



RELATIONSHIP BETWEEN NEUTROPHIL-LYMPHOCYTE RATIO, PLATELET-LYMPHOCYTE RATIO, AND FETAL GROWTH RETARDATION

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Abstract

Background: Fetal growth restriction (FGR) is one of the causes of morbidity and mortality in Indonesia. Inflammation is believed to be one of the factors causing the incidence of FGR, especially in preeclampsia/eclampsia (PE/E) cases. Various studies suggest that neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were significant in predicting the incidence of PE in high-risk patients. However, there have been no studies investigating relationship between the NLR and PLR ratio on the incidence of FGR in patients, especially with preeclampsia/eclampsia.

Methods: This study is an observational-analytic study with a case control approach using secondary data. Total sampling was done on all FGR subjects with PE/E from January 2017 until December 2019. Subjects were then grouped into early onset PE/E group with FGR and without FGR.

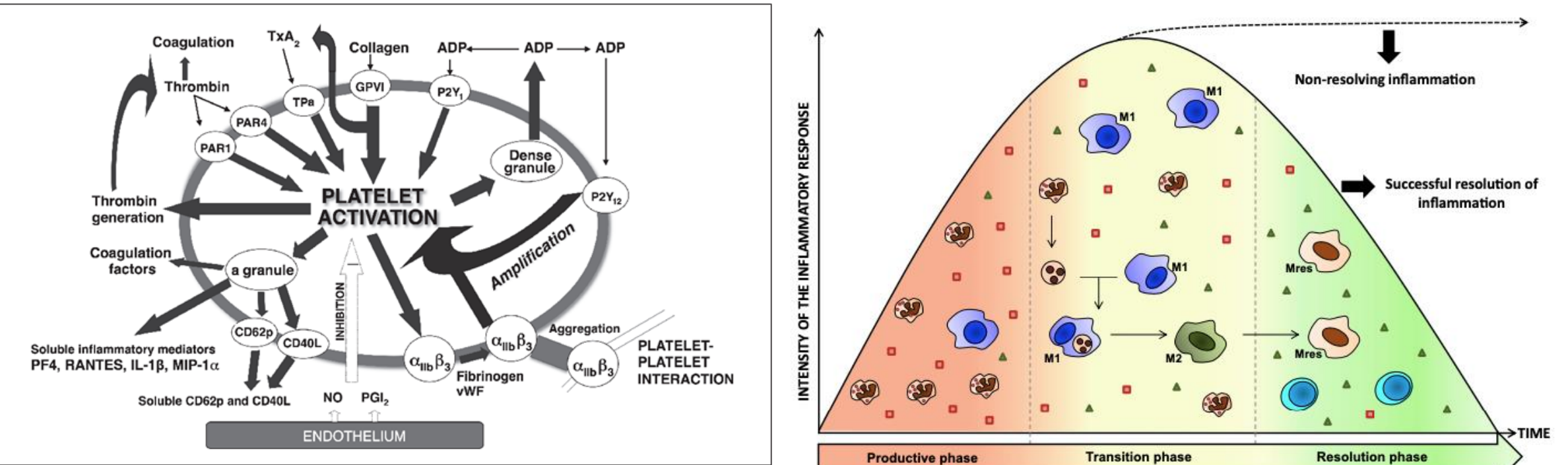
Results: A total 342 patients, of which 137 patients in the FGR group and 205 patients in the no FGR group. A total of 10 samples in the FGR group had to be excluded because they did not match the research criteria, while 7 samples in the without FGR group had to be excluded because they did not match the research criteria. The NLR was statistically significant (p <0.05) with OR 2.362, CI 1.456-3.831. The PLR was obtained statistically significant (p <0.05) with OR 3.527, CI 2.125-5.854.

Conclusion: Higher NLR and PLR was found in FGR group than in non-FGR group.

Introduction

Preeclampsia (PE) and eclampsia (E) are forms of pathological conditions occurring during pregnancy. PE/E is characterized by increased in blood pressure, seizures, and peripheral organ damage in pregnant women at a minimum of 20 weeks of gestation. Early onset PE/E can lead to complications for both mother and fetus. The most common complication in the fetus is fetal growth retardation (FGR). Fetal growth retardation is a fetus that does not grow according to its ability.¹⁻³

The incidence of PE/E in Indonesia is about 100,000 cases a year or about 5.3% of all pregnancy, with the incidence of FGR being found to vary from 3-10%. The theory thought to play a role in the pathophysiology of PE/E is an exaggerated systemic inflammatory response due to damage to one or more of the maternal immune systems. During pregnancy, there is an increased immune response to inflammation.^{5,6}



Picture 1. Platelet activation and body response in inflammation process

Methodology

This is an analytic observational study using case control design. Analysis using secondary data was done at Ulin Regional Hospital, Banjarmasin, Indonesia during the period of January 2017 to December 2019. This study used 5% error bound and 95% confidence interval limit, with power of the test considered to be 90%. Subjects for this study were all pregnant women with early onset preeclampsia/eclampsia who were recruited using total sampling method. The inclusion criteria for this research were all pregnant women with preeclampsia/eclampsia, singleton pregnancy, and gestational age of 20-24 weeks old. The exclusion criteria for this study were incomplete medical record data, mother with anemia, acute infection, malignancy, premature rupture of membrane, obese, coagulopathy, or fetus with congenital anomaly. Subjects were then grouped into FGR group and non-FGR group.

Variables analyzed in this were neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and fetal growth retardation (FGR). NLR and PLR were counted using automated leukocyte count, while FGR was diagnosed by plotting the estimated birth weight of fetus using ultrasonographic examination. If the estimated birth weight was less than the 10th percentile of the given gestational age, FGR diagnosis was erected. Leukocyte count and ultrasound examination were done at the time of admission. NLR was then categorized into high (> 4.06) and low (≤ 4.06), while PLR was categorized into high (> 135.8) and low (≤ 135.8).

All human studies had been approved by the Helath Research Ethics Committee of Faculty of Medicine, Lambung Mangkurat University with ethical clearance number 179/KEPK-FK UNLAM/EC/V/2020. Collected data were then analyzed using SPSS for Macintosh ver. 20. Characteristics of subjects and examination results were analyzed accordingly.

Results

Table 1. Baseline Characteristics of Subjects

Variables	FGR	Non-FGR	p
Maternal age (years)	25 ± 7,71	26 ± 5,92	0,081
Gravid	1 (1-3)	2(2-4)	0,077
Parity	0 (0-2)	1(0-4)	0,051
Gestational age during admission (weeks)	31,81 ± 4,19	32,5 ± 3,79	0,089
Gestational age during birth (weeks)	32 ± 2,51	33 ± 2,11	0,068

Table 2. Analysis of Markers Between Groups

Variables	FGR	Non-FGR	p
Neutrophil (x10 ³ /mm ³)	8,3 (3,2)	7,9 (3,1)	0,038
Platelet (x10 ³ /mm ³)	245,81 ± 56,31	210,11 ± 59,38	0,042
NLR	3,87 (1,88)	2,89 (1,4)	< 0,001
PLR	118,82 (23,20)	112 (25,29)	0,021
Lymphocyte (x10 ³ /mm ³)	2,1 (0,73)	2,32 (0,62)	0,073

Table 3. Analysis of NLR Category Between Groups

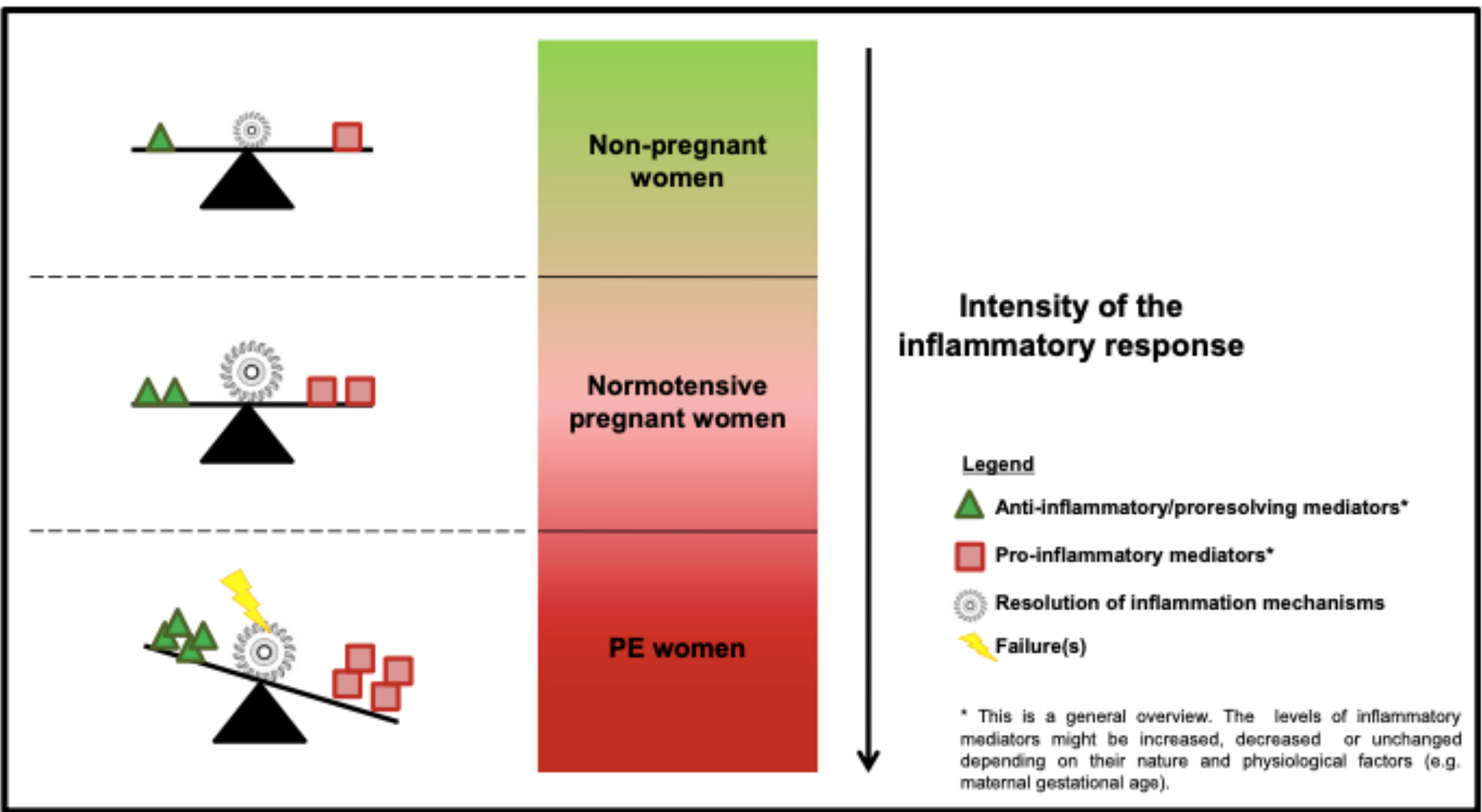
NLR	FGR	Non-FGR	p	Odds Ratio
High	71 (60%)	66 (40%)	< 0.001	2.36
Low	46 (40%)	101 (60%)		(1.45 – 3.83)

Table 4. Analysis of PLR Category Between Groups

PLR	FGR	Non-FGR	p	Odds Ratio
High	84 (72%)	70 (42%)	< 0.001	3.527
Low	33 (28%)	97 (58%)		(2.12 – 5.85)

Discussion

Based on the study, it was found that mothers with PE/E and FGR tend to have higher NLR and PLR. These results are in line with the theory put forward by Perucci et al (2017) that patients with preeclampsia/eclampsia with FGR had higher inflammation incidence than patients without FGP⁸



Picture 2. Inflammation mechanism in non pregnant, normotensive, and PE women

In this study, the value of the odds ratio between LPR and the incidence of FGR was 3.527. This result showed that patients with high LPR had 3.527 times higher risk of developing FGR in their fetus. In normal pregnancy, platelet production is relatively constant and does not increase significantly. However, in PE/E cases, uncontrolled platelet activation and increased platelet destruction occur as a consequence of endothelial damage. Higher platelet activation in PE/E patients can cause FGR due to activated platelets closing the damaged vascular tissue by creating a blockage. However, at a higher degree, platelet activation can cause placental thrombosis which will aggravate uteroplacental blood flow.

The limitation for this study were its retrospective nature and limited scale. Follow-up studies in the form of prospective studies involving many teaching hospitals and larger samples carried out on patients at risk of suffering from PE/E in the first trimester of pregnancy can certainly be beneficial in predicting the incidence of IUGR in patients with PE/E.

Conclusions

It is concluded in this study that mothers with preeclampsia/eclampsia and FGR tend to have higher NLR and PLR than mothers with preeclampsia/eclampsia but without FGR.