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Severe Preeclampsia Women With Low Serum L - Arginine Levels

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Abstract: The results of serum l - arginine low levels affect the age of the mother, this is shown at p-value 0.057 <0.05. And serum l - arginine levels affect medication administration where the p-value is 0.011 <0.05. age and medication administration influence the occurrence of low serum l - arginine levels in severe preeclampsia women.

Keywords: Normal Pregnant Women, Severe Preeclampsia, Severe Preeclampsia With Complications, Serum L - Arginine Levels.

1. INTRODUCTION

Preeclampsia is an obstetric problem that cannot be resolved comprehensively in the world, likewise in Indonesia. The occurrence of major complications in pregnancy is due to hypertensive disease in pregnancy, including gestational hypertension, preeclampsia (PE), and eclampsia, and accounted for 14% of maternal mortality(1)**.** Preeclampsia is a special symptom in pregnancy marked with high blood pressure and proteinuria after 20 weeks of pregnancy occurring in 8% of pregnant women(2)**.** The cause of pre-eclampsia until now is not known. Severe pre-eclampsia experienced by pregnant women does not occur by itself, many risk factors can affect the incidence of severe pre-eclampsia: Mother's age, parity, gestational age, number of children, the number of ANC visits, and the History of Hypertension(3).

Arginine can increase NO, relax blood vessels so that it plays a role in treating angina and several other cardiovascular problems. In general, arginine can be found in vegetable and animal proteins such as milk production, meat and especially in fish (7% of total protein) and nuts (15% of total protein). The Food Drug Administration (FDA) classifies its use as Generally Recognized as Safe (GRAS)(4).

Vitamin l - arginine supplementation with antioxidants resulted in a significant reduction in the risk of preterm birth indicated compared with placebo. Furthermore, the existing literature suggests that l -arginine has a direct effect on blood pressure in animal models, normal humans, hypertensive patients, women with pre-eclampsia, and healthy pregnant women. However, it should be noted that women with gastric ulcers should not give l - arginine because it can worsen the symptoms of the disease. For protection from pre-eclampsia, it is best if vitamin l - arginine and antioxidants are added before 24 weeks of gestation(5). In humans, administration of l - arginine can improve uteroplacental circulation and decrease maternal blood pressure, and oxidative stress can play a key role in the

development of endothelial dysfunction and preeclampsia(6). Research has been conducted to find the relationship between l - arginine, and preeclampsia. Several studies reported that there was statistical significance between l - arginine supplementation and Nitric Oxide levels in women with preeclampsia. This study also showed that there was an increase in nitric oxide levels in the blood after l - arginine supplementation and women who had both l - arginine supplementation and l - arginine supplementation had a lower chance of developing preeclampsia compared with those who did not receive l - arginine supplementation or less l - arginine levels in the body. This study demonstrates the specificity of nitric oxide as a marker for the development of preeclampsia(7). Therefore, based on the background of the above problems, it is necessary to research preeclampsia mothers with low serum l - arginine levels.

2. MATERIALS & METHODS

This research was used for secondary data (medical records). Characteristics of patients with normal pregnant women, severe preeclampsia, and severe preeclampsia with complications along with data on serum l-arginine levels.

Time and place of research

This research was conducted in September - October 2020 in Makassar. The study was conducted in 4 hospitals in Makassar, namely: RSU Dr. Wahidin Sudirohusodo, Hasanuddin University Teaching Hospital, Sitti Khadijah 1 Mother and Child Hospital, Sitti Fatimah Maternal, and Child Health Hospital.

Research Stage

This research is a retrospective descriptive study using medical record data by reviewing the characteristics of the patient, the treatment room, and the supplements provided. In addition, other supporting data are serum l - arginine levels in the sample group of normal pregnant women, severe preeclampsia, and severe preeclampsia with complications. Data analysis using statistical analysis with descriptive statistical test and chi-square statistical test.

3. RESULT & DISCUSSION

Table 1: Characteristics of Respondents

Variable	**Normal (n=30)**	**Severe preeclampsia (n=30)**	**Severe preeclampsia with complications (n=12)**	**Total**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Age				
Low risk	18 (25.0)	22(30.6)	9 (12.5)	49 (68.1)
High risk	12 (16.7	8(11.1)	3(4.2)	23 (31.9)
Paritas				
Primigravida	10 (13.9)	10(13.9)	3 (4.2)	23 (31.9)
Multigravida	19 (26.4)	16 (22.2)	9 (12.5)	44 (61.1)

Grande multigravida	1 (1.4)	4 (5.6)	0 (0.0)	5 (6.9)
BMI				
Thin	3 (4.2)	0 (0.0)	2 (2.8)	5 (6.9)
Normal	18(25.0)	13 (18.1)	4 (5.6)	35 (48.6)
Fat	3(4.2)	5 (6.9)	1 (1.4)	9 (12.5)
Obesity	6 (8.3)	12 (16.7)	5 (6.9)	23 (31.9)
Pregnancy Distance				
No risk	18 (25.0)	20 (27.8)	8 (11.1)	46 (63.9)
Risky	12 (16.7)	10 (13.9)	4 (5.6)	26 (36.1)
History of preeclampsia/eclampsia				
No history	30 (41.7)	20 (27.8)	6 (8.3)	56 (77.8)
There is a history	0 (0.0)	10 (13.9)	6 (8.3)	16 (22.2)
Serum l – arginine levels				
Normal	1 (1.4)	4 (5.6)	1 (1.4)	6 (8.3)
Low	29 (40.3)	26 (36.1)	11 (15.3)	66 (91.7)
Ward				
Childbirth	30 (41.7)	30 (41.7)	9 (12.5)	69 (97.2)
ICU	0 (0.0)	0 (0.0)	3 (4.2)	3 (4.2)
Medication				
Antibiotics	1 (1.4)	0 (0.0)	2 (2.8)	3 (4.2)
Analgesics	0 (0.0)	2 (2.8)	1 (1.4)	3 (4.2)
Calcium antagonists	0 (0.0)	4 (5.6)	3 (4.2)	7 (9.7)
Antibiotics + Analgesics	29 (40.3)	13 (18.1)	1 (1.4)	43 (59.7)
Antibiotics + Anti inflammatory	0 (0.0)	1 (1.4)	0 (0.0)	1 (1.4)
Antibiotics + Calcium Antagonists	0 (0.0)	0 (0.0)	1 (1.4)	1 (1.4)
Analgesics + Calcium Antagonist	0 (0.0)	7 (9.7)	3 (4.2)	10 (13.4)
Antibiotics + Analgesics + Calcium Antagonist	0 (0.0)	3 (4.2)	1 (1.4)	4 (5.6)
Supplement				
Dietary supplements	0 (0.0)	5 (6.9)	2 (2.8)	7 (9.7)
Iron supplements	23 (31.9)	15 (20.8)	7 (9.7)	45 (62.5)
Vitamin	1 (1.4)	9 (12.5)	3 (4.2)	13 (18.1)
Dietary supplements + Iron supplements	6 (8.3)	1 (1.4)	0 (0.0)	7 (9.7)

Length of treatment				
1 – 3 days	20 (27.8)	18 (25.0)	4 (5.6)	42 (58.3)
4 – 6 days	8 (11.1)	8 (11.1)	7 (9.7)	23 (31.9)
7 – 14 days	2 (2.8)	4 (5.6)	1 (1.4)	7 (9.7)

The number of samples in this study was 72 samples. In Table 1, the characteristics of respondents obtained are: Based on the largest age group, namely the low-risk age category as many as 49 people (68.1%). For most parity with the multigravida category as many as 44 people (61.1%). Most categories of BMI in normal BMI with 35 people (48.6%). Most pregnancy spacing with the category not at risk was 46 people (63.9%). The most preeclampsia history was in the category that did not have a history of preeclampsia, there were 56 people (77.8%). The group with the highest serum l -arginine levels in the low category were 66 people (91.7%). Meanwhile, for the treatment room in the puerperal room, there were 69 people (95.8%). The group of drugs given antibiotics and analgesics was 43 people (59.7%). Most types of supplements were in the category of iron supplements as many as 45 people (62.5%). The length of treatment who underwent treatment for 1-3 days was 42 people with a proportion (58.3%).

Table 2: Characteristics of Respondents Based on Serum L - Arginine Levels

Characteristics	**Serum L - Arginine Levels**				***P-Value***
	Normal		**Low**		
	n	**%**	**n**	**%**	
Mother status					
Normal	1	1.4	29	40.3	0.375
Severe preeclampsia	4	5.6	26	36.1	
Severe preeclampsia with complications	1	1.4	11	15.3	
Age					
Low risk	2	2.8	47	65.3	0.057
High risk	4	5.6	19	26.4	
Paritas					
Primigravida	1	1.4	22	30.6	0.496
Multigravida	4	5.6	40	55.6	
Grande multigravida	1	1.4	4	5.6	
BMI					
Thin	0	0.0	5	6.9	0.385
Normal	2	2.8	33	45.8	
Fat	2	2.8	7	9.7	
Obesity	2	2.8	21	29.2	
Pregnancy Distance					
No risk	5	6.9	41	56.9	0.300
Risky	1	1.4	25	34.7	
History of preeclampsia/eclampsia					
No history	5	6.9	51	70.8	0.732

There is a history	1	1.4	15	20.8	
Ward					
Childbirth	5	6.9	64	88.9	0.110
ICU	1	1.4	2	2.8	
Medication					
Antibiotics	0	0.0	3	4.2	0.011
Analgesics	1	1.4	2	2.8	
Calcium antagonists	1	1.4	6	8.3	
Antibiotics + Analgesics	1	1.4	42	58.3	
Antibiotics + Anti inflammatory	1	1.4	0	0.0	
Antibiotics + Calcium Antagonists	0	0.0	1	1.4	
Analgesics + Calcium Antagonist	2	2.8	8	11.1	
Antibiotics + Analgesics + Calcium Antagonist	0	0.0	4	5.6	
Supplement					
Dietary supplements	1	1.4	6	8.3	0.845
Iron supplements	3	4.2	42	58.3	
Vitamin	1	1.4	12	16.7	
Dietary supplements + Iron supplements	1	1.4	6	8.3	
Length of treatment					
1 – 3 days	3	4.2	39	54.2	0.816
4 – 6 days	2	2.8	21	29.2	
7 – 14 days	1	1.4	6	8.3	

**p:<0.05*

**Chi-Square test*

Table 2 shows that the study respondents in the group of normal pregnant women, severe preeclampsia and severe preeclampsia with complications based on maternal status, parity, BMI, pregnancy distance, history of preeclampsia, treatment room, supplements, and length of treatment were not significantly different. Meanwhile, age and drug variables have significant differences.

Arginine is considered an unnecessary amino acid in many species, including humans. However, in certain physiological (growth, pregnancy) or pathophysiological conditions with certain conditions arginine is required in preterm birth, sepsis, and diabetes can cause arginine to be important. Usually, these conditions can benefit from exogenous arginine supplementation, because this amino acid is required for NO, creatine, polyamine, and protein synthesis(8).

L - arginine is categorized as a semi-essential amino acid, under normal circumstances the body can meet its needs through the synthesis of l - arginine, but in pregnant conditions, the need for l - arginine will increase(9). L - arginine is the most important source in the regulation of nitric oxide so that in pregnancy there will be a period of increased deposition in maternal and fetal tissues so that increased NO synthesis is needed to be a major contributor to maternal vascular expansion in pregnancy and blood flow to the

placenta. This makes the need for l - arginine to be an essential amino acid in pregnant women(10).

Higher homocysteine and ADMA levels observed in patients with early preeclampsia may indicate an association between the levels of these factors and the time of clinical manifestations of preeclampsia. They might too indicates that maternal serum homocysteine levels are higher and ADMA correlates with severity and can be decisive early onset of the disease clinically. Increased ADMA level and eNOS level unchanged at Pregnancy complicated by severe preeclampsia conclusion that nitric oxide deficiency in this pregnancy the distraction results not from reduced eNOS levels or activity, rather, from elevated levels of asymmetric dimethylarginine, an endogenous eNOS inhibitor. The results of this study also suggest that ADMA and homocysteine reduction can be goals in the prevention and treatment of preeclampsia(11).

Preeclampsia is associated with reduced NO· bioavailability and L - arginine/ADMA ratio and elevated levels of ADMA and 3-nitrotyrosine. Measurements of these parameters can help in the early prediction of endothelial dysfunction in preeclampsia. Elevated ADMA levels may precede hypertension and proteinuria and hence could be used for predicting preeclampsia. Preeclampsia predisposes women to have a preterm delivery, IUGR, and low birth weight babies. Exogenous supplementation with L - arginine during pregnancy could be explored as a therapeutic agent to increase the Larginine/ADMA ratio and improve endothelial function in preeclampsia and pregnant women at risk of developing preeclampsia(12).

New therapeutic options emerge as we understand the rise of preeclampsia. Increase NO pathway, by overcoming eNOS block and neutralizing the increased ADMA values and with homocysteine reduction, maybe a perspective goal in the treatment and prevention of PE. Still new, prospective clinical trials are needed to safely develop effective management strategies with the use of pharmacological modulators of the NO system, which seems promising for preeclampsia treatment(13).

3. CONCLUSION

Characteristics of mothers who have low serum l - arginine levels are normal pregnant mother status, low-risk age, multigravida, normal BMI, no risk pregnancy interval, no history of preeclampsia, postpartum care room, antibiotics and analgesics, iron supplements, and duration of treatment 1 - 3 days. Maternal characteristics based on serum l - arginine levels can be seen that age affects serum l - arginine levels in severe preeclamptic mothers to be low and drug administration also significantly affects low serum l - arginine levels in severe preeclampsia women.

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