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Original Research Article

Evaluating association between thrombocytopenia and hypertension in pregnancy and its fetomaternal outcome

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ABSTRACT

Background: Hypertension in pregnancy is common complication of pregnancy with incidence 5-15% and associated with maternal and perinatal mortality and morbidity. Platelet count is most simple, rapid and economical method of prediction of pregnancy induced hypertension. The aim and objective of study was to corelate with severity of thrombocytopenia and its association with fetal and maternal outcome.
Methods: This study was a case control study and was conducted in department of obsterics and gynecology, SVBP hospital attached to LLRM medical college, Meerut, from October 2020 To June 2022. Total number of 100 pregnant females out of which 50 pregnant females with hypertension as cases and 50 pregnant females without hypertension as control were included in study. Observations were tabulated, analysed and conclusions were drawn.
Results: Out of 50 cases 43 patients developed preeclampsia thus giving incidence of 43 % and out of which 21 patients had mild thrombocytopenia,13 moderate thrombocytopenia and 4 severe thrombocytopenia. The mean age amongst cases was 26.73±5.19SD and the mean age amongst control was 28.09±4.83. There was very high significant relationship between the degree of thrombocytopenia with severity of hypertension during pregnancy (at $p < 0.01$). 24% fetuses had preterm birth, 8% had fetal growth restriction, 2% were IUD and 2% mortality. 2% of mothers had DIC,8% had post-partum hemorrhage, 6% had abruption ,4% had pulmonary edema and 6% mortality.
Conclusions: Thrombocytopenia is most common and can be life threatening complication of pregnancy induced hypertension. Therefore, platelet count can be used as an early, easy, simple, most economical and rapid test to assess severity of preeclampsia and to prevent its progression to eclampsia, HELLP syndrome and DIC.

Keywords: HELLP, PIH, Pregnancy induced Thrombocytopenia

INTRODUCTION

Hypertensive disorders of pregnancy is a global problem and complicating approximately 10-17% of pregnancies. The incidence of Pregnancy induced hypertension (PIH) in India is about 5% to 15%. Hypertensive disorders in pregnancy are the most common medical complications of pregnancy and is a serious health risk during pregnancy for both mother as well as fetus. Pre-eclampsia is defined as hypertension, occurring after 20 weeks of pregnancy, together with proteinuria.[1] A variety of hematological abnormalities may occur in women with pregnancy induced hypertension of which thrombocytopenia is the most common.

Platelets are produced in bone marrow and their lifespan in blood is about 2 weeks before they get destroyed in the reticuloendothelial system.[2] Thrombocytopenia is defined as platelet count less than 1.5 lakh cells/mm3 and is the most common hematological disorder in pregnancy after anemia. Normal platelet count ranges from 1.5 -4.5 lakh cells/mm3. Gestational thrombocytopenia accounts for 70-

80% of all cases of thrombocytopenia in pregnancy. Hypertensive disorders accounts for 20% of cases and immune thrombocytopenic purpura for about 3-4% of cases of thrombocytopenia in pregnancy. Thrombocytopenia in pregnancy is classified on the basis of platelet count as mild (platelet count from 100 × 10^3 to 150 × 10^3/µl), moderate (platelets 50-100 × 10^3/µl), and severe (<50 × 10^3/µl). Thrombocytopenia (platelet count<1.5 lac cells/mm3) is found in approximately 20% of all cases during pregnancy and it may be due to hemodilution, increased consumption of platelets due to abnormal activation of the coagulation system or hormonal inhibition of megakaryocytopoesis.[1,3] Gestational thrombocytopenia (GT) or thrombocytopenia during pregnancy occurs in late gestation and is commonly mild (>100*10^3/ul), and resolves after delivery. Several studies have reported thrombocytopenia in 4-13% of neonates of GT's mothers. GT is a benign condition and severe thrombocytopenia rarely occurs. Thrombo-cytopenia can also be due to idiopathic thrombocytopenic purpura (ITP) which occurs due to formation of autoantibodies. ITP is usually severe during pregnancy and severe thrombocytopenia may occur in 5-10% of neonates of mothers with ITP. It generally improves after delivery. In pre-eclampsia, usually thrombocytopenia is mild to moderate but patients with eclampsia can develop severe thrombocytopenia and are more likely to have HELLP (Hemolysis, Elevated Liver enzymes, Low Platelet count) syndrome. The pathophysiology responsible for this is incomplete or abnormal invasion of uterine arteries by trophoblasts cells leading to release of cytokines and chemokines resulting in inflammation in microvasculature, endothelial dysfunction, abnormal activation of coagulation pathway and fibrinolysis.[1,3]

Currently, there is no screening test that would help in identifying whether pregnancy will be associated with PIH or assess its severity. A number of other tests like D-dimer, soluble vascular endothelial growth factor receptor and platelet distribution width, flbronectin level, decrease anti thrombin III level, decrease in α2 anti trypsin, increase in sFlt-1 (soluble Fms like tyrosine kinase-1) concentration, decrease in circulating free PlGF (placental growth factor) are though more sensitive but expensive, time consuming, require well equipped hospital and not suitable for routine purpose.[3,4] Hence, the present study was conducted to investigate the effect of hypertension in pregnancy on the platelet count and to study the pregnancy outcome, maternal and fetal complications in pregnant women with hypertension with low platelet count.

METHODS

This study was a hospital-based case control study conducted in the department of obstetrics and gynecology, SVBP Hospital attached to LLRM Medical College, Meerut, from October 2020 to June 2022. Study was approved by institution's ethical committee and in every case written informed consent was obtained from pregnant females. Fifty pregnant women with hypertension were taken as cases and fifty pregnant females without hypertension were taken as a control visiting the SVBP Hospital, LLRM College. The aim of the study was to analyze the association of low platelet count with hypertension in pregnancy and its feto-maternal outcome. All consenting pregnant females age >18 yrs and BMI <30 kg/m^2 were included in the study while all non-consenting pregnant females age <18 yrs OR >35 yrs, BMI >30 kg/m^2, twin pregnancy, pre-existing renal or vascular disease, seizure disorder, liver disorder, established coagulation and hematological disorder, connective tissue disorder, and drug induced thrombocytopenia were excluded. Pregnant females as cases were those with BP>140/90 MMHG after 20 weeks of gestation on two occasions 4-6 hours apart and those with BP within normal range were taken as control.

Procedure

Two milliliters of blood sample was drawn aseptically using a dry sterile disposable syringe and needle from the median ante cubital vein of all the subjects and control participants into EDTA vials. The blood was diluted with the diluents (1% ammonium oxalate) by 1 in 20 dilutions (0.02 ml of blood and 0.38 ml of diluents) and the platelet count was performed through automated blood count analyzer with other routine antenatal hematological evaluation of the patient. All women enrolled were monitored by platelet count estimation in third trimester or at the time of admission and effect was observed on platelet count in pregnant women with hypertension and its fetomaternal outcome. Blood pressure measurements twice daily and Complete blood count, LFT, KFT, Peripheral blood film were conducted on twice weekly or weekly basis depending upon the severity of hypertension. Peripheral smear was done to exclude ITP, Leukamia, lymphoproliferative diseases and those who received drugs like aspirin and other antiplatelet drugs were excluded from study. Patients were followed up till delivery and their fetomaternal outcomes were assessed. Data was collected and subjected to statistical analysis - SPSS 22.00 for windows; SPSS inc, Chicago, USA. Difference between two groups was determined using t test as well as chi square test and the level of significance was set at $p<0.05$.

RESULTS

Total number of patients analyzed were 100, out of which 50 patients non-hypertensive patients were taken as controls and 50 patients with hypertension were taken as cases. Out of 50 hypertensive patients, 43 developed preeclampsia thus giving an incidence of 43%. Out of these 43 preeclampsia patients 27 were mild preeclampsia and 16 patients developed severe preeclampsia. The mean age amongst cases was 26.73±5.19 SD and the mean age amongst controls was 28.09±4.83 SD. Hence, both the groups were comparable in terms of age distribution. The maternal outcomes among the study groups is shown in (Table 6).

Table 1: Age distribution among the study groups.

Age Group (years)	Gestational HTN		Pre-eclampsia without severe Features		Pre-eclampsia with Severe Features		Severe pre-eclampsia with HELLP syndrome		Eclampsia		Control	
	N	%	N	%	N	%	N	%	N	%	N	%
18-20	1	2	2	4	0	0	0	0	0	0	2	4
21-30	0	0	21	42	12	24	1	2	2	4	32	64
31-35	0	0	6	12	4	8	2	4	1	2	16	32
Total	1	2	27	54	16	32	3	6	3	6	50	100
P value	0.73											

Table 2: Distribution of cases according to severity of hypertension.

Hypertension	Case	
	N	%
Gestational HTN	1	2
Pre-eclampsia without severe Features	27	54
Pre-eclampsia with Severe Features	16	32
Severe pre-eclampsia with HELLP syndrome	3	6
Eclampsia	3	6
Total	50	100

Table 3: Comparison of platelet parameters between cases and control.

Parameters	Case		Control		P value
	Mean	SD	Mean	SD	
Platelet Count×10^9/l	147.30	34.68	284.65	63.20	<0.01**
PCT %	0.12	0.04	0.23	0.03	0.006*

**: highly significant, *: statistically significant

Table 4: Comparison of platelet parameters among cases according to severity of hypertension.

Hypertension	Platelet Count×10^9/l		PCT %	
	Mean	SD	Mean	SD
Gestational HTN (N=1)	184.83	33.27	0.14	0.05
Pre-eclampsia (N=27)	158.36	32.41	0.17	0.03
Severe pre-eclampsia (N=16)	132.04	31.54	0.12	0.02
Severe pre-eclampsia with HELLP syndrome (N=3)	127.45	36.82	0.13	0.03
Eclampsia (N=3)	116.88	35.13	0.15	0.04
P value	0.003*		0.042*	

*statistically significant

Table 5: Comparison of thrombocytopenia among cases according to severity of hypertension.

Hypertension	Thrombocytopenia			
	Normal	Mild	Moderate	Severe
Gestational HTN (N=1)	1	0	0	0
Mild pre-eclampsia (N=27)	10	16	1	0
Severe pre-eclampsia (N=16)	1	5	9	1
Severe pre-eclampsia with HELLP syndrome (N=3)	0	0	2	1
Eclampsia (N=3)	0	0	1	2
Total	12	21	13	4
p value	0.008*			

*statistically significant

Caesarean section, maternal complication and maternal mortality was revealed more in cases as compared to control group. Maternal mortality was high among cases as compared to control but the difference was not statistically significant. The fetal outcomes among the study groups. Preterm birth, SGA, APGAR score<7,

NICU admission, FGR and IUFD was reported more in cases as compared to control group and all the outcomes were significant statistically (Table 7).

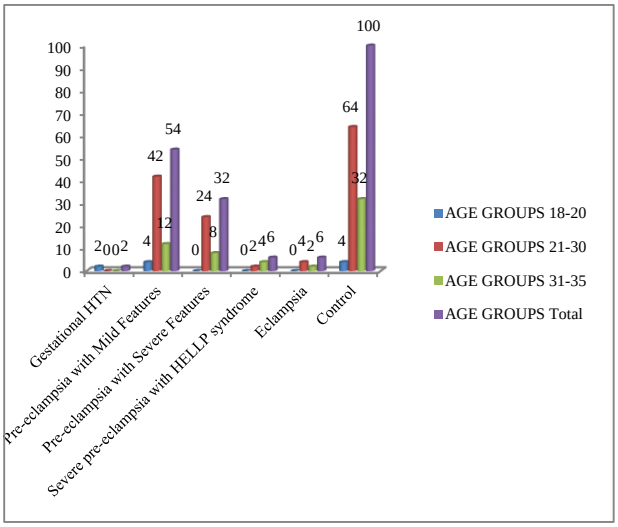

Figure 1: Age distribution among the study groups.

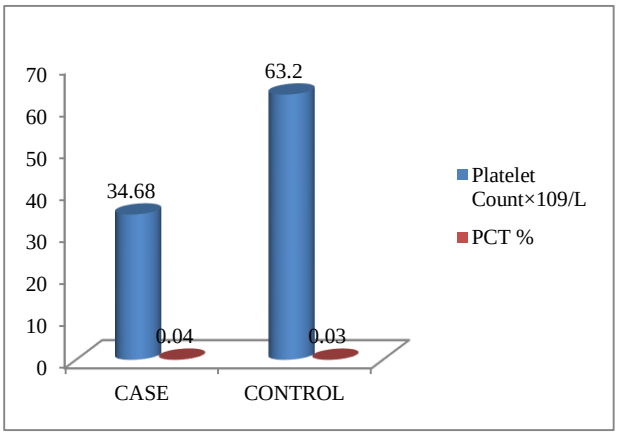

Figure 2: Comparison of platelet parameters between cases and control.

Table 6: Maternal outcomes among the study groups.

Outcomes	Case		Control		P value
	N	%	N	%	
Mode of delivery					
Vaginal	18	36	39	78	<0.01
Caesarean section	32	64	11	22	
Maternal complication					
No	35	70	47	94	0.006
Yes	15	30	3	6	
PTVD	6	12	2	4	
HELLP	1	2	0	0	
PPH	4	8	1	2	
Abruption	3	6	0	0	
Pulmonary edema	2	4	0	0	
Maternal mortality					
Yes	1	6	0	0	0.59
No	49	94	50	100	

Table 7: Fetal outcomes among the study groups.

Outcomes	Case		Control		p value
	N	%	N	%	
Gestational status					
Preterm birth	12	24	2	4	<0.01
Term birth	38	76	48	96	
Fetal weight					
SGA	11	22	4	8	0.038
AGA	34	68	43	86	
LGA	5	10	3	6	
APGAR score					
<7	18	36	7	14	<0.01
>7	32	64	43	86	
NICU admission	12	24	1	2	0.003
FGR	4	8	0	0	
IUFD	2	4	0	0	
Mortality					
Yes	1	2	0	0	0.72
No	49	98	50	100	

DISCUSSION

Thrombocytopenia is defined as platelet count less than 150×10^3/µl or platelet count below the 2.5th percentile for pregnant patients. Thrombocytopenia is encountered in 7-8 % of all pregnancies, out of which 75 % of them is associated with an unknown cause. PIH is the most common medical disorder in pregnancy and is one of the important causes of multiorgan failure and maternal mortality which is preventable, if diagnosed and treated at appropriate time. Many studies have reported thrombocytopenia as a sign of worsening hypertensive disease in pregnant females. Some investigators have proposed biochemical markers to predict the severity of hypertensive disorders of pregnancy like Placental tissue protein 13 and Endoglin's; but these tests cannot be used for simple, low-cost screening. Therefore, there is a need to identify a simple, easily available test specifically designed for routine use in a hospital environment in particular those suitable at a rural setup.[2]

This study was a case control study, which was conducted in the department of obstetrics and gynecology, SVBP hospital attached to LLRM medical college, Meerut, from October 2020 to June 2022. Fifty pregnant women with hypertension and fifty subjects without hypertension served as a control visiting the SVBP Hospital, LLRM College. The aim of the study was to analyze the association of low platelet count with hypertension in pregnancy and its feto maternal outcome. In the present study; 2% of the subjects had gestational HTN, 54% had Pre-eclampsia without severe Features, 32% had Pre-eclampsia with Severe Features, 6% had severe pre-eclampsia with HELLP syndrome, and 6% had eclampsia. Similar findings were observed in a study done by Wolde et al which showed that preeclampsia as the most common hypertensive disorders of pregnancy (51.9%); followed by eclampsia (23.4%), HELLP syndrome (8.9%), and simple

gestational HTN (5.1%). The findings of both the studies were comparable.[5]

The mean age amongst cases was 26.73±5.19 SD and the mean age amongst controls was 28.09±4.83 SD. High incidence of hypertension was seen in age group 21-30 yrs. It was seen that among 18-20 years age group, 2% subjects had gestational HTN, 4% had pre-eclampsia with mild features. Among the 21-30 years age group, 42% subjects had pre-eclampsia without severe features, 24% had pre-eclampsia with severe features, 2% had severe pre-eclampsia with HELLP syndrome, and 4% had eclampsia. Among 31-35 years age group, 12% subjects had pre-eclampsia without severe features, 8% had pre-eclampsia with severe features, 4% had severe pre-eclampsia with HELLP syndrome, and 2% had eclampsia. The findings were not significant statistically. The findings were comparable to study done by Elseed et al in their study 50 females with preeclampsia had mean age of 32.20±3.21 years while 50 normal healthy pregnant females had mean age of 30.68±2.85 years.[6] Our findings corelated with the study of Hussein et al where majority of participants who were diagnosed with hypertension associated with pregnancy were be-tween 25 to 29 years old.[7] Thus, there was no significant finding in any of above study showing co-relation of age with severity of hypertension in pregnancy. In this study, hypertension during pregnancy were more common in multigravida women as compared to primigravida among cases. Among Primi gravida women, 2% subjects had gestational HTN, 10.5% had pre-eclampsia without severe features, 14% had pre-eclampsia with severe features, and 2% had severe pre-eclampsia with HELLP syndrome, and 2% had eclampsia. Among Multi gravida women, 44% subjects had pre-eclampsia without severe features, 14 % had pre-eclampsia with severe features, 4% had severe pre-eclampsia with HELLP syndrome, and 4% had eclampsia. Abalos et al in their study similarly reported that most women had more than one pregnancy (multigravida).[7-9] Continuous review of the records showed multigravidas and multiparas tend to be affected by hypertension more than the primi gravidas and primiparas. Similar findings were observed, in the same study of Hussein et al and Al-Ghamdi et al they found that higher prevalence of hypertension amongst multipara with hypertension were admitted.7[-10] In contrast a study from Ethiopia showed 66.7% of cases with PIH studied by Wolde et al were nulliparous, another study in contrast to the present study was a study done by Riaz et al where 60% of the cases were primigravida and Donimath et al where majority of patients were primigravida.[5,8,11]

In the present study; mean platelet count and PCT % was found to be significantly lower in cases as compared to controls. Mean platelet count was 184.83±33.27, 158.36±32.41, 132.04±31.54, 127.45±36.82, and 116.88±35.13 respectively among subjects with gestational HTN, mild pre-eclampsia, severe pre-eclampsia, severe pre-eclampsia with HELLP syndrome and eclampsia. The findings were significant statistically and was consistent with the study done by Rupakala et al in which they showed that 30 cases had normal platelet count and 120 cases had derranged platelet count.[12] Severe thrombocytopenia was reported more in eclampsia subjects followed by severe pre-eclampsia with HELLP syndrome while moderate thrombocytopenia was found more in severe pre-eclampsia women. This showed that increasing severity of hypertension is associated with decrease in platelet count. The thrombocytopenia in pregnancy-induced hypertension is moderate, and the platelets rarely drop below 20,000/l. Hemorrhage is an uncommon event unless the patient develops disseminated intravascular coagulation, but thrombocytopenia can be a sign of worsening hypertensive disease. A slowly decreasing platelet count and worsening disease can be detected before the clinical manifestations of pregnancy induced hypertension and necessary action can be taken accordingly. When accompanied by microangiopathic hemolytic anemia, hemolysis, elevated liver enzymes, and low platelets, HELLP syndrome is diagnosed. Similar findings were obtained in study by Meshram et al where they found lower platelet counts in preeclampsia and eclampsia than in healthy pregnant controls.[13] Caesarian section, maternal complication including HELLP Syndrome and PPH and maternal mortality was revealed more in case as compared to control group. HELLP syndrome and PPH was found in 10% of the cases respectively which was high as compared to control but not statistically significant thus larger sample size is needed for confirmation. In a study by Rupakala et al the incidence of HELLP syndrome was 6%. Riaz et al reported an incidence of 5%.[11-14] 32 Meshram et al reported an incidence of 10.63% and in their study documented similar findings by Sibai et al 9.8%. In our study incidence of help syndrome was 2% amongst cases. Abalos et al in their study mentioned that maternal outcome recorded no maternal deaths; however, 4% maternal complications (i.e., post-partum hemorrhage and HELLP syndrome) and more caesarean section deliveries were observed.[9] Our findings were comparable to findings of above-mentioned studies. Only single maternal mortality was reported in our study which was a referred case of ecclampsia with aspiration pneumonitis. Preterm birth, SGA, APGAR score <7, NICU admission, FGR and IUFD was reported more in case as compared to control group. It was seen that all the outcomes were significant statistically. One neonatal mortality was reported where baby was preterm (31.2 WOG), low birth weight (1.1 kg), severe fetal growth restriction with mother showing features of eclampsia. Even though, a larger percentage of term babies were documented, prematurity was still a common complication of hypertensive disorder associated with pregnancy. In a research conducted by Bangal et al a considerable incidence of prematurity was identified in babies of women with mild to severe pregnancy-induced hypertension and eclampsia.[15] Another study of Brown and Buddle established that fetal outcomes differ according to the type of hypertension.[16] For example, women with superimposed pre-eclampsia had earlier deliveries, with lower average birth weights babies and more SGA babies.[17] The “Born Too Soon” report by Raina

and Mehta provides estimates for global comparisons.[17] According to this report, annually 15 million babies are born before 37 weeks gestation with one of the causes being PIH. Intrauterine deaths, intrauterine growth restriction, prematurity and perinatal asphyxia are common complications in the baby born to mother of pregnancy induced hypertension as mentioned by Sandhya et al in their study.[18] 4% Intrauterine death, 8% intrauterine growth restriction, 24% prematurity amongst cases was reported from our study as compared to only 4% prematurity with no intrauterine death and intrauterine growth restriction amongst control.

CONCLUSION

The study concluded that platelet count (PLTs count) and plateletcrit (PCT) were significantly decreased in pregnant women with hypertensive disorder of pregnancy, especially preeclampsia. Thrombocytopenia worsens as PIH progresses from gestational hypertension to eclampsia, so platelet parameters especially (PLTs count and PCT) can be used for assessing and predicting of the risk of severe preeclampsia and prevent progression to HELLP syndrome and DIC by timed delivery. This method is not only rapid but also cheaper. It can be done even in rural hospitals.

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