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Original Research Article.

A Comparative Study on Neutrophil to Lymphocyte Ratio as Predictor of Severe Pre-Eclampsia between Normotensive and Pre-Eclamptic Women

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ABSTRACT

Background: Pregnancy-induced hypertension (PIH) is the most common medical disorder of pregnancy contributing significantly to maternal/fetal morbidity and mortality. It is common practice to investigate the etiology of symptoms and monitor disease activity by monitoring markers of inflammation. However, information related to leukocytes count and its differentials is limited in patients with pre-eclampsia. Based on these conflicting data, the current study was conducted in order to compare neutrophil to lymphocyte ratio (NLR) in pregnant women with and without pre-eclampsia.

Materials & Methods: This is a hospital based comparative longitudinal study on 50 healthy pregnant women (controls) and 50 women with pre-eclampsia (cases) attending antenatal opd and admitted in labour room and fulfilling inclusion /exclusion criteria and give written and informed consent in obstetrics and gynaecology department S.M.S. Medical College Jaipur from May 2016 to May 2017.

Results: Our study showed that the mean age of pre-eclamptic group was 27.60±6.47 years and in control group was 26.98 ± 6.33 yrs. Systolic and diastolic BP was significantly higher in (P<0.0001*** each) in pre-eclamptic group as compared to control group. Our study showed that the mean value of hemoglobin and WBC was non-significant (P=0.172 & P= 0.051 respectively) but neutrophils, lymphocyte and NLR was statistically significant (P=0.025**, P= 0.04** & P=0.001** respectively) when compare to between groups.

Conclusion: We concluded that the neutrophil to lymphocyte ratio is increased in women who have pre-eclampsia, this may serve as a predictor for the disease. Hence establishing cost-effective bio-markers help in early prediction of disease which in turn helps in early treatment and slow down progression of disease.

Keywords: Pre-Eclampsia, Pregnancy, Hypertension, NLR, Neutrophil.

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INTRODUCTION

The Incidence of hypertensive disorder was 10-14% in complicating pregnancy. They contribute to mortality as high as 30% in India.[1] Mor et al (2010)[2] proposed that pregnancy is split into three distinctive states: first trimester proinflammatory (TH_1 mediated), second trimester anti-inflammatory (TH_2 mediated) and third trimester returned to a heightened inflammatory state.

It is common practice to investigate the etiology of symptoms and monitor disease activity by monitoring markers of inflammation. These markers include – Acute phase proteins and the cells involved in innate immunity (leucocytes). Leucocytes, one of the markers of inflammation are measured clinically as part of a full blood count.[3] Inflammation is "an essential response provided by the immune system that ensures survival during infection and tissue damage". As inflammation is usually initiated by the innate immune system, cells involved in innate response are pivotal in the inflammatory processes.

The activation of neutrophils may occur in the presence of some cytokines (i.e. TNF α) and of some chemoattractants released during an inflammatory process. During neutrophils activation, there is metabolic activation and release of their granules in blood and in tissues, contributing to increase the inflammatory response and/or oxidative stress.[3] However, information related to leukocytes count and its differentials is limited in patients with pre-eclampsia. Based on these conflicting data, the current study was conducted in order to compare neutrophil to lymphocyte ratio (NLR) in pregnant women with and without pre-eclampsia.

MATERIALS AND METHODS

This is a hospital based comparative longitudinal study on 50 healthy pregnant women(controls) and 50 women with pre-eclampsia (cases) attending antenatal OPD and admitted in labour room and fulfilling inclusion /exclusion criteria and give

written and informed consent in obstetrics and gynaecology department S.M.S. Medical College Jaipur from May 2016 to May 2017.

Inclusion Criteria

- Normal pregnant women 28-40 wks of GA.
- Pregnant women with pre-eclampsia between 28-40 wks of GA were recruited.

The definitions used for pre-eclampsia in this study are those of "ACOG 2014 guidelines of hypertension in pregnancy"

Exclusion Criteria

- Patients with history of membrane rupture.
- Patients with history of any infection.
- Patients with multiple pregnancies were excluded.
- Presence of fetal anomalies and maternal or fetal infection.
- Pregestational and gestational diabetes mellitus.
- Pregnant women with cardiovascular disease, and renal or liver diseases.
- Pregnant women in labour.

Methodology

All the patients satisfying the above criteria were selected for the study. The tests were carried out in hospitalized patients and pregnant women attending antenatal clinics. A detailed history was taken, general physical and systemic examination including the obstetrics examination. Per speculum examination were done to look for any evidence of vaginal infection clinically.

Peripheral venous blood sample were taken. Total and differentials leukocyte counts were measured by an automated hematology analyzer along with full blood count. Neutrophils and lymphocytes level are measured and neutrophil to lymphocyte ratio in the obtained blood samples are determined. Data were entered in microsoft excel sheet and analyzed statistically.

RESULTS

Our study showed that the mean age of pre-eclamptic group was 27.60±6.47 years and in control group was 26.98 ± 6.33 yrs. The comparison of mean value of Parity and BMI was statistically non-significant (P=0.104 & P=0.23 respectively) but gestational weeks in significantly (P=0.0003***) lower in pre-eclamptic group as compared to control group. Systolic and diastolic BP was significantly higher in (P<0.0001*** each) in pre-eclamptic group as compared to control group (table 1).

Our study showed that the mean value of hemoglobin and WBC was non-significant (P=0.172 & P=0.051 respectively) but neutrophils, lymphocyte and NLR was statistically significant (P=0.025**, P= 0.04** & P=0.001** respectively) when compare to between groups (table 2).

Table 1: Demographic and clinical data in study groups

Variables	Pre-eclamptic group	Control group	P-Value
Age in years	27.60 ± 6.47	26.98 ± 6.33	0.502
Parity	0.87 ± 1.04	1.07 ± 1.09	0.104
BMI (kg/m ²)	24.1 ± 3.6	23.5 ± 1.5	0.23
Gestational wks	35.3 ± 2.6	37.9 ± 1.3	0.0003
Systolic BP, mm Hg	156.44 ± 13.8	108.16 ± 11.15	<0.001
Diastolic BP, mm Hg	101.39 ± 9.73	67.54 ± 7.55	<0.001

Table 2: FBC comparison

Variables	Pre-eclampsia	Normal pregnant	P value
Haemoglobin	11.46 ± 1.30	11.09 ± 1.22	0.172
WBC (10^3 per ml)	13.34 ± 3.39	9.76 ± 2.01	0.051
Neutrophils (10^3 per ml)	11.01± 3.28	6.80 ± 1.80	0.025
Lymphocyte(10^3 per ml)	1.65± 0.45	2.23± 0.51	0.04
NLR	7.39± 3.51	3.20 ± 1.08	0.001

Table 3: NLR distribution in cases

NLR	No. of pregnant women with pre-eclampsia	Percentage
3.88 – 5.87	13	26%
6.88 – 8.87	26	52%
8.88 – 10.90	11	22%

DISCUSSION

Women with severe pre-eclampsia develop a variety of hematologic aberrations which have an impact on the pregnancy outcome so that aggressive therapy can be initiated to prevent maternal and neonatal morbidity and mortality.[4]

Our study showed that the median NLR value of the pre-eclampsia group was significantly higher than that of the control [7.39±3.51 vs 3.20±1.08; p<0.001]. A study done by Kurtoglu E et al (2015)[5] found NLR in preeclamptic group was significantly higher than that of normal group (p=0.023) and area under ROC curve was found statistically significant (p=0.023).

As shown in the current study, WBC count of pre-eclamptic women were higher than those of the women with normal pregnancy, suggesting an increased inflammatory response in pre-eclampsia. Leukocytosis, mainly related to neutrophilia, is a common findings in normal pregnancy. After 8 wks, neutrophilia

begins to occur, and neutrophil count stabilizes in the second half of pregnancy. Accordingly, the control group of our study, which was comprised of women with normal pregnancy, had normal counts of WBC, neutrophils and lymphocytes.

Greer et al.[6] first showed that neutrophil activation is confined to the maternal circulation in pregnancy-induced hypertension, where it may contribute to vascular damage. Soluble markers of neutrophil activation, released in the circulation from the degranulation of activated neutrophils, are also increased in pre-eclamptic patients.[7-10] Further evidence of enhanced inflammation in preeclampsia has been demonstrated through the uncontrolled increased activation of the complement system compared with normal pregnancy. Activation of the complement system amplifies inflammation, promotes chemotaxis of inflammatory cells and generates proteolytic fragments that enhance phagocytosis by neutrophils and monocytes.[11]

This study compares the difference in commonly tested haematological parameters undertaken in the normal pregnant women and pregnant women with pre-eclampsia. It evolves from work presented in this study, which demonstrates that women who develop pre-eclampsia involve changes in markers of inflammation. Therefore, NLR has been proposed as an easily measurable objectives marker of systemic inflammation and a prognostic factor for a variety of diseases, including endometriosis, primary ovarian insufficiency, gestational trophoblastic disease and ovarian hyperstimulation syndromes.[12]

NLR has become popular recently so that many studies have been done to find out the predictive value of NLR in many different topics, particularly cancers. Pretreatment NLR has been mentioned to be significantly elevated and useful as a prognostic indicator by several researchers.

CONCLUSION

We concluded that the neutrophil to lymphocyte ratio is increased in women who have pre-eclampsia; this may serve as a predictor for the disease. Hence establishing cost-effective bio-markers help in early prediction of disease which in turn helps in early treatment and slow down progression of disease. However, large scale prospective study needed to determine the optimal NLR value and its prognostic significance in the diagnosis of pre-eclampsia.

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