed in the study [9].

In contrast to the findings in the present study, a study by Monteiro G et al., studied a typical Indian population with retrospective data which showed that the mean platelet count was significantly decreased in the group that contained pregnant women with hypertension from 20th week onwards

when compared to controls [10]. Their study also states that platelet count is a predictor of progression of severity of pregnancy induced hypertension. In a case series by Onisai M et al., the median platelet count was lower in the patients with 5 of their selected patients showing thrombocytopenia as low as 6000 platelets/cmm. Also the median platelet volume was higher in that group [4]. Absence of statistical significance can also be due to significant number of multigravida in the study tending to have a higher platelet count. As per the study by Onisai M et al., primiparas who are pre-eclamptics tended to have lower platelet count [4].

MPV was increased in comparison to control subjects of the present study, though not statistically significant. The MPV was near similar in all the 4 sub-groups of the present study in comparison to the MPV of the control group. A study by Kashanian M et al., followed up 35 pre-eclamptics cases over 269 normotensives whose mean platelet count was decreased (similar to our study) but did not show statistical significance but mean platelet volume was significantly higher (contrast to our study) [11]. MPV was also increased in a study by Boriboonhirunsarn D et al., [12]. Al-Sheeha et al., reported that MPV and PDW did not show significant difference between normotensives and pre-eclamptics and suggested a ratio of platelet count/MPV is valid predictor of pre-eclampsia [13]. A study by Altinbas S et al., discussed that there is an increase in the MPV in normal pregnant controls and failed to provide a difference between all stages of pre-eclamptic eclamptic syndrome stages [14]. However, this study didn't provide any additional benefit to predict pre-eclampsia using Doppler velocimetry and MPV values contradicting Piazze J et al., study [6].

Unlike the previously quoted studies that have performed serial monthly assessment of platelet indices from the 20th week of gestation, the present study recorded the platelet indices only during admission. This could be one of probable cause for absence of statistical significance for increase in MPV and decrease in platelet count. It has been suggested to record sequential platelet count and indices throughout pregnancy in order to assess the role of platelet parameters in development of pre-eclampsia and its severity [9]. Another probable cause is the distribution of the patients with a significant group of patients presenting with mild pre-eclampsia showing relatively less toxic effects on hematological parameters.The study by Ceyhan T et al., concluded that variations in methods of measurement adopted by researchers which are used for automated blood counts could be a reason for controversies between different studies, especially for MPV [8].

The present study portrayed an increase in PDW with statistical significance only in the mild pre-eclampsia and severe pre-eclampsia group. Yet, it is clearly observed that the PDW is higher in rest of the groups than the pregnant controls. A study by Dadhich S et al., showed significant increases in PDW (pre-eclamptic subjects - 47.19% versus 29.4% of control subjects) and MPV (44.5% vs 9.22%). The platelet count decreased to 9.22% in comparison with control 44.5% [15]. In contrast the study by Alisi PN et al., shows that there is only a mild increase in the PDW values [16]. The increase in PDW probably reflects increased platelet turnover which would support the idea that platelet survival time is decreased resulting in increased destruction of platelets [17]. The variation in the platelet distribution width would also suggest that endothelial dysfunction seen in pre-eclampsia, would result in production of younger and larger platelets of varying sizes in order to compensate for the reduction in platelet count as the disease progresses [18]. Kirbas A et al., reported the utility of PDW in the early diagnosis in pre-eclampsia and eclampsia [19]. Kurtoglu E et al., concurred with the present study that platelet indices are a beneficial indicator of pre-eclampsia and eclampsia [20]. The platelet indices from various studies in comparison to our study are elucidated in [Table/Fig-2].

Studies	Mean Platelet count (10^9/L)	Mean MPV (in fL)	PDW (in %)
Vijaya C et al., [7]	155.5+31.300	10.38+1.66	15.50+2.68
Alisi P et al., [15]	108.0±30.02	12.04±1.70	9.52±0.75
Monteiro et al., [9]	121.6±90.55	-	-
Kashanian et al., [10]	185.6±60.1	10.16 ± 1.2	-
Annam V et al., [16]	-	9.9	10.38
Present study	226.16±99.72	10.67	13.42

[Table/Fig-2]: A comparison of studies regarding mean platelet count, mean platelet volume and platelet distribution width in pre-eclamptic eclamptics syndrome cases.

LIMITATION

One obvious limitation of the study is sample size. It is possible more accurate results could be deciphered on a larger sample size. However, the sample size in this study was sufficient to provide statistically significant results. The study was also focused on platelet parameters and did not assess the findings in relation to the foetal outcome.

CONCLUSION

Additional studies with PDW and the increase in MPV seen in pre-eclampsia and eclampsia may yield further insights on the underlying pathophysiology of these conditions. The increase in PDW provides a tool in the early diagnostic assessment of pre-eclampsia and eclampsia. Currently, the platelet count is only used as one of the criteria for the diagnosis of pre-eclampsia. However, assessing the PDW and MPV, along with platelet count may be beneficial as an indicator of pre-eclampsia and eclampsia. Changes in platelet indices may provide a cue towards potential worsening of pre-eclampsia and eclampsia status of the patient. The present study has potential areas of further research where platelet indices can be correlated to check if there exists an association with

increased maternal floor infarction in the study group. In conjunction, the alteration of MPV and PDW values can be assessed for using it as a tool for predicting pre-eclampsia or used as adjunct to clinical parameters of diagnosing pre-eclampsia.

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