

Frequency of abnormal platelet indices among women presenting with preeclampsia

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ABSTRACT

Objective: To determine the Frequency of abnormal platelet indices among women presenting with preeclampsia

Material and methods: This descriptive cross sectional study was conducted in duration of six months from 20-02-2017 to 19-08-2017, at Department of Obstetrics and Gynaecology Unit III, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana. In total 95 women of age 18-40 years, having pregnancy 20 to 40 weeks, alive singleton fetus and confirmed preeclampsia were included. Patients with history of chronic hypertension, Idiopathic Thrombocytopenic Purpura, using anticoagulant drugs within last one month, multiple gestation and morbid obesity were excluded. Mean \pm SD, frequencies & percentages were calculated. Chi-square was used as test of significance with a P value ≤ 0.05 as significant.

Results: Mean \pm SD age of patients was 29.52 ± 6.17 years (Range 18 to 40). Mean \pm SD parity was 1.71 ± 1.11 children (Range 1-4). Mean \pm SD gestational age was 30.39 ± 4.90 weeks (Range 21-38). The mean platelet volume was 12.80 ± 6.82 fl, mean platelet count in mm³ was $2,22,997 \pm 1,00,093$ while mean platelet distribution width was 11.05 ± 5.95 fl. Thrombocytopenia was found positive among 32.6%. Frequency of abnormal platelet indices was 22.1% (n = 21).

Conclusion: Preeclampsia is very dangerous condition posing life threat to mother and the fetus. The current study found that platelet volume and platelet distribution width both increase while platelet count decreases among women who develop the preeclampsia..

Keywords: Preeclampsia; Platelet count; Platelet volume; Platelet distribution width; Thrombocytopenia.

INTRODUCTION

Hypertensive disorders of pregnancy are among the most frequent and adverse outcomes of pregnancy worldwide. These include chronic hypertension, gestational hypertension, as well as two main important forms of hypertensive disorders i-e; preeclampsia and eclampsia. Preeclampsia (PE) is associated with higher rates of maternal, fetal and infant mortality and morbidity. It complicates 2-5% of pregnancies in developed countries and 18% in developing countries. Asian women with preeclampsia have worse pregnancy outcomes than others. The World Health Organization (WHO) estimates that preeclampsia is directly responsible for 10% of direct maternal mortality in Asia. In Pakistan it varies in different research studies conducted at different hospital settings from 1.9% to 19%.

Preeclampsia is a condition characterized by hypertension and proteinuria and can lead to renal and liver disorders, convulsions and clotting disorders. Exact cause & pathophysiological aspects of PE remain unclear despite extensive investigations.ⁱ However; it is thought the major pathophysiological processes include the alterations in hemostatic system, such as the endothelial cell damage, platelet activation and enhanced intravascular thrombin generation.ⁱⁱ

Increased platelet activity is associated with increased platelet size and is common in PE. Large platelets that contain more dense granules are metabolically and enzymatically more active than small platelets.^{iii,iv} Additionally, mean platelet volume (MPV), a determinant of platelet activation has been recognized as an independent risk factor in PE.^v Platelet activation is measured in terms of reduced platelet count and increased MPV.^{vi} These are elevated in PE much before the onset of clinical symptoms and hence may be useful as predictors for the onset of the disease.^{11,14} MPV is routinely done during antenatal checkup at low cost. Increased MPV was detected among 25% PE women while none (0%) of the normotensive. Also it was found that 65.6% PE women had increased platelet distribution width (PDW) compared to only 9.4% of normotensive women.¹⁵

A study done by Dadhich S, et al reported that 19.4% preeclamptic patients compared to 7.4% normotensive patients presented with thrombocytopenia.^{vii} Further it was noted that MPV was more among PE patients (44.5%) compared to normotensive patients (9.22%) & finally; increase in PDW was detected among PE patients (47.19%) compared to (29.4%).¹⁶ Improving the outcome for preeclampsia necessitates accurate and early prediction of the disease to identify women at high risk, enabling prophylaxis with antiplatelet agents such as aspirin, as well as early intervention.^{viii}

Presentation of preeclampsia is common in our population which leads to many fetal and maternal complications. Clinical research is mandatory to assess the platelet indices in different populations which develop PE. Larkana is an area with majority of rural population living around it. Though some studies reported lowered platelet indices in PE in other populations, but it has not been studied in our population.^{ix} This was the rationale to conduct this study. The results of this study provide the magnitude of abnormal platelet indices among pregnant women which develop PE. Further the study is to help us in future to manage such patients on earlier basis to reduce the maternal & fetal morbidity & mortality.

MATERIAL AND METHODS

Study setting: Obstetrics and Gynaecology Unit III, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana.

Duration of study: Six months period from 20-02-2017 to 19-08-2017.

Study design: Cross sectional study

Sample size: WHO's sample size calculator used with following data;

P = 19.4% Prevalence of thrombocytopenia in preeclamptic patients. [15]

Confidence interval = 95%

Margin of error = 8%

The sample size calculated come was 94 ~ 95.

Sampling technique: Non probability consecutive.

Sample selection:

Inclusion Criteria:

- Age of patient between 18-40 years
- Gestational age between 20-40 weeks on clinical history & Ultrasonology
- Confirmed case of preeclampsia as per operational definitions
- Primigravida and multigravida both
- Parity from 0 to 4.
- Singleton alive fetus confirmed on Ultrasonology
- Booked cases as per our OPD record.
- Willingness of woman to participate in the study

Exclusion Criteria:

- Known case of chronic hypertension
- Multiple gestation, twin pregnancy
- Morbid obesity [body mass index (BMI) ≥ 40 Kg/m²]
- Intrauterine fetal death confirmed through Ultrasonology
- Known case of hypercholesterolemia, ischaemic heart diseases, diabetes mellitus, renal disease or hepatic dysfunction (confirmed through past history & medical record)
- History of asthma requiring steroidal treatment or patient using
- History of Idiopathic Thrombocytopenic Purpura
- History of using anticoagulant drugs within last one month

Confounders: MPV increases in diabetes mellitus, hypercholesterolemia, acute ischemic stroke. These were excluded.

History of smoking: These were controlled through stratification during data analysis. Patient was labeled to be smoker if she smoked >10 cigarettes per day for >6 months. Patient was labeled to be ex-smoker if she had quit smoking before last 6

months then.

DATA COLLECTION PROCEDURE: Data collection was done in OPD of obstetrical Unit III of SMBBMU, Larkana. Pregnant women, who were eligible as per selection criteria and provided valid written consent, were included in the study. Only confirmed cases of preeclampsia were enrolled in the study. Platelet indices were evaluated by taking blood for haematological analysis. After taking all aseptic precaution, 2 ml of venous blood was collected from each patient with disposable syringe by venipuncture for haematological analysis. Blood was taken into a vial containing Ethylene Diamine Tetra Acetate (EDTA) and mixed well to prevent clot formation for platelet count and platelet indices. Platelet indices and platelet count were measured in Haematology auto-analyzer (SYSMEX-XE 5000) within 2 hours of blood collection. Total platelet count, mean platelet volume (MPV) and platelet distribution width (PDW) were measured. Laboratory investigations were done from the central laboratory of the SMBBMU.

Primary outcome variable was detection of abnormal platelet indices (Total platelet count, MPV, PDW) among patient of preeclampsia. Study variables included name, maternal age, parity, gestational age, address, blood pressure values, spot urine dipstick proteins. Data were collected on prescribed proforma by the investigator herself. Preeclampsia was treated as per the protocol of the institution.

STATISTICAL ANALYSIS: SPSS version 21 was used for data entry and analysis. The continuous variables like maternal age, parity, gestational age, total platelet count, MPV, PDW were expressed in mean & standard deviation (Mean ± SD). Categorical variables like address (Rural / Urban), detection of abnormal platelet indices were expressed in frequencies and percentages.

RESULTS

The current study was undertaken on 95 pregnant women who had presented with preeclampsia at department of Obstetrics and Gynecology Unit III, Sheikh Zaid Women Hospital Larkana, to determine the frequency of abnormal platelet indices in them.

The mean ± SD age of these women was 29.52 ± 6.17 years with a range from 18 to 40 years. The mean ± SD parity was 1.71 ± 1.11 children which ranged from minimum 01 child to a maximum 4 children. (Table 1) The mean ± SD gestational age was 30.39 ± 4.90 weeks with a range from 21 to 38 weeks.

The mean platelet volume was 12.80 ± 6.82 fl (Famtoliters), ranging between 3.63 to 28.6 fl. The mean platelet count in mm³ was 2,22,997 ± 1,00,093 ranging between 85000 to 4,30,000 mm³. The mean platelet distribution width was 11.05 ± 5.95 fl, ranging between 4 to 28 fl. (Table 1)

It was found that 8.42% (n=8) patients were of group aged 18 to 20 years, those who aged from 21 -30 years were 42.11% (n = 40), while those who aged from 31 -40 years were 49.47% (n = 47). (Figure 1)

About nineteen percent women (n = 18) were nulliparous, those having 1 -2 children were 61.1% (n = 58) while those having 3-4 children were 20% (n = 19). (Table 1)

Figure 2 shows the gestational age distribution and according to that a vast majority women 74.74% (n = 71) had presented gest age of 25-36 weeks; younger gest age i-e; upto 24 weeks were 16.84% (n = 16) while 8.42% (n = 8) women had presented gest age of 37 and above weeks. (Figure 2)

Distribution of smoking status of patients presented with preeclampsia resulted in the picture that equal number of women i-e; 16.8% (n = 16) had history of being current smoker and past smoker each. A vast majority however; was non-smoker 66.3% (n = 63). (Table 3)

Approximately two thirds of all women 64.21% (n = 61 out of 95) were from the rural areas. (Figure 3)

Thrombocytopenia was found positive among 32.6% (n = 31) women. (Table 4)

Figure 4 shows the categorization of all women according to the degree of proteinuria they had presented with as detected on the urine dipstick method.

Primary outcome variable of the study was to note down the frequency of abnormal platelet indices among 95 women who had presented with preeclampsia and it was detected positive among 22.11% (n = 21) women. (Figure 5)

Table: 1. Descriptive statistics.

variable	Minimum	Mean (± SD)	Maximum
Age of the Patient	18	29.52 ± 6.17	40
Number of children	0	1.71 ± 1.11	4
Gestational age	21	30.39 ± 4.90	38
Gravida	1	2.87 ± 1.15	5
Mean platelet volume in (fl)	3.63	12.80 ± 6.82	28.60

Platelet count in mm ³	85000	2,22,997 ± 1,00,093	4,30,000
Platelet distribution width (fl)	4	11.05 ± 5.95	28

Figure: 1. Percentage of patients (presented with preeclampsia) as per age categories

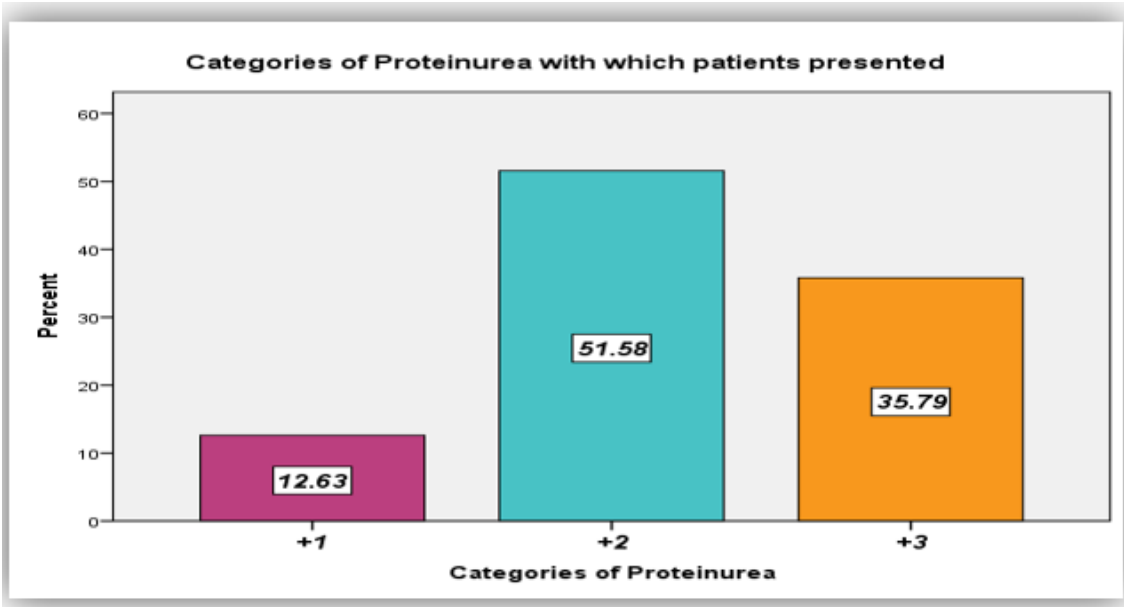


Table: 2. Number of children (Parity).

Parity	Frequency	Percent
Nulliparours	18	18.9
1-2 Children	58	61.1
3-4 Children	19	20
Total	95	100

Figure: 2. Frequency gestational ages with which patients presented with preeclampsia.

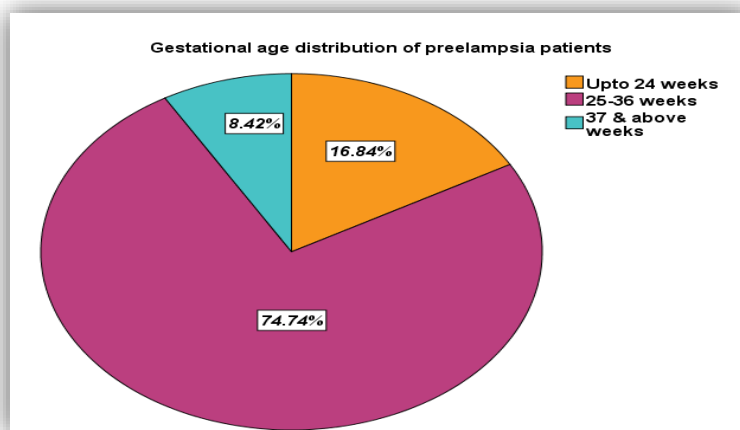


Table: 3. Distribution of smoking status of patients presented with preeclampsia

Smoking status	Frequency	Percent
Smoker	16	16.8
Ex-Smoker	16	16.8
Non-smoker	63	66.3
Total	95	100

Figure: 3. Percentage of patients (presented with preeclampsia) as per residence.

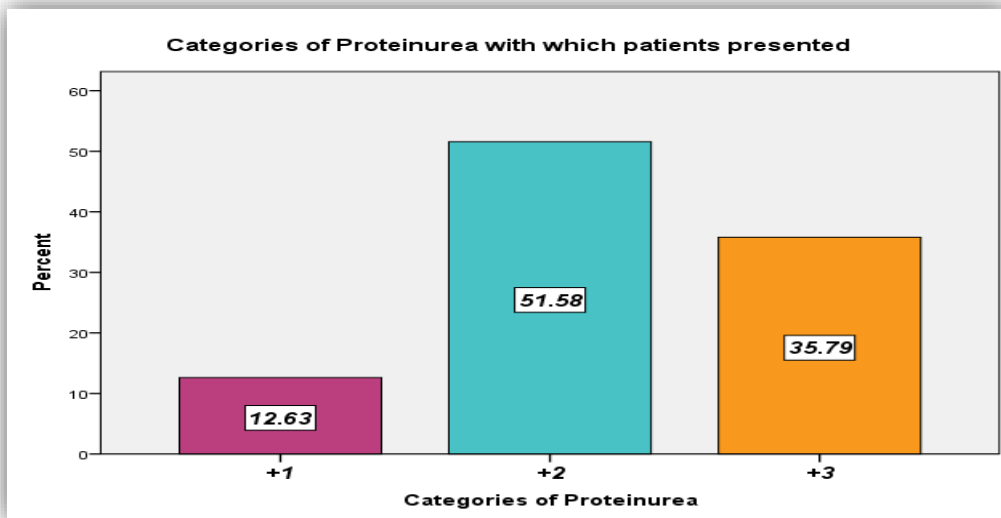
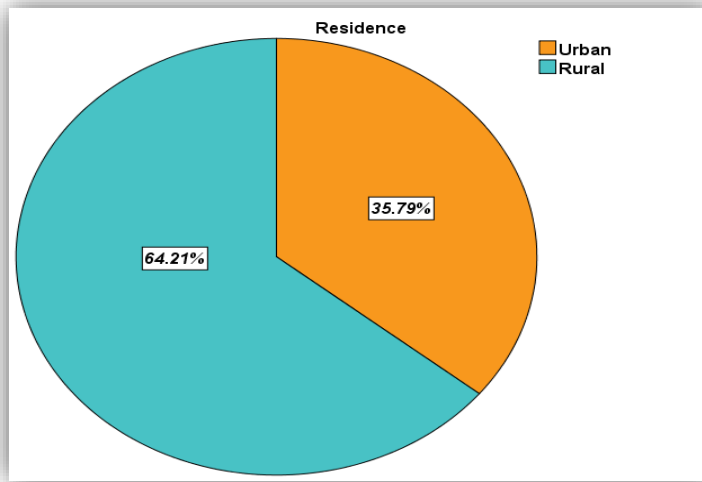


Figure: 4. Frequency of proteinuria with which preeclampsia patients presented

Table: 4. Distribution of thrombocytopenia among patients presented with preeclampsia

Thrombocytopenia	Frequency	Percent
Yes	31	32.6
No	64	67.4
Total	95	100

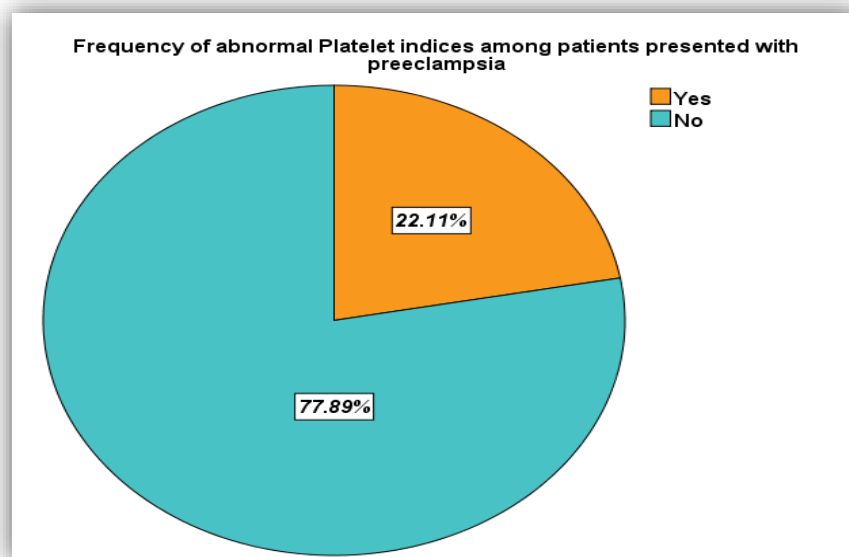


Figure: 5. Frequency of abnormal platelet indices among patient presenting with preeclampsia (n =95).

DISCUSSION

Preeclampsia has been complicating the human pregnancies since a very long and unknown period of time. It is responsible for huge proportion of maternal and fetal morbidity and mortality. Further; it is associated with a high risk of IUGR, preterm delivery, placental abruption. Its long term postpartum consequences in affected women are still more.^{4,8,11,21,23,44,45,x,xi} Preeclampsia has long been in hard hands of the researchers but knowledge of its exact pathophysiology has still not been fully achieved. Though; there many pathophysiological mechanisms have come forth with variety of factors known to be responsible for the diverse subsets of PE yet; these do not completely explain the disease process. One of these includes impaired vascular remodeling of the maternal–fetal interface, excessive immune response to paternal antigens, systemic inflammatory response, and dysfunctional placental or endothelial response. All of processes are modulated by genetic and environmental parameters.^{7,8,10,12,19,23,24}

The abnormal vascular response is thought to be associated with increased systemic vascular resistance, enhanced platelet aggregation, activation and alteration of the coagulation system, and endothelial cell dysfunction and all these are believed to play an important role in the pathogenesis of preeclampsia. An explanation to the fact of fall in the platelet count- the most frequent abnormality- is probably due to consumption during low grade intravascular coagulation.^{9,16,21,22}

Platelet indices such as platelet count (PC), mean platelet count (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR) are widely available and are cost-effective parameters to monitor maternal and fetal mortality and morbidity occurring from preeclampsia. To highlight the importance and evaluate the association of abnormal vascular response especially platelet parameters with preeclampsia, the current study was undertaken in a public sector tertiary care obstetric care setup.

It was found in this study that almost a quarter (22.11%) of pregnant women admitted with diagnosis of preeclampsia was having abnormal platelet indices. Among all patients the mean MPV was 12.80 ± 6.82 fl, mean PDW was 11.05 ± 5.95 fl, while mean platelet count was 2,22,997 ± 1,00,093/mm³ however; the overall prevalence of thrombocytopenia (<1,50,000/mm³) was 32.6%. Other studies have reported mimicking statistics among women presenting with preeclampsia. One study found that platelets count was 2,36,500/mm³, mean platelet volume was 10.0 fL while platelet distribution width, was 12.7 fl (11.4-15.8).^{xii} Nooh AM, et al. reported PC was 1,91,000/mm³ ± 40,300, MPV was 10.8 ± 1.7 fL while PDW was 24.4 ± 3.6 % in preeclampsia patients. Changes in platelet indices noted in this study are in agreement with those reported by other

researchers.^{7-11,13,19,xiii,xiv,xv,xvi} However; there are variable results on record as well. Like one study by Kamel Ammar WAE, et al., from Egypt found that PLT count mean \pm SD was $1,34,880 \pm 34,005/\text{mm}^3$ and MPV mean \pm SD was 11.294 ± 1.1714 fl while PDW mean \pm SD was 17.394 ± 2.137 fl.²⁹

Conflicting results have been published regarding changes in platelet indices in normotensive pregnancies and PE. Some investigators found no difference in values of these indices between PE and controls,^{xvii,xviii} whereas others demonstrated lower PC and higher MPV and PDW in PE.^{xix} These researchers concluded that controversies between different studies, especially for MPV, probably are due to variations between different methods of measurement which are used for automated blood counts.

It can be fairly accepted here that platelet indices are simple, cheap and practical tools in predicting severity of PE. Comparing all cases of preeclampsia with abnormal vascular parameters however; some researchers concluded that WBC, HCT, RDW, PC, PDW, MPV, and PC to MPV ratio were not significantly different when mild and severe preeclampsia women were compared.³⁰ On the other hand Seung Woo Yang and coworkers have reported that among platelet indices, the PDW is significantly higher in women with severe PE than in women with mild PE, and is positively correlated with the MAP.¹⁶ Therefore, the PDW can serve as a candidate marker for predicting the severity of PE. Likewise; a study from Egypt by Kamel Ammar WAE, et al., found that the platelet count decreased, while MPV, PDW and PLCR increased with severity of preeclampsia, poor maternal prognosis and poor fetal prognosis.¹²⁹ However; it is noteworthy that some researchers failed to confirm PC and MPV as predictors of preeclampsia.^{17,26}

In the current study we noted that mean age of patients was 29.52 ± 6.17 years (Range = 18 to 40 years). However; almost half of population was in 3rd and 4th decade of life each. A study done by Kashanian M, et al. reported that the mean age of women was 27 ± 5.5 (15-43) years old.^{xx} Another study by Al Sheeha MA, et al.,¹¹ found that mean \pm SD age of preeclampsia was 30.6 ± 6.0 years which is in concordance with the current study results. Younger age cases of preeclampsia are also on record.^{xxi} Study by Dadhich S, et al.¹⁵ reported that the mean age range of the pregnant women was 23.45 ± 3.23 years while another study by Nooh AM, et al. reported mean \pm SD age was 24.1 ± 4.1 years.¹⁵ In the contrast, a study by Cehan T and coworkers¹²⁶ which has been conducted as a case control study, 56 pre-eclamptic women with 43 normotensive pregnant women were compared according to MPV and platelet count. Additionally; it was worth noting that in the current study that proportion of abnormal platelet indices in preeclampsia was double in women of younger age (18-20 years) compared to elder age women (31-40 years; p value = 0.085).

It is well accepted fact that the preeclampsia is more common in primigravida women. A study reported that 53.84% of patients in the preeclampsia group were primigravida while in the current study we found that 19% women were primigravid.¹⁵ This difference is can be declared due to the chance alone. On the other hand, Han L, et al. documented that all pregnant women in their study were nulliparous.³⁰ It is very unique finding of the current study that there was very minimal if any difference of frequency of abnormal platelet indices in women having preeclampsia was there in relation to the parity (P value = 0.992).

Women participating in current study had presented with mean \pm SD gestational age of 30.39 ± 4.90 weeks (Range 21 to 38). But it was important finding that proportion of abnormal platelet indices was highest in women of upto 24 weeks gestational age which eventually decreased to nil in women with 37 & above weeks gestational age (P value = 0.105). Comparing to the current study, a study by Al Sheeha MA, et al.,³⁰ found that mean \pm SD gestational age was 33.8 ± 4.3 weeks. This resemblance reiterates the fact that preeclampsia affects the third trimester just like first trimester. Study by Kashanian M, et al. reported that mean platelet volume in the 1st and 3rd trimesters of pregnancy are higher in women which potentially can develop preeclampsia, but has low predictive value and is not a good predictor of preeclampsia.²⁹ The study further; found that mean platelet volume in the 1st trimester and the third trimester of pregnancy of pre-eclamptic women was significantly higher than normotensive women (10.2 ± 1.06 fl VS 9.68 ± 1.09 fl with P value = 0.008) & (10.16 ± 1.23 fl VS 9.62 ± 1.12 fl, p value = 0.009) respectively. Han L, et al.,³⁰ reported that In the third trimester, the platelet count (PC) of these pregnant women sharply reduced to 164.9 ± 51.1 109/L from 185.7 ± 47.2 109/L in the first trimester (P value < 0.05), but their mean platelet volume (MPV) significantly elevated from 9.5 ± 1.1 fL during early pregnancy to 10.4 ± 1.4 fL during late pregnancy (P value < 0.05). Nevertheless, there were no significant differences in PDW or platelet ratio (Pt Ratio) between the first and the third trimesters (P value < 0.05). Another study by Akhila NR, et al., shows that MPV was significantly increased from first trimester to third trimester in women with gestational hypertension than in normal pregnant women.²⁰

Validity of changes in MPV in predicting PE has been extensively investigated. Dundar et al., in a previous large longitudinal study suggested that increase of MPV may precede development of PE symptoms by approximately 4.6 weeks (range 2.8-5.9 weeks). They suggested that sensitivity and specificity of MPV value at 24-28 gestational weeks with a cut-off value of 8.5 fL for predicting PE development were 78% and 86%, respectively. Accordingly, they concluded that women with MPV > 8.5 fL at 24-28 weeks were almost three times at risk of PE development (OR: 2.83). In the light of these results, they suggested that serial MPV monitoring may assist obstetricians and other healthcare givers in predicting development of PE. Different studies have different results regarding MPV and platelet count in preeclampsia. In a study by Jaremo et al.¹⁶ severe preeclampsia was accompanied with higher MPV, and preeclamptic women had a higher MVP and lower platelet count during the third trimester of gestation compared to post pregnancy stage of normotensive women. This study concluded that the severity of preeclampsia could be determined by MPV. The study by Dundar et al.,¹⁴ showed that MPV gradually

increases during pregnancies which will be terminated to preeclampsia, and this increase starts from 24 weeks of pregnancy and continues to the post partum stage.

There is a postulated association of smoking habit with occurrence of preeclampsia. In this regard, in the current study it was noted that proportion of women having history of being smoker and ex-smoker was 16.8% each while the remaining two third women (66.3%) were non-smokers. Though non-significant (P value = 0.550) yet, proportionally higher frequency of abnormal platelet indices among preeclampsia patients was noted in the smoker women (31.2%) compared to the ex-smokers (25%) and non-smokers (19%). Further women from urban areas had 1.5 times more risk of developing abnormal platelet indices during preeclampsia compared the women coming from rural background (P value = 0.153).

Studies like Nooh AM, et al. reported mean \pm SD BMI was 27.3 ± 3.1 Kg/m² or other which documented that mean \pm SD age body mass index, kg/m² was 31.0 ± 6.3 ,³⁰ and Han L, et al. documented that the mean \pm SD BMI at term was 23.8 ± 0.8 .¹³⁰ However; the current study did not checked for the BMI in preeclampsia.

The limitation of this study was that it was a cross sectional study which is unable to prove the role of platelet parameters in prediction and assessing the severity of preeclampsia in the course of the pregnancy period. Despite of this the current study has come up with some important clues regarding the health of women who are at risk of preeclampsia. It found that platelet count, MPV and PDW are useful to detect the risk of preeclampsia and these can play a role in predicting preeclampsia. Thus; the estimation of platelet indices during ANC when women blood drawn during early, mid, and late second trimester could be followed for the development of preeclampsia and predict the prognosis of the mother and the fetus. It therefore; may be considered as an easy, reliable, economic and rapid method for detection of preeclampsia and assessment of its severity. Further research is also recommended through this study by including more study participants which would help to assess whether or not preeclampsia can be predicted in the early second trimester in a similar way.

CONCLUSION

Preeclampsia is very dangerous condition posing life threat to mother and the fetus if it is not quickly diagnosed and treated. It is far better to be able to predict the condition and take preemptive measure to reduce the chance of any materno-fetal morbidity. An excessive and recently worked upon method is to measure abnormal platelet indices in order to foretell the occurrence of preeclampsia.

The current study found that platelet volume and platelet distribution width both increase while platelet count decreases among women who develop the preeclampsia. Age, gestational age, parity, history of smoking and urban living are some of the important variables which can also be studied thoroughly in future researches to evaluate the predictive value of platelet indices for preeclampsia prediction

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