Study of Lowered Platelet Count as a Prognostic Index in Hypertensive Disorders of Pregnancy

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Abstract

INTRODUCTION: Hypertensive disorders complicate 5-10% of all pregnancies, and together, they form one member of the deadly triad, along with bleeding and infection that contribute significantly to the maternal morbidity and mortality rates.

MATERIAL & METHODS: This study designed as a comparative study with pregnant women of term gestation with hypertension and normotensive women. It is a prospective study carried out in the Department of Obstetrics and Gynaecology at Guntur Medical College and Hospital, Guntur, during the period of February 2018 to January 2019. Pregnant women with known bleeding disorders, on anticoagulant therapy, with abruptio placentae, with IUD, and with established DIC were excluded.

RESULTS: The mean platelet count observed among cases of preeclampsia, severe preeclampsia, and eclampsia was 1.89, 1.56, and 1.14 lakh/mm3, respectively. The difference in the mean platelet count among cases and controls was statistically significant. The association of platelet count with the severity of different degrees of hypertension in pregnancy was analyzed statistically and was highly significant.

CONCLUSIONS: Platelet count is a very important investigation for eclampsia and pre-eclampsia, as it is directly related to the maternal and perinatal outcome. Routine and regular monitoring of platelet count can be included in the routine antenatal checkup among pregnant women with hypertension.

Key Words: Eclampsia, pre-eclampsia, platelet count, prognostic index

Date of Submission: 01-01-2021

Date of Acceptance: 13-01-2021

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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 bleeding and infection that contribute significantly to the maternal morbidity and mortality rates.1 Out of which pre-eclampsia and eclampsia constitute 70% and chronic hypertension 30%. The incidence of eclampsia is 1 in 100 to 1 in 2000 pregnancies. It remains one of the important causes of maternal death worldwide, accounting for 15-20% of maternal deaths in developing as well as developing countries.2

During the coagulation and fibrinolytic cycle, profound changes occur in a healthy pregnancy, causing a hypercoagulable state. There is a clear possibility that the hypercoagulable pregnancy may be accentuated during eclampsia and preeclampsia.3

Out of all the hematological changes that occur in pre-eclampsia and eclampsia, thrombocytopenia is the most common hematological abnormality found.4 It has known that an underlying coagulation abnormality increases the risk of bleeding complications, especially during operative delivery or during the placement of an epidural catheter for regional anesthesia.5

There is considerable evidence to support the fact that intravascular coagulation occurs in severe preeclampsia and eclampsia. Post mortem studies in women who died of eclampsia have shown fibrin deposition in the blood vessels of several organs. Renal biopsy specimen by immunofluorescence has demonstrated the deposition of fibrinogen related material within renal glomeruli.

Further support has come from a demonstration of high molecular weight fibrin complexes in the plasma of women with severe pre-eclampsia and eclampsia. There have been many reports of changes in blood coagulation and fibrinolysis compatible with a process of intravascular coagulation in severe pre-eclampsia and eclampsia.

Preeclampsia and eclampsia of varying degrees of severity form a considerable portion of admissions in our hospital. In these patients, different degrees of disseminated intravascular coagulation can contribute significantly to the morbidity and, sometimes, even to mortality. Early assessment of the severity of preeclampsia and eclampsia is necessary to prevent complications and increased maternal and fetal morbidity and mortality.

It was thus essential to study the occurrence of disorders in the coagulation system concerning the severity of pre-eclampsia and eclampsia. The research is therefore carried out to determine the extent of pre-eclampsia and eclampsia by a method that is rapid, cheaper, and readily available so that they will guide us for management before the patient goes into complications.

II. Aims And Objectives:

To evaluate the platelet indices and their significance in the assessment of hypertensive disorders and to detect coagulation failure early and manage before it worsens. This study is therefore conducted to determine the severity of preeclampsia, eclampsia through platelet count estimation, which is a simple, rapid, cheaper, and readily available prognostic lab method, to prevent further complications.

III. Material & Methods

This study titled "Study of lowered platelet count as a prognostic index in hypertensive disorders of pregnancy" was conducted in the Department of Obstetrics and Gynaecology at Guntur Medical College and Hospital, Guntur, from February 2018 to January 2019.

The study was designed as a comparative study and included a total of 196 patients. Ninety-eight controls well matched with the study population, which included a total of 98 patients with pre-eclampsia and eclampsia. The selection of patients based on the following:

INCLUSION CRITERIA:

Pregnant women of term gestation with pre-eclampsia and eclampsia. The control group consists of Pregnant women of term gestation with normal blood pressure.

EXCLUSION CRITERIA:

Pregnant women

i) With known bleeding disorders

ii) On anticoagulant therapy

iii) With established DIC

iv) Known case of ITP & SLE

Besides complete obstetric examination, a detailed history taken with particular attention to hemorrhagic complications, thromboembolic episode, epilepsy, hepatic or renal disorder, and drug intake, which can alter platelet count and function.

All the patients included under the study first underwent the preliminary workup according to the proforma already made. Then blood was withdrawn for platelet count. The following methods did the platelet count. MANUAL PLATELET COUNT

Principal

Blood is diluted with a diluted fluid that causes lysis of RBC but has no effect on platelets, counted in the Neubauer hemocytometer.

Reagents

1% Aqueous solution of Ammonium oxalate.

A fresh solution prepared and filtered before use.

Procedure

Using either a Thomas WBC pipette or tube method, a 1:20 dilution solution is to be prepared. EDTA venous blood is preferable to capillary blood since some platelets are unavoidably lost from the letter because they adhere to the edges of the wound. This gives falsely low values.

Mix for two minutes on a mechanical mixer. Then fill both sides of Neubauer counting and allow the platelets to settle for 20 minutes in Petri dish, on the bottom of which is a moist disc of filter paper it is essential that the preparation not be left in the pipette or tube for any undue length of time before transferred to the counting chamber and count the number of platelets, which will appear as small retractile bodies, in 5 squares in the central ruled area of a Neubauer hemocytometer. It should be noted that leukocytes are not affected by the diluting fluid and will be readily visible. Leukocytes, however, are much larger than platelets and are unlikely to cause any confusion.

Platelet counting is facilitated by using a phase-contrast microscope. Alternatively, a light microscope may be used with condenser well down.

Calculation.

Area of 5 squares in central ruled area - 0.2 sq.mm

volume of 5 squares in central ruled area - $0.2 \times 0.1 \text{uL} = 0.02 \mu \text{L}$

Dilution of blood sample - 1:20 IFR = NUMBER OF PLATELTES COUNTED IN 0.02UI

Then number of platelets / μ L = R X 20 X 1/0.2= R X 20 X 50

= R X 1000

Normal Values

Normal values are 1,50,000 to 4,50,000 per mm3.

STATISTICAL METHODS APPLIED

1. Descriptive analysis

2. Chi-square test

3. Analysis Of Variance (ANOVA)

IV. Results:

A total of 196 subjects were included in this study "Study of lowered platelet count as a prognostic index in hypertensive disorders of pregnancy."

n=98 were normal pregnant (Group NP)

n=98 were with pre-eclampsia and eclampsia

Out of these 98 cases:n=55 cases were with pre-eclampsia (Group PE), n=33 were with severe preeclampsia (Group SEVERE PE), and n=10 were with eclampsia (Group E).

Age-wise distribution of cases with preeclampsia and eclampsia and control group showed that in healthy pregnant controls, the maximum cases were in the age group of 21-25 years, i.e., 48 (50.8%) cases with mean age being 22.6 \pm 4.2 years. Most of the cases in group PE n=55 were in the age group of 18-25 years, i.e., 40 (72.73%) cases with mean age 23.47 \pm 4.25 years. The maximum numbers of cases in group SEVERE PE n=33 were in the age group of 21-25 years, i.e., 15 (45.45%) cases with mean age 23.49 \pm 3.72 years. Similarly, in group E n=10, maximum numbers of patients were in the age group of 18-25 years, i.e., 9 (90%) cases with mean age was 22.2 \pm 4.94 years.

Parity wise distribution showed that in control group n=98, 27.55% were primipara and 72.45% were multipara. In group PE n=55, 61.82% were primipara, while 38.18% were multipara In group SEVERE PE n=33, 36.36% were primipara, and 63.64% were multipara. Similarly, in group E n=10, 80% primipara, and 20% were multipara.

In this study, in preeclampsia eclampsia group n=98, 33.7% of cases were booked, and 66.3% of cases were unbooked. In the control group, 58% of cases were booked, and 42% of the cases were unbooked. Cases distribution by platelet count and clinical diagnosis:

In control group n=98: 4.08% had Platelet Count in the range 1.0-1.5 Lakh/mm³; in Group PE 29.09% had 1lakh- 1.5 lakh/mm³; in group SEVERE PE n=33: 6.06% had platelet count below 50,000/mm³; 33.33% had between 50,000 - 1 lakh/mm³; 18.18% had between 1lakh - 1.5lakh/mm³ and 42.42% had in the normal range. In Group E n=10: 40% had Platelet Count in the range 50,000 - 1 lakh/mm³ and 40% had between 1.0-1.5 lakh/mm³; 20% had in the normal range. ANOVA test of platelet count among cases and controls showed p-value to be less than 0.001, hence the platelet count has a highly significant difference among cases and controls.

Clinical diagnosis	Ν	Mean	S.D.	Min	Max	F value	P value
NP	98	2.5005	0.8151	1.02	4.2	18.49	0.000
PE	55	1.886	0.824	0.72	3.9	10.49	0.000
Severe PE	33	1.56	0.896	0.4	3.53		
Е	10	1.142	0.386	0.64	1.9		

 Table 1: Platelet count according to clinical diagnosis

Distribution of urine albumin in cases and controls:

In Group NP n=98: 91.8% had no proteinuria, 5.1% had traces, 2.04% had 1+ and 1.02% had 3+; in Group PE n=55: 10.91% had no proteinuria and traces, 49.09% had 1+ and 21.82% had 2+, 7.27% had 3+; in group SEVERE PE n=33: 6.06% had no proteinuria, 3.03% had traces, 27.27% had 1+, 24.24% had 2+, 21.21% had 3+ and 18.18% had 4+ and in Group E, n=10: 10% had 1+, 40% had 2+, 30% had 3+, 20% had 4+.

Out of n=196, n= 81 were primigravidae – 13.58% had platelet count below 11akh/mm³, 20.99% had between 1 to 1.5 lakh/mm³ and 65.43% had normal platelet count.

n=115 were multigravidae – 11.3% had platelet count below 11akh/mm³, 11.3% had between 1 to 1.5 lakh/mm³ and 77.39% had normal platelet count.

Blood pressure versus platelet count: In the control group n=98, with normal blood pressure, 2% had thrombocytopenia with counts of 1 to 1.5 lakh/mm³. In cases n=98, n=60 had blood pressure in the range of >140/90 to <160/110 mm of Hg, and n=38 had a blood pressure of \ge 160/110 mm of Hg. n=60 with a blood pressure of <160/110 mm of Hg, 16.67% had a platelet count below 1 lakh/mm³, and 26.67% had a platelet count of 11akh to 1.5 lakh/mm³. n=38 with a blood pressure of \geq 160/110 mm of Hg, 36.8% had a platelet count of below 1 lakh/mm³, and 31.6% had a platelet count of 1 to 1.5 lakh/mm³.

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Platelet outcome per mm ³	<140/90	SBP- 140-159 DBP- 90-109	≥ 160/110	Total	
< 50,000	0	0	2 (5.2%)	02	
50,000-1 Lakh	0	10 (16.67%)	12 (31.6%)	22	
1 lakh-1.5 lakh	2 (2%)	16 (26.67%)	12 (31.6%)	30	
≥ 1.5 lakh	96 (98%)	34 (56.66%)	12 (31.6%)	142	

Table 2: Blood Pressure versus platelet count

Distribution of cases according to management: In the present study, group NP, n=98, 61 (62%) cases delivered vaginally, and 37 (38%) cases underwent LSCS.

In group PE, n=55, 14 (25.5%) cases delivered vaginally and 41 (74.5%) cases underwent LSCS. 43 (78%) cases were given antihypertensive drugs, and 7 (13%) cases were given Inj. MgSO4.In group severe PE, n=33, 20 (60%) cases delivered vaginally and 13 (40%) cases underwent LSCS. All cases were given antihypertensive drugs, and17 (52%) cases were given Inj. MgSO4. In group E, n=10, 5 (50%) cases delivered vaginally and 5 (50%) cases underwent LSCS. All cases were given antihypertensive drugs and Inj. MgSO4.

Table No 3: Distribution of cases according to management								
Management	NP	%	PE	%	Severe	%	E	%
_					PE			
VD	61	62	14	25.5	20	60	5	50
LSCS	37	38	41	74.5	13	40	5	50
				1	1	1		

 $\mathbf{T}_{\mathbf{r}}$ by $\mathbf{N}_{\mathbf{r}}$ $\mathbf{N}_{\mathbf{r}}$

Table 100 4. Distribution of material complications among cases							
Group	Imminent	HELLP	DIC	Pulmonary	PPH	Mortality	
	Eclampsia	Syndrome		edema			
PE, n=55	7	0	0	0	0	1	
Severe PE, n=33	17	2	1	2	2	2	
E, n=10	0	4	2	2	2	1	
Total n=98	24	6	3	4	4	4	

Table No 4: Distribution of maternal complications* among cases

*In the same case, more than one complication was seen. Therefore, the percentages are not calculated It was observed that the most common maternal complication was imminent eclampsia 24 out of 98 cases in this study. n= 2 cases of mortality with a platelet count below 50,000/cumm, n=2 cases of death with a platelet count between 11akh/cumm to 1.51akh/cumm were noted.

All control group cases were healthy.

Table No 5: Distribution of fetal complications among cases

Group	IUGR	RDS	MAS	Mortality
PE, n=55	7	3	5	1
Severe PE, n=33	7	4	7	6
E, n=10	5	1	0	2
Total, n=98	19	8	12	9

The most common fetal complication of preeclampsia and eclampsia cases seen was IUGR. RDS in 8 cases, MAS in 12 cases.

Mortality was present in 9 cases. Out of 9 cases of mortality, 5 had a platelet count <1.5 lakh/mm³, and 4 had a platelet count of >1.5 lakh/mm³.

V. Discussion

Out of all the hematological abnormalities that occur in hypertensive disorders of pregnancy, thrombocytopenia is the most common. There is a progressive fall of mean platelet count with increasing severity of the disease.

The present study was done to assess the severity of preeclampsia and eclampsia with a focus on platelet count estimation and hence, prove its prognostic significance. It was seen that there was a significant decrease in platelet count in preeclampsia and eclampsia cases when compared to control groups.

As far as age is concerned, there is no or little difference noted between the control group and cases with preeclampsia and eclampsia in this study.

Most of the cases in normal pregnant group (75%) and cases with preeclampsia and eclampsia were in the age group of 18 to 25 years of age which is comparable with the study of Chaware et al where the maximum number of patients preeclampsia, severe preeclampsia, and eclampsia were in the age group of 20 - 24 years.⁶ The mean age in the present study is 23.5 ± 4.16 years, which is comparable to Sharma Sk et al.⁷ and Prakash J et al.⁸ The younger age of occurrence of preeclampsia and eclampsia could be due to the early age of marriage and early pregnancy in this country compared to western countries.

Preeclampsia is primarily regarded as a disease of first pregnancy. Out of 98 cases in the study group, 56% were primigravidae, and 44% were multigravidae. The findings of the present study (56%) and many other studies such as Leduc et al.41 (65%) and Naaz A et al.⁹ (60%) also confirm that preeclampsia and eclampsia are more prevalent in primigravida.

Platelet count among cases: In the present study, thrombocytopenia is seen in 41.8% of cases in preeclampsia group (n=55), 57.6% of cases in severe preeclampsia group (n=33), 80% of the cases in the eclampsia group (n=10). It was seen that the platelet count in severe preeclampsia and cases with eclampsia were very significantly lower than the healthy pregnant control, whereas the platelet count in preeclampsia was not significantly lower than the healthy pregnant control.

In the present study, we observe that as the severity of the disease increases to severe preeclampsia and eclampsia, a decreasing trend of platelet count is seen, and the association is statistically significant.

A similar association was shown by Poulri et al.¹⁰ thrombocytopenia was present in 5 out of the 100 PIH cases and in which 4 were eclampsia and 1 was severe preeclampsia. Therefore, thrombocytopenia is mostly a feature of eclampsia.

In the present study, we observe that the lowest platelet count group severe PE (n=33) is $21,000/\text{mm}^3$, and in Group E (n=10) is $78,000/\text{mm}^3$.

A continuous decline in platelet count as pregnancy advances was shown by Faye et al.¹¹, and Shah A R et al.¹² indicated that there is a possibility of platelet destruction during pregnancy. This, together with hemodilution and platelet trapping, results in a decrease in platelet count¹³.

In all the studies including the present one, the mean platelet counts in the controls were>2.2 lakh/mm³, and it also demonstrated a decreasing trend as the severity of pre-eclampsia increased even though in most of the studies the mean platelet counts were in the normal range of 1.53 lakh/mm³. But in eclampsia, the mean platelet count was seen to be below 1 lakh/mm³. The mean platelet counts in both the case and control group were compared with other studies conducted by Chaware SA et al.,¹⁴and Mohapatra S et al¹⁵.

McCrae¹⁶ has suggested that thrombocytopenia may precede the various other manifestations of preeclampsia, and thus should be considered in the event of isolated thrombocytopenia seen in the late second or third trimester.

Some authors have suggested that thrombocytopenia is caused due to peripheral consumption, endothelial damage, and reduced life span. Altered platelet membrane with accelerated aggregation and destruction have also been suggested¹³.

Meshram et al.¹⁷, in a hospital-based study, found lower platelet counts in preeclampsia and eclampsia in healthy pregnant controls. Low platelet count was seen in 29.31% of cases with preeclampsia and in 44.44% of cases with eclampsia.Studies by Khan A et al.¹⁸ from Pakistan found a fall in platelet counts in cases with PIH.

In the present study, we observe that as the severity of hypertension increases and a decreasing trend of platelet count is seen and the association is statistically significant. A similar association was shown by Poluri et al.¹⁰

In the control group n=98, with normal blood pressure, 2% had a low platelet count. In the study group, the low platelet count is seen in 44% of cases with a blood pressure of <160/110 mm of Hg, and 69% of cases with a blood pressure of $\geq 160/110$ mm of Hg.

Thrombocytopenia is directly proportional to pre-eclampsia severity. A platelet count below one lakh per mm3 indicates increased risk for DIC and HELLP Syndrome. Disseminated intravascular coagulation had implicated in the pathogenesis of pre-eclampsia and eclampsia for a long time.

The severity of proteinuria in pre-eclampsia had regarded by some as a predictor of adverse outcomes for the mother.¹⁹ This is correlated with our study, where the degree of proteinuria found to increase with the severity of pre-eclampsia and eclampsia.

In the present study, the rate of maternal complications increased as the severity of disease increased. The complication rate was higher in cases of severe preeclampsia and eclampsia.

In the control group, maternal complications were present only in 4 cases, which had primary PPH.

In preeclampsia group n=55, 7 had imminent eclampsia, and one maternal death occurred due to hepatorenal syndrome. In severe preeclampsia group n=33, 17 had imminent eclampsia, 2 cases developed HELLP syndrome, 1 had DIC, 4 had PPH, 2 had pulmonary edema, and two maternal deaths noted.

In eclampsia group n=10, 2 had pulmonary edema, 2 had DIC, 4 had HELLP syndrome, and one maternal death occurred.

In this study, there were 4 cases of mortality due to PPH, DIC, which deteriorated to cerebral edema and cerebral damage leading to multiorgan dysfunction syndrome, acute kidney injury, and death.

In the present study, the most common fetal complication was IUGR and is present in 7 cases with preeclampsia, 7 cases with severe preeclampsia, and 5 with eclampsia.

RDS was seen in 3 cases with preeclampsia, 4 with severe preeclampsia, and 1 with eclampsia.MAS was observed in 5 with preeclampsia, 7 with severe preeclampsia.

Mortality was seen in 9 cases, one preeclampsia, six severe preeclampsia, and two eclampsia cases. Out of 9 cases of mortality, 5 had a platelet count <1.5 lakh/mm³, and 4 had a platelet count of >1.5 lakh/mm³.

In the control group NP, n=98, 95% delivered healthy babies with no fetal complications, and 5% had IUGR.

In the present study, we observed that cases with low platelet count had increased risk of maternal and fetal complications. Most of the cases who developed impending eclampsia had a platelet count in the range of <1.5 lakh per cumm.

Out of 98 cases with preeclampsia eclampsia syndrome, who presented with low platelet count 6 cases developed HELLP syndrome of which 4 cases had a platelet count below 1 lakh/mm³. 4 cases developed pulmonary edema with a low platelet count, of which 2 cases had a platelet count below 1lakh/mm³, and 3 cases land into DIC with a low platelet count of which 2 cases had a platelet count below 50,000/mm³.

4 cases of mortality noted in the present study, of which 2 cases had a platelet count below 50,000/mm³ and 2 cases had a platelet count of 11akh to 1.5 lakh/mm³.

The aims of pharmacotherapy are to reduce morbidity, prevent complications, and correct eclampsia. The drug of choice to treat and prevent eclampsia is magnesium sulfate.²⁰

Evidence of DIC in the setting of severe preeclampsia and eclampsia should prompt immediate delivery. The decision of whether to proceed with the induction of labor or cesarean delivery depends on parity, cervical Bishop's score, the motivation of the pregnant woman, and the severity of the disease.

Moderate to severe thrombocytopenia may be a contraindication to regional anesthesia because of the risk of spinal hematoma²¹.

Eclamptic convulsions are life-threatening emergencies and require the proper treatment to decrease maternal morbidity and mortality.

Delivery is the only definitive treatment for eclampsia. Several organizations have developed screening, treatment, and prevention guidelines for preeclampsia and eclampsia^{22,23}.

Pharmacotherapy goals are to reduce morbidity, prevent complications, and correct eclampsia. The drug of choice to treat and prevent eclampsia is magnesium sulfate.

In the present study, group NP, n=98, 62% of cases delivered vaginally, and 38% of cases underwent LSCS. In group PE (n=55) 25.5% of cases delivered vaginally and 74.5% of cases underwent LSCS. 78% of cases were given antihypertensive drugs, and 13% of cases were given Inj. MgSO4.

In severe PE (n=33), 60% of cases delivered vaginally, and 40% of cases underwent LSCS. All cases were given antihypertensive drugs, and 52% of cases were given Inj. MgSO4.

In group E(n=10), 50% of cases delivered vaginally, and 50% of cases underwent LSCS. All cases were given antihypertensive drugs and Inj. MgSO4.

Out of the total study population cases with preeclampsia and eclampsia (n=98), 3% of cases went into coagulation failure. They were treated with fresh frozen plasma, and platelet concentrates apart magnesium sulfate and antihypertensive drugs followed by delivery.

Although the incidence of eclampsia has declined in recent years, mainly due to the improvement of healthcare, serious adverse outcomes still exist.²⁴

VI. Conclusions:

It can be concluded from the present study that the platelet countestimation can be taken as an early, simple, rapid, and low-cost routine procedure for the assessment of the severity of hypertensive cases and their subsequentmanagement. But, alone, it cannot be upon to assess the severity of the disease.

Hence the other parameters like prothrombin time, INR, activated partialthromboplastin time, Thrombin time, D-dimer levels, and fibrinogen levels should be used for a definite diagnosis and management of the coagulation failure inpreeclampsia and eclampsia patients. There are still doubts, however, as to the cost of the tests required for all patients to be carried out.

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Dr.B.S.V.Sivaranjani, et. al. "Study of Lowered Platelet Count as a Prognostic Index in Hypertensive Disorders of Pregnancy." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(01), 2021, pp. 50-56.

DOI: 10.9790/0853-2001065056