Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

The Coagulation Profile on Pregnancy Induced Hypertensive Patients in Third Trimester of Pregnancy – The Prospective and Observational Study.

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Received: March 2018
Accepted: April 2018

ABSTRACT

Background: Hypertensive disorders are the most important cause of maternal and perinatal morbidity and mortality. The aim of present study is to know the changes in certain parameters of coagulation profile in pregnancy induced hypertensive patients in third trimester of pregnancy, so that treatment can be planned to reduce maternal morbidity and mortality. **Methods:** The study was undertaken at Department of Obstetrics and Gynecology, NIMS Medical College and Hospital, Rajasthan for the period of 1 year on 100 patients diagnosed with PIH. **Result:** Mean BT, CT were in normal range in all patients of PIH; but CT was significantly higher in E group than PE &GTN. Mean CRT was poor in patients with E group and normal in patients of PE & GTN group. Mean platelet counts & serum fibrinogen levels found to be decreased with severity of PIH. Prolonged mean PT & aPTT were observed in patients with E. **Conclusion:** Inclusion of coagulation profile with routine investigations leads to early prediction of severity of PIH and subsequent complications.

Keywords: Coagulation profile, pregnancy induced hypertension, third trimester.

INTRODUCTION

Hypertensive disorders are the most important cause of maternal and perinatal morbidity and mortality.[1] Hypertensive disorders complicate 5-10% of all pregnancies and together they form one member of deadly triad along with hemorrhage and infection that contribute greatly to the maternal morbidity and mortality.[2] According to estimates, approximately 50,000 women die from eclampsia across the world.[3] The timely management of eclampsia can decrease maternal and fetal morbidity and mortality.

Several classifications of hypertension in pregnancy have been used in the past, out of which only two have received the widest acceptance, that of ACOG and that of ISSHP2. Hypertension in pregnancy is defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or by increase in SBP ≥ 30 mmHg, or in DBP ≥ 15 mmHg, from preconception or first trimester blood pressure confirmed by two measuring, 6 hours apart.[4] Hypertension in pregnancy is major cause of maternal mortality and substantial cause of neonatal morbidity and mortality. 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.[5] In addition to the risk they present to the pregnancy, hypertensive disorders of pregnancy have been linked to future high blood pressure and cardiovascular disease in women.[6-8]

The Pregnancy induced hypertension results in several systemic abnormalities including alteration in the coagulation profile. The pregnancy induced hypertension activates the coagulation cascade. The preeclampsia itself is a highly thrombotic and pro-coagulant state, with platelet activation and consumption, promoting of thrombin formation, promoting of fibrin formation and destruction.[9,10] In spite of these changes, in most cases of preeclampsia the coagulation anomalies do not have major clinical significance and the usual coagulation investigations are not modified. About 20% of the patients have altered coagulation.[11]

Profound changes in coagulation and fibrinolytic system occur during normal pregnancy causing a hypercoagulable state. There is distinct possibility of accentuation of hypercoagulable state of pregnancy during preeclampsia and eclampsia. Women with pregnancy induced hypertension may develop a variety of hematological changes. Thrombocytopenia is the most common hematological abnormality found.[12] The platelet

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count is routinely measured in women with any form of gestational hypertension. The other tests like prothrombin time, activated partial thromboplastin time, bleeding time and clotting time are more sensitive.[13-18]

Early assessment of severity of preeclampsia and eclampsia is necessary to prevent increased maternal and fetal morbidity and mortality and complications like HELLP syndrome.[19-21] Hence, this study is undertaken to assess the severity of preeclampsia, eclampsia and coagulopathy by a method that is rapid, cheaper and easily available, so that it will guide us for management before the patient lands into complications.

The aim of present study is to know the changes in certain parameters of coagulation profile in pregnancy induced hypertensive patients in third trimester of pregnancy, so that treatment can be planned to reduce maternal morbidity and mortality.

MATERIALS AND METHODS

A Prospective type of observational study is done in Obstetrics & Gynecology Department of NIMS Medical College, Jaipur for a period of one year on 100 pregnant women in third trimester (after 28 weeks of gestation) diagnosed with pregnancy induced hypertension.

Inclusion criteria

1. Singleton pregnancy
2. Those who will gave consent for study

Exclusion criteria

1. Pre-existing medical disorders - Diabetes Mellitus, Renal disease, any coagulopathies, Chronic Hypertension.
2. Smoker
3. Multi-fetal gestation
4. Age > 35 years
5. Placental abruption or previa
6. Sepsis
7. IUD
8. Established DIC

All the patients included into study were subjected to detailed history, examination and investigation with the proforma as appended after taking consent. Finally after making diagnosis from clinical examination and investigations; patients divided into 3 groups: gestational hypertension, preeclampsia and eclampsia.

Gestational Hypertension: New onset hypertension developing after 20 weeks of gestation in a previously normotensive woman having BP 140/90 and without proteinuria. Gestational hypertension is also called transient hypertension if preeclampsia does not develop and the blood pressure has returned to normal by 12 weeks' postpartum. In this study final diagnosis was made after 12 weeks follow up when BP returned to normal.

Pre-eclampsia: The diagnostic criteria used to define pre-eclampsia were:

1. 20 weeks of gestation
2. Blood pressure of 140/90 mmHg or greater when readings taken twice six hours apart.
3. Proteinuria of 1+ or greater by dipstick method in two random samples when measured 6 hours apart.

These patients were further categorized into three different categories.

Eclampsia: Pre eclampsia associated with seizures.

All the studied cases will be subjected to routine investigations and special investigations like Platelet count, Prothrombin time, Activated partial thromboplastin time, Bleeding time, Clotting time, Clot retraction time and serum fibrinogen assay.

1. Bleeding time (BT): By Duke's method; Abnormal if >7.1 minute (430 seconds).
2. Clotting time (CT): By Wright's capillary tube method; abnormal if >10 minute (600 seconds).
3. Platelet Count: By using Sysmex Corporation Kobe, Japan "Automated Haematology Analyzer" KX-21 - It is an automatic multi-parameter blood cell counter for in vitro diagnostic use in clinical laboratories; thrombocytopenia if <1,50000 lakhs/cumm.
4. Prothrombin time (PT): By using KCI Amelung Trinity Biotech Pic. Coagulometer; Abnormal if >15 sec.
5. Activated partial thromboplastin time (aPTT): By using KCI Amelung Trinity Biotech Pic. Coagulometer; abnormal if >35 sec.
6. Clot retraction time manually; after 4 hr is said to be poor and after 24 hr is said to be non retraction.
7. Plasma fibrinogen level; by Clauss method (Normal range 150-400 µg/dl).

The data thus collected was compiled by using Excel sheet. The data was transferred to Statistical Package for Social Services (SPSS vs 20). The categorical variables were presented as frequencies and percentages and Quantitative variables were presented as measures of central tendency. Chi square test was used as test of significance for categorical variables. Independent Samples T test was used as test of significance for quantitative variables. P value <0.05 was taken as significant.

RESULTS

The distribution of the study group according to gravidity had shown that, about 66.7% of the patients with gestational hypertension and 60.8% of the patients with preeclampsia were primigravida, whereas 40% of the patients with eclampsia were gravida 2 and 40% were multigravidae. There was no statistically significant difference between the gravid status of the patients with gestational hypertension, preeclampsia and eclampsia [Table 1, Figure 1].

The mean bleeding time of the patients with gestational hypertension was 4.6 mins, among the patients with preeclampsia was 5.7 min and among

the patients with eclampsia was 6.4 mins. The Bleeding time was prolonged for more than 5 min in 38.1% of the gestational hypertension patients, 58.1% of the preeclampsia patients and 80% of the patients with eclampsia. There was no statistically significant difference in the bleeding time between the patients with gestational hypertension, preeclampsia and eclampsia [Table 2, Figure 2].

Table 1: Distribution of the study groups according to gravidity.

Gravida	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
Primigravida	14 (66.7)	45 (60.8)	1 (20.0)
Gravida 2	4 (19.0)	19 (25.7)	2 (40.0)
Gravida 3	1 (4.8)	7 (9.5)	0
Multigravida	2 (9.5)	3 (4.1)	2 (40.0)
Total	21	74	5

$\chi 2$ value= 12.018; df=6; p value>0.05, NS

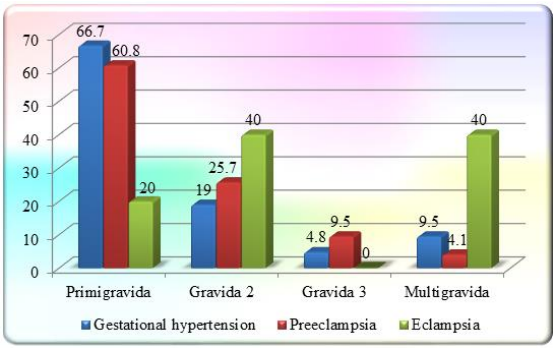

Figure 1: Graphical representation showing distribution of the study groups according to gravidity.

Table 2: Distribution of the study groups according to bleeding time

Bleeding time (5.49±1.79) (Normal: <7.1 minutes)	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
< 5 min	61.9)	31 (41.9)	1 (20)
> 5 min	8 (38.1)	43 (58.1)	4 (80)
Total	21	74	5
Mean ± SD	4.6 ± 1.3	5.7 ± 1.9	6.4 ± 1.3

$\chi 2$ value= 3.976; df=2; p value=0.137, NS

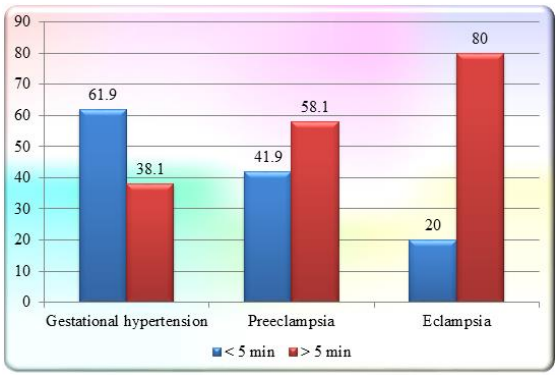

Figure 2: Distribution of the study groups according to bleeding time.

Table 3: Distribution of the study groups according to clotting time.

Clotting time (5.16±1.409)	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
< 5	18 (85.7)	37 (50)	0
>5	3 (14.3)	37 (50)	5 (100)
Total	21	74	5
Mean ± SD	4.2 ± 0.7	5.3 ± 1.3	7.5 ± 1.6

$\chi 2$ value= 14.863; df=2; p value=0.001,Sig

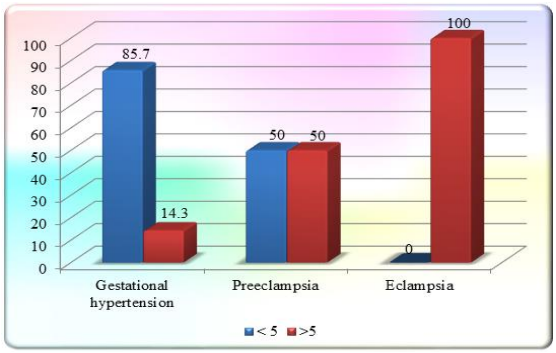

Figure 3: Distribution of the study groups according to clotting time

The mean clotting time of the gestational hypertension patients was 4.2 mins, in patients with preeclampsia was 5.3 mins and eclampsia patients was 7.5 minutes. The clotting time was more than 5 mins in 14.3% gestational hypertension patients, 50% of the preeclampsia patients and all the patients with eclampsia. This difference in clotting time was statistically significant between the patients with gestational hypertension, preeclampsia and eclampsia [Table 3, Figure 3].

Table 4: Distribution of the study groups according to clot retraction time

Clot retraction time (2.29±1.5)	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
Normal	20 (95.2)	68 (91.9)	0
Poor (>4 hr)	1 (4.8)	6 (8.1)	5 (100.0)
Total	21	74	5
Mean ± SD	2.0 ± 0.7	2.1 ± 1.0	7.2 ± 1.2

$\chi 2$ value= 38.77; df=2; p value=0.000, Sig

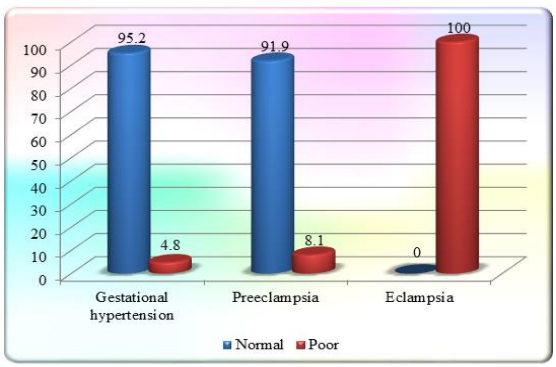

Figure 4: Distribution of the study groups according to clot retraction time

The mean clot retraction time of the patients with gestational hypertension was 2.0 mins in gestational hypertension patients, 2.1 mins in patients with preeclampsia and 7.2 min in patients with eclampsia. The clot retraction time was poor in 4.8% of the gestational hypertension patients, 8.1% of the patients with preeclampsia and all the patients with eclampsia [Table 4, Figure 4].

Table 5: Distribution of the study groups according to platelet count

Platelet count (1.61±0.83)	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
< 1 lac	0	16 (21.6)	3 (60.0)
1 – 2.5 lac	12 (57.1)	57 (77.0)	2 (40.0)
> 2.5	9 (42.9)	1 (1.4)	0
Total	21	74	5
Mean ± SD	2.6 ± 1.1	1.4 ± 0.5	0.9 ± 0.2

$\chi 2$ value= 39.011; df=4; p value=0.000, Sig

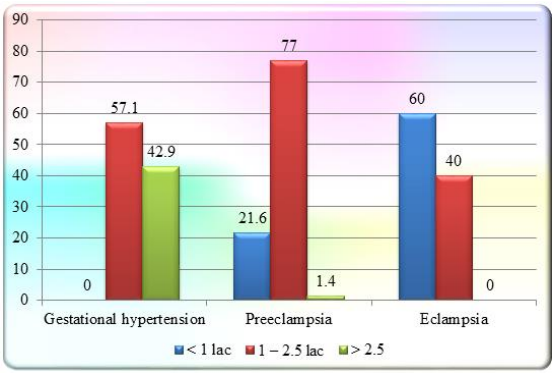

Figure 5: Distribution of the study groups according to platelet count

Table 6: Distribution of the study groups according to prothrombin time

Prothrombin time (17.28±4.47)	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
Normal	5 (23.8)	31 (41.3)	0
Prolonged (>15 sec)	16 (76.2)	43 (58.7)	5 (100)
Total	21	74	5
Mean ± SD	16.6 ± 3.0	16.9 ± 4.2	27.6 ± 3.8

$\chi 2$ value= 5.282; df=2; p value=0.071, NS

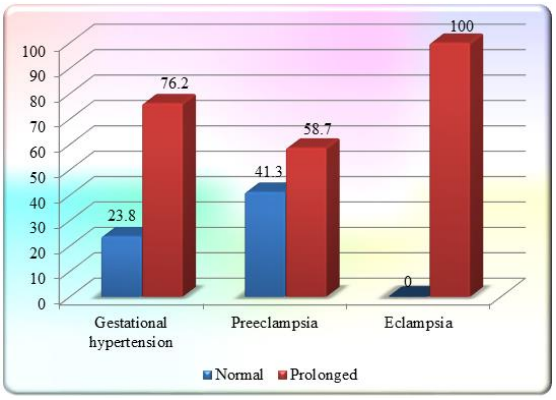

Figure 6: Distribution of the study groups according to prothrombin time

The mean platelet count of the gestational hypertension patients was 2.6 lakhs/ dl, 1.4 lakhs/dl in patients with preeclampsia and 0.9 lakhs /dl in patients with eclampsia. The platelet count was less than a lakh in none of the patients with gestational hypertension, 21.6% of the patients with preeclampsia and 60% of the patients with eclampsia. There was a statistically significant difference between the platelet count of patients with gestational hypertension, preeclampsia and eclampsia [Table 5, Figure 5].

The mean prothrombin time of patients with gestational hypertension was 16.6 secs, preeclampsia patients was 16.9 secs and eclampsia patients was 27.6 secs. About 76.2% of the patients with gestational hypertension, 58.7% of the patients with preeclampsia and all the patients of eclampsia had prolonged prothrombin time [Table 6, Figure 6].

Table 7: Distribution of the study groups according to aPTT levels

aPTT (34.93±8.44)	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
Normal	18 (85.7)	37 (50.0)	0
Prolonged(> 35 sec)	3 (14.3)	37 (50.0)	5 (100)
Total	21	74	5
Mean ± SD	29.4 ± 4.6	35.8 ± 8.1	51.2 ± 4.8

$\chi 2$ value= 14.863; df=2; p value=0.001, Sig

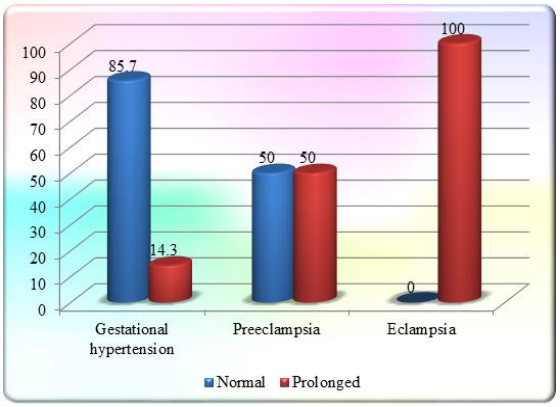

Figure 7: Distribution of the study groups according to aPTT levels

Table 8: Distribution of the study groups according to fibrinogen levels

Fibrinogen (330.76± 59.06)	Gestational hypertension n (%)	Preeclampsia n (%)	Eclampsia n (%)
Increased (>400)	0	5 (6.9)	1 (20.0)
Normal (150-400)	21 (100)	69 (93.2)	4 (80)
Total	21	74	5
Mean ± SD	276.5 ± 38.8	252.4 ± 64.1	207.8 ± 19.5

$\chi 2$ value= 3.15; df=2; p value=0.207, NS

The mean aPTT among the patients with gestational hypertension was 29.4 secs, 35.8 secs in patients with preeclampsia and 51.2 secs in patients with

eclampsia. The aPTT was prolonged in 14.3% of the patients with gestational hypertension, 50% of the patients with preeclampsia and all the patients with eclampsia. There was a statistically significant difference between the clotting time of patients with gestational hypertension, preeclampsia and eclampsia [Table 7, Figure 7].

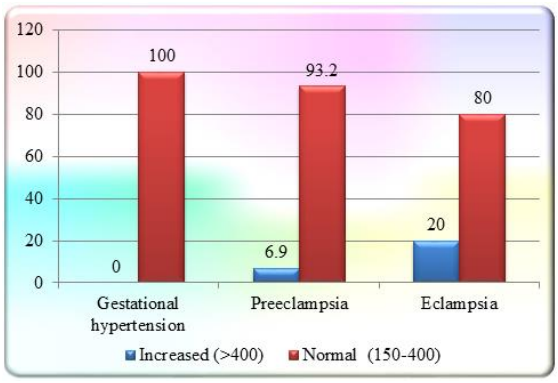

Figure 8: Distribution of the study groups according to fibrinogen levels

The mean fibrinogen levels of the patients with gestational hypertension was 276.5 µg/dl, 252.4 µg/dl in patients with preeclampsia and 207.8 µg/dl in patients with eclampsia. The plasma fibrinogen levels was increased in 6.9% of the preeclampsia patients and 20% of the eclampsia patients. This difference in plasma fibrinogen levels was not statistically significant between the gestational hypertension, preeclampsia and patients with eclampsia [Table 8, Figure 8].

DISCUSSION

Hypertensive disorders are the most important cause of maternal and perinatal morbidity and mortality1. According to estimates, approximately 50,000 women die from eclampsia across the world. The timely management of eclampsia can decrease maternal morbidity and mortality and fetal morbidity and mortality.[22-24]

Profound changes in coagulation and fibrinolytic system occur during normal pregnancy causing a hypercoagulable state. There is distinct possibility of accentuation of hypercoagulable state of pregnancy during eclampsia and pre eclampsia. Women with pregnancy induced hypertension may develop a variety of haematological changes. Thrombocytopenia is the most common haematological abnormality found.[12] The platelet count is routinely measured in women with any form of pregnancy induced hypertension. The other tests like prothrombin time, activated partial thromboplastin time, bleeding time and clotting time are more sensitive.[25,26]

The mean bleeding time of the patients with gestational hypertension was 4.6 mins, among the patients with preeclampsia was 5.7 min and among the patients with eclampsia was 6.4 mins. The Bleeding time was prolonged for more than 5 min in 38.1% of the gestational hypertension patients, 58.1% of the preeclampsia patients and 80% of the patients with eclampsia. In a study by Vijayalakshmi et al,[27] the mean bleeding time among the cases with mild preeclampsia was 3.5 min, in severe preeclampsia was 4.8 min and in cases of eclampsia was 5.3 mins.82 In a study by Priyadarshini et al,[28] the mean bleeding time was 5.03 min among the patients with preeclampsia and 3.65 mins among the normal pregnant women; this study result was almost similar to result of preeclampsia group of present study. But results of present study was different to Vijayalakshmi et al,[27] study may be because of different sample size.

The mean clotting time of the gestational hypertension patients was 4.2 mins, in patients with preeclampsia was 5.3 mins and eclampsia patients was 7.5 minutes. The clotting time was more than 5 mins in 14.3% gestational hypertension patients, 50% of the preeclampsia patients and all the patients with eclampsia. In a study by Vijayalakshmi et al,[27] the mean clotting time was 4.2 min in mild preeclampsia, 5.4 min in severe preeclampsia was 5.4 min and in eclampsia the mean clotting time was 5.6 min. In a study by Priyadarshini et al,[28] the mean clotting time was 5.03 mins among the patients with peeclampsia and 3.65 min among the normal pregnant women. Mean clotting time of PE and GTN group present study was comparable to respective group of Vijayalakshmi et al,[27] study but Mean clotting time of E group was high may be due to different studied subjects. And result of Priyadarshini et al,[28] was nearly comparable to this study.

The mean platelet count of the gestational hypertension patients was 2.6 lakhs/ mm3, 1.4 lakhs/ mm3 in patients with preeclampsia and 0.9 lakhs/ mm3 in patients with eclampsia. The platelet count was less than a lakh in none of the patients with gestational hypertension, 21.6% of the patients with preeclampsia and 60% of the patients with eclampsia. In a study by Jahromi et al,[29] the mean platelet count of women with severe preeclampsia was 1.57 lakhs/ mm3 and in normal pregnant women had 2.33 lakhs/cumm. In a study by Nirmala et al,[30] the mean platelet count was 2.65 lakhs/ mm3 in the patient with pregnancy induced hypertension, 2.72 lakhs/ mm3 in women with later normal pregnancy and 2.72 lakhs/ mm3 among the controls. The mean platelet count in mild preeclampsia was 2.1 lakhs/mm3, severe preeclampsia was 0.8 and eclampsia was 0.7 lakhs/cumm.82 In a study by Hannsaford et al6, none of the gestational hypertension cases, 1 case of imminent eclampsia had severe platelet counts and 1 case of severe preeclampsia had severe thrombocytopenia. In a study by Naaz et al,[31] the mean platelet count was 1.86 lakhs /mm3 among the cases and 2.76

lakhs/mm3 among the controls. Mean platelet count of PE group of current study were nearly comparable to same group of Jahromi et al,[29] and Priyadarshini et al,[28] study but not of other group of this study to other reviewed studies due to different sample size.

The mean prothrombin time of patients with gestational hypertension was 16.6 secs, preeclampsia patients was 16.9 secs and eclampsia patients was 27.6 secs. About 76.2% of the patients with gestational hypertension, 58.7% of the patients with preeclampsia and all the patients of eclampsia had prolonged prothrombin time. In a study by Jahromi et al,[29] the mean prothrombin time was 13.59 secs among women with severe reeclampsia and 12.5 secs in normal pregnant women. In a study by Nirmala et al,[30] the mean prothrombin time was 13.41 sec among the patients with pregnancy induced hypertension, 13.24 secs in late normal pregnancy and 13.14 secs among controls. In a study by Nirmala T et al,[30] the mean PT was 12.19 secs in Mild GH, 13.07 sec in severe GH, 12.47 in mild preeclampsia was 11.68 secs. About 3 cases of Mild GH, 2 cases of severe GH, 6 cases of mild preeclampsia and 4 cases of severe preeclampsia had prolonged PT.81 In a study by Vijaya Lakshmi et al27, the mean prothrombin time among the patients with mild preeclampsia was 12.4 sec, in severe preeclampsia it was 16.1 secs and in eclampsia cases it was 15.8 secs. In a study by Priyadarshini et al,[28] the mean prothrombin time was 15.27 secs among the patients with preeclampsia and 13.72 secs among the cases with normal pregnancy. It was found that results of PE group of this study were similar to PE group of Vijaya Lakshmi et al and Priyadarshini et al;[27,28] and nearly comparable to Jahromi et al study.[29] Discrepancy in results of other group of this study to others may be due to different no. of cases in their study and some unknown reasons.

The mean aPTT among the patients with gestational hypertension was 29.4 hours, 35.8 in patients with preeclampsia and 51.2 in patients with eclampsia. The aPTT was prolonged in 14.3% of the patients with gestational hypertension, 50% of the patients with preeclampsia and all the patients with eclampsia. In a study by Jahromi et al,[29] the Partial thromboplastin time among the women with severe preeclampsia was 38.7 secs and in normal pregnant women 34.24 secs. In a study by Nirmala et al,[30] the mean aPTT among the patients with mild GH was 25.11 secs, severe GH was 25.97 secs, Mild preeclampsia was 26.74 secs and severe preeclampsia was 27.33 secs. In a study by Vijaya Lakshmi et al,[27] the mean aPTT among the mild preeclampsia cases was 33.6 sec, in severe preeclampsia cases was 44.6 secs and 42.4 secs in eclampsia cases. The aPTT was prolonged in 6 mild GH, 2 in severe GH, 10 in Mild preeclampsia and 14 in Severe preeclampsia cases.81 In a study by Priyadarshini et al,[28] the mean aPTT was 34.2 sec among the patients with preeclampsia and 22.16 among the cases with normal pregnancy. Result of GTN group of this study were nearly similar to result respective group of Nirmala et al,[30] and Vijaya Lakshmi et al.[27] Result of PE group of this study were nearly similar to result respective group of Priyadarshini et al and Jahromi et al,[28,29] And result were not comparable in eclampsia group of present study to respective group of Vijaya Lakshmi et al study.[27]

The mean fibrinogen levels of the patients with gestational hypertension was 276.5 µg/dl, 252.4 µg/dl in patients with preeclampsia and 207.8 µg/dl in patients with eclampsia. The plasma fibrinogen levels was increased in 6.9% of the preeclampsia patients and 20% of the eclampsia patients. In a study by Jahromi et al,[29] the mean plasma fibrinogen level among the women with severe preeclampsia was 238.78 µg/dl and 298.08 µg/dl among the normal pregnant women. In a study by Naaz et al,[31] the mean fibrinogen level among the cases was 346.5 mg/dl and 276.75 mg/dl among the controls. Result of present study were nearly similar to result of Jahromi et al,[29] but was dissimilar to result of Naaz et al may be due to different sample size.[31]

CONCLUSION

Mean BT, CT were in normal range in all patients of PIH; but CT was significantly higher in E group than PE &GTN.

Mean CRT was poor in patients with E group and normal in patients of PE & GTN group.

Mean platelet counts & serum fibrinogen levels found to be decreased with severity of PIH.

Prolonged mean PT & aPTT were observed in patients with E.

However further studies with a large sample size and serial assessment of coagulation parameters are required to corroborate these findings and their relation with the progression and severity of PIH.

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How to cite this article: Sonal, Mathur S. The Coagulation Profile on Pregnancy Induced Hypertensive Patients in Third Trimester of Pregnancy – The Prospective and Observational Study. Ann. Int. Med. Den. Res. 2018; 4(4):OG01-OG07.

Source of Support: Nil, **Conflict of Interest:** None declared