

# Antithrombin-III level and Platelet Count in Pregnancy Induced Hypertension (PIH): A Cross-Sectional Study from a Tertiary Care Centre of North-Eastern India

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## ABSTRACT

**Introduction:** Pregnancy Induced Hypertension (PIH) is one of the most common disorders seen in human pregnancies. Approximately 1,00,000 women die worldwide per annum because of eclampsia. It is said that pre-eclampsia and eclampsia contribute to death of a woman every 3 minute worldwide. In India the incidence of pre-eclampsia is reported to be 8-10% of the pregnancy. It is the third leading cause of maternal mortality responsible for 17% of maternal deaths. Hence, this study was undertaken to determine the changes in the level of plasma Antithrombin-III and Platelet count in pre-eclamptic woman and its correlation with severity of disease in order to evaluate if it can be used as a marker of severity of pregnancy induced hypertension (PIH).

**Material and Methods:** Total 90 PIH cases in their third trimester of pregnancy comprising of 30 Mild Pre-eclampsia, 30 Severe Pre-eclampsia and 30 Eclampsia patients were enrolled for the study. The necessary laboratory investigations required for the study was carried out in the Advanced Hematology, Service Laboratory under Department of Pathology in a tertiary care centre of North-eastern India by using SYSMEX XS-800i 5 part haematology analyzer and SYSMEX CA-500 series Coagulometer. Data were analyzed using MS Excel 2007 and GraphPad Prism 7.

**Results:** In PIH patients Antithrombin-III level and Platelet count shows a gradual and almost linear reduction in various groups ranging from mild pre-eclampsia to eclampsia.

**Conclusion:** It was concluded from the study that the reduction of platelet count and antithrombin-III are the main predictors to predict and monitor the severity of PIH.

**Keywords:** Antithrombin-III, Eclampsia, Platelet Count, Pre-Eclampsia, Pregnancy induced Hypertension

## INTRODUCTION

Pregnancy induced hypertension (PIH) still remains a nightmare for every obstetrician. Eclampsia is an easily recognizable event and has been described in the medical literature as long as 4200 ago. Approximately 1, 00, 000 women die worldwide per annum because of eclampsia.<sup>1</sup> It is said that pre-eclampsia and eclampsia contribute to death of a woman every 3 minute worldwide.<sup>2</sup> In India the incidence of pre-eclampsia is reported to be 8-10% of the pregnancy.<sup>3</sup> It is the third leading cause of maternal mortality responsible for 17% of maternal deaths.<sup>3,4</sup> Pre-eclampsia was diagnosed according to American College of Obstetrics and Gynaecology (ACOG) criteria;<sup>5</sup> a blood pressure higher than 140/90 mm of Hg, edema and proteinuria >300mg/24 hours or  $\geq 1+$  dipstick method after 20<sup>th</sup> week of gestation. Patient with blood pressure > 140/90 mm of Hg but <160/110 mm of Hg without proteinuria were included in the mild cases. And patient with blood pressure  $\geq 160/110$  mm of

Hg, proteinuria and presence of headache, visual disturbances, upper abdominal pain, oliguria and thrombocytopenia were included in severe cases. Eclampsia is defined as pre-eclampsia associated with seizures.

Antithrombin-III (AT-III) which is an  $\alpha$ -2-globulin, exercises potent activity against thrombin and other serine proteases generated during coagulation. The mature antithrombin molecule has a molecular weight of 58, 200 d with 432 amino acids.<sup>6,7</sup> The liver is the primary source of antithrombin synthesis and posttranslational glycosylation.<sup>8</sup> The fall in the platelet count is most frequent abnormality and is probably due to consumption during low-grade intravascular coagulation.<sup>9</sup> Hence, this study was undertaken to determine the changes in the level of plasma Antithrombin-III and Platelet count in pre-eclamptic woman and its correlation with severity of disease in order to evaluate if it can be used as a marker of severity of pregnancy induced hypertension (PIH).

## MATERIAL AND METHODS

A hospital based cross-sectional study was conducted for a period of one year from July 2014 to June 2015. All antenatal cases diagnosed as PIH both indoor and outdoor, in the Department of Obstetrics and Gynaecology, in a tertiary care centre of North-Eastern India, were enrolled for the study. 90 cases of PIH in their third trimester, comprising of 30 Mild Pre-eclampsia, 30 Severe Pre-eclampsia and 30 Eclampsia patients were included.

Ethical clearance was obtained from the Institutional Ethics Committee for conducting the study. Details of the study were explained to the subjects and written informed consent was taken from all the study subjects.

For Hematological parameters, blood was collected by venepuncture using a plastic syringe and 21-gauge needle, directly into two vials. One of the vials containing 0.5 ml sodium citrate (3.2%, 0.11M) to give a ratio of 9 volumes of blood to 1 volume of sodium citrate was used for coagulation studies while the other vial containing EDTA as anticoagulant was used for platelet count. Blood samples so collected were

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transported without delay to the Advanced Haematology service Laboratory, Pathology Department, in a tertiary care centre of North-Eastern India.

The platelet count was done in SYSMEX XS-800i 5 part haematology analyser with the blood collected in the EDTA vial and Antithrombin-III was done in SYSMEX CA 500 automated analyzer.

**Criteria for selection of cases**

Pregnant females in their third trimester with signs and symptoms of PIH were included in the study. Criteria for selection is elevation of systolic blood pressure above 140mm of Hg and/or diastolic blood pressure above 90mm of Hg or a rise in former of at least 15mm of Hg above baseline value on at least two occasions and at least 6 hours apart. All the patients fulfilling these criteria with or without edema or proteinuria after 20 weeks of pregnancy were included in the study.

**Exclusion criteria**

1. All cases with pre-existing hypertension other than PIH.
2. Patients having co morbid conditions such as
  - Severe anaemia
  - Diabetes mellitus
  - H/o auto immune disorder.
  - H/o I.T.P. (Idiopathic Thrombocytopenic Purpura)
  - H/o receiving drugs like aspirin, anti-coagulants etc
3. Patients who didn't give consent for the study.

**STATISTICAL ANALYSIS**

Data were presented with percentages and mean with standard deviation. Statistical significance among the groups were assessed using ANOVA (Analysis of Variance) followed by Bonferroni. Data were analyzed using MS Excel 2007 and GraphPad Prism 7.

**RESULTS**

Majority (75.56%) of PIH cases belonged to the 20–29 years age group. The mean platelet count among the mild pre-eclampsia cases was 2, 05, 530 (± 41994.85) per mm<sup>3</sup> and 1, 03, 370 (± 19255.96) per mm<sup>3</sup> among the eclampsia cases. The platelet count decreased significantly with the increase in severity.

The mean AT-III level among the mild pre-eclampsia cases was 101.81 (± 6.57)%. It was found to be 84.59 (± 8.14)% and 76.00 (± 7.42)% among the severe preeclampsia and eclampsia cases respectively. A statistically significant decrease in the AT-III level was observed with the increase in severity of PIH.

All (100%) the mild pre-eclampsia cases had normal AT-III level whereas in severe pre-eclampsia and eclampsia cases only 53.30% and 46.70% had normal AT-III level respectively. A statistically significant association was observed between severity of PIH and AT-III level.

Majority (86.70%) of the mild pre-eclampsia cases had normal platelet count. Among the eclampsia cases, all (100%) had abnormal platelet count. A statistically significant association was observed between severity of PIH and platelet count.

**DISCUSSION**

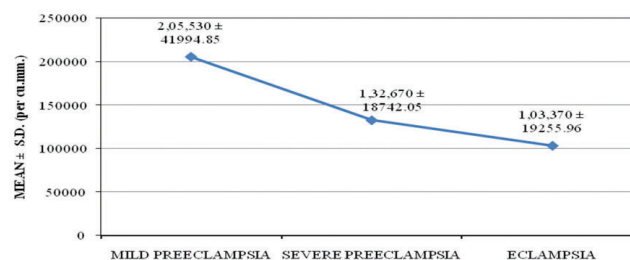
In the present study, the AT-III level was found to be normal in all (100%) of the mild pre-eclampsia cases, whereas in severe pre-eclampsia and eclampsia cases only 53.30% and 46.70% had normal AT-III level respectively. Decrease in the

Study group	Platelet Count [mean ± S.D. (per cu.mm.)]	p value
Mild Preeclampsia	2, 05, 530 ± 41994.85	p < 0.05
Severe Preeclampsia	1, 32, 670 ± 18742.05	
Eclampsia	1, 03, 370 ± 19255.96	
Mild Preeclampsia vs. Severe Preeclampsia		p < 0.05
Mild Preeclampsia vs. Eclampsia		p < 0.05
Severe Preeclampsia vs. Eclampsia		p < 0.05

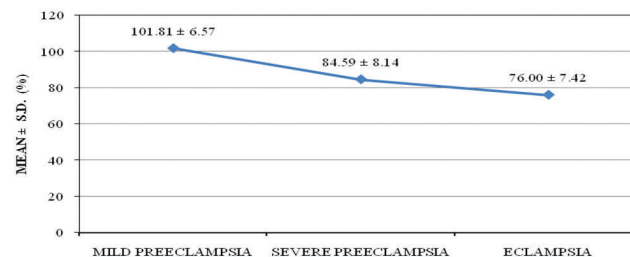
**Table-1:** Correlation of platelet count with the severity of PIH

Study group	AT-III [Mean ± S.D. (%)]	p value
Mild Preeclampsia	101.81 ± 6.57	p < 0.05
Severe Preeclampsia	84.59 ± 8.14	
Eclampsia	76.00 ± 7.42	
Mild Preeclampsia vs. Severe Preeclampsia		p < 0.05
Mild Preeclampsia vs. Eclampsia		p < 0.05
Severe Preeclampsia vs. Eclampsia		p < 0.05

**Table-2:** Correlation of AT-III level with the severity of PIH



**Figure-1:** Correlation of platelet count with the severity of PIH



**Figure-2:** Correlation of AT-III level with the severity of PIH

AT-III level with the increase in severity of PIH was found to be statistically significant.

Sarkar PD et al.<sup>10</sup> (2013) in their study found that the mean AT-III level in mild pre-eclamptic and severe pre-eclamptic study subjects was 78.32 (± 3.09)% and 70.84 (± 6.90)% respectively. The decrease in AT-III in severe pre-eclamptic women was highly significant compared to that of mild pre-eclamptic pregnant women.

In a study conducted by Cengiz D et al.<sup>11</sup> (2010) on natural coagulation inhibitors and active protein c resistance in pre-eclampsia found that AT-III values were significantly lower in pre-eclamptic patients than in the control groups (p=0.001).

Marietta M et al.<sup>12</sup> (2007) in their study on antithrombin plasma level in pre-eclampsia patients observed a statistically significant decrease in the antithrombin plasma level with worsening of pre-eclampsia.

Srivastava M et al.<sup>13</sup> (1995) in their study on antithrombin-III level in pregnancy induced hypertension observed that the

antithrombin-III activity decreased linearly with the increase in the severity of PIH. The AT-III activity was observed to be positively correlated with PIH.

The findings of the present study are therefore in accordance to the study conducted by Sarkar PD et al.<sup>10</sup> (2013), Cengiz D et al.<sup>11</sup> (2010), Marietta M et al.<sup>12</sup> (2007) and Srivastava M et al.<sup>13</sup> (1995).

In the current study, the platelet count decreased significantly with the increase in severity.

Chauhan P et al.<sup>14</sup> (2014) in their study observed a statistically significant decrease in platelet count with an increase in severity of PIH.

Sarkar PD et al.<sup>10</sup> (2013) in M.G.M. Medical College, Indore conducted a study to determine the changes in the level of plasma Antithrombin-III (AT-III) and platelet count in pre-eclamptic women and its comparison with healthy non-pregnant women and normal pregnant women and observed a statistically significant difference in the platelet count between healthy non-pregnant women and pre-eclamptic women and normal pregnant women and pre-eclamptic women.

Mohapatra S et al.<sup>15</sup> (2007) in their study in S.C.B Medical College, Cuttack observed that there is an inverse relationship between the severity of PIH and platelet numbers.

Vrunda JK et al.<sup>16</sup> (2004) in their study on platelet count in PIH patients observed that thrombocytopenia is directly proportional to the severity of PIH.

Shete AN et al.<sup>17</sup> (2013), Government Medical College, Aurangabad, conducted a study to assess the Physiological stress during Pregnancy Induced Hypertension and observed a significant decrease in platelet count.

In a study conducted by Sultana R et al.<sup>18</sup> (2012) on platelet count in preeclampsia, it was observed that the mean platelet count in cases and controls were 1, 44, 260±96, 472 and 1, 98, 100±51, 219 respectively. The study revealed that low platelets count is associated with pre-eclampsias.

The findings of the current study therefore correlates with the study conducted by Chauhan P et al.<sup>14</sup> (2014), Sarkar PD et al.<sup>10</sup> (2013), Mohapatra S et al.<sup>15</sup> (2007), Vrunda JK et al.<sup>16</sup> (2004), Shete AN et al.<sup>17</sup> (2013) and Sultana R et al.<sup>18</sup> (2012).

## CONCLUSION

In the light of the results obtained from the present study, we can say that both the haematological parameters (platelet count and antithrombin-III) show considerable derangement in patients suffering from pregnancy induced hypertension. These coagulation parameters can therefore be used to predict and monitor the severity of the disease. Timely measurement of these parameters and prompt treatment might reduce systemic complications and maternal deaths due to pregnancy induced hypertension.

## REFERENCES

1. Shah M R. Hypertensive disorders in pregnancy. 1st edn published by Jaypee. 2007:1-10.
2. Cunningham F G, Leveno K J, Bloom S L, Hauth J C, Gilstrap III. L. C, Wenstrm K. D. Hypertensive disorders in pregnancy. Ch 37 In William Obstetrics. 21st edn published by McGraw Hill Company. 2002:871-907.
3. Krishna Menon M. K. and Palaniappan B. Hypertensive disorders of pregnancy. In MudlairMenon (Ed.). Clinical

Obstetrics. 9th edn. Orient Longman Madras. 1994;133-159.

4. Mackay AP, Berg CJ. Pregnancy related mortality from pre-eclampsia and eclampsia. *Obstet. Gynecol.* 2001;97: 533-538.
5. Management of Preeclampsia. Washington, DC: American College of Obstetricians and Gynecologists; 1986. ACOG Technical Bulletin No. 91.
6. Bock SC, Wion KL, Vehar GA, et al. Cloning and expression of the cDNA for human antithrombin III. *Nucleic Acids Res.* 1982;10:8113-8125.
7. Petersen TE, Dudek-Wojciechowski G, Sottrup-Jensen L, et al. Primary structure of antithrombin III (heparin cofactor): partial homology between alpha 1 antitrypsin and antithrombin III. In: Collen D, Wiman B, Verstraete M, eds. *The Physiological Inhibitors of Blood Coagulation and Fibrinolysis.* Amsterdam, The Netherlands: Elsevier Science. 1979:43-54.
8. Prochownik EV, Orkin SH. In vivo transcription of a human antithrombin III "minigene". *J Biol Chem.* 1984; 259:15386-15392.
9. Halligan A, Bonnar J, Sheppard B, et al. Haemostatic, fibrinolytic and endothelial variables in normal pregnancies and pre-eclampsia. *Br J Obstet Gynaecol.* 1994;101:488.
10. Sarkar PD, Sogani S. Association of antithrombin-III and platelet count with pregnancy induced hypertension. *Int J Reprod Contracept Obstet Gynecol.* 2013;2:398-401.
11. Cengiz D, ImdatDilek. Natural coagulation inhibitors and active protein c resistance in preeclampsia. *CLINICS.* 2010; 65:1119-1122.
12. Marietta M, Simoni L, Pedrazzi P, Facchini L, D'amico R, Facehinetti F. Antithrombin plasma levels decrease is associated with preeclampsia worsening. *Journal compilation 2008 Blackwell Publishing Ltd, Int. Jnl. Lab. Hem:* 1-6.
13. Srivastava M, Bali S, Pandey J, NayarV, Talib VH. Pregnancy Induce Hypertension and Antithrombin-III. *Indian J Pathol Microbiol.* 1995;38:257-260.
14. Chauhan P, Rawat U, Bisht V, Purohit RC. Comparison of Coagulation Profile in Pre-Eclamptic and Eclamptic Patients with Normotensive Pregnant Patients. *Journal of Evolution of Medical and Dental Sciences.* 2014;3:3208-3215.
15. Mohapatra S, Pradhan BB, Satpathy UK, Mohanty A, Pattnaik JR. Platelet estimation: its prognostic value in pregnancy induced hypertension. *Indian J Physiol Pharmacol.* 2007;51:160-4.
16. Vrunda JK, Shaila S. Lowered platelet count: A Prognostic Index in Pregnancy Induced Hypertension. *J Obstet Gynecol Ind.* 2004;54:235-6.
17. Shete AN, Garkal KD, Deshmukh PR. Physiological Parameters in Pregnancy Induced Hypertension. *International Journal of Recent Trends in Science And Technology.* 2013;7:24-25.
18. Sultana R, Karim SM, Atia F, Ferdousi S, Ahmed S. Platelet Count In Preeclampsia. *J. Dhaka National Med. Coll. Hos.* 2012;18:24-26.

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