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Role of platelet indices in non-thrombocytic pih

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***Abstract*---**Background: Thrombocytopenia seen in PIH may be due to increased adherence of platelets at the site of damaged vascular endothelium leading to increased consumption and secondary platelet destruction and activation. Variation in platelet count is associated with changes in platelet indices, plateletcrit and PDW depicts the average size and variation respectively. Aims and Objectives: To evaluate and study platelet indices in the assessment of severity of pre-eclampsia and eclampsia that have normal platelet count. Materials and Methods: Prospective study to determine the Role of Platelet Distribution width and Plateletcrit in the department of OBGY, KIMS, Karad (Apr. 2021 to Sept. 2021). Result: Sample size: 123. 95% of pre-eclampsia patients and 99% of eclampsia patients had increased PDW. 68% of pre-eclampsia patients and 82% of eclampsia patients had decreased plateletcrit. Diagnostic cut-off value of PDW 17.45 fl. in preeclampsia and 17.25 in fl. in eclampsia. Plateletcrit was significantly lower (< 0.17) in preeclampsia and eclampsia. Conclusion: Platelet indices should be done as it has a significant relationship with severity of PIH, i.e., increase in PDW and decrease in plateletcrit and even to decide the time for delivery.

***Keywords*---**platelet indices, non-thrombocytic, pre-eclampsia, eclampsia.

Introduction

Pregnancy induced hypertension is one of the serious complications of pregnancy affecting 5-10% of pregnancies and presenting with hypercoagulable state. Most common haematological abnormality occurring in women with PIH is thrombocytopenia which at times becomes life threatening. (1-3) Pre-eclampsia is a multisystem disorder in which there is abnormal vascular response in from of increased vascular resistance, platelet aggregation, activation of coagulation system with resultant endothelial cell dysfunction and reduced organ perfusion. It

is a worldwide issue that affects 10 to 17 percent of all pregnancies. PIH is prevalent in India, with rates ranging from 5% to 15%.(4) PIH is responsible for 14% of all maternal fatalities worldwide. (5) Some biological measures, such as angiogenic markers and placental tissue, have been proposed. Some researchers have looked into protein 13 (PP-13), soluble endoglin, and soluble fms-like tyrosine kinase1.(4,6)These procedures, on the other hand, are not ideal for routine screening that is simple, low-cost, and quick.

Thrombocytopenia in pregnancy induced hypertension might be due to increased adherence of platelets at the site of damaged vascular endothelium that leads to increased consumption and secondary destruction of platelets. There is activation of platelets along with decreased degranulation leading to reduced platelet life span and increased number of immature platelets in blood. The variation in platelet count is associated with changes in platelet indices i.e., Mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit.

Large platelets are more reactive than smaller ones due to increased number and size of pseudopodia leading to increased PDW while plateletcrit depicts total mass of platelets, which is the product of total platelet count and MPV reflects changes in bothnumber and size of the platelets. MPV and PDW depict the average size and heterogenicity in platelet morphology respectively as described. Therefore, when thrombocytopenia is due to peripheral platelet destruction, platelet production is stimulated with increased number of large platelets in blood, leading to increased MPV. (7) Plateletcrit is an indicator of platelet activity in the blood hence low plateletcrit reflects low platelet activity. (8-11) Decrease in platelet count (<1,00,000/L) is considered as an indicator of severity of the disease is the characteristic of worsening of pregnancy induced hypertension, however in few studies because of uncontrolled platelet activation and aggregation, even in non-thrombocytopenic states, worsening of PIH cases has been reported. Therefore, purpose of this study was to evaluate new markers of platelet activation such as platelet indices in non-thrombocytopenic patients.

Aims and Objectives

Aim:
To evaluate platelet indices in the assessment of pre-eclampsia and eclampsia that have normal platelet counts.

Objectives:

1) To study plateletcrit in normal and pre-eclampsia patients.
2) To study platelet distribution width in normal and pre-eclampsia patients.
3) To study the relation of platelet indices with severity of pre-eclampsia.

Materials and Methods
Methodology

This was a prospective observational study to determine the Role of Platelet Distribution width and Plateletcrit in the assessment on nonthrombocytopenic pre-eclampsia and Eclampsia.

Patients with inclusion criteria admitted in Department of Obstetrics and Gynaecology in a tertiary care centre from January 2020 to June 2021 were included

Sample size: - 123 patients

Inclusion Criteria: -
On basis of blood pressure and proteinuria, patients were divided into three groups:
Group 1: Normal – Pregnant women of more than 20 weeks of gestational age.
Group 2: Pre-eclampsia – Including both: -

1) Non-severe - Patients with BP ≥ 140/90mmHg but ≤160/110 mmHg with urine albumin positive on dipstick method.
2) Severe - Patients with BP ≥ 160/110 mmHg with urine albumin positive on dipstick method

Group 3: Eclampsia – Patients with BP ≥ 140/90mmHg with urine albumin positive on dipstick and convulsions/coma.

Exclusion Criteria:
Previous history of: -

- Haemorrhagic disorder
- Epilepsy
- Hypertension
- Drug intake affecting platelet count.
- Diabetes mellitus
- Renal disease
- Dengue positive status
- Viral fever
- Harris Platelet Syndrome

Data Acquisition, Facilities and Equipment:

Once a patient satisfied the inclusion criteria for the study, she was administered the study proforma. The patients were briefed about the procedure and consent was taken. CBC counts and platelet indices were done on the ANC patients and put in category to follow-up for the outcome and study completion.

Blood samples were taken under all aseptic precautions and sent to lab for routine investigations and platelet indices. Reports were collected and followed up for study completion.

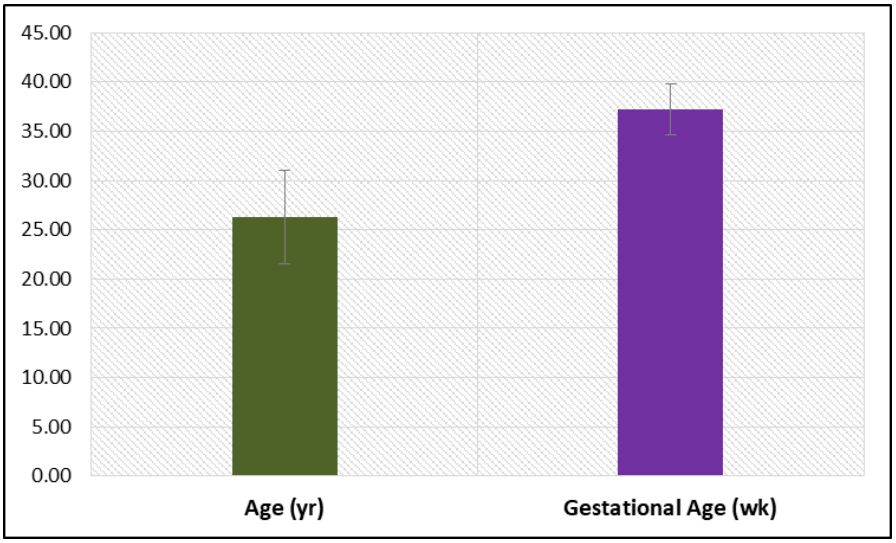
Results

Observations & Results

Table 1
Descriptive Summary of Age, Gestational Age, SBP and DBP of Study Cases

Age (yr)	26.27	4.73
Gestational Age (wk)	37.24	2.57
SBP	139.67	17.13
DBP	87.48	12.12

The mean age of the study cases was 26.27±4.73 yr. The mean gestational age was 37.24±2.57 wk. While mean SBP and DBP were 139.67±17.13 mmHg and 87.48±12.13 mmHg respectively.



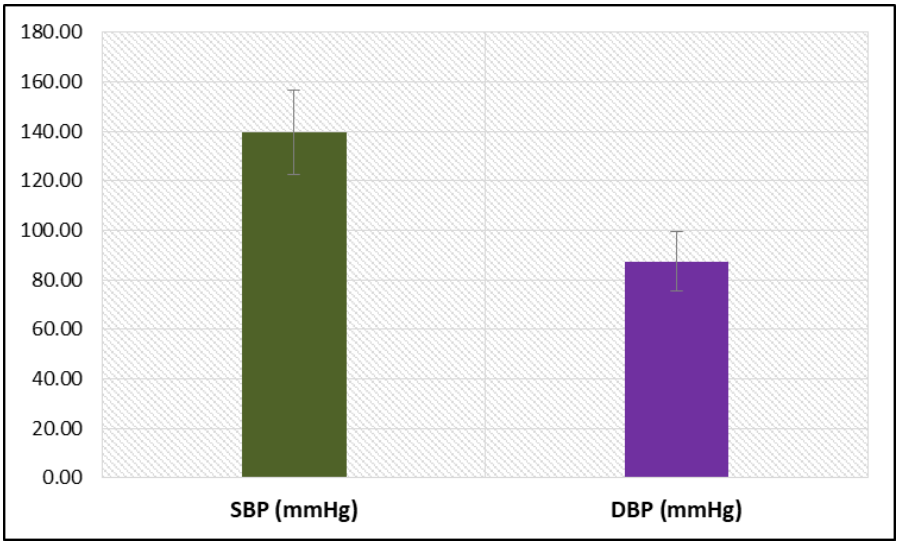


Table 2
Distribution of Cases according to Parity, Period of Gestation and SES

Variable		No.	%
Parity	Primigravida	44	35.8
	Multigravida	79	64.2
Period of Gestation	< 37 wk	36	29.3
	37 - 38 wk	28	22.8
	38 - 39 wk	36	29.3
	39 - 40 wk	12	9.8
	> 40 wk	11	8.9
SES	III	51	41.5
	IV	64	52.0
	V	8	6.5

Out of 123 study cases, 44 (35.8%) were Primigravida cases while 79 (64.2%) were Multigravida cases. 29.3% cases have period of gestation less than 37 weeks, while 8.9% have POG more than 40 weeks. The proportion of cases with POG 37-38 wk, 38-39 wk and 39-40 wk was 22.8%, 29.3% and 9.8% respectively. The cases with SES III, IV and V were arrived in proportion 41.5%, 52% and 6.5% respectively.

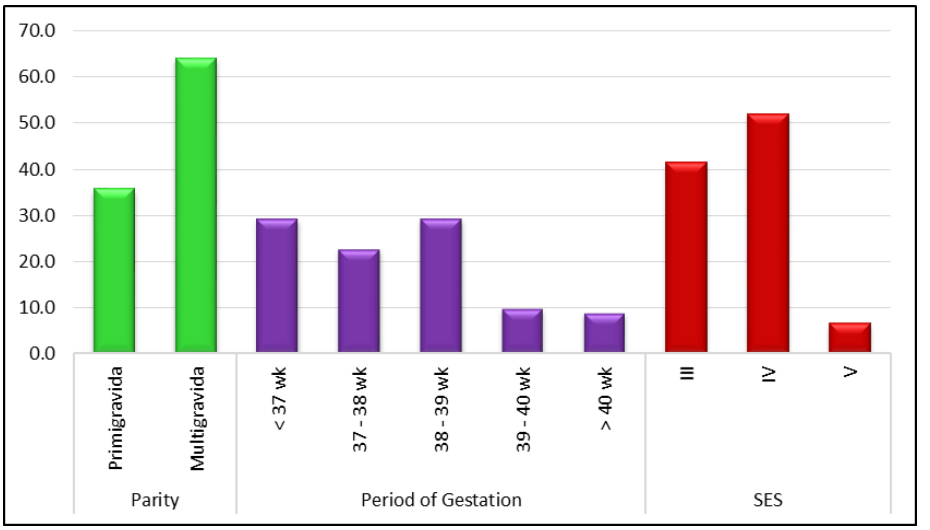


Table 3
Descriptive Summary of PC, PDW and Plateletcrit of Study Cases

Variable	Mean	SD
Platelet count (L/cu. mm)	2.24	0.59
PDW (fl)	17.54	1.26
Plateletcrit	0.17	0.06

The mean platelet count of the study cases was 2.24±0.59 L/cu.mm. The mean PDW (fl) was 17.54±1.26 and mean Plateletcrit was 0.17±0.06.

Table 4
Distribution of Cases according to Urine Albumin Status

Urine Albumin	No.	%
Negative	67	54.5
Positive	56	45.5
Total	123	100.0

The urine albumin was found to be positive in 56 (45.5%) cases while in rest 67 (54.5%) cases it was negative.

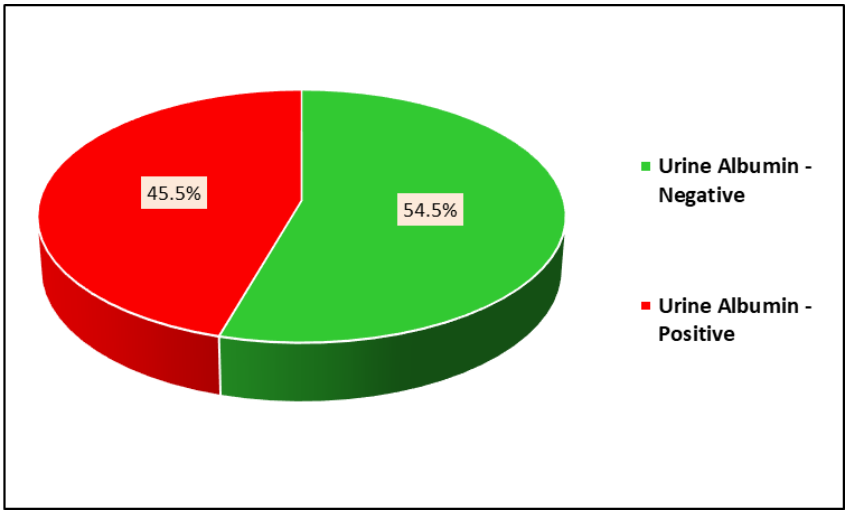


Table 5
Distribution of Cases according to Diagnosis

Diagnosis	No	%
Normal	67	54.47
Non Severe Pre Eclampsia	21	17.07
Severe Pre Eclampsia	24	19.51
Eclampsia	11	8.94
Total	123	100.00

The non-severe pre eclampsia was found in 21 (17.07%) cases while severe preeclampsia and eclampsiain were observed in 24 (19.51%) and 11 (8.94%) cases respectively. Rest 67 (54.47%) study cases were normal.

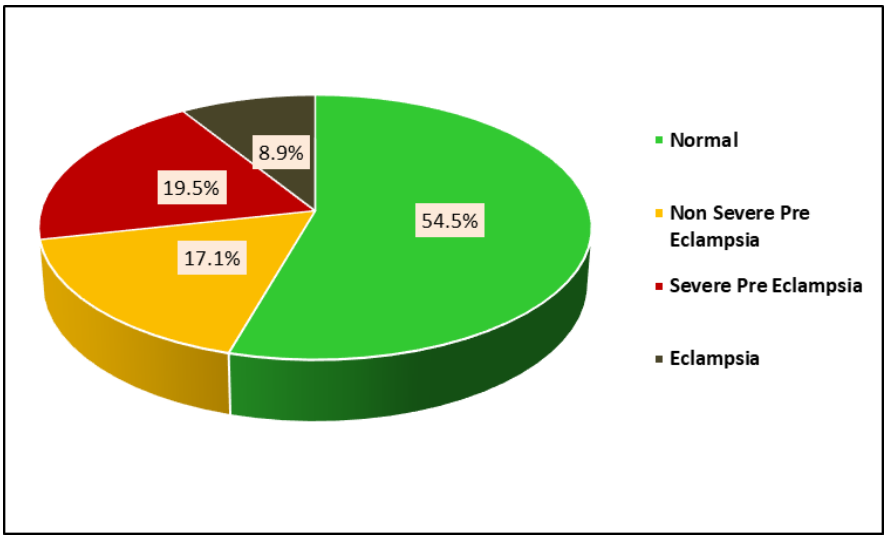


Table 6
Distribution of Cases according to Mode of delivery and Maternal/Fetal Outcome

Variable		No.	%
Mode of Delivery	PTVD	10	8.1
	FTVD	35	28.5
	LSCS	78	63.4
Maternal outcome	HELLP syndrome	1	0.8
	Neuro transfer	1	0.8
	Stable	117	95.1
	Wound gape	4	3.3
Fetal Outcome	Motherside	102	82.9
	NICU	15	12.2
	IUD	5	4.1
	Stillbirth	1	0.8

Out of 123 study cases, PTVD, FTVD and LSCS were included in 8.1%, 28.5% and 63.4% cases respectively. Maternal outcome was stable in 117 cases, while HELLP syndrome, neuro transfer and wound gap were observed in 1 (0.8%), 1 (0.8%) and 4 (3.3%) cases respectively. The fetal outcome was motherside in 102 (82.9%) cases while NICU and IUD admission were observed in 15 (12.2%) and 5 (4.1%) cases respectively.

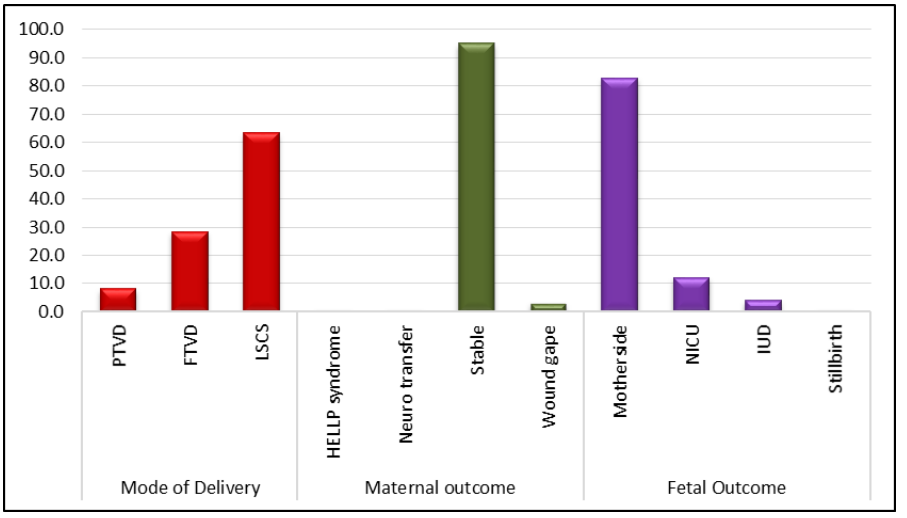


Table 7
Comparison of Age between Normal, Pre eclampsia and Eclampsia Cases

Group	Age in years		ANOVA	
	Mean	SD	F-value	p-value
Normal	26.16	4.36	.253	.859
Non Severe Pre Eclampsia	26.00	3.85		
Severe Pre Eclampsia	27.00	5.62		
Eclampsia	25.82	6.65		

On comparing the mean age among various type of cases, it was found that the mean age was minimum in eclampsia cases (25.82±6.65) yrs and maximum in severe pre eclampsia cases (27.00±5.62) yrs. However no significant difference was observed in mean ages between the groups (p=0.859).

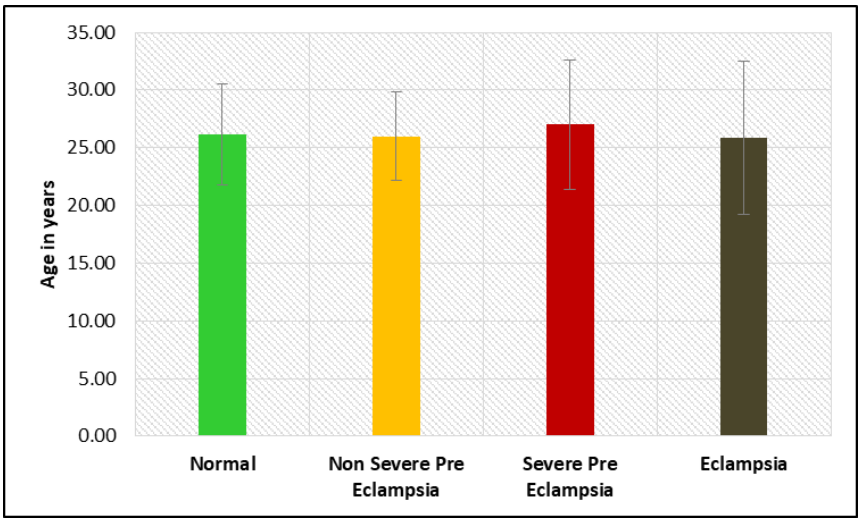


Table 8
Comparison of GA between Normal, Pre eclampsia and Eclampsia Cases

Group	Gestational age (wk)		ANOVA	
	Mean	SD	F-value	p-value
Normal	37.52	2.44	1.927	.129
Non Severe Pre Eclampsia	37.72	1.88		
Severe Pre Eclampsia	36.65	3.03		
Eclampsia	35.94	3.05		

On comparing the mean gestational age among various type of cases, it was found that the mean GA was minimum in eclampsia cases (35.94±3.05 wk) and maximum in non-severe pre eclampsia cases (37.72±1.88 wk). However no significant difference was observed in mean GA between the groups (p=0.129).

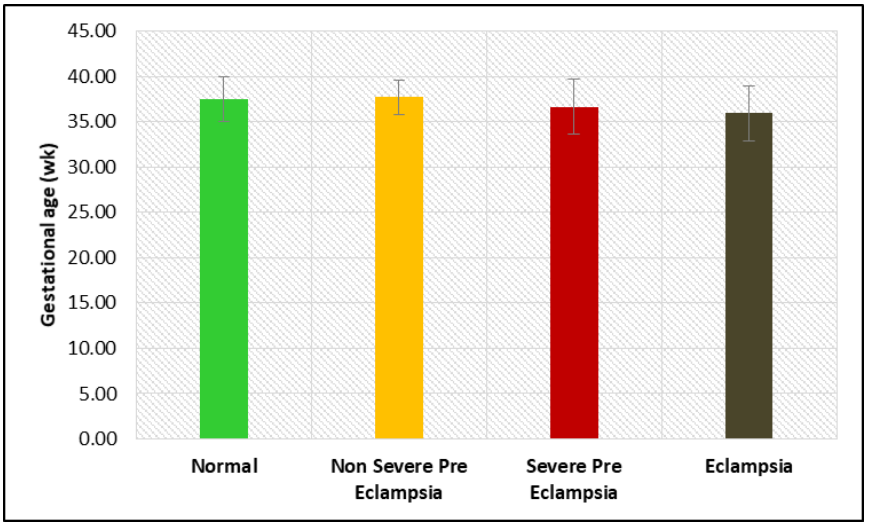


Table 9
Comparison of SBP between Normal, Pre eclampsia and Eclampsia Cases

Group	SBP		ANOVA	
	Mean	SD	F-value	p-value
Normal	128.96	9.23	54.683	<0.001
Non Severe Pre Eclampsia	142.38	7.68		
Severe Pre Eclampsia	160.83	13.16		
Eclampsia	153.64	20.63		

On comparing the mean SBP among various type of cases, it was found that the mean SBP was minimum in normal cases (128.96±9.23) mmHg and maximum in severe pre eclampsia cases (160.83±13.16) mmHg. Highly significant difference was observed in mean SBP among the groups (p<0.001).

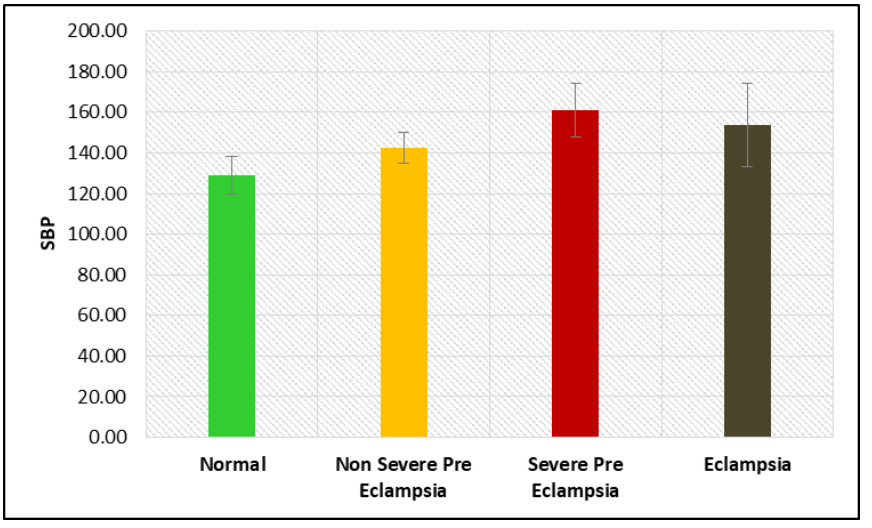


Table 10
Comparison of DBP between Normal, Pre eclampsia and Eclampsia Cases

Group	DBP		ANOVA	
	Mean	SD	F-value	p-value
Normal	79.40	6.72	59.235	**<0.001**
Non Severe Pre Eclampsia	91.43	4.78		
Severe Pre Eclampsia	101.25	9.47		
Eclampsia	99.09	13.00		

On comparing the mean DBP among various type of cases, it was found that the mean DBP was minimum in normal cases (79.40±6.72) and maximum in severe pre eclampsia cases (101.25±9.47). Highly significant difference was observed in mean DBP among the groups (p<0.001).

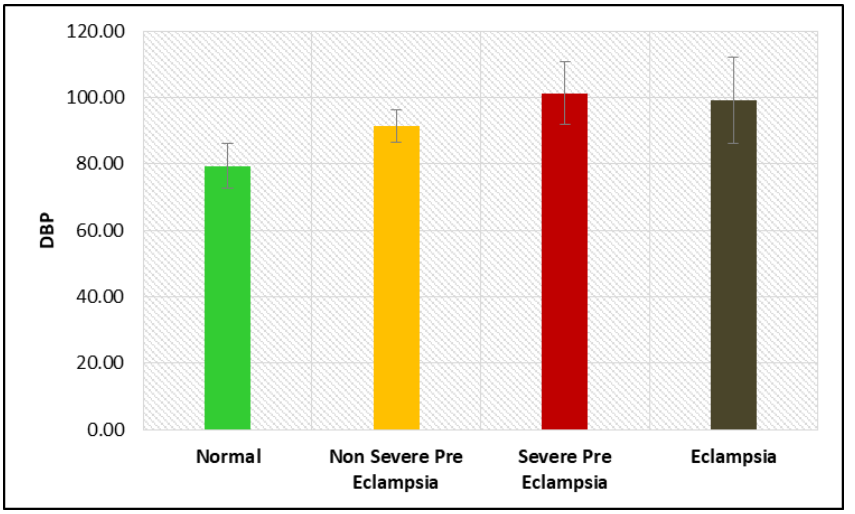


Table 11
Comparison of Parity, POG, SES and Urine Albumin between Normal, Pre eclampsia and Eclampsia Cases

Variable		Normal		No severe Pre Eclampsia		Severe Pre Eclampsia		Eclampsia		chi sq	p-value
		No.	%	No.	%	No.	%	No.	%		
Parity	Primi	15	34.1%	13	29.5%	11	25.0%	5	11.4%	12.97	**0.005**
	Multi	52	65.8%	8	10.1%	13	16.5%	6	7.6%		
POG	< 37 wk	15	41.7%	6	16.7%	9	25.0%	6	16.7%	8.60	0.736
	37 - 38 wk	18	64.3%	5	17.9%	4	14.3%	1	3.6%		
	38 - 39 wk	19	52.8%	7	19.4%	7	19.4%	3	8.3%		
	39 - 40 wk	9	75.0%	1	8.3%	2	16.7%	0	0.0%		
	> 40 wk	6	54.5%	2	18.2%	2	18.2%	1	9.1%		

SES	III	32	62.7%	8	15.7%	7	13.7%	4	7.8%	8.51	0.203
	IV	34	53.1%	11	17.2%	13	20.3%	6	9.4%		
	V	1	12.5%	2	25.0%	4	50.0%	1	12.5%		
UA	Negative	64	95.5%	2	3.0%	1	1.5%	0	0.0%	100.28	**<0.001**
	Positive	3	5.4%	19	33.9%	23	41.1%	11	19.6%		

The proportion of severity was much increased in primigravida cases than the multigravida cases. The significant association of eclampsia severity was found with parity (p=0.005). No significant association of eclampsia severity was found with period of gestation (p=0.736) and socio-economic status (p=0.203). The proportion of urine albumin positive cases was more as severity of eclampsia increased. The significant association of eclampsia severity was found with presence of urine albumin (p<0.001).

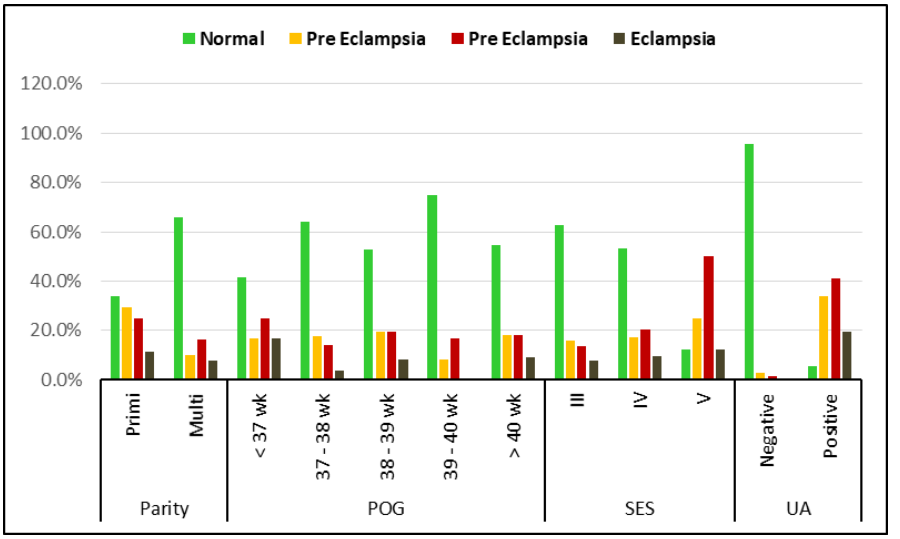


Table 12
Comparison of Platelet Count between Normal, Pre eclampsia and Eclampsia Cases

Group	Platelet count (L/cu. mm)		ANOVA	
	Mean	SD	F-value	p-value
Normal	2.38	0.63	4.498	**.005**
Non Severe Pre Eclampsia	2.29	0.49		
Severe Pre Eclampsia	2.00	0.42		
Eclampsia	1.85	0.58		

On comparing the mean platelet count among various type of cases, it was found that the mean platelet count was minimum in eclampsia cases (1.85±0.58) and maximum in normal cases (2.38±0.63). Highly significant difference was observed in mean platelet count among the groups (p=0.005).

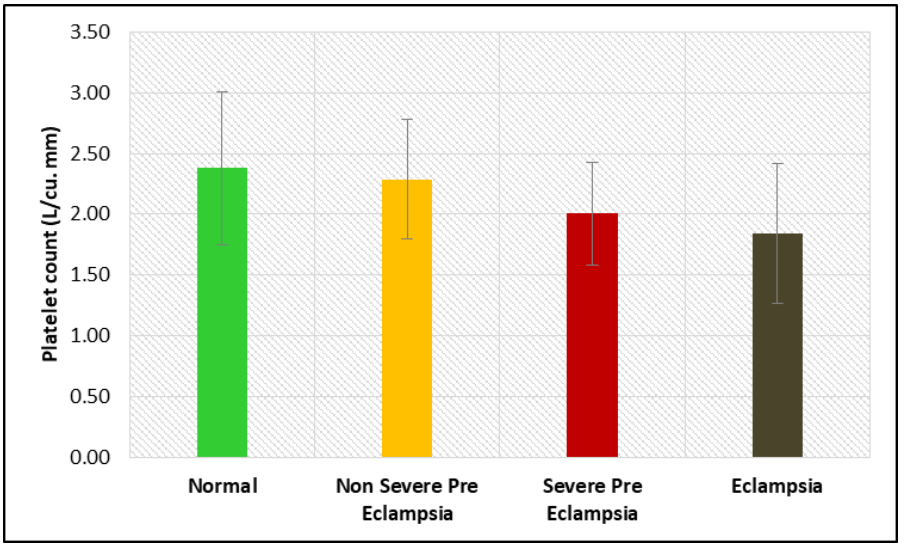


Table 13
Comparison of PDW between Normal, Pre eclampsia and Eclampsia Cases

Group	PDW (fl)		ANOVA	
	Mean	SD	F-value	p-value
Normal	17.33	1.46	1.406	.244
Non Severe Pre Eclampsia	17.79	0.65		
Severe Pre Eclampsia	17.84	0.94		
Eclampsia	17.70	1.36		

On comparing the mean PDW among various type of cases, it was found that the mean PDW was minimum in normal cases (17.33±1.46) and maximum in severe pre eclampsia cases (17.84±0.94). However no significant difference was observed in mean PDW among the groups (p=0.244).

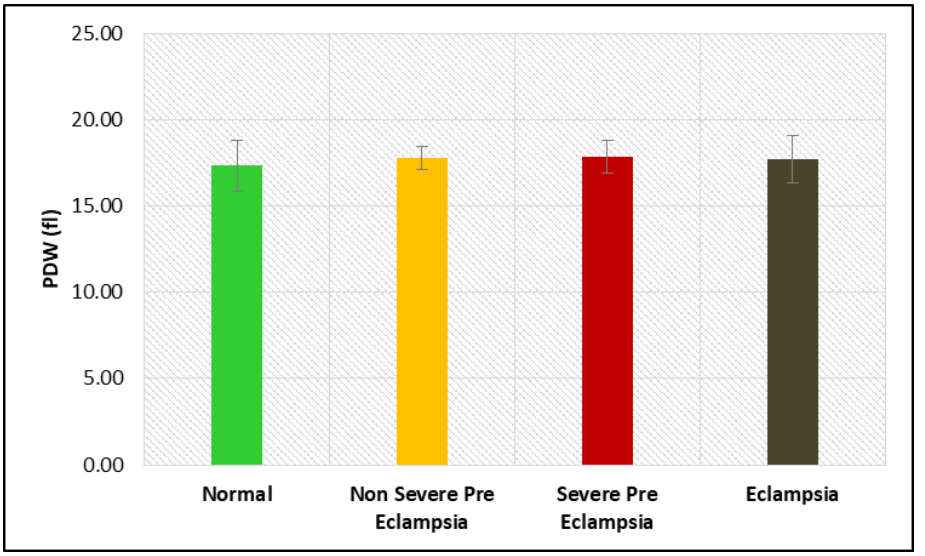


Table 14
Comparison of plateletcrit between Normal, Pre eclampsia and Eclampsia Cases

Group	Platelet crit		ANOVA	
	Mean	SD	F-value	p-value
Normal	0.18	0.07	3.893	**.011**
Non Severe Pre Eclampsia	0.16	0.04		
Severe Pre Eclampsia	0.14	0.04		
Eclampsia	0.15	0.05		

On comparing the mean Platelet Crit among various type of cases, it was found that the mean PCr was minimum in severe pre eclampsia cases (0.14±0.04) and maximum in normal cases (0.18±0.07). The significant difference was observed in mean PCrit among the groups (p=0.011).

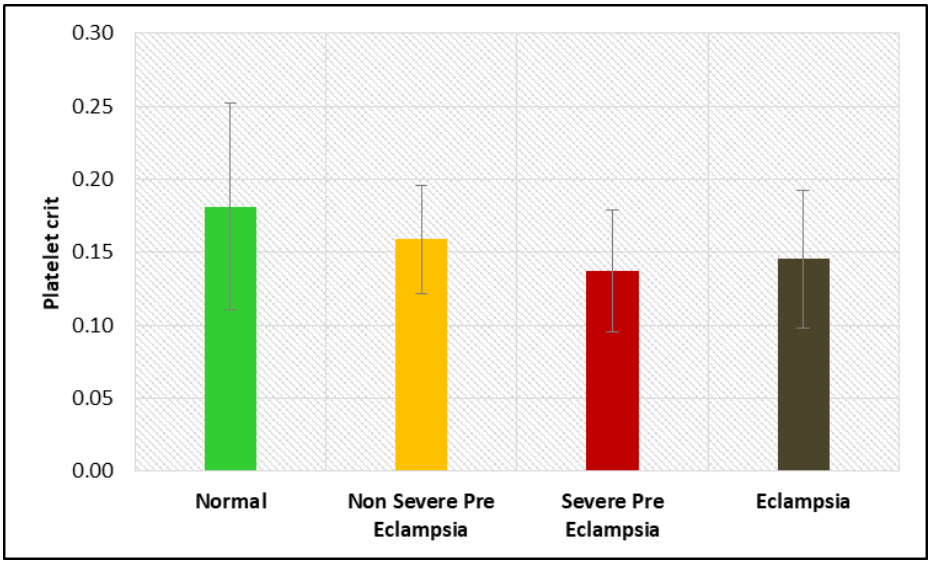


Table 15
Comparison of Mode of delivery between Normal, Pre eclampsia and Eclampsia Cases

Variable		Normal		Pre Eclampsia		Pre Eclampsia		Eclampsia		chi sq	p-value
		No.	%	No.	%	No.	%	No.	%		
Mododel	PTVD	5	50.0%	2	20.0%	2	20.0%	1	10.0%	10.49	0.105
	FTVD	25	71.4%	7	20.0%	3	8.6%	0	0.0%		
	LSCS	37	47.4%	12	15.4%	19	24.4%	10	12.8%		

No significant association of eclampsia severity was found with mode of delivery (p=0.105). However eclampsia cases more in LSCS and normal were more in FTVD.

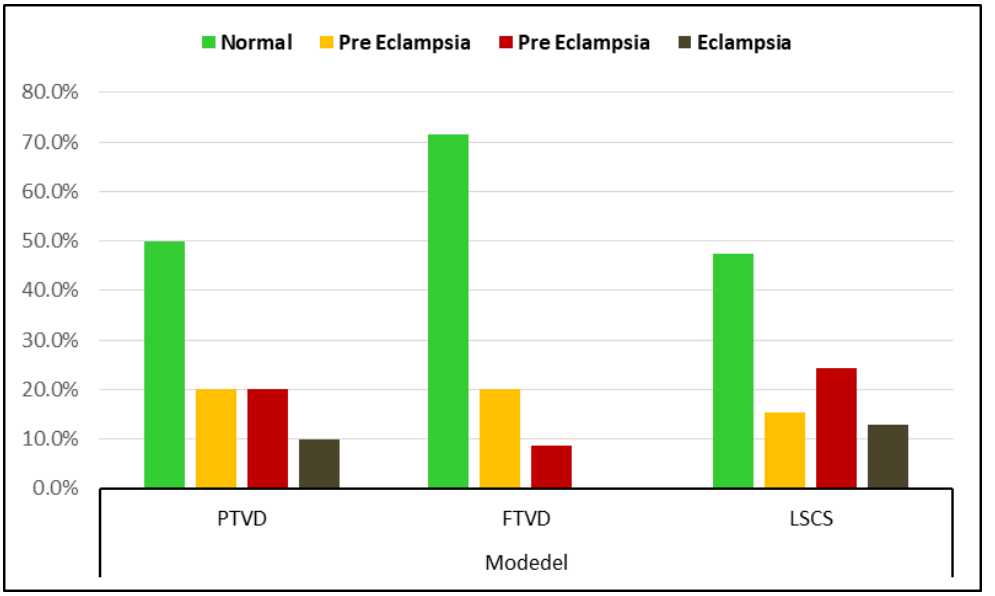
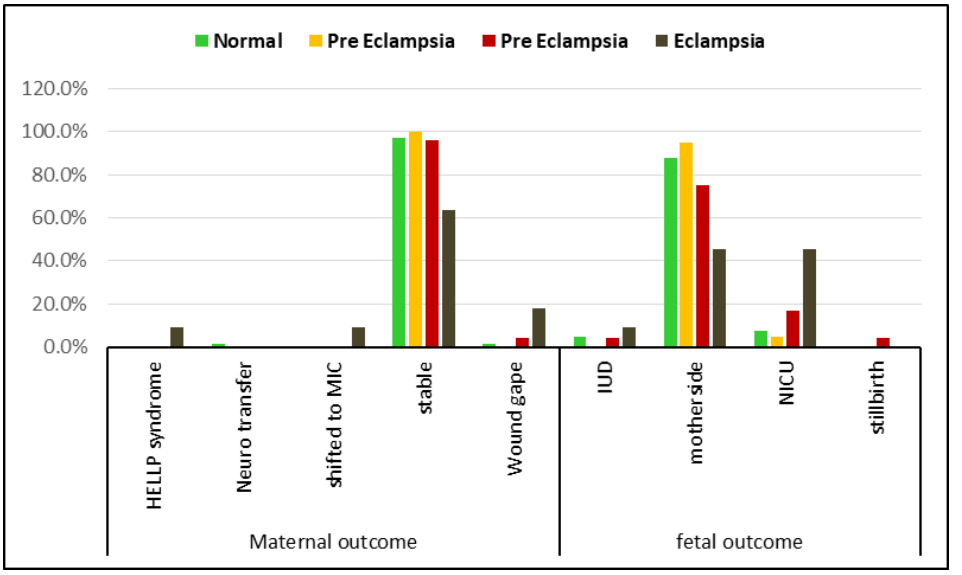


Table 16
Comparison of Maternal/Fetal Outcomes between Normal, Pre eclampsia and Eclampsia Cases

Variable		Normal		Pre Eclampsia		Pre Eclampsia		Eclampsia		chi sq	p-value
		No.	%	No.	%	No.	%	No.	%		
Mater-nal outcome	HELLP syndrome	0	0.0%	0	0.0%	0	0.0%	1	9.1%	31.35	**0.002**
	Neuro transfer	1	1.5%	0	0.0%	0	0.0%	0	0.0%		
	shifted to MIC	0	0.0%	0	0.0%	0	0.0%	1	9.1%		
	stable	65	97.0%	21	100.0%	23	95.8%	7	63.6%		
	Wound gape	1	1.5%	0	0.0%	1	4.2%	2	18.2%		
fetal outcome	IUD	3	4.5%	0	0.0%	1	4.2%	1	9.1%	20.89	**0.013**
	motherside	59	88.1%	20	95.2%	18	75.0%	5	45.5%		
	NICU	5	7.5%	1	4.8%	4	16.7%	5	45.5%		
	stillbirth	0	0.0%	0	0.0%	1	4.2%	0	0.0%		

The significant association of eclampsia severity was found with maternal outcome (p=0.002). Among normal cases, 97% were stable, among non severe preeclamisa cases 100% were stable while in eclampsia cases, HELLP syndrome was found in 1 case and wound gape in 2 cases.



Discussion

Pre-eclampsia is multisystem disorder, characterized by abnormal vascular response to placentation that is associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of coagulation system and endothelial dysfunction. It is important cause of maternal and perinatal morbidity and mortality as it is associated with high risk of IUGR, pre-term delivery, placental abruption etc. Furthermore, it has long term consequences as women who experience this disorder represent a high-risk group for subsequent premature cardiovascular, cerebrovascular, peripheral arterial diseases and other chronic illnesses later in life.

Uncontrolled platelet activation and aggregation are expected in pre-eclampsia and eclampsia patients (14). In non-thrombocytopenic pregnancy, in response to platelet activation, there is increase in bone marrow turnover that leads to production of new enlarged platelets that further leads to maintenance of normal platelet count but mean platelet volume and PDW increase due to large platelets. This might be the reason of increased PDW even in some of the normal controls as pregnancy itself is a hypercoagulable state.

In our study, mean platelet count were decreased (Mean: 1.95 L/cu.mm) but the values were within normal range (1.5 to 4.5 L/cu.mm). Many studies found showing similar results (5,7,10,11). Mean platelet distribution width (PDW) was found to show a significant increase and the value was above normal range (9-14 fl) in all the groups (17.37 fl in normal; 17.74 fl in pre-eclampsia; 18.81 fl in eclampsia) including few of the controls. Similar observation was seen in other studies as well (12,13,14,15). Increase in mean PDW can be directly linked with the degree of thrombocytopenia. By above values, p-value turned out to be < 0.001 therefore, PDW can be taken as an important parameter in the assessment of pregnancy induced hypertension as a reflection of ongoing platelet activation

even in non-thrombocytopenic conditions. Furthermore, serial estimation of mean PDW can be of great help in understanding the severity of the disease.

Mean plateletcrit was found to show a significant decrease in our study (0.17 in normal; 0.13 in pre-eclampsia; 0.11 in eclampsia). The p-value turned out to be < 0.001 suggesting that plateletcrit can be taken as an important parameter in the assessment of pregnancy induced hypertension and like PDW, plateletcrit can also reflect the severity of the disease. A number of studies showed similar results (1,2,3,4,12). In my study, PDW showed 60.7% sensitivity and 68.7% specificity for prediction of pre-eclampsia and 66.7% sensitivity and 46.7% specificity for prediction of eclampsia. Plateletcrit showed 57.1% sensitivity and 98.5% specificity for prediction of pre-eclampsia and 81.3% sensitivity and 53.3% specificity for prediction of eclampsia.

Conclusion

There was a significant relationship between platelet indices and severity of pregnancy induced hypertension. There was increase in PDW and decrease in plateletcrit with severity of PIH. Hence instead of relying on platelet count alone, PDW and plateletcrit should also be assessed in patients of pregnancy induced hypertension. Estimation of these parameters will also help us to decide further management of the patient along with prevention of further progression to HELLP syndrome and DIC. Women with preeclampsia have a higher risk of adverse newborn outcomes such as intrauterine growth restriction and fetal distress. Platelet indices can be utilised as efficient biomarkers that are both easy and affordable to obtain, especially in developing nations like India. Platelet indices can be utilised as a predictive tool to assist prediction of pre-eclampsia to improve fetomaternal outcomes.

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