A Comparative Study of Coagulation Profile in Pre-Eclamptic and Normotensive Pregnant Females

Pratibha Meena¹, Amit Gupta², Shailendra Meena³, Rupinder Kalra⁴

¹(Department Of Pathology, L N Medical College and Research Centre, India)  
²(Department Of Pathology, L N Medical College and Research Centre, India)  
³(Department Of Community Medicine, L N Medical College and Research Centre, India)  
⁴(Department Of Pathology, L N Medical College and Research Centre, India)

Corresponding author: Pratibha Meena

Abstract: Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with hemorrhage and infection that results in maternal and perinatal morbidity and mortality. In developing countries with uncared pregnancy, this entity on many occasions remains undetected till major complications supervene. The abnormalities of coagulation parameters like prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen levels are usually observed in severe preeclampsia and Eclampsia. Our study aimed to analyse the utility of coagulation tests (prothrombin time, activated partial thromboplastin time and plasma fibrinogen and FDP levels) in pre-eclampsia so as to prevent fatal complications and early detection, careful monitoring and appropriate management of gestational hypertension to reduce the morbidity and mortality of both mother and child. The present study is a prospective case control study carried out in Department of Pathology and Department of Obstetrics and Gynecology in J. K. Hospital Bhopal associated with L.N. Medical College over a period from May 2016 to October 2017. Total 140 subjects, 70 control and 70 cases were enrolled in the study. In preeclampsia group, the mean prothrombin time and mean activated partial thromboplastin time was found to increase gradually with progression of disease in present study. In present study the mean fibrinogen level found to be significantly decreased in cases than in controls. There was gradual decrease of fibrinogen level with progression of disease from mild pre eclampsia to severe pre-eclampsia and was statistically significant. The mean fibrin degradation products (FDP) levels in the present study were significantly increased as compared controls. Low fibrinogen levels and increase in fibrin split products (D-Dimer) with increasing severity of preeclampsia suggest these products may serve as a marker of coagulopathy and the aggressive management towards early delivery may result in decreasing morbidity and mortality.

Date of Submission: 15-03-2018  
Date of acceptance: 30-03-2018

I. Introduction

Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with hemorrhage and infection that results in maternal and perinatal morbidity and mortality. In developing countries with uncared pregnancy, this entity on many occasions remains undetected till major complications supervene.¹

During pregnancy the concentration of coagulation factors VII, VIII, IX, X XII and von willebrand factor rise significantly accompanied by a relevant increase in the concentration of plasma fibrinogen. Plasma fibrinolytic activity is reduced due to liberation plasminogen inhibitor from the placenta². All of these events can continuously trigger the cycle of coagulation and fibrinolysis in pregnancy, complicating pregnancy with preeclampsia.³

Preeclampsia usually occurs in the last trimester of pregnancy and more commonly in primiparas. It is characterized by maternal endothelial dysfunction presenting clinically with hypertension, oedema and proteinuria.⁴ The onset of convulsion in a woman with preeclampsia that cannot be attributed to other cause is termed as eclampsia.⁵ Due to low socioeconomic status, apathetic attitude, poor health education and lack of regular antenatal supervision the incidence of preeclampsia is more in developing countries like India.⁶

The abnormalities of coagulation parameters like prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen levels are usually observed in severe preeclampsia and Eclampsia⁷,⁸ and even in the presence of normal platelet count.⁹

The measurement of aPTT seems to be important for early detection of coagulation abnormalities in patients with severe preeclampsia who have normal platelet counts¹⁰. There is significant increase in partial
thromboplastin time activated with Kaolin (PTTK) and thrombin time (TT) in preeclampsia. Similarly the fibrin degradation products were also increased.

Low fibrinogen levels and increase in fibrin split products (D-dimer) is noted with increasing severity of preeclampsia. Many authors suggest these products may serve as an early marker of coagulopathy and the aggressive management towards early delivery may result in decreasing morbidity and mortality.

The aPTT and the PT reflect the function of endogenous and exogenous coagulation pathways respectively. A certain degree of coagulative dysfunction occurs in the endogenous coagulative pathway of severe preeclampsia patients while their exogenous coagulative do not change greatly.

Preeclampsia and Eclampsia of varying degree of severity forms a considerable portion of admissions in our hospital. In these patients, varying degree of disseminated intravascular coagulation (DIC) can contribute significantly to the morbidity.

Hence present study is aimed to analyse the utility of coagulation tests (prothrombin time, activated partial thromboplastin time and plasma fibrinogen and FDP levels) in pre-eclampsia so as to prevent fatal complications that’s leading to Postpartum collapse, electrolyte imbalance, pulmonary edema, acute renal failure, hepatic rupture, central haemorrhage, abruptio placentae, ophthalmological problems, disseminated intravascular coagulation and hemolysis, elevated liver enzymes and low platelet, and early detection, careful monitoring and appropriate management gestational hypertension to reduce the morbidity and mortality of both mother and child.

II. Material And Methods

The present study is a prospective case control study carried out in Department of Pathology and Department of obstetrics and gynecology in J. K. Hospital Bhopal associated with L.N.MEDICAL COLLEGE over a period from May 2016 to October 2017. Total 140 subjects, 70 control and 70 cases were enrolled in the study.

Study Design: Prospective case control study

Study Location: This was a tertiary care teaching hospital based study done in Department of Pathology and Department of obstetrics and gynecology in J. K. Hospital Bhopal associated with L.N.MEDICAL COLLEGE.

Study Duration: May 2016 to October 2017.

Sample size: Total 140 subjects.

Subjects & selection method: The study included 70 normotensive pregnant women without any complications and pregnant women with signs and symptoms of preeclampsia in third trimester of gestation. 70 Cases of preeclampsia were categorized on the basis of blood pressure based upon classification according to the scheme of the Working Group of the NHBPEP- National High Blood Pressure Education Program (2000).

Inclusion criteria:

For cases

1. Include pregnant women with sign and symptoms of preeclampsia in 3rd trimester
2. BP >140/90 mm Hg after 28 weeks of gestation
3. Proteinuria > 300mg/24 hours ‘or’
4. If 24 hour urine is not available then a protein concentration >1+ (concentration) on dipstick - a minimum of two random
   Urine samples collected at least 4-6 hours apart.

For controls

Gestation Age and gestation matched normal pregnant women in 3rd trimester would constitute the control

Exclusion criteria:

Pregnant women with known
1. History Of Essential Hypertension
2. With known liver disease
3. Renal Disorder
4. Hydatidiform mole
5. With known bleeding disorder
6. On Anticoagulant therapy
7. With Abruptio placentae
8. Intrauterine foetal death
9. In labour
10. With established DIC
11. Idiopathic Thrombocytopenic purpura
12. History of illicit drug use
13. Any associated inflammatory disease or sepsis

III. Procedure Methodology

The selected cases of preeclampsia for study were further subdivided into mild and severe preeclampsia
(i) **Mild preeclampsia:** patient having systolic blood pressure between 140-160 mmHg, diastolic blood pressure between 90-110 mmHg and proteinuria upto 1+ (dipstick method).

(ii) **Severe preeclampsia:** patient having systolic blood pressure between >160 mmHg, diastolic blood pressure >110 mmHg plus one or more of the following criteria: proteinuria >1+, headache, visual disturbance, upper abdominal pain, oliguria (<400 ml/24 hours), serum creatinine elevated >1.2 mg/dl, marked elevation of serum transaminase AST or ALT, fetal growth restriction and pulmonary edema

All the subjects will undergo following blood investigations using venous blood and sample will be processed as soon as possible (Within 1 hr of sample collection) maintaining at room temperature.

IV. Coagulation Tests

Blood sample was collected in plastic tube of 3.2% citrate anticoagulant (9;1 ratio, 9 parts of blood added to 1 part of anticoagulant). The blood sample in citrate bulb was immediately centrifuged at 3000 rpm (approximately 2000g) for 15 minutes and the supernatant plasma was transferred to a clean polystyrene tube. This plasma sample was used for studying Prothrombin time (PT), Activated partial thromboplastin time (aPTT) and plasma fibrinogen levels and test done by mechanical clot detection method using STAGO semi-automated coagulation analyzer and FDP (Fibrin degradation products) levels by slide agglutination method. Tests were conducted within 4 hours of collection.

V. Statistical Analysis

The statistical software namely statistical package for the social sciences (SPSS) version 22 is used for analysis of data. Analysis of variance (ANOVA) is used to compare the variables. Data is expressed as mean± standard deviation. The p-value was calculated for each parameter and p<0.05 is considered statistically significant. Bar diagrams were used for graphical representation of this data.

VI. Results

The present study was carried out in the department of pathology and Department of obstetrics and gynecology in J.K. Hospital Bhopal associated with L.N. MEDICAL COLLEGE over a period from May 2016 to October 2017.

In the present study, we have studied coagulation profile (PT, aPTT, Plasma Fibrinogen and FDP levels) in total 70 cases of preeclampsia (grouped as mild and severe preeclampsia) in 3rd trimester of pregnancy and 70 normotensive age and gestation matched pregnant women in 3rd trimester were studied as controls.

Preeclampsia group included 31 (44.30%) cases of mild pre eclampsia, 39 (55.70%) cases of severe preeclampsia. (Table I, CHART A).

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cases</td>
<td>70</td>
<td>100</td>
</tr>
<tr>
<td>a.</td>
<td>Mild PE</td>
<td>31</td>
<td>44.30</td>
</tr>
<tr>
<td>b.</td>
<td>Severe PE</td>
<td>39</td>
<td>55.70</td>
</tr>
<tr>
<td>2</td>
<td>Controls</td>
<td>70</td>
<td>100</td>
</tr>
</tbody>
</table>

CHART A: Distribution of cases in mild and severe preeclampsia

**Table 1: Showing distribution of cases (subgroup) and control**
A Comparative Study Of Coagulation Profile In Pre-Eclamptic And

Age:

The mean age ± Standard deviation (SD) of the cases was 25.12 ± 3.65 years. Age distribution of the preeclampsia cases revealed maximum 58 (82.84%) cases were in the range of 20-29 years. There were only two (2.85%) cases of preeclampsia, one in mild preeclampsia and one in severe pre eclampsia, above 35 years of age as shown in table II and CHART B below.

<table>
<thead>
<tr>
<th>Age group (Years)</th>
<th>Control (%)</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild PE (%)</td>
<td>Severe PE (%)</td>
</tr>
<tr>
<td>20-24</td>
<td>33 (47.5)</td>
<td>8</td>
</tr>
<tr>
<td>25-29</td>
<td>28 (41.25)</td>
<td>15</td>
</tr>
<tr>
<td>30-34</td>
<td>6 (7.5)</td>
<td>7</td>
</tr>
<tr>
<td>35-40</td>
<td>3 (3.75)</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>70 (100)</td>
<td>31 (44.30)</td>
</tr>
<tr>
<td>Mean Age ±SD</td>
<td>25.17 ± 3.85</td>
<td>26.19 ± 3.72</td>
</tr>
<tr>
<td>Range</td>
<td>20-35</td>
<td>20-35</td>
</tr>
</tbody>
</table>

CHART B: Age wise distribution of patient in mild and severe preeclampsia and control

Gestational Age:

The mean gestational age in cases was 33.55 ± 3.93 weeks in present study. In subgroups of cases, the mean gestational age was 33.94 ± 3.54 and 33.30 ± 4.43 weeks in mild pre eclampsia and severe pre eclampsia respectively as shown in table III and CHART C.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>Gestational Age (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cases</td>
<td>70</td>
<td>33.55 ± 3.93</td>
</tr>
<tr>
<td></td>
<td>a. Mild PE</td>
<td>31</td>
<td>33.94 ± 3.54</td>
</tr>
<tr>
<td></td>
<td>b. Severe PE</td>
<td>39</td>
<td>33.30 ± 4.23</td>
</tr>
<tr>
<td>2</td>
<td>Controls</td>
<td>70</td>
<td>34.66 ± 3.70</td>
</tr>
</tbody>
</table>
A Comparative Study Of Coagulation Profile In Pre-Eclamptic And

CHART C: Mean gestational age ± SD in control and mild and severe preeclampsia

Prothrombin Time

The mean prothrombin time in cases was 14.30 ± 1.67 seconds with the range of 11.5 to 24.5 seconds whereas the mean prothrombin time observed in controls was 12.62 ± 0.82 seconds with the range of 10.3 to 13.8 seconds as shown in table IV and CHART D below.

Table IV: Showing mean prothrombin time (PT) in mild and severe preeclampsia and controls.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>PT (sec)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cases</td>
<td>70</td>
<td>11.5 – 24.5</td>
<td>14.30 ± 1.67</td>
</tr>
<tr>
<td>2</td>
<td>Controls</td>
<td>70</td>
<td>10.3 – 13.8</td>
<td>12.62 ± 0.82</td>
</tr>
<tr>
<td>a.</td>
<td>Mild PE</td>
<td>31</td>
<td>11.5 – 15.3</td>
<td>13.69 ± 0.69</td>
</tr>
<tr>
<td>b.</td>
<td>Severe PE</td>
<td>39</td>
<td>11.7 – 24.5</td>
<td>14.77 ± 2.03</td>
</tr>
</tbody>
</table>

The prothrombin time was found to be increased in cases as compared to that in the controls and this difference was found to be statistically significant. (p=0.000, < 0.05)

The mean value of prothrombin time in mild pre eclampsia was 13.69 ± 0.69 seconds and in severe pre eclampsia it was 14.77 ± 2.03 seconds. Thus the mean prothrombin time was found to increase with increasing severity of disease. (Table IV, Chart D)

Statistically when compared with the controls the increase in mild pre eclampsia and in severe pre eclampsia was significant (P =0.0000, < 0.05). The increase in mean prothrombin time in mild pre eclampsia and in severe pre eclampsia when compared with that in mild pre eclampsia were also found to be statistically significant (p=0.0032, and 0.001, <0.05).

Activated partial thromboplastin time:

The present study observed mean activated partial thromboplastin time in cases as 33.99 ± 4.5 seconds with the range of 25.6 – 70.1 seconds whereas in the control group it was 31.00 ± 1.62 seconds with the range between 26.2 – 33.1 seconds as shown in table V and CHART E below.
A Comparative Study Of Coagulation Profile In Pre-Eclamptic And

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>aPTT (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Range</td>
</tr>
<tr>
<td>1</td>
<td>Cases</td>
<td>70</td>
<td>25.6 – 70.1</td>
</tr>
<tr>
<td>a. Mild PE</td>
<td>31</td>
<td>27.0 – 37.0</td>
<td>31.94 ± 2.36</td>
</tr>
<tr>
<td>b. Severe PE</td>
<td>39</td>
<td>26 – 47</td>
<td>35.61 ± 5.20</td>
</tr>
<tr>
<td>2</td>
<td>Controls</td>
<td>70</td>
<td>26.2 – 33.1</td>
</tr>
</tbody>
</table>

Statistically this increase in aPTT in cases as compared to that in the controls was found to be significant (p=0.000, <0.05).

The mean aPTT in different subgroups of cases was 31.94 ± 2.36 seconds in mild preeclampsia and 35.61 ± 5.20 seconds in severe preeclampsia. Thus there was progressive increase in aPTT with progression of disease. (Table V, CHART E)

On statistical analysis, when compared with the controls, the increase in aPTT was significant in mild preeclampsia (p=0.0219, <0.05) and in severe preeclampsia (p= 0.000, <0.05).

The comparison of aPTT values amongst the subgroups of cases, showed increase in severe preeclampsia as compared to that in mild preeclampsia were statistically significant (p= 0.000, <0.05).

**Fibrinogen**

In the present study, the mean fibrinogen level in cases was found to be 229 ± 54.95 mg/dl with the range of 130-320 mg/dl whereas in the control group it was 295.9 ± 32.32 mg/dl with the range of 250-398 mg/dl as shown in table VI and CHART F below.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>Fibrinogen (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Range</td>
</tr>
<tr>
<td>1</td>
<td>Cases</td>
<td>70</td>
<td>130-320</td>
</tr>
<tr>
<td>a. Mild PE</td>
<td>31</td>
<td>165-320</td>
<td>244.29 ± 57.11</td>
</tr>
<tr>
<td>b. Severe PE</td>
<td>39</td>
<td>130-315</td>
<td>217.18 ± 50.74</td>
</tr>
<tr>
<td>2</td>
<td>Controls</td>
<td>70</td>
<td>250-398</td>
</tr>
</tbody>
</table>

Thus the mean fibrinogen level was found to be decreased in cases as compared to that in the controls and statistically this difference was found to be significant (p=0.000, <0.05).
A Comparative Study Of Coagulation Profile In Pre-Eclamptic And

CHART F: Mean fibrinogen level ± SD in case (subgroup) and control

Amongst the subgroups of cases, the mean fibrinogen levels in mild pre eclampsia, and severe pre eclampsia were 244.29 ± 57.11mg/ dl and 217.18 ± 50.74 mg/dl respectively. (Table VI, CHART F). Thus there was inverse relationship between fibrinogen level and severity of disease.

On statistical analysis, using multiple comparison Anova test, when the fibrinogen level in subgroups of case were compared with that in the controls, the decrease in fibrinogen level was significant in mild preeclampsia (p=0. 000, < 0.05) and in severe preeclampsia (p=0.000, <0.05). The comparison of fibrinogen level in the subgroups of cases showed the decrease of fibrinogen level in mild pre eclampsia and in severe pre eclampsia were statistically significant (p=0.000, <0.05).

Fibrin degradation products:

The mean fibrin degradation products (FDP) level in cases was 177.50 ± 198.71 ng/ml with range from 0 – 600 ng/ml where as FDP level was non-detectable in controls (i.e. < 200 ng/ml by semi quantitative method that will be equivalent to zero) as shown in table VII and CHART G below.

Table VII: Showing mean Fibrin degradation products levels in case (subgroup) and control.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>FDP (ng/ml)</th>
<th>Range</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cases</td>
<td>70</td>
<td></td>
<td></td>
<td>125.71 ± 174.19</td>
</tr>
<tr>
<td>a.</td>
<td>Mild PE</td>
<td>31</td>
<td>0-200</td>
<td>25.86 ± 68.55</td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td>Severe PE</td>
<td>39</td>
<td>0-600</td>
<td>205.00 ± 191.87</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Controls</td>
<td>70</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Statistically this increase in mean FDP level in cases as compared to that in controls was found to be significant (p=0.000, <0.05)

CHART G: Mean FDP value ± SD in case (subgroup) and control

The FDP was detectable in 29 (41.42%) cases. In mild preeclampsia group, only four cases showed detectable FDP level of 200 ng/ml. In severe pre eclampsia 25 of the 39 (64.10%), cases showed elevated FDP levels. The mean FDP value in these groups were found to be 205.00 ± 191.87 ng/this increase in FDP levels in was found to be significant (p=0.000, <0.05) as compared to the controls (Table VII, CHART G)
The comparison of FDP level amongst the subgroups showed significant increase in severe pre eclampsia as compared to the cases of mild pre eclampsia (p=0.0019, <0.05)

VII. Discussion

In the present study, we compared the coagulation profile (PT, aPTT, levels of plasma fibrinogen and FDP) in 70 cases of pre-eclampsia in 3rd trimester of pregnancy with 70 normotensive age and gestation matched pregnant women as controls.

The distribution of the cases showed, there were 31 (44.30%) cases of mild pre eclampsia and 39 (55.70%) cases of sever preeclampsia. (Table I, CHART A)

The mean age of the cases was 25.12 ± 3.65 years, Maximum 68 (82.82%) cases were between 20-29 years of age. (Table II, CHART B). 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. But it was clear that most patients in normal pregnant control group and patients with pregnancy induced hypertension were in age ranging between 21 to 29 years.

Priyadarshini and Mohanty (2014), Chauhan et al (2014), Jaleel and Baseer (1997), Nazli et. Al (2012) and Kumar et . Al. (2015) also found maximum cases between 21-30 years of age, similar to the present findings. Younger age of occurrence of pre eclampsia testifies the early age of marriage and pregnancy in our country as compared to western countries.

The mean gestational age observed in cases in the present study was 33.55 ± 3.93 weeks. In subgroups of cases the mean gestational age in mild pre eclampsia, and severe pre eclampsia were found to be 33.94 ± 3.54 and 33.22 ± 4.23 weeks respectively.

The mean prothrombin time in cases (14.30 ± 1.67 seconds) was found to be significantly increased as compared to that in the controls (12.62 ± 0.82 seconds) in the present study and was significant (Table IV, CHART D) R. Anuradha (2015) observed significant increase in prothrombin time in cases (17.1 ± 0.98 seconds) as compared to that in controls (16.7 ± 0.77 seconds),Priyadarshini and Mohanty (2014) also found significant increase in prothrombin time in cases (15.27 ± 3.47 seconds) as compared to that in controls (13.72 ± 1.97 seconds) .both studies are in accordance with the our study.

In the subgroups of cases also there was gradual increase in prothrombin time from mild preeclampsia (13.69 ± 0.69 seconds) to severe pre-eclampsia (14.77 ± 2.03 seconds). Thus the prothrombin time was found to increase with progression of disease. (Table IV, CHART D)

Chauhan et.al (2014) found mean prothrombin time in mild pre eclampsia 13.78 ± 1.82 seconds, severe pre eclampsia 13.83 ± 1.82 seconds and eclampsia 14.14 ± 1.50 seconds. Chaware et al(2015) observed prothrombin time in mild pre-eclampsia, and severe preeclampsia was 13.92 sec ± 1.03 sec and 14.22 ± 1.1 sec (12.4- 18 sec) respectively, Jahromi and Rafiee (2009) found mean prothrombin time in normal pregnant women is 12.18 seconds and in severe pre eclampsia is 13.59 seconds. Antony et. al (1990) found mean PT in mild PIH as 12.15 ± 1.16 and in sever PIH as 12.8 ± 1.41 seconds. These authors also found the increase in mean prothrombin time with progression of disease similar to the present findings. However, Agarwal et al(1978) also found no significance increase in PT.

The present study observed mean activated partial thromboplastin time in cases as 33.99 ± 4.5 seconds and in the controls as 31.00 ± 1.62 seconds (Table V, CHART E). Thus the aPTT was increased in cases as compared to the controls and statistically this difference was found to be significant.

Dave et. al (2014) found mean aPTT in cases as 36.70 ± 12.35 seconds and in controls as 34.24 ± 2.52 seconds. Meshram d p (2014) observed aPTT 33.17 ± 3.24 seconds in control and 37 ± 6.0 seconds in pre-eclampsia Jahromi and Rafiee (2009) observed mean aPTT in cases as 38.70±10.35 sec and in controls as 34.24 ± 2.52 seconds. These differences in aPTT values in cases and controls were statistically significant and thus the findings of these authors are in accordance with the present findings.

The mean aPTT in subgroups of cases was 31.46 ± 2.38 seconds in mild pre eclampsia and 34.77 ± 3.24 seconds in control and 37.32 ± 4.58 seconds in severe pre eclampsia. Thus there was gradual increase in aPTT with progression of disease. (Table VI, CHART E).

Chauhan et. al (2014) also found similar gradual increase in mean aPTT from 29.31 ± 3.39 seconds in controls, to 29.50 ± 1.78 sec in mild pre eclampsia, 30.80 ± 1.62 sec in sever pre eclampsia and 32.84 ± 2.01 in eclampsia. Chaware S A et al (2015) also found gradual increase in levels of aPTT from 28.2 seconds in controls to 28.5 seconds in mild pre eclampsia to 30.6 seconds in severe pre eclampsia. Antony et. al (1998) observed mean aPTT in controls as 28 ± 1.13 seconds, in mild PIH as 29.8 ± 3.27 seconds and in sever PIH as 32.04 ± 3.62 seconds which also showed gradual increase with progression of disease. Thus the findings of these authors are in accordance with the present study.

The aPTT and PT reflects the function of endogenous and exogenous coagulation pathways respectively. Normal late pregnancy shows a physiological hypercoagulable state with decreased levels of aPTT and PT and increased levels of fibrinogen compared to early pregnancy. This result may be caused by platelet
consumption and aggregation followed by a secondary regeneration (Han et. al 2014)\textsuperscript{13}. However with the onset of preeclampsia in particular severe pre eclampsia, there may develop complex disorders in exogenous and endogenous coagulation pathways which may relate to increased PT and aPTT in these conditions. As pre eclampsia and eclampsia syndrome is considered as a multisystem inflammatory disorder (Staff et. al 2013)\textsuperscript{24} and as the diagnostic criteria involve elevated serum transaminase levels suggesting increased certainty of pre eclampsia (Cunningham et. al 2010)\textsuperscript{6}, it indicates hepatic insult in pre eclamptic syndrome. The liver damage is usually associated with increased prothrombin time level and this is likely to be the mechanism for increased prothrombin time in cases of pre eclampsia.

Similarly the significant prolongation of aPTT in severe pre eclampsia occurs due to activation and consumption of coagulation factors. (Redman 1979\textsuperscript{25}, de Boer et. al 1985\textsuperscript{5} especially factor VIII. (Weiner et. al 1984\textsuperscript{27}). Present study observed significant decrease in mean fibrinogen level in cases of pre eclampsia as compared to that in the controls (229.56 ± 54.95 vs 295.9 ± 32.32 mg/dl) – Table VI, CHART H. Similar findings have also been observed by Dave et. al (2014)\textsuperscript{18}, Acmaz et. al (2008)\textsuperscript{3}, Srivastava et. al (1995)\textsuperscript{12}, Jahromi and Rafiee (2009)\textsuperscript{10}.

Dave et. al (2014)\textsuperscript{12} found fibrinogen level of 236.78 ± 66.58 mg/dl in pre eclamptic women and 298.08 ± 32.37 mg/dl in normotensive pregnant women. Acmaz et. al (2008)\textsuperscript{3} observed mean fibrinogen level in pre eclampsia patients as 422.87 ± 126.32 mg/dl and in controls as 477.91 ± 108.38 mg/dl. Jahromi and Rafiee (2009)\textsuperscript{10} found mean fibrinogen level in severe pre eclampsia patients as 238.78 ± 54.58 mg/dl and in controls as 298.08 ± 32.38 mg/dl.

In the subgroups of cases, present study observed a gradual decrease in fibrinogen level with increasing severity of disease. (Table VI, CHART F.). Srivastava et. al (1995)\textsuperscript{12} also noted similar trend in fibrinogen level with values of 370.3 mg% in mild pre eclampsia, 350.9 mg% in severe pre eclampsia.

In the present study the mean fibrin degradation products (FDP) level was found to be 125.71 ± 174.19 ng/ml in cases and it was non-detectable in controls by semi quantitative method. The difference in the levels of FDP in cases and controls was statistically significant. (Table VII, CHART G)

Mirza asif baig (2013)\textsuperscript{28}, Jahromi and Rafiee (2009)\textsuperscript{10} and Dave et. al (2014)\textsuperscript{18} also found significantly higher levels of FDP in cases as compared to controls, similar to the present findings.

The increase in FDP was seen in 29 (41.4%) cases in the present study. In subgroups of cases only 4 of 31 (12.9%) cases showed elevated FDP levels in mild pre eclampsia while in severe pre eclampsia 25 of 39 (64.10%) cases showed elevated FDP levels. The mean level of FDP in severe pre eclampsia was 205.00 ± 199.87 ng/ml (Table VII, CHART G). Thus the FDP level was found to increase significantly with the increasing severity of disease.

Kumar et. al (2015)\textsuperscript{17} found 24.1% cases of mild pre eclampsia and 40%) cases of severe pre eclampsia to have elevated levels of FDP. Dave et. al (2014)\textsuperscript{22} found high FDP levels in 15% cases of pre eclampsia whereas none of the control showed elevated FDP levels. FitzGerald et. al (1996)\textsuperscript{9} observed presence of D-dimer in 5 of 28 (17.85%) cases of mild pre eclampsia and, 17 of 40 (42.5%) cases of severe pre eclampsia included in their study. Antony et. al (1998)\textsuperscript{20} found normal range of FDP in all normotensive and mild PIH cases while 28% cases of severe PIH showed high FDP levels. Thus these authors also found elevation of FDP with progression of disease, similar to the present findings.

VIII. Conclusion

1. In preeclampsia group, the mean prothrombin time and mean activated partial thromboplastin time was found to increase gradually with progression of disease from mild pre-eclampsia to severe pre-eclampsia in present study. The mean prothrombin time and mean activated partial thromboplastin time observed in normotensive pregnancy of 3rd trimester also found to be significantly higher than that in the preeclampsia.

2. In present study the mean fibrinogen level found to be significantly decreased in cases (< 250 mg/dl was observed in 55.71% ) than in controls. There was gradual decrease of fibrinogen level with progression of disease from mild pre eclampsia to severe pre-eclampsia and was statistically significant.

3. The mean fibrin degradation products (FDP) levels in the present study were significantly increased as compared controls. The mean FDP levels in severe pre-eclampsia were found to be significantly higher than in the mild pre eclampsia. However FDP measurement does not seem to be an appropriate screening test since it is expensive and also it can be achieve by aPTT.

4. Low fibrinogen levels and increase in fibrin split products (D-Dimer) with increasing severity of preeclampsia suggest these products may serve as an marker of coagulopathy and the aggressive management towards early delivery may result in decreasing morbidity and mortality.

5. Of the total 70 cases, present study observed abnormal aPTT results > 35 seconds in 31.43% cases of pre eclampsia. So measurement of aPTT seems to be important for early detection of coagulation abnormalities in patient with severe preeclampsia who have normal platelet counts.
References


[23] Mirza Asif Baig:MD (Pathology) Former Assistant Professor BLDUs Shri B. M. Patil Medical College, Hospital & Research Centre Bijapur, Karnataka, India; Coagulation Profiles in PIH – a) To Determine Coagulation Index to Distinguish Severe Preeclampsia from Normal Pregnancy b) To Assess the Correlation of Coagulation Parameters in Normal Pregnancy & in Varying Grades of Preeclampsia; International Journal of Science and Research (IJSR) Index Copernicus Value (2013): 6.14 Volume 4 Issue 8, August 2015 www.iosrjournals.org