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PROSPECTIVE ANALYSIS OF COAGULATION PROFILE IN PREECLAMPSIA-ECLAMPSIA SYNDROME COMPLICATING PREGNANCY PATIENTS AND ITS CORRELATION WITH FETAL OUTCOMES IN A TERTIARY CARE CENTRE.

Pathology

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ABSTRACT

Background: Preeclampsia-eclampsia syndrome complicating pregnant women are at potential risk of developing various coagulation disorders and is one of the major cause of perinatal morbidity and mortality.

Aim: To assess the coagulation profile of patients having preeclampsia complicating pregnancy and to compare it with coagulation profile of normal pregnant women . In addition, to analyse the effect of deranged coagulation profile with fetal outcomes.

Methods: Prospective analysis of coagulation profile of 60 cases and 60 controls were done and their fetal outcomes were compared.

Results : In this present study, there is significant prolongation of clotting time, prothrombin time, activated partial thromboplastin time in preeclampsia-eclampsia group when compared to normotensive pregnant women. This deranged coagulation profile had significant association with unfavourable fetal outcomes.

Conclusion: Estimation of coagulation profile will help to identify preeclampsia-eclampsia complicating pregnant women with compromised coagulation status. Thus identification of such high risk group among preeclampsia-eclampsia complicating pregnant women would help to deliver prompt and effective medical care thereby reducing maternal and perinatal morbidity and mortality.

KEYWORDS:

Coagulation profile, preeclampsia, eclampsia, normotensive, fetal outcomes.

INTRODUCTION:

Pregnancy associated hypertension is one of the commonest medical disorder of pregnancy encountered in clinical practice. Preeclampsia is the most common hypertensive disorder of pregnancy affecting 2-10% of all pregnancies [1]. If this condition is left untreated, it may progress to eclampsia and eventually become fatal. Hypertensive disorders of pregnancy accounts for 16% of maternal deaths in developed countries [2]. According to a study conducted by Majhi et al[3], the proportion of maternal deaths among eclampsia patients is 25% in Indian population. Preeclampsia-eclampsia syndrome is one of the major cause of maternal and perinatal morbidity and mortality, especially in developing countries like India [4]. The main pathophysiology of preeclampsia include endothelial cell injury, vasoconstriction, activation of platelets and coagulation factors leading to microthrombus formation, which eventually leads to ischemic damage and multiorgan dysfunction[5,6,7,8,9] . The levels of clotting factors and fibrinogen increases in normal pregnancy[10]. Preeclampsia complicating pregnant women showing low levels of clotting factors and fibrinogen may indicate an underlying disorder of consumption coagulopathy like disseminated intravascular coagulation [11,12] . Coagulation abnormalities increase the risk of bleeding complications.

AIM & OBJECTIVES:

1. To assess the coagulation profile of patients having preeclampsia-eclampsia complicating pregnancy and to compare it with coagulation profile of normotensive pregnant women.
2. To correlate the coagulation parameters with fetal outcomes in Preeclampsia -eclampsia complicating pregnancy.

MATERIALS AND METHODS:

It is a prospective study conducted at Department of Pathology in association with Department of Obstetrics and Gynaecology at Government Vellore Medical College and Hospital, Vellore, Tamil Nadu for a period of 6 months from 1st July to 31st December 2016.

STUDY POPULATION:

The cases and controls were selected from pregnant women admitted for labour at our tertiary care centre. Sixty Preeclampsia-eclampsia syndrome patients were taken as cases and sixty normotensive pregnant women matched for age were enrolled as controls.

SAMPLE SIZE: 60 cases and 60 controls.

STUDY DURATION: 6months (1st July to 31st December 2016).

INCLUSION CRITERIA FOR CASES:

1. Age 18 to 35 years.
2. Preeclampsia women were selected based on the recent American College of Obstetricans And Gynaecologists(ACOG) Guidelines[13] as follows:

(A) Pregnant women having new onset of hypertension ≥140/90 mmHg appearing for the first time after 20 weeks of gestation and proteinuria ≥300 mg/24 hours or ≥1+ measured by dipstick test.

(B) In the absence of proteinuria, pregnant women having new onset of hypertension with new onset of any of the following criteria:

Platelet count<1 lakh/cu.mm,
Serum creatinine >1.1 mg/dl,
Elevated serum Aspartate transaminase/Alanine transaminase > 70 IU/L,
Cerebral symptoms and visual disturbances,
Pulmonary edema.

3. Eclampsia-Preeclampsia women developing convulsions before, during or 48 hours after delivery.

INCLUSION CRITERIA FOR CONTROLS:

Normotensive pregnant women aged between 18-35 years, in third trimester of pregnancy not associated with any other complications were included as controls.

EXCLUSION CRITERIA:

Cases and controls with the following disorders, such as hydatidiform mole, twin pregnancy, epilepsy, chronic hypertension, gestational hypertension, bleeding diathesis, gestational diabetes mellitus and those with history of renal or liver diseases before pregnancy were excluded from the study.

METHODOLOGY:

After obtaining Institutional Ethical Committee approval, the study population was selected as per the inclusion and exclusion criteria. Informed consent was obtained and under aseptic precautions, venous blood sample was collected from antecubital vein by venepuncture. Bleeding time was estimated and clotting time estimation was done in blood samples without the addition of an anticoagulant. EDTA was used as an anticoagulant for platelet estimation. Trisodium citrate was used as an anticoagulant for prothrombin time and activated partial thromboplastin time estimation. The study groups (both cases and controls) were subjected to coagulation profile assessment using the following methods:

1. Bleeding time - Duke`s method.
2. Clotting time - Capillary tube method.
3. Platelet count - Fully automated quantitative hematology analyser(Sysmex k X21).
4. Prothrombin time(PT) - Automated blood coagulation analyser (Sysmex CA50 Japan).
5. Activated partial thromboplastin time(APTT) - Automated blood coagulation analyser(Sysmex CA50 Japan).

Both cases and controls were followed till their hospital stay and the maternal and fetal outcomes were observed.

STATISTICAL ANALYSIS:

Mean and standard deviation of all variables were calculated. The statistical significance was calculated using student t test. P value <0.05 was considered significant.

Maternal and fetal outcomes of cases having deranged coagulation profile was compared with the outcomes of cases having normal coagulation profile and the statistical significance was calculated using chi square test.

RESULTS:

The study was carried out from 1st July to 31st December 2016 in the Department of Pathology in association with Department of Obstetrics and Gynaecology at Government Vellore Medical College and Hospital, Vellore. A total of 120 women (60 cases and 60 controls) were included in this study.

- Both cases and controls were in the age group of 18-35 years.
- Out of 60 controls, 26(43.3%) were primigravida and 34(56.7%) were multigravida. Out of 60 cases 28(46.7%) were Primigravida and 32(53.3%) were multigravida.
- The mean gestational age in controls was 34.07 weeks in the range of 31-38 weeks and the mean gestational age in cases was 35.23 weeks in the range of 31-38 weeks.
- The mean blood pressure in controls was 110/72mm Hg and the mean blood pressure in cases was 152/106 mm Hg.

Table.1 : COMPARISON OF COAGULATION PROFILE IN PATIENTS WITH PREGNANCY INDUCED HYPERTENSION AND NORMOTENSIVE PREGNANT WOMEN.

Tests	Normotensive pregnant women (controls) n=60	Patients with preeclampsia-eclampsia (cases) n=60	P value
Bleeding time (minutes)	1.39±1.18	1.40±1.2	0.84
Clotting time (minutes)	3.33±1.8	5.94±2.4	0.000738
Platelet count (lakh cells/cu.mm)	2.65±1.63	2.48±1.57	0.09
Prothrombin time (seconds)	13.52±3.7	15.95±4	0.000729
Activated Partial Thromboplastin Time (seconds)	34.4±5.87	34.96±5.9	0.004992

The mean Bleeding time in cases was 1.40±1.2minutes, which is higher than control group.

The mean Clotting time in cases was 5.94±2.4minutes, while that of control group was 3.33±1.8minutes. Prolonged clotting time was seen in about 16.67% of cases.

The mean platelet count in cases was 2.48±1.57 lakhs/cu.mm and in controls was 2.65±1.63 lakhs/cu.mm. Platelet count was lower in preeclampsia-eclampsia syndrome when compared to that of control group. Reduced Platelet count was seen in about 6.67% of cases.

The mean Prothrombin time in cases was 15.95±4seconds while that of control group was 13.52±3.7seconds. Prolonged Prothrombin time was seen in 96.67% of cases.

The mean Activated Partial Thromboplastin time in cases was 34.96±5.9seconds. Prolonged APTT was observed in 40% of cases(Table.1).

There was statistically significant prolongation of clotting time, prothrombin time and Activated Partial Thromboplastin time in preeclampsia-eclampsia syndrome complicating pregnant women when compared to normotensive pregnant women(P value is <0.05).

Table. 2: COMPARISON OF FETAL OUTCOMES IN NEWBORNS BORN TO PATIENTS WITH PREGNANCY INDUCED HYPERTENSION AND NORMOTENSIVE PREGNANT WOMEN.

Fetal outcomes	Normotensive pregnant women (controls) n=60	Patients with preeclampsia-eclampsia (cases) n=60
Low APGAR score	2	12
Low birth weight	10	32
Perinatal death	0	0

Out of 60 cases, 44 women(73.3%) with pregnancy induced hypertension had unfavourable fetal outcomes. Among cases, 12 newborns(20%) showed low APGAR score and 32(53.3%) showed low birth weight.

Out of 60 controls, 2 newborns(3.33%) showed low APGAR score and 10(16.67%) showed low birth weight(Table.2).

Among 60 cases, 16(26.7%) women showed normal coagulation profile while 44(73.3%) women showed deranged coagulation profile (Table.3).

Table.3 : COMPARISON OF FETAL OUTCOMES IN PATIENTS WITH PREECLAMPSIA-ECLAMPSIA SYNDROME IN RELATION TO COAGULATION PROFILE:

Fetal outcomes	Normal coagulation profile (n=16)	Deranged coagulation profile(n=44)	P Value
Low APGAR score	3	9	0.44
Low birth weight	5	27	0.019

Among the newborns born to PIH mothers with normal coagulation profile 50% showed unfavourable outcomes. Among newborns born to PIH mothers with deranged coagulation profile 81.8% showed unfavourable outcomes, that includes 9 newborns (20.4%) with low APGAR score and 27 newborns(61.4%) with low

birth weight(Table.3). There is significant correlation between deranged coagulation profile of preeclampsia patients and low birth weight(P value <0.05).

As all the cases were well managed, no adverse maternal outcome was observed in the study group.

DISCUSSION:

Preeclampsia is the most common hypertensive disorder of pregnancy affecting 2- 10% of all pregnancies [1]. Preeclampsia is characterised by hypertension (≥140/90 mmHg) after 20 weeks of gestation with or without proteinuria and multiorgan dysfunction. About 1 in 200 women with untreated preeclampsia develop eclampsia characterised by convulsions. Eclampsia can also develop without any obvious signs of preeclampsia. About 10 to 20% of women with severe preeclampsia develop another potentially life threatening complication called HELLP syndrome(Hemolysis, Elevated liver enzymes and Low platelet count). Severe preeclampsia can also affect the fetus by impairing blood and oxygen flow leading to growth retardation or stillbirth. Infants delivered early due to preeclampsia may have complications associated with prematurity, such as respiratory distress caused by underdeveloped lungs.

Namawar Jahromi et al[14] observed that normal platelet count could not rule out the presence of other significant clotting abnormalities and hence suggested to evaluate activated partial thromboplastin time for early detection of coagulation abnormalities in patients with severe preeclampsia even in those who have normal platelet counts.

In this study, preeclampsia-eclampsia patients were found to have statistically significant prolongation of clotting time similar to the observation made by Girija Priyadharshini et al[15]. Prothrombin time is also significantly prolonged in the preeclampsia patients similar to the study done by Han L et al[16] . Activated partial thromboplastin time is prolonged in 40% of the cases that is consistent with similar studies conducted by Han L et al[16], Chaware et al[17], RutviDave et al[18], Girija Priyadharshini et al[15] and Namawar Jahromi et al[14].

No significant unfavourable maternal outcomes were noted in this study. The maternal hemodynamic system usually adapts to hypertension by hemodilution, increased production of clotting factors and activation of fibrinolytic system. The release of procoagulants during labour triggers the imbalance between coagulation and fibrinolytic system in some of the preeclampsia-eclampsia complicating pregnant women thereby resulting in unfavourable maternal outcome.

In this present study, 32 cases (53.3%) of preeclampsia complicating pregnant women delivered low birth weight babies which is comparable with other studies conducted by Meshram et al [19] and Ludec et al[20]. There is significant correlation between preeclampsia-eclampsia syndrome patients having deranged coagulation profile with unfavourable fetal outcomes(81.8%) which is consistent with the studies conducted by Meshram et al[19] and P W Howie et al[21].

Fetus is more sensitive to hypoxia and reduced blood flow induced by vasoconstriction and microthrombi formed as a result of compromised coagulation status. So, the neonates born to preeclampsia-eclampsia complicating pregnant women presented with higher incidence of unfavourable fetal outcomes than the control group.

Preeclampsia- eclampsia syndrome complicating pregnant women present with frequent coagulation abnormalities than the normotensive pregnant women. The derangement in coagulation studies has the potential to identify individuals at risk of developing life threatening complications such as DIC and has significant association with poor fetal outcomes such as intrauterine growth retardation, stillbirth and low birth weight.

Limitations of this study were small sample size and only one time assessment of coagulation profile was done before child birth. Serum fibrinogen and d-dimer tests were not done due to financial constraints.

Further studies with larger sample size is required to assess the incidence of maternal and fetal outcomes in PIH complicating pregnancy. Studies with serial assessment of coagulation profile are needed to identify preeclampsia complicating pregnant women at risk of progression to severe coagulopathy.

CONCLUSION:

Pregnancy induced hypertension is one of the most common maternal complication encountered in our hospital. If left untreated, it may produce unfavourable outcomes and may even lead to maternal or fetal death. From this study, it is concluded that estimation of coagulation profile will help to identify preeclampsia-eclampsia complicating pregnant women with compromised coagulation status. Thus, identification of such high risk group among preeclampsia-eclampsia complicating pregnant women would help to deliver prompt and effective medical care thereby improving maternal and fetal outcomes.

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