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**RESEARCH**

## Difference in Mean Levels of Calcium Magnesium Ratio and Sodium Potassium Ratio of Maternal Serum Between Severe Preeclampsia and Eclampsia

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**Abstract**

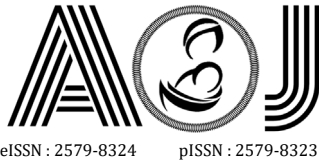
The high incidence of preeclampsia and eclampsia causes the importance of early detection especially eclampsia which is the main cause of maternal morbidity and mortality and bad perinatal outcome. The etiology was unknown, but is related to changes in electrolyte status. Electrolytes such as calcium ( $Ca^{2+}$ ), Magnesium ( $Mg^{2+}$ ), sodium ( $Na^+$ ) and potassium ( $K^+$ ) play an important role in pre-eclampsia and eclampsia because they contribute significantly in vascular smooth muscle function. This study was done to analyze the differences in mean levels of calcium magnesium ratio and sodium potassium ratio of maternal serum in severe preeclampsia and eclampsia. We performed an observational comparative with cross sectional study on 16 women with severe preeclampsia and 16 women with eclampsia who met the inclusion criteria and there were no exclusion criteria. The samples were recruited in Dr. M Djamil general hospital Padang, Solok District Hospital, and Pariaman District Hospital from May 2015 to January 2016. The levels of calcium serum were examined by atomic absorption spectrophotometry (AAS), magnesium levels were examined by enzymatic metode, sodium and potassium levels were examined by ion selection electrode (ISE). The differences in mean levels of calcium magnesium ratio and sodium potassium ratio between the two groups was analyzed by using independent *t* test. The mean levels of calcium magnesium ratio in severe preeclampsia was significantly higher than eclampsia. The mean levels of sodium potassium ratio in severe preeclampsia was significantly lower than eclampsia.

**Keywords:** Calcium magnesium ratio, sodium potassium ratio, severe preeclampsia, eclampsia

**INTRODUCTION**

Severe preeclampsia and eclampsia are a group of symptoms that can occur in pregnancy and childbirth. These changes need to be well recognized because their effect is a problem that contributes to the well-being and safety of the mother and the fetus she is carrying. The reported incidence of severe preeclampsia and eclampsia varies widely. <sup>1</sup>

Preeclampsia is an important problem in the obstetric field because it is still the main cause of maternal death compared to bleeding and infection. Preeclampsia is a pregnancy-specific syndrome in the form of reduced organ perfusion due to vasospasm and endothelial activation that occurs after 20 weeks. Proteinuria is an important sign of preeclampsia in



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addition to hypertension with or without edema. Preeclampsia consists of mild preeclampsia and severe preeclampsia. Meanwhile, eclampsia is the occurrence of seizures in a woman with preeclampsia that is not caused by anything else.

Savitz and Zhang, who conducted a study in North Carolina (USA), found the incidence of hypertension in pregnancy was 43.1 per 1000 single pregnancies. WHO noted that the incidence of severe preeclampsia ranges from 0.51% to 38.4%. Meanwhile, the incidence of severe preeclampsia in Indonesia ranges from 3-10%. The incidence of preeclampsia in the United States ranges from 2–6% in nulliparous women. In all cases of preeclampsia, 10% occurred before 34 weeks of gestation. Overall, the incidence of preeclampsia ranges from 5-14% of all pregnancies.

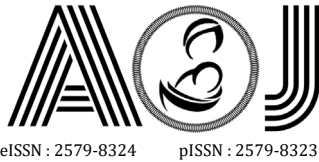
Nationally, the prevalence of eclampsia ranges from 7-10% and continues to increase every year. The frequency of eclampsia in developing countries ranges from 0.3% to 0.7%. It is different from developed countries where the frequency of eclampsia is only in the range of 0.05-0.1%. Research by Kusuma, et al at RSUPN Dr. Cipto Mangunkusumo Jakarta found 36 cases of eclampsia during 2008. Research conducted in Perjan M. Djamil Padang in 1998 - 2002 found the incidence rate of preeclampsia 5.5% or 663 cases and eclampsia 0.88 % or 106 cases out of 12034 deliveries, 65% of preeclampsia cases were term pregnancies.<sup>4</sup>

During the period 1 January 2005 to 31 December 2007 at BLU RS DR. M. Djamil Padang had 220 cases of severe preeclampsia (4.99%) and eclampsia as many as 47 people (1.07%) from 4407 deliveries. Medical record data of patients treated in the obstetrics and gynecology department of Dr. M. Djamil Padang during 2011 had the incidence of preeclampsia as many as 125 cases (8.31%) out of 1395 deliveries. This figure increases every year, namely as many as 193 cases (11.47%) from 1,682 deliveries during 2012, and as many as 206 cases (12.02%) from 1,714 deliveries during 2013.

Given the high incidence of preeclampsia and eclampsia, it is important to be able to detect this condition early, especially the incidence of eclampsia which causes worse maternal and perinatal morbidity and mortality. With early detection, it is hoped that interventions can be carried out in the course of the disease so that it does not cause bad consequences for the welfare of the mother and fetus.<sup>8,9</sup>

The exact etiology is unknown but may be related to changes in electrolyte status. Although relatively easy to examine with modern investigative techniques, electrolyte measurements in preeclamptic women are often overlooked. Electrolytes such as Calcium (Ca<sup>2+</sup>), Magnesium (Mg<sup>2+</sup>), Sodium (Na<sup>+</sup>), and Potassium (K<sup>+</sup>) play an important role in preeclampsia and eclampsia as they make a significant contribution to vascular smooth muscle function. Ca<sup>2+</sup> plays an important role in vascular smooth muscle function.<sup>10</sup>

A decrease in plasma Ca<sup>2+</sup> concentration leads to an increase in blood pressure.<sup>11</sup> Mg<sup>2+</sup> acts as a co-factor for many enzymes (eg sodium-potassium ATPase) and is involved in peripheral vasodilation. Several studies have shown that Ca<sup>2+</sup> and Mg<sup>2+</sup> have a relaxing



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effect on the blood vessels of pregnant women.<sup>12</sup> The ratio of calcium and magnesium is important in the excitability and transmission of nerve cell signals.

Research by Idogun et al. Found that low extracellular calcium and magnesium concentrations also decreased the ratio of calcium to magnesium in their study. These extracellular changes explain why some of his patients experience seizures (eclampsia) because a small decrease in extracellular calcium and / or magnesium will lead to increased excitability and burning bursts, altering physiological and pathophysiological processes such as increasing long-term potentiation, pain transmission, epileptogenesis, and nerve damage. The increase in extracellular calcium and magnesium will have the opposite effect on this process.

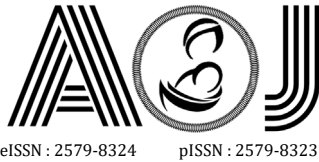
According to Wang et al, the effect of these extracellular divalent ions on signal transmission may explain some of the pathophysiological effects of hypocalcemia and hypomagnesemia.<sup>13</sup> Deficiency of Ca and Mg results in clinical manifestations that can be observed in preeclampsia because these two ions are important in cellular metabolism and neuronal metabolism and maintain cell membrane stability. Meanwhile, sodium and potassium ions are the main ions in the formation of action potentials in muscle fibers which will cause muscle contraction.

## METHOD

This study is a comparative observational study with a cross-sectional design that was conducted on 16 women with preeclampsia and 16 women with eclampsia who met the inclusion criteria and there were no exclusion criteria. Samples were taken at RSUP Dr. M Djamil Padang from May 2015 to January 2016.

The inclusion criteria were women diagnosed with preeclampsia or eclampsia in the obstetric emergency room of Dr. M Djamil Padang Hospital, Solok Hospital, and Pariaman Regional Hospital and were willing to take part in the study for blood sampling. Exclusion criteria were a history of hypertension before pregnancy or before 20 weeks of gestation, a history of kidney disease, liver disease, diabetes mellitus, or suffering from extensive burns (> 20% TBSA) and being receiving anti-seizure therapy.

Examination of sodium and potassium levels was carried out using the ion selection electrode (ISE) method, an examination of calcium levels was carried out by the Atomic Absorption Spectrophotometry (AAS) method at the Dr. M Djamil Padang General Hospital Laboratory and magnesium levels were examined by enzymatic methods at the Prodia Padang Laboratory. Statistical analysis was performed using SPSS version 20 program. Differences in the mean ratio of calcium to magnesium and the mean ratio of sodium to potassium in maternal serum were tested by independent t.



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**RESULTS****Research Sample Characteristics**

The subjects of this study consisted of 16 preeclampsia and 16 eclampsia people. There was no difference in the characteristics of the gestational age and the gravida group between the two groups with a p-value of  $> 0.05$ , but there was a significant difference in the characteristics of maternal age with a p-value of  $< 0.05$ , as shown in Table 1.

**The difference in mean maternal serum calcium-magnesium ratio between severe preeclampsia and eclampsia**

The analysis was performed with the t-Independent test. Table 2 shows the mean difference in maternal serum calcium-magnesium ratio between preeclampsia and eclampsia ( $4.3 + 0.92$  vs  $2.93 + 0.47$ ). There is a very significant difference with  $p < 0.000$ .

**The difference in mean maternal serum sodium-potassium ratio between severe preeclampsia and eclampsia**

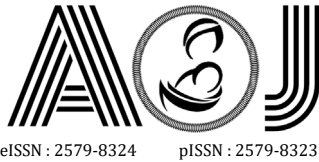
The analysis was performed using an independent t-test. Table 3 shows the mean difference in maternal serum sodium-potassium ratio between preeclampsia and eclampsia ( $31.16 + 4.36$  vs  $39.46 + 6.2$ ). There is a very significant difference with  $p < 0.000$ .

**DISCUSSION**

There are three characteristics in the subjects of this study, namely maternal age, gestational age, and gravida status. The two groups (preeclampsia and eclampsia) were equal in terms of gestational age (mean  $36.25 + 3.84$  weeks and  $35.81 + 2.74$  weeks, with  $p = 0.713$ ) and gravida status (mean  $1.63 + 1.03$  and  $1.31 + 0.79$  with  $p = 0.342$ ). Meanwhile, in terms of maternal age, there were significant differences (maternal age mean was  $30.56 + 7.05$  years and  $24.94 + 7.25$  years, with  $p = 0.034$ ). However, there is no theory that age affects the occurrence of seizures.

**Tabel 1. Karakteristik Subjek Penelitian Antara PEB dan Eklamsia**

Karakteristik	PEB n=16	Eklamsia n=16	p
Usia ibu ( $\bar{x} \pm SD$ ), tahun	$30,56 \pm 7,05$	$24,94 \pm 7,25$	0,034
Usia kehamilan ( $\bar{x} \pm SD$ ), minggu	$36,25 \pm 3,84$	$35,81 \pm 2,74$	0,713
Gravida ( $\bar{x} \pm SD$ )	$1,63 \pm 1,03$	$1,31 \pm 0,79$	0,342
Kelompok Gravida			
- Primigravida	10 (62,5%)	13 (81,25%)	0,238
- Multigravida	6 (37,5%)	3 (18,75%)	



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The mean maternal serum calcium-magnesium ratio in preeclampsia was  $4.3 + 0.92$ , whereas in eclampsia it was  $2.93 + 0.47$ , with  $p = 0.000$  meaning that there was a significant difference in the mean ratio of maternal serum calcium magnesium between preeclampsia and eclampsia.

The ratio of calcium to magnesium is important in the excitability and transmission of nerve cell signals. Research by Idogun (2007) found that low extracellular calcium and magnesium concentrations also decreased the ratio of calcium to magnesium in his study. These extracellular changes explain why some of his patients experience seizures (eclampsia) because a small decrease in extracellular calcium and / or magnesium leads to increased excitability and burning bursts, altering physiological and pathophysiological processes such as increasing long-term potentiation, pain transmission, epileptogenesis, and nerve damage.<sup>13,14</sup>

This is consistent with the results of this study where the mean ratio of maternal serum calcium magnesium in eclampsia was lower than preeclampsia, namely:  $2.93 + 0.47$  vs  $4.3 + 0.92$ , with  $p = 0.000$

**Tabel 2. Perbedaan Rerata Rasio Kalsium Magnesium Serum Maternal Antara PEB dan Eklamsia**

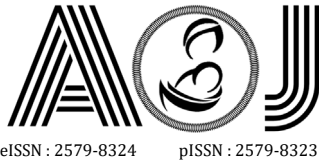
Variabel	PEB n=16	Eklamsia n=16	p
Kalsium ( $\bar{x} \pm SD$ ), mg/dl	$8,68 \pm 0,75$	$7,85 \pm 0,68$	0,003
Magnesium ( $\bar{x} \pm SD$ ), mg/dl	$2,18 \pm 0,72$	$2,78 \pm 0,68$	0,019
Rasio Kalsium Magnesium ( $\bar{x} \pm SD$ )	$4,3 \pm 0,92$	$2,93 \pm 0,47$	0,000

The mean maternal serum sodium level in preeclampsia was  $133.25 + 3.4$  mmol / L, while in eclampsia  $137.88 + 11.82$  mmol / L, with  $p = 0.143$  meaning that there was no significant difference in the mean maternal serum sodium level between preeclampsia and eclampsia. The mean maternal serum potassium level in preeclampsia was  $4.37 + 0.72$  mmol / L, whereas in eclampsia  $3.57 + 0.58$  mmol / L, with  $p = 0.002$ , it means that there was a significant difference in the mean maternal serum potassium levels between preeclampsia and eclampsia.

**Tabel 3. Perbedaan Rerata Rasio Natrium Kalium Serum Maternal Antara PEB dan Eklamsia**

Variabel	PEB n=16	Eklamsia n=16	p
Natrium ( $\bar{x} \pm SD$ ), mmol/L	$133,25 \pm 3,4$	$137,88 \pm 11,82$	0,143
Kalium ( $\bar{x} \pm SD$ ), mmol/L	$4,37 \pm 0,72$	$3,57 \pm 0,58$	0,002
Rasio Natrium Kalium ( $\bar{x} \pm SD$ )	$31,16 \pm 4,36$	$39,46 \pm 6,2$	0,000





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The normal level of serum sodium is around 136 - 145 mmol / L. In preeclampsia, the mean serum sodium level was 133.25 + 3.4 mmol / L, while in eclampsia, the low normal level was 137.88 + 11.82 mmol / L. Normal serum potassium levels are around 3.5 - 5.1 mmol / L. In preeclampsia, the mean normal serum potassium level was 4.37 + 0.72 mg / dl, while in low eclampsia, it was normal, namely 3.57 + 0.58 mg / dl. It appears that low serum potassium levels play a greater role in pathogenesis. preeclampsia-eclampsia versus serum sodium levels.

The mean maternal serum sodium-potassium ratio in preeclampsia was 31.16 + 4.36, while in eclampsia 39.46 + 6.2, with  $p = 0.000$ , it means that there was a significant difference in the mean ratio of maternal serum calcium magnesium between preeclampsia and eclampsia. The presence of sodium and potassium depends on the active transport of  $\text{Na} + / \text{K} + / \text{ATPase}$ . Hypertension in pregnancy is an early sign of abnormality in the transport of sodium-potassium across the vascular smooth muscle cell membrane which functions to regulate blood pressure.<sup>17,18</sup>

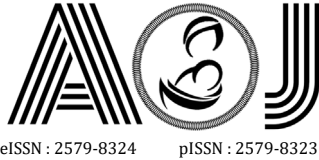
Decreased levels of potassium will reduce sodium excretion, apparently through changes in sodium reabsorption in the proximal tubule of the kidney, resulting in increased blood pressure.<sup>19,20</sup>

Manjareeka reports that there is an increase in serum sodium levels in preeclampsia compared to normal pregnancy and a decrease in serum potassium levels in preeclampsia compared to normal pregnancy.<sup>21</sup>

Thus, the sodium-potassium ratio will increase in preeclampsia compared to normal pregnancy. This is consistent with the results of this study where the mean ratio of maternal serum sodium-potassium in eclampsia was higher than preeclampsia, namely: 39.46 + 6.2 vs 31.16 + 4.36, with  $p = 0.000$ . Seizures are a clinical manifestation due to excessive electrical discharge in brain neuron cells due to the impaired function of these neurons in the form of physiology, biochemistry, and anatomy. Nerve cells, like living cells in general, have a membrane potential. The membrane potential is the potential difference between intracellular and extracellular. The intracellular potential is more negative than the extracellular.

The pathophysiology of seizures occurs due to an increase in the body's chemical reactions, thus oxidation reactions occur more rapidly, and as result oxygen will be depleted more quickly, leading to a hypoxic state. Active transport that requires ATP is disrupted so that intracellular Na and intracellular K are increased.<sup>22</sup>

The presence of conditions where there is an increase in sodium levels and a decrease in vascular potassium levels is likely to further facilitate seizures.



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**CONCLUSION**

The mean maternal serum calcium-magnesium ratio was significantly higher in preeclampsia than in eclampsia. The mean maternal serum sodium-potassium ratio was significantly lower in preeclampsia than in eclampsia.

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