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Research Article
Differences in Mean Levels of Maternal Resistin Serum between Early Onset Preeclampsia (EOPE) and Late Onset Preeclampsia (LOPE)

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Abstract

Objective: To analyze the differences in mean levels of maternal resistin serum in early onset preeclampsia (EOPE) and late onset preeclampsia (LOPE). **Method:** An analytical cross sectional study was performed with 20 women with early onset preeclampsia (EOPE) and 20 women with late onset preeclampsia (LOPE) who met the inclusion criteria and there were no exclusion criteria. The samples were recruited in Dr.M. Djamil General Hospital, Padang from July-October, 2015. The levels of maternal resistin serum was examined by enzyme-linked immunosorbent assay (ELISA). The differences in mean levels of maternal resistin serum between the two groups was analyzed by using independent t-test. **Result:** The mean levels of maternal resistin serum in late onset preeclampsia was higher than early onset preeclampsia (8.891±6.219 ng mL^{-1} vs 2.526±1.603 ng dL^{-1}, p = 0.000). **Conclusion:** The mean levels of maternal resistin serum in late onset preeclampsia was significantly higher than early onset preeclampsia.

Key words: Maternal resistin serum, early onset preeclampsia, late onset preeclampsia

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Preeclampsia is one of the major causes of morbidity and mortality of the mother and fetus. World Health Organization (WHO) reported the number of deaths caused by preeclampsia by 16% in developing countries[1]. Preeclampsia resulting 3-25 fold increased risk obstetric complications and is the cause of 30-40% of perinatal deaths in Indonesia[2].

The incidence of preeclampsia ranges between 5-10% of all pregnancies[1]. Incidence of preeclampsia in the United States, Canada and Western Europe ranges between 2-5% of all pregnancies and higher, 4-18% in some developing countries in Africa[3]. The incidence of preeclampsia in Indonesia ranged between 3-10%[2].

In Dr.M. Djamil General Hospital in Padang during the year 2011, the incidence of preeclampsia was 8.31%, on 2012 was 11.47% and on 2013 was 12.02%.

Preeclampsia is divided into early onset preeclampsia (EOPE) (<34 weeks) and late onset preeclampsia (LOPE) (>34 weeks) of pregnancy based on the onset of clinical manifestations of preeclampsia. The EOPE and LOPE has a different pathogenesis. The PEAD is often associated with impaired uteroplacental perfusion caused by disruption of trophoblast invasion, while LOPE is often associated with the presence of extrinsic and maternal factors[4,5].

Preeclampsia is a protean syndrome, in which multiple organ systems can be affected compared to the others. Preeclampsia is mainly characterized by hypertension and proteinuria or may be associated with abnormalities in laboratory test results that renal function, hepatic or hemostasis after 20 weeks of pregnancy[1,6].

Analysis of risk factor for preeclampsia is needed to mitigate the adverse effects of preeclampsia. One among of these risk factor is resistin which is associated with inflammation and insulin resistance, so that resistin was a maternal risk factor that associated with LOPE[7].

Resistin is an adipose tissue-specific secretory factor (ADSF), a hormone secreted by adipose tissue that induces insulin resistance in muscle and liver. Resistin stimulated by inflammatory conditions that produce proinflammatory cytokines[7,8].

Preeclampsia is associated with inflammation and insulin resistance which is affected by resistin. Resistin is associated with late onset preeclampsia because it was a maternal factors, so there was an increasing of maternal resistin serum levels in late onset preeclampsia[7,8].

Previous study reported an elevated of maternal resistin serum levels associated with a systemic inflammatory response and insulin resistance which is both of them are increased in preeclampsia compared to normal pregnancy[9-12]. The other study showed the mean of Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) and high sensitivity C-reactive protein (hs-CRP) was higher in late onset preeclampsia than early onset preeclampsia group. From various studies on the above it could be estimated that the inflammatory factor and insulin resistance are associated with higher levels of resistin more dominant in late onset preeclampsia group compared to early onset preeclampsia group.

The HOMA-IR could be used as an indicator of insulin resistance, but not for inflammatory states, contrary hs-CRP could be used as an indicator of inflammation, but not for insulin resistance. Resistin is expected to describe both of them, because it was associated with insulin resistance and inflammation[7].

MATERIALS AND METHODS

This study is an analytical cross sectional study with 20 women of early onset preeclampsia (EOPE) and 20 women of late onset preeclampsia (LOPE) who met the inclusion criteria and there were no exclusion criteria. The samples were recruited in Dr.M. Djamil General Hospital, Padang from July-October, 2015.

The inclusions criteria were women who detected early onset preeclampsia or late onset preeclampsia in obstetrics emergency ward of Dr.M. Djamil General Hospital, Padang and willing to follow the research for taking blood samples. The exclusions criteria were diabetes mellitus (random blood sugar as >200 mg dL^{-1}), had suffered coronary heart disease, chronic kidney disease, chronic liver disease and obesity (BMI before pregnancy >25 kg m^{-2}).

Maternal resistin serum was examined by enzyme-linked immunosorbent assay (ELISA) method in Biomedic Laboratory in Medical Faculty of Andalas University. Statistical analysis was conducted by using SPSS program 20th version. The data distribution was normal with p>0.05. The differences mean levels of maternal resistin serum was analyzed by using independent t-test.

RESULTS

Characteristics of research subjects: Forty patients of research subjects consisted 20 patients of early onset preeclampsia (EOPE) and 20 patients of late onset preeclampsia (LOPE). Mean levels of maternal age in EOPE group is 34.4±5.144 years, whereas in LOPE group is 32.9±6.324 years with p = 0.416. According to maternal age

Table 1: Characteristics of research subjects between early onset preeclampsia and late onset preeclampsia

Characteristics	EOPE (n = 20)	LOPE (n = 20)	Total (%)	p
Maternal age group				
<20 years	0 (0%)	0 (0%)	0	
20-35 years	8 (40%)	10 (50%)	45	0.537
>35 years	12 (60%)	10 (50%)	55	
Maternal age ($\bar{x}$±SD) years	34.4±5.144	31.9±6.314		0.416
Gravidity group				
Primigravid	6 (30%)	7 (35%)	32.5	0.744
Miltigravid	14 (70%)	13 (65%)	67.5	
Gravidity ($\bar{x}$±SD)	2.4±1.314	2.65±1.461		0.573
BMI group				
Underweight	0 (0%)	0 (0%)	0	
Normoweight	14 (70%)	12 (60%)	65	0.520
Overweight	6 (30%)	8 (40%)	35	
BMI ($\bar{x}$±SD)	22.55±1.595	22.59±1.812		0.946

Table 2: Mean levels of maternal resistin serum in early onset preeclampsia and late onset preeclampsia

	EOPE		LOPE	
Variable	Mean	SD	Mean	SD
Maternal resistin serum (ng mL^{-1})	2.526	1.603	8.891	6.219

Table 3: Mean levels difference of maternal resistin serum in early onset preeclampsia and late onset preeclampsia

Variable	Mean difference	CI (95%)	p
Maternal resistin serum (ng mL^{-1})	6.365	3.3835-9.3475	0.000

groups, study of subjects in early onset preeclampsia consists 8 patients (40%) in group of maternal age 20-35 years old, 12 patients (60%) in group of maternal age >35 years old, none in group of maternal age <20 years old. Research subjects of late onset preeclampsia consists of 10 patients (50%) in group of maternal age 20-35 years old, 10 patients (50%) in group of maternal age >35 years old, none in group of maternal age <20 years old.

Mean levels of gravidity in early onset preeclampsia (EOPE) group is 2.4±1.314, whereas in late onset preeclampsia (LOPE) group is 2.65±1.461 with p = 0.573. According to gravidity groups, study of subjects in early onset preeclampsia consists 6 patients (30%) in group of primigravida, 14 patients (70%) in group of multigravida. Research subjects of late onset preeclampsia consists of 7 patients (35%) in group of primigravida, 13 patients (65%).

Mean levels of Body Mass Index (BMI) in early onset preeclampsia (EOPE) group is 22.551±1.595, whereas in late onset preeclampsia (LOPE) group is 22.588±1.4812 kg m^{-2} with p = 0.946. According to BMI groups, study of subjects in EOPE consists 14 patients (70%) in group of normal weight, 6 patients (30%) in group of overweight, none in group BMI underweight. Research subjects of late onset preeclampsia consists 12 patients (60%) in group of normal weight, 8 patients (40%) in group of overweight, none in group BMI underweight.

There were no statistically significant differences regarding maternal age, group of maternal age, gravidity, group of gravidity, BMI and group of BMI characteristic between those two groups with p>0.05 showed in Table 1.

Mean levels of maternal resistin serum in early onset preeclampsia and late onset preeclampsia: Mean levels of maternal resistin serum was higher in late onset preeclampsia than early onset preeclampsia (8.891±6.219 ng mL^{-1} vs 2.526±1.603 ng dL^{-1}), showed in Table 2.

Differences in mean levels of maternal resistin serum between late onset preeclampsia and early onset preeclampsia: The data distribution was normal with Kolmogorov Smirnov test. Analysis was performed with independent t-test. Table 3 showed the differences in mean levels of maternal resistin serum between early onset preeclampsia and late onset preeclampsia as 6.365 ng mL^{-1} with Confidence Interval (CI) 95% 3.384-9.347. There is a high significant differences with p<0.001.

DISCUSSION

The mean levels of maternal serum resistin in early onset preeclampsia (EOPE) group was 2.526±1.603 ng mL^{-1} whereas in late onset preeclampsia (LOPE) group was 8.891±6.219 ng mL^{-1} (Table 2), with a mean difference 6.365 ng dL^{-1}, 95% CI 3.384-9.347. Statistical test showed p<0.001, that the mean levels of maternal serum resistin significantly was higher in LOPE than EOPE (Table 3).

Resistin is a hormone secreted from adipose tissue that induces insulin resistance in muscle and liver. Resistin stimulated by inflammatory conditions that produce proinflammatory cytokines. Resistin contribute to the inflammatory disorders such as coronary heart disease,

chronic kidney disease and liver cirrhosis as well as insulin resistance in diabetes mellitus through the activation of proinflammatory cytokines varied which depending on the organs affected[7,8].

Insulin resistance and inflammation were the condition associated to preeclampsia. This factor related to the role of resistin through the release of proinflammatory cytokines. The relationship between resistin and preeclampsia is connected by those which is a maternal factor in preeclampsia. Therefore, resistin is associated to late onset preeclampsia, so the levels of maternal resistin serum was increased in late onset preeclampsia[7,8].

Inflammation and insulin resistance have been investigated, that the comparasion between HOMA-IR and hs-CRP in EOPE and LOPE. This study reported the results that mean levels of HOMA-IR and hs-CRP were higher in LOPE compared to EOPE (HOMA IR: 4.86±5.50 vs 3.99±5.97 and hsCRP: 123.08±38.67 vs 26.54±34.7 mg L^{-1}). This study suggested that the inflammatory factor and insulin resistance were more dominant in LOPE compared to EOPE.

A similar results was reported in which the mean levels of maternal resistin serum was higher in preeclampsia compared to normal pregnancy related to an increase in insulin resistance and the response systemic inflammation that happened in preeclampsia particularly late onset preeclampsia[9-12].

A cross sectional study in which two groups of pregnant women with preeclampsia (n = 15) and normal pregnancy (n = 23) demonstrated th mean levels of maternal resistin serum was higher in preeclampsia (5.68±0.41 ng mL^{-1}) compared to normal pregnancy (4.65±0.32 ng mL^{-1}), p = 0.028. The mean levels of maternal resistin serum related to the mean of HOMA-IR and proinflammatory cytokines that were elevated in preeclampsia compared to normal pregnancy. The mean of HOMA-IR (2.5±0.8 vs 1.4±0.1), IL-6 (6.34±1.02 vs 2.80±0.31) and TNF-α (1.89±0.18 vs 1.23±0.10)[9].

Another cross-sectional study on two groups of pregnant women, which were preeclampsia (n = 29) and normal pregnancy (n = 30), found that mean levels of maternal resistin serum was higher in preeclampsia 61.98±32.26 ng dL^{-1}, compared to normal pregnancy 38.06±31.26 ng dL^{-1}, p = 0.013. Insulin resistance is thought related the increasing the levels of maternal resistin serum, because the mean of HOMA-IR was higher in preeclampsia compared to normal pregnancy (4:44±4:02 vs 3.99±2.82)[10].

A cross sectional study was conducted on two groups of pregnant women, which are preeclampsia (n = 50) and normal pregnancy (n = 50). The median levels of maternal resistin serum were higher in preeclampsia 61 ng mL^{-1} compared to normal pregnancy 25.5 ng mL^{-1}, p = 0.033. Insulin resistance is thought related the increasing the levels of maternal resistin serum, because the median of HOMA-IR was higher in preeclampsia compared to normal pregnancy (4.7 vs 3.6)[11].

A cross sectional study was conducted on two groups of pregnant women, which are preeclampsia (n = 16) and normal pregnancy (n = 22). The mean levels of maternal resistin serum was higher in preeclampsia (12.06±0.973 ng mL^{-1}) compared to normal pregnancy (7.35±1.195 ng mL^{-1}), p = 0.041. Inflammatory factors is thought related the increasing the levels of maternal resistin serum in preeclampsia. There was an increasing mean levels of TNFα in preeclampsia compared to normal pregnancy (15.23±0.674 vs 12.84±0.348 ng mL^{-1}, p = 0.021)[12]. Based on that description, there was a correlation between previous studies and this study[9-12].

The mean levels of HOMA-IR and hs-CRP were higher in late onset preeclampsia than early onset preeclampsia, so according to those studies above, the insulin resistance and inflammation that were higher in late onset preeclampsia than early onset preeclampsia related to the levels of maternal resistin serum that was higher in late onset preeclampsia than early onset preeclampsia. It was appropriate with the results of this research that the mean levels of maternal resistin serum in late onset preeclampsia was significantly higher than early onset preeclampsia with p<0.001.

CONCLUSION

The mean levels of maternal resistin serum was higher significantly in late onset preeclampsia (LOPE) compared to early onset preeclampsia (EOPE).

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