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Original Article

Pathology Section

Platelet Count and Platelet Distribution Width: Potential Predictive Biomarkers for Preeclampsia and Eclampsia

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ABSTRACT

Introduction: Hypertensive disorders of pregnancy are one of the most common obstetric pathologies, affecting approximately 8-10% of all pregnancies worldwide, including entities like preeclampsia and eclampsia. Preeclampsia increases the risk of maternal morbidity and mortality, foetal mortality, and preterm birth. Early identification of preeclampsia and eclampsia helps in the effective management and favourable outcome of pregnancy.

Aim: To determine the relationship between platelet parameters, namely Platelet Count (PC) and Platelet Distribution Width (PDW), with preeclampsia and eclampsia.

Materials and Methods: A hospital-based analytical cross-sectional study was conducted in the Department of Pathology in collaboration with the Department of Obstetrics and Gynaecology, including 100 pregnant women attending the antenatal clinic in Jorhat Medical College and Hospital, Jorhat, Assam, India, for a duration of one year (from June 2021 to July 2022). Pregnant women meeting the inclusion criteria were selected and divided into two broad groups: a comparison group comprising normotensive pregnant women (n=50) and a study group (n=50), which further included subgroups of preeclamptic women (n=35) and eclamptic women (n=15). A 5 mL venous blood sample was drawn and collected in an Ethylenediaminetetracetic acid (EDTA) vial from both groups and analysed using a six-part fully automated haematology cell counter (SYSMEX XN-550) for PC and PDW. Changes in PC and PDW were compared between the two groups using a student t-test with GraphPad software. A p-value of <0.05 was considered statistically significant.

Results: The mean PC in preeclampsia was 185.714±69.56×10^3/µL, while in eclampsia, it was 147.53±56.927×10^3/µL. The mean value of PDW in preeclampsia was 18.4314±4.184 fL, while in eclampsia, it was 14.86±3.854 fL. A decrease in PC was found to be statistically significant in eclampsia (p-value <0.001). PDW was statistically significantly different among normotensive, preeclamptic, and eclamptic participants (p-value <0.001). The increase in PDW was higher in eclamptic patients compared to preeclamptic patients.

Conclusion: Hence, the estimation of PC and PDW can be used as a screening test for the early identification of preeclampsia and eclampsia. Platelet parameters may act as an indicator of preeclampsia and eclampsia. The prognosis of preeclampsia and eclampsia in pregnant women can also be assessed, making them effective prognostic markers as PDW correlates with disease severity. Moreover, these indices are cost-effective and easily available.

Keywords: Maternal mortality, Pregnancy, Prognostic makers, Platelet activation

INTRODUCTION

Pregnancy is a physiological process that is normally associated with significant changes in the haemostatic mechanism to maintain placental function during pregnancy and prevent excessive bleeding during delivery. Pregnancy complications caused approximately 289,000 deaths of pregnant women worldwide in 2013, and 99% of those women were from developing countries [1]. Pregnancy-induced hypertension is one of the most frequently encountered pregnancy-related medical complications, alongside gestational diabetes mellitus. Hypertensive disorders of pregnancy occur in 10% of all pregnant women worldwide. The present study was aimed to determine the relationship of platelet parameters, namely PC and PDW, with preeclampsia and eclampsia.

Preeclampsia is a multisystem disorder of unknown aetiology. According to the International Society for the Study of Hypertension in Pregnancy (ISSHP), preeclampsia is defined as de novo hypertension (systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg on atleast two occasions measured four hours apart) in previously normotensive women, occurring at or after 20 weeks of pregnancy, together with proteinuria (300 mg/24 hours protein: creatinine ratio >0.3; ≥1+dipstick) or without proteinuria in the presence of any evidence of end-organ damage like thrombocytopenia, renal insufficiency, impaired liver function, pulmonary oedema, new-onset headache unresponsive to medication, or visual symptoms [2,3]. Development of convulsions in a case of preeclampsia, which cannot be attributed to another cause, is termed eclampsia.

Preeclampsia usually occurs in the last trimester of pregnancy and more commonly in primiparas, with a higher incidence in the first pregnancy, especially in women aged less than 20 years. While the exact mechanisms leading to preeclampsia are still being studied, it is clear that the placenta plays a central role in the pathogenesis of the syndrome, as evident from observations that symptoms disappear rapidly after delivery of the placenta [4]. An initiating event in preeclampsia has been proposed to be reduced perfusion of the placenta, which leads to widespread dysfunction of the maternal vascular endothelium by mechanisms that remain to be defined. Risk factors for preeclampsia include age over 35 years or teenage pregnancy, nulliparity, a long interval between pregnancies, a family history of preeclampsia, and the presence of any co-morbidity like chronic hypertension, diabetes mellitus, renal disease, obesity, collagen vascular disorders like Systemic Lupus Erythematosus (SLE). Obesity, maternal low birth weight, blacks, and Asians are other risk factors. Abnormal placental vasculature, diffuse endothelial dysfunction, imbalance of angiogenic and antiangiogenic factors, vasoconstriction, increased vascular permeability, and coagulation abnormalities with alteration of the haematological profile are the principal pathophysiological aberrations in preeclampsia [4,5]. Vascular leakage/dysfunction caused by Hypertensive Disorders of Pregnancy (HDP) leads to increased platelet consumption, resulting

in increased platelet activation. In these patients, the production of new platelets begins in the bone marrow to compensate for platelet consumption [6].

Increased platelet consumption causes a reduction in PC. Active turnover of platelet production in the bone marrow due to peripheral consumption leads to an increase in both MPV and PDW. As the severity of preeclampsia increases, platelet consumption also increases [7]. Therefore, certain indices are used to estimate platelet number and function, which can be useful for assessing the severity of preeclampsia. PC, PDW, Mean Platelet Volume (MPV), and Plateletcrit (PCT) are markers of platelet activation [8,9]. MPV and PDW increase with elevated blood pressure [8]. These alterations in parameters have a major impact on the final outcome of pregnancy, such as seizures (eclampsia), ischaemic heart disease, stroke, type II diabetes, venous thromboembolism, haemorrhagic and hepatic damage, Haemolysis Elevated Liver Enzyme Low Platelet Count (HELLP) syndrome, renal dysfunction, as well as preterm delivery and abruptio placentae [8]. Therefore, early detection of these clinical entities, i.e., preeclampsia, will help initiate aggressive therapy at the very early stage and thus decrease maternal and neonatal morbidity and mortality. Hence, the objective of present study is to assess whether PC and indices like PDW can be useful screening tests for the early identification and prognosis assessment of pregnant women with hypertension.

MATERIALS AND METHODS

A hospital-based analytical cross-sectional study was conducted in the Department of Pathology in collaboration with the Department of Obstetrics and Gynaecology at Jorhat Medical College and Hospital, Jorhat, Assam, India, from June 2021 to July 2022. Clearance from the Institutional Ethics Committee was obtained prior to the commencement of the study (IEC NO. SMEJ/JMCH/MEU/841/Pt-2/2011/3681). Routine clinical specimens were used as samples in present study after obtaining written consent from all the patients. The present study comprised 100 pregnant women who met the inclusion criteria. They were divided into two broad groups: a comparison group consisting of normotensive pregnant women (n=50) and a study group (n=50) which further included subgroups of preeclamptic women (n=35) and eclamptic women (n=15).

Inclusion criteria: Women in the age range of 18 to 45 years with blood pressure at or above 140/90 mmHg on atleast two occasions, six or more hours apart after 20 weeks of the present pregnancy, with or without proteinuria, oedema, convulsions, and coma were included.

Exclusion criteria: Cases with hypertension prior to this pregnancy and hypertension secondary to other causes were excluded. Additionally, cases with associated diabetes mellitus, anaemia, and multiple gestations were excluded.

Study Procedure

History and clinical examination, including general and systemic examination, as well as obstetrics examination, were be performed. A 5 mL venous blood sample were drawn and collected in an EDTA vacutainer (Ethylenediaminetetraacetic) as an anticoagulant, following all aseptic precautions. The blood samples were analysed using a six-part fully automated haematology cell counter (Sysmex XN-550 from Japan) to determine PC and PDW. The normal range for PC is considered to be 150-410×10^9/L [10], and the normal range for PDW is 9 to 14 fL [11], respectively.

STATISTICAL ANALYSIS

A comparison was made between the above-mentioned platelet indices in the comparison group and the study group. Changes in PC and PDW were compared between the two groups using a student's t-test with GraphPad software. A p-value of <0.05 was considered statistically significant.

RESULTS

In the present study, PC and PDW were studied in a total of 100 pregnant women, including 50 pregnant women in the study group. Preeclampsia contributed 35% (n=35), eclampsia contributed 15% (n=15), and the remaining 50 pregnant women were in the comparison group, which consisted of normotensive pregnant women. The age range of the subjects was from 17 to 38 years. The majority of cases in both preeclampsia 12 (34.29%) and eclampsia 8 (53.33%) were in the age group of 20-25 years. The age distribution of cases (preeclamptic and eclamptic) and normotensive pregnant women is shown in [Table/Fig-1].

Age group (years)	Study group				Comparison group	
	Preeclamptic pregnant women (n=35)		Eclamptic pregnant women (n=15)		Normotensive pregnant women (n=50)	
	No.	%	No.	%	No.	%
42-45	0	0	0	0	0	0
38-41	1	2.86	1	6.66	1	2
34-37	2	5.71	1	6.66	5	10
30-33	7	20	2	13.33	7	14
26-29	9	25.71	1	6.66	15	30
22-25	12	34.29	8	53.33	16	32
18-21	3	8.57	2	13.33	5	10
Total	35		15		50	
Mean age	26.09		23.4		24.94	
SD	5.408		5.302		5.19	
p-value	0.326		0.319			

[Table/Fig-1]: Age distribution of preeclamptic, eclamptic and normotensive pregnant women.
SD: Standard deviation

The mean age of the comparison group was 24.94±5.19 years, while in preeclampsia it was 26.09±5.408 years, and in eclampsia it was 23.4±5.302 years. There was no significant age difference between the different study groups and the comparison groups when compared separately [Table/Fig-2]. All demographic and baseline characteristics were compared in [Table/Fig-2]. Except age of patient and gestational age (eclamptic vs normotensive), other characterstics showed a statistically significant difference between the participants in all groups.

Characteristics	Preeclamptic pregnant women	Eclamptic pregnant women	Normotensive pregnant women	p-value
Age (years)	26.09±5.408	23.4±5.302	24.94±5.19	PE vs N=0.3259 E vs N=0.1857
BMI (kg/m^2)	27.091±3.437	26.18±3.76	21.8±2.75	PE vs N <0.0001 E vs N <0.0001
Age of gestation (weeks)	35.28±3.49	36.467±2.099	37.28±2.138	PE vs N <0.0001 E vs N=0.199
Systolic blood pressure (mm/Hg)	156.057±12.305	170.93±18.467	121±10	PE vs N <0.0001 E vs N <0.0001
Diastolic blood pressure (mm/Hg)	99.83±8.98	101.33±8.633	72±8.1	PE vs N <0.001 E vs N <0.0001

[Table/Fig-2]: Demographic and baseline characteristics of subjects.
BMI: Basic metabolic index

The distribution of cases according to parity showed that the majority of cases in both preeclampsia and eclampsia were primigravida [Table/Fig-3]. In the present study, the mean PC in preeclampsia was 185.7±69.56×10^3 lac/cum, in eclampsia it was 147.5±56.927×10^3 lac/cumm, and in the comparison group it was 208.1±63.965×10^3 lac/cumm [Table/Fig-4]. There was a decrease in mean PC in both preeclampsia and eclampsia. On statistical analysis, when the mean

PC in different subgroups of the study groups was compared with that in the controls, the decrease in PC in eclampsia was significant (p<0.0016, <0.05), but not in preeclampsia (p=0.13, p>0.05). PDW was found to be statistically significant with a p-value <0.05. This implies that there is a significant difference between the PDW values of preeclampsia and normal pregnant women, as well as between eclampsia and normal pregnant women [Table/Fig-4,5].

	Study group				Comparison group	
	Preeclamptic pregnant women (n=35)		Eclamptic pregnant women (n=15)		Normotensive pregnant women (n=50)	
Parity	N	%	N	%	No.	%
Primi	19	54.28	9	60	26	52
Multi	16	45.714	6	40	24	48

[Table/Fig-3]: Distribution of women with preeclampsia and eclampsia according to gravida/parity.

Parameters (Mean±SD)	Study group		Comparison group	p-value	S/NS
	Preeclamptic pregnant women	Eclamptic pregnant women	Normotensive pregnant women		
Platelet Count (PC) (×10^3 cumm/L)	185.7±69.56	147.5±56.927	208.1±63.965	PE vs N=0.13 E vs N <0.016	NS S
Platelet Distribution Width (PDW) (fL)	18.431±4.184	19.5±3.43	14.86±3.854	PE vs N=0.0001 E vs N <0.0001	S S

[Table/Fig-4]: Mean Platelet Count (PC) and mean of Platelet Distribution Width (PDW) in Preeclamptic (PE), Eclamptic (E) and Normotensive (N) pregnant women.
S: Significant; NS: Non significant

Platelet distribution width (fL)	Study group				Comparison group	
	Preeclamptic pregnant women (n=35)		Eclamptic pregnant women (n=15)		Normotensive pregnant women (n=50)	
	No.	%	No.	%	No.	%
25.0-26.99	3	8.57	3	20	2	4
23.0-24.99	4	11.43	1	6.67	3	6
21.0-22.99	4	11.43	2	13.33	2	4
19.0-20.99	6	17.14	3	20	5	10
17.0-18.99	5	14.29	4	26.66	4	8
15.0-16.99	6	17.14	1	6.67	6	12
13.0-14.99	4	11.43	0	0	15	30
11.0-12.99	3	8.57	1	6.67	8	16
9.0-10.99	0	0	0	0	5	10
Total	35		15		50	
Mean value of PDW	18.4314		19.5		14.86	
SD	4.184		3.43		3.854	
p-value	0.0001		<0.0001			

[Table/Fig-5]: PDW in preeclampsia, eclampsia and normal pregnancy.

DISCUSSION

Preelclampsia is believed to be a threat to public health, especially in developing countries, affecting approximately 8% of all pregnancies globally. Each year, more than four million women are affected by preeclampsia, highlighting the seriousness of the disease [12]. Most pregnant women present with symptoms such as headache, upper abdominal pain, or visual disturbances during the last trimester of pregnancy [13]. Preeclampsia and eclampsia are the most common causes of low platelet count during pregnancy [14]. Hypercoagulability is consistently associated with hypertensive disorders of pregnancy, particularly preeclampsia [15]. Preeclampsia can also lead to long-term consequences such as premature cardiovascular, cerebrovascular, peripheral arterial diseases, and other chronic illnesses in affected women [16-18].

Several studies by Mohapatra S et al., Sultana R et al., Dadhich S et al., Vijay C et al., Singh A and Verma R, Gupta A et al., have evaluated platelet indices to predict outcomes and understand the pathogenesis of preeclampsia [14,19-23]. Vijay C et al., concluded that platelet indices can serve as an early, cost-effective, and rapid method for assessing the severity of pregnancy-induced hypertension cases [14]. However, although the mean platelet count in the present study was reduced compared to control subjects, it did not reach statistical significance.

In present study, most cases (34.29%, n=12 out of 35) belonged to the age group of 22-25 years, similar to the findings reported by Singhal P et al., where the maximum number of cases (48.75%, n=39 out of 80) were in the age group of 20-24 years [24]. Systolic blood pressure and diastolic blood pressure also showed a significant increase in the study group, which is supported by other studies conducted by Attahir A et al., Karatke A et al., Singh A and Verma R, and Temur M et al., [Table/Fig-6,7] [22,25-27].

The majority of cases (88.57% of preeclampsia cases and 93.33% of eclampsia cases) in our study were from rural areas. This finding is consistent with the study by Naseer et al., who found that the majority (48%, n=48) of patients with preeclampsia belonged to rural areas [28]. Although most subjects in our study showed a normal platelet count, 14% of women in the comparison group, 31.42% of women with preeclampsia, and 46.66% of cases with eclampsia exhibited thrombocytopenia. This decrease in platelet count was more significant in eclampsia when compared with the comparison group, while it was not significant in cases of preeclampsia.

Ceyhan T et al., and Temur M et al., did not find a significant decrease in platelet count in cases of preeclampsia [Table/Fig-8] [14,21,22,26,27]. In contrast, Vijay C et al., Mohapatra S et al., Sultana R et al., Dadhich S et al., Singh A and Verma R, Gupta A et al., found a significant decrease in platelet count in cases of preeclampsia [Table/Fig-9] [9,14,19-23,27,29].

Name of the author, year and place of study	Mean systolic blood pressure (mmHg)			
	Preeclamptic pregnant women	Eclamptic pregnant women	Normotensive pregnant women	p-value
Attahir A et al., [25] (2010) Zaria, Nigeria	167.60±2.75	-	116.40±0.73	Significant
Karatke A et al., [26] (2015) Turkey	149±25	-	128±13	0.001
Singh A and Verma R [22] (2018) Raipur, India	151.9±14.8	157.6±15.8	120.5±7.1	PE vs N=0.0001 E vs N=0.0001
Temur M et al., [27] (2021) Bursa, Turkey	155.76±13.98	-	108.02±12.13	0.001
Present study Jorhat, India	156.057±12.305	170.93±18.467	121±10	PE vs N <0.0001 E vs N <0.0001

[Table/Fig-6]: Comparative analysis of Mean systolic blood pressure in all subjects for various studies and present study [22,25-27].

Name of the author, year and place of study	Mean diastolic blood pressure (mmHg)			
	Preeclamptic pregnant women	Eclamptic pregnant women	Normotensive pregnant women	p-value
Attahire A et al., [25] (2010) Zaria, Nigeria	107.48±8.01	-	76.80±8.67	S
Karatke A et al., [26] (2015) Turkey	84±16	-	71±23	<0.001
Singh A and Verma R [22] (2018) Meerut, India	98.3±9.7	102±11.7	79.7±6.2	<0.0001
Temur M et al., [27] (2021) Bursa, Turkey	98.39±9.34	-	64.90±9.27	<0.001
Present study Jorhat, India	99.83±8.98	101.33±8.633	72±8.10	<0.0001

[Table/Fig-7]: Comparative analysis of mean diastolic blood pressure in all subjects for various studies and present study [22,25-27].

Name of the author, year and place of study	Preeclamptic pregnant women	Mean value of Platelet Distribution Width (PDW) (fL)		p-value
		Eclamptic pregnant women	Normotensive pregnant women	
Dadhich S et al., [21] (2012) Bikaner	21.80±2.08	-	16.70±0.82	0.001
Vijay C et al., [14] (2014) Bangalore, India	15.50+2.68	16.78+3.13	11.08+2.42	-
Karatke A et al., [26] (2015) Turkey	18.2±3.5	-	16.3±2.1	0.004
Singh A and Verma R [22] (2018) Meerut, India	16.9±1.09	17.4±1.03	16.5±0.86	<0.0001
Temur M et al., [27] (2021) Bursa, Turkey	17.11±0.80	NA	17.29±0.82	0.014
Present study Jorhat, India	18.431±4.184	19.5±3.43	14.86±3.854	PE vs N <0.0001 E vs N <0.0001

[Table/Fig-8]: Comparative analysis of PDW and significance in subjects for various studies [14,21,22,26,27].

Name of the author, year and place of study	Mean Platelet Count (PC) (×10³ lac/cumm)			p-value
	Preeclamptic pregnant women	Eclamptic pregnant women	Normotensive pregnant women	
Ceyhan T et al., [9] (2006) Turkey	227±71	-	220±79	Not significant
Mohapatra S et al., [19] (2007) Cuttack	182.00±45.00	130.00±49.00	238.00±33.00	PE vs N <0.01 E vs N <0.01
Sultana R et al., [20] (2012) Dhaka	144.26±96.47	-	198.1±51.219	0.001
Dadhich S et al., [21] Bikaner, India	175.42±31.22	-	231.80±40.52	0.001
Vijay C et al., [14] (2014) Bangalore, India	155.500±31.300	131.00±33.280	218.40±28.250	PE vs N<0.0001 E vs N<0.0001
Singh A and Verma R [22] (2018) Raipur, India	196.2±88.7	147.8±53.3	280.0±89.8	PE vs N <0.005 E vs N <0.005
Gupta A et al., [23] (2018) Bhopal, MP, India	1.68±74.22	-	229.61±73.27	p<0.05
Temur M et al., [27] (2021) Bursa, Turkey	227.22±78.58	-	236.69±64.30	0.133
Taşin C et al., [29] (2022) Mersin, Turkey	206.500±96.485	-	222.6±60.992	0.03
Present study Jorhat, India	185.7±69.56	147.5±56.927	208.1±63.965	PE vs N=0.13 E vs N <0.001

[Table/Fig-9]: Comparative analysis of mean PC with other studies [9,14,19-23,27,29].

In the present study, the mean values of PDW showed a significant increase in both subgroups of the study group. These findings were consistent with the studies conducted by Vijay C et al., Dadhich S et al., Singh A and Verma R, Karatke A et al., Temur M et al., who also reported a significant increase in PDW in both preeclampsia and eclampsia [Table/Fig-8] [14,21,22,26,27].

Limitation(s)

This is a hospital-based study, and therefore the results cannot be generalised to the broader community. The sample size is small, and the number of eclampsia cases is less compared to the number of preeclampsia cases.

CONCLUSION(S)

In the present study, a significant relationship was found between platelet indices and the severity of Pregnancy-induced Hypertension (PIH). There was an increase in PDW with an increase in the severity of PIH, with higher values observed in eclampsia compared to preeclampsia and normal pregnant individuals. It was also observed that a normal platelet count does not rule out a severe disease. Therefore, the assessment of PDW should be done to evaluate the severity of preeclampsia and eclampsia in addition to platelet count, rather than relying on platelet count alone. Hence, the estimation of platelet count and PDW can be used as a screening test for early identification of preeclampsia and eclampsia. Platelet

parameters can serve as indicators of these conditions and can be used as effective prognostic markers because PDW correlates with disease severity. Moreover, these indices are cost-effective and easily available. Therefore, it can be concluded that platelet indices are important and essential investigations for the management of patients with pregnancy-induced hypertension.

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