Original Research Article

Comparison Of Platelet Indices and Coagulation Profile in Preeclamptic/ Eclamptic with Normotensive Pregnant Females

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ABSTRACT
Background: Hypertensive disorders are the most common medical complications of pregnancy. Due to low socioeconomic status, poor health education and lack of regular antenatal supervision, the incidence of preeclampsia is more in developing countries like India. Pregnancy induced hypertension is an important health issue that has to be dealt especially in the developing countries. It is a hypertensive disorder which usually appears after the 20th week of gestation.

Methods: The prospective case control study was conducted In Department of Pathology, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonepat for the duration of one year from February 2021 to February 2022 on 110 pregnant women, 55 normotensive and 55 with PIH. The study parameters included Platelet count, Platelet Distribution Width (PDW), Mean Platelet Volume (MPV), Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT), thrombin time(TT), serum fibrinogen, D-dimer, protein C and protein S.

Results: Platelet count decreased in pre-eclampsia but had no significant difference when compared to normotensive women. Mean platelet volume, Platelet distribution width, Serum fibrinogen, D-dimer showed significant difference in pre-eclamptic patients. Protein C was found within normal range. Protein S found marginally deranged in pre eclamptic women.

Conclusion: Thus, authors came to the conclusion that platelet indices and coagulation profile can be used as a reliable early indicator of onset and severity of preeclampsia and eclampsia.

Keywords: Coagulation, Eclampsia, Preeclampsia, Platelet

INTRODUCTION

Hypertensive disorders are the most common medical complications of pregnancy and are important causes of maternal and perinatal morbidity and mortality affecting 7-15% of all pregnancies. It is associated with 16% of all maternal mortality and 20% of all perinatal mortality in India.[1] Due to low socioeconomic status, poor health education and lack of regular antenatal supervision, the incidence of preeclampsia is more in developing countries like India.[2] Pregnancy induced hypertension (PIH) is an important health issue that has to be dealt with, especially in the developing countries where the incidence and the rate of adverse outcome are higher.[3] It is a hypertensive disorder which usually appears after the 20th week of gestation and results in multiorgan failure if left untreated.[4]

Hypertension is the most common medical problem encountered during pregnancy, complicating up to 10% of pregnancies.[5] Hypertensive disorders during pregnancy are classified into 4 categories, as recommended by the National High Blood Pressure Education Program (NHBPEP) Working Group on High Blood Pressure in Pregnancy: (i) Chronic hypertension (ii) Preeclampsia-eclampsia (iii) Preeclampsia superimposed on chronic hypertension and (iv) Gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy). This terminology is preferred over the older but widely used term "pregnancy-induced hypertension" (PIH) because it is more precise[6].

In clinically healthy pregnant women, BP steadily decreases up to the middle of gestation and then increases up to the day of delivery, with final BP values similar to those found early in pregnancy in the same women. For women who developed gestational hypertension or preeclampsia, BP is stable during the first half of pregnancy and then continuously increases until delivery. These predictable patterns of BP variability during pregnancy are somehow independent from the continuous linear increase in maternal weight with gestational age.[7]

PIH can present in the form of gestational hypertension, preeclampsia or eclampsia. Gestational hypertension is blood pressure (BP) ≥140/90 mmHg but without proteinuria. Preeclampsia is characterized by the new onset of hypertension (≥140 mmHg systolic or ≥ 90 mmHg diastolic) after 20 weeks of gestation, associated with proteinuria (spot urine protein/creatinine ≥30 mg/mmol (0.3 mg/mg) or ≥300 mg/day or at least 1g/L ('2+') on dipstick testing. Eclampsia is defined as the presence of new onset grand-mal seizures in a woman with preeclampsia, after excluding the presence of other causes of seizures. There is no effective treatment for preeclampsia and eclampsia, in addition to the termination of pregnancy.[8]

METHODS:

A prospective case control study was conducted in Department of Pathology, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonepat for the duration of one year from February 2021 to February 2022. Normotensive, preeclamptic and eclamptic pregnant females of age between 20-30 years with single live foetus of gestational age 24 weeks to 40weeks were included in our study. Pregnant females with Hydatidiform Mole, Multifoetal Pregnancy, Intrauterine Foetal Demise, Diabetes Mellitus (Gestational or Overt) and with Other medical conditions like Essential hypertension/chronic hypertension, Chronic kidney disease, Cardiac disorders, Connective tissue diseases, Autoimmune disorders and Tuberculosis were not included in our study. Platelet indices (MPV, PDW, PC) with EDTA anticoagulant blood was run on automated hematology analyser. For PT, INR, APTT, TT, fibrinogen, D-dimer, Protein C and S blood was collected in 3.8% trisodium citrate vacutainer in 1:9 ratio. The sample was centrifuged for 15 minutes at 3500 rpm and the plasma was separated and run on coagulation analyser ACL Elite pro.

RESULTS

A total of 110 pregnant females were included in the study, out of which 55 were controls and 55 were in case group. In the case group 19(34.5%) were in age group 20-22, 20(36.4%) were in age group 23-26 and 16(29.1%) were in age group 27-30.In the control group 18(32.7%) were in age group 20-22, 12(21.8%) were in age group 23-26 and 25(45.5%) were in age group 27-30. The mean age of women who were case and control were 24.73±3.21 and 25.29±3.66 respectively**.** In case group 38(69.1%) women were primigravida while 17(30.9%) were multigravida. In control 22(40%) were primigravida and 33(60%) were multigravida.

Table 1 Shows correlation of haematological assay between two groups

		Mean	±Std. Deviation	P value
Platelet count (lakh/cumm)	Case	1.704	±0.73	0.92
	Control	1.716	±0.57	
MPV (fl)	Case	12.35	±1.43	0.001 (S)
	Control	8.89	±0.93	
PDW (%)	Case	17.75	±1.23	0.001 (S)
	Control	12.82	±1.303	

The mean platelet count was 1.704 lakh/cumm with standard deviation of 0.73 lakh/cumm in cases and 1.71 lakh/cumm with standard deviation of 0.57 lakh/cumm in control. The p value was 0.92 which was statistically not significant. The average mean platelet volume was 12.35 ±1.43 fl in case and 8.89 fl ±o.93 fl in control. The p value was 0.001 which was statistically significant. The platelet distribution width was 17.75±1.23% in cases and 12.82±1.30% in control.

Table 2 Shows correlation of coagulation assay between two groups

		Mean	±Std. Deviation	P value
SERUM FIBRINOGEN(g/L)	Case	5.45	±0.95	0.001 (S)
	Control	3.57	±0.703	
D-DIMER(ng/mL)	Case	1021.25	±585.330	0.001 (S)
	Control	427.38		
APTT(seconds)	Case	39.876	±1.7990	0.001 (S)
	Control	24.236	±0.8252	
TT(seconds)	Case	19.395	±1.3552	0.001 (S)
	Control	10.013	±0.6087	
PROTEIN C (IU/Dl)	Case	99.78	±12.91	0.18
	Control	96.54	±12.69	
PROTEIN S (IU/dL)	Case	124.27	±10.904	0.46
	Control	125.61	±8.23	

Serum fibrinogen in preeclamptic women was 5.45±0.95g/L and 3.57±0.70g/L in control group. In case group, D-Dimer came out to be 1021.25±585.33 ng/ml and 427.38±83.05 ng/ml in control. APTT value in case group was 39.876±1.799 seconds and 24.236±0.82 seconds in control. In case group, TT value came out to be 19.39±1.35 seconds and 10.013±o.608 seconds in control group. Protein C in case group was 99.78±12.91 IU/dL and 96.±12.69 IU/dL in control group. In case group, Protein S came out to be 124.27±10.94 IU/dl and 125.61±8.23 IU/dl in control group.

DISCUSSION

There are variety of haematological changes occurs in PIH, out of which thrombocytopenia is the most common abnormality seen due to increased consumption of platelets during low-grade intravascular coagulation.[9,10] This study was undertaken to assess the severity of PIH and coagulopathy related adverse effects by using haematological/coagulation parameters helped in the management of PIH patient. It was observed that mean maternal age was 25.29±3.66 years in

normotensive group while 24.73±3.21 years in pre-eclamptic group and study showed that 69.1% and 40% were primigravida while 30.9% and 60% were multigravida in pre-eclamptic and normotensive groups respectively. The result was comparable with the studies conducted by Duan et al[11] and Mobeen et al[12] where the average age and parity was similar in normotensive and pre-eclamptic group and there was no significant difference found.

In our study mean platelet count was 1.716 lakh/cumm in normotensive women and 1.704 lakh/cumm in pre-eclamptic women. The p value was 0.92 which was statistically not significant. Although platelet count remained well above the lower limit (>1.5 lakh/cumm), it was noted that the platelet count in our study decreased. Pregnancy itself is a thrombocytopenic condition and with pre-eclampsia in pregnancy platelet count further decrease but it stayed well above the normal. Our findings regarding platelet count are consistent with the study by Lakshmi et al[13]. They too did not report a significant difference between normal and mild preeclampsia and severe preeclampsia patients and suggested that decreased platelet count may be due to the gestation itself, rather than the pre-eclampsia.

In our study the mean platelet volume was 8.89fl in normotensive women while 12.35fl in pre-eclamptic women. The platelet distribution width in normotensive women was 12.82% and 17.75% in pre-eclamptic women. The p value was 0.001 which was statistically significant. Our results are comparable with the other studies and showed significant results as shown in Table no. 3. The increase in both the MPV and PDW, which are the markers of platelet activation, suggests an active turnover of platelet production in the bone marrow due to peripheral consumption. The increase in values of both the MPV and PDW along with increased BP, further suggests that they are also elevated in severe pre-eclampsia with higher elevations of BP.

Table 3 Correlation of MPV and PDW in the present study with the other studies

Studies	Normotensive		Pre-eclamptic		P VALUE
	MPV	PDW	MPV	PDW	
Thalor et al[14]	10.5	13.3%	11.8	16.1%	0.01
Giles et al[15]	8.7	12%	9.8	6%	0.01
Present study	8.89	12.82%	12.35	17.75%	0.001

In the present study D-dimer in normotensive women came out to be 405.37±91.274 ng/ml and 915.19±276.07 ng/ml in mild pre-eclamptic women and 1267.29± 943.59 ng/ml in severe pre-eclampsia. D-Dimer value significantly increases with severity of preeclampsia. Our results are comparable with the results of study done by Duan et al[11]. In their study D-dimer in a normotensive females were 1.05mg/L while in pre–eclamptic it was 3.05mg/L. Similar results were present in a study done by Gulec et al[16].

In present study activated prothrombin time (APTT) was found 39.87±1.79 seconds in pre eclamptic women while it was 24.23±0.82 seconds in normal pregnant women. Prothrombin time (PT) was found 13.07±0.49 seconds in pre eclamptic women while it was 9.12±0.65 seconds in normal pregnant women.

Table 4 Correlation of APTT and PT in the present study with the other studies

Studies	Normotensive		Pre-eclamptic		P VALUE
	APTT	PT	APTT	PT	
Priyadarshani et al[17]	22.16±4.70	13.72±1.97	34.20±11.46	15.27±3.47	<0.001
Swetha et al[18]	29.45±2.29	13.23±0.94	36.20±4.95	15.41±1.13	<0.001
Present study	24.23±O.82	9.12±0.65	39.87±1.79	13.07±0.49	<0.001

In a study conducted by Han et al[19] there was slight increase in TT. In their study mean TT in normal pregnant women was 12.9±0.6secondes while in pre eclamptic it was 13.5±1.2. In present study thrombin time (TT) was found19.3±91.35 seconds in pre eclamptic women while it was10.01±0.60 seconds in normal pregnant women. TT value significantly increased in pre eclamptic patients as compared to normal women

In present study value Protein C in preeclamptic women was 99.78±12.91 IU/dL and 96±12.69 IU/dL in normal women. In pre eclamptic women, Protein S came out to be 124.27±10.94 IU/dl and 125.61±8.23 IU/dl in normotensive. The p value was 0.18 which was statistically not significant. In a study conducted by Okoye et al[20] showed that mean protein C did not differ in normal pregnant women and pre eclamptic women. But protein S values were found higher in pre eclamptic (54.58%±10.24%) women then in control group (47.23%±10.27%).

CONCLUSION
Present study revealed changes in the platelet indices and coagulative parameters in normotensive women which were compared to pre-eclamptic women. Platelet count decreased in pre-eclampsia but had no significant difference when compared to normotensive women. Mean platelet volume, Platelet distribution width, Serum fibrinogen, D-dimer showed significant difference in pre-eclamptic patients. With increasing severity of blood pressure in pregnant women changes were noted in the haemostatic parameters. Coagulative parameters like PT, APTT, TT showed significant difference in values between normotensive and preeclampsia patients Protein C was found within normal range. Protein S found marginally deranged in pre eclamptic women.

Furthermore, some normotensive women who had deranged values of these parameters progressed to pre-eclampsia (mild and severe) and some of the pre-eclamptic women having mild disease progressed to severe disease. Hence according to the present study, the haemostatic parameters could be used as markers for detection of pre-eclampsia, as well as markers for its severity and can be helpful for the management of complications in relation to pre-eclampsia.

REFERENCES
1. Dutta DC. Pregnancy induced hypertension. In: Dutta DC, editors. Textbook of Obstetrics including perinatalogy and contraception. 7th edn. Kolkata: New Central Book Agency (P) Ltd 2011. p. 219-40.

2. Villar K, Say L, Gulmezoglu AM. Eclampsia and preeclampsia: a health problem for 2000 years. In: Critchley H, MacLean AB, Poston L, editors. Preeclampsia. London: RCOG Press 2003. p. 189-207

3. Campbell OM, Graham WJ. Maternal survival series steering group. Strategies for reducing maternal mortality: getting on with what works. Lancet 2006;368(9543):1284-99.

4. Mohapatra S, Pradhan BB, Satpathy UK, Mohanthy A, Pattnaik JR. Platelet estimation: Its prognostic value in pregnancy induced hypertension. Indian J Physiol Pharmacol 2007;51:160-4.

5. Chaithra H, Ramesh ST, Ahmad R. A Comparative Study of Coagulation Profile and Haematological Parameters in Pregnancy Induced Hypertension (PIH). Trop J Pathol Microbiol 2021;7(3):150-54.

6. Cunningham FG, Norman FG, Kerneth JL, Lary CG, Hauth JC, Wenstom KD. Hypertensive disorders in pregnancy. In: ASeilis, SR Noujaim, K Davis, editors. Williams Obstetrics international Edn 22nd Edn, New York: McGraw Hill; 2001;p. 567-618.

7. Ayala DE, Hermida RC, Mojón A, Fernández JR, Silva I, Ucieda R, et al. Blood pressure variability during gestation in healthy and complicated pregnancies. Hypertension 1997;30(3):611-8

8. Tranquilli AL, Brown MA, Zeeman GG. The definition of severe and early-onset preeclampsia. Statements from the International Society for the Study of Hypertension in Pregnancy (ISSHP). Pregnancy Hypertens 2013;3(1):44-7.

9. Rosevear SK, Liggins GC. Platelet dimensions in pregnancy-induced hypertension. N Z Med J 1986;99(802)356-7.

10. Annam V, Srinivasa K, Yatnatti SK, Med SD. Evaluation of platelet indices and platelet counts and their significance in pre-eclampsia and eclampsia. Int J Biol Med Res 2011;2(1):425-8.

11. Duan Z, Li C, Leung WT, Wu J, Wang M, Ying C, et al. Alterations of several serum parameters are associated with preeclampsia and may be potential markers for the assessment of PE severity. Dis Markers 2020;13;1-7

12. Mobeen SH, Rashid NI, Iqbal IR, Khalid A, Iqbal K. Prevalence of Thrombocytopenia among Normal Pregnant and Preeclamptic Females attending Antenatal Care. PJMHS. 2019;13(4):2.

13. Lakshmi CV. Comparative Study of Coagulation Profile in Mild Pre-eclampsia, Severe Pre-eclampsia, and Eclampsia. Int J Sci Res 2016;4(4):180-3.

14. Thalor N, Singh K, Pujani M, Chauhan V, Agarwal C, Ahuja R. A correlation between platelet indices and preeclampsia. Hematol Transfus Cell Ther 2019;41:129-33.

15. Giles C. The platelet count and mean platelet volume. Br J Haematol 1981;48(1):31-7.

16. Kucukgoz GU, Tuncay OF, Baris GA, Buyukkurt S, Seydaoglu G, Ferhat UI, et al. An analysis of C- reactive protein, procalcitonin, and D- dimer in pre- eclamptic patients. Am J Reprod Immunol 2012;68(4):331-7.

17. Priyadarshini GP, Mohanty RR. Assessment of coagulation profile and its correlation with severity of preeclampsia in women of Odisha-a comparative cross-sectional study. Inter J Basic Applied Physiol. 2014;3(1):234-40

18. Swetha AG, Puranik N, Kammar KF. A comparative study on coagulation profile and neutrophil-lymphocyte ratio in pregnancy-induced hypertension. Natl J Physiol Pharm Pharmacol 2018;8(3):400-5.

19. Han L, Liu X, Li H, Zou J, Yang Z, Han J, et al. Blood coagulation parameters and platelet indices: changes in normal and preeclamptic pregnancies and predictive values for preeclampsia. PloS One 2014;9(12):1-14

20. Okoye HC, Eweputanna LI, Okpani AO, Ejele OA. Associations between pre- eclampsia and protein C and protein S levels among pregnant Nigerian women. Int J Gynecol Obstet 2017;137(1):26-30.