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Original Research Article

Significance of leukocyte and platelet counts in hypertensive disorders of pregnancy - A retrospective study in a tertiary care hospital

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ABSTRACT

Background: Hypertensive disorders in pregnancy are a spectrum of disorders ranging from gestational hypertension, pre-eclampsia to eclampsia and chronic hypertension superimposed by pre-eclampsia. With an incidence of 7-15% complicating pregnancies, several theories have been stated to define the pathogenesis. Inflammation per se is also found to have its part in the pathogenesis of hypertension.

Objective: To evaluate and compare the inflammatory mediators namely the leukocyte count, platelet count, absolute neutrophil count, absolute lymphocyte count, neutrophil lymphocyte ratio and platelet lymphocyte ratio among the hypertensive disorders in pregnancy.

Materials and Methods: This is a retrospective study done at a tertiary care hospital including all women admitted with hypertension in pregnancy from 26th April 2016 to 31st March 2019. Patients with singleton pregnancy with hypertension were included and those with prelabour rupture of membranes or concomitant infection were excluded. Patients were divided into four groups, chronic hypertension, and gestational hypertension, non-severe and severe preeclampsia. The total and differential leukocyte counts at admission were accessed from the medical records and statistical analysis was done.

Results: Out of 4860 deliveries, 294 patients were diagnosed with hypertensive disorders (6.04%). Of the 294, those belonging to chronic hypertension, gestational hypertension, non-severe and severe preeclampsia were 43 (14.6%), 128(43.5%), 52(17.7%) and 71(24.1%) respectively. A p value of < 0.05 was considered significant. It was found that there was a significant difference among the groups in mean age and chronic hypertension was found to have a higher mean age than the other groups. The mean platelet count was also found to be significantly higher in chronic hypertension as compared to other groups. There was no significant difference in both mean total and mean differential leukocyte counts, ANC, ALC, NLR and PLR among the four groups.

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1. Introduction

Hypertensive disorders in pregnancy are a spectrum of disorders ranging from gestational hypertension, pre-eclampsia to eclampsia and chronic hypertension superimposed by pre-eclampsia.¹ With an incidence of 7-15%,² several theories have been stated to define the pathogenesis of hypertension in pregnancy like

immunological theory, genetic theory, abnormal placental invasion and exaggerated inflammatory response.³ During the inflammatory response, the leukocytes are activated which releases cytokines, interleukin-8 and tumour necrosis factor α which leads to endothelial dysfunction. A recent study has found an interaction with the activated leukocytes and platelets which triggers and exaggerates inflammation in the arterial endothelium. The exaggerated systemic inflammatory response causes endothelial dysfunction

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which predates the clinical manifestation of preeclampsia. The haematological parameters, the Platelet-to-Lymphocyte ratio (PLR) and Neutrophil-to Lymphocyte ratio (NLR), have been recently applied to be systemic inflammatory response markers,⁴ could be options for evaluation of adverse maternal and fetal outcomes in preeclampsia. Mihi et al in 2010 showed that in preeclampsia, there is an exacerbation of a generalized inflammatory response, physiologically present during the last trimester of gestation.⁵

The haematological parameters, the PLR and NLR, have been recently applied to be systemic inflammatory response markers, which could be options for evaluation of severity of preeclampsia. Studies have been done to compare the changes in systemic inflammatory response markers between the normal pregnancies and preeclampsia. There is limited data comparing the markers between the various hypertensive disorders in pregnancy, this study is designed to assess the leucocyte and platelet counts in the hypertensive disorders in pregnancy and its relation to the severity of the condition.

The objective of the study is to evaluate and compare the inflammatory mediators namely the leukocyte count, platelet count, absolute neutrophil count, absolute lymphocyte count, neutrophil lymphocyte ratio and platelet lymphocyte ratio among the hypertensive disorders in pregnancy.

2. Materials and Methods

This was a retrospective study conducted in a tertiary care hospital - Pondicherry Institute of Medical Sciences, Pondicherry, India, from 26th April 2016 to 31st March 2019. The study included all singleton pregnancies with hypertensive disorders of pregnancy who delivered in our institution. Those with multifetal gestation, prelabour rupture of membranes, any concomitant infection like urinary tract infection, dental infection, fever 48 hours before or during or 48 hours after admission were excluded from the study. The total leukocyte count, differential leukocyte counts and platelet counts at admission were taken into consideration.

A pilot study was conducted with a sample size of 10 per group for the four hypertensive disorders of pregnancy. Sample size was calculated based on the pilot study to estimate the difference between means using the formula below with alpha error as 5%, power as 80%, error of margin as 3 for platelet to lymphocyte ratio and the mean & standard deviation based on the pilot study (10 subjects in each group). Minimum sample per group was found to be 54 per group.

Formula used for sample size calculation $n = 2 \frac{Z^2(1-\alpha/2)\sigma^2}{d^2}$

where Z is the standard normal deviate, d is the error of margin; sigma is the average standard deviation of means.

Records of all women who delivered between 1st January 2016 to 31st March 2019 with any hypertensive disorder of pregnancy fulfilling the selection criteria were included and were divided into 4 groups chronic hypertension, gestational hypertension, mild preeclampsia and severe preeclampsia. The total and differential leukocyte counts and platelet count at admission were accessed from the electronic medical records. The absolute neutrophil and absolute lymphocyte count were used to calculate the neutrophil to lymphocyte ratio and the platelet to lymphocyte ratio. Correlation analysis between the total and differential leucocyte count, platelet count, PLR, NLR, absolute neutrophil count and absolute lymphocyte count and the 4 hypertensive groups was done.

3. Results

Out of the 294 samples, the mean age was found to be 27.30 ± 5.245 . 43(14.6%) participants had chronic hypertension, 128(43.5%) had gestational hypertension, 52(17.7%) had non-severe preeclampsia and 71(24.1%) had severe preeclampsia. The tests of significance used were ANOVA test for means of parameters and Kruskal-Wallis (KW) test for median of parameters. The mean ages among the study groups were – chronic hypertension was 30.07 ± 5.289 , gestational hypertension was 26.34 ± 5.011 , non-severe preeclampsia was 26.75 ± 5.129 and severe preeclampsia was 27.73 ± 5.180 . Table 1 shows the summary of the results of statistical analysis. There was no statistically significant difference among patients with GH, NSP and SP. While, as expected, CH was seen in patients with higher age group. There was no statistically significant difference among the groups in mean total leukocyte count ($p = 0.117$), Mean lymphocyte count ($p = 0.097$), Mean neutrophil count ($p = 0.143$). Median eosinophil count ($p = 0.853$), median basophil count ($p = 0.730$) and median monocyte count ($p = 0.738$) also had no statistically significant differences among the groups. The difference in mean platelet count among the groups was statistically significant ($p = 0.008$). A sub-analysis by Tukey post hoc test revealed that the platelet count of CH patients were statistically significantly higher than the other groups, while there was no statistically significant difference between the GH, NSP and SP patients. The other parameters studied also showed no statistically significant difference among the groups viz., the mean absolute neutrophil count, median basophil count ($p = 0.084$), mean absolute lymphocyte count ($p = 0.324$), median platelet to lymphocyte ratio ($p = 0.451$), median neutrophil to lymphocyte ratio ($p = 0.219$).

4. Discussion

A total of 294 samples were evaluated which included subjects with gestational hypertension, chronic hypertension, mild preeclampsia and severe preeclampsia.

Table 1: Summary of statistical analysis

Grp (N)	Mean TC (X 1000 cells/ MI)	Mean L %	Mean N %	Median E %	Median M %	Median B %	Mean platelet count (X 10 ⁵ /mL)	Mean ANC (X1000 cells/ml)	Mean ALC (X1000 cells/ml)	Median PLR	Median NLR
CH (43)	11.96	18	74	2	3	0	265.37	8.97	2.15	14.0	3.80
GH (128)	11.91	18	75	1	4	1	231.85	9.11	2.03	12.9	4.25
NSP (52)	13.46	16	77	1	4	0	222.69	10.5	2.03	12.3	4.49
SP (71)	12.27	19	73	1	4	0	228.06	9.25	2.22	12.5	3.80
Total (294)	12.28	18	75	1	4	0	234.22	9.38	2.09	12.8	4.02
*Test	ANOVA	ANOVA	ANOVA	KW	KW	KW	ANOVA	ANOVA	ANOVA	KW	KW
p value	0.117	0.097	0.143	0.853	0.738	0.730	0.008	0.084	0.324	0.451	0.219

TC: Total leukocyte count, L: Lymphocytes, N: Neutrophils, E: Eosinophils, M: Monocytes, B: Basophils, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, PLR: Platelet to lymphocyte ratio, NLR: Neutrophil to lymphocyte ratio, KW: Kruskal-Wallis test

Only chronic hypertension was found to occur in older age group as compared to other hypertensive disorders in pregnancy. Mean platelet count was increased in chronic hypertension group. No statistical significant variation was found in the rest of the parameters among the groups. Several other studies showed conflicting results.⁴⁻⁶

Sitowah et al⁶ in 2018, published a cross-sectional study done at University of Gondar hospital. The study compared mild and severe preeclamptic subjects with healthy pregnant women. With a sample size of 126, the parameters studied were mean WBC count, mean ANC, mean AMC, mean PTC, Platelet distribution width (PDW), mean NLR and median of platelet-to-large cell ratio (P-LCR) which were significantly increased; while Absolute lymphocyte count (ALC) and platelet count (PTC) were significantly decreased in PE groups. Chronic hypertension and gestational hypertension were not considered in this study. In the current study no significant difference was found among the groups of concern while normotensive antenatal women were not considered for our study.

Yavuzcan et al.⁴ compared women with severe preeclampsia, healthy pregnant and non-pregnant women. The parameters of concern were leukocytes, neutrophils, lymphocytes, mean platelet volume (MPV), and systemic inflammatory response (SIR) markers (neutrophil-lymphocyte ratio/platelet-lymphocyte ratio). It was found that there was no statistically significant difference in MPV, NLR and PLR ($p=0.081$, $p=0.721$, $p=0.098$) among severe PE and healthy pregnant women. Again, this study considered only severe preeclampsia vs healthy pregnant women, while the other hypertensive disorders were not taken into consideration.

Toptas et al,⁷ studied NLR and PLR in patients with preeclampsia and healthy pregnant women. Their sample included 93 women with PE and 94 normal pregnant women with similar maternal age and gestation at deliver. There were similar PLR and NLR among the groups. A subgroup analysis showed that subjects with severe PE had similar NLR but lower PLR levels compared to those with mild PE. But NLR did not show any such significant difference in subgroup analysis.

Aly et al⁸ tried to derive the association between biochemical markers released from neutrophils in preeclampsia. According to the study, syncytiotrophoblast microvillous membranes (STBMs) act on maternal neutrophils to produce superoxide radicals in preeclamptic women and their correlation was showed to be statistically significant from cultured STBMs ($P = .007$). Maternal TPA levels were also significantly increased among PE women than healthy controls ($P = .005$). Superoxide production by maternal neutrophils from cultured STBMs among PE women and healthy women showed statistical significant difference (P values $.006$). A dose-response relationship was observed. They concluded that “STBMs in maternal

blood induce neutrophils to generate superoxide radicals that may cause endothelial dysfunction in women with preeclampsia”.

Canzoneri et al.,⁹ conducted a retrospective study in 240 women who delivered at Louisiana State University Health Sciences Center– Shreveport, Louisiana. They compared preeclamptic women with normal pregnant women. They found that total leukocyte count and neutrophil counts were increased. There were no statistical differences among the groups in monocyte and lymphocyte counts.

Mihu et al⁵ in their study, concluded that TLC and neutrophil counts positively correlated with diastolic blood pressure values and hence can be considered as markers of inflammatory response in preeclampsia. Again gestational hypertension and chronic hypertension were not considered in this study. Women with preeclampsia on a whole were compared to normotensive pregnant women.

Another study by Ceyhan et al¹⁰ found there is no significant difference between the TLC and platelet counts. The current study shows no significant variation in TLC while mean platelet count was found to be elevated in chronic hypertensives.

A recent study in 2024 by Zhu et al¹¹ suggested that leucocytosis in pregnancy was associated with increased rates of obstetric complications related to placenta like placenta previa, oligohydramnios and fetal growth restriction. Further studies with higher sample size are required to show the effects of leucocytosis in pregnancy.

A study conducted in a maternity unit in Sudan in 2022¹² showed a significant increase in WBC count and neutrophils. It also showed an increased NLR and decreased lymphocyte count in SP as compared to NSP suggesting NLR as a prognostic marker of severity of preeclampsia.

Another study by Guimiot F et al¹³ in 2024 showed the importance of different immunological aspects leading to preeclampsia and had suggested that studying the genetics of endometrial cells in menstruation in women at risk of developing hypertension in pregnancy may lead to innovations in therapy in the future. The two stage pathophysiology of SP has been emphasised in a study by Kornacki et al¹⁴ in 2023, where abnormal placentation as a result of improper cardiac and cardio-vascular adaptation in pregnancy which basically also signifies the immunologic impairment in hypertension in pregnancy.

Chronic hypertension occurs in older age group as compared to other hypertensive disorders of pregnancy ($p=0.001$). Chronic hypertension in pregnancy have a higher platelet count than other groups and the difference is statistically significant ($p=0.008$). There is no correlation between age and platelet count in pregnancy ($p = 0.387$). Other parameters namely the total and differential leukocyte counts, NLR, PLR, ANC and ALC showed no statistically significant association. Further research is required to establish association if any.

In another recent study in 2024 by Kapci et al.¹⁵ showed the prognostic value of inflammatory markers NLR and Systemic Immune-Inflammation Index - SIII ((Platelet × Neutrophil)/Lymphocyte ratio) in preeclampsia. Use of these markers is a cost effective way of managing hypertensive disorders in pregnancy.

A cross-sectional study conducted in Ethiopia in 2024¹⁶ also studied the parameters in complete hemogram in preeclampsia patients. Similar to the results of our study, this study also showed most of the parameters related to leukocytes were not showing much statistical difference except the relative lymphocyte count, NLR and the Red blood cell distribution width (RDW- SD).

5. Conclusion

Further research about the predictors of severity and prognosis in hypertensive disorders of pregnancy is required to reduce the associated maternal morbidity and mortality. Cost effectiveness and easy accessibility of such tests would help in ensuring improved standards of care and reduction in complications in Indian women.

6. Sources of Funding

No funding was involved

7. Conflict of Interest

The authors declare that they have no conflict of interest.

8. Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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