ALTERATION OF COAGULATION PROFILE IN PRE-ECLAMPSIA AND ECLAMPSIA PATIENTS AT TERTIARY LEVEL HOSPITAL

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Abstract:

Background: *Preeclampsia and eclampsia is associated with a risk of abnormal hemostasis that occurs most commonly secondary to thrombocytopenia. Automated analyze technique measures whole blood coagulation and has been used to manage coagulation defects in obstetric patients.*

Objective: *To find out the alteration of coagulation profile beyond physiological level in pre-eclampsia and eclampsia patients for early detection and planning of management.*

Method: *It was a observation type of cross sectional study carried out Department of Obs& Gynae, Dhaka Medical College Hospital, Dhaka. Severe pre-eclamptic and eclamptic patients admitted in the department of Obstetrics &Gynaecology, Dhaka Medical College Hospital during the period of July 2018 to December 2018. Data were collected as predesigned data collection sheet and for coagulation profile. Collection of venous sample about 5ml of blood were done without a pressure cuff allowing the blood to enter the syringe by continuous free flow and sending to the laboratory for coagulation assay by automated analyzer Sysmex CA500.*

Results: *In this study mean age was 26.94 years, majority 56% age group was 26-30 years of age. The mean gestational age was 32.36 weeks. All the coagulation parameters were altered in 6% of the patients, 4 parameters were altered in 10% of the patients, 3 parameters were altered in 16% of the patients 2 and 1 parameters were altered in 24% and 44% patients respectively.*

Regarding coagulation profile, thrombocytopenia was present in 22% patients, prothombin time was prolonged in 10% of the patients, APTT was prolonged in 20% of the patients, and fibrinogen level was reduced in 40% of the patients and FDP was elevated 32% of the patients. Out of 50 severe preeclamptic and eclamptic patients, 6% of the patients developed DIC in whom all the coagulation parameters were altered.

Conclusion: *In this study, in patients of severe pre-eclampsia and eclampsia 22% patients had thrombocytopenia. 6% of the patients had alteration of all the coagulation parameters. Coagulation indices were altered not only in the patients with reduced platelet count but also in the patients with normal platelet count. Among the patients, 6% of the patients developed DIC, PPH developed in 12% of the patients and maternal death occurred in 4% of the patients.*

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Introduction

Preeclampsia is defined as the presence of a systolic blood pressure (SBP) greater than or equal to 140 mm Hg or a diastolic blood pressure (DBP) greater than or equal to 90 mm Hg or higher, on two occasions at least 4 hours apart in a previously normotensive patient, or an SBP greater than or equal to 160 mm Hg or a DBP greater than or equal to 110 mm Hg or higher. In addition to the blood pressure criteria, proteinuria of greater than or equal to 0.3 grams in a 24-hour urine specimen, a protein (mg/dl)/creatinine (mg/dl) ratio of 0.3 or higher, or a urine dipstick protein of 1+ (if a quantitative measurement is unavailable) is required to diagnose preeclampsia.[1]

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Eclampsia is defined as seizures that cannot be attributable to other causes in a woman with preeclampsia.[1]

Severe preeclampsia and eclampsia may be associated with thrombocytopenia and coagulation abnormalities indicating intravascular coagulation. Syndrome of hemolysis, elevated liver enzymes and low platelets is a complication of severe preeclampsia and eclampsia. With routine screening tests, coagulation disorders of preeclampsia and eclampsia can be detected. The detection of coagulation failure will be helpful to obstetrician in treating the patients who probably may go in to D.l.C. From the historical point of view, it was first stated that only serial measurements of platelet count were adequate for antepartum screening.[2] Later, combination of platelet count and APTT, platelet count and liver function test,[3] platelet count and lactate dehydrogenase,[4] platelet count and antithrombin[5] suggested for early detection and screening of the patients with pre-eclampsia and eclampsia. 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 fibrinogen levels are found in patients with platelet of less than 100,000/mm3, So, the physician can follow only the platelet counts of the patients with severe pre-eclampsia. On the other hand, another study suggested the evaluation of PT, APTT and fibrinogen in the patients with severe preeclampsia and eclampsia for whom operative delivery or regional anesthesia is planned to prevent bleeding complications.[6]

The most interesting of acquired haemostatic diseases is Disseminated Intravascular Coagulation, a term coined by Hardway and McKay in 1959. Pregnancy is accompanied by changes in the haemostatic system, resulting in hypercoagulable states, ranging from venous thromboembolism to DIC.[7] Disseminated intravascular coagulation is always a secondary phenomenon triggered by specific disorder.[8] Obstetric conditions associated with DIC includes pre-eclampsia, eclampsia, abruptio placenta, retained dead fetus, placenta accreta, prolong shock and amniotic fluid embolism.[9] DIC occurs approximately42.8% patients with eclampsia,2-4% cases of pre-eclampsia with HELLP syndrome.[10] DIC is the most common maternal complication with a reported frequency varying from 4-38%.

Materials and Methods

This study was conducted in the department of Obstetrics and Gynecology department of Dhaka Medical College Hospital. This was a cross-sectional observational study. Patients with severe pre-eclampsia and eclampsia with pregnancy between 28 to 40 weeks gestational age were included in this study. Patients with diabetes mellitus, hemorrhagic disorder, epilepsy and renal disorder were excluded from the study. The participants were selected purposively. Informed written consent was obtained from all the participants. Main outcome variable studied were a) CBC, b) APTT, c) Prothrombin time and d) Fibrinogen level.

Results

Among the sample mean age was 26.94 (±3.97), minimum age was 19 and maximum age was 35 years. Majority of the sample that is 56% were from 26-30 years of age. Among the sample mean gestational age was 32.36 (±3.42) weeks. Among the sample mean systolic BP was 175.80±24.16 mmHg and minimum 130 and maximum 180 mmHg, mean diastolic BP was 108.80±10.57 mmHg minimum 90 and maximum 130 mmHg

Table-I

Demography of the study population

Trait	Frequency n=50	Percent
Age in years Mean (SD)- 26.94(±3.97)		
<20 years	05	10.0
2 1-25 years	09	18.0
26-30 years	28	56.0
> 30 years	08	16.0
Gestational age mean(SD)- 32.36(±3.42)		
28-32 wks32-36 wks	1630	32.060.0
>37 wks	04	08.0
Systolic BP Mean (SD)	175.80±24 16	
Diastolic BP Mean (SD)	108.80±10.57	

Table II

Laboratory findings (Serum and urinary biochemical markers) and ultrasonographical observation expressed in frequency and percentage among the sample.

Test findings	Frequency	Percentage
AST		
• <40 IU/L	35	70
• ≥40IU/L	15	30
ALT		
• <45 IU/L	35	70
• ≥45 IU/L	15	30
LDH		
• <225 IU/L	40	80
• ≥225 IUL	10	20
Serum bilirubin		
• <1.2mg/dl	43	86
• ≥1 .2 mg/dl	7	14
Serum creatinine		
• <1. 2 mg/dl	44	88
• ≥1 .2 mg/dl	6	12
24 hrs urinary protein		
• < 5gm	0	0
• ≥5gm	50	100
USG		
(IUGR and oligohydramnios)		
• Present		
• Absent	842	1684

Out of 50 sever pre-eclamptic patients' serum AST and ALT were elevated in 30% patients, LDH was elevated in 20% Patients and serum bilirubin was raised in 14% patients. 24 hrs urinary protein was 5gm or more, in all the patients though serum creatinine level was elevated in 12% patients. USG revealed IUGR and oligohydramnios in 16% patients.

Table-III

Coagulation parameters among 50 patients with pre-eclampsia and eclampsia (Results were expressed in mean (±SD) and range).

Parameters (Minimum-Maximum)	Mean ±SO	R a n g e
Platelet count (in lakh/mm^3)	2.01 (±0.40)	0.90-2.60 x100^3(/mm_3)
Prothombin time (in sec)	12.51(±1.34)	11-19min
APTT (in sec)	31.24(±7.12)	11.90-53.0
Fibrinogen Level (mg/dl)	313±112.72	150-495
FDP (ug/ml)	10.84±2.46	4-15.50

Table shows though all the parameters of coagulation profile were altered in many cases among the sample as shown in the range but while considering the mean values only FDP level was altered.

Table IV

Relationship between the platelet count and other abnormal couagulation parameters among the sample.

Platelet count (Iakh/$mm^{3)}$	No of the patients N (%)	Prolonged PT (%)	Prolonged APTT (%)	Low fibrinogen (%)	Elevated FDP (%)
>1.5(lakh/$mm^{3)}$	39 (78)	04	04	16	04
1-1.5(lakh/$mm^{3)}$	08(16)	04	10	12	12
<1 (Iakh/$mm^{3)}$	03(6)	02	04	06	06

Among the sample, thrombocytopenia was associated with alteration in other parameters in most of the sample. Even in case of normal platelet count, there was alteration in other parameters.

Table-V

Obstetric complications among the sample

Outcome	No. of the patients	Percentage
DIC	03	6
PPH	06	12
Maternal death	02	4
IUD	05	10

Out of 50 severe preeclamptic patients 6% patient developed DIC, maternal death occurred in 4% cases. PPH developed in 12% patients and IUD occurred in 10% patients.

Discussion

Preeclampsiaand eclampsia is associated with a risk of abnormal hemostasis that occurs most commonly secondary to thrombocytopenia. Coagulation parameters has been measured and used to manage coagulation defects in obstetric patients. There are several studies on this issue in preeclamptic and eclamptic women to assess changes in coagulation.[4,5,6]

This observational type of cross-sectional study was carried out among the severe pre-eclamptic and eclamptic patients in the Department of OBS & Gynae in DMCH. Total 50patients of severe preeclampsia and eclampsia were enrolled in this study.

In this study mean age was 26.94 (±3.97), majority 56% age group was 26-30 years of age which is similar to Dadhich S et al.[15] study, who found that the mean age range 23.45 ± 3.23 years. Similar study by Namavar Jahromi et al.[16] also observed the mean age 27.44±7.65 years.

In this study mean gestational age was 32.36(±3.42) weeks with the range of 28 to 40 weeks. Similar findings were seen in studies conducted by Leduc Line et al. and Vrunda et al.[4,17]

Present study showed out of 50 sever pre-eclamptic and eclamptic patients serum AST and ALT were elevated in 30% patients, LDH elevated in 20% Patients and serum billirubin was raised in 14% patients. 24 hrs urinary protein was 5gm or more in all the patients though serum creatinine level was elevated in 12% patients. USG revealed IUGR and oligohydramnios was present in 16% patients.

In this study platelet count «as reduced in 22% patients. Dadhich et al.[15] reported the decreasein platelet count with progression of gestation was more significant as severity of preeclampsiaincreases from mild-to-severe. They also observedhighly significant decrease in platelet count in earlier gestation that is 32 to 36 weeksin severepreeclampsia and eclampsia patients as compared to mild one. Jahromi etat.[16] in a study observed that theincidence of thrombocytopenia was 50% among the pre-eclampticpatients. The higher incidence of thethrombocytopenia was probably because that study included the eclamptic patients along with pre-eclamptic patients.

In present study, prothrombin time was prolonged in 10% patients and APPT was, prolonged in 20%, reduced fibrinogen Level in 40% and FDP was elevated in 32% patients. Regarding coagulation parameters all the parameter were altered in 6% patients, 4 parameters were altered in 10% patients, 3 parameters were altered in 16% patients 2 and 1 parameters were altered in 24% and 44% patients respectively.

Present study showed thrombocytopenia was associated with alteration in other parameters in most of the sample. Even in case of normal platelet count, there was alteration in other parameters.

Present study showed out of 50 severe preeclamptic and eclamptic patients, 6% patients developed DIC in whom all the coagulation parameters were altered. 2 patients died from coagulation failure. PPH occurred in 12% patients and Intra uterine death occurred among 10% patients. In present study when the platelet count was normal in 78% patients then PT, APTT were prolonged in 4% patients, fibrinogen level was reduced in 16% patients and FDP was elevated in 6% patients. When the platelet count was 1-1.5 lakh/mm^3 in 16% patients then prothrombin time was prolonged in 4% patients, APTT was prolonged in 10% patients, FDP was elevated in 12 patients and fibrinogen level was reduced in 12% patients. When the platelet count was <1 lakh/mm^3 in 6% patients then PT was prolonged in 2 patients.

APTT wasprolonged in 4% patients, fibrinogen level was reduced in 6% patients and fibrinogen was elevated in 6% patients. Though low platelet count was significantly associated with alteration of other coagulation parameter but at the same time some of the parameters were altered when the platelet count was normal. Jahromi et al.[16] reported that if low platelet count considered as a reflection of the alteration of the coagulation parameter, a high percentage of the cases with real coagulation abnormalities will be missed. Even, among the 25 patients who had platelet counts of more than 1.5 lakh /mm^3. 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 and eclampsia who have normal platelet counts. Metz et al.[18] and Jharomi et al.[16]are in agreement with the result of this study and against the concept that all preeclamptic and eclamptic patients with a coagulation abnormality have platelet count <100,000/ mm^3.

The study showed the importance of measurement of all the coagulation indices among the severe per-eclamptic and eclamptic patients to assess the coagulationstatus. There was a significant association between the low platelet count and alteration of other coagulation parameters. Coagulation parameters should be thoroughly evaluated in severe pre-eclamptic and eclamptic patients for early detection of coagulopathy and prevention of obstetric complications as a squealae of the coagulopathy. So, coagulation profile in severe pre-eclamptic and eclamptic patients should be assessed for early detection of coagulopathy and planning of appropriate management.

Conclusion

In this study, in patients of severe pre-eclampsia and eclampsia 22% patients had thrombocytopenia. 6% of the patients had alteration of all the coagulation parameters. Coagulation indices were altered not only in the patients with reduced platelet count but also in the patients with normal platelet count. Among the patients, 6% of the patients developed DIC, PPH developed in 12% of the patients and maternal death occurred in 4% of the patients.

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