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SHORT COMMUNICATION

Coagulation Factors in Severe Preeclampsia

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Abstract

Background: Preeclampsia is an idiopathic multisystem disorder specific to human pregnancy and the puerperium and hematological abnormalities may develop in preeclamptic women. This study was designed to determine coagulation parameters in patients with severe preeclampsia in Shiraz, southern Iran.

Methods: From 2002 to 2005, coagulation indices including platelet count, prothrombin time (PT), activated partial thromboplastin time (aPPT), plasma fibrinogen, and fibrin degradation products (FDP) were measured within 24 hours of admission for fifty women with severe preeclampsia and fifty normal pregnant women. The patients with coagulopathies were excluded. Abnormal coagulation indices were compared between the two groups.

Results: The mean value of platelet counts were significantly lower while the mean values of aPPT and FDP were higher in the preeclamptic patients. However, the mean values of plasma fibrinogen and PT did not show any statistical difference between these two groups. Fifty percent of the patients with severe preeclampsia showed thrombocytopenia, 10% prolonged PT, 30% prolonged PTT, 28% hypofibrinogenemia, and 32% elevated FDP. Prolonged aPTT was seen in 6% of patients with platelet counts of more than $150\times10^3/mm^3$ at the admission time. However, these patients showed evidence of coagulopathies and needed to receive blood or blood products later in their hospital course.

Conclusion: In case an abnormal platelet count or aPTT is detected in a patient with severe preeclampsia, a coagulopathic disorder should be clinically suspected.

Keywords: Thrombocytopenia; Severe preeclampsia; Coagulation tests; Activated partial thromboplastin time; Iran

Introduction

Preeclampsia is an idiopathic multisystem disorder specific to human pregnancy and the puerperium.[1] Hematological abnormalities such as thrombocytopenia and decrease in some plasma clotting factors may develop in preeclamptic women.[2] Subtle changes consistent with disseminated intravascular coagulation (DIC) are potentially serious. Thus, coagulation testing is common in these patients for evidence of DIC[3,4] and HELLP (hemolysis, enzyme elevation and low platelet) syndrome. From the historical point of view, it was first stated that only serial measurements of platelet count was adequate for intrapartum screening.[5] Later, combination of platelet count and aPTT,[3] platelet count and liver function tests,[6] platelet count and lactate dehydrogenase,[4] platelet count and antithrombin[7] were suggested for early detection and screening of the patients with preeclampsia. However, there are still doubts as to the cost-effectiveness of the tests needed to be performed on all patients.

It was shown that abnormal PT, aPTT and fibrinigen levels are found in patients with platelet counts of less than $100,000/mm^3$, so the physician can safely follow only the platelet counts of the patients with severe preeclampsia.[5] On the other hand, another study suggested the evaluation of PT, aPTT and fibrinogen in the patients with severe preeclampsia for whom operative delivery or regional anesthesia is planned to prevent bleeding complications.[8]

In this study we aimed to compare the coagulation parameters in the patients with severe preeclampsia and normal pregnant women and to determine whether a normal platelet count can assure the physician that no other clinically significant clotting abnormalities are present in the patients with severe preeclampsia.

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Materials and Methods

This prospective study was performed during three years (2002-2005) on the referred patients to the prenatal clinics and hospitals of Shiraz University of Medical Sciences. One-hundred women in their third trimester of pregnancy were enrolled, fifty with severe preeclampsia and fifty with normal pregnancies. The criteria for severe preeclampsia included sustained blood pressure of at least 160/110 mmHg or higher with persistent proteinuria of 2^+ or greater on urine dipstick or elevated creatinine (>1.2mg/dL) or liver enzyme abnormalities or eclampsia.[2] Coagulation indices including platelet count, PT, aPTT, total serum fibrinogen level (by Clauss method), and fibrin degradation products (FDP) were measured simultaneously for each patient within 24 hours of admission. The tests were repeated if clinically indicated thereafter. These patients were followed. Coagulopathy was diagnosed in a patient if transfusion of any blood products or coagulation factors became necessary due to bleeding or hemolysis in her hospital course.

The patients who had any confounding conditions that could have altered the coagulation tests such as placental abruption or previa, sepsis, stillborn or heavy vaginal bleeding were not included in the study. Thrombocytopenia was defined as platelet count <150,000/mm.[3] PT and aPTT were considered abnormal if they were >15 seconds and >40 seconds, respectively. Fibrinogen was considered low if it was <250 mg/dL and FDP was considered elevated if it was ≥5 µg/mL.

The features for HELLP syndrome were: 1) hemolysis defined by abnormal peripheral smear and increased bilirubin >1.2 mg/dL and 2) elevated liver enzymes at a level of twice the upper normal limit for the laboratory as: serum aminotransferase ≥70 U/L 3) and low platelets defined as platelet counts $<100\times10^3/\mu L$.[9,10]

Statistical analyses were performed by Chi Square, 2- tailed t and Fisher's exact tests. Statistical significance was considered at $p<0.05$.

Results

Out of 50 patients with severe preeclampsia, 22 (44%) were admitted to the intensive care unit and 28 (56%) were managed in the high risk obstetric center. Among the patients with severe preeclampsia, 12 (24%) had the criteria of HELLP syndrome, 6 (12%) were eclamptic, and 2 (4%) had HELLP syndrome and eclampsia simultaneously. The clinical and paraclinical findings of the patients with severe preeclampsia and the control group at the admission time are compared in Table 1. The mean value of platelet counts was lower ($p<0.001$) and the mean values of aPTT ($p<0.005$) and FDP ($p<0.001$) were higher in preeclamptic patients. However, the mean values of plasma fibrinogen and PT showed no statistical difference between the two groups ($p>0.05$).

Simultaneous abnormalities in coagulation tests of patients with severe preeclampsia are presented in Table 2. The patients with severe preeclampsia were classified according to their platelet counts (Table 3). There was a significant correlation between thrombocytopenia and

Table 1: Clinical and paraclinical characteristics of the study groups

Variable	Women with severe preeclampsia	Normal pregnant women	*p*-value (by 2-tailed t-test)
Age (years)	27.44±7.65	24.66±4.52	0.030
Gravida (number)	2.82±2.43	2.08±1.39	0.066
Gestational age (weeks)	35.12±3.89	35.54±3.41	0.564
Systolic BP (mmHg)	175.80±24.16	108.40±8.65	<0.001
Diastolic BP (mmHg)	108.80±10.57	62.80±7.01	<0.001
Hemoglobin (g/dL)	10.83±2.33	12.18±1.46	<0.001
White blood cells (/mm^3)	11597.60±4905.86	9650.00±2498.42	<0.001
Platelet×10 ^{3} (/mm^3)	157.76±86.69	233.04±55.6	<0.001
Prothrombin time (s)	13.59±4.04	12.50±0.76	0.067
Partial thromboplastin time (s)	38.70±10.35	34.24±2.52	0.005
Plasma fibrinogen (mg/dL)	238.78±64.58	298.08±32.37	0.166
Elevated fibrin degradation products (%)	16	0	<0.001

Table 2: Simultaneous abnormalities of coagulation tests in the patients with severe preeclampsia

Coagulation abnormality	No.	Thrombocytopenia No. (%)	Prolonged PT No. (%)	Prolonged PTT No. (%)	Low fibrinogen No. (%)	Elevated FDP No. (%)
Thrombocytopenia (<150×10^3/mm^3)	25	-	5 (20.0)	12 (48.0)	6 (24.0)	15 (70.0)
Prolonged PT 15-35s	5	3 (60.0)	-	3 (60.0)	0	3 (60.0)
Prolonged PTT 41-90s	15	12 (80.0)	3 (20.0)	-	5 (33.3)	10 (66.6)
Low fibrinogen (<250mg/dL)	14	6 (42.8)	0	6 (42.8)	-	4 (28.5)
Elevated FDP (≥5µg/mL)	16	15 (93.7)	3 (18.7)	10 (62.5)	4 (25.0)	-

Table 3: Simultaneous coagulation abnormalities of patients with severe preeclampsia according to their platelet counts

Platelet count	No.	Prolonged PT No. (%)	Prolonged aPTT No. (%)	Low fibirongen No. (%)	Elevated FDP No. (%)
≥150×10^3/mm^3	25	2 (8.0)	3 (12)	8 (32.0)	1 (4.0)
100-150×10^3/mm^3	12	2 (16.7)	5 (41.7)	2 (16.7)	4 (33.3)
≤100×10^3/mm^3	13	1 (7.7)	7 (53.8)	4 (30.8)	11 (84.6)
P value		0.700	0.015	0.700	<0.001

Significance of each test is calculated related to platelet counts of less than150×10^3/mm^3 Values are expressed as: Number (%)

prolonged aPTT (p=0.010). Also, there was a strong correlation between elevated FDP and thrombocytopenia (p<0.001) in patients with severe preeclampsia.

Platelet counts were less than 150×10^3/ml in 25 cases, ranging 20-142×10^3/µL. Among the patients with platelet counts of more than 150×10^3/µL, there were three cases with prolonged aPTT (6%). One of them showed simultaneous elevation of FDP. These 3 cases developed DIC in their hospital course.

Discussion

In this study, the comparison of normal pregnant women to the preeclamptic patients for mean PT and mean plasma fibrinogen showed no statistically significant difference. Also, following the clinical course of the disease in the preeclamptic patients with isolated prolongation of PT or hypofibrinogenemia showed no coagulopathies. Similar results have been reported previously.[11-13] Thrombocytopenia is relatively frequently reported in severe preeclampsia with the occurrence range of 30-50%.[14-16] The incidence of thrombocytopenia in our study was 50%. This high incidence probably occurred because we included only the cases with severe preeclampsia or eclampsia, many of whom were admitted in the intensive care unit.

As our results show, if we only considered the platelet counts of ≤100×10^{-3}/µL, we would miss a high percentage of the cases with real coagulation abnormalities. Even, among the 25 patients who had platelet counts of more than 150×10^3/µL, 3 cases had simultaneous prolongation of aPTT and one patient had an elevated FDP. These 3 patients showed evidence of DIC in their hospital course. So, we concluded that platelet count >150,000/mm^3 cannot assure the physician that no other significant clotting abnormalities are present. However, the measurement of aPTT seems to be important for early detection of coagulation abnormalities in patients with severe preeclampsia who have normal platelet counts. Our results are in agreement with the results of Metz et al.[3] and against the concept that all preeclamptic patients with a coagulation abnormality have platelet count <100,000/mm^3.[5]

In this study, there was only one patient with raised FDP and a platelet count of more than 150×10^3/µL who had a simultaneous prolongation of aPTT. FDP measurement does not seem to be an appropriate screening test since it is expensive and of little help in diagnosis (2%), and also it can be achieved by measuring aPTT. This study shows that

measurement of PT, fibrinogen and FDP are unnecessary in severe preeclampisa when there is no clinical evidence of bleeding or a condition which may produce coagulopathy. However, these results suggest that combining platelet count and aPTT are useful to detect an early ongoing coagulopathy in all patients with severe preeclampsia who will develop DIC. However, more research in this field is required to find the ideal screening method. In conclusion, an ongoing coagulopathy should be suspected and clinically judged if either thrombocytopenia or prolongation of aPTT is found in a patient with severe preeclampsia.

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