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Original Research Article

A comparative study of coagulation profile and platelet indices at term in pre-eclamptic, eclamptic and normal pregnancy along with fetomaternal outcome

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ABSTRACT

Background: Hypertensive disorders of pregnancy is reported to cause about 60-80% of maternal deaths. Platelet indices are biomarkers of platelet activation. Among these platelet indices, mean platelet volume (MPV), and platelet distribution width (PDW), platelet large cell ratio (PLCR) is a group of platelet parameters. When platelets are activated, they become larger in size which causes increased platelet indices such as MPV, PDW and PLCR. So, platelet indices can give an idea of platelet activation. A comparative study of coagulation profile and platelet indices at term in pre-eclamptic, eclamptic and normal pregnancy along with fetomaternal outcome.
Methods: This study was carried out in department of obstetrics and gynaecology in collaboration with department of pathology, Rabindranath Tagore Medical College (RNTMC), Udaipur. Cases were selected by systematic random sampling. Bleeding time (BT), clotting time (CT), prothrombin time (PT), mean platelet volume (MPV), platelet distribution width (PDW), and activated partial thromboplastin time (aPTT) to analyse hypertensive disorders in pregnancy (HDP) during the period January 2021 to December 2021.
Results: Significant difference was seen in bleeding time (seconds), prothrombin time (seconds), aPTT (seconds) between normal pregnancy as compared to pre-eclampsia and eclampsia. (p value <0.05). Patients' admission in neonatal intensive care unit (NICU) was significantly higher in eclampsia (p<0.0001) and pre-eclampsia (p<0.0001) as compared to normal pregnancy (66.67%, 43.24% versus 2% respectively).
Conclusions: We conclude that coagulation profile like (BT, CT, PT, and aPTT), platelet counts along with platelet indices- MPV, PDW are useful markers, which were significantly raised in patients with preeclampsia and eclampsia. Platelet indices along with coagulation profile emerges as an important, simple, cost effective and effortless tool for predicting severity of pregnancy induced hypertension (PIH).

Keywords: HDP, PIH, MPV, PDW, PLCR, aPTT

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) are the common complications that are found during pregnancy with incidence rates reported to be about 2% to 8%.[1] These disorders can have a negative effect on the gestational outcomes. One of the most deleterious gestational hypertensive disorders is pre-eclampsia (PE), which is characterized by gestational hypertension as well as nephrotic impairment with proteinuria.[2] It is associated with increased rates of mortality during pregnancy.[3]

The prevalence of hypertensive disorders of pregnancy, gestational hypertension and preeclampsia are 5.2–8.2%,

1.8–4.4% and 0.2–9.2%, respectively.[4] The prevalence of maternal and fetal complications associated with HDP vary by region and healthcare facility type.[5] HDP has been reported to cause about 60-80% of all maternal deaths.[6]

The American high blood pressure education program working group report indicates that about 30% of HDP in that country were due to chronic hypertension while 70% of the cases were PE.[7]

PE is diagnosed when the patient is presenting with blood pressure (BP) ≥140/90 mmHg appearing for the first time after 20 weeks of gestation and proteinuria over 300 mg/24 hour or over 30 mg/dl. Eclampsia is the occurrence of convulsions or coma unrelated to other cerebral conditions with signs and symptoms of pre-eclampsia. Eclampsia is defined when seizures appear in woman that meets the criteria for PE.[2]

Thrombocytopenia is characteristic of worsening PE as it signifies platelet activation and aggregation as well as microangiopathic hemolysis.[8]

Platelet indices are biomarkers of platelet activation. They allow extensive clinical investigations focusing on the diagnostic and prognostic values in a variety of settings without bringing extra costs. Among these platelet indices, mean platelet volume (MPV), and platelet distribution width (PDW), platelet large cell ratio (PLCR) is a group of platelet parameters.[9]

MPV, which is commonly used as a measure of platelet size, indicates the rate of platelet production and platelet activation. The MPV has been shown to correlate with the function and activation of platelets. The importance of MPV has been emphasized as an inflammation marker in some diseases such as PE.[10]

Platelet activation begins in the first month of pregnancy in women with risk for PE. Studies suggested that when platelets are activated, they become larger in size which causes increased platelet indices such as MPV, PDW and PLCR. So, platelet indices can give an idea of platelet activation.[10]

Aims and objectives

A comparative study of coagulation profile and platelet indices at term in pre-eclamptic, eclamptic and normal pregnancy along with fetomaternal outcome.

METHODS

This case control study was carried out in department of obstetrics and gynaecology in collaboration with department of pathology of Rabindranath Tagore (RNT) Medical College, Udaipur. Cases were selected by systematic random sampling, as per inclusion and exclusion criteria.

Inclusion criteria

Females with singleton pregnancy were included in the study. For study group, women between 37 to 40 weeks of gestation with PE and eclampsia; and for the control group, normotensive pregnant women between 37 to 40 weeks of gestation were included in the study.

Exclusion criteria

Patients with pre-existing medical disorders like diabetes mellitus, renal disease, coagulopathies, chronic hypertension and hepatitis, sepsis, ITP, and severe trauma history; 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; and women with multiple pregnancies and congenital malformed foetus were excluded from the study.

Tests to assess the platelet function

Bleeding time

It is the interval from oozing of blood after a cut or injury till arrest of bleeding.

Platelet count

Total number of platelets in the blood is referred to as the platelet count.

Platelet indices: MPV and PDW

MPV and PDW are two simple methods of assessing platelet function and reflect the platelet production rate and activation. MPV reflects the size of platelets and PDW directly measures the variability in platelet size.

Tests to assess the coagulation system

Clotting time (CT)

It is the time interval from oozing of blood after a cut or injury till the formation of clot.

Prothrombin time (PT)

It is the time taken by blood to clot after adding tissue thromboplast into it.

Activated partial thromboplastin time (aPTT)

It is the period required for clot formation in recalcified blood plasma after contact activation and the addition of platelet substitutes.

Details of the study protocol was explained to patients; informed consent was obtained; detailed history was

taken; and general physical, systemic and obstetric examination was done.

Statistical analysis

The data was collected in Microsoft excel and the final analysis was done using statistical package for social sciences (SPSS) software, version 21.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

RESULTS

50 pregnant women between 37 to 40 weeks of gestation with PE and eclampsia and 50 normotensive pregnant women between 37 to 40 weeks of gestation were included in the study. BT, platelet count, platelet indices, CT, PT, aPTT was assessed, maternal and fetal outcome was observed and results are as follows.

Mean age (years) of study subjects was 23.96±4.2 with median (25th-75th percentile) of 23 (21-26).

Distribution of bleeding time (seconds) was comparable between normal pregnancy, PE and eclampsia (normal {90 to 240 seconds}: 100% versus 97.22% versus 100% respectively, deranged: 0% versus 2.78% versus 0% respectively) (p value=0.5).

Distribution of clotting time (seconds) was comparable between normal pregnancy, PE and eclampsia (normal {180 to 300 seconds}: 48% versus 61.11% versus 50% respectively, deranged: 52% versus 38.89% versus 50% respectively) (p value=0.472).

Proportion of patients with prothrombin time (seconds): deranged was significantly lower in normal pregnancy as compared to PE (p value=0.001) and eclampsia (p value <0.0001) (deranged: 22% versus 55.56% and 92.86% respectively).

Distribution of aPTT (seconds) was comparable between normal pregnancy, PE and eclampsia (normal {24 to 36 seconds}: 76% versus 77.78% versus 78.57% respectively, deranged: 24% versus 22.22% versus 21.43% respectively) (p value=1).

No significant difference was seen in clotting time (seconds) (p value=0.3) between normal pregnancy, PE and eclampsia.

Significant difference was seen in bleeding time (seconds), prothrombin time (seconds), aPTT (seconds) between normal pregnancy as compared to PE and eclampsia (p value <0.05) (Table 2).

Mean±SD of platelet count (lacs/cubic mm) in normal pregnancy was 3.07±0.59 which was significantly higher as compared to PE (1.74±0.75) (p value<0.0001) and eclampsia (1.42±0.68) (p value<0.0001). Mean±SD of platelet count (lacs/cubic mm) in PE was 1.74±0.75 and eclampsia was 1.42±0.68 with no significant difference between them (p value=0.128).

Mean±SD of MPV (cubic µm) in eclampsia was 11.61±1.01 which was significantly higher as compared to normal pregnancy (9±0.79) (p value<0.0001) and PE (10.52±1.31) (p value=0.001). Mean±SD of mean platelet volume (cubic µm) in normal pregnancy was 9±0.79 which was significantly lower as compared to PE (10.52±1.31) (p value<0.0001).

Mean±SD of PDW (cubic µm) in eclampsia was 18.53±2.65 which was significantly higher as compared to normal pregnancy (12.43±1.11) (p value<0.0001) and PE (16.9±3.09) (p value=0.023). Mean±SD of platelet distribution width (cubic µm) in normal pregnancy was 12.43±1.11 which was significantly lower as compared to PE (16.9±3.09) (p value<0.0001) and eclampsia (18.53±2.65) (p value<0.0001) (Table 3).

Distribution of IUGR was comparable between PE and eclampsia (absent: 58.33% versus 57.14% respectively, present: 41.67% versus 42.86% respectively (p value=0.939).

Proportion of patients with IUGR was significantly higher in eclampsia and pre-eclampsia as compared to normal pregnancy (42.86% (p value <0.0001) and 41.67% (p value <0.0001) versus 0% respectively) (Figure 1).

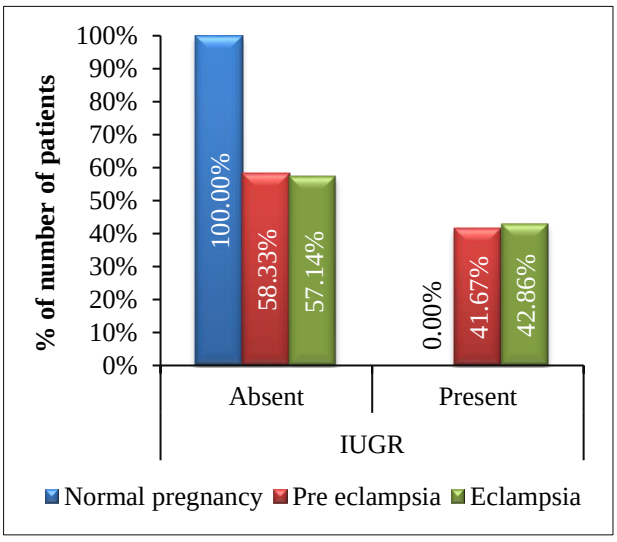

Figure 1: Comparison of IUGR between normal pregnancy, PE and eclampsia.

Proportion of patients with NICU admission was significantly higher in eclampsia (p value <0.0001) and PE (p value <0.0001) as compared to normal pregnancy (present: 66.67%, 43.24% versus 2% respectively). Distribution of NICU admission was comparable between eclampsia and PE (p value=0.126) (Table 4).

Table 1: Comparison of age (years) between normal pregnancy, pre-eclampsia and eclampsia.

Age (years)	Normal pregnancy (n=50)	Pre-eclampsia (n=36)	Eclampsia (n=14)	P value
Mean±SD	23.22±2.66	25.17±5.67	23.5±3.63	0.67 N versus PE:0.383 N versus E:0.941 PE versus E:0.593
Range	19-31	18-37	18-32	

Table 2: Comparison of coagulation profile between normal pregnancy, pre-eclampsia and eclampsia.

Coagulation profile	Normal pregnancy (n=50)	Pre-eclampsia (n=36)	Eclampsia (n=14)	P value
Bleeding time (seconds)				
Mean±SD	146.74±22.25	192.67±25.12	211.43±16.2	<0.0001§ N versus PE:<0.0001 N versus E:<0.0001 PE versus E:0.068
Range	114-196	146-246	186-236	
Clotting time (seconds)				
Mean±SD	309.66±77.31	282±56.14	304.07±66.37	0.3§ N versus PE:0.139 N versus E:0.994 PE versus E:0.308
Range	210-510	214-396	214-452	
Prothrombin time (seconds)				
Mean±SD	11.23±1.25	13.86±1.84	16.01±2.23	<0.0001‡ N versus PE:<0.0001 N versus E:<0.0001 PE versus E:<0.0001
Range	9.2-13.9	9.9-18	10.2-20	
aPTT (seconds)				
Mean±SD	27.84±4.64	31.52±7.81	34.23±5.22	0.0004§ N versus PE:0.013 N versus E:0.0002 PE versus E:0.066
Range	12-35.7	12.8-56	28-46	

‡ ANOVA, § Kruskal Wallis test

Table 3: Comparison of platelet count and platelet indices between normal pregnancy, pre-eclampsia and eclampsia.

Platelet count and indices	Normal pregnancy (n=50)	Pre-eclampsia (n=36)	Eclampsia (n=14)	P value
Platelet count (lacs/cubic mm)				
Mean±SD	3.07±0.59	1.74±0.75	1.42±0.68	<0.0001‡ N versus PE:<0.0001 N versus E:<0.0001 PE versus E:0.128
Range	1.8-4.2	0.7-3.8	0.3-2.8	
Mean platelet volume (cubic µm)				
Mean±SD	9±0.79	10.52±1.31	11.61±1.01	<0.0001‡ N versus PE:<0.0001 N versus E:<0.0001 PE versus E:0.001
Range	7.6-11.2	6.8-12.5	9.8-14.1	
Platelet distribution width (cubic µm)				
Mean±SD	12.43±1.11	16.9±3.09	18.53±2.65	<0.0001‡ N versus PE:<0.0001 N versus E:<0.0001 PE versus E:0.023
Range	9.5-14.4	10-23.5	15.1-22.9	

‡ ANOVA

Table 4: Comparison of birth weight (kg), APGAR score, NICU admission between normal pregnancy, pre-eclampsia and eclampsia.

Foetal outcome	Normal pregnancy	Pre-eclampsia	Eclampsia	P value
Birth weight (kg), mean±SD	3.01±0.32	6.85±0.89	2.25±0.59	<0.0001§
APGAR score, mean±SD	7.66±0.52	14.41±25.79	6.53±0.64	<0.0001§
NICU admission (%)	1 (2)	16 (43.24)	10 (66.67)	<0.0001*

* Fisher's exact test, § Kruskal Wallis test

DISCUSSION

Platelets adhere to the injured blood vessel to prevent blood loss through a discrete series of steps involving platelet adhesion to the wounded area and platelet activation, i.e. generation of intracellular chemical signals that are initiated by platelet adhesion. These signals cause rapid morphological changes such as extension of pseudopodia, platelet–platelet aggregation, and granule secretion.

This renders platelet indices, such as MPV and PDW, as valuable prognostic markers for thromboembolic diseases and platelet activation.

The present study was conducted in department of gynecology and obstetrics in collaboration with department of pathology of RNT Medical College, Udaipur. 50 pregnant women between 37 to 40 weeks of gestation with PE and eclampsia and 50 normotensive pregnant women between 37 to 40 weeks of gestation were included in the study. BT, CT, platelet count, platelet indices, PT, aPTT was assessed, maternal and fetal outcome was observed.

Mean age of our study subjects was 23.96 years with median of 23. Here, median age (years) in normal pregnancy was 23, in PE was 23 and eclampsia was 23 with no significant difference between them (p value=0.67). Similar results were observed by Thalor et al who found mean age of the patients with pre-eclampsia was 26 years.[10] Mohapatra et al found women with mild PIH had mean age group of 29.3 years, with PE had mean age-25.5 years, and those with eclampsia with mean age 25.7 years.[11]

Meena et al found mean age of the cases as 25.12 years, with maximum 68 (82.82%) cases were between 20-29 years of age.[12] It appears that as far as age is concerned, there is no or little difference between normal healthy pregnant women and patients with different degrees of severity of pregnancy induced hypertension. But it was clear that most patients in normal pregnant control group and patients with pregnancy induced hypertension were in age ranging between 21 to 29 years.

In our study mean±SD of platelet count (lacs/cubic mm) in normal pregnancy was 3.07±0.59 which was significantly higher as compared to pre-eclampsia (1.74 ± 0.75) (p value<0.0001) and eclampsia (1.42±0.68) (p value<0.0001).

MPV is the measurement of average size of platelets. The increase of MPV in conditions of increased platelet turnover is probably mediated by several cytokines (interleukins 6 and 11 and thrombopoietin) that affect megakaryocyte ploidy and result in the production of larger and more reactive platelets.[12]

The MPV values evaluated in our study were 9.0±0.79 fl for the control, 10.52±1.31 fl for PE, and 11.61±1.01 fl for eclampsia group. We found that there was a progressive rise when the values generated in normotensive pregnant women were compared with those of preeclamptic and eclamptic women in the present study. This significant difference in MPV can be attributed to both, complication of PE and the state of pregnancy itself.

This suggests the role of platelets in pathogenesis of hypertensive disorders of pregnancy. Hence, any increase in MPV must be carefully monitored to help in early diagnosis so that proper line of management can be chosen and an impending thrombotic event leading to maternal and neonatal morbidity or mortality can be prevented.

PDW is the distribution width on 20% frequency level with the peak taken as 100%.[13] The PDW is useful in differentiating reactive thrombocytosis from the essential type, especially when it is combined mathematically with the MPV and platelet count to obtain a discriminant function.[14]

Our observations showed that PDW was significantly elevated among the patients as compared with the control group. In our study mean±SD of PDW (cubic µm) in normal pregnancy was (12.43±1.11) which was significantly lower as compared to eclampsia (18.53±2.65) and pre-eclampsia (16.9±3.09) (p value≤0.0001).

Manchanda et al also found that compared to controls, among the patients with PE and eclampsia, there were higher values of MPV (10.46 versus 11.52 versus 8.45), PDW (15.57 versus 16.34 versus 11.01). This was in accordance with the increased BP. The study showed that that platelet indices are increased among patients with PIH than women with normal pregnancies.[9]

Haldar et al also found that among the patients with mild PE, severe PE and eclampsia, there was a decrease in the platelet count (/cu mm) (181541.7 versus 170291.7 versus 128291.7 versus 260000, p<0.05) and an increase in the MPV (fl) (10.32 versus 11.21 versus 12.97 versus 8.20,

p<0.05), PDW (%) (15.41 versus 18.717 versus 20.6 versus 12.5).[15]

Alkholy et al in their study found that among the patients with PE and eclampsia there was a decrease in the platelet count (183.940 versus 139.340 versus 249.120, p<0.001) and an increase in the MPV (9.82 versus 11.07 versus 8.50), and PDW (14.26 versus 17.09 versus 11.01). The results showed that because of increase in platelet destruction as well as platelet turnover among patient having preeclampsia, reducing PC, and increase in MPV and PWD, there is a role in prediction of PE.[16]

Annam et al study found that among the patients with PE and eclampsia there was a decrease in the platelet count (1,55,500 versus 1,31,000 versus 2,18,440) and an increase in the coagulation parameters MPV (10.38 versus 11.03 versus 8.63), PDW (15.51 versus 16.78 versus 11.07). The study stressed on the occurrence of intravascular coagulation among patients with hypertensive disorders of pregnancy. An association was also found between platelet indices and PE severity.[17]

In our study, significant difference was seen in bleeding time (seconds), prothrombin time (seconds), aPTT (seconds) between normal pregnancy as compared to PE and eclampsia (p value <0.05).

Median (25th-75th percentile) of bleeding time (seconds) in normal pregnancy was 140 (130-158) which was significantly lower as compared to PE (186 (177.5-212)) (p value <0.0001) and eclampsia (211 (197-223)) (p value<0.0001).

Median (25th-75th percentile) of PT (seconds) in normal pregnancy was 11.45 (10.2-12.1) which was significantly lower as compared to PE (14.15 (12.95-14.75) (p value <0.0001) and eclampsia (16.3 (15.15-17.125)) (p value <0.0001). Median (25th-75th percentile) of PT (seconds) in PE was 14.15 (12.95-14.75) which was significantly lower as compared to eclampsia (16.3 (15.15-17.125)) (p value <0.0001).

Median (25th-75th percentile) of aPTT (seconds) in normal pregnancy was 27.45(24.275-31.4) which was significantly lower as compared to PE (30.2 (27.85-35.45)) (p value=0.013) and eclampsia (32 (30.8-35.9)) (p value=0.0002). Chaithra et al study showed increased prothrombin time (sec) in the cases group is 16.70 (sec) as compared to the 12.25 (sec) control group.[18] Also there was an increase in aPTT (sec) in cases group is 32. 75 (sec) as compared to 25.59 (sec) control group. The difference was statistically significant. The findings were in concordance with the study done by Lakshmi et al shows increased PT and aPTT in severe PE and eclampsia.[19] The study done by Kumar et al shows thrombocytopenia and coagulation abnormalities particularly showing an increase in aPTT.[20]

Chauhan et al also found that among the patients with PE and eclampsia there was a decrease in the platelet count (157.18 versus 222.93) and an increase in the bleeding time (322.46 versus 186.60) (p<0.001). PT, aPTT, and CT were comparable.[21]

Swetha et al found that among the patients with PE and eclampsia there was a decrease in the platelet count (1.14 versus 1.00 versus 2.17) and comparable PT (15.52 versus 15.45 versus 15.41, p>0.05), and an increase in aPTT (37.21 versus 37.29 versus 36.20, p<0.05), CT (min) (6.07 versus 6.72 versus 4.67, p<0.05), BT (min) (4.66 versus 4.79 versus 2.72, p<0.05).[22] Haldar et al found increase in PT (severe PE versus eclampsia versus control 15.7 versus 16.7 versus 13.8 sec), and aPTT (29.7 versus 31.2 versus 40.4 versus 26.6, p<0.05).[15]

Patients with IUGR was significantly higher in eclampsia and PE as compared to normal pregnancy. (42.86% (p value<0.0001) and 41.67% (p value<0.0001) versus 0% respectively). Proportion of patients with mode of delivery LSCS was significantly higher in PE (47.22%, p value=0.025) and eclampsia (57.14%, p value=0.018) as compared to normal pregnancy (24%). Proportion of patients with NICU admission was significantly higher in eclampsia (p value <0.0001) and PE (p value <0.0001) as compared to normal pregnancy (present: 66.67%, 43.24% versus 2% respectively).

Limitations

Follow-up of the patients was not possible to examine the prognostic value of our findings. As the pathophysiology of PIH is complex and elusive so exact prediction of prognosis of disease still remains a challenge, there is no single marker or lab investigation which can strongly predict the prognosis of disease. So future research in this field is necessary.

CONCLUSION

We can conclude that the values of different parameters in coagulation profile denote the severity of the disease to some extent. Our study indicated that coagulation profile (BT, CT, PT, aPTT), platelet counts along with platelet indices- MPV, PDW are useful markers, which were significantly raised in patients with PE and eclampsia.

Platelet indices along with coagulation profile emerges as an important, simple, cost effective and effortless tool for predicting severity of PIH. These are routine tests which can be performed in every government hospital and can help to reduce the maternal and fetal morbidity and mortality associated with pregnancy induced hypertension.

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