

## Estimation of Platelet Count As A Prognostic Marker for Feto-Maternal Outcome in Preeclampsia & Eclampsia

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### Abstract:

**Introduction:** Preeclampsia and eclampsia contribute greatly to the maternal morbidity and mortality. Thrombocytopenia is the most common hematological abnormality of all that occur in preeclampsia, and the frequency of maternal thrombocytopenia is dependent on the intensity of the disease process and duration of preeclampsia syndrome.

**Material and methods:** A hospital based observational study was conducted which included 150 normotensive pregnant females as controls and 150 cases of preeclampsia of varying severity (mild preeclampsia, severe preeclampsia and eclampsia). Study subjects were studied with Haemoglobin, Bleeding time, Clotting time and Platelet count and feto-maternal outcome was compared between both study groups.

**Results:** Platelet Count was found to be significantly lower in preeclampsia cases as compared to control group. The feto-maternal outcome was observed to be poor in thrombocytopenic cases as compared to their normal platelet count counterpart subjects.

**Conclusion:** Thrombocytopenia correlates well with the disease severity and poor perinatal and maternal outcome in patients of preeclampsia syndrome. Platelet count being a low cost, rapid and easily available investigation, hence can be used as a tool for screening the patients for prediction of disease severity and clinical outcome.

**Keywords:** Bleeding time, Eclampsia, Platelet Count, Preeclampsia

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### I. Introduction

Hypertensive disorders complicate 5%-10% of all pregnancies and together they form one member of the deadly triad, along with hemorrhage and infection that contribute greatly to the maternal morbidity and mortality rates. Preeclampsia is diagnosed when the patient is presenting with Blood Pressure (BP)  $\geq$ 140/90 mm Hg appearing for the first time after 20 weeks of gestation and proteinuria over 300 mg/24 hour or over 30mg/dl proteinuria is present. Eclampsia is defined when seizures appear in woman that meets the criteria for preeclampsia (1). Preeclampsia is important because it is a multisystem disorder linked to the significant morbidity and mortality of mother and fetus. Mother may develop DIC (Disseminated Intravascular Coagulation), acute renal failure, stroke, acute pulmonary edema, cerebral edema, and placental abruption, and liver hemorrhage/rupture, transformation in chronic hypertension or even maternal death (2). Fetal sufferance due to placental insufficiency, IUGR (Intra-Uterine Growth Retardation), preterm labour and may include pregnancy loss (3).

In preeclampsia there will be abnormal trophoblast invasion. The result is placental ischemia followed by release of number of vasoactive factors that alter the endothelial function; the platelet function all leads to change the balance between vasoconstriction and vasodilation and the final consequence is endothelial dysfunction, generalized vasoconstriction and consequent hypertension with signs and symptoms of preeclampsia. Endothelial dysfunction is associated with excessive platelet activation, thrombosis in microcirculation, end organ dysfunction/necrosis and placental infarction (2). Decreased platelet concentrations with eclampsia were first described by Stancke in 1922 (4). Up to 50% preeclampsia associated with thrombocytopenia which is proportional to severity of disease. Thrombocytopenia may be severe and potentially life threatening. Due to accelerated platelet destruction, there is a shortened platelet life span, increased number of megakaryocytes in bone marrow and an increased number of immature platelets seen in peripheral blood

smear. Thrombocytopenia is characteristic of worsening preeclampsia as it signifies platelet activation and aggregation as well as microangiopathic hemolysis. Hence this study is undertaken to evaluate the platelet count as a prognostic marker to assess the severity of preeclampsia and eclampsia.

## **II. Material & Methods**

Total 300 Pregnant women were included in the study for a period of 1.5 years from July 2015 to Dec 2016 at JLN Medical College Ajmer (Raj). Healthy normotensive females who were between 28 weeks of gestation till term of pregnancy without any sign and symptoms of preeclampsia were considered as control. Pregnant females between 28 weeks of gestation till term with signs and symptoms of preeclampsia/eclampsia, admitted to ANC (Ante Natal Care) ward were selected and grouped as per criteria described in classification of hypertensive disorders of pregnancy according to ACOG (American Congress of Obstetricians and Gynecologists).

### **The study groups were divided as follows:**

1. Healthy normotensive pregnant controls-150
2. Patients with mild preeclampsia -90
3. Patients with severe preeclampsia-31
4. Patients with Eclampsia-29

### **2.1 Inclusion criteria:**

- Singleton pregnancy
- Cephalic presentation
- Patients giving informed consent to take part in study

### **2.2 Exclusion criteria:**

- Patients with history of intake of any systemic drug which significantly interfere with coagulation-fibrinolysis mechanism.
- Patients with history/known case of congenital or acquired disease of coagulation pathway.
- Patients with chronic hypertension.
- Contracted pelvis, cephalo-pelvic disproportion, multiple pregnancies, short stature (<150cm), congenital malformed foetus, amniotic fluid abnormalities i.e. moderate to severe polyhydramnios/oligohydramnios
- Patients/control subjects not willing to participate in study.

Detailed history, important clinical findings and relevant investigations were noted as per case performa. Whole blood sample was obtained by anterior cubital vein venepuncture, the blood sample was obtained without a pressure cuff and by continuous free flow by the negative pressure.

## **III. Observations, Results & Discussion**

**3.1 Observations & Results :** Statistical analysis was performed with the SPSS, Trial version 23 for Windows statistical software package (SPSS inc., Chicago, IL, USA) and Primer. The Categorical data were presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data were presented as mean and standard deviation and were compared using by students t-test and ANOVA Test. Probability P value <0.05 was considered statistically significant. As depicted in table no1 the eclampsia group had maximum percentage of subjects ageing <25 years while maximum numbers of >25 years subjects dominated in severe preeclampsia group.

Mean age was observed to be lowest among eclampsia group ( $22.93 \pm 4.28$ , range 18 to 35 years) while it was higher among control group i.e.  $23.38 \pm 3.25$  (range 19 to 35 years) and highest among severe preeclampsia group i.e.  $26.26 \pm 4.56$  years (range 18 to 35 years). On stratification of the study subjects according to their obstetric history maximum percentage of primigravidae subjects (72.41%) was found in eclampsia group, while it was minimum in severe preeclampsia group (29.03%). As evident from table no1, the percentage of thrombocytopenic subjects was higher among preeclampsia and eclampsia group (30%, 64.52% & 55.17%) as compared to control group (16%) and the difference among study groups upon application of chi-square test was statistically significant (P value <0.001).

As shown in table no 2, the mean hemoglobin in mild preeclampsia, severe preeclampsia and eclampsia was found to be  $9.52 \pm 1.44$  gm% (range 6 to 14.6 gm%),  $9.72 \pm 2.17$  gm% (range 4.5 to 13.7 gm%) and  $10.47 \pm 2.35$  gm% (range 6.9 to 15.6 gm%) respectively. The difference in mean hemoglobin was statistically significant with severity of pregnancy induced hypertension. (P value 0.043) The mean platelet count in mild preeclampsia severe preeclampsia, eclampsia was  $195.33 \pm 67.61 \times 1000 / \text{cumm}$  (range 90 to

425),  $142.65 \pm 67.38 \times 1000 / \text{cumm}$  (range 34 to 289 ) and  $177.38 \pm 89.95 \times 1000 / \text{cumm}$  ( range 32 to 365 ) respectively. Mean platelet count of preeclampsia and eclampsia were significantly lower than control group. Lowest value of mean platelet count was observed among severe preeclampsia group.

The bleeding time in mild preeclampsia was  $3.1 \pm 1.12$  min (range 1.5 to 6.4 min.), in severe preeclampsia was  $3.98 \pm 1.3$  min. (range 1.2 to 6.5 min) in eclampsia it was  $3.77 \pm 1.29$  min ( range 2 to 6.8). The difference in bleeding time among the study groups was found statistically significant (P value  $< 0.001$ ). The clotting time in mild preeclampsia was  $5.17 \pm 1.6$  min. (range 3 to 11 ), in severe eclampsia  $6.18 \pm 1.6$  min. (range 3.2 to 11 ) in eclampsia  $5.9 \pm 1.7$  min ( range 3.3 to 11 ) . The difference among the study subjects in clotting time was found to be statistically significant (P value  $< 0.001$ ).

As depicted in table no 3, a higher percentage of the subjects of mild preeclampsia, severe preeclampsia and eclampsia were found to have unfavourable maternal outcome as compared to control group subjects. The difference of percentage among study groups was found to be significant on application of chi square test (P Value  $< 0.001$ ). Similarly the difference among the study groups on the basis of percentage of unfavourable foetal outcome was also found to be significant as presented in table no 3. As shown in the above table no 4, we found a positive correlation between low platelet count and unfavorable maternal outcome as a significantly higher percentage of subjects observed to have unfavorable outcome in low platelet count group while majority of normal platelet count subjects had favorable maternal outcome. This comparative analysis was done including subjects having severe hypertensive disease (severe preeclampsia and eclampsia). Similarly though unfavorable fetal outcome was dominantly seen in both normal and low platelet groups, the percentage of unfavorable outcome was observed to be higher in low platelet subjects while percentage of favorable outcome was observed to be higher in normal platelet subjects (refer table no 4).

**3.2 Discussion:** Pregnancy is associated with complex and still incompletely understood changes involving blood coagulation. Information regarding behaviour of platelets in normal pregnancy has shown varying trends. The study evaluated and compared various haematological parameters in normal pregnancy versus hypertensive pregnancies of varying severity. In our study we found that the mean age of the subjects presented with eclampsia was significantly lower ( $22.93 \pm 4.28$  years) than the control group ( $23.38 \pm 3.25$  years) while the mean age of mild and severe preeclampsia group was found to be higher than control group. This finding was in accordance of previous studies done for instituting risk factors for eclampsia and younger age is one of them (5).

Corrie Macdonald-Wallis et al while studying risk factors for preeclampsia found that young maternal age, higher pre-pregnancy BMI (Body Mass Index), nulliparity and twin pregnancy were all associated with increased odds of experiencing proteinuria. (6). In our study we found that eclampsia group had a significantly higher fraction (72%) of primipara as compared to control group and preeclampsia groups. Preeclampsia group had a higher percentage of subjects belonging to multipara group compared to controls. These results favor extremes of parity as an established risk factor for preeclampsia and eclampsia. Our present study indicates that a significantly higher mean hemoglobin levels were observed among eclampsia group subjects as compared to control and eclampsia group. This observation is attributable to hypoproteinemia, fluid leak and subsequent hemoconcentration in eclampsia group subjects. Similar observations were made previously eg. Cordina, Mark, et al (7) found that higher maternal hemoglobin was observed among cases of severe preeclampsia and eclampsia and inverse correlation was found between the centile weight of the newborn and the maternal hemoglobin. Also, significantly higher hemoglobin levels were found in pregnancies complicated by fetal growth retardation and perinatal distress compared with those in pregnancies with good outcomes. Similar inferences were also made by other workers eg. Hamideh Pakniat et al (8) while studying hemoglobin and hematocrit levels in eclampsia.

Role of Platelet count in prediction of severity of hypertensive disease of pregnancy has been studied widely and varied inferences have been made (9-16, 18). In our study we observed that the number of thrombocytopenic subjects was higher in cases of eclampsia and severe preeclampsia as compared to the control group and mild preeclampsia group with a statistically significant difference. More importantly the mean platelet count was also significantly lower in subjects belonging to eclampsia and severe preeclampsia case groups as compared to control and mild preeclampsia group. These two extrapolations indicate that there might be some important mechanism which interferes with platelets life span thus reducing the number of functional platelets in circulation. A comparison of mean platelet count in our study with previous studies (10, 12, and 17) is being presented in the table no 5. Comparing with previous studies, results of our study are not much differ except having a higher mean platelet value among eclampsia (1.77 lakh/cumm) when comparing to severe preeclampsia group (1.42 lakh/cumm). The results are here affected by a very high standard deviation value (89.95) among eclampsia group compared to other study groups.

An absolute decrease value of platelet count is not much significant until it is reflected in clinical picture in terms of feto-maternal outcome. For further clarification, we compared the normal and

thrombocytopenic subjects of eclampsia and severe preeclampsia and found that a significantly higher number of thrombocytopenic subjects had unfavorable maternal outcome compared to normal platelet count subjects group while a positive correlation was found between normal platelet count and favorable maternal outcome. Thus it can be narrated that platelet count can serve as a predictor of maternal outcome as the count has a negative correlation with the severity of hypertensive disease.

On the other side when the fetal outcome was compared among thrombocytopenic and normal subjects of severe hypertensive disease (eclampsia and preeclampsia) again a negative and stronger correlation found between platelet count and severity of disease. Bleeding time (BT) is essentially is known as a measure of platelet function hence estimation of bleeding time is considered as to quantitate the functional circulating platelet count. A comparison of mean bleeding count estimated in our study with some recent studies is presented in table no 6. From the table no 6 it is evident that in recent studies there is prolongation of bleeding time along the spectrum of the hypertensive disease of pregnancy. The normal range of bleeding time varies over a wide range and considered normal in 2-9 minutes, though it varies along different races, geographical populations and different age groups. So absolute value of mean bleeding time is of not much value but the difference among the study groups (as observed significant) indicates that a decrease in functional platelets population might be responsible for the rise in bleeding time. In our present study pattern of increase in bleeding time followed the pattern of fall in platelet count and hence maximum absolute mean bleeding time was observed in severe preeclampsia group rather than eclampsia group but the difference of mean value among these two was not significant statistically.

The normal expected range for clotting time is 4-10 minutes. Estimation of clotting time provides assessment of overall function of coagulation factors. We estimated mean clotting time among all four study groups and a comparative analysis was done in respect of some recent studies, details of which are being presented in the following table no 6. As evident from the results and the table no 6, according to the most of recent studies the rise in mean clotting time (CT) along the severity of preeclampsia was not significant though it followed the pattern of severity of the disease. Likewise in our study the increase in clotting time in eclampsia as compared to mild and severe preeclampsia was not observed but the overall rise in mean CT in case group compared to control was higher. Laxmi CV et al (20) while studying coagulation profile in PIH (Pregnancy Induced Hypertension) reported a significantly raised clotting time among the study groups (as shown in table no 6). The author concluded that an ongoing coagulopathy should be suspected if thrombocytopenia along with prolongation of CT, PT (prothrombin time) and aPTT (activated partial thromboplastin time) is found and treatment should be started at the earliest. It can be inferred from studies that clotting time values observed to be high in preeclampsia cases but it may or may not follow along the severity pattern of the disease. Overall according to our present study the feto-maternal outcome worsens along the severity of preeclampsia and the hematological parameters (specifically the platelet count) closely follows the disease pattern with highly significant correlation.

**Figures And Tables**

**Table no 1:** Distribution of the subjects according to age, Obstetric history and number of thrombocytopenic subjects

S N		CONTROL	MILD PE	SEVERE PE	ECLAMPSIA	P Value
1	Number of subjects	150	90	31	29	
2	Subjects age ≤25 years	123 (82%)	55 (61.10%)	15 (41.90%)	24 (82.80%)	
3	Subjects age >25 years	27 (18%)	35 (38.90%)	16 (58.10%)	5 (17.20%)	
4	Mean age	23.38 ± 3.25	25.22 ± 4.55	26.26 ± 4.56	22.93 ± 4.28	
5	No of Primi gravidae	8 (56%)	4 (37.78%)	9 (29.03%)	2 (72.41%)	1
6	No of thrombocytopenic subjects	2 (16%)	4 (30%)	7 (64.52%)	1 (55.17%)	6 < 0.001
		control (N=150)	mild PE (N=90)	severe PE (N=31)	Eclampsia (N=29)	P value LS

**Table No. 2:** Mean Hemoglobin, Platelet count, Bleeding time & Clotting time among the study groups

**Table no 3:** Distribution of the subjects according to maternal & fetal outcome

O u t c o m e		Control (N=150)	Mild PE (N = 9 0 )	Severe PE ( N = 3 1 )	Eclampsia ( N = 2 9 )	Total	P Value
Maternal	Favorable	1 3 8 ( 9 2 % )	6 4 (71.11%)	1 4 (45.16%)	1 4 (48.28%)	2 3 0	< 0 . 0 0 1
	Unfavorable	1 2 ( 8 % )	2 6 (28.89%)	1 7 (54.84%)	1 5 (51.72%)	7 0	
F o e t a l	Favorable	1 0 1 (67.33%)	5 8 (64.44%)	4 (12.90%)	9 (31.03%)	1 7 2	< 0 . 0 0 1
	Unfavorable	4 9 (32.67%)	3 2 (35.56%)	2 7 (87.10%)	2 0 (68.97%)	1 2 8	

**Table No 4:** Association of Platelet Count with maternal and fetal outcome in (severe preeclampsia+ Eclampsia) cases

Maternal outcome	F a v o r a b l e		U n f a v o r a b l e		n o o f c a s e s	
	N	%	N	%		
Platelet Count L o w ( < 1 . 5 l a c / c u m m )	1	1	3 0 . 5 6	2 5	6 9 . 4 4	3
N o r m a l ( 1 . 5 - 4 l a c / c u m m )	1	7	7 0 . 8 3	7	2 9 . 1 7	2
	2	8		3 2		6
F o e t a l O u t c o m e	F a v o r a b l e		U n f a v o r a b l e		n o o f c a s e s	
	N	%	N	%		
Platelet Count L o w ( < 1 . 5 l a c / c u m m )	7		1 9 . 4 4	2 9	8 0 . 5 6	3
N o r m a l ( 1 . 5 - 4 l a c / c u m m )	6		2 5 . 0 0	1 8	7 5 . 0 0	2
	1	3		4 7		6

**Table: 5** Comparison of platelet count (lakh/cumm) in present study with other studies in controls and cases.

	control(N=150)	mild PE(N=90)	severe PE(N=31)	Eclampsia(N=29)	P value LS
<b>Mean</b>	Mean ±SD(Min to max)				
<b>Hemoglobin (range)</b>	<b>9.62±1.32</b> (6.6 to 13.8)	<b>9.52±1.44</b> (6 to 14.6)	<b>9.72±2.17</b> (4.5 to 13.7)	<b>10.47±2.35</b> (6.9 to 15.6)	0.043
<b>Platelet count</b>	<b>216.13±69.02</b> (70 to 421)	<b>195.33±67.61</b> (90 to 425)	<b>142.65±67.38</b> (34 to 289)	<b>177.38±89.95</b> (32 to 365)	<0.001
<b>Bleeding time</b>	<b>2.72±1.06</b> (1.4 to 9.36)	<b>3.1±1.12</b> (1.5 to 6.4)	<b>3.98±1.3</b> (1.2 to 6.5)	<b>3.77±1.29</b> (2 to 6.5)	<0.001
<b>Clotting time</b>	<b>4.2±1.05</b> (2.5 to 8.4)	<b>5.17±1.6</b> (3 to 11)	<b>6.18±1.6</b> (3.2 to 11)	<b>5.9±1.7</b> (3.3 to 11)	<0.001

A u t h o r s	c o n t r o l	Mild Preeclampsia	Severe preeclampsia	E c l a m p s i a
S h r i v a s t a v a ( 1 9 9 5 )	1 . 9 4	1 . 7 9	1 . 6 4	1 . 5 2
J a m b h u l k a r ( 2 0 0 1 )	2 . 3 8	2 . 3 0	1 . 7 0	1 . 5 1
J o s h i e t a l ( 2 0 0 4 )	2 . 2 0	2 . 0 0	1 . 4 0	1 . 3 0
D a v i e s e t a l ( 2 0 0 7 )	2 . 5 7	2 . 3 0	1 . 7 7	-
E l l o r a D e v i e t a l ( 2 0 1 2 )	2 . 4 4	1 . 8 2	1 . 4 2	-
M A S a m e e r e t a l ( 2 0 1 4 )	2 . 4 2	2 . 3 9	1 . 6 0	1 . 5 1
P r e s e n t s t u d y	2 . 1 6	1 . 9 5	1 . 4 2	1 . 7 7

### III. Conclusions

Preeclampsia/eclampsia is largely a preventable condition and the severity of this syndrome and feto-maternal outcome significantly related to coagulation status. Platelet count, bleeding time, clotting time have predictive value in severe cases of preeclampsia. Among the hematological parameters platelet count being a simple, low cost, rapid and easily available investigation and can be used as an important tool for screening the patients for prediction of disease severity and clinical outcome. Early detection and prompt treatment have a significant role in reducing the morbidity and mortality of mother and fetus.

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