

“A Study on Coagulation Profile in Pregnancy Induced Hypertension Cases”

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Abstract: *Pregnancy is a physiological process in women but it may be associated with certain risks to the health and life of both the mother and child. Hypertensive disorders complicating pregnancy are common and form one of the deadly triad along with haemorrhage and infection that results in maternal and perinatal morbidity and mortality. Pregnancy can induce hypertension in normotensive women or aggravate already existing hypertension or appears for the first time during pregnancy. The identification of this clinical entity and effective management play a significant role in the outcome of pregnancy, both for the mother and the baby. In the developing countries with uncared pregnancy, this entity on many occasions remains undetected till major complications supervene.*

In modern obstetric practice, hypertensive disorders of pregnancy are understood to encompass a clinical spectrum of abnormalities ranging from minimal elevation in blood pressure to severe hypertension with multiorgan dysfunction [1].

This study is aimed to evaluate coagulation profile in hypertensive disorders of pregnancy.Changes in coagulation profile that occur in normal pregnancy includes the biochemical adaptation especially the hematological changes that occur in response to pregnancy are profound.The levels of several blood coagulation factors are increased during pregnancy.Plasma fibrinogen increases about 65% late in pregnancy.The increase in fibrinogen concentration contributes significantly to the striking increase in ESR.There is moderate decrease in platelet count as pregnancy progresses.Hence it is useful to evaluate these biochemical markers to prevent the complications like pre-eclampsia,eclampsia, abruption placenta,intrauterine infection etc.

Key words: *fibrinogen levels,platelet count,pre-eclampsia,eclampsia*

I. Introduction.

Hypertensive disorders during pregnancy are associated with high maternofetal mortality and morbidity in both underdeveloped and developed countries [2]. Approximately 70% of hypertensive disorders are due to gestational hypertension this condition is called pre eclampsia [3].

Pre eclampsia/eclampsia has been called the “**Disease of Theories**”. Although it is a relatively common entity and has been the subject of a large body of research, the search for an inciting agent and a unifying pathophysiological mechanism has generated more questions than answers. Even the definition of a disease has been a source of controversy. Nevertheless, research has yielded a great deal of information that has markedly improved maternal and foetal outcomes, and work continues to enhance efforts at prevention of this often devastating condition [1].

Foetal neonatal jeopardy results primarily from compromised placental perfusion and the need for preterm delivery in severe cases. In developed countries, up to 25% of all prenatal deaths are attributable to hypertensive disorders of pregnancy, the major maternal hazards are the consequences of severe hypertension, grand mal seizures and damage to other end organs. In many areas of the world, hypertensive disorders of pregnancy are not the most common cause of maternal death because with modern management, preeclampsia can be ameliorated and eclampsia largely prevented [1].

One way to reduce the impact of arterial hypertension on maternal mortality is to establish the correct diagnosis of hypertensive disorders of pregnancy, and to proceed with an early intervention when it is diagnosed. The clinical signs are considered to be a late manifestation of a disease that has been present since the first trimester of gestation due to “Diagnostic delay”. Many tests have attempted to establish the diagnosis of preeclampsia as early as possible, often even before the patient present arterial hypertension. Tests reported for the early diagnosis of hypertensive disorders are Doppler ultrasound assessment of maternal and foetal circulation, uric acid concentration, the supine pressure test, the angiotensin test, microalbuminuria, plasma

fibronectin concentration, plasma antithrombin activity, calciuria, prothrombin time, platelet count, fibrinogen levels, APTT and other tests, all of which are of debatable efficacy and practicality[4].

How pregnancy incites or aggravates hypertension remains unsolved despite decades of intensive research. Indeed, hypertensive disorders remain among the most significant and intriguing unsolved problems in obstetrics. This study is aimed to evaluate some biochemical markers in hypertensive disorders of pregnancy which includes:

1. Platelet count
2. Prothrombin time
3. Activated partial Thromboplastin time
4. Fibrinogen levels.

Changes in coagulation profile that occur in normal pregnancy includes the biochemical adaptation especially the haematological changes that occurs in response to pregnancy are profound the levels of several blood coagulation factors are increased during pregnancy.

Plasma fibrinogen increases about 65% late in pregnancy. The increase in fibrinogen concentration contributes significantly to the striking increase in ESR. Other clotting factors that increase appreciable during normal pregnancy are factors- VII, VIII.IX & X. prothrombin and factors V and XII do not change. Whereas factors XI and XIII decrease slightly. There is moderate decrease in platelet count as pregnancy progresses.

Disseminated Intravascular Coagulation (DIC) is always a secondary phenomenon trigger by specific obstetrics complications which are listed below [5]:

- Preeclampsia
- Eclampsia
- Abruptio placenta
- Intrauterine infection
- Retained dead foetus
- Placenta accrete
- Hydatidiform mole
- Prolonged shock
- Amniotic fluid embolism.

Hence it is useful to evaluate these biochemical markers to prevent the above cited complications.

II. Aims And Objectives

The present study was undertaken at Department of Biochemistry, SVS Medical College and Hospital, the following are aims

A.To study the following parameters in antenatal women after 20 weeks of pregnancy :

1. Activated partial Thromboplastin time
2. Prothrombin time
3. Fibrinogen levels
4. Platelet count

B.To find out any alterations in the above parameters in pregnancy induced hypertension.

C.To compare the above biochemical parameters between the test group and control group.

D.To correlate the outcome of pregnancy with the above biochemical parameters

III. Materials And Methods

The present study is carried out in the Department Of Biochemistry, SVS Medical College Mahaboobnagar. All the subjects included in the study are admitted in Department Of Obstetrics And Gynaecology, SVS Medical College Mahaboobnagar during the year 2010-2011.

A total number of 20 normal antenatal women without PIH are included in control group and a total number of 20 diagnosed cases of PIH are taken as test group. The biochemical parameters of test group is estimated and compared with those of control group. The test group is selected on the basis of vital signs like blood pressure more than 140/90 mmHg and clinical features like oedema, headache, vomiting, epigastric pain, convulsions etc.

The following biochemical parameters are included in present study.

- 4.1. APTT
- 4.2. PT
- 4.3. Fibrinogen
- 4.4. Platelet count

Cases-20 in number (test group)

Inclusion criteria:

1. Age - 18-35years.
2. Antenatal women with hypertension with or without proteinuria, pre-eclampsia and eclampsia.

Exclusion criteri

1. History of chronic hypertension before completion of 20 weeks of pregnancy.
2. History of Diabetes.

Control – 20 in number

Inclusion criteria

Age group: 18-35 years

Antenatal women without hypertension/pre eclampsia/eclampsia.

Exclusion criteria

Patients with cardiovascular/renal/hepatic complications are excluded from the study.

Method of collection of data

Case history and physical examination findings of both cases and controls are obtained.

Sample collection for the estimation of APTT, PT, and Fibrinogen:

- Venous blood without undue stasis is collected from peripheral vein by vene puncture under aseptic conditions.
- This blood is transferred into an anticoagulated tubes without delaying the mixing of blood with anticoagulant.
- Exactly 9 parts of freshly collected blood is mixed with 1 part of trisodium citrate (0.11 mol/litre).
- The sample is centrifuged for 15minutes at 3000 rpm and the plasma is separated.
- The separated plasma is transferred in a clean and dry test tube and is tested within 2-3 hours of blood collection.

Instruments used

- Centrifuge machine
- Semi-auto analyser (hemostar, tulip group)

ADDITIONAL MATERIAL REQUIRED

- 10 x 75 mm glass test tubes, pipettes, sample cups, magnet rod.

Sample collection for estimation of platelet count

- Venous blood without undue stasis is collected from peripheral vein by vene puncture under aseptic conditions.
- K2 EDTA is used as an anti coagulant to prepare the anticoagulant blood sample (the dose of K2 EDTA is 1.5 mg/ml blood).
- Anticoagulant blood is mixed up.

Instrument used.

- Auto-analyser (cell counter)

Statistical analysis Mean and standard deviation of all variables are calculated. The statistical significance is assured using students T-test. P values less than 0.05 are considered significant.

Controls

Table No: I

S.No	Systolic BP (mmHg)	Diastolic BP (mmHg)	APTT (Seconds)	PT (Seconds)	Fibrinogen (mg/dl)	Platelet Count /lakhs	Gravida	Foetal Complications
1.	90	50	24.2	10.7	220	3.0	Multi	O
2.	90	60	22.1	12.1	210	3.2	Primi	ND
3.	110	70	28.7	13.2	266	3.0	Multi	ND
4.	120	80	23.0	12.9	250	3.5	Multi	O
5.	120	70	25.3	10.5	294	3.0	Primi	O
6.	100	60	27.5	13.6	235	2.8	Primi	O
7.	130	80	30.8	14.0	280	2.5	Multi	O
8.	110	70	31.2	11.9	270	2.3	Primi	ND
9.	110	80	21.4	12.6	295	2.2	Multi	ND
10.	120	80	22.0	13.2	260	2.0	Multi	ND

11.	110	70	24.5	11.1	340	2.0	Multi	ND
12.	110	70	30.5	10.5	230	2.8	Primi	O
13.	120	80	26.4	14.2	260	2.4	Multi	O
14.	100	70	28.6	13.9	350	3.0	Primi	ND
15.	90	60	21.5	12.7	285	3.2	Multi	O
16.	110	70	22.1	13.5	280	2.8	Primi	ND
17.	120	70	23.3	11.2	290	2.4	Multi	ND
18.	100	70	24.1	11.5	320	3.1	Multi	O
19.	110	80	27.6	10.8	310	3.2	Primi	O
20.	120	80	26.2	15.7	290	2.9	Primi	O
Total	2190	1420	511	249.8	5535	55.3		
Mean	109.5	71.0	25.55	12.49	276.75	2.76		
SD	11.46	8.52	3.23	1.45	37.31	0.42		

ND- normal delivery O – Delivery outcome not known: 1

Cases

Table No: II

S.No	Systolic BP (mmHg)	Diastolic BP (mmHg)	APTT (Seconds)	PT (Seconds)	Fibrinogen (mg/dl)	Platelet Count /lakhs	Gravida	Foetal Complications
1.	150	100	29.9	14.4	360	1.8	Primi	ELSCS
2.	160	100	33.8	14.6	340	1.8	Primi	ELSCS
3.	160	110	33.6	18.0	310	1.6	Primi	IUGR
4.	140	100	31.6	16.7	220	2.3	Multi	ND
5.	140	100	31.0	13.2	220	2.1	Multi	ND
6.	170	120	32.3	16.1	370	1.2	Primi	IUD
7.	150	110	33.2	16.2	370	2.1	Multi	ELSCS
8.	150	110	31.2	17.0	410	1.7	Primi	LSCS
9.	150	110	33.5	14.3	280	1.9	multi	LSCS
10.	150	110	31.4	14.4	390	1.8	Primi	ELSCS
11.	160	100	35.2	15.9	110	1.85	Primi	IUD
12.	150	110	28.8	16.9	370	1.85	Primi	ELSCS
13.	170	110	34.5	18.5	315	1.63	Multi	IUD
14.	140	110	31.3	18.5	420	2.30	Primi	ND
15.	180	130	29.4	16.3	260	1.90	Primi	IUGR
16.	140	100	35.2	19.1	315	2.50	multi	ND
17.	140	110	32.4	17.5	390	1.80	Primi	ND
18.	150	100	32.1	18.9	350	1.50	multi	ELSCS
19.	160	110	36.3	17.8	380	1.68	Primi	ELSCS
20.	170	110	37.4	19.7	450	1.9	Multi	IUD
Total	3080	2160	657.1	334	6630	37.21		
Mean	154	108	32.85	16.7	331.5	1.86		
SD	11.87	7.67	2.34	1.83	81.30	0.29		

ND-5, LSCS-2, ELSCS-7, IUGR-2, IUD-4.

IV. Summary Of Results

Table No: III

Sl.No	Investigation	Statistical Parameter	Control subjects	Test group
1	Systolic Blood Pressure(mmHg)	Mean	109.5	154
		SD	11.46	11.88
		SEM		
		t-test		
		p-Value		
2	Diastolic Blood Pressure (mmHg)	Mean	71.0	107.5
		SD	8.52	7.86
		SEM		
		t-test		
		p-Value		
3	Activated Partial Thromboplastin time (APTT) Seconds	Mean	25.5	32.85
		SD	3.23	2.34

		SEM	0.72	0.52
		t-test	8.17	
		p-Value	<0.0001	
			Control subjects	Test group
4	Prothrombin Time (PT) Seconds	Mean	12.49	16.7
		SD	1.45	1.83
		SEM	0.32	0.41
		t-test	8.03	
		p-Value	<0.001	
			Control subjects	Test group
5	Fibrinogen(mg/dl)	Mean	276.75	346.5
		SD	37.31	64.16
		SEM	8.34	14.35
		t-test	4.20	
		p-Value	=0.002	
			Control subjects	Test group
6.	Platelet Count (Lacs/cumm)	Mean	2.76	1.86
		SD	0.42	0.29
		SEM	0.09	0.06
		t-test	7.74	
		p-Value	<0.01	

SD : Standard Deviation,SEM: Standard Error of Mean

V. Results

In the present study the biochemical parameters like Activated partial thromboplastin time, Prothrombin time, Fibrinogen levels and Platelet count were estimated in 20 controls and 20 cases in normotensive and hypertensive pregnant women respectively.

Table I, II,III and IV shows the biochemical profile in cases and controls.

- I. The mean and standard deviation of systolic blood pressure (mmHg) in controls is 109.5 ± 11.46 as compared to 154 ± 11.88 in test group. The difference is statistically significant, as shown in chart no: 01.
- II. The mean and standard deviation of diastolic blood pressure (mmHg) in controls is 71 ± 8.52 as compared to 107.5 ± 7.86 in test group. The difference is statistically significant, as shown in chart no: 02.
- III. The mean and standard deviation of Activated partial thromboplastin time (seconds) in controls is 25.5 ± 3.23 as compared to 32.85 ± 2.34 in test group. The difference is statistically significant, as shown in chart no: 03.
- IV. The mean and standard deviation of Prothrombin time (seconds) in controls is 12.49 ± 1.45 as compared to 16.7 ± 1.83 in test group. The difference is statistically significant, as shown in chart no: 04.
- v The mean and standard deviation of Fibrinogen levels (mg/dl) in controls is 276.75 ± 37.31 as compared to 346.5 ± 64.16 in test group. The difference is statistically significant, as shown in chart no: 05.
- V. The mean and standard deviation of Platelet count (lakhs/cu mm) in controls is 2.76 ± 0.42 as compared to 1.86 ± 0.29 in test group. The difference is statistically significant, as shown in chart no: 06.
- VI. The mean and standard deviation of age distribution in controls is 24.55 ± 4.86 as compared to 25.45 ± 4.02 in test group, as shown in table no :05 & 06 and chart no: 09 & 10.
- VII. From table IV , the parity of the two groups was similar. The percentage composition of primigravidae and multigravidae within the group and between the two groups were similar.

Table No: IV showing parity distribution

Parity distribution	Control		Cases	
	Number	Percentage	Number	percentage
Primi	09	45%	12	60%
Multi	11	55%	08	40%
Total	20	100	20	100

Table No: V showing the age distribution of control group

Age in years	No: of control subjects	Percentage
18-23	10	50%
24-29	06	30%
30-35	04	20%
Total	20	100%

The mean age was 24.55 years with a standard deviation of 4.86 years.

Table No: VI showing the age distribution of cases group

Age in years	No: of control subjects	Percentage
18-23	06	30%
24-29	11	55%
30-35	03	15%
Total	20	100%

The mean age was 25.45 years with a standard deviation of 4.02 years.

VI. Discussion

Preeclampsia is a serious and life threatening complication in pregnant women. It is a pregnancy specific disorder which rates among one of the major causes of maternal and foetal morbidity and mortality.

More number of cases are seen in underdeveloped and developing countries due to late diagnosis and inadequate antenatal services.

In the present study the biochemical parameters like Activated Partial Thromboplastin Time, Prothrombin Time, Fibrinogen Levels And Platelet Count are studied in normotensive and hypertensive(PIH)pregnant women.

The results of the present study are discussed under two groups:

1. Control subjects (normal pregnant women)
2. pregnancy-induced hypertension subjects as cases.

Control group:

A total number of 20 normotensive pregnant women were studied. The age group of these subjects ranges from 18-35 years.

All these subjects are normotensive and healthy pregnant women. The results of estimation of Activated Partial Thromboplastin time, Prothrombin time Fibrinogen level and Platelet count are within normal limits.

Case group:

A total number of 20 cases of PIH have been studied. The age group of these subjects ranges from 18-35 years.

All cases showed classical triad of hypertension, proteinuria and oedema. In addition to above symptoms the eclampsia patients are presented with convulsions.

All subjects showed an increase in plasma APTT levels when compared with normal pregnant women the levels are within normal range and the difference is statistically significant.

All subjects showed an increase in plasma Prothrombin Time when compared with normal pregnant women the levels are within normal range and the difference is statistically significant.

There is significant increase in plasma fibrinogen levels in cases when compared with normal pregnant women, the levels are within normal range and the difference is statistically significant.

There is significant decrease in platelet count in cases when compared with normal pregnant women, the levels are within normal range and the difference is statistically significant.

Biochemical changes consistent with intravascular coagulation and less often erythrocyte destruction may complicate preeclampsia and especially eclampsia. Changes in coagulation profile that occur in normal pregnancy includes the biochemical adaptation especially the haematological changes that occur in response to pregnancy are profound. The levels of several blood coagulation factors are increased during pregnancy.

APTT is a measure of classic intrinsic pathway and is prolonged by deficiency of pre-kalikein, HMW kininogen, factors XII, XI, IX, VIII, X, V, II, fibrinogen and presence of inhibitors.

Shortening of APTT may be seen in patients with compensated low grade consumptive coagulopathy.

Prothrombin time measures the integrity and adequacy of classic extrinsic pathway, especially the factors- VII, X, V, II and fibrinogen, a combination of these factors or the presence of an inhibitor.

Prolongation of prothrombin time may bbe associated with the deficiency of coagulation factors mentioned above.

Plasma fibrinogen increases about 65% late in pregnancy. The increase concentration contributes significantly to the striking increase in ESR. Other clotting factors that increase appreciably during normal

pregnancy are factors- VII, VIII, IX, X. Prothrombin and factors- V, XII do not change. Whereas factors- XI and XIII decreases slightly. There is moderate decrease in platelet count as pregnancy progresses.

Maternal thrombocytopenia can be induced acutely by preeclampsia, eclampsia. Overt thrombocytopenia defined by platelet count less than 1,00,000/ μ l is an ominous sign.

Platelet aggregation is increase in preeclamptic women. Immunological processes or simply platelet deposition at sites of endothelial damage may be the cause. Thrombocytopenia in such disorders is associated with a prolonged bleeding time. The clinical significance of thrombocytopenia in addition to obvious impairment in coagulation is that it reflect the severity of pathological process. The lower the platelet count, the greater are maternal and foetal mortality and morbidity. The addition of elevated liver enzymes to this clinical picture is even more ominous and a combination of events is referred to as HELLP syndrome [Haemolysis, Elevated Liver Enzymes and Low Platelet Count].

Pregnancy outcome:The outcome of pregnancy in the present study among 20 control subjects 9 delivered normally and in remaining 11 subjects the delivery outcome is not known. Where as in 20 cases, 5 subjects delivered normally, 2 subjects underwent LSCS, in 7 cases ELSCS was done, 2 subjects had foetus with IUGR and 4 with IUD.

VII. Conclusion

A comparative study was done between a normal pregnant women and women with PIH on the levels of APTT, PT, and Fibrinogen level and platelet count in blood.

The patients were clinically diagnosed based upon history, clinical symptoms, signs and levels of blood pressure.

In all the blood samples obtained from controls and cases APTT, PT, fibrinogen levels and platelet count were estimated by standard methods. For this study the results showed a significant rise in APTT, PT, fibrinogen levels. Whereas decrease levels of platelet count I in cases with PIH. But in the control subjects the values for all above parameters are within normal limits.

From this study it is concluded that estimation of these biochemical parameters plays an important role in the diagnosis of PIH and the evaluation of risk factors, early detection and effective antenatal services, prompt and proper management will decrease the materno-foetal mortality, morbidity and also perinatal mortality.

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