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A Single Tertiary Care Center's Experience: Can High First Trimester NLR and PLR Be an Early Predictor of Preeclampsia?

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Abstract

The purpose of the current research was to ascertain if the first-trimester platelet to lymphocyte ratio (PLR) and neutrophil to lymphocyte ratio (NLR) would be helpful predictors of later preeclampsia. **Material and Methods:** Our hospital retrospectively reviewed the medical records of 146 women (mean age 27.27 years; age range 20-36 years) with preeclampsia and healthy controls. Clinical features and first-trimester haematological markers, such as haemoglobin, neutrophil, lymphocyte, platelet, NLR, and PLR, were assessed for both groups. To determine the ideal NLR and PLR values for preeclampsia prediction, receiver operating characteristic curve (ROC) analysis was also carried out.

Results: Of the 146 patients in this research, 70 (~47.9%) had preeclampsia, while the remaining 76 (52.1%) had normotension. The preeclamptic women had substantially higher amounts of lymphocytes ($p < 0.001$), NLR ($p < 0.0001$), and PLR ($p < 0.0001$) in the haematological parameters. However, the preeclamptic women's haemoglobin concentration ($p \sim 0.436$), platelets ($p \sim 0.124$), and neutrophils ($p \sim 0.07$) were neither substantially high nor low. The independent strong predictive factors on multivariate regression analysis were PLR (OR 1.02; 95% CI 1.01-1.04; $p = 0.01$) and NLR (OR 2.17; 95% CI 1.04-4.51; $p = 0.03$). The area under the curve for both NLR and PLR in the ROC study was 0.800. Preeclampsia was predicted by the cut-off values of NLR > 2.78 and PLR > 109 , with corresponding sensitivity of 80.0% and 85.7% and specificity of 71.1% and 65.8%.

Conclusions: We found that a high NLR and PLR during the first trimester is a reliable indicator of preeclampsia later on.

Keywords: preeclampsia; platelet to lymphocyte ratio (PLR); neutrophil to lymphocyte ratio (NLR)

Introduction

Preeclampsia is a multisystem illness in which a pregnant woman who was previously normotensive develops new-onset hypertension and proteinuria after 20 weeks of gestation.¹ It is one of the most prevalent pregnancy problems, accounting for 12% of maternal deaths worldwide and affecting 5–10% of pregnant women.^{2,3} Its pathophysiology and aetiology are yet unknown. The common suggested explanation is that a gravid woman's altered immune response results in aberrant placentation and increased maternal inflammation.

Increased capillary permeability, microvascular thrombosis, and elevated vascular tone are the results of multisystemic endothelial dysfunction.⁴ The justification for early preeclampsia identification is that it would enable prompt beginning of preventative treatment to lower the risk of preeclampsia-related death and morbidity.^{5–8} Table 1.9-11 summarises suggested biomarkers for preeclampsia early identification. In clinical practice, these biomarkers and the uterine artery pulsatility index for early preeclampsia diagnosis are not widely accepted.

Category	Name of biomarker
Angiogenic marker	VEGF, sflt-1, PIGF, sEng
Renin angiotensin system related	Antibodies against the AT1 receptor
Immunological markers	PP-13, PAPP-A , ADAM12
Metabolic marker	Visfatin
Endocrinological markers (Maintenance of spiral artery function)	Activin A, Inhibin A

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VEGF stands for vascular endothelial growth factor; sFlt-1 for soluble fms-like tyrosine kinase-1; PIGF for placental growth factor; sEng for soluble endoglin; AT1 receptor for angiotensin II receptor type 1; ADAM12 for metalloprotease 12; PP-13 for placenta protein 13; and PAPP-A for pregnancy-associated plasma protein .

A Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are two examples of systemic inflammatory response indicators that have recently attracted a lot of attention in a variety of clinical situations. Increased cardiovascular risk and death in some cancers are strongly linked to elevated levels of systemic inflammatory response markers.¹⁴. It is still unknown how systemic inflammatory response indicators might be used to predict preeclampsia in its early stages.

Therefore, the purpose of this study was to evaluate the predictive value of the systemic inflammatory response markers neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in the early detection of preeclampsia.

Materialand Methods

This research was conducted between June 2017 and March 2018 at the obstetrics and gynaecology department of Santokba Durlabhji Memorial Hospital cum Medical Research Institute in Jaipur, Rajasthan, India. It is a retrospective observational study. Our institution conducted a retrospective evaluation of the medical records of 146 women (mean age 27.27 years; age range 20-36 years) who had preeclampsia and healthy controls. The requirements for both groups' inclusion and exclusion are

Inclusion Criteria

Test group- 70 Preeclamptic women diagnosed as per American College of Obstetricians and Gynecologists (ACOG) criteria. All preeclamptic patients were diagnosed between 24 to 40 weeks of gestation.

Control group- 76 pregnant women delivered between 37 to 41 weeks, appropriate for gestational age, without any history of complications throughout the pregnancy

Exclusion criteria

Patients with systemic diseases,
History of hematopoietic system disorders,
Malignancies,
Acute or chronic inflammatory disease

Our center used an automated system to conduct a complete blood count (CBC) throughout the first trimester (between 7 and 13 weeks of gestation). Clinical features and first-trimester haematological markers, such as haemoglobin, neutrophil, lymphocyte, platelet, NLR, and PLR, were assessed for both groups. This retrospective investigation was approved by the institutional ethics committee.

To determine the ideal NLR and PLR values for preeclampsia prediction, receiver operating characteristic curve (ROC) analysis was also carried out.SPSS version 11.0 (Chicago, Illinois) was used to analyse the data. $P < 0.05$ is regarded as the significant threshold.

Result

Of the 146 patients, 70 (~47.9%) were preeclamptic patients and remaining 76 (52.1%) were normotensive in present study. Clinical characteristics of the recruited patients are shown in tabular form in table number 2. In the haematological parameters, lymphocyte ($p < 0.001$), NLR ($p < 0.0001$) and PLR ($p < 0.0001$) levels were significantly elevated in the preeclampsia women. Whereas other parameters neutrophil ($p \sim 0.07$), platelet ($p \sim 0.124$) hemoglobin concentration ($p \sim 0.436$) were not significantly high or low in the preeclamptic women.

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Table 2. Clinical characteristics of the recruited patients

Parameters	Pre eclampsia group (n=70) (Mean $\pm$ SD)	Normotensive group (n=76) (mean $\pm$ SD)	P value
Maternal age (in years)	27.5 $\pm$ 3.6	27.1 $\pm$ 3.5	0.579
Hemoglobin	11.4 $\pm$ 1.4	11.7 $\pm$ 1.1	0.43
Birth weight (in kg)	2.7 $\pm$ 0.5	3.9 $\pm$ 0.4	0.02
Gestational age at delivery (In weeks)	39.5 $\pm$ 2.2	40.7 $\pm$ 2.3	0.03
Neutrophyl (103/mm-3)	6.9 $\pm$ 1.4	6.2 $\pm$ 1.8	0.07
Lymphocyte (103/mm-3)	2.5 $\pm$ 1.6	2.0 $\pm$ 0.5	<0.001
Platelet (103/mm-3)	280.4 $\pm$ 80.4	253.8 $\pm$ 65.6	0.125
NLR	3.53 $\pm$ 0.9	2.6 $\pm$ 0.9	<0.001
PLR	151.2 $\pm$ 48.0	106.1 $\pm$ 33.7	<0.001

NLR- neutrophil-to-lymphocyte ratio; PLR Platelet-to-lymphocyte ratio

On multivariate regression analysis, NLR (OR 2.17; 95% CI 1.04-4.51; p = 0.03) and PLR (OR 1.02; 95% CI 1.01-1.04; p = 0.01) were the independent powerful predictive variables as shown in table number 3.

Table 3. Significant predictors of preeclampsia in multivariate regression analysis

Markers	Odd ratio	95% CI	P value
NLR	2.2	1.04-4.51	0.03
PLR	1.02	1.01-1.04	0.01
Lymphocyte	1.1	0.95-1.87	0.105

CI- confidence interval; NLR- neutrophil-to-lymphocyte ratio; PLR Platelet-to-lymphocyte ratio

In the ROC analysis (Figure 1), for both NLR and PLR area under curve was 0.800. The cut-off values of NLR > 2.78 and PLR > 109 predicted preeclampsia with the sensitivity of 80.0% and 85.7% and specificity of 71.1% and 65.8%, respectively as shown in tabular form in table number 4.

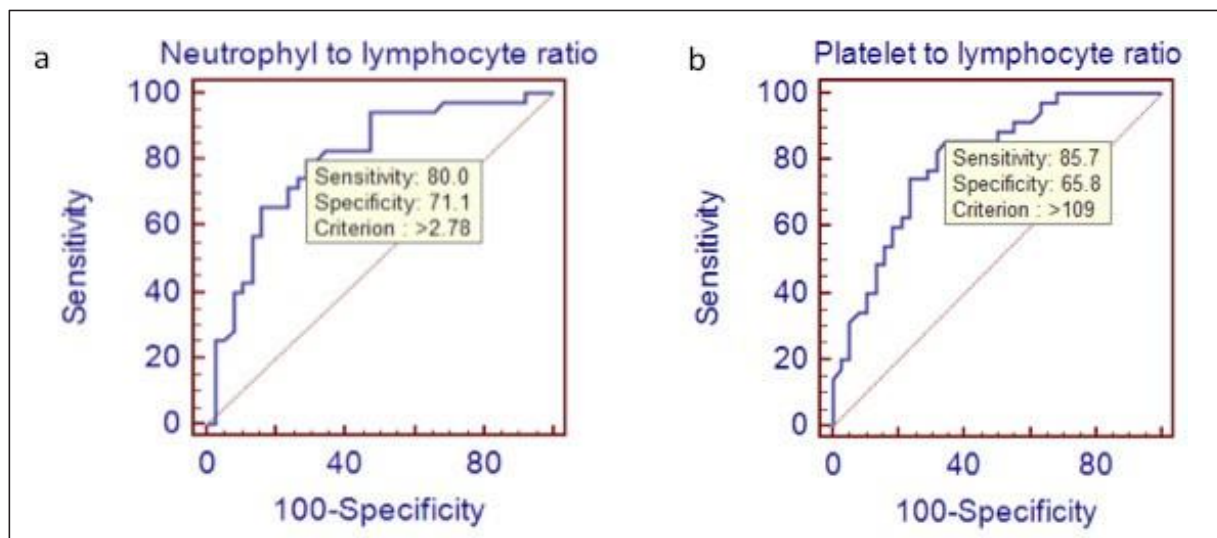


Figure 1. Receiver operating characteristic (ROC) curves for (a) neutrophil-to-lymphocyte ratio (NLR) and (b) Platelet-to-lymphocyte ratio (PLR) to predict the early diagnosis of preeclampsia. The area under the ROC curves for both parameters was 0.800.

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Table 4. Cut- offs value for first trimester NLR and PLR in predicting eclampsia

Markers	AUC (95% CI)	Sensitivity	Specificity	Cut-off value	P value
NLR	0.800 (0.690 to 0.885)	80.0%	71.1%	>2.78	0.0001
PLR	0.800 (0.690 to 0.885)	85.7%	65.8%	>109	0.0001

AUC- Area under the curve; NLR- neutrophil-to-lymphocyte ratio; PLR Platelet-to-lymphocyte ratio

Discussion

Abnormal placentation, which is the consequence of an altered immunological response and severe inflammation in the mother, causes preeclampsia. indicators of the systemic inflammatory response, such as PLR and NLR, that suggest an elevated state of inflammation. in order to anticipate preeclampsia during the first trimester of pregnancy. The purpose of the current research was to evaluate the systemic inflammatory markers NLR and PLR in preeclamptic individuals during the first trimester.

Gezer et al. (2015), Oylumlu et al. (2016), and Kurtogluet al. (2017) evaluated the NLR and PLR parameters in the early prediction of preeclampsia and found that NLR was considerably greater in preeclamptic patients compared to the control group. While Kurt et al. (2019) found that NLR was not significantly different between the PE and control groups of patients, Mannaertset al. (2018) found that NLR was higher and PLR was lower in the PE group compared to the controls, while the neutrophil count was significantly higher in the PE patient group. While neutrophil ($p \sim 0.07$), platelet ($p \sim 0.124$), and haemoglobin concentration ($p \sim 0.436$) were not statistically high or low in the preeclamptic women in the current research, lymphocyte, NLR, and PLR levels were considerably higher.

NLR (OR 1.43) and PLR (OR 1.38) were the most potent prognostic factors close to the sample, according to Gezer et al.'s multivariate regression analysis. This investigation should be carried out in a vast geographic region with a large sample size in order to generalise our findings to the whole population.

This is a retrospective study so unidentified confounding factors has been introduces.

Present study was not correlated with the other radiological and biochemical for preeclampsia

Summary

CBC is the most often recommended haematological test among all the first trimester biomarkers and sonological indicators; we only need to pay close attention to the NLR and PLR. This would be economical and maybe most advantageous for the whole community, not just expectant mothers. Since elevated NLR and PLR have been linked to increased inflammation, results obtained in acute inflammatory conditions should not be interpreted. Elevated NLR and PLR may be seen in pregnant women with haematopoietic systemic disorders or chronic inflammatory conditions.

Conclusions

We came to the conclusion that a high NLR and PLR during the first trimester is a reliable indicator of preeclampsia later on. Therefore, we recommended that pregnant women with high NLR and PLR in the first trimester of pregnancy be carefully watched for preeclamptic symptoms such proteinuria and hypertension.

Limitations of Present Study

Present study was conducted in the limited geographical area and on relatively small sized

Th is is a retrospective study so unidentified confounding factors has been introduces.

Present study was not correlated with the other radiological and biochemical for preeclampsia

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