Coagulation profile in cases of pre-eclampsia and eclampsia

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ABSTRACT

Pregnancy Induced Hypertension (PIH) is a syndrome of hypertension with or without proteinuria (Preeclampsia) proteinuria and oedema. With additional symptoms like coagulation abnormalities and liver function abnormalities. Preeclampsia is a severe multi-systemic pregnancy-specific, hypertension disorder usually occurring after 20 weeks of gestation, characterised by new onset of hypertension and proteinuria, and it regresses after delivery of the concepts. The present cross-sectional case-control study was carried out in the Department of Pathology of a tertiary care hospital. Study of Coagulation profile in Preeclampsia and Eclampsia comprised of 258 cases which were categorised as preeclampsia, eclampsia and control group with 86 cases in each group. A total number of 258 patients were studied who were categorised as the control group, preeclampsia group and Eclampsia group with 86 cases in each. Preeclampsia was further classified as mild Preeclampsia (48/86) and severe Preeclampsia (38/86). Results-Majority of occurrences were noted in 21 to 25 years of age group, i.e. 45 patients of Eclampsia (52%), Eclampsia (67.44%) and Severe Preeclampsia (63.95%) were found to be more common in Primigravid patients. In Eclampsia group, 40% had mild thrombocytopenia. In Severe preeclampsia group, 37% had mild thrombocytopenia. In Mild preeclampsia group, 67% (32/48) cases showed platelet counts within a healthy range. In Eclampsia group, (13/86), i.e., 15% had prolonged bleeding time (>9 mints) In Severe preeclampsia group, (3/38), i.e. 8% had prolonged clotting time (>11 mins) In Mild preeclampsia group and control group, none had prolonged clotting time (>11 mins). In Eclampsia group, (37/ 86), i.e., 43% had prolonged prothrombin time. Study concluded that coagulation profile could help to assess the severity of Preeclampsia and Eclampsia and thus can help to reduce complications if treated early.

INTRODUCTION

Pregnancy Induced Hypertension (PIH) is a syndrome of hypertension with proteinuria (Preeclampsia) or without proteinuria and oedema with additional symptoms including coagulation abnormalities, liver function abnormalities (Barron, 1999), sodium retention, and/or hyperreflexia. Preeclampsia is a severe multi-systemic pregnancy-specific, hypertension disorder usually occurring after 20 weeks of gestation, characterised by new onset of hypertension and proteinuria.
and it regresses after delivery of the conceptus. It may progress to EclampsiaEclampsia if left untreated (Obstetrics, 2009). Eclampsia means a fever of rapid onset is a dangerous complication of pregnancy with a sudden onset. It has the feature of developing tonic-clonic seizures in a patient who has developed Preeclampsia. Preeclampsia and EclampsiaEclampsia are collectively called hypertensive disorders of Pregnancy or toxemia of Pregnancy (Chesley, 1985).

Around 5,85,000 women die each year due to Pregnancy-related causes, 13% are due to hypertensive disorders of pregnancy, particularly Eclampsia (Ahmad et al., 2008). Both developed and developing countries are facing significant public health threat for Preeclampsia, contributing to maternal and perinatal morbidity and mortality (World Health Organization, 2002). The prevalence of Preeclampsia in developing countries ranges from 1.8% to 16.7%. The incidence of Preeclampsia in India and Maharashtra is 5.56% and 39.5%, respectively Agrawal and &amp;Walai (2010). While in India, the prevalence of EclampsiaEclampsia is 1.5%, and it is the cause for about 8 - 14% of maternal mortality, i.e. 200 mothers per day (National Eclampsia Registry) (Cunningham et al., 2014). It probably accounts for 50,000 maternal deaths a year worldwide.

The impact of the disease is felt more severely in developing countries, and most preeclampsia cases remain unrecognized until severe complication such as EclampsiaEclampsia develops (Igberase and Ebeigbe, 2006). Significant preeclampsia complications and Eclampsia include central nervous system injuries such as:

Seizures, IHD, type II diabetes mellitus, venous thromboembolism, haemorrhagic and ischemic strokes, hepatic damage, HELLP syndrome, renal dysfunction, aspiration pneumonia, pulmonary oedema, cardiopulmonary arrest, fetal growth retardation, placental abruption, fetal death, preterm delivery, increased frequency of cesarean delivery, in comparison with women without a history of the hypertensive disorders of pregnancy (Mattar and Sibai, 2000). The uteroplacental vasculature insufficiency, vasospasm, pathologic vascular lesions in multiple organ systems, enhanced lipid peroxidation, systemic endothelial dysfunction, platelet activation and subsequent activation of the coagulation system in the microvasculature and many undefined factors contribute in the development of Pregnancy-induced hypertension (Redman, 1991). Platelets play an essential role in the pathogenesis of Preeclampsia. Activation of platelets takes place when they come in contact with the damaged or activated endothelial wall (Onisai and Vasilache, 2007). Increased consumption of platelets causes thrombocytopenia which is a vital sign of severe Preeclampsia (Onisai et al., 2009a). If we look at the past, present and think of future, it is evident that only the name has been changing from toxemia of pregnancy to gestosis and so on, but the disease continues unabated (Goodlin, 1986).

**Aim**

To study coagulation profile in patients of Preeclampsia and Eclampsia.

**Objectives**

1. To study the changes in coagulation profile (platelet count, bleeding time, clotting time, prothrombin time and activated partial thromboplastin time) in patients of Preeclampsia and Eclampsia in the third trimester of pregnancy.
2. To correlate the coagulation parameters with the severity of Preeclampsia and Eclampsia.
3. To study coagulation parameters in a normoten- sive gestational age-matched pregnant woman in the third trimester of pregnancy (as controls).
4. To compare coagulation parameters between the control, preeclampsia and eclampsia patients.

**MATERIALS AND METHODS**

The present study is an analytical case-control study, carried out in the Department of Pathology. Our study includes cases of Preeclampsia and Eclampsia coming to the Department of Obstetrics and Gynaecology for two years. Written informed consent was taken from all the cases and controls included in the study for the investigations and research purpose.

**Inclusion criteria**

Newly diagnosed Preeclampsia and eclampsia patients in the third trimester of age 18 to 30 years.

**Preeclampsia Group**

Patients with BP more than 140/90 mm of Hg with urine albumin > 1+ on dipstick or > 300 mg/24 hour urine.

**Eclampsia Group**

Patients with BP more than 140/90 mm of Hg with urine albumin > 1+ on dipstick or > 300 mg/24-hour urine with convulsions or coma. Normotensive Pregnant women in their Third Trimester formed the control group.

**Exclusion Criteria**

Age < 18 years and > 30 years.
1. Previous History of hypertension.
2. Previous history of diabetes mellitus, renal disease, thyroid disorder.
3. Patients in Sepsis.
4. Previous History of known bleeding disorders.
5. After the probable clinical diagnosis, the consent was taken from the patients.
6. The blood sample was drawn from all the patients under aseptic precautions to perform haematological tests, coagulation tests such as Bleeding time, Clotting time, Prothrombin time, Activated Partial Thromboplastin time And D dimer.

The following tests were carried out in the preeclampsia and eclampsia cases admitted in our hospital.

**Haematological tests**

1. Complete blood count- it included Haemoglobin, Total leucocytes count, Differential leucocytes count and platelet count. For complete blood count, the blood sample was taken in EDTA vacutainer. The blood was tested in 5 part Sysmex XT 1800i automated haematology analyser. The count was then noted down.
2. Erythrocyte Sedimentation Rate (ESR) – Done by Westergren method.

**Coagulation tests**

For all the coagulation tests, the blood was collected in Trisodium citrate vacutainer.

1. Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) - Done on StagosemiautomatedCoagulometer.
3. Bleeding time - The bleeding time of patient was done by Dukes method.
4. Clotting time - Done by the capillary method.

Biochemical tests – For all Biochemical tests, the blood was collected in plain vacutainer.

1. Serum creatinine – Done on Automated analyser using the principle of the Jaffe method.
3. Blood sugar – Done on the semiautomated analyser
4. Liver function test – Done on automated biochemistry analyser.

**Other investigations** – Proteinuria by Dipstick Method, USG.

**Complete blood count**

It was done on Sysmex XT 1800i Automated haematology analyser with five parts differential function for in-vitro diagnostics. XT 800i can analyse 24 parameters of the blood sample.

**Sample collection** - Plasma samples are recommended for use with Quanta D-Dimer test.

**Measuring range** – The Quanta D-Dimer reagent has been designed to measure DDimer concentration in the range of 200- 4000 ng/ml. The Quanta D-Dimer assay is linear between the measuring range under the described assay conditions.

**Normal range** – D-Dimer assay – 200 to 250ng/ml [Quanta D-Dimer kit].

**RESULTS AND DISCUSSION**

The present study is a case-control study, carried out over two years in the Department of Pathology in our institute. In our study, 258 patients were studied in total who were admitted to the antenatal ward/labour room of the Department of Obstetrics and Gynecology.

Patients were categorised as Preeclampsia group and Eclampsia group and Control group with 86 patients in each. Preeclampsia group was further classified into Mild Preeclampsia and severe Preeclampsia. A maximum number of patients were from the age group of 21 to 25 years in Preeclampsia (45%) and Eclampsia (52%), while in the control group a maximum number of patients belonged to 26- 30 years (43%). The mean age of women in study groups were 23.34 ± 2.62 years for Preeclampsia, 23.82 ± 2.55 years for Eclampsia. Also, for the control group, it was 22.13 ± 3.17 years. In the present age-matched case-control study, pregnant women were in the age range...
group of 18 to 30 years, and gestational age was >28 weeks. In 52% eclampsia patients, 45% of preeclampsia patients were in the age group of 21-25, among the control group, 43% of patients in the age group of 21 to 25 years.

**Gestational age**

Gestational age of the patients in the control group was between 28-39 weeks, while in case of Preeclampsia, it was between 28-40 weeks and Eclampsia it was between 28-40 weeks. Mean with SD of gestational age for the control group, Preeclampsia and Eclampsia were 34.57 ± 2.66, 36.64 ± 1.64, 36.62 ± 1.78 weeks respectively.

**Clinical features in Preeclampsia and Eclampsia**

In eclampsiagroup, the headache was the most common symptom which was present in 32 patients (37%) followed by Nausea and vomiting in 31 patients (38%), epigastric pain in 13 patients (15%), blurring of vision in 13 patients (11%) and reduced urine output in 5 patients (6%). In severe preeclampsia eclampsiagroup, the headache was present in 17 patients (44%) followed by Nausea and vomiting in 16 patients (41%), epigastric pain in 7 patients (19%), blurring of vision in 2 patients (4%) and while none had reduced urine output. In Mild preeclampsia group, Nausea and vomiting were the most common symptom, 19 patients (26%) followed by headache in 21 patients (10%) and epigastric pain in 6 patients (3%). At the same time, none had blurring of vision or reduced urine output.

**Comparison of Biochemistry tests in Preeclampsia and Eclampsia**

In eclampsia group, all biochemical markers were raised. For proteinuria all 86 patients (100%), for sr. creatinine 48 patients (56%), for SGPT 52 patients (60%), for LDH 48 patients (56%), for SGOT 47 patients (55%), for Alkaline Phosphatase 31 patients (36%) and for Total Bilirubin 5 patients (6%) had values above normal range. In severe preeclampsia group, for proteinuria all 38 patients (100%), for sr. creatinine 15 patients (39%), for SGPT 5 patients (12%), for LDH 16 patients (43%), for SGOT 5 patients (13%), for Alkaline Phosphatase 8 patients (21%) and for Total Bilirubin 2 patients (4%) had values above normal range. While in mild preeclampsia group, for proteinuria 48 patient (100%), sr. creatinine 17 patients (8%), for SGOT 3 patients (6%), for SGPT 4 patients (8%) and none had raised values of Total Bilirubin, Alkaline phosphatase, and Lactate dehydrogenase.

**Distribution of anaemia in patients of Pregnancy Induced Hypertension and Control group**

In eclampsia group, 21 patients (24%) patients had severe anaemia, while among critical preeclampsia group 13 patients (15%) had severe anaemia as compared to mild Preeclampsia in which only three patients (6%) had severe anaemia. In the control group, none of the patients had severe anaemia, and 93% had haemoglobin values of more than 11 gm/dl.

**Degree of thrombocytopenia in the individual categories**

In eclampsia group, 34 (40%) patients had mild thrombocytopenia, and 24 (28%) had moderate thrombocytopenia, and 14 (16%) patients were found to have severe thrombocytopenia. In critical preeclampsia group, 14 (37%) patients had mild thrombocytopenia, and 09 (23%) patients had moderate thrombocytopenia, whereas 06 (16%) patients had severe thrombocytopenia. In mild preeclampsia group, 14 (29%) patients had mild thrombocytopenia, and 2 (4%) had moderate thrombocytopenia, and none had severe thrombocytopenia. Among the control group, platelet count was found to be in the normal range in all i.e. 100% of the patients.

**Mean and SD of Platelet count with individual categories of the study group**

The mean platelet count of patients in eclampsia group was 1.30 ± 0.28, in severe Preeclampsia, it was 1.70 ± 0.42, while in mild Preeclampsia it was 2.20 ± 0.58. And for the control group, it was 2.40 ± 1.9 lakh. Thus the mean platelet count was found to be reduced in Eclampsia and severe Preeclampsia.

**Distribution of patients according to bleeding time**

In Eclampsia group, 13 cases (15%) had bleeding time more than nine mints, 57 cases (66%) had BT between 3-9 mints and 16 cases (19%) had less than three mints. In severe preeclampsia group, 5 cases (13%) had bleeding time more than 9 mints, 25 cases (66%) had BT between 3-9 mints and 8 cases (21%) had less than three mints. In mild preeclampsia group, no one had bleeding time more than 9 mints, 17 cases (35%) had BT between 3-9 mints and 11 cases (65%) had less than three mints. Bleeding time was found to be in the normal range in all control patients.

Pregnancy-induced hypertension is a severe and life-threatening complication in pregnant women. It is a pregnancy-specific disorder which rates among one of the major causes of maternal and fetal morbidity and mortality. More number of cases are seen in underdeveloped and developing countries due to late diagnosis and inadequate antenatal services. Women with Preeclampsia and Eclampsia, create a variety of coagulation abnormalities. These coag-
ulation abnormalities have an impact on the outcome of delivery of these patients so that aggressive therapy is required to prevent maternal and neonatal morbidity and mortality. The obstetricians rely upon laboratory tests for further management. The present study was aimed at analysing the coagulation changes in patients of Preeclampsia and Eclampsia attending our tertiary care hospital.

In our study, 258 patients were studied in total who were admitted to the antenatal ward/ labour room of the Department of Obstetrics and Gynecology. These patients were categorised as Preeclampsia group and Eclampsia group and Control group with 86 patients in each. Preeclampsia group was further classified in Mild Preeclampsia and severe Preeclampsia. In Total 172 patients of Preeclampsia and Eclampsia were included for analysis of coagulation profile with Eighty-Six age and gestational age-matched controls.

In the present study majority of preeclampsia and eclampsia patients were in the age group of 21-25 years, which is similar to other studies. The mean age of women in study groups were 23.34 ± 2.62 years for Preeclampsia, 23.82 ± 2.55 years for Eclampsia/Eclampsia. Also, for the control group, it was 22.13 ± 3.17 years. A maximum number of patients were from the age group of 21 to 25 years. In Eclampsia 45 patients (52%), severe preeclampsia 17 patients (45%), mild preeclampsia 22 patients (46%) belonged to of 21-25 years age group. Also, in the control group, a maximum number of patients belonged to 21-25 years, i.e. 37 patients (43%). Our findings correlated well with a study done by Shetty et al. 229 and Chaware et al. (2015). It appears that as far as age is concerned, there is no or little difference between normal healthy pregnant women and patients with different degrees of severity of pregnancy-induced hypertension. Most patients in the normal pregnant control group and patients with Preeclampsia and Eclampsia were in age ranging between 21 to 25 years. The present study is comparable to Annam et al. (2011); Sivakumar et al. (2007); Prakash et al. (2006) studies. However, in a study done by Onisai et al. (2009b), they observed that the mean age of PIH cases was 29.8 years.

Gestational Age
Mean with SD of gestational age for the control group, Preeclampsia and Eclampsia were 34.57 ± 2.66 weeks, 36.64 ± 1.64 weeks and 36.62 ± 1.78 weeks respectively. The present study showed 55 cases (64%) with Preeclampsia and 58 cases (68%) of Eclampsia/Eclampsia were primigravida. Whereas 65 cases(75%) were primigravida and 21 cases (25%) were multigravida, in the control group. So, PIH was common in primigravida as compared to multigravida in the current study.

Our findings of increased incidence of Preeclampsia and Eclampsia in primipara were in agreement with Thiagarajah et al. (1984) who reported Preeclampsia and Eclampsia/Eclampsia in about 61% in primipara as compared to 39% multipara. Kumar Pet al 228 also found Preeclampsia and Eclampsia to be more common in primipara. Sultana et al. (2015) also showed in their study that most of the patients of mild Preeclampsia, severe Preeclampsia and Eclampsia were primigravidas.

Clinical Features
In eclampsia group, the headache was the most common symptom which was present in 32 patients (37%) followed by Nausea and vomiting in 31 patients (38%), epigastric pain in 13 patients(15%), blurring of vision in 13 patients (11%) and reduced urine output in 5 patients (6%). In severe preeclampsia eclampsia group, the headache was present in 17 patients (44%) followed by Nausea and vomiting in 16 patients(41%), epigastric pain in 7 patients(19%), blurring of vision in 2 patients (4%) and while none had reduced urine output. In Mild preeclampsia group, Nausea and vomiting were the most common symptom, 19 patients (26%) followed by headache in 21 patients (10%) and epigastric pain in 6 patients(3%). At the same time, none had blurring of vision or reduced urine output. Our findings were similar to Shetty et al. 229 Her study revealed, Eclampsia/Eclampsia and severe preeclampsia patients had a headache as the predominant symptom in 52 cases (46.43%). The other symptoms followed by epigastric pain in 21 (18.75%), blurring of vision in 8 (7.14%), reduced urine output in 6 (5.35%), vomiting in 8 (7.14%), and giddiness in 3 (2.68%) cases. On the other hand, mild preeclampsia case was asymptomatic.

Biochemical Tests
Proteinuria: Proteinuria is a vital sign of Preeclampsia, and diagnosis of Preeclampsia is doubtful in its absence. In the present study, proteinuria was present in all the cases (100%) of mild Preeclampsia, severe Preeclampsia and Eclampsia. Our study findings were in concordance with Jambhulkar et al. (2001).

Total Bilirubin
Serum bilirubin level was raised in 2 patients (4%) of severe preeclampsia group and was normal in the remaining patients. While in eclampsia group, five patients (6%) had raised serum bilirubin levels and...
the remaining patients had serum bilirubin levels within the normal range. The highest level of serum bilirubin of 13.5 mg/dl was seen in a case of HELLP, the range being 1.3-13.5 mg/dl.

**SGOT & SGPT**

Serum glutamic oxaloacetic aminotransferase (SGOT) appears to be the dominant transaminase released into the peripheral circulation with severe Preeclampsia and HELLP syndrome.

In the present study, Raised AST values correlated well with the severity of the disease. Also, all patients with HELLP had higher values when compared to non-HELLP

Our study was in concordance with Chaware et al. (2015); 7. It was seen that the platelet count in severe preeclampsia group and eclampsia group were very significantly lower than the healthy pregnant Control. In contrast, the platelet count in mild Preeclampsia was not markedly lower than the healthy pregnant Control. Joshi SR et al. 235 observed thrombocytopenia in 43.75% and 55% patients of severe Preeclampsia and Eclampsia, respectively. Chauhan et al. 246 also saw a statistically significant decrease in platelet count with an increase in severity of Preeclampsia and Eclampsia. (Joshi and sapre, 2004) observed thrombocytopenia in 21.8% and 39.3% patients of severe Preeclampsia and Eclampsia, respectively. (Mohaptra et al., 2007). An inverse relationship between the severity of pregnancy-induced hypertension and platelet count was found.

In our study, mean bleeding time was found to be 4.3 mints in the eclampsia group, while it was 2.8 mints in severe preeclampsia group, 2.6 mints in mild preeclampsia group, and in the control group, it was 2.4 mints. Present study findings were comparable with Chauhan P et al. 242 with bleeding time being 4.70 mints in eclampsia group, 3.24 mints in severe preeclampsia group. In comparison, it was 2.94 mints in mild preeclampsia group and 1.86 mints in the control group.

Joshi et al. 235 in their study found that bleeding time was not significantly prolonged in varying severity of Preeclampsia. However, found that there is a significant increase in bleeding time in Eclampsia Eclampsia. In our study, mean clotting time was found to be 4.24 mints in the eclampsia group, while it was 4.24 mints in severe preeclampsia group, 4.21 mints in mild preeclampsia group, and in the control group, it was 4.10 mints.

Our study findings were similar to the findings by Chaware et al. (2015) in which clotting time was 4.20 mints in mild preeclampsia group, 4.25 mints in the severe preeclampsia group while 4.10 mints in the control group. Prolonged clotting time was seen in 8 (9%) patients of eclampsia group, 3 (8%) patients of severe Preeclampsia while none of the patient in mild preeclampsia group and Control had prolonged clotting time. In the present study, clotting time increases slightly in Preeclampsia and Eclampsia compared to normal pregnant women. However, the increase was not statistically significant. In our study, the mean prothrombin time was found to be 14.44 secs in the eclampsia group. In comparison, it was 14.10 secs in severe preeclampsia group, 13.72 secs in mild preeclampsia group, and in the control group it came out to be 13.60 secs.

PT was prolonged (More than 16 sec) in 7 (15%) of mild Preeclampsia, 39% of severe Preeclampsia and 43% of eclampsia cases. In the control group, all cases were found to be within the normal range. Our finding was comparable to the findings of (Joshi and sapre, 2004; 7) In our study, mean APTT was found to be 31.42 secs in the eclampsia group. At the same time, it was 30.30 secs in the severe preeclampsia group, 28.40 secs in mild preeclampsia group, and in the control group, it was 28.10 secs. Our study result was in concordance with a study done by 7 Joshi and sapre (2004).

APTT is a measure of a classic intrinsic pathway and is prolonged by a deficiency of pre-kallikrein, HM kininogen, factors XII, XI, IX, VIII, X, V, II, and fibrinogen.

**Disseminated Intravascular coagulation**

D dimer was done in 67/172 (38.95%) patients of Preeclampsia and Eclampsia. Values were > 200 ng in 23/67 (34.32%) patients while it was < 200 ng in 21/67 (31.34%) patients. It was undetectable in 23/67 (34.32%) patients. Out of 7 patients of HELLP, D dimer values were found to be positive >200ng) in 5/7 (71.42%) patients of which three patients were from severe preeclampsia group and two patients were from eclampsia group.

**CONCLUSIONS**

The study concluded that the coagulation profile could help to assess the severity of Preeclampsia and Eclampsia and thus can help to reduce complications if treated early.

**Funding source**

The authors declare that they have no funding support for this study.

**Conflicts of interest**

The authors declare that they have no conflict of interest for this study.
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