INTRODUCTION

Preeclampsia is a pregnancy-specific syndrome, which increases morbidity and mortality of both mother and fetus, and it is responsible for 4-8% of pregnancy complications. Based on the onset, ACOG (American College of Obstetrics and Gynecology) classified preeclampsia in two groups: early onset preeclampsia for those occurred before the 34th gestational week, and late onset preeclampsia for those occur after the 34th gestational week. This classification is made according to the significant differences in fetomaternal outcome of both groups. Immunological, genetic, biochemical, and inflammatory factors are still discussed as the underlying mechanisms of preeclampsia.

Preeclampsia growth factor is pregnancy specific hormone involved in trophoblastic invasion and fetal growth. This hormone is first detected in the third gestational week, the level of which keeps rising with placental growth. However, this does not occur in pregnancy complicated by preeclampsia. PlGF level is a dependable marker to predict preeclampsia.

PlGF and TNF-α serum in preeclampsia

Abstract

Objective: To analyze the difference of PlGF and TNF-α serum level between early-onset and late-onset preeclampsia.

Method: This is a cross-sectional analytic comparative study comparing serum level of PlGF and TNF-α between groups with early- and late-onset preeclampsia. Each group consists of 32 subjects who met inclusion criteria and presented to Dr. Hasan Sadikin Hospital or its district hospitals in September - November 2012. Statistical analysis was performed with Kolmogorov Smirnov test, Shapiro-Wilk test, and non-parametric Mann-Whitney test.

Result: Mean of PlGF serum level in the group with early-onset preeclampsia is 53.0344 ± 38.07140 pg/ml, while mean of which in the group with late-onset preeclampsia is 241.8063 ± 192.8373 pg/ml (p<0.0001). Mean of TNF-α serum level in the group with early-onset preeclampsia is 2.7733 ± 0.97533 pg/ml, while mean of which in the group with late-onset preeclampsia is 2.5061 ± 0.84872 pg/ml (p=0.235).

Conclusion: Serum level of PlGF in early-onset preeclampsia is lower than the level of which in late-onset preeclampsia (p<0.0001). There is no significant difference of TNF-α serum level between the early- and late-onset preeclampsia (p=0.235).

Keywords: early onset, late onset preeclampsia, PlGF, preeclampsia, TNF-α

Abstrak

Tujuan: Menganalisis perbedaan kadar PlGF dan TNF-α antara preeklampsia awitan dini dan lambat.


Hasil: Rerata PlGF serum pada kelompok preeklampsia awitan dini adalah 53,0344 ± 38,07140 pg/ml, sedangkan pada kelompok preeklampsia awitan lambat adalah 241,8063 ± 192,8373 pg/ml (p<0,0001). Rerata TNF-α serum pada kelompok preeklampsia awitan dini adalah 2,7733 ± 0,97533 pg/ml, sedangkan pada kelompok preeklampsia awitan lambat adalah 2,5061 ± 0,84872 pg/ml (p=0,235).

Kesimpulan: Kadar PlGF pada preeklampsia awitan dini lebih rendah daripada preeklampsia awitan lambat (p<0,0001). Tidak ditemukan perbedaan yang bermakna pada kadar TNF-α antara preeklampsia awitan dini dan lambat (p=0,235).

Kata kunci: PlGF, preeklampsia awitan dini, preeklampsia awitan lambat, TNF-α

Correspondence: Christofani Ekapatria, Jln. Teluk Peleng no 62A Pasar Minggu Jakarta Selatan, Telephone: 08122188611, Email: christoekapatria@yahoo.com
TNF-α induces vasoconstriction, and is involved in micro vascular protein leakage and hypertriglyceridemia.11 Rise in TNF-α level is found in patients with preeclampsia.11-14

No study has reported comparison of angiogenic factor (PIGF) and inflammatory factor (TNF-α) between early onset and late onset preeclampsia in Indonesia. This is seen as an interesting topic, as the result would bring us closer to understand more about some factors to predict preeclampsia.

METHOD

This was a cross-sectional analytic comparative study, comparing serum level of PIGF and TNF-α between groups with early and late onset preeclampsia. Each group consisted of 32 subjects with gestational age of 20 weeks or more, single live fetus, who regularly have antenatal care, not showing any signs of infection, and clinically diagnosed with preeclampsia before and after the 34th gestational week from the last menstrual period, not having any history of hypertension nor kidney or liver disorder before pregnancy, and presented to Dr. Hasan Sadikin Hospital or its district hospitals in September - November 2012.

Five ml of blood sample were collected by cubital vein phlebotomy. The blood was stored for ±30 minutes in vacutainer, to be centrifuged in 3000 rpm thereafter for 10 minutes. The serum were stored in plastic tubes at –20°C. Then the serum level of PIGF and TNF-α were measured by ELISA method. The results recorded were serum level of PIGF in pg/ml and serum level of TNF-α in pg/ml.

RESULT

Characteristics of subjects in both groups are analyzed by Mann-Whitney test for numerical data and Kolmogorov-Smirnov test for categorical data. They are maternal age (in categories of <20 year old, 20-35 year old, and >35 year old), parity (in categories of 0, 1-3, and 4+), and BMI before pregnancy (with mean of 22.2538±1.19469 in subjects with early-onset preeclampsia, and 23.1509±1.90633 in those having late-onset preeclampsia). Both groups do not show any significant difference in maternal age (p=0.627), parity (p=1.000), or BMI before pregnancy (p=0.073).

Saphiro-Wilk test for normality was done on the PIGF and TNF-α serum level from the 64 subjects. p value of <0.05 shows the data from both groups are not normally distributed. Thus, the data was analyzed with Mann-Whitney nonparametric test. SPSS version 18.0 for windows was used in analyzing data.

<table>
<thead>
<tr>
<th>Table 1. Comparison of PIGF serum level between early onset and late onset preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>SD</td>
</tr>
</tbody>
</table>

Note: *Mann-Whitney test

<table>
<thead>
<tr>
<th>Table 2. Comparison of TNF-α serum level between early-onset and late-onset preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>SD</td>
</tr>
</tbody>
</table>

Note: *Mann-Whitney test

Table 1 shows PIGF serum level of the group with early-onset preeclampsia compared with late-onset preeclampsia. The level is significantly lower in the group with early onset preeclampsia. Whereas Table 2 shows a nonsignificant result (p>0.05), therefore TNF-α serum level of both groups is not significantly different.

DISCUSSION

The two-stage model of preeclampsia proposes that the first stage of preeclampsia is dominantly caused by poorly perfused placenta. This condition explains the lower PIGF level in the early onset compared with late onset preeclampsia, where greater extent of placental damage takes place.15 A study done by Ogge in 2011 explained that placental damage in early onset preeclampsia is histopathologically more extensive due to the greater degree of lesion following the wider infarction, and chronic inflammation such as vasculitis and villitis, which causes decidual arteriopathy and further re-
duction of villi surface volume. In early onset preeclampsia, trophoblastic inadequate invasion to maternal spiral artery accounts for reduced perfusion to umbilical artery, which causes fetal restriction. The significantly different level of PlGF shown in this study may be affected by some factors, one of them is the very low level of which in early onset preeclampsia may follow more damage in placenta, although histopathological examination was not performed in this study. Furthermore, the PlGF serum level in late onset preeclampsia is higher, some approaching the level of which in normal pregnancy, because of the minimally damaged or even intact placenta. Compared with the other angiogenic factors, PlGF serum level is superior for detecting preeclampsia, as PlGF is placental specific.

This study reports a non-significant difference in TNF-α serum level. This result can be explained by theory of pathogenesis proposed by Roberts, in which endothelial dysfunction following the increased level of cytokine, such as TNF-α, is the second stage of preeclampsia. Placental abnormalities in the first stage may induce release of placental factors into maternal circulation. This leads to glomerular endotheliosis, vascular permeability, and inflammatory response marked by increased level of cytokines such as TNF-α, further causing various organ damage by mechanism of hypoperfusion. According to former studies by Ogge and Huppertz, placental abnormality in preeclampsia may have occurred in the first trimester, even when clinical manifestations are not observable yet, leaving a more extensive placental damage. Earlier hypoxia condition happened in placenta leads to earlier placental damage, thus cytokine expression ensues earlier. This is consistent with a former study by Haider. Referring to the study by Robert JM and Hubel CA in 2009, the second stage of preeclampsia may occur even without the first stage, when maternal risk factors such as obesity and diabetes were clinically significant to generate clinical manifestations of preeclampsia syndrome. Founds reported an enhancement of TNF-α production by adipocytes in preeclamptic women.

Further study including objective tests for kidney and liver function in TNF-α measurement, or investigating other factors to predict preeclampsia, is encouraged.

CONCLUSION

Serum level of PlGF in early-onset preeclampsia is lower than in late onset preeclampsia. There is no significant difference of TNF-α serum level between the early and late onset preeclampsia.

REFERENCES


