

## Platelet volume indices in gestational hypertension: An observational study

Nagalakshmi Vijaykumar<sup>1\*</sup>, Deepti Dixit<sup>2</sup>, Sanjivani S. Jadhav<sup>3</sup>, Asha Neravi<sup>4</sup>,  
Usha Kiran Naidu<sup>4</sup> and Rishab Patil<sup>5</sup>

<sup>1</sup>Department of Physiology, SDM College of Medical Sciences and Hospital, Manjushree Nagar, Sattur, Dharwad-580009, Karnataka, India, <sup>2</sup>Department of Pathology, SDM College of Medical Sciences & Hospital, Manjushree Nagar, Sattur, Dharwad-580009, Karnataka, India, <sup>3</sup>Department of Physiology, JGMM Medical College, Gabbur Cross, Hubballi-580028, Karnataka, India,

<sup>4</sup>Department of OBG, SDM College of Medical Sciences & Hospital, Manjushree Nagar, Sattur, Dharwad-580009, Karnataka, India and <sup>5</sup>Under graduate student, SDM College of Medical Sciences & Hospital, Manjushree Nagar, Sattur, Dharwad-580009, Karnataka, India

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**Abstract: Background & Objectives:** The incidence of gestational hypertension is increasing in India which accounts for various maternal morbidity & mortality. As gestational hypertension is hypercoagulability state we wanted to assess platelet volume indices in gestational hypertension. **Materials and Methods:** This is a cross-sectional, case-control study conducted in the Department of Physiology, in collaboration with OBG and Pathology after obtaining institutional ethical clearance. Study includes 60 (n=60) hypertensive as cases and 60 (n=60) normotensive as controls who were in third trimester of pregnancy. Blood pressure was measured using mercury sphygmomanometer and those who had BP values more than 140/90 mmHg without proteinuria were taken as cases and those with normal values were taken as controls. Platelet volume indices were measured using sysmex automated flow meter. Statistically analyzed using t test and pearson's correlation by SPSS 20 software. **Results:** Mean platelet volume, platelet distribution width and large cell platelet ratio were higher in hypertensive pregnant female when compared to normotensives which is not statistically significant. (10.72±1.08 Vs 10.61±1.08 p= 0.56, 12.69± 2.79 Vs 12.57±2.85 p= 0.80, 30.75± 8.50 Vs 29.75±8.70 p= 0.52) plateletcrit was lower in hypertensive when compared to normotensive. (0.23± 0.08 Vs 0.24±0.04 p=0.48) there was no statistical significant correlation exists between BP and platelet volume indices. **Conclusion:** Our study concludes no strong association of platelet volume indices with severity of hypertension amongst gestational hypertension.

**Keywords:** Pregnancy Induced Hypertension, Plateletcrit, Mean Platelet Volume.

### Introduction

Pregnancy induced Hypertension (PIH) is seen in up to 10% of pregnancies and represents a significant cause of maternal and perinatal morbidity and mortality [1].

According to National High Blood Pressure Education Program and The American College of Obstetricians and Gynecologists (ACOG) practice bulletins, hypertension in pregnancy can be classified as Gestational hypertension, Preeclampsia - eclampsia, chronic hypertension and preeclampsia superimposed upon chronic hypertension [2]. Based on values, Systolic blood pressure (SBP) >140 mmHg and/or Diastolic

blood pressure (DBP) > 90mmHg or both is recommended as Gestational hypertension. If SBP > 140 mmHg and / or DBP > 90 mmHg present before pregnancy or before 20 weeks of gestation is considered as chronic hypertension. If SBP > 160 mmHg and DBP > 90 mmHg present along with proteinuria is recommended as preeclampsia. If SBP > 160 mmHg and DBP > 90 mmHg along with proteinuria develops in chronic hypertensive patient then is recommended as preeclampsia superimposed on chronic hypertension [2].

Elderly primi, previous history of preeclampsia, obesity before pregnancy,

ethnicity, multiple gestations, and underlying medical conditions such as renal disease and diabetes mellitus imposes more risk to develop PIH [3]. Gestational hypertension accounts for various maternal and perinatal morbidity and mortality, like increased risk of prematurity, birth of infants who are small for their gestational age, intrauterine death, placental abruption, and cesarean delivery [4].

Platelets, which are the important component of blood play crucial role in coagulability of blood. It also plays role in thrombus formation. There are various markers to assess the platelet activation and function. Mean platelet volume (MPV) is one of the markers, which is average size of platelets. When there is increased platelet activity, generally it increases its size, with lots of granules and increases coagulability state. Platelet distribution width (PDW) is the variance in size of platelets indicates platelet activation. Platelet distribution width is also marker of platelet reactivity and thrombolytic failure [5].

Various studies demonstrate use of platelet indices like MPV and PDW as a marker for the development of hypertension during pregnancy [6-7] but few studies shows no association between platelet volume indices with hypertension during pregnancy. As review of literature shows varied results, we wanted to study platelet volume indices in gestational hypertension and also to see their association with severity of hypertension.

### Material and Methods

*Study Design:* This is a cross-sectional, case-control study that was conducted in the Department of Physiology in association with Obstetrics and Gynecology and Pathology, SDM Medical College after obtaining institutional ethical clearance. (Ref: SDMIEC: 44: 2020) Study was conducted between June 2021 to December 2021.

*Study population:* Our accessible study population was pregnant females who are in third trimester who were attending OBG OPD'S or in wards in the age group of 25- 40 years. Our target population was those were diagnosed as hypertensive by the obstetrician. Pregnant females with normal blood pressure were taken as

controls. All the participants were explained about the procedure and written consent taken.

*Inclusion criteria:* Hypertensive pregnant females and normotensive pregnant females who are in third trimester of pregnancy in the age group of 25- 40 years.

*Exclusion Criteria:* Pregnant females with Gestational Diabetes mellitus, hematological disorders, history of multiple pregnancies and neurological disorders were excluded from the study.

*Sample size:* sample size was decided based on incidence of hypertensive pregnancies amongst general population who are visiting SDMCMS&H, with study duration in mind (6 months). Study includes 60 (n=60) hypertensive pregnant females as cases and 60 (n=60) normotensive pregnant females as controls.

*Study protocol:*

*a) Estimation of Blood pressure:* Subjects were made to lie down in supine position for 10 minutes. At the end of 10 minutes blood pressure was recorded using mercury sphygmomanometer with female seated with her legs uncrossed and back supported. (Anand agencies, Bengaluru) an appropriate sized cuff was used to get accurate readings. Initially BP was recorded by palpatory method to avoid auscultatory gap. Then cuff was inflated 20 mmHg more than SBP value then slowly deflated. Ist phase of Korotkoff sound i. e appearance of sound was considered as systolic blood pressure (SBP) and disappearance of sound i.e phase IV or V taken as Diastolic Blood pressure. (DBP) Values were recorded in mmHg units.

Those who got BP values more than 140/90 mmHg, BP was recorded again by the procedure mentioned above after 20 minutes. Pregnant females who had SBP > 140 mmHg and / or DBP > 90mmHg were considered as gestational hypertensive and included in study as cases. Those pregnant females who developed SBP 100-140 mmHg and DBP 60-90 mmHg were taken as normotensive and included in study as controls.

*b. Recording of platelet volume indices:* 5cc of blood collected in EDTA vacutainer under aseptic precautions using venupuncture. Various platelet volume indices like mean platelet volume (MPV) in femtolitres, Platelet distribution width (PDW) in femtolitres, platelet large cell ratio (P-LCR) and plateletcrit (PCT) are estimated by Sysmex KX21-N automated flow meter using principle of impedance and optical light scatter.

*Statistical Analysis:* Analysis of above case-control, cross-sectional study was performed using SPSS software version 20. Intra group analyses of variables were done by unpaired T test. Pearson’s correlation used to test the association of severity of blood pressure values with various platelet volume indices. Values were expressed as mean ± standard deviation (SD). p < 0.05 considered as statistically significant and <0.01 as highly significant.

**Results**

The study includes 60 hypertensive pregnant females (n= 60) and 60 normotensives pregnant females as controls (n= 60). Table 1 shows demographical details of cases and controls. Mean age of cases and controls were 30.13± 5.32 and 26.38± 3.61. Amongst hypertensive out of 60, 21 (35%) were primigravida, 38 (63%) were second gravid and 1 (2%) was third gravid. Amongst normotensives 42 (70%) were primigravida, 18 (30%) were second gravid. Regarding pregnancy outcome in hypertensive 45 (75%) underwent caesarian section and in normotensives 28 (47%) underwent caesarian section. The average fetal weight born for hypertensive females was 2.22±0.50 Kg and amongst normotensives was 2.81±0.32 Kg.

	<b>Hypertensive (n=60)</b>	<b>Normotensive (n=60)</b>
<b>Age (years)</b>	30.13± 5.32	26.38± 3.61
<b>Age distribution</b>		
25-30 years	41 (69%)	50 (83%)
30-35 years	17 (28%)	10 (17%)
35-40 years	02 (03%)	0 (0%)
<b>Gravid score</b>	Primigravida -21 (35%)- Second gravid- 38 (63%) Third gravid 1 (2 %)	Primigravida- 42 (70%) Second gravid- 18 (30%) Third gravid- 0%
<b>Pregnancy outcome</b>		
LSCS	45 (75 %)	28 (47%)
Vaginal delivery	15 (25 %)	32 (53 %)
Fetal weight (Kg)	2.22±0.50	2.81±0.32
Values are expressed as Mean±SD		

Table 2 shows comparison of study parameters amongst cases and controls. There was a statistically significant increase in SBP amongst hypertensive compared to normotensives. (151.10± 8.81 Vs 110.63±8.51 p=0.01\*\*) there was a significant increase in DBP amongst hypertensive compared to normotensives. (90.86± 6.61 Vs 68.36±5.23 p=0.01\*\*) The platelet count (10<sup>3</sup>/microL) is lower in hypertensive compared to normotensive which is not significant. (380.00±20.0 Vs 430.00± 70.0 p= 0.09). The Mean Platelet Volume is high in hypertensive compared to normotensives which is not

statistically significant. (10.72± 1.08 Vs 10.61±1.08 p= 0.56) Platelet Distribution Width is high in hypertensive compared to normotensives which is not significant. (12.69± 2.79 Vs 12.57±2.85 p= 0.80) Platelet -Large cell ratio was high in hypertensive compared to normotensive which is not significant. (30.75± 8.50 Vs 29.75±8.70 p= 0.52) Plateletcrit was lower in hypertensive compared to normotensives which is not statistically significant. (0.23± 0.08 Vs 0.24 ± 0.04 p=0.48).

Parameters	Hypertensive (n=60)	Normotensive (n=60)	t value	p value
Systolic Blood Pressure (mm of Hg)	151.10± 8.81	110.63±8.51	25.57	0.00**
Diastolic Blood Pressure (mm Hg)	90.86± 6.61	68.36±5.23	20.65	0.00**
Platelet count (10 <sup>3</sup> /microL)	380.00±20.0	430.00± 70.0	-0.607	0.09
Mean Platelet Volume (fl)	10.72± 1.08	10.61±1.08	0.57	0.56
Platelet Distribution Width (fl)	12.69± 2.79	12.57±2.85	0.242	0.80
Platelet Large Cell Ratio	30.75± 8.50	29.75±8.70	0.63	0.52
Plateletcrit	0.23± 0.08	0.24±0.04	-0.70	0.48

Values are expressed as Mean ± SD, p< 0.05\* considered as significant, p< 0.01 \*\* considered as highly significant.

Table 3 shows correlation between Blood pressure and Platelet indices in hypertensive pregnant females. There exists a weak positive correlation between both Systolic and Diastolic BP with MPV, PDW and L-CPR. There exists a weak negative correlation between Systolic blood pressure & Plateletcrit which is not significant.

	Systolic Blood pressure (mmHg)	Diastolic Blood Pressure (mmHg)
Mean Platelet Volume (fl)	r= 0.05 p= 0.51	r=0.04 p=0.64
Platelet Distribution Width (fl)	r= 0.01 p= 0.85	r= 0.01 p=0.89
Platelet- Large Cell Ratio	r=0.05 p=0.55	r= 0.04 p=0.62
Plateletcrit	r= -0.06 p=0.48	r=-0.15 p=0.08

r= + positive correlation: r= - Negative correlation: p< 0.05 considered as significant\*

### Discussion

All the 60 hypertensive pregnant females had gestational hypertension with SBP equal to or greater than 140 mmHg or DBP equal to or greater than 90 mmHg or both [4]. 15 (25%) of them had systolic blood pressure of equal to or greater than 160 mmHg and 45 (75%) of them had systolic blood pressure 140 to 160 mmHg & none of them developed preeclampsia. 42 (70%) had DBP equal to or greater than 90 mmHg and 18 (30%) had DBP between 80 to 90 mmHg. Out

of 60, 18 (30%) had only elevated SBP of more than 140 mmHg and normal DBP values whereas 42 (70%) had both elevated SBP of more than 140 mmHg and DBP of greater than 90 mmHg. Our study showed that hypertension was more common in females with second pregnancy than in females who were primigravida and also more in age group of 25-30 years. The retrospective study conducted in referral hospital, Ethiopia in 6826 total deliveries, 199 had hypertension during pregnancy. It shows that hypertension during pregnancy was more common in elderly primi of more than 35 years old [8]. Most of hypertensive pregnant females underwent caesarian section than vaginal delivery.

Mean platelet volume which is an average dimension of each platelet varies from 7.5 to 12 fl is a marker of platelet activity. Physiologically there is an inverse relation between platelet count and MPV to maintain a constant platelet mass. Platelets with MPV more than 15 fl are more active releases more granules and increases platelet aggregation and clot formation [9]. In normal pregnancy due to increased consumption of platelets in utero-placental circulation there is decreased platelet count and reduced lifespan of platelets. As pregnancy induces strain on vascular endothelium, there can be vascular damage and this leads to slight increase in MPV [10]. Our study shows MPV in normotensive pregnant females is 10.61 fl. Study conducted by Gustavo shows MPV in normotensive pregnant females was 10.1 fl [11].

Our study shows average MPV in hypertensive pregnant females is 10.72fl. Our study shows that MPV is higher in hypertensive females when compared to normotensive control which is not significant. Results of our study is comparable to Study conducted by Gustavo which shows that MPV significantly increases in preeclampsia compared to normotensive pregnant females. There study shows MPV in preeclampsia was 11.3fl [11]. Prospective study conducted by Mine Kanat shows that MPV significantly increases in preeclampsia. Study shows MPV of more than 10.5 fl in late first trimester of pregnancy indicates intrauterine growth restriction [12].

Systemic metaanalysis done by Ioannis Bellos shows that MPV was significantly higher in preeclamptic women compared to controls [13]. Case control study done by Thalor also shows statistically significant difference in MPV in preeclampsia females [14]. However Study conducted by Suhail in pregnant females with PIH in third trimester shows no significant difference in MPV compared to pregnant females without PIH. There study shows MPV in PIH pregnant females was 7.14 fl and in pregnant females without PIH was 7.89fl [15]. Even study done by Ismail shows that there no difference in MPV in hypertensive pregnant females [16].

Platelet distribution width is the distribution width on 20% frequency level with the peak taken as 100%. PDW mainly depends on platelet activation with the formation of more pseudopods and platelet morphological change [17]. Our study shows that average PDW in hypertensive pregnant females was  $12.69 \pm 2.79$ fl when compared to  $12.57 \pm 2.85$ fl in normotensive pregnant females. Our study shows increased PDW in hypertensive female which is not statistically significant. However results of various studies show that there is statistically significant increase exists in PDW in hypertensive pregnant females compared to normotensive pregnant females [18-20].

Plateletcrit which is an indicator of total platelet mass ranges 0.20 - 0.35 % in subjects with normal platelet count [21]. Our study showed increased plateletcrit in hypertensive females compared to normotensive which is not statistically significant. ( $0.23 \pm 0.08$  Vs  $0.24 \pm 0.04$   $p=0.48$ ) results of our study is similar to study

done by Nitesh which showed lower PCT in hypertensive than normotensives but not statistically significant & cause for lower PCT in hypertensive could be due to thrombocytopenia [14] however study done by Abha singh showed reduced PCT even in non thrombocytopenic hypertensives [20].

Platelet large cell ratio (P-LCR) is defined as percentage of platelets that have platelet volume exceeds than 12fl in the total count which is inversely related to platelet count and directly related to MPV [21]. Our study showed increased P-LCR in hypertensive than normotensive which is not statistically significant. ( $30.75 \pm 8.50$  Vs  $29.75 \pm 8.70$   $p=0.52$ ) however study shows significant increase in L-CPR in hypertension compared to normotensive. Increase in P-LCR could be attributed to bone marrow activation by unknown stimulus [18].

Our study also shows the correlation between Blood pressure and platelet volume indices. There was weak positive correlation exists between SBP and MPV, PDW and P-LCR which was not statistically significant. ( $r=0.05$   $p=0.51$ ,  $r=0.01$   $p=0.85$ ,  $r=0.05$   $p=0.55$ ) we found weak negative correlation between SBP and plateletcrit which is not statistically significant. ( $r=-0.06$   $p=0.48$ ) there was weak positive correlation exists between DBP and MPV, PDW & P-LCR which is not statistically significant. ( $r=0.04$   $p=0.64$ ,  $r=0.01$   $p=0.89$ ,  $r=0.04$   $p=0.62$ ) we found negative correlation between DBP and PCT which is not statistically significant. ( $r=-0.15$   $p=0.08$ ) however studied shows significant positive correlation between BP and MPV & PDW [14].

*Strength of study:* Our study shows altered platelet volume indices in pregnancy induced hypertension. Our study opens up the further research scope, in which follow up study can be done in pregnant females to see the effect of altered platelet indices value with the chances of development of hypertension. Study should also be done to set up a cutoff value for MPV to predict development of future hypertension. Our study shows the importance of platelet indices as a predictor of development of hypertension.

**Limitations of study:** Small sample size is one of the limiting factors of our study. As the study was planned for ICMR, STS keeping the duration in mind 60 sample sizes was decided.

## Conclusion

Our study concludes that platelet volume indices such as Mean platelet volume, platelet distribution width, plateletcrit and large cell platelet ratio will not be significantly altered in gestational hypertension.

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\*All correspondences to: Dr. Nagalakshmi V., Professor, Department of Physiology, SDM College of Medical Sciences & Hospital, Manjushree Nagar, Sattur, Dharwad-580009, Karnataka, India. E-mail: drlakshmi26@yahoo.com