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Original Article

Pathology Section

Comparison Study of Coagulation Profile in Normal Term Pregnancy and Pregnancy Induced Hypertension

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ABSTRACT

Introduction: Pregnancy Induced Hypertension (PIH) is one of the commonest medical disorders in pregnancy, which is divided into three categories: gestational hypertension, pre-eclampsia and eclampsia. Hypercoagulable state in pregnancy and presence of any provocative factor can easily upset the normal balance culminating into Disseminated Intravascular Coagulation (DIC). In PIH, due to endothelial injury, the delicate haemostatic mechanism is triggered, which leads to coagulation failure.

Aim: To compare the coagulation profile in normal term pregnancy and PIH during third trimester and to diagnose the severity of hypertensive disorders in pregnancy with coagulation parameters, clinical profile and to compare it with healthy controls.

Materials and Methods: The present prospective study included 25 normotensive pregnant women and 80 pregnant women with signs and symptoms of pre-eclampsia and eclampsia in third trimester of gestation, over a period of one year. Study included clinical profile, age wise and parity distribution and coagulation parameters like platelet count, Prothrombin Time (PT), activated Partial Thromboplastin Time (aPTT) and D-dimer in PIH and compared with healthy controls.

Results: Most of the cases (56.25%) were in the age group 20-24 years and most were primipara. Mean systolic blood pressure in mild pre-eclampsia, severe pre-eclampsia and eclamptic patients was 146 mmHg, 164 mmHg and 168 mmHg, while the mean diastolic blood pressure was 94 mmHg, 110 mmHg, 106 mmHg, respectively. The significant proteinuria in mild pre-eclampsia, severe pre-eclampsia and eclampsia was 12 (34.29%), 17 (60.71%), and 09 (52.94%) respectively. Oedema was less severe in mild pre-eclampsia, whereas headache, blurring of vision and right upper abdominal pain were seen in severe cases of PIH. The mean haemoglobin in mild pre-eclampsia, severe pre-eclampsia and eclampsia was 10.8 gm/dL, 11.1 gm/dL, 11.5 gm/dL, respectively, whereas, platelet count was significantly lower than that of healthy pregnant control. There was prolongation of prothrombin time and significant difference between PT, aPTT D-dimer in mild pre-eclampsia, severe pre-eclampsia and eclampsia and that of healthy controls.

Conclusion: The degree of thrombocytopenia increases with severity of disease. Early assessment of severity of PIH can be done to prevent complications and to monitor the disease progression.

Keywords: Coagulation parameters, Eclampsia, Pre-eclampsia

INTRODUCTION

The Pregnancy Induced Hypertension (PIH) is one of the commonest medical disorders in pregnancy diagnosed by obstetricians in clinical practice. It is divided into three categories: Gestational hypertension, pre-eclampsia and eclampsia [1]. Gestational hypertension is defined as development of new arterial Hypertension (blood pressure ≥140/90 mmHg) measured on two separate occasions more than 6 hours apart without the presence of protein in the urine and diagnosed after 20 weeks of gestation. Pre-eclampsia, is a multisystem disorder of unknown aetiology characterised by development of hypertension to the extent of 140/90 mmHg or more with proteinuria after the 20th week in a previously normotensive and non-proteinuric women. Its clinical types include mild and severe. Eclampsia is defined as when pre-eclampsia is complicated with convulsions and/or coma, which may occur quite abruptly, without any warning manifestations [1]. In PIH due to endothelial injury, the delicate haemostatic mechanism is triggered, which leads to coagulation failure [2]. In PIH, blood pressure alone is not always a dependable indicator of severity. Convulsions are usually preceded by unrelenting severe headache or visual disturbances; thus these symptoms are considered ominous. Oedema of pre-eclampsia is pathological; it usually involves the face and hands. Proteinuria is an important indicator of severity because it usually develops late in the course of the disease. The seizures may appear before, during or after labour. Seizures develop more than 48 hours postpartum, however especially in primipara may be encountered upto 10 days postpartum [2]. In India, gestational hypertension continues to be responsible for the largest proportion of perinatal death resulting from prematurity and Intra Uterine Growth Retardation (IUGR) and is a major contributor to perinatal and maternal morbidity and mortality [1]. The aim of the study was to compare the coagulation profile in normal term pregnancy and PIH during third trimester and to diagnose the severity of hypertensive disorders in pregnancy including coagulation parameters, clinical profile and their comparison with healthy controls.

MATERIALS AND METHODS

The present prospective study included normotensive pregnant women (control) and pregnant women with signs and symptoms of pre-eclampsia and eclampsia in third trimester of gestation, who attended the Department of Obstetrics and Gynaecology and were referred to Department of Pathology of Sarojini Naidu Medical College, Agra, Uttar Pradesh, India over a period of one year (March 2015 to February 2016). The ethical clearance number for the present work is ST/PG Thesis Proforma/IEC-2014/2015/14 dated 30.01.2015. The study was carried out on 80 pregnant women with PIH who

visited antenatal clinic and maintained complete follow-up records and were compared with 25 normal term (controls pregnant women (less controls because of high cost of tests), after taking informed consent. Inclusion criteria for the study were: Pregnant women in third trimester of gestation with pre-eclampsia and eclampsia, normotensive pregnant women in 3rd trimester of gestation (controls). Exclusion criteria were: Patients with bleeding disorders, patients on anticoagulant therapy, abruption placenta, Intrauterine Device (IUD), twin pregnancy, with established Disseminated Intravascular Coagulation (DIC), renal disorder and hydatidiform mole.

Haematological investigations performed were platelet count- by automated hematology analyser, Prothrombin Time (PT) and activated Partial Thromboplastin Time (aPTT) by fully automated coagulometer, and D-dimer fluorescence immunoassay.

STATISTICAL ANALYSIS

Statistical analysis was done comparing coagulation profile in normal term pregnancy and PIH using student's t-test. Statistical software used was Matlab 9.0 and MS Excel. p value less than 0.05 was considered as statistically significant.

RESULTS

Out of 80 cases of PIH studied, 35 had mild pre-eclampsia, 28 had severe pre-eclampsia, and 17 had eclampsia. Maximum women with PIH were in the age group of 20-24 years age group followed by 25-29 years, 15-19, >30 years, whereas in healthy control group, maximum cases were in the age group of 20-24 years followed by 25-29 years 15-19 years and >30 years. The range in this group was 18-30 years and mean of 23.8 years. Thus, about 92% of pregnant control cases had age in between 20-29 years. Most of the patients with mild pre-eclampsia, severe pre-eclampsia and eclampsia were in the age group 20-24 years followed by age group of 25-29 years. Parity distribution in patients with various categories of PIH cases and healthy control group are shown in [Table/Fig-1].

Observations on the clinical parameters as mean systolic and diastolic blood pressure, proteinuria, pathological oedema in mild pre-eclampsia, severe pre-eclampsia and eclamptic patients is presented in [Table/Fig-2]. Symptoms like headache, blurring of vision and right upper abdominal pain were seen in severe cases of PIH. The mean Hb concentration in mild pre-eclampsia, severe pre-eclampsia and eclampsia was 10.8 gm/dL (5.1-13.9), 11.1 gm/dL (6.2-14.5), 11.5 gm/dL (7.9-15.0), respectively [Table/Fig-2].

Statistical analysis of coagulation profiles in healthy pregnant control group, mild pre-eclampsia, severe pre-eclampsia and eclampsia for Platelet count, PT, aPTT and D-dimer of normal pregnancy is shown in [Table/Fig-3].

It was seen that the platelet count in mild pre-eclampsia, severe pre-eclampsia and cases with eclampsia were significantly lower than that of healthy pregnant control {248400±56397 (150000-390000)}.

S. No.	Parity	Mild pre-eclampsia		Severe pre-eclampsia		Eclampsia		Total		Healthy control group (n=25)	
		No.	%	No.	%	No.	%	No.	%	No.	%
1.	Primipara	17	48.57	19	67.86	12	70.59	48	60.00	10	40
2.	II para	11	31.43	6	21.43	3	17.65	20	25.00	7	28
3.	III para or > III para	7	20.00	3	10.71	2	11.76	12	15.00	8	32
4.	Total	35	100.00	28	100.00	17	100.00	80	100.00	25	100

[Table/Fig-1]: Table showing parity distribution in patients with various categories of PIH cases and healthy control group.

S. No.	Parameter	Mild pre-eclampsia (n=35)	Severe pre-eclampsia (n=28)	Eclampsia (n=17)
1.	Systolic BP mm of Hg Mean (range)	146 (130-150)	164 (140-240)	168 (140-200)
2.	Diastolic BP mm of Hg Mean (range)	94 (82-110)	110 (100-190)	106 (80-120)
3.	Urine protein- Nil	-	1	1
	1+	23	10	7
	2+	10	12	6
	3+	2	5	3
	4+			
4.	Oedema- Nil	3	-	-
	+1	21	4	3
	+2	10	14	10
	+3	1	10	4
5.	Symptoms indicating severity like headache, blurring of vision, right upper abdominal pain		15	11
6.	Haemoglobin gm% (Mean)	10.8 gm/dL (5.1-13.9)	11.1 gm/dL (6.2-14.5)	11.5 gm/dL (7.9-15.0)

[Table/Fig-2]: Table showing clinical profile of cases of mild pre-eclampsia, severe pre-eclampsia, eclampsia.

Tests	Control	Mild pre-eclampsia	Severe pre-eclampsia	Eclampsia
Platelet count	248400±56397 (150000-390000)	177571±42259 (110000-310000) p<0.0001	117857±27535 (70000-190000) p<0.0001	108823±32573 (40000-180000) p<0.0001
PT (second)	11.06±1.27 (8.8-13.1)	13.29±1.36 (11.3-16) p<0.0001	13.95±0.99 (12.4-16.3) p<0.0001	15.43±2.07 (12.3-20.0) p<0.0001
aPTT (second)	28.66±1.97 (24.4-31.2)	31.48±3.40 (24.4-38.9) p<0.000458	35.44±3.31 (30.2-42.0) p<0.0001	39.86±3.51 (32.2-43.6) p<0.0001
D-dimer (ng/ml)	413.12±58.52 (301.79-510.39)	2038.74±510.7 (921.78-3124.01) p<0.0001	5922.4±3441.45 (2297.12-14257.12) p<0.0001	5565.07±2434.63 (1100.08-9310.06) p<0.0001

[Table/Fig-3]: Table showing comparison of coagulative profile between control, mild pre-eclampsia, severe pre-eclampsia, eclampsia (Mean levels, standard deviation and range).
p>0.05 not significant, p<0.05 significant, p<0.01 highly significant

There was prolongation of PT and significant difference between PT in mild pre-eclampsia, severe pre-eclampsia and eclampsia and that of healthy controls {11.06±1.27 second (8.8-13.1)}.

There was significant difference between aPTT in mild pre-eclampsia, severe pre-eclampsia and eclampsia and that of healthy controls {28.66±1.97 second (24.4-31.2)}.

There was significant difference between D-dimer in mild pre-eclampsia, severe pre-eclampsia and eclampsia and that of healthy controls {413.12±58.52 ng/mL (301.79-510.39)}.

DISCUSSION

In the present study, most of the patients in control group and patients with PIH were in the age ranging between 20-29 years; which was in accordance with the study of Meshram DP et al., who observed mean of 24.55 years in pre-eclampsia and 24.30 years in eclampsia; Chaware SA et al., who observed mean age of 24 years (19-33 years) in mild pre-eclampsia, 22.7 years (19-35 years) in severe pre-eclampsia and 23.9 (19-35) in eclampsia and Naaz A et al., observed mean age for PIH was 24.55±4.86 years [3-5]. Eclampsia was more common in primipara. Present study finding of increased incidence of PIH in primipara was in concordance with Meshram DP et al., who reported PIH about 66.50% in primipara compared to 33.50% in multiparity [3]. Chaware SA et al., and Nirmala T et al., also found PIH more common in primipara (62.5% and 61%, respectively) [4,6].

In present study, clinical parameters in cases of different severities of PIH showed that the mean systolic blood pressure in mild pre-eclampsia, severe pre-eclampsia and eclamptic patients were in concordance with studies of Jahromi BN and Rafiee SH, who found systolic blood pressure of 175.80±24.16 mmHg and diastolic blood pressure was 108.80±10.57 mmHg in severe pre-eclampsia [7]. Meshram DP et al., also found increased systolic blood pressure in pre-eclampsia (167.55 mmHg) and eclampsia (171.33 mmHg) and increased diastolic blood pressure in pre-eclampsia (115.72 mmHg) and eclampsia (119.5 mmHg) [3]. Naaz A et al., found systolic blood pressure in PIH 154±11.88 mmHg and diastolic blood pressure was 107.5±7.86 mmHg [5]. Chaware SA et al., also found increased systolic blood pressure in mild pre-eclampsia, severe pre-eclampsia and eclampsia (mean) to be 144 mmHg, 161 mmHg and 164 mmHg, respectively; and increased diastolic blood pressure to be 96 mmHg, 112 mmHg and 106 mmHg, respectively [4].

Protienuria were in concordance with the results of Chaware SA et al., who found significant proteinuria in mild, severe pre-eclampsia and eclampsia 30%, 97.5% and 93.3%, respectively [4]. Oedema was less severe in mild pre-eclampsia and pathological oedema (2+ to 3+) was seen only in 11 (31.43%) cases while in severe pre-eclampsia, oedema of hand and feet and generalised oedema was seen in 24 (85.71%) cases and in eclampsia, pathological oedema was observed in 14 (82.35%) of cases. Present study findings related to oedema were in concordance with Chaware SA et al., [4].

Symptoms like headache, blurring of vision and right upper abdominal pain were similar with findings of Chaware SA et al., who found these symptoms indicating severity in severe pre-eclampsia and eclampsia 57.5% and 70%, respectively. The mean haemoglobin concentration showed little difference in haemoglobin concentration in different severity of pre-eclampsia as was shown by Chaware SA et al., [4].

Platelet count was found to be lower in PIH which was in concordance with Meshram DP et al., Chaware SA et al., Osmanagaoglu MA and Topcuoglu K, Mohapatra S et al., Baig MA and Mishra DP et al., except in case of mild pre-eclampsia [3,4,8-11]. Osmanagaoglu MA and Topcuoglu K, studied platelet counts in severe pre-eclamptic women only [8]. Mohapatra S et al., found blood platelets as 2.38 lacs/mm^3±0.33 in control group, 2.23 lacs/mm^3±0.19 in mild PIH, 1.82 lacs/mm^3±0.45 in pre-eclampsia and 1.21 lacs/mm^3±0.49 in ecplampsia [9]. This indicated that there was an inverse relationship between the severity of PIH and platelets number. Meshram DP et al., found that platelet count in pre-eclampsia (1.60±0.51 lacs/mm^3) and eclampsia (1.51±0.68 lacs/mm^3) was significantly lower than that in control group (2.42±0.62 lacs/mm^3) [3]. Baig MA, found that platelet count in mild pre-eclampsia (1.81±0.52 lacs/mm^3) and severe pre-eclampsia (1.05±0.63 lacs/mm^3) was lower than that in control group (1.92±0.41 lacs/mm^3) [10]. Chaware SA et al., observed the platelet count in case of mild pre-eclampsia 2.23±0.36 lac/mm (p=0.0634), in severe pre-eclampsia 1.73 lac/mm±0.56 (p<0.0001) and eclampsia 1.38±0.58 lac/mm (p<0.0001) [4]. They observed that the platelet count in severe pre-eclampsia and cases with eclampsia were very significantly lower than the healthy pregnant control, whereas the platelet count in mild pre-eclampsia was not significantly lower than the healthy pregnant control.

In present study, PT was in concordance with Nirmala T et al., and Baig MA, except in case of mild pre-eclampsia [6,10]. Baig MA, found increase in PT of 11.8±3.2 seconds in mild pre-eclampsia and 19.6±5.7 seconds in severe pre-eclampsia as compared to normal pregnant control 10.9±2.1 seconds [10]. Nirmala T et al., observed PT of 12.47±3.62 seconds and 11.68±2.47 seconds in mild pre-eclampsia and severe pre-eclampsia, respectively and found no statistically significant abnormality in mild pre-eclampsia but observed statistically significant abnormality in severe pre-eclampsia [6]. Present study was in discordance with Meshram DP et al., Chaware SA et al., and Jambulkar S et al., [3,4,12]. Jambhulkar S et al., observed no abnormality in PT in mild pre-eclampsia and severe pre-eclampsia [12]. Meshram DP et al., found PT time 13.67±1.06 second, 13.73±2.24 second (6.89%), 13.82±2.02 second (8.33%) in normal control, pre-eclampsia and eclampsia, respectively that was not significantly prolonged (p>0.05) in pre-eclampsia and eclampsia [3].

Chaware SA et al., found PT in mild pre-eclampsia, severe pre-eclampsia and eclampsia 13.92±1.03 second (11.3-16 second) (p=0.5592), 14.22±1.1 second (12.4-18 second) (p=0.0839) and 14.4±1.41 second (12.3-20 second) (p=0.0101), respectively [4]. PT was slightly prolonged as compared to healthy pregnant control.

In this study, aPTT was in concordance with, Meshram DP et al., Chaware SA et al., (except in mild pre-eclampsia), Baig MA and Jhambhulkar S et al., (except in mild pre-eclampsia) [3,4,10,12]. Jhambhulkar S et al., noted no significant prolongation in aPTT values in mild pre-eclampsia and normal pregnant control groups but found significant prolongation of aPTT (p<0.05) in severe pre-eclampsia cases when compared to normal pregnant controls [12]. Meshram DP et al., observed that the mean aPTT in pre-eclampsia was 37.44±6.60 second with p-value <0.001 which was significantly prolonged when compared with healthy control [3]. Similarly in eclampsia the mean activated partial thromboplastin was 37.69±5.61 second with p-value <0.001 which was again significantly prolonged as compared to control. Baig MA, found prolongation of aPTT in mild pre-eclampsia (51.6±11.5 second) and severe pre-eclampsia (78.7±22.7 second) when compared with normal control group (39.6±1.2 second) [10]. Chaware SA et al., also found in mild pre-eclamptic patients, aPTT 28.5±2.52 second (24.1-33.7) and there was no significant prolongation (p=0.57) when compared with healthy controls [4]. The aPTT in severe pre-eclampsia was 30.6±6.39 second (24.3-50) and it was significantly prolonged (p=0.0232) when compared with healthy controls. The aPTT in eclampsia was 31.03±6.49 second (24.5-49.2) and it was significantly prolonged (p=0.0232) when compared with controls.

In present study, D-dimer values were increased in PIH which was in concordance with Chaware SA et al., and Baig MA, who also found an increase in D-dimer values in severe pre-eclampsia and eclampsia when compared with healthy controls [4,10].

Limitation(s)

In present study number of control samples were less as compared to study group due to high cost of tests performed.

CONCLUSION(S)

This study showed that the degree of thrombocytopenia increases with severity of disease (lower the platelet count, greater the maternal and foetal morbidity and mortality). Early assessment of severity of PIH is necessary to prevent complications like HELLP syndrome and DIC. The coagulation parameters, especially platelet count, aPTT and D-dimer can be safely used as an early indicator for the assessment of severity of PIH and to monitor the progession of gestational hypertension to pre-eclampsia.

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