Coagulation Profile Study in Pregnancy Induced Hypertension

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Abstract

Background & Aims: Hypertensive disorders represent the most common medical complication of pregnancy. Hypertensive disorders remains leading cause of direct maternal and fetal mortality. Coagulation profile study in pregnancy induced hypertension helps inearly diagnosis of pregnancy induced hypertension and assessing the severity of pregnancy induced hypertension at earlier stage and help to prevent severe complications like disseminated intravascular coagulation and HELLP syndrome. To estimate platelet count, prothrombin time and activated partial thromboplastin time in pregnancy induced hypertension. To estimate above parameters in normal pregnancy. To compare above parameters between normotensive women and women with pregnancy induced hypertension. **Material and Method:** 100 newly diagnosed patients of pregnancy induced hypertension and 100 normal healthy controls were included in the study. After taking consent, their blood samples were collected. These samples were transported to the laboratory and processed without delay for prothrombin time, activated partial thromboplastin time and platelet count. The results of these parameters were noted, compared and analysed statistically. **Result:**In our study, we observe that pregnancy induced hypertension is common in primipara. There was a statistically significant difference between study group and control group for all three parameters($p<0.001$). Comparison between each study group and control group showed significant difference ($p<0.05$) between prothrombin time and activated partial thromboplastin time . Prothrombin time and activated partial thromboplastin time showed significant increase value when compared to normal group although the mean value are normal or near normal in range. **Conclusions:** It can be concluded from this study that the pregnancy induced hypertension causes a significantchanges in haematological parameters. These parameters should be regularly monitored to prevent serious complications like disseminated intravascular coagulation and HELLP syndrome, hence to decrease morbidity and mortality.

Keywords: - Pregnancy induced hypertension, Disseminated intravascular coagulation, activated partial thromboplastin time , prothrombin time.

Introduction

Hypertensive disorders represent the most common medical complication of pregnancy affecting 7% and 15% of all gestations and accounts for approximately a quarter of all antenatal admissions. According to world health organization's systemic review on maternal mortality worldwide, hypertensive disease remains a leading cause of direct maternal mortality. Together with hemorrhage and infection, hypertensive forms the deadly triad that contributes to morbidity and mortality during pregnancy and childbirth.

Pregnancy induced hypertension is an elevated blood pressure that appears first time in pregnancy as a result of gravid state. It is one of the most common cause of increased mortality and morbidity in the mother and fetus[1].

Although maternal mortality is much lower in high-income countries than in developingcountries, the

incidence of pre-eclampsia has risen in the United States of America. This might be related to an increased prevalence of predisposing disorders such as chronic hypertension, diabetes and obesity. About 16% of maternal deaths were attributed to hypertensive disorders in developed countries and over half of these hypertension – related deaths were preventable.

Hypertensive disorders are responsible for not only maternal deaths but also substantial morbidity for the pregnant women. One-third of severe maternal morbidity was a consequence of hypertensive conditions in United Kingdom. Five percent of women with severe pre- eclampsia or eclampsia were admitted to intensive care. Long term impact of hypertension in pregnancy in the form of chronic hypertension and increased lifetime cardiovascular risk is also present.

Hypertensive disorders also carry a risk for a baby. Hypertension and/or proteinuria is the leading single identifiable risk factor in pregnancy associated still birth. Pre-eclampsia is strongly associated with fetal growth restriction, low birth weight, spontaneous or iatrogenic preterm delivery, respiratory distress syndrome, admission to neonatal to intensive care and cerebral palsy.

Pre-eclampsia is a combination of elevated blood pressure, proteinuria and edema. Eclampsia is the presence of convulsion along with above features of pre-eclampsia.

Normal pregnancy is a hypercoagulable state due to elevation of the most of coagulation factors and reduced anticoagulant activity[2]. In pregnancy induced hypertension, there is an accentuation of hypercoagulable state as a result of injury to the endothelium[3].

Coagulation profile study in pregnancy induced hypertension are platelet counts, prothrombin time and activated partial thromboplastin time. These parameters are helpful in assessing the severity of coagulation abnormalities in pregnancy induced hypertension at earlier stage, prior to the occurrence of complications.

Although many risk factors are attributed to the chance of developing pregnancy induced hypertension (PIH), most such patients are healthy nulliparous women with no obvious risk.

Aim:

Aim of the study is to estimate changes that occur in coagulation parameters in pregnancy induced hypertension in comparison to normal pregnancy.

Material & method:

Study site:

The present study was conducted in department of Obstetrics and Gynecology and Department of Pathology, Government Medical College and Sir. T. Hospital, Bhavnagar, Gujarat, after IRB approval during period of July 2020 to July 2021.

Inclusion criteria:

- Age >18 years newly diagnosed PIH antenatal women.
- For control group >18 years normal healthy antenatal women.

Exclusion criteria:

1. Pre existing medical disorders – Diabetes Mellitus
   Renal disease
   Any coagulopathies
   Chronic Hypertension
2. Smokers
3. Multifetal Gestation
4. Placental abruption or previa

Study design: Pregnant women fitting in above criteria were divided in case and control groups.

Cases further classified in following groups depending on their presentation:

- Gestational hypertension: **:**New-onset hypertension (systolic BP of 140 mm Hg or more or diastolic BP of 90 mm Hg or more, or both on two occasions at least 4 hours apart) develops after 20 weeks‟ gestation, during labour, or in the first 24-hours postpartum, without proteinuria or any other severe systemic features of pre- eclampsia, in previously normotensive nonproteinuric woman.
- Pre-eclampsia: Pre-eclampsia is a disorder of pregnancy associated with new onset of hypertension, which occurs most often after 20 weeks‟ gestation and frequently near term. Although often accompnied by new onset proteinuria, hypertension, and other signs or symptoms of

pre-eclampsia may present in some women in the absence of proteinuria. Hypertension is associated with proteinuria greater than 0.3 g/L in a 24-hour urine collection, dipstick reading of 2+ by qualitative urine examination or protein creatinine ratio of 0.3 mg/dl or more after 20 weeks" gestation.

- Eclampsia: Convulsions occuring in a patient with pre-eclampsia are known as eclampsia and are among the more severe manifestation of the disease.

Recruitment and procedure:

Samples of newly diagnosed cases of PIH of any (second, third) trimester were collected in Vacu Care EDTA and citrate vacutte. At the same time samples of normal healthy control women of same gestational age were collected. These samples were immediately transported to the hematology laboratory and processed without delay for prothrombin time (PT), activated partial thromboplastin time (APTT) and platelet count (PC). The results of these parameters were noted , compared and analyzed statistically.

Methodology:

1. Platelet count was done by 5 PART automated cell counter- Nihoncohdenmek 9100 with impendence method.
2. PT was done on fully automated Stago Compact Max. NEO-OPTIMAL kit is used. The international sensitivity index (ISI) for lyoplastin was 1.2.
3. APTT was done on fully automated Stago Compact Max. CK-PREST & $Cacl_2$ ready to use kit is used. PT and APTT done by magnetic steel ball method.

Technical details:

I) Collection of blood

A. For PT and APTT: 2 ml venous blood of patients was collected in 3.2% citrate vacutte.

B. For platelet count: 2 ml of blood was collected in EDTA vacutte.

II) Processing of sample for coagulation studies:

Samples of the patient and control subject were immediately transported to the laboratory and were centrifuged at 3000-4000 revolutions for 15-30 minutes to obtain platelet poor plasma. Platelet poor plasma was used in PT and APTT. Both the control and patient's samples were tested within 6 hours of collection of blood sample.

1. Platelet Count

2 ml of blood was collected in EDTA vacutainer. Blood was processed in the automated cell counter. Platelet count was obtained.

2. PT and APTT

2 ml blood was collected in 3.2% sodium citrate vacutainer. It was centrifuged. It was further processed in automated coagulometer (Stago compact Max), for evaluation of prothrombin time and activated partial thromboplastin time.

Statistical Analysis:

- Study and control group data of all parameters was tabulated in microsoft office Excel worksheet, and descriptive statistics were calculated as mean and standard deviation at 95% confidence interval.
- Comparison of PT, PC and APTT between study and control group was done using chi square test with the help of 2x2 tables and the data was compared and p-value <0.05 was considered significant.
- Comparison of platelet count, PT, APTT between the subgroups of the study group in gestational hypertension, pre-eclampsia and eclampsia were done by chi square test.
- All statistical analysis was done by using OPEN EPI.

- The difference was considered statistically significant when the calculated p- value was less than 0.05.

Results:

A total of 200 pregnant females were included in the study, out of which 100 females were normotensive and formed the control group and 100 with PIH (BP > 140/90mm Hg) were studied.

63 cases of gestational hypertension, 31 of pre-eclampsia and 6 of eclampsia were detected, where maximum cases were observed between 18-29 yrs of age. Pregnancy induced hypertension was more common in primipara. The mean value of platelet count was 2.5,2.08 and 1.4 in GHT , PE and eclampsia respectively. Mean prothrombine time was 15.08,16.7 and 17.65 respectively where as mean APTT values were 26.72, 28.3 and 31.56 in GHT, PE and eclampsia respectively.In above values confidence limit of 95% was considered.

Table 1: Distribution of cases according to age and diagnosis

Age in years	Control group (100)	Study group (100)	GHT	PE	E	TOTAL
18-23 YEARS	26	39	23	13	3	104
24-29 YEARS	52	47	30	15	2	146
>30 YEARS	22	14	10	03	01	50
TOTAL	100	100	63	31	06	

GHT= gestational hypertension; PE = pre-eclampsia; E= eclampsia

Maximum number of cases in both the groups, control and study group are between 18 to 29 years of age.

Table 2: Distribution of cases according to parity

Parity	Control group%	Cases %
Primipara	49	52
Multipara	51	48

In the present study PIH was more common primipara.

Table 3: Comparison of platelet count, PT and APTT between control and overall values of study group

	Control group	Study group	P value	Significance
Platelet count	2.9±0.60	2.3±0.86	<0.001	Significance
PT	12.9±1.21	15.71±2.4	<0.001	Significance
APTT	26.50±2.05	27.50±3.3	<0.001	Significance

Decrease in platelet count is statistically significant ($p<0.001$). There is statisticallysignificant increase in PT ($p<0.001$) and APTT ($p<0.001$).

Table 4: Comparison of mean values of platelet count, PT and APTT with individual categories of study group.

	Control group	GHT	PE	E
Platelet count	2.9±0.6	2.5±0.87	2.08±0.70	1.4±0.81
PT	12.92±1.21	15.08±1.9	16.70±2.8	17.65±3.7
APTT	26.50±2.05	26.72±2.9	28.30±3.2	31.56±4.8

As shown in table the mean values of PT and APTT fall in normal range in all groups, but when compared with increasing grade of severity it shows gradual increase.

Table 5: Comparison of platelet count, PT and APTT of control with GHT, PE and eclampsia.

	Control group	GHT	P value	significance	PE	Eclampsia	P value	Significance
PC	2.9±0.6	2.5±0.87	<0.05	Significance	2.08±0.70	1.4±0.81	>0.05	Not Significance
PT	12.92±1.21	15.08±1.9	<0.05	Significance	16.70±2.8	17.65±3.7	<0.05	Significance
APTT	26.50±2.05	26.72±2.9	<0.05	Significance	28.30±3.2	31.56±4.8	<0.05	Significance

Results are statistically significant when p<0.05. When coagulation parameters were compared betweencontrol group and GHT group significant difference noted. When coagulation parameters were compared between control group and PE group significant difference between PT and APTT and not statistical difference noted in PC in this study. When coagulation parameters were compared between control group and E group significant difference between PT and APTT and not statistical difference noted in PC in this study.

Thrombocytopenia was seen in 9.6% of pre-eclampsia cases, 9.5% of gestational hypertension cases and 16.66% of eclampsia cases. PT was prolonged in 22.2% cases of gestational hypertension , 38.70% of pre-eclampsia cases and 50% cases of eclampsia.

Discussion:

In the present study the platelet count and coagulation parameters like PT and APTT were studied in normotensive and hypertensive (PIH) pregnant women.

Table 1 shows age wise distribution of women with pregnancy induced hypertension. In healthy pregnant controls, the maximum cases were in the age group 24-29 years (52%) cases followed by 26 cases in the age group of 18-23 years. The range in this group was 19-35 years with mean of 26 years. Thus about 78% of pregnant control cases had the age in between 19- 29 years. Most of the patients with GHT were in age group of 24-29 years (47.61%) cases followed by 23 (36.50%) cases in the age group 18-23 years. The mean age was 25 years with range of 19- 38years. The maximum number of cases in Pre-eclampsia were in age group of 24-29 years 15 (48.38%) cases, followed by 13 (41.93%) cases in the age group 18-23 years. Mean age was 24.6 years with range of 19-42 years. In eclampsia maximum number of patients were in age group of 18-23 years 3 (50%) cases , followed by 2 (33.33%) in age group 24-29 years . The mean age was 24.83 years with range of 20-35 years. It appears that as far as the age is concerned, there is no or little difference between normal healthy pregnant women and patients with different degrees of severity of pregnancy induced hypertension. But it was clear that most patients in normal pregnant control group and patients with pregnancy induced hypertension were in between 19-29 years. Many authors stated their observation of age as mean of 22.7 years in pre-eclampsia by Kitzmiller JL *et al* (1974)[4],22.4±6.9 years by J. Metz *el al* (1994)[5], 24.75 years (range -19-32) by J. Prakash(2006)[6].P.W. Howie (1971)[7] noted mean age for pre-eclampsia as 25 years.

Table 6: Comparative studies on parity and PIH

	Leduc et al [8]	Naaz A et al [9]	Present study
Primipara	65%	60%	58%
Multipara	35%	40%	42%

The findings of the present study and many other studies such as Joshi SR[10], also confirm that PIH is more prevalent in primigravida with approximately same % as other studies. Metz et al (1994) [11] described PIH and pre-eclampsia of 71% and 79% respectively in primipara.

APTT :

The activated partial thromboplastin time (APTT) in pre- eclampsia was 28.30sec ± 3.2 sec and was significantly prolonged (p-<0.05) when compared with normal healthy pregnant controls. The activated partial thromboplastin time (APTT) in eclampsia was 31.56±4.secs and was significantly prolonged (p-<0.05) when compared with normal healthy pregnant controls. So in our study APTT was significantly

prolonged when compared with healthy controls. Sibai et al (1982) observed APTT of 29.9±6.6 secs in eclampsia while in control group it was 26.4± 1.8 sec. Comparison revealed p value of <0.005 which was highly significant.Antony et al (1998)[12] and Jambhulkhar at el (2001)[13] noted significant prolongation of APTT (p value <0.05) in pre-eclampsia and eclampsia cases when compared to the normal pregnant controls. Osmanangaoglu (2005)[14] noted a significant difference (p<0.0001) with regard to APTT between pre-eclampsia and eclampsia with the control group. The findings of APTT in our study correlates well with other study.

Platelet count:

Table 7: Mean platelet count (lac/ cumm)

	GHT	PREECLAPSIA	ECLAMPSIA
Chauhan P[15]	1.73±0.25	1.45±0.24	1.21±0.22
Mohapatrta S[16]	2.23±0.19	1.82±0.45	1.21±0.49
Sarkar PD[17]	1.98±0.41	1.47±0.32	-
Mirza AB[18]	1.81±0.52	1.05±0.64	-
Kulkarni[19]	1.84	1.19	1.18
Lakshmi VC	2.1±0.5	0.8±0.3	0.7±0.3
Present study	2.5±0.87	2.08±0.73	1.4±0.81

There was fall in mean platelet count with increasing severity of PIH in present study. Reduction in platelet count can be attributed to platelet activation, platelet aggregation and platelet consumption which can be present during and even before the onset of disease. Platelet activation may lead to increased generation of thromboxane A2 and serotonin release, in turn increase vasoconstriction and platelet aggregation. Thrombocytopenia in PIH is also supported by Whingham KAE, Redman[20], Kelton[21] , Baker and Cunningham[22], Rowland[23] and Harlow[24].

In control cases there was no thrombocytopenia. In GHT total of 7 patients had thrombocytopenia , while 1 patient had count below 50,000/cumm. In PE total 5 patients had thrombocytopenia, while 1 patient had count below 50,000/cumm. In all cases of PIH (100) thrombocytopenia was seen in 17% cases. The thrombocytopenia in our study well correlate with other authors who reported thrombocytopenia of 4% to 50% in mild to severe cases of pre-eclampsia and eclampsia.

Prothrombin time:

There was statistically significant increase in PT between control and study group in present study. The results were comparable with the studies of Priyadarshini G (p<0.05)[25] and Naaz A (p <0.001)[26], while Chauhan P (p >0.05) showed no statistically significant difference. PT showed statistically significant increase when compared to control group . Even though the mean value of PT in each group is normal or near normal range there was statistical difference between values of cases and controls. As the severity of PIH increased the values of PT shifted from lower limit to upper limit of normal. So gradual increase of PT in pregnant female measured by repeated testing may point towards the possibility of PIH and can help in early detection. Similar findings were seen in studies of Priyadarshini G[(25)] and Naaz A.[(26)]

Conclusion:

- Pregnancy Induced Hypertension is common in primipara.
- Comparison between study group and control group showed that the deacrese in platelet count and increase in PT and APTT are all statistically significant(p<0.001).
- Comparison between control group and each study group showed significant difference (p<0.05) between platelet count , PT and APTT, except in pre-eclampsia and eclampsia where the platelet count showed no significant deacrese.
- PT and APTT showed significant increase value (p<0.05) when compared to control group.
- Although the mean values are normal or near normal in range.
- Present study revealed changes in the coagulation parameters in women with pregnancy induced hypertension which was compared to normotensive pregnant women.

- Platelet count showed inverse relationship with severity of pregnancy induced hypertension.
- Prothrombin time and Activated Partial Thromboplastin time showed prolonged values with pregnancy induced hypertension.
- Coagulation abnormalities include HELLP syndrome and disseminated intra vascular coagulation contribute the causes for maternal deaths in pregnancy induced hypertension.
- Present study can be helpful in identifying the coagulation abnormalities in relation to pregnancy induced hypertension in earlier stage and can be helpful for the management of complications in relation to pregnancy induced hypertension.
- Maternal and fetal mortality and morbidity can be reduced with the help of this study.

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