

**A Comparative Study to Assess Neutrophil Lymphocyte Ratio as a Severity Marker for Preeclampsia in Patients**

**Attending Antenatal Clinic at SMS Medical College, Jaipur**

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**Abstract**

**Background:** In recent years, there was more focus on Neutrophil/Lymphocyte ratio (NLR) which denotes the ratio of Neutrophils, representing the active nonspecific inflammatory mediator initiating the first line of defense, to lymphocytes representing the regulatory or protective component of inflammation. It provides prognostic as well as diagnostic information about subclinical inflammation beyond conventional risk factors. It is a reliable marker of low grade inflammation in pre-eclampsia.

**Methods:** Hospital based comparative study conducted at department of Obstetrics and Gynaecology, SMS medical college and associated hospitals, Jaipur.

**Results-**The mean neutrophil level was higher in preeclampsia group. The mean lymphocyte level is higher in mild preeclampsia group. The mean NLR in severe preeclampsia group is  $4.01 \pm 0.13$  whereas in mild preeclampsia group is  $2.74 \pm 0.08$  which is significant in severe preeclampsia.

**Conclusion:** In our study NLR values are definitely raised among the severe preeclampsia group compared to the mild preeclampsia which signify their role in contributing to the early diagnosis of the condition.

**Keywords:** NLR, Preeclampsia, Severe.

**Introduction**

Hypertensive disorders complicate 5-10% of all pregnancies and contribute greatly to maternal morbidity and mortality. Importantly more than half of these hypertension related deaths are preventable<sup>1</sup>. The reported incidence of HDP 5.38% while Pre-eclampsia, Eclampsia and HELLP syndrome accounted for 44%, 40% and 7% of complications respectively<sup>2</sup>

Preeclampsia is a major cause of maternal and fetal or neonatal mortality and morbidity<sup>3</sup>. Pre-eclampsia occurs in 3.7% of pregnancy and contributes to 18% maternal mortality. Pre-eclampsia is a condition that occurs only during pregnancy. Pre-eclampsia is a multisystem disorder of unknown etiology<sup>4</sup>.

The differential white blood cell counts are an easily measurable, available and reliable parameter that can be used as a severity index of the systemic inflammatory immune response. In recent years, there was more focus on Neutrophil/Lymphocyte ratio (NLR) which denotes the ratio of Neutrophils, representing the active nonspecific inflammatory mediator initiating the first line of defense, to lymphocytes representing the regulatory or protective component of inflammation. It

provides prognostic as well as diagnostic information about subclinical inflammation beyond conventional risk factors. It is a reliable marker of low grade inflammation in pre-eclampsia<sup>5,6</sup>.

**Material and Methods**

**Type of Study:** Hospital based comparative study.

**Study Design:** Cross sectional study.

**Place Of Study:** Department of Obstetrics and Gynaecology, SMS medical college and associated hospitals, Jaipur.

**Duration:** From June 2018 to august 2019.

**Study Participants:** Pregnant women over 20 weeks of gestation with mild preeclampsia, and severe preeclampsia.

**Sample Size:** Sample size was calculated at 95% confidence level assuming standard deviation of 3.1 in neutrophil lymphocyte ratio as per results of seed article.

At the precision of 1, minimum 37 preeclampsia patients were required as sample size, which was further enhanced to 41 preeclampsia patients in each group as final sample size, expecting 10% attrition.

**Sampling Procedure:** 41 pregnant (>20 weeks) women having mild pre eclampsia and 41 pregnant (>20 weeks) women having severe pre eclampsia were included on first cum first basis after beginning the study assuming 10% drop outs.

**Inclusion Criteria:** A singleton pregnancy over 20 weeks of gestation with mild preeclampsia and with severe preeclampsia.

**Exclusion Criteria**

1. Patients with history of chronic renal disease.
2. Chronic Hypertension.
3. History of pre-existing diabetes or gestational diabetes.
4. Cardiovascular illness.

5. Any infectious diseases.
6. Chronic medical disorders.
7. History of smoking.
8. Those with a fetal structural or genetic anomaly.
9. History of membrane rupture.

**Methodology**

- All eligible pregnant women fulfilling inclusion criteria were explained about nature and purpose of the study.
- After taking their informed written consent, detail history, general and systemic examination was done.
- Blood samples was collected in tubes containing EDTA vial.
- The neutrophil counts and lymphocyte counts were estimated and then neutrophil lymphocyte ratio was calculated.
- All information and reports was recorded on a pre designed Proforma and was entered in Microsoft excel sheet to prepare master chart.

**Statistical Analysis**

- Appropriate parametric test was used for linear variables and non parametric tests was used for categorical variables as per natural and yield of data.
- P value <0.05 was considered as significant data was analysed using medcalc 16.4 version statistical software.

**Observations and Results**

Table 1: Distribution of study participants according to maternal age in 2 groups

Age (in years)	Group A Mild preeclampsia		Group B Severe preeclampsia		Total	
	No.	%	No.	%	No.	%
20-25	17	41.46	16	39.02	33	40.24
26-40	24	58.54	25	60.97	49	59.75
Total	41	100.00	41	100.00	82	100.00

Chi-square = 0.000 with 1 degree of freedom; P = 1.000 (NS)

Mild : Mean ± SD = 27.02 ± 5.02 years

Severe : Mean ± SD = 26.78 ± 4.45 years

The above table shows the age wise distribution of 2 group subjects. In group A, out of 41 study subjects maximum i.e. 24 (58.54%) subjects were lying in the age group 26-40 years followed by 17 (41.46%) were lying in the age group 20-25 years.

The mean age of this group was = 27.02 ± 5.02 years

In group B, out of 41 study subjects, most of the subjects i.e. 25 (60.97%) subjects were lying in the age group of 26-40 years followed by 16 (39.02%) were lying in the age group 20-25 years. The mean age of this group was = 26.78 ± 4.45 years.

Table 2: Mean NEUTROPHIL ( $10^9$ /liter) count in study group

	Group A Mild preeclampsia		Group B Severe preeclampsia	
	Mean	SD	Mean	SD
Neutrophil ( $10^9$ /liter)	7.80	0.13	9.51	0.14
Range	7.40-8.02		9.23-9.78	
P value	P<0.001			

The above table shows the relation between mean Neutrophil level with the severity of pre-eclampsia. The mean Neutrophil level in severe pre-eclampsia was  $9.51 \pm 0.14$  and in mild pre eclampsia was  $7.80 \pm 0.13$ . So the results showing that the mean neutrophil level was increasing with severity of pre-eclampsia.

Table 3: Mean Lymphocyte ( $10^9$ /liter) level in study group

	Group A Mild preeclampsia		Group B Severe preeclampsia	
	Mean	SD	Mean	SD
Lymphocyte ( $10^9$ /liter)	2.85	0.06	2.37	0.07
Range	2.74-3.01		2.23-2.63	
P value	P<0.001			

The above table shows the relation between mean lymphocyte level with the severity of pre-eclampsia. The mean lymphocyte level in severe pre-eclampsia was  $2.37 \pm 0.07$  and in mild pre eclampsia was  $2.85 \pm 0.06$ . So the results showing that the mean lymphocyte level was decreasing with severity of pre-eclampsia.

Table 4: Mean Neutrophil Lymphocyte Ratio level in 2 study groups

	Group A Mild preeclampsia		Group B Severe preeclampsia	
	Mean	SD	Mean	SD
NLR	2.74	0.08	4.01	0.13
Range	2.58-2.92		3.66-4.21	
P value	P<0.001			

The above table shows mean NLR level of group A was  $2.74 \pm 0.08$  and mean NLR of group B was  $4.01 \pm 0.13$ , which is significantly higher than group A.

### Discussion

Pre-eclampsia is a multisystem disorder characterized by a blood pressure of 140/90 mm of Hg or more on two occasion at least 4 hours apart after 20 weeks of gestation in women with previously normal BP may be associated with proteinuria, thrombocytopenia, renal insufficiency, impaired liver function, cerebral and visual symptoms.<sup>1</sup>

Pre-eclampsia is a result of imbalance between factors produced by the placenta and maternal adaptation to these factors. Abnormal placentation with impaired trophoblastic invasion at the beginning of pregnancy (weeks 8– 18) followed by inadequate remodelling of the uterine spiral arteries leading to hyper activation of maternal immunological response and progressive endothelial damage. Pre-eclampsia has pre-clinical (symptomless) and clinical stages, only the latter phase can be detected by clinical screening and is outcome of placental dysfunction secondary to maternal inflammatory reaction. It is probable that pre-eclampsia results from abnormal trophoblastic growth and differentiation, develops at any time after the earliest stages of implantation. The primary dysfunction may be immunologic response to fetal alloantigens, as first pregnancy preponderance of pre-eclampsia. Immunological response leads to activation of platelets, activation of neutrophils, secretion of pro-inflammatory cytokines and autoantibodies by leukocyte. These activated leukocytes like neutrophils, lymphocytes infiltrate in maternal systemic circulation precipitate vasoconstriction which is the background pathophysiology of preeclampsia. Neutrophil-lymphocyte ratio (NLR) is indicator of systemic subclinical inflammatory markers.<sup>7</sup>

We conducted a hospital based cross sectional study to assess Neutrophil Lymphocyte ratio as a severity marker for pre-eclampsia in patients attending antenatal clinic at S.M.S Medical College, Jaipur. Total 82 patients in which, 41 patients with mild pre-eclampsia (group A) and 41 patients with severe pre-eclampsia (group B) on first cum basis, fulfilling inclusion criteria were enrolled in the study.

In present study mean neutrophil counts ( $10^9/L$ ) in cases with mild pre-eclampsia and severe pre-eclampsia was

$7.80 \pm 0.13$ ,  $9.51 \pm 0.14$  respectively. Neutrophil counts are more increased in severe PE than mild PE. The difference between two groups was statistically significant ( $p$  value  $< 0.001$ ). Similar result was reported by Lurie et al<sup>8</sup> they concluded that mean neutrophil counts increased with severity of preeclampsia.

In present study mean lymphocyte count ( $10^9/L$ ) in mild pre-eclampsia and severe pre-eclampsia was  $2.85 \pm 0.06$ ,  $2.37 \pm 0.07$  respectively. Lymphocyte counts are more decreased in severe PE than mild PE. The difference between two groups was statistically significant ( $p$  value  $< 0.001$ ). Similar result was reported by Lurie et al.<sup>8</sup> They concluded that mean lymphocyte counts decreased with severity of preeclampsia.

In present study mean NLR level in group A (mild PE) & group B (severe PE) were  $2.74 \pm 0.08$  and  $4.01 \pm 0.13$  respectively. The result was statistically significant ( $P$  value  $< 0.001$ ). Similar results were reported by Salah Serin, Fazil Avci, Onder Ercan, Murat Bakacak et al<sup>9</sup>, Anat Hershko Klement et al<sup>10</sup>, Mehmet Toptas et al.<sup>11</sup> In that study NLR of mild preeclampsia group was  $4.8 \pm 3.7$  and NLR of severe preeclampsia was  $6.5 \pm 4.8$  and  $p$  value was 0.032.

### Conclusion

In our study NLR values are definitely raised among the severe preeclampsia group compared to the mild preeclampsia which signify their role in contributing to the early diagnosis of the condition.

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