

Comparative Study of Hypertensive Disorders of Pregnancy with Normotensive Pregnancies through Evaluation of Coagulation Profile and Platelet Count

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Abstract

Pregnancy-induced hypertension (PIH) is the major cause of maternal and fetal mortality and morbidity and it contributes to 16% of mortality in pregnant mothers in developed and developing countries. Aim of this study was to estimate, evaluate and compare platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT), D-Dimer and fibrinogen levels in patients with hypertensive disorders of pregnancy with normotensive pregnancies and further correlate the derangements in platelet count, PT, APTT, D-Dimer and fibrinogen levels with the clinical outcomes. For this a prospective case control study was conducted for two years in the Department of Pathology, JNMCH, AMU on total 128 pregnant females comprising of diagnosed cases of PIH and normal pregnant females were taken as controls. Platelet count, PT, APTT, D-Dimer and fibrinogen levels in 128 pregnant females (31 Severe Preeclampsia (BP above 160/110 mmHg), 37 Non-Severe Preeclampsia (BP ranges between 140/90 mmHg and 160/110 mmHg), and 60 Normal Pregnant Females) were evaluated and then correlated with the clinical outcomes. Analysis of variance (ANOVA) followed by post hoc Scheffe test has been used for statistical analysis. In this study, the mean platelet count significantly decreases while mean D-Dimer significantly increases with increasing severity of PIH. The mean PT, mean APTT and mean fibrinogen levels for the severe PIH group were significantly higher as compared to non-severe PIH and normal pregnancy groups. Statistical difference was not significant between the normal pregnancy group and the non-severe PIH group. Maternal and Fetal complications are more common with severe PIH, decreased platelet count and deranged coagulation profile. Therefore this study concludes that platelet count and D-dimer levels can be used to monitor the progression of pregnancy-induced hypertension and raised PT, APTT and fibrinogen levels are fairly good indicators of severe pregnancy-induced hypertension.

Keywords: PIH, Platelet count, PT, APTT, D-Dimer, Fibrinogen.

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Introduction

Pregnancy is one of the important stages of women's life with blessings and noble service of nature. Though pregnancy is a normal physiological process, not a disease, the mother and fetus are susceptible to certain risks. Regardless of a feeling of wellbeing, many women are surprised, when faced with unpleasant outcomes such as Pregnancy-induced hypertension (PIH) and other similar complications which can sometimes lead to intrauterine growth retardation (IUGR) and intrauterine death (IUD). Hypertension in pregnancy is one of the common problems for expectant mothers along with infection and postpartum hemorrhage. Women with pre-existing disorders are more likely to have certain

complications during pregnancy than those with normal blood pressure.

Pregnancy-induced hypertension (PIH) is an elevated blood pressure that develops after five months of pregnancy. Hypertension before 20 weeks of gestation almost always is due to chronic hypertension. Preeclampsia is a combination of elevated blood pressure, proteinuria and edema. Eclampsia is the presence of convulsions along with the above three features of preeclampsia. Pregnancy-induced hypertension is rare before the third trimester (1).

Pregnancy-induced hypertension (PIH) is a multiple organ disease unique to a pregnancy and can cause

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maternal complications like eclampsia, HELLP syndrome, acute renal failure, cerebrovascular accidents, etc. It influences the fetus like fetal growth restriction, oligohydramnios and fetal distress. Apart from pregnancy related complications, preeclampsia may lead to future cardiovascular as well as metabolic disease in women. Risks are common in every society and every setting but in developed countries, the risks have been largely overcome because every pregnant woman has access to special care. Young women with a first pregnancy, pregnant women having age less than 20 years and those having age more than 40 years, women with multiple fetuses, pregnant diabetics, pregnant women with pre-existing hypertension or history of preeclampsia or PIH in a previous pregnancy and pregnant women with pre-existing kidney disease are more vulnerable to PIH (1).

Pregnancy is a hypercoagulable state due to the elevation of most of the coagulation factors and reduced anticoagulant activity. In pregnancy-induced hypertension, there is an accentuation of hypercoagulable state because of injury to the endothelium. Profound changes in the coagulation and fibrinolytic system occur during normal pregnancy causing a hypercoagulable state (2). In preeclampsia and eclampsia, there is evidence of disseminated intravascular coagulopathy (DIC) affecting widespread organs of the body as opposed to selective DIC only at the placental site in normal pregnancy. This process appears to be initiated by the release of thromboplastin into the circulation. There is reduction of platelets and degree of thrombocytopenia reflects the severity of pathology. There is also reduction of fibrinogen, antithrombin III and plasminogen level in the blood. The underlying coagulation abnormality increases the risk of bleeding complications, especially during operative delivery and during the placement of an epidural catheter for regional anesthesia. Anticipation of these coagulation disturbances in patients of preeclampsia can prevent significant maternal morbidity and mortality. Early assessment of the severity of PIH is necessary to prevent complications like HELLP (Haemolysis, Elevated Liver enzymes, Low Platelet count) syndrome (3).

Pregnancy-induced hypertension is one of the major causes of death among women in the reproductive age group. Around 5 lakh women die each year from maternal causes, and for every woman who dies, 20 or

more suffer from injuries, infection and disabilities during pregnancy or childbirth. The incidence of PIH in India is about 7-10% of all antenatal admissions. Over half a million women die each year from pregnancy related causes. In many low income countries, complications of pregnancy and childbirth are the leading cause of death among women of reproductive years. Out of the several forms of hypertensive disorders of pregnancy (like gestational hypertension, preeclampsia, eclampsia and chronic hypertension), eclampsia is a most important form of maternal mortality (3).

Identification of certain predictors like platelet count and coagulation profile would be useful to differentiate hypertensive pregnant women who are at risk of progression to preeclampsia or development of adverse outcomes.

The aim of the present study is to find out the changes that occur in the coagulation parameters in pregnancy-induced hypertension and to compare it with normotensive pregnant women.

This study may help in reducing the mortality and morbidity that are caused by the coagulation abnormalities of pregnancy-induced hypertension. The overall goal of these analyses is to provide information that can improve the diagnostic accuracy in the evaluation of pregnant patients with suspected or known preeclampsia.

Material and Methods

A prospective case control study was conducted for two years in the Department of Pathology, JNMCH, AMU on total 128 pregnant women from the Department of Obstetrics and Gynecology, J. N. Medical College and Hospital, AMU, Aligarh, in which 60 pregnant women were selected for the control group with normal blood pressure. The remaining 68 pregnant women with a systolic blood pressure of 140 mmHg and above and diastolic blood pressure of 90 mmHg and above were divided into two groups. The non-severe PIH group consists of 37 pregnant women with blood pressure between 140/90 mmHg and 160/110 mmHg. The severe PIH group consists of 31 pregnant women with systolic blood pressure above 160 mmHg and diastolic blood pressure above 110 mmHg with symptoms like vomiting, headache, visual disturbances, upper abdominal pain, oliguria, convulsion, low platelet count, elevated serum enzymes and creatinine.

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Detailed medical and obstetric history was taken from the study group and the procedure was explained. After getting consent, the Platelet count was done by using BeneSphera 3 part Hematology Analyser while PT, APTT, D-Dimer, Fibrinogen were done by using Automated Analyser ACL TOP 500 CTS Model. Results of the following tests were evaluated and then correlated with the clinical outcomes.

Statistical Package for Social Sciences (SPSS) version 25 has been used for statistical analysis for applying Analysis of variance (ANOVA) followed by post hoc Scheffe test. The study was approved by the board of studies and Institutional Ethics Committee, J.N. Medical College, AMU, Aligarh. Informed consent was obtained from each participant. The participants were assured about privacy and confidentiality before proceeding with the study.

Results

The present case control study was carried out on 128 pregnant females admitted in the labour room of the Department of Obstetrics and Gynecology, J. N. Medical College and Hospital, AMU, Aligarh. The patients selected for the study were 60 normal pregnant women and 68 patients with pregnancy-induced hypertension (PIH). The 68 PIH patients were classified as 37 non-severe PIH patients and 31 severe PIH patients. The study was carried out for the period from November 2019 to November 2021.

| Age group (years) | CLINICAL DIAGNOSIS | | | | | | Total |
|-------------------|--------------------|------------|----------------|------------|------------|------------|------------|
| | Normal pregnancy | % | Non severe PIH | % | Severe PIH | % | |
| 18-20 | 5 | 9 | 3 | 8 | 3 | 10 | 11 |
| 21-25 | 27 | 45 | 22 | 60 | 21 | 67 | 70 |
| 26-30 | 26 | 43 | 9 | 24 | 4 | 13 | 39 |
| 31-35 | 2 | 3 | 3 | 8 | 3 | 10 | 8 |
| Total | 60 | 100 | 37 | 100 | 31 | 100 | 128 |

Table 1: Distribution of Patients according to Age

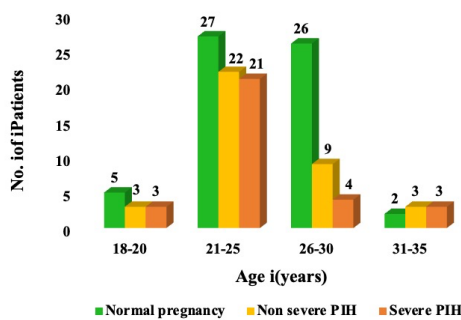


Chart 1: Distribution of Patients according to

Age

Table 1 and chart 1 show the age distribution of patients among study groups. The age group of patients ranges from 18 to 35 years. 67% of patients in the severe PIH group, 60% of patients in the non-severe PIH group, and 45% of patients in the normal pregnancy group were in the age group 21-25 years. 9% and 3% of patients were in the age group 18-20 years and 31-35 years respectively in the normal pregnancy group. In the non-severe PIH group, the percentage composition in the age group 18-20 years and in the age group 31-35 years was 8% each. However, 10% of patients were in the age group 18-20 years as well as in the age group 31-35 years in the severe PIH category.

| | No. of Patients | Mean Age (years) | Std. Deviation |
|-------------------------|-----------------|------------------|----------------|
| Normal Pregnancy | 60 | 25.18 | 2.68 |
| Non Severe PIH | 37 | 24.7 | 3.01 |
| Severe PIH | 31 | 24.32 | 3.32 |
| Total | 128 | 24.84 | 2.94 |

Table 2: Mean Age (years) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

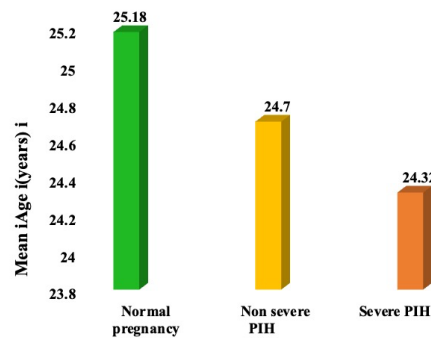


Chart 2: Mean Age (years) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

Table 2 and chart 2 shows that the mean age of normal pregnancy, non-severe PIH and severe PIH patients were 25.18 years, 24.7 years and 24.32 years respectively.

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| Parity | CLINICAL DIAGNOSIS | | | | | | Total |
|--------------|--------------------|------------|----------------|------------|------------|------------|------------|
| | Normal pregnancy | % | Non severe PIH | % | Severe PIH | % | |
| Primipara | 34 | 57 | 23 | 62 | 22 | 71 | 79 |
| Multipara | 26 | 43 | 14 | 38 | 09 | 29 | 49 |
| Total | 60 | 100 | 37 | 100 | 31 | 100 | 128 |

Table 3: Distribution of Patients according to Parity

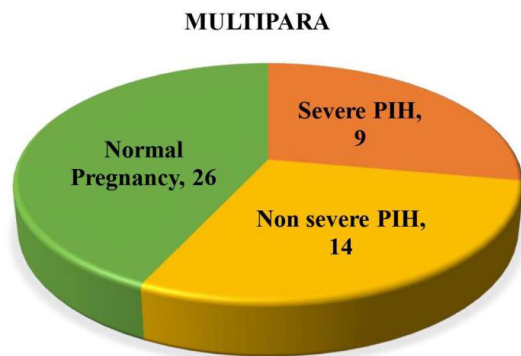
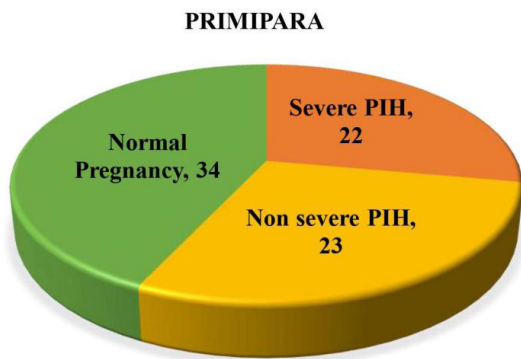


Chart 3: Distribution of Patients according to Parity

Table 3 and chart 3 show the distribution of patients according to parity. 71% of patients in the PIH group, 62% patients in the non-severe PIH group and 57% patients in the normal pregnancy group were primipara. The percentage composition of multipara was 29%, 38% and 43% in severe PIH group, in non-severe PIH group and normal pregnancy group respectively.

| Platelet count (lakhs/m | CLINICAL DIAGNOSIS | | | | | | Total |
|-------------------------|--------------------|---|----------|---|--------|---|-------|
| | Normal pregna | % | Non seve | % | Severe | % | |

| m ³) | ncy | | re PIH | | PIH | | |
|------------------|-----------|------------|-----------|------------|-----------|-----------|------------|
| <1.5 | 02 | 3 | 02 | 5 | 19 | 61 | 23 |
| 1.5-2.5 | 14 | 23 | 28 | 76 | 12 | 39 | 54 |
| 2.5-3.5 | 34 | 57 | 07 | 19 | 00 | 0 | 41 |
| >3.5 | 10 | 17 | 00 | 0 | 00 | 0 | 10 |
| Total | 60 | 100 | 37 | 100 | 31 | 10 | 128 |

Table 4: Distribution of Patients according to Platelet Count

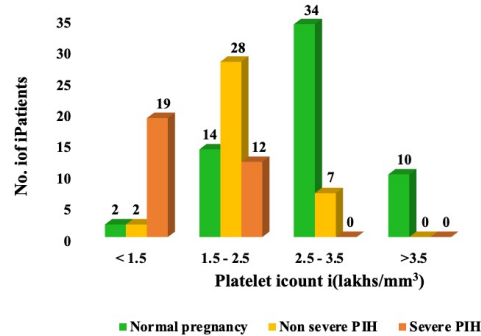


Chart 4: Distribution of Patients according to Platelet Count

Table 4 and chart 4 show the distribution of patients according to platelet count. 61% patients in severe PIH group, 5% patients in non-severe PIH group and 3% patients in normal pregnancy group had platelet count less than 1.5 lakhs/mm³. However, no patient in the non-severe PIH group had a platelet count of more than 3.5 lakhs/mm³. In the severe PIH group, no patient had platelet count more than 2.5 lakhs/mm³.

| | No. of Patients | Mean | Std. Deviation |
|-------------------------|-----------------|-------------|----------------|
| Normal Pregnancy | 60 | 2.89 | 0.80 |
| Non Severe PIH | 37 | 2.22 | 0.57 |
| Severe PIH | 31 | 1.47 | 0.53 |
| Total | 128 | 2.35 | 0.88 |

Table 5: Mean Platelet Count (lakhs/mm³) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

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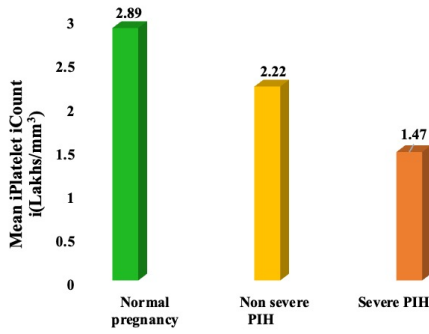


Chart 5: Mean Platelet Count (lakhs/mm³) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

Table 5 and chart 5 show that the mean platelet count of normal pregnancy, non-severe PIH and severe PIH patients were 2.89 lakhs/mm³, 2.22 lakhs/mm³ and 1.47 lakhs/mm³ respectively.

| | Sum of squares | Df | Mean square | F | P-value |
|-----------------------|----------------|------------|-------------|---------|---------|
| Between Groups | 41.8171 | 2 | 20.9085 | 44.7528 | 0.000 |
| Within Groups | 58.4001 | 125 | 0.4672 | | |
| Total | 100.217 | 127 | | | |

Table 6: Analysis of variance (ANOVA) of Platelet Count among groups: Normal Pregnancy, Non severe PIH and Severe PIH

On applying ANOVA (Analysis of variance), the p value was significant (p value < 0.05) for the platelet count between the normal pregnancy, non-severe PIH and severe PIH groups.

| Mean Platelet Count (I) | Mean Platelet Count (J) | Mean Difference (I-J) | CV | F _s |
|-------------------------|-------------------------|-----------------------|--------|----------------|
| Normal Pregnancy | Non Severe PIH | 0.668* | 6.1373 | 21.8593 |
| | Severe PIH | 1.41468* | 6.1373 | 87.5561 |
| Non Severe PIH | Normal Pregnancy | -0.668* | 6.1373 | 21.8593 |
| | Severe PIH | 36.48* | 6.1373 | 48046.4 |

| | | | | |
|------------|------------------|-----------|--------|---------|
| | Severe PIH | | 8 | |
| Severe PIH | Normal Pregnancy | -1.41468* | 6.1373 | 87.5561 |
| | Non Severe PIH | -36.48* | 6.1373 | 48046.4 |

*The mean difference is significant as the F_s value (post hoc Scheffe test) is higher than the CV (Critical value for post hoc Scheffe test)

Table 7: Post hoc Scheffe test of platelet count among groups: Normal Pregnancy, Non Severe PIH and Severe PIH

Post hoc Scheffe test analysis revealed that the mean difference in the platelet count between normal pregnancy and non-severe PIH, normal pregnancy and severe PIH as well as non-severe PIH and severe PIH groups were significant as the F_s value for platelet count was more than the critical value for post hoc Scheffe test in all comparison groups.

| Prothrombin time (seconds) | CLINICAL DIAGNOSIS | | | | | | Total |
|----------------------------|--------------------|------------|----------------|------------|------------|------------|------------|
| | Normal pregnancy | % | Non severe PIH | % | Severe PIH | % | |
| <10 | 10 | 17 | 16 | 43 | 03 | 9 | 29 |
| 10-12 | 36 | 60 | 18 | 49 | 07 | 23 | 61 |
| 12-14 | 14 | 23 | 03 | 8 | 14 | 45 | 31 |
| >14 | 00 | 0 | 00 | 0 | 07 | 23 | 07 |
| Total | 60 | 100 | 37 | 100 | 31 | 100 | 128 |

Table 8: Distribution of Patients according to Prothrombin Time

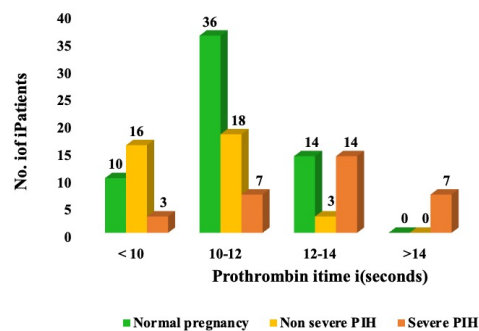


Chart 6: Distribution of Patients according to Prothrombin Time

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Table 8 and chart 6 show the distribution of patients according to prothrombin time. PT was prolonged (>12 seconds) in 68% of patients in severe PIH group, 8% in non-severe PIH group and 23% in normal pregnancy group.

| | No. of patients | Mean | Std. Deviation |
|------------------|-----------------|--------------|----------------|
| Normal Pregnancy | 60 | 11.11 | 1.37 |
| Non Severe PIH | 37 | 10.28 | 1.44 |
| Severe PIH | 31 | 13.17 | 2.76 |
| Total | 128 | 11.37 | 2.11 |

Table 9: Mean Prothrombin Time (seconds) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

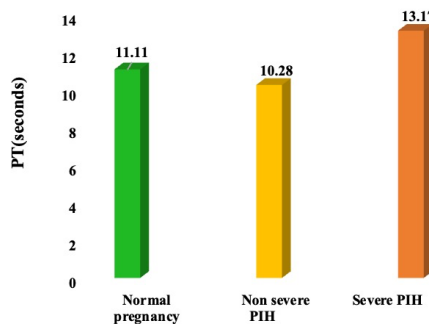


Chart 7: Mean Prothrombin Time (seconds) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

Table 9 and chart 7 show that the mean prothrombin time of normal pregnancy, non-severe PIH and severe PIH were 11.11 seconds, 10.28 seconds and 13.17 seconds respectively.

| | Sum of squares | Df | Mean square | F | P-value |
|----------------|----------------|------------|-------------|---------|---------|
| Between Groups | 148.416 | 2 | 74.208 | 22.3668 | 0.000 |
| Within Groups | 414.723 | 125 | 3.31778 | | |
| Total | 530.183 | 127 | | | |

Table 10: Analysis of variance (ANOVA) of Prothrombin Time among groups: Normal Pregnancy, Non severe PIH and Severe PIH

On applying ANOVA (Analysis of variance), the p value was significant (p value < 0.05) for the prothrombin time between the normal pregnancy, non-severe PIH and severe PIH groups.

| Mean PT (I) | Mean PT (J) | Mean Difference (IJ) | CV | F _s |
|----------------|------------------|----------------------|---------|----------------|
| Normal | Non Severe PIH | 0.82122 | 6.13738 | 4.652 |
| Pregnancy | Severe PIH | -2.06597* | 6.13738 | 232.054* |
| Non Severe PIH | Normal Pregnancy | -0.82122 | 6.13738 | 4.652 |
| | Severe PIH | 2.88718* | 6.13738 | 191.502* |
| Severe PIH | Normal Pregnancy | 2.06597* | 6.13738 | 232.054* |
| | Non Severe PIH | 2.88718* | 6.13738 | 191.502* |

*The mean difference is significant as the F_s value (post hoc Scheffe test) is higher than the CV (Critical value for post hoc Scheffe test)

Table 11: Post hoc Scheffe test of Prothrombin Time among groups: Normal Pregnancy, Non severe PIH and Severe PIH

Post hoc Scheffe test analysis revealed that the mean difference in the prothrombin time between normal pregnancy and severe PIH groups as well as between non-severe PIH and severe PIH groups were significant as the F_s value for prothrombin time was more than the critical value for post hoc Scheffe test, while the mean difference in the prothrombin time between normal pregnancy and non-severe PIH groups was not significant as the F_s value for prothrombin time was less than the critical value for post hoc Scheffe test.

| APTT (seconds) | CLINICAL DIAGNOSIS | | | | | | Total |
|----------------|--------------------|---|------------|---|------------|---|-------|
| | Normal pregnanc | % | Non severe | % | Severe PIH | % | |
| | | | | | | | |

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|) | y | | PIH | | | | |
|--------------|-----------|------------|-----------|------------|-----------|------------|------------|
| 20-25 | 12 | 20 | 06 | 16 | 03 | 10 | 20 |
| 25-30 | 16 | 27 | 15 | 40.5 | 05 | 16 | 26 |
| 30-35 | 27 | 45 | 15 | 40.5 | 06 | 19 | 35 |
| 35-40 | 05 | 8 | 01 | 3 | 11 | 36 | 41 |
| >40 | 00 | 0 | 00 | 0 | 06 | 19 | 06 |
| Total | 60 | 100 | 37 | 100 | 31 | 100 | 128 |

Table 12: Distribution of Patients according to APTT

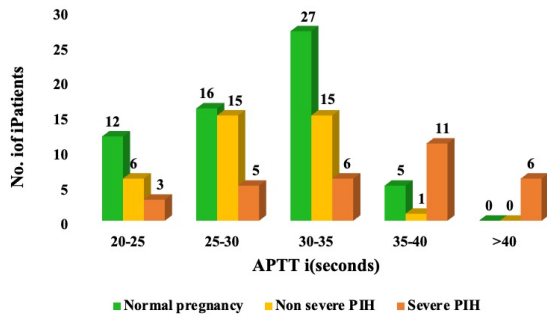


Chart 8: Distribution of Patients according to APTT

Table 12 and chart 8 show the distribution of patients according to APTT. APTT was prolonged (>40 seconds) in 19% of patients in the severe PIH group, however APTT was within the normal range in all patients of the non-severe PIH group and normal pregnancy group.

| | No. of Patients | Mean | Std. Deviation |
|-------------------------|-----------------|--------------|----------------|
| Normal Pregnancy | 60 | 29.36 | 3.79 |
| Non Severe PIH | 37 | 28.85 | 3.77 |
| Severe PIH | 31 | 35.16 | 6.92 |
| Total | 128 | 30.62 | 5.36 |

Table 13: Mean APTT (seconds) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

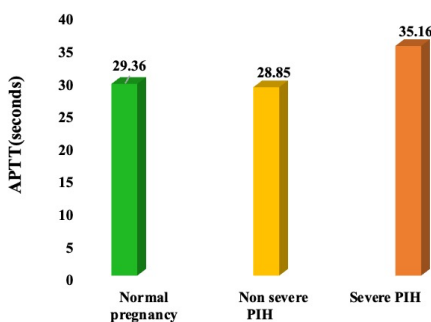


Chart 9: Mean APTT (seconds) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

Table 13 and chart 9 show that the mean APTT of normal pregnancy, nonsevere PIH and severe PIH patients were 29.36 seconds, 28.85 seconds and 35.16 seconds respectively.

| | Sum of squares | Df | Mean square | F | P-value |
|-----------------------|----------------|------------|-------------|---------|---------|
| Between Groups | 848.908 | 2 | 424.454 | 18.9542 | 0.000 |
| Within Groups | 2797.73 | 125 | 22.3818 | | |
| Total | 3646.64 | 127 | | | |

Table 14: Analysis of variance (ANOVA) of APTT among groups: Normal Pregnancy, Non severe PIH and Severe PIH

On applying ANOVA (Analysis of variance), the p-value was significant (p value < 0.05) for APTT between the normal pregnancy, non-severe PIH and severe PIH groups.

| Mean APTT (I) | Mean APTT (J) | Mean Difference (I-J) | CV | F _s |
|------------------|------------------|-----------------------|---------|----------------|
| Normal Pregnancy | Non Severe PIH | 0.51198 | 6.13738 | 0.268 |
| | Severe PIH | -5.79473* | 6.13738 | 30.665* |
| Non Severe PIH | Normal Pregnancy | -0.51198 | 6.13738 | 0.268 |
| | Severe PIH | -6.30671* | 6.13738 | 29.975* |
| Severe PIH | Normal Pregnancy | 5.79473* | 6.13738 | 30.665* |
| | Non Severe PIH | 6.30671* | 6.13738 | 29.975* |

*.The mean difference is significant as the F_s value (post hoc Scheffe test) is higher than the CV (Critical value for post hoc

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Scheffe test)

| | | | |
|--------------|------------|---------------|--------------|
| Total | 128 | 238.68 | 91.21 |
|--------------|------------|---------------|--------------|

Table 15: Post hoc Scheffe test of APTT among groups: Normal Pregnancy, Non severe PIH and Severe PIH

Post hoc Scheffe test analysis revealed that the mean difference in the APTT between normal pregnancy and severe PIH groups as well as between non severe PIH and severe PIH groups were significant as the Fs value for APTT was more than the critical value for post hoc Scheffe test, while the mean difference in the APTT between normal pregnancy and non-severe PIH groups was not significant as the Fs value for APTT was less than the critical value for post hoc Scheffe test.

Table 17: Mean D-Dimer (ng/ml) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

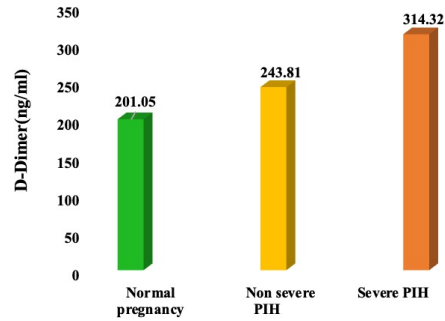


Chart 11: Mean D-Dimer (ng/ml) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

| D-Dimer (ng/ml) | CLINICAL DIAGNOSIS | | | | | | Total |
|-----------------------|--------------------|------------|----------------|------------|------------|------------|------------|
| | Normal pregnancy | % | Non severe PIH | % | Severe PIH | % | |
| Normal (≤ 232) | 50 | 83 | 24 | 73 | 18 | 60 | 92 |
| Increased (> 232) | 10 | 17 | 13 | 27 | 13 | 40 | 36 |
| Total | 60 | 100 | 37 | 100 | 31 | 100 | 128 |

Table 16: Distribution of patients according to D-Dimer

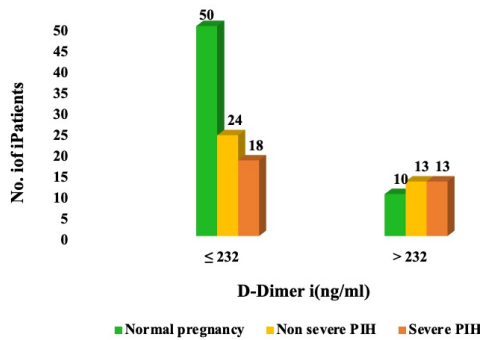


Chart 10: Distribution of patients according to D-Dimer

Table 16 and chart 10 show the distribution of patients according to D-Dimer levels. 40% of patients had increased D-dimer level (> 232 ng/ml) in severe PIH group as compared to 27% of patients in non-severe PIH group and 17% of patients in normal pregnancy group.

Table 17 and chart 11 show that mean D-Dimer levels of normal pregnancy, non-severe PIH and severe PIH were 201.05 ng/ml, 243.81 ng/ml and 314.32 ng/ml respectively.

| | Sum of squares | Df | Mean square | F | P-value |
|-----------------------|----------------|------------|-------------|----------|---------|
| Between Groups | 262711.6 | 2 | 131355.8 | 21.35363 | 0.000 |
| Within Groups | 768931.3 | 125 | 6151.45 | | |
| Total | 1031643 | 127 | | | |

Table 18: Analysis of variance (ANOVA) of D-Dimer levels among groups: Normal Pregnancy, Non severe PIH and Severe PIH

On applying ANOVA (Analysis of variance), the p value was significant (p value < 0.05) for D-Dimer levels between the normal pregnancy, non-severe PIH and severe PIH groups.

| | No. of Patients | Mean | Std. Deviation |
|-------------------------|-----------------|--------|----------------|
| Normal Pregnancy | 60 | 201.05 | 32.41 |
| Non Severe PIH | 37 | 243.81 | 64.49 |
| Severe PIH | 31 | 314.32 | 136.29 |

| Mean D-Dimer(I) | Mean D-Dimer(J) | Mean Difference (I-J) | CV | F _s |
|------------------|-----------------|-----------------------|----------|----------------|
| Normal Pregnancy | Non Severe PIH | -42.7608* | 6.137377 | 6.803* |

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| | | | | |
|----------------|------------------|-------------------|--------------|-------------|
| ncy | Severe PIH | - 113.2 73* | 6.137 377 | 42.6 33* |
| | Normal Pregnancy | 42.76 08* | 6.137 377 | 6.80 3* |
| Non Severe PIH | Severe PIH | - 70.51 18* | 6.137 377 | 13.6 33* |
| | Normal Pregnancy | 113.2 73* | 6.137 377 | 42.6 33* |
| Severe PIH | Non Severe PIH | 70.51 18* | 6.137 377 | 13.6 33* |
| | Severe PIH | 113.2 73* | 6.137 377 | 42.6 33* |

*The mean difference is significant as the F_s value (post hoc Scheffe test) is higher than the CV (Critical value for post hoc Scheffe test)

Table 19: Post hoc Scheffe test of D-Dimer levels among groups: Normal Pregnancy, Non severe PIH and Severe PIH

Post hoc Scheffe test analysis revealed that the mean difference in the D-Dimer levels between normal pregnancy and non-severe PIH, normal pregnancy and severe PIH as well as non-severe PIH and severe PIH groups were significant as the F_s value for D-Dimer levels was more than the critical value for post hoc Scheffe test in all comparison groups.

| Fibrinogen (mg/dl) | CLINICAL DIAGNOSIS | | | | | | Total |
|--------------------|--------------------|------------|----------------|------------|------------|------------|------------|
| | Normal pregnancy | % | Non severe PIH | % | Severe PIH | % | |
| Normal (180-360) | 58 | 97 | 31 | 84 | 23 | 74 | 112 |
| Increased (>360) | 02 | 3 | 06 | 16 | 08 | 26 | 16 |
| Total | 60 | 100 | 37 | 100 | 31 | 100 | 128 |

Table 20: Distribution of patients according to Fibrinogen

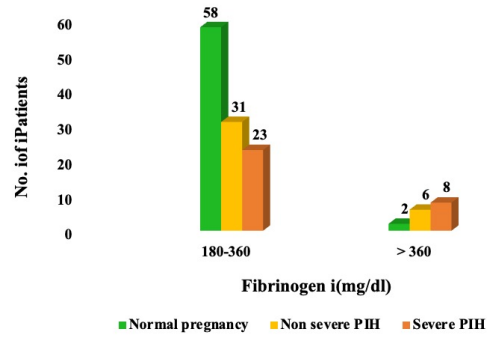


Chart 12: Distribution of patients according to Fibrinogen

Table 20 and chart 12 show the distribution of patients according to fibrinogen. 26% of patients had increased fibrinogen level (>360 mg/dl) in severe PIH group as compared to 16% of patients in non-severe PIH and 3% of patients in normal pregnancy group.

| | No. of Patients | Mean | Std. Deviation |
|------------------|-----------------|---------------|----------------|
| Normal Pregnancy | 60 | 250.67 | 78.01 |
| Non Severe PIH | 37 | 285.60 | 96.04 |
| Severe PIH | 31 | 371.07 | 88.01 |
| Total | 128 | 289.92 | 94.51 |

Table 21: Mean Fibrinogen (mg/dl) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

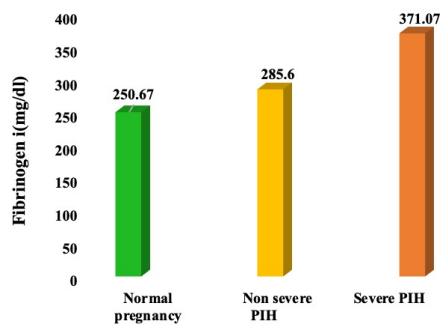


Chart 13: Mean Fibrinogen (mg/dl) for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

Table 21 and chart 13 show that the mean Fibrinogen levels (mg/dl) of normal pregnancy, non-severe PIH and severe PIH were 250.67 mg/dl, 285.6 mg/dl and 371.07 mg/dl respectively.

| | Sum of squares | Df | Mean square | F | P-value |
|--|----------------|----|-------------|---|---------|
| | | | | | |

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| | | | | | |
|-----------------------|----------------|------------|----------|----------|-------|
| Between Groups | 297259.1 | 2 | 148629.5 | 22.18934 | 0.000 |
| Within Groups | 837280.1 | 125 | 6698.241 | | |
| Total | 1134539 | 127 | | | |

Table 22: Analysis of variance (ANOVA) of Fibrinogen levels among groups: Normal Pregnancy, Non severe PIH and Severe PIH

On applying ANOVA (Analysis of variance), the p value was significant (p value < 0.05) for Fibrinogen levels between the normal pregnancy, non-severe PIH and severe PIH patients.

| Mean Fibrinogen (I) | Mean Fibrinogen (J) | Mean Difference (I-J) | CV | F _s |
|---------------------|---------------------|-----------------------|----------|----------------|
| Normal Pregnancy | Non Severe PIH | -34.9279 | 6.137377 | 4.168 |
| | Severe PIH | -120.398* | 6.137377 | 44.233* |
| Non Severe PIH | Normal Pregnancy | 34.9279 | 6.137377 | 4.168 |
| | Severe PIH | 85.470* | 6.137377 | 18.396* |
| Severe PIH | Normal Pregnancy | 120.398* | 6.137377 | 44.233* |
| | Non Severe PIH | 85.470* | 6.137377 | 18.396* |

*.The mean difference is significant as the F_s value (post hoc Scheffe test) is higher than the CV (Critical value for post hoc Scheffe test)

Table 23: Post hoc Scheffe test of Fibrinogen levels among groups: Normal Pregnancy, Non severe PIH and Severe PIH

Post hoc Scheffe test analysis revealed that the mean difference in the fibrinogen levels between normal pregnancy and severe PIH groups as well as between non severe PIH and severe PIH groups were

significant as the F_s value for fibrinogen levels was more than the critical value for post hoc Scheffe test, while the mean difference in the fibrinogen levels between normal pregnancy and non-severe PIH groups was not significant as the F_s value for fibrinogen levels was less than the critical value for post hoc Scheffe test.

| Adverse Maternal Outcome | Normal Pregnancy (n=60) | Non Severe PIH (n=37) | Severe PIH (n=31) |
|--|-------------------------|-----------------------|-------------------|
| HELLP syndrome | 0 | 1 (2.7%) | 5 (13.5%) |
| Disseminated intravascular coagulopathy (DIC) | 0 | 1 (2.7%) | 3 (9.7%) |
| Placental abruption | 0 | 0 | 3 (9.7%) |
| Maternal Death | 0 | 0 | 2 (6.5%) |

Table 24: Adverse Maternal Outcome for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

Table 24 shows the adverse maternal outcome for normal pregnancy group, non-severe PIH group and severe PIH group. The most common complications of severe PIH identified in this study were HELLP syndrome (13.5%), disseminated intravascular coagulopathy (9.7%) and placental abruption (9.7%).

| Adverse Maternal Outcome | Mean Platelet count (lakhs/mm ³) | Mean PT (seconds) | Mean APTT (seconds) | Mean D-Dimer (ng/ml) | Mean Fibrinogen (mg/dl) |
|--|--|-------------------|---------------------|----------------------|-------------------------|
| HELLP syndrome | 1.34 | 11.46 | 35.6 | 332.16 | 377.33 |
| Disseminated intravascular coagulopathy | 1.5 | 11.4 | 36.2 | 444.75 | 355.25 |

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| | | | | | | | | | | | |
|-----------------------------|------|-------|------|-------|--------|--------------------------|------|-------------|-------------------|--------|--------|
| pathy (DIC) | | | | | | mm³) | | nds) | er (ng/ml) | | |
| Placental abrupti on | 1.65 | 13.23 | 35.3 | 269.0 | 343.66 | Still birth | 1.22 | 11.4 | 32.43 | 245.71 | 346 |
| Maternal Death | 1.12 | 10.6 | 42.9 | 180.5 | 326.0 | Low birth weigh t | 1.57 | 12 | 33.18 | 237.75 | 350.25 |

Table 25: Correlation of Adverse Maternal Outcome with Platelet Count and Coagulation Profile

Table 25 shows the correlation of adverse maternal outcome with platelet count and coagulation profile. The mean platelet count in patients with HELLP syndrome was less than 1.5 lakhs/mm³ along with raised mean D-Dimer (>232 ng/ml) and raised mean fibrinogen (>360 mg/dl). Mean D-Dimer was high and correlated well with patients developing DIC as a complication of PIH. Mean PT was prolonged (> 12 seconds) and mean D-Dimer was raised in patients with placental abrupti on. The mean platelet count was 1.12 lakhs/mm³ and mean APTT was prolonged (>40 seconds) in cases of maternal mortality.

| Fetal Outcome | Normal Pregnancy (n=60) | Non Severe PIH (n=37) | Severe PIH (n=31) |
|-------------------------|--------------------------------|------------------------------|--------------------------|
| Healthy newborn | 58 (96.6%) | 33 (89.2%) | 18 (58%) |
| Still birth | 1 (1.7%) | 1 (2.7%) | 5 (16%) |
| Low birth weight | 1 (1.7%) | 3 (8.1%) | 8 (26%) |

Table 26: Fetal Outcome for Normal Pregnancy, Non Severe PIH and Severe PIH Patients

Table 26 shows the fetal outcome for normal pregnancy group, non-severe PIH group and severe PIH group. There were 16% stillbirth and 26% low birth weight in severe PIH group as compared to 2.7% stillbirth and 8.1% low birth weight in non-severe PIH group.

| Fetal Outcome | Mean Platelet count (lakhs/) | Mean PT (secods) | Mean APT T (secods) | Mean D-Dim | Mean Fibrin ogen (mg/dl) |
|----------------------|-------------------------------------|-------------------------|----------------------------|-------------------|---------------------------------|
|----------------------|-------------------------------------|-------------------------|----------------------------|-------------------|---------------------------------|

Table 27: Correlation of Fetal Outcome with Platelet Count and Coagulation Profile

Table 27 shows the correlation of fetal outcome with platelet count and coagulation profile. The mean platelet count was less than 1.5 lakhs/mm³ along with raised mean D-Dimer (>232 ng/ml) in mothers of stillborn babies while low birth weight was mainly associated with raised mean D-Dimer.

Discussion

Hypertensive disorders are among the commonest medical disorders during pregnancy and continue to be a major cause of maternal and perinatal morbidity and mortality worldwide (4). Preeclampsia is an idiopathic multisystem disorder specific to human pregnancy and the puerperium (5).

Hematological abnormalities such as thrombocytopenia and a decrease in plasma clotting factors may develop in preeclamptic women. Subtle changes consistent with disseminated intravascular coagulation (DIC) are potentially serious. Thus, coagulation testing should be common in these patients for evidence of DIC and HELLP syndrome (Haemolysis, Elevated Liver Enzymes and Low Platelet Count). From the historical point of view, it was first stated that only serial measurements of platelet count were adequate for intrapartum screening (6). Later, combination of platelet count and APTT, platelet count and liver function tests, platelet count and lactate dehydrogenase, platelet count and antithrombin60 were suggested for early detection and screening of the patients with preeclampsia (7-9).

We conducted a case-control study to compare hypertensive disorders of pregnancy with normotensive pregnancies through evaluation of coagulation profile and platelet count.

Age and Parity:

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In the present study the mean age of normal pregnancy, non-severe PIH and severe PIH groups were 25.18 years, 24.7 years and 24.32 years respectively. The distribution of the study group according to parity had shown that 71% of the patients with severe PIH, 62% of the patients with non-severe PIH and 57% of the patients with normal pregnancy were primipara, whereas the percentage composition of multipara was 29%, 38% and 43% in severe PIH group, in non-severe PIH group and in normal pregnancy group respectively.

Sonal et al., 2018 showed that about 66.7% patients in gestational hypertension group and 60.8% patients in preeclampsia group were primigravida, whereas 40% of the patients with eclampsia were gravida 2 and 40% were multigravida (10). **Naaz et al., 2015**, in their study found that the mean age was 24.55 years in normal pregnant women with 45% primipara and 55% multipara. However, 60% primipara and 40% multipara in cases of pregnancy-induced hypertension had a mean age of 25.45 years (11). In a study by **Mohapatra et al., 2007**, women with mild PIH had mean age of 29.3 ± 2.8 years, women with preeclampsia had a mean age of 25.5 ± 3.6 years and women with eclampsia had a mean age of 25.7 ± 3.1 years. The control group included normal pregnant women with a mean age of 24.7 ± 3.4 years (12). The studies mentioned above correlated well with the present study.

Platelet Count:

Hematological abnormalities such as thrombocytopenia and reduction in some plasma clotting factors may develop in preeclamptic women. Transient mild thrombocytopenia is seen due to increased platelet consumption during pregnancy. A continuous decline in platelet count as pregnancy advances indicates that there is the possibility of platelet hyper-destruction during pregnancy. This together with hemodilution and platelet trapping results in decreased platelet count. Thrombocytopenia may precede various other manifestations of preeclampsia, and thus should be considered in the event of isolated thrombocytopenia seen in the late second or third trimester.

In the present study the mean platelet count of normal pregnancy, non-severe PIH and severe PIH groups were 2.89 lakhs/mm³, 2.22 lakhs/mm³ and 1.47 lakhs/mm³ respectively with significant P-value. The platelet count was less than 1.5 lakhs/mm³ in 3% of

the patients with normal pregnancy, 5% of the patients with non-severe PIH and 61% of the patients with severe PIH. The difference in mean platelet count was significant among all the groups.

Shete et al., 2013 showed that the mean platelet count in normal pregnancy was 3.41 lakhs/cubic mm and in severe PIH was 1.27 lakhs/cubic mm with significant p-value (13). **Jahromi et al., 2009** revealed that the mean platelet count of normal pregnancy and severe PIH were 2.33 lakhs/cubic mm and 1.5 lakhs/cubic mm with a significant p-value (14). **Sameer et al., 2014**, in their study found that the mean platelet count in normal pregnancy was 2.39 lakhs/cubic mm and in severe PIH was 1.6 lakhs/cubic mm with a significant p-value (15). **Mohapatra et al., 2007** exhibited that the mean platelet count in normal pregnancy was 2.38 ± 0.33 lakhs/cubic mm, mean platelet count in non-severe PIH was 1.82 ± 0.45 lakhs/cubic mm and mean platelet count in severe PIH was 1.21 ± 0.49 lakhs/cubic mm with significant P-value (12). Platelet count in the present study is in accordance with the studies conducted by other authors.

In present study, thrombocytopenia was a consistent finding, a systematic fall in platelet counts in relation to the severity of PIH was noted, Majority of cases with preeclampsia had thrombocytopenia and a decrease in platelet count was statistically significant from normal pregnancy to non-severe PIH to severe PIH, hence thrombocytopenia may help in identifying progression as well as the severity of the disease. However, its absence does not rule out a severe disease. Therefore, overall consideration of various laboratory tests and not only just one test has been made obvious. Platelet count is a simple, low cost, and rapid routine screening test. As normal platelet count does not rule out a severe disease, the present study shows that platelet count alone cannot be relied upon to assess the severity of PIH.

Prothrombin Time:

During pregnancy, the haemostatic system changes towards a more procoagulant state and lower levels of anticoagulants like protein S and C are seen. There is also increased level of coagulation factors. Prothrombin time is a functional test to measure enzymatic activity that leads to clot formation. Prothrombin time (PT) is used to evaluate for the status of the extrinsic coagulation pathway.

In the present study the mean prothrombin time for normal pregnancy, nonsevere PIH and severe PIH

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groups were 11.11 seconds, 10.28 seconds and 13.17 seconds respectively with significant p-value. About 23% of patients of normal pregnancy, 8% patients of non-severe PIH and 68% patients of severe PIH had prolonged PT with statistically significant difference between normal pregnancy and severe PIH group, non-severe PIH and severe PIH group. Statistical difference was not significant between normal pregnancy and non-severe PIH group.

In a study by **Priyadarshini et al., 2014**, the mean prothrombin time was 13.72 seconds among the cases with normal pregnancy and 15.27 seconds among the patients with preeclampsia with significant p value (16). **Lefkou et al., 2020**, in their study found that the mean value of prothrombin time in mild preeclampsia was 13.24 ± 0.80 seconds, in severe preeclampsia was 14.77 ± 0.96 seconds and in pregnant controls was 12.23 ± 0.59 seconds ($p < 0.05$ and $p < 0.001$ respectively) (17). In a study by **Jahromi et al., 2009**, the mean prothrombin time was 12.50 ± 0.76 seconds in normal pregnant women and 13.59 ± 4.04 seconds among women with severe preeclampsia with no statistically significant difference (p-value of 0.067) between the two groups (14). **Aref et al., 2012**, in their study showed that the mean prothrombin time for normal pregnancy and severe PIH patients were 13.24 ± 0.86 seconds and 13.41 ± 0.68 seconds respectively with P-value more than 0.05 (18). **Mushtaque T., 2013** revealed that the mean prothrombin time for normal pregnancy, non-severe PIH and severe PIH patients were 10.95 ± 1.12 seconds, 10.17 ± 0.75 seconds and 9.81 ± 0.89 seconds respectively and was statistically significant with p-value < 0.000 (19). Results of our study were similar to the study by **Priyadarshini et al., 2014** and nearly comparable to results of **Lefkou et al., 2020**. The discrepancy in results of this study to other studies mentioned above may be due to differences in sample size in their study.

As per findings of this study, PT can be used to identify severe PIH as well as the progression of disease from non-severe PIH to severe PIH but may not be used to identify the progression of disease from normal pregnancy to non-severe PIH as mean PT was not statistically significant between these groups. PT alone may not be helpful in identifying the severe PIH as it is not increased in every case of severe PIH. Evaluation of the intrinsic coagulation pathway by APTT and other coagulation parameters are required in conjunction with PT as a screening test to help in

monitoring the coagulation disorder in pregnancy-induced hypertension.

Activated Partial Thromboplastin Time:

With the development of preeclampsia, coagulation dysfunction is more significant, breaking the dynamic balance of hypercoagulable state in normal pregnancy and developing into a pathological hypercoagulable state. APTT can be used as a marker to distinguish normal hypercoagulable state of pregnant women from pathological hypercoagulable state caused by preeclampsia by detecting abnormal coagulation function of intrinsic coagulation pathway.

In present study the mean APTT for normal pregnancy, non-severe PIH and severe PIH patients were 29.36 seconds, 28.85 seconds and 35.15 seconds respectively, with significant P-value. APTT was increased in 19% of severe PIH group only. Statistically significant difference was found between normal pregnancy and severe PIH group, non-severe PIH and severe PIH group. Statistical difference was not significant between normal pregnancy and non-severe PIH group.

In a study by **Priyadarshini et al., 2014**, the mean APTT was 22.16 seconds among the normal pregnancy and 34.2 seconds among the patients of preeclampsia with significant p value (16). In a study by **Jahromi et al., 2009**, the mean activated partial thromboplastin time was 34.24 ± 2.52 seconds in normal pregnant women and 38.70 ± 64.58 seconds among women with severe preeclampsia with statistically significant difference (p value of 0.005) between the two groups (14). **Lefkou et al., 2020**, in their study found that the mean activated partial thromboplastin time was increased in mild preeclampsia and was 32.64 ± 1.83 seconds and in severe preeclampsia it was 35.59 ± 1.53 seconds and in pregnant controls it was 29.53 ± 1.62 seconds ($p < 0.001$) (17). Results of this study were nearly similar with the studies concluded by other authors.

In present study, although mean APTT was in normal reference range in most patients of all the groups, but significant increase in mean APTT was seen with severe PIH. APTT can be used to identify severe PIH as well as progression of disease from non-severe PIH to severe PIH but may not be used to identify progression of disease from normal pregnancy to non-severe PIH as mean APTT was not statistically significant between these groups. Therefore APTT

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provides more accurate information in severe preeclampsia patients and can be used as a reliable marker for assessing the severity of preeclampsia.

D-Dimer:

Preeclampsia is a multifactorial disease which is associated with microvasculature fibrin deposition and maternal organ dysfunction. D-dimer has been used as a marker of formation of fibrin degradation products in vivo. D-dimer has emerged as a useful diagnostic tool for thrombotic conditions because its plasma concentration has a high negative predictive value for venous thromboembolism especially seen in severe preeclampsia patients.

In present study mean D-Dimer levels of normal pregnancy, non-severe PIH and severe PIH were 201.05 ng/ml, 243.81 ng/ml and 314.32 ng/ml respectively with significant P-value. About 17% of patients of normal pregnancy, 27% patients of nonsevere PIH and 40% patients of severe PIH had raised D-Dimer. The difference in mean D-Dimer was significant among all the groups. In the current study D-dimer levels of severe PIH group and non-severe PIH group as compared to normal pregnancy group were significantly high, which is consistent with the study conducted by **Tacoosian et al., 2007** and **Bozkurt et al., 2015**. **Tacoosian et al., 2007**, in their study demonstrated to have D-Dimer levels of 721.43 ± 401.13 ng/ml in severe preeclampsia as compared to the D-Dimer levels of 322.26 ± 117.65 ng/ml in control group ($p < 0.001$) whereas **Bozkurt et al., 2015** reported that the average D-Dimer levels were 634 ± 228 ng/ml, 1426 ± 430 ng/ml, 2067 ± 580 ng/ml in control group, preeclamptic patients and eclamptic patients respectively (20, 21). The D-Dimer levels in preeclampsia and eclampsia patients were significantly higher than the control group ($p = 0.034$, $p = 0.020$) (21).

In this study increased D-dimer in PIH patients was indicating that with the development of PIH, the risk of vascular thromboembolism disease was increased. This study assessed plasma D-Dimer in PIH patients and normotensive pregnant women to define its diagnostic value in pregnancy induced hypertension. The findings of our study clearly highlighted that the D-dimer is a good indicator to monitor progression of the disease from normotensive pregnant to non-severe PIH to severe PIH. There is need for additional comprehensive coagulation studies throughout

pregnancy, in order to fully elucidate the diagnostic as well as prognostic role of D-Dimer in PIH.

Fibrinogen:

Fibrinogen is a major coagulation protein. In preeclampsia, the concentration of total fibrinogen is increased as compared to normal pregnancy. This may be a reflection of the exaggerated inflammatory response, and subsequent endothelial activation as key pathophysiological mechanisms in preeclampsia.

In present study mean Fibrinogen levels of normal pregnancy, non-severe PIH and severe PIH were 250.67 mg/dl, 285.6 mg/dl and 371.07 mg/dl respectively with significant P-value. 3% patients of normal pregnancy, 16% patients of non-severe PIH and 26% patients of severe PIH had prolonged Fibrinogen. Statistically significant difference was found between normal pregnancy and severe PIH group, non-severe PIH and severe PIH group. Statistical difference was not significant between normal pregnancy and non-severe PIH group.

In a study by **Naaz et al., 2015**, the mean fibrinogen level among the hypertensive pregnant women was 346.5 mg/dl and was 276.75 mg/dl among the normotensive pregnant women. The difference was statistically significant with p value < 0.002 (11). In the study conducted by **Manten et al., 2003**, it was found that the median (range) total fibrinogen concentration in the pre-eclampsia group was 5.04 (3.25-6.51) g/l and in the healthy pregnant control group was 4.19 (3.61-5.38) g/l ($p < 0.05$) (22). Results of present study were nearly similar to the results of **Naaz et al., 2015** and **Manten et al., 2003**. **Jahromi et al., 2009**, in their study found no statistically significant difference between normal pregnant women and preeclamptic patients for fibrinogen levels which were 298.08 ± 32.37 mg/dl and 238.78 ± 64.58 mg/dl in normal pregnant women and women with severe preeclampsia respectively with p-value of 0.166 (14). Discrepancy in results of this study to other studies mentioned above may be due to difference in sample size in their study.

This study indicated that increased plasma fibrinogen may provide information for future risk of developing thromboembolic disorder in PIH. Therefore, estimation of the plasma fibrinogen levels in PIH can help in minimizing the further complications like disseminated intravascular coagulation thereby

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reducing both maternal and fetal mortality and morbidity.

Maternal and Fetal outcome:

With the development of preeclampsia, the coagulation factors get reduced along with platelet consumption forming micro thrombus. This would lead to ischemia and hypoxia of vital organs and the development of eclampsia, HELLP syndrome, disseminated intravascular coagulation (DIC), and multiple organ dysfunction syndrome (MODS), which seriously threaten the life of mother and child and primarily cause maternal and fetal death.

The most common complications of severe PIH identified in this study were HELLP syndrome (13.5%), disseminated intravascular coagulopathy (9.7%) and placental abruption (9.7%). There were 2.7% cases of both HELLP syndrome and disseminated intravascular coagulopathy in non-severe PIH patients. In present study, maternal death was recorded in 6.5% cases with severe PIH group whereas no maternal death was there in non-severe PIH group and in normal pregnancy group. **Mahran et al., 2017** quoted that in patients of eclampsia, the most common complication was HELLP syndrome (15.6%) followed by postpartum haemorrhage (9.6%) and disseminated intravascular coagulopathy (7.6%) along with 1.6% maternal mortality, which was in accordance with our study (23). The findings in present study differ from studies done by **Sobande et al., 2007** and **Chibber et al., 2016**, where no maternal deaths were reported in patients with severe PIH (24, 25) and also **Chibber et al., 2016** reported that placental abruption was the most common complication in severe PIH patients (25). The present study highlighted that maternal complications were more common with decreased platelet count and deranged coagulation profile.

There were 16% of stillbirths and 26% of low birth weight in severe PIH group while 2.7% of stillbirths and 8.1% of low birth weight in non-severe PIH group and 1.7% of both stillbirths and low birth weight in normal pregnancy group. **Sobande et al., 2007** reported that the perinatal mortality rate was 16.6% and 14.1% among the eclamptics and severe pre-eclamptic patients respectively (24). **Bilano et al., 2014** showed that perinatal mortality was 3.26% in preeclampsia and eclampsia in Latin America. In Asian countries with low or middle income, the perinatal mortality in preeclampsia and eclampsia

varies from 1.3% in Vietnam to 15.76 % in Nepal (26). **Odegard et al., 2000** observed 12% low birth weight infants in patients of severe preeclampsia (27). Results of the current study was nearly similar to the study done by **Sobande et al., 2007**, **Bilano et al., 2014** and **Odegard et al., 2000**. The present study highlighted that stillbirths and low birth weight were more common with decreased platelet count and deranged coagulation profile.

After the onset of complications such as HELLP syndrome and DIC, the diagnosis is simplified but the treatment becomes difficult. Pregnancy-induced hypertension can also lead to adverse perinatal outcomes such as intra uterine growth retardation, preterm delivery, low birth weight and stillbirths. Thus it is important to diagnose the impending complications at subclinical stage so that early therapeutic measures can be instituted. Therefore from our study, the estimation of platelet count, PT, APTT, D-Dimer and Fibrinogen levels especially in patients of severe PIH can be helpful not only in the early diagnosis of haemostatic failure but also to guide the clinicians towards necessary therapeutic measures thereby reducing maternal and fetal morbidity and mortality.

Conclusion

The present case-control study was conducted on total 128 pregnant females comprising of diagnosed cases of PIH and normal pregnant females were taken as controls. Platelet count, PT, APTT, D-Dimer and fibrinogen levels in 128 pregnant females (31 Severe Preeclampsia (BP above 160/110 mmHg), 37 Non-Severe Preeclampsia (BP ranges between 140/90 mmHg and 160/110 mmHg), and 60 Normal Pregnant Females) were evaluated and then correlated with the clinical outcomes.

In this study, the mean platelet count significantly decreases while mean D-Dimer significantly increases with increasing severity of PIH. The mean PT, mean APTT and mean fibrinogen levels for the severe PIH group were significantly higher as compared to non-severe PIH and normal pregnancy groups.

Statistical difference was not significant between the normal pregnancy group and the non-severe PIH group. Maternal and Fetal complications are more common with severe PIH, decreased platelet count and deranged coagulation profile.

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The statistical results and the reviewed articles suggest that the coagulation profile is an important tool in the early detection of coagulation failure and its management before the condition worsens. Therefore this study concludes that platelet count and D-dimer levels can be used to monitor the progression of pregnancy-induced hypertension and raised PT, APTT and fibrinogen levels are fairly good indicators of severe pregnancy-induced hypertension.

Predicting the development of severe preeclampsia has consistently been a difficult problem. However, so far, no effective and reliable prediction methods are available. Several published studies have shown the degree of hypercoagulability is positively correlated with the severity in patients of preeclampsia. Therefore, monitoring the status of coagulation-fibrinolysis system through evaluation of platelet count and coagulation profile including PT, APTT, D-Dimer and Fibrinogen, in preeclampsia patients could be helpful in assessing the disease severity leading to early clinical intervention and improvement in the prognosis of mother and infant.

Strength of the study

1. The present study can be helpful in identifying the patients with pregnancy induced hypertension at an early stage.
2. Maternal and fetal complications can be predicted early and patients with pregnancy-induced hypertension can be followed accordingly for antenatal care.

Limitation of the study

1. Simple, cheaper and cost-effective tests like bleeding time and clotting time should also be used for the diagnosis of coagulation defects in pregnancy induced hypertension.
2. This study was not performed on the serial estimation of platelet count and coagulation profile at regular intervals from the first trimester to predict the severity of pregnancy-induced hypertension and its complications, as it was difficult to follow up patients due to hindrance in outpatient services provided throughout the COVID pandemic.
3. The sample size of the present study is low due to the COVID pandemic. A better study can be performed with a large sample size for more precise results.

Declarations

Funding: No external funding was received for this study.

Conflict of Interest: The authors declare no conflict of interest.

References

1. Cunningham F.G, Kenneth J. Leveno, Steven L. Bloom, John C. Hypertensive Disorders. In: Kenneth J. Leveno, Steven L. Bloom. Eds. Williams Obstetrics. 24th ed. New York: McGraw-Hill; 2014:728-79.
2. Kashanian M, Hajjarian M, Khatami E, Sheikhsari N. Evaluation of the value of the first and third trimester maternal mean platelet volume (MPV) for prediction of pre-eclampsia. *Pregnancy Hypertens: Int. J. Women's Cardiovascular health.* 2013;3(4):222-226.
3. Vijayalakshmi S, Kavitha D. Comparative analysis of coagulation profile in pregnancy induced hypertensive women and in normotensive pregnant women in a tertiary care hospital. *Int. J. Sci. Res.* 2020;9(1):62-64.
4. Mishra R. Ian Donald's practical obstetric problems. 6th ed. New Delhi, BI Publications; 2007:280-309.
5. Norwitz ER, Hsu CD, Repke JT. Acute complications of preeclampsia. *Clin Obstet Gynecol* 2002;45(2):308-29.
6. Leduc LI, Wheeler JM, Kirshon BR, Mitchell P, Cotton DB. Coagulation profile in severe pre eclampsia. *Obstet Gynecol* 1992;79(1):14-28.
7. Metz J, Cincotta R, Francis M, DeRosa L, Balloch A. Screening for consumptive coagulopathy in preeclampsia. *Int J Gynecol Obstet* 1994;46(1):3-9.
8. Kramer RL, Izquierdo LA, Gilson GJ, Curet LB, Qualls CR. "Preeclamptic labs" for evaluating hypertension in pregnancy. *J Reprod Med.* 1997;42(4):223-28.
9. Barron WM, Heckerling P, Hibbard JU, Fisher S. Reducing unnecessary coagulation testing in hypertensive disorders of pregnancy. *Obstet Gynecol.* 1999;94(3):364-70.
10. 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):1-7.
11. Naaz A, Sushma P, Ahmed MM, Sarma DV, Baig AA, Reddy K. A Study on Fibrinogen Levels and Platelet Count in Pregnancy Induced Hypertension. *Int. J. Sci. Res.* 2015;5(3):1-8.
12. Mohapatra S, Pradhan BB, Satpathy UK, Mohanty A, Pattnaik JR. Platelet estimation: its prognostic value in pregnancy induced hypertension. *Indian J. Physiol. Pharmacol.* 2007;51(2):160-64.

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13. Shete Anjali N, K.D Gaikal, Prathiba R. Deshmukh. Physiological parameters in Pregnancy Induced Hypertension. *Int. j. recent trends sci. technol.* 2013;7(1):24-25.
14. Jahromi BN, Rafiee SH. Coagulation factors in severe pre eclampsia. *Iran. Red Crescent Med.* 2009;11(3):321-24.
15. Sameer MA, Meshram DP, Despande, Sadupandi. *J. Med. Dent. Sci.* 2014;13(4):39-43.
16. Priyadarshini GP, Mohanty RR. Assessment of coagulation profile and its correlation with severity of preeclampsia in women of odisha-a comparative cross-sectional study. *Int J Basic Applied Physiol.* 2014;3(1):234-40.
17. Lefkou E, Van Dreden P, Rousseau A, Gerotziafas GT. Differences in the Coagulation Profile in Women with Mild and Severe Preeclampsia. *Blood.* 2020;136:15-26.
18. Aref WM, Mazny AE, Mazny AE. Liver dysfunction and ultrasonographic findings in pregnancy induced hypertension compared to late normal pregnancy. *Am. J. Sci.* 2012;8(8):74-78.
19. Mushtaque T. A comparative study of coagulation profile in term normal pregnancy, preeclampsia and eclampsia. 2013
20. Tacosian Z, Hajseyed Javadi E, Farzam SA, Javadi A. Evaluation of correlation between pre- eclampsia with D-Dimer. *J. Qazvin Univ. Med. Sci.* 2007;11(1):62-66.
21. Bozkurt M, Yumru AE, Sahin L, Salman S. Troponin I and D-Dimer levels in preeclampsia and eclampsia: prospective study. *Clin Exp Obstet Gynecol.* 2015;42(1):26-31.
22. Manten GT, Sikkema JM, Franx A, Hameeteman TM, Visser GH, De Groot PG, Voorbij HA. Increased high molecular weight fibrinogen in pre-eclampsia. *Thrombosis research.* 2003;111(3):143-47.
23. Mahran A, Fares H, Elkhateeb R, Ibrahim M, Bahaa H, Sanad A, Gamal A, Zeeneldin M, Khalifa E, Abdelghany A. Risk factors and outcome of patients with eclampsia at a tertiary hospital in Egypt. *BMC pregnancy and childbirth.* 2017 Dec;17(1):1-7.
24. Sobande AA, Eskandar M, Bahar A, Abusham A. Severe pre-eclampsia and eclampsia in Abha, the south west region of Saudi Arabia. *J Obstet Gynaecol.* 2007;27(2):150-4.
25. Chibber R, Al-Hijji J, Amen A, Fouda M, Kaleemullah ZM, El-Saleh E, et al. Maternal and perinatal outcome of eclampsia over a decade at a tertiary hospital in Kuwait. *J. Matern.-Fetal Neonatal Med.* 2016;29(19):3132-37.
26. Bilano VL, Ota E, Ganchimeg T, Mori R, Souza JP. Risk factors of preeclampsia/ eclampsia and its adverse outcomes in low- and middle-income countries: a WHO secondary analysis. *PloS one.* 2014;9(3).
27. Odegard RA, Vatten LJ, Nilsen ST, Salvesen KA, Austgulen R. Preeclampsia and fetal growth. *Obstet Gynecol.* 2000;96(6):950-55.