COMPARISON OF CERULOPLASMIN SERUM LEVEL IN EARLY ONSET AND LATE ONSET SEVERE PREECLAMPSIA

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Abstract **:** This research is supposed to find the difference in ceruloplasmin serum level between patient with early and late onset severe preeclampsia. This is a comparative analytic study with cross sectional design. Study subjects were pregnant women admitted to obstetric ward and emergency room of H. Adam Malik General Hospital and USU Medical Faculty satellite hospitals, who fulfilled the inclusion criteria. 40 subjects were obtained, with 20 cases of early onset severe preeclampsia and 20 cases of late onset severe preeclampsia. From 40 subjects obtained, the average ceruloplasmin serum level was higher in subjects with early onset severe preeclampsia (0,899 g/L) compared to late onset severe preeclampsia (0,663 g/L) with p-value <0.05. From Pearson correlation test, a weak inverted correlation (- 0,668) between gestational age of subjects with early onset severe preeclampsia and ceruloplasmin serum level (p-value 0,001), and a strong inverted correlation (- 0,802) between gestational age of subjects with late onset severe preeclampsia and ceruloplasmin serum level (p-value < 0,05) were found. Average serum level of ceruloplasmin is higher in subjects with early onset severe preeclampsia compared to late onset severe preeclampsia (p-value <0.05). There's a strong inverted correlation between gestational age, whether in early or late onset severe preeclampsia with ceruloplasmin serum level. With the increase of gestational age, the level of ceruloplasmin will decrease.

Keyword **:** Preeclampsia, early onset, late onset, ceruloplasmin.

I.   INTRODUCTION

Preeclampsia - eclampsia (PE-E) is still one of the diseases and is often found in a mother both during pregnancy, childbirth and the puerperium. Because the influence it creates is a problem that largely determines the safety / well-being of the mother and fetus. Although progress in the field of antenatal and neonatal care has been achieved, PE-E is still a cause of maternal and fetal morbidity and mortality. [1,2,3]

Preeclampsia is a syndrome characterized by hypertension and proteinuria that occurs in the second and third trimesters of pregnancy. This can cause disseminated intravascular coagulation (DIC), vasospasm, sodium retention, and seizures; the occurrence of seizures in preeclampsia women marks the onset of eclampsia. Preeclampsia is a major cause of the high rates of maternal morbidity and mortality worldwide, [4] occurring 5% to 7% in first pregnancies and 13% to 18% recurring in subsequent pregnancies.[5,6] Although mortality rates from preeclampsia and eclampsia are highest in undeveloped countries, the burden of disease and death in developed countries is still quite large. In the United States, nearly 20% of deaths after 20 weeks' gestation are related to complications from preeclampsia and eclampsia.[7]

In a retrospective study conducted by Simanjuntak for five years (1993-1997), there were 5-10% maternal deaths in severe cases of preeclampsia.[8] Other meta-analysis studies from the Cochrane Review mentioned the prevalence of patients with severe preeclampsia with gestational age below 34 week is 50% of the number of pregnancies with severe preeclampsia. [9,10]

The etiology and pathogenesis of preeclampsia is still difficult to understand. Preeclampsia is characterized by vasospasm, increased peripheral vascular resistance and decreased organ perfusion. There is some evidence that various manifestations of preeclampsia, including changes in vascular reactivity, vasospasm, and abnormalities in various organ systems, originate from pathological changes in maternal vascular endothelium.[11,12]

The hypothesis that is receiving a lot of attention right now is a free radical reaction that results in an event that endangers the vascular endothelial defense function in preeclampsia. When there are free radicals exceeding the capacity of the antioxidant defense mechanism when oxidation stress occurs [11,12,13,14,15]

Several studies conducted by Ruder et al (2009), Wruch et al (2009), and Talaulikar and Manyonda (2009) suggest that oxidative stress may be a major factor causing preeclampsia. Atamer et al (2005) and Fainaru et al (2003) reported that an increase in serum hydroperoxide levels was associated with high oxidative stress. [16] Sidabutar E (2005) suggested that there was a decrease in the level of the antioxidant enzyme, the enzyme superoxide dismutase in preeclampsia patients.[17]

Other studies have shown an increasement in serum ceruloplasmin levels in preeclampsia patients (Guller et al, 2008; Engin-Ustùn et al, 2005; Orhan et al, 2001). This conclusion is based on several experiments that the levels of placental ceruloplasmin, proteins with complete antioxidants (Guller et al., 2008; Hellman and Gitlin, 2002; Patel et al., 2002) were markedly increased in patients with preeclampsia compared with patients with normal pregnancies at the same gestational age (gestational age) Guller et al., 2008). The possibility of placental hypoxia associated with preeclampsia (Redman and Sargent, 2005; Kaufmann et al, 2003) increases the expression of placental ceruloplasmin in macrophages and monocytes (Sarkar et al, 2003).[16]

II. RESEARCH METHODOLOGY

This study uses a comparative analytic study that compares the group of pregnancies with early onset severe preeclampsia (PE) and those with late onset severe preeclampsia using a cross sectional design.

The study was conducted at the Department of Obstetrics and Gynecology, Medical Faculty University of North Sumatra/ General Hospital Adam Malik Medan and Network Hospitals of University of North Sumatera such as Sundari Hospital Medan, Tk. II Puteri Hijau KESDAM II / BB Hospital Medan, Hajj Mina Hospital Medan. from July to October 2013.

After calculating, it was found that the sample size needed for each group was 17 people. The subjects of the study were all pregnant women who examined their pregnancies in obstetric clinics and emergency rooms at the General Hospital H Adam Malik Medan and the Network Hospitals of University of North Sumatera that met the inclusion criteria, namely: a. Pregnant with early onset severe preeclampsia b. pregnant with late onset severe preeclampsia c. primigravida or multigravida d. willing to participate in research. While the exclusion criteria are a. pregnancy with liver disease b. damaged blood sample. From this study total sample of 40 people were obtained with details of 20 cases of pregnant women with early onset severe preeclampsia and 20 cases of pregnant women with late onset severe preeclampsia.

Patients who meet the sample acceptance requirements are given an explanation of the research to be carried out and the patient signs an agreement if they are willing. 5 cc of venous blood is taken by using germ free disposable tools and by trained health workers. Blood samples are stored in special containers, labeled with code then sent to the Prodia laboratory within $\pm$ 60 minutes. Data about patients taken according to the variables needed.

All participants were given an explanation of the purpose and method used in this study, the study was conducted after there was a voluntary agreement from each participant by signing an informed consent letter.

III. RESULTS AND DISCUSSIONS

From table 1, it can be seen the characteristics of patients with early onset and late onset severe preeclampsia at General Hospital H. Adam Malik Medan and Network Hospitals of University of North Sumatera. From the age characteristics found that most patients with severe preeclampsia both early onset (95%) and late onset (75%) come from the age group 19-35 years. Based on parity found that most patients with severe preeclampsia both early onset (55%) and late onset (50%) are from primigravida. Based on the level of education found that most patients with severe preeclampsia both early onset (75%) and late onset (70%) have a high school education.

Tabel 1. Characteristics of Research Sample

Characteristics		Severe preeclampsia	
		Early Onset N (%)	Late Onset N (%)
Age (years)	19 – 35	19 (95%)	15 (75%)
	> 35	1 (5%)	5 (25%)
Parity	Primigravida	11 (55%)	10 (50%)
	Secundigravida	5 (25%)	4 (20%)
	Multigravida	4 (20%)	6 (30%)
Education Level	Elementary School	1 (5%)	1 (5%)
	Junior High School	4 (20%)	5 (25%)
	Senior High School	15 (75%)	14 (70%)
	Bachelor	0 (0%)	0 (0%)

From table 2 it can be seen that the average serum seruloplasmin level in patients with early onset severe preeclampsia is higher (0.899 g / L) compared to late onset severe preeclampsia (0.663 g / L) with a p-value <0.05.

Tabel 2. Comparison of Ceruloplasmin Serum Levels between Pregnancy with Early Onset Severe Preeclampsia and Pregnancy with Late Onset Severe Preeclampsia

	Diagnostic	Mean Ceruloplasmin (g/L)	N	Std. Deviation	P value
Cerulopasmin Serum Levels	Early Onset	0,899	20	0,155	< 0,05
	Late Onset	0,663	20	0,137	< 0,05

The results of this study are in accordance with the study by Ghaseminejad et al (2009), in a case control study finding that the average serum levels of ceruloplasmin were higher in women with preeclampsia than in the control group. They also found higher ceruloplasmin levels in women with severe preeclampsia compared to mild preeclampsia, and higher levels in early onset preeclampsia compared to late onset preeclampsia.[18]

From the Pearson correlation test (Tables 3 and 4), a weak inverse correlation (- 0.668) was found between the gestational age of the mother with severe early onset preeclampsia with serum ceruloplasmin levels (p-value 0.001), and the presence of a strong inverse correlation (- 0.802) between gestational age of mothers with late onset severe preeclampsia and serum levels of ceruloplasmin. (p-value <0.05). With increasing gestational age, serum seruloplasmin levels will decrease. This is consistent with the findings of Perveen et al (2002) who found a decrease in serum ceruloplasmin levels with increasing gestational age.[19]

Table 3. . Correlation between Ceruloplasmin Serum Level and Gestational Age with Early Onset Severe Preeclampsia

		Ceruloplasmin levels (g/L)	Gestational Age (weeks)
Ceruloplasmin levels (g/L)	Pearson Correlation	1	-,668
	P-value		,001
	N	20	20
Gestational Age (weeks)	Pearson Correlation	-,668	1
	P-value	,001	
	N	20	20

Table 4. . Correlation between Ceruloplasmin Serum Level and Gestational Age with Late Onset Severe Preeclampsia

		Ceruloplasmin levels (g/L)	Gestational Age (weeks)
Ceruloplasmin levels (g/L)	Pearson Correlation	1	-,802
	P-value		,000
	N	20	20
Gestational Age (weeks)	Pearson Correlation	-,802	1
	P-value	,000	
	N	20	20

IV. CONCLUSIONS

The mean serum ceruloplasmin level in early onset severe preeclampsia is higher than the late onset (p-value <0.05). There is a strong inverse correlation between gestational age with severe preeclampsia both early onset and late onset with serum ceruloplasmin levels (p-value <0.05).

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