ORIGINAL ARTICLE

Coagulation Profile in Pregnancy Induced Hypertension

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Abstract

Preeclampsia and Eclampsia affect the fetus because of uteroplacental insufficiency leading to risk for intra-uterine growth restriction and premature and operative deliveries and adverse effects of maternal drugs.Studies report the frequency of abnormal coagulation profile in patients with pre-eclampsia and eclampsia to be between 0% and 50%. Hence their estimation offers an early, simple, rapid assessment of Pregnancy Induced Hypertension (PIH) for its severity and the risk of complications. These tests may be considered as screening tests and follow up to be routinely performed in the antenatal workup of women with PIH.

***Keywords**: Pregnancy Induced Hypertension, Coagulation profile, Preeclampsia, Eclampsia, Prothrombin Time*

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Introduction

Normal pregnancy is associated with remarkable changes in the uteroplacental intravascular coagulation mechanism, in the form of increased production of coagulation factors leading to a hypercoagulable state and suppression of fibrinolysis. This resulting 'hypercoagulability' is beneficial at the time of placental separation [1] but is accentuated in pre-eclampsia. [2]Preeclampsia affects the fetus because of uteroplacental insufficiency. In consequence, these children are at risk for intra-uterine growth restriction and may be delivered prematurely. They may also suffer from the consequences of the high rate of operative deliveries and the adverse effects of maternal drugs. [3]Eclampsia is often preceded by premonitory signs including a headache, visual disturbances, epigastric pain, constricting sensations in the thorax, apprehension, excitability, and hyperreflexia. Most eclamptic convulsions occur prepartum, intrapartum, or within 48 hours postpartum, but there is an unusual entity labeled late postpartum eclampsia that occurs from 48 hours to several weeks after delivery.[4]Studies report the frequency of abnormal Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) in patients with pre-eclampsia and eclampsia to be between 0% and 50% found that minor abnormalities of PT, aPTT, and fibrinogen levels were frequent. These were found mostly in patients with severe pre-eclampsia. It is recommended that a baseline coagulation profile is probably sufficient in patients with a hypertensive disorder of pregnancy. The aim of the present study was to determine coagulation profile (Bleeding Time (BT), Clotting Time (CT), PT and aPTT in cases of PIH and to compare and correlate the values with normotensive pregnant subjects.

Materials and Methods

The present prospective case-control study was carried out in the Department of Pathology of Jawaharlal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital at Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha from August 2011 to July 2013 and included pregnant women admitted in Obstetrics Department. Cases were selected, after taking a detailed history and thorough clinical examination and records. The study has been conducted on two groups of pregnant women:

Group I: Comprised 50 normal healthy women in the second and third trimester of pregnancy.

Group II: Comprised 150 healthy pregnant women who were further categorized into subgroups.

Normal healthy pregnant women who developed hypertension for the first-time during pregnancy after 20 weeks of gestation were included in this PIH category.The further categorization was done according to the following diagnostic criteria. [4]

1. **Gestational hypertension**- Blood pressure elevation of greater than 140 mm Hg systolic or 90 mm Hg diastolic in a previously normotensive woman for the first time after mid-pregnancy, but in whom proteinuria is not identified.
2. **Preeclampsia** - Hypertension (blood pressure greater than 140 mm Hg systolic or 90 mm Hg diastolic) associated with proteinuria > 0.3g/l in a 24-hour urine collection or 1+ dipstick or greater urinary protein levels in random urine collection, after 20 weeks of gestation in a previously normotensive woman.
3. **Severe Preeclampsia** - Preeclampsia, with systolic blood pressure >160 mm Hg and diastolic blood pressure > 110 mm Hg.
4. **Eclampsia** - Onset of convulsions in women with pre-eclampsia that cannot be attributed to other causes.

Exclusion Criteria: Hemorrhagic diathesis, functional uterine bleeding, placental abruption or previa, diabetes, respiratory, circulatory, renal and hepatic disorders, known cases of hypertension and subjects taking drugs affecting coagulation profile. All the subjects in group I and group II underwent the battery of investigations of complete urine examination, hematological investigations, and coagulation profile.

Hemoglobin, RBC, WBC, and Platelet estimation was performed in all subjects. The normal range of hemoglobin in pregnancy was considered as 11 -11.7 g/dl in the 2nd trimester and 10.6 – 10.9 g/dl in the third trimester. Bleeding time [5] was done by Ivy's method. It utilizes the principle that cessation of bleeding from standard incision depends on the adequate number of platelets and on the ability of the platelets to adhere to the subendothelium and to form aggregates. Clotting time (CT)[6,-8] was done by Lee and White method. It is a measure of the plasma clotting factors. Prothrombin Time (PT) [9]The test measures the CT of plasma in the presence of an optimal concentration of tissue extract (thromboplastin) and indicates the overall efficiency of the extrinsic clotting system. Activated Partial Thromboplastin Time (aPTT) [9] - The test measures the CT of plasma after the activation of contact factors (kaolin, silica, or ellagic acid) but without added tissue thromboplastin and so indicates the overall efficiency of the intrinsic pathway. Both PT and aPTT were performed on Coagulometer CL analyzer, Instrumentation Laboratory, Warfarin group, Italy. The results were analyzed statistically to draw a comparison between the groups. The statistical data were processed using Microsoft Excel to draw the values of significance. Tests of significance applied were Chi-square and 'Z' test for statistical analysis to suggest the relationship between the observed abnormal values of chosen laboratory tests in the study with hypertensive disorders of pregnancy and its importance in antenatal care.

Results

A total of 200 subjects were included in the study. The maximum number of cases 78 (52%) had preeclampsia followed by cases of severe preeclampsia 32 (21.33%), eclampsia 21 (14%) and gestational hypertension with 19 (12.67%) cases. The maternal age distribution, cases according to Gestational age and Coagulation profile of study subgroups and control group is depicted in Table No. 01. It was observed that in the subgroups, the maximum number of cases was admitted for PIH in the gestation age group of > 36-40 weeks. A minimum number of cases in the study were observed in >40-44 weeks of gestation. PT was found to be significantly raised in cases of severe preeclampsia ($p = 0.001$) and eclampsia ($p = 0.0003$). Even in the total study group, PT appeared to be significantly prolonged as compared to control with highest prolongation of 27.7 seconds and 'p' value of 0.045.

None of the cases of gestational hypertension showed abnormal prolongation of aPTT. Three cases (3.85%) of preeclampsia showed prolongation of aPTT of which 2 cases had prolonged aPTT in range of >40-45 seconds and 1 case in the range of >45-50 seconds.

Table 1: Showing the details of maternal age coagulation profile of study subgroups and controls

	Study Group (150)	Gestational hypertension (19)		Preeclampsia (78)		Severe Preeclampsia (32)		Eclampsia (21)		Total (150)		Control Group (50)	
		No	%	No	%	No	%	No	%	No	%	No	%
Maternal Age in years	**<20**	0	0	2	2.56	2	6.25	0	0	4	2.67	1	2
	20-29	15	78.95	66	84.62	24	75	19	90.48	124	82.67	47	94
	30-39	4	21.05	10	12.82	6	18.75	2	9.52	22	14.66	2	4
	Mean	**26.05**		**24.4**		**24.31**		**24.19**		**24.56**		**23.4**	
	SD	**4.6**		**3.75**		**4.48**		**4.37**		**4.11**		**2.94**	
	Range	**20-35**		**19-36**		**19-37**		**20-35**		**19-37**		**19-37**	
Gestational Age in weeks	**≥ 20-24**	1	5.26	2	2.56	1	3.12	2	9.52	6	4	2	4
	>24-28	1	5.26	4	5.13	5	15.62	5	23.81	15	10	7	14
	>28-32	1	5.27	6	7.69	2	6.25	2	9.52	11	7.33	10	20
	>32-36	5	26.32	19	24.36	11	34.38	5	23.81	40	26.67	13	26
	>36-40	11	57.89	46	58.98	13	40.63	7	33.34	77	51.33	18	36
	>40-44	0	0	1	1.28	0	0	0	0	1	0.67	0	0
	Mean	35.63		36.36		34.41		32.38		35.29		33.82	
	SD	4.41		4.05		4.62		5.22		4.57		4.42	
	Range	24-40		20-42		24-40		24-39		20-42		24-40	
BLEEDING TIME IN MINUTES	**2 to 7 (Normal Range)**	19	100	78	100	31	96.88	20	95.24	148	98.67	50	100
	>7	0	0	0	0	1	3.12	1	4.76	2	1.33	0	0
	Mean	**2.23**		**2.23**		**2.72**		**3.24**		**2.48**		**2.3**	
	SD	**0.53**		**0.75**		**1.56**		**1.87**		**1.2**		**0.83**	
	Range	**1 – 3.3**		**1.3 - 4**		**1.3 – 10**		**2 – 11**		**1.0-11.0**		**1.3 - 4**	
	'p' value	**NA**		**NA**		**0.080 NS,p>0.05**		**0.023 S,p<0.05**		**0.316 NS,p>0.05**			
Clotting Time (In Mins)	**4-12 (Normal Range)**	19	100	78	100	31	96.87	20	95.24	148	98.67	50	100
	>12	0	0	0	0	1	3.12	1	4.76	2	1.33	0	0
	Mean	4.51		4.72		5.34		6.1		5.02		4.75	
	SD	0.44		0.61		2.28		3.05		1.68		0.55	
	Range	4 – 5.3		4.0-6.0		4 – 17		4.3 -19		4.19		4 – 6	
	'p' value	NA		NA		0.081 NS,p>0.05		0.023 S,p<0.05		0.316 NS,p>0.05			
Prothrombin Time (In Sec)	**11-16 (Normal range)**	19	100	76	97.44	28	87.5	18	85.72	141	94	50	100
	>16-22	0	0	2	2.56	2	6.25	1	4.76	5	3.33	0	0
	> 22-28	0	0	0	0	2	6.25	2	9.52	4	2.67	0	0
	Mean	**11.99**		**12.48**		**13.85**		**14.33**		**12.97**		**11.97**	
	SD	**0.3**		**1.08**		**3.7**		**4.23**		**2.56**		**0.31**	
	Range	**11.4 – 12.4**		**11.5 – 18.6**		**11.5 – 27.7**		**11.4 – 27.5**		**11.4 – 27.7**		**11.2 –12.6**	
	Chi Square Value	**NA**		**3.04**		**12.9**		**16.05**		**6.18**			
	'p' value	**NA**		**0.08 (NS,p>0.05)**		**0.001 S, p<0.05**		**0.0003 S,p<0.05**		**0.045 S,p<0.05**			
Activated Partial Thromboplastin Time (in sec)	**26-40 (Normal range)**	19	100	75	96.15	26	81.25	16	76.19	136	90.67	50	100
	>40-45	0	0	2	2.57	3	9.38	2	9.52	7	4.66	0	0
	>45-50	0	0	1	1.28	3	9.38	2	9.52	6	4	0	0
	>50-55	0	0	0	0	0	0	1	4.77	1	0.67	0	0
	Mean	30.52		32.08		34.73		35.67		32.95		30.54	
	SD	1.77		2.93		5.72		6.66		4.52		1.35	
	Range	**27.5 – 34**		**27.5 – 47.1**		**28 – 48.1**		**30 – 50.1**		**27.5 – 50.1**		**27.5 – 33**	
	Chi Square Value	**NA**		**4.08**		**19.99**		**23.2**		**9.42**			
	'p' value	**NA**		**0.12 NS,p>0.05**		**S,P<0.0001**		**S,P<0.0001**		**0.009 S,p<0.05**			

Out of 32 cases of severe preeclampsia, 6 cases (18.75%) showed prolonged aPTT with 3 cases in the range of >40-45 seconds and another 3 cases in the range of >45-50 seconds. 5(23.81%) out of 21 cases of eclampsia showed prolongation of aPTT, 2 cases in the range of > 40-45 seconds, 2 in the range of >45-50 seconds and 1 case in the range of >50-55 seconds. The

subgroups of severe preeclampsia and eclampsia had the standard deviation of 5.72 and 6.66 respectively and therefore had a significant 'p' value of 0.0001 in both. Overall 14 cases (9.33%) out of 150 cases in the study group showed prolongation of aPTT.

Discussion

In the present study, mean gestational age of 35.63±4.41 weeks was observed in gestational hypertension subgroup [10-16]. The similar mean age of 24.4±3.75 yrs was observed in preeclampsia subgroup in the present study. Distribution of subjects of study group according to Gestational age at admission in study subgroups: In preeclampsia subgroup, the mean gestational age was found to be 36.36±4.05 weeks while in severe preeclampsia subgroup it was 34.41±4.62 weeks. Mean gestational age of 32.38±5.22 weeks was observed in eclampsia subgroup. The mean gestational of the total study group in the present study was 35.29±4.57 weeks when patients were admitted because of clinical or laboratory manifestations of PIH. Observations similar to the present study in cases of gestational hypertension for weeks of gestation were seen by Fitzgerald *et al;*[12] and Metz et al. [11] Observations similar to the present study in cases of pre-eclampsia for weeks of gestation were seen by other similar studies done in this field [12-16] The present study in cases of severe preeclampsia for weeks of gestation were seen by Fitzgerald *et al;*[12] (35.1 weeks) and Dogru *et al;*[16] (34.38±1.68 weeks), Lopez–Llera *et al;*[18](35.5±5.6 weeks).

The present study considered the BT of 2-7 minutes as normal and over 7 minutes as prolonged BT. Considering these values, 3.12% of women of severe preeclampsia group and 4.76% of women in eclampsia subgroup showed prolongation of BT generally inferring that there was no significant prolongation of BT. This observation of the present study is contrary to the observation of Ramanathan *et al;*[20] and Pritchard *et al;* [19] but in agreement with the observations of other studies [22-26]. However, Sheth *et al;*[27] have reported an increase in CT which was not statistically significant in the group of 30 eclamptic females. The observations of the present study of CT are in agreement with the above authors with exception of one case each (3.12%, 4.76%) of severe preeclampsia and eclampsia subgroups respectively. The control group also did not show prolonged CT similar to Dube *et al;*[21] Though many studies have been reviewed for present work to know the importance of PT in context of various classes of pregnancy-induced hypertension, none of the studies has given the distribution of prolongation of PT over its ranges and its distribution over the classes except for Fitzgerald *et al;* [12] who did not observe any prolongation of PT in subgroup of gestational hypertension of 5 cases but observed prolonged PT in 1 out of 28 cases of preeclampsia and 11 out of 40 cases of severe preeclampsia. One case of eclampsia showed no prolongation of PT. The present study found no case of prolonged PT in gestational hypertension subgroup while 2 cases (mean - 12.48±1.08 seconds) out of 78 cases of preeclampsia, 4 cases (mean - 13.85±3.7 seconds) out of 32 cases of severe preeclampsia and 3 cases (mean - 14.33±4.23 seconds) out of 21 cases of eclampsia subgroup showed prolongation of PT. These observations are comparable with the observation of Fitzgerald *et al;*[12] in subgroups of gestational hypertension and preeclampsia only. In this study, the mean values of PT showed no statistical difference between the two groups. The average PT in the study of Lopez–Llera*et al;*[17] performed in 31 out of 33 severely toxemic eclamptic patients averaged 13.7±2.3 seconds against 12.6±0.8 seconds in the corresponding controlled plasma.

The present study has found significant 'p' value in the subgroup of severe preeclampsia and eclampsia for PT and it was also significant when total study group of PIH of 150 cases was concerned. The present study is in agreement with studies of Davidson, Phillips [13], for prolongation of PT in preeclampsia subgroup and Lopez–Llera *et al;* [17] for prolongation of PT in eclampsia subgroup through the control of these studies and present study varies a little for comparison. The observations of the present study are discordant with the study of Jahromi*et al;*[22] in the subgroup of severe preeclampsia. The present study observed significant 'p' value of aPTT in subgroups of severe preeclampsia, eclampsia which is similar to Jahromi*et al;*[22] and Jambhulkar *et al;*[26]and also in the total study group. Kramer *et al;* [28] in the study of

244 patients did not perform the analysis of aPTT prolongation in subgroups of PIH, however, found that 3 out of 244 patients showed mild prolongation of aPTT. Kazimoglu *et al;*[29]reported prolonged aPTT in 2 out of 52 patients which were associated with increased levels of LDH. These observations of Kramer *et al;*[28]and Kazimoglu *et al;*[29] have not specified the prolongation of aPTT in identified in subgroups of PIH.

Conclusion

BT and CT are concluded to do possess no significance in predicting, suggesting or suspecting the PIH as well as its grades and the risk of development of consumptive coagulopathy. However, prolonged PT and aPTT are concluded to be reliable indicators of consumptive coagulopathy expected with PIH. aPTT is more dependable and consistent across the clinical subgroups of PIH of preeclampsia, severe preeclampsia and eclampsia and its mean of prolonged duration is comparable to the severity of PIH. It is obvious from the results of the study that there is a definite statistical difference in values of, PT and aPTT in groups of severe preeclampsia and eclampsia when compared with control. Their estimation is highly recommended as screening and follows up in the antenatal care.

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