Research Article

Platelet dysfunction in pre-eclamptic mothers

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Abstract

Background: Pre-eclampsia (PE) is a pregnancy-specific hypertensive disorder leading to a high proportion of hospital admission, labor induction, maternal as well as fetal morbidity and mortality. However it is fortunate that with timely detection and prompt management, this disease can often be ameliorated and eclampsia can be prevented.

Objective: The objective of this study is to find out the changes in total platelet count (TPC), bleeding time (BT), and clotting time (CT) in pre-eclamptic pregnant women as compared with normal pregnant women.

Material and Methods: This was a case–control study which included 60 pregnant women of more than 20 weeks of gestation. Out of these, 30 subjects were normotensive and 30 subjects were diagnosed with pre-eclamptic women. Patients having a past history of hypertension, renal diseases, diabetes during non-pregnant state, drug administration altering hematological profile, and autoimmune disorder were excluded from the study. Blood pressure was measured in all the cases and control subjects and three blood tests, i.e., BT, CT, and TPC were performed for each.

Results: There was a significant fall in TPC in PE cases as compared with normal ($P < 0.01$). But there is significant increase in BT and CT ($P < 0.01$) in PE as compared with normal pregnant women.

Conclusion: From this study, it was observed that BT, CT, and TPC can be used as predictive tests not only for disease process, but also for fetal outcome. This can also help us in early diagnosis and treatment of severe PE in which maternal mortality rate is very high.

KEY WORDS: Pre-eclampsia, bleeding time, clotting time, total platelet count

Introduction

Toxemia of pregnancy, a disease peculiar to the human race, has been recognized since antiquity. Pre-eclampsia (PE) is characterized clinically by new onset hypertension (blood pressure ≥ 140/90 mmHg) and proteinuria (more than 0.3 g/l in 24-h urine collection or by 1+ qualitative urine examination) after 20 weeks of gestation. It is responsible for a high proportion of hospital admission and labor induction accounting for more than 60,000 maternal deaths per year in developing countries.[1] Worldwide more than 10% of perinatal and neonatal mortality are associated with PE.[2] The incidence of PE in pregnant women ranges between 10% to 14% in primigravida and 5.7% to 7.3% in multigravida women.[3] In PE, uteroplacental unit is one of the organs which is affected by capillary damage and leads to subsequent placental ischemia.[4] It has been suggested that significant stimulation of erythropoesis occurs in PE reflecting an underlying placental hypoxic condition.[5] Although there is convincing evidence that intravascular coagulation is associated with toxemia of pregnancy, the underlying cause which initiates such coagulation is obscure. Changes in the coagulation system in established PE are well documented and distinguish other hypertensive disorders coinciding with pregnancy. It has been reported that the possibility of lower platelet count was higher in PE compared with normotensive mothers.[6] In

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addition, PE has been reported to be a risk factor for neonatal infections leading to an increase in neonatal morbidity and mortality.[7] Platelet function tests are simpler measures of coagulation profile and helpful for monitoring high-risk pregnancies as well as preventing associated hazards for both mother and fetus.[8] Therefore this study was proposed to compare bleeding time (BT), clotting time (CT), and total platelet count (TPC) of case and control so that preventive measures can be taken to avoid high-risk pregnancies as well as expect better fetal outcome.

Material and Methods

This study was conducted in the Department of Physiology, Veer Surendra Sai Institute of Medical Sciences and Research (VIMSAR), Burla, Sambalpur, Odisha, India. The study was conducted from December 2014 to August 2015 after getting approval by Institutional Ethical Committee VIMSAR. It was a case–control study in which 30 preeclamptic women were taken as case and 30 normal pregnant women were taken as control. Pregnant women more than 20 weeks of gestational age with systolic blood pressure more than 140 mmHg, diastolic blood pressure more than 90 mmHg and urine protein more than 0.3 g in 24 h urine sample were taken as case. Pregnant women more than 20 weeks of gestational age with normal blood pressure and without proteinuria were taken as control. Pregnant women less than 20 weeks of gestation, having history of hypertension, diabetes mellitus, renal disease, any endocrinal disease, or organic disorders were excluded from this study. Subjects were selected from the outpatient department (OPD) of obstetrics and gynecology. Subjects clearly understood about the purpose and the output of study. To assess the platelet dysfunction, the blood samples were tested for BT, CT, and TPC. Subjects were brought to the Department of Physiology and the above-mentioned hematological tests were performed in the hematology laboratory. A written consent was taken from each subject, both case and control, to perform BT, CT, and TPC. BT was done by Duke's method, CT was done by Wright's glass capillary tube method and TPC was performed by the Rees Ecker method. Then data analysis was done by the statistical software SPSS version 16. Statistical test implemented was unpaired *t*-test. *P*-value < 0.05 was considered to be significant. Generation of tables and graphs was done by Microsoft word.

Results

Distribution of subjects was shown in pie chat form as shown in Figure 1. Comparison of BT, CT, and TBC is shown in Table 1. Mean BT of case was 197 s (3 min 17 s) whereas mean BT of control was 108 s (1 min 48 s). This difference in BT between case and control was found significant at $P < 0.01$ and is shown in Table 1 and Figure 2. Mean CT of case was 408 s (6 min 48 s) whereas mean CT of control was 273 s (4 min 33 s). This difference in BT between case and control was found significant

Figure 1: Distribution of subjects as case and control.

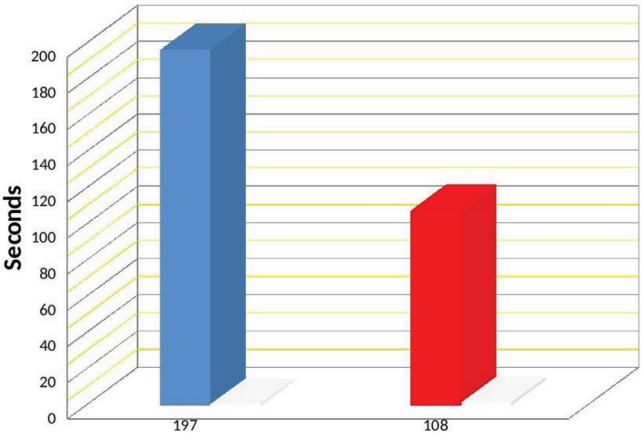

Figure 2: Mean bleeding time of case (blue colour) and control (red colour) groups.

at $P < 0.01$ as shown in Table 1 and Figure 3. Mean TPC of case was 1.23 lakhs and mean TPC of control was 1.87 lakhs. This variation in TPC was found significant at $P < 0.01$ as shown in Table 1 and Figure 4.

Discussion

In this study, it was found that the BT of case was more than that of control and the difference is significant ($P < 0.01$). Similarly, we found that the CT of case was more than the control and the difference was significant ($P < 0.01$). Also we found that TPC of case was less than the control and the difference was significant ($P < 0.01$).

Table 1: Comparison of variables

Variable	Case (mean ± SD)	Control (mean ± SD)	*t*-Test	*P*-value
BT (s)	197±36.69	108±22.36	11.38	<0.01
CT (s)	408±64.61	273±25.63	10.62	<0.01
TPC (lakh/cm)	1.23±0.32	1.87±0.41	–6.84	<0.01

This table shows comparison of different parameters. Data expressed in mean ± SD form. Statistical test used was unpaired *t*-test. $P < 0.05$ was considered to be significant.

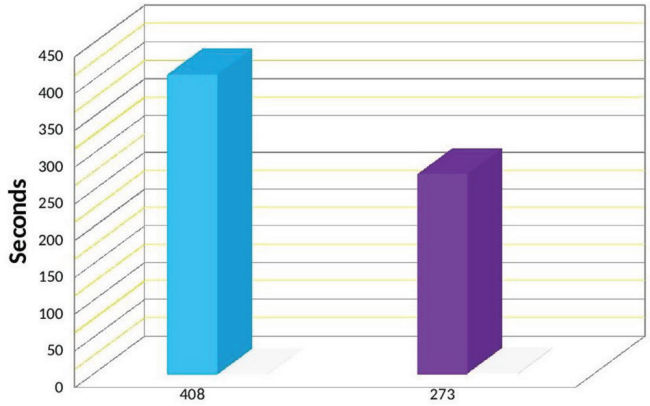

Figure 3: Mean clotting time of case (blue colour) and control (violet colour) groups.

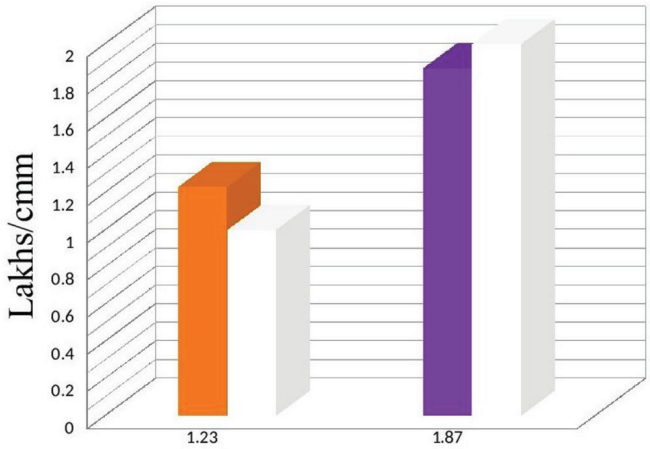

Figure 4: Mean platelet count of case (orange colour) and control (violet colour) groups.

Blood in the normal circulating system remain in the fluid state. The fluidity of the blood in the body depends on the special physical properties of the intact vascular system, on the rate of blood flow, and on the presence of natural anticoagulants. Blood clots due to some essential reaction in coagulation cascade of the blood which converts soluble protein fibrinogen into insoluble fibrin by means of enzyme thrombin. Thrombin does not exist in the circulation as such but as an inactive precursor prothrombin. The activation of prothrombin depends on the presence of calcium ions and factors which are derived from the damaged tissue, disintegrating platelets, and from plasma itself. The formation of prothrombin in liver depends on the availability of Vitamin K in adequate amount (Samson Wright, 1972).[9] Two properties of platelet, namely adhesiveness to the damaged lining of blood vessels and aggregation of platelets, are important in hemostasis. Uteroplacental unit is one of the organs which is affected by capillary damage in hypertensive pregnant women. Although the exact cause of PE is not known, the dysfunctioning of endothelium and interaction with platelets seems essential for the development of PE.[10] Aggregation of platelets further compromises blood flow through placenta and else accompanied with a decrease in the number of platelets in blood. Hence platelets are of paramount importance in hemostasis and thrombus formation. Without an adequate number of platelets, the initial stage of hemostasis is seriously hampered. Hence low and falling platelet count should always be taken as a parameter of severe disease. A subset of PE, HELLP Syndrome (hemolysis, elevated liver enzymes and low platelet count), is always accompanied with a low platelet count and further 10% of patients with more prevalent form of PE have low platelet count.[11,12]

In the present study, the maximum number of cases in the study group and the control group was between 17 and 25 years of age. None of the control cases had proteinuria. Similar findings were also reported by Howie et al.[13] In this study, it was observed that all the established case of PE has significant low platelet count with variable degrees. Redman et al[8] reported that although platelet counts would not be a good screening test for PE, repeated reading in some patients can be useful in monitoring high-risk pregnancies. The time of onset of coagulation disturbances is a matter of controversy. Redman et al in their study found that a fall in the circulating platelet count in pregnancy is primarily a feature of PE and this reduction in platelet count occurred early in the development of PE. They found that lower platelet count in severe eclampsia is associated with abnormal activation of the coagulation system and they believed that it would reflect increased platelet consumption. It has been reported that possibility of thrombocytopenia was higher in newborns of pre-eclamptic mothers who have hypertension and especially thrombocytopenia, compared with normotensive mothers.[14] PE has been reported to be a risk factor for neonatal neutropenia and infections in premature newborn.[7,15] Previous studies shown that normoblast increases in babies of PE mothers and this is secondary to uteroplacental hypoperfusion.[16] The clinical spectrum of PE ranges from mild to severe. Hence, maternal hypertension constituted a significant risk for polycythemia, low platelet count, neutropenia and infection in newborn independent of fetal growth.[17] BT is a combined measure of platelet number, capillary function, and platelet adhesiveness. In the present study, increased BT was found significantly increased in PE cases than normal pregnant state. Dube et al reported a similar increase in BT in all patients with toxemia.[18] CT of the PE cases was increased significantly

in comparison to normal pregnant women. These findings were contradicted to the study by Bellar et al; they reported increased CT in PE than normal pregnant women but the difference was not significant.[19]

Strength and Limitations

In this study BT, CT, and TPC were estimated as good indices of coagulation profile which are helpful for the detection of severity of PE. But the limitations of this study that we recruited small sample, did not correlate the coagulation profile with the blood pressure of subjects. Therefore, further study required with a larger sample for better analysis. Also longitudinal study required for serial changes with severity of PE.

Conclusion

From this study, it was found that BT, CT, and TPC can be used as predictive tests not only for disease process, but also for fetal outcome. These tests are also helpful for early diagnosis and treatment of severe PE. Although at present, medical science has developed with modern techniques, the prevention of disease PE has not been succeeded completely. The severity and complications of PE can be controlled by early detection and treatment during antenatal period. Hence, it is essential to diagnose this disease at its early stage by simple and sensitive biochemical tests in high-risk pregnant women. An alert and well-informed obstetrician acts in time and is rewarded in the end by healthy mother and fetus.

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