

**Original Article**

**DIFFERENCES OF MAGNESIUM SERUM LEVELS BEFORE AND AFTER THE ADMISSION OF MgSO<sub>4</sub> IN PREECLAMPSIA PATIENTS**

**SARMA N. LUMBANRAJA, MUHAMMAD RAFI J. ADNANI, SARAH DINA, MUARA P. LUBIS, HANUDSE HARTONO, DERI EDIANTO**

**Department of Obstetrics and Gynecology, Medical Faculty, Universitas Sumatera Utara, H. Adam Malik General Hospital Medan  
Email: sarmalumbanraja@yahoo.com**

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**ABSTRACT**

**Objective:** The definitive treatment of preeclampsia until the fetus and placenta are delivered with magnesium sulfate (MgSO<sub>4</sub>) is a modality for the prevention and treatment of eclampsia. This study aims to determine the differences in serum magnesium (Mg) levels between before and after administration of MgSO<sub>4</sub> in preeclampsia patients.

**Methods:** This research was an analytical study with experimental design with one group pre and post-test control group design in 4 hospitals in Medan City, North Sumatera, Indonesia from July to November 2019, the preeclampsia group and as a control group is the normal pregnant women. Statistical analysis was performed to determine differences in initial serum Mg levels in the two groups, and differences in serum Mg levels before and after administration of MgSO<sub>4</sub> in the preeclampsia group.

**Results:** The study was conducted on 50 samples, divided into 2 groups with a total of 25 samples each. The mean Mg of serum in the preeclampsia group was 1,39 mEq/l (SD±0,28) lower than the control group, which was 1,53 mEq/l (SD±0,17) (p = 0.004). The average Mg level in preeclampsia patients before administration of MgSO<sub>4</sub> was 1,39 mEq/l (SD±0,28), after MgSO<sub>4</sub> administration, the average Mg level became 4,90 mEq/l (SD±0,37) (p<0,001).

**Conclusion:** MgSO<sub>4</sub> administration provides a significant increase in serum Mg levels in preeclampsia women. Serum Mg levels in preeclampsia patients are significantly lower than in women with normal pregnancies.

**Keywords:** Preeclampsia, Eclampsia, Magnesium sulfate

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**INTRODUCTION**

Maternal Mortality Rate (MMR) is a reflection of the quality of maternal health services in a country. According to the 2015 Indonesian Demographic and Health Survey (IDHS), the maternal mortality rate in Indonesia is 305 per 100,000 live births. This fig. is still far from the Sustainable Development Goals (SDGs) target, namely that in 2030 it is expected that the maternal mortality rate in all countries will decrease to 70 per 100,000 live births [1, 2].

Preeclampsia is the second largest cause of maternal death worldwide, with 192 people dying every day either by preeclampsia or its complications [3, 4]. This disease is a collection of symptoms of hypertension in pregnancy, which has complicate 2-10% of all pregnancies and this event is 7 times higher in developing countries (2.8% of all live births) [5, 6]. Complications of preeclampsia involve various organ systems. Eclampsia also contributes to 50,000 maternal mortality rates annually worldwide [7, 8].

Preeclampsia is defined as multisystemic disease characterized by hypertension after 20 w of gestation in women who were previously normotensive, with/without proteinuria and symptoms that indicate target organ injury [5]. The pathophysiology of multisystem disorders in preeclampsia is still poorly understood and the etiology is not fully understood [9].

Several studies have reported that decreasing serum Mg levels during pregnancy might be a contributor to the etiology and pathogenesis of preeclampsia [10]. Although there are various results regarding differences in serum Mg levels in preeclampsia and normal pregnant women, [11-14] giving MgSO<sub>4</sub> is the options that are considered to increase serum Mg levels [15, 16].

Decreased serum Mg levels in preeclampsia women is still controversial and there are still rarely studies that assess serum Mg levels in preeclampsia women before and after MgSO<sub>4</sub>

administration. Therefore, this study was conducted to see differences in serum magnesium levels before and after the administration of the MgSO<sub>4</sub> regimen in preeclampsia patients.

**MATERIALS AND METHODS**

This research is an analytical study with experimental design with one group pre and post-test control group design at H. Adam Malik General Hospital, USU Hospital, Pirngadi General Hospital Medan, Sundari General Hospital (Medan City, North Sumatera Indonesia) from July to November 2019. The population of this research is pregnant women who come to the delivery room in 4 hospitals and had been diagnosed with preeclampsia based on history taking, physical examination, and workup examination.

Samples were selected by consecutive sampling method, which included all the populations that were obtained and met the research criteria. The sample was divided into two groups, namely the preeclampsia group and the normal pregnant group as a control. The inclusion criteria of this study were: 1) diagnosed with preeclampsia with severe feature according to PNPk POGI 2016; 2) non-preeclampsia patients are pregnant patients with normal blood pressure; 3) willing to participate in research. After calculating the minimum sample size obtained is 25 research subjects. So that the total research subjects were 50 people where 25 people were pregnant women with preeclampsia and 25 without preeclampsia.

Age variables are classified into 3 categories: 1) <20 y; 2) 20-35 y; 3) >35 y. The parity variable is classified into 2: 1) primigravida (first pregnancy); and 2) multigravida (more than one pregnancy). Preeclampsia is defined as new hypertension that occurs in pregnancy or over 20 w accompanied by organ disorders, hypertension with systolic  $\geq$  160 mmHg or diastolic  $\geq$  110 mmHg at two measurements at least within 4 h, when the patient is at rest, sitting position or half lie down, use the mercury sphygmomanometer, where Korotkoff I shows

systolic pressure, and Korotkoff V shows diastolic pressure. Normal pregnancy is defined as a pregnant patient of the third trimester of pregnancy with normal blood pressure.

As controls, serum Mg levels were taken in normal pregnant patients at the age of the third trimester of pregnancy. In the preeclampsia group, the level of serum Mg was measured before and after MgSO<sub>4</sub> administration with a loading dose of 4 grams MgSO<sub>4</sub> followed by a maintenance dose of 1 gram per hour MgSO<sub>4</sub>. Measurement of serum Mg levels was carried out using spectrophotometry in the laboratory. Side effects after MgSO<sub>4</sub> administration in patients with preeclampsia were also noted.

Data were analyzed using statistical software. Data were analyzed descriptively to see the frequency distribution of the studied variables. Numerical data will be presented as mean±SD, while data for side effects will be displayed in percentage values. To see the difference in serum Mg levels in preeclampsia and control patients, the Mann Whitney test was used because the data were not normally distributed. To analyze differences in serum Mg levels before and after MgSO<sub>4</sub> administration, the Wilcoxon test was used because the data were not normally distributed. The results of the analysis were

significant if the p value<0.05.

## RESULTS

This study used a sample of 50 people in total, which were divided into 2 groups with a total of 25 samples each, the preeclampsia and control groups (normal pregnancy). Table 1 presents all samples of the preeclampsia group were 20-35 y old, whereas in the normal pregnancy group there were 24 samples (96.0%) aged 20-35 y and only 1 sample (4.0%) aged>35 y. The average age of the sample in the preeclampsia group was 26.3 y (SD±2.64), with the youngest age of 23 y and the oldest at 33 y, and the median age was 25 y. In the normal pregnancy group, the average age was 29.2 y (SD±3.93), with the youngest age being 24 y and the oldest being 38 y, and the median age being 29 y.

In the preeclampsia group, there was a greater proportion of primigravidas compared to multigravidas (88.0% vs 12.0%), whereas the opposite occurred in the control group (36.0% vs 64.0%). This is presented in table 1. The Saphiro-Wilk test used to analyze the age and parity characteristics in the sample shows that the data are not normally distributed (p<0.05).

**Table 1: Characteristics of study subjects**

| Characteristic | Preeclampsia |        | Normal pregnancy |       |
|----------------|--------------|--------|------------------|-------|
|                | N            | %      | n                | %     |
| <b>Age</b>     |              |        |                  |       |
| <20 y          | 0            | 0,0%   | 0                | 0,0%  |
| 20-35 y        | 25           | 100,0% | 24               | 96,0% |
| >35 y          | 0            | 0,0%   | 1                | 4,0%  |
| <b>Parity</b>  |              |        |                  |       |
| Primigravid    | 22           | 88,0%  | 3                | 36,0% |
| Multigravid    | 9            | 12,0%  | 16               | 64,0% |

Table 2 presents the average Mg level in preeclampsia patients is 1,39 mEq/l (SD±0,28) with a median of 1,35 mEq/l, whereas in the control group the average is 1,53 mEq/l (SD±0,17), with a median of 1,35 mEq/l. The Saphiro-Wilk test shows that the data are not normally distributed

(p<0.05) in the data. Analysis of differences between serum Mg levels in the two groups was performed using the Mann-Whitney test, which showed a statistically significant difference between serum Mg levels in the preeclampsia group and the control group (p<0.05).

**Table 2: Differences in serum mg levels in the preeclampsia and normal pregnancy groups**

| Group            | $\bar{x} \pm SD$ | Median (min-max) | P Value*     |
|------------------|------------------|------------------|--------------|
| Preeclampsia     | 1,39±0,28        | 1,35 (1,00-2,02) | <b>0,004</b> |
| Normal Pregnancy | 1,53±0,17        | 1,53 (0,89-1,82) |              |

\*Mann Whitney

Table 3 presents analysis using the Saphiro-Wilk test, which showed the data were not normally distributed (p<0.05). The average Mg level in preeclampsia patients before MgSO<sub>4</sub> administration was 1,39 mEq/l (SD±0,28). The lowest Mg level before administration of MgSO<sub>4</sub> in the sample was 1,00 mEq/l, while the highest was 2,02

mEq/l. After the administration of MgSO<sub>4</sub>, the average Mg level became 4,90 mEq/l (SD±0,37), with the lowest serum Mg level of the patient being 4,19 mEq/l and the highest 5,94 mEq/l. The Wilcoxon test used to analyze differences in Mg levels before and after MgSO<sub>4</sub> administration showed that there were statistically significant.

**Table 3: Differences in serum magnesium levels before and after administration of MgSO<sub>4</sub>**

| Group  | $\bar{x} \pm SD$ | Median (min-max) | P Value*         |
|--------|------------------|------------------|------------------|
| Before | 1,39±0,28        | 1,35 (1,00-2,02) | <b>&lt;0,001</b> |
| After  | 4,90±0,37        | 4,86 (4,19-5,94) |                  |

\*Wilcoxon

Table 4 presents the most common side effect was flushing (76.0%), with an average serum Mg level of 4,87 mEq/l. The highest serum Mg level 5,94 mEq/l was obtained in 1 sample that had side effects of headache. 12.0% of the sample did not experience side effects of

serum Mg levels, with an average serum Mg level of 4,41 mEq/l. There were no other side effects such as missing tendon reflexes, respiratory depression, respiratory arrest, until cardiac arrest in the samples in this study.

**Table 4: Side effects of increased serum Mg levels after MgSO<sub>4</sub> administration**

| Side effect         | n  | %      | Mean mg serum level (mEq/l) |
|---------------------|----|--------|-----------------------------|
| Headache            | 1  | 4,0%   | 5,94                        |
| Nausea              | 2  | 8,0%   | 5,31                        |
| Flushing            | 19 | 76,0%  | 4,87                        |
| Without Side Effect | 3  | 12,0%  | 4,41                        |
| Total               | 25 | 100,0% |                             |

## DISCUSSION

This research was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine, University of North Sumatra and at H. Adam Malik General Hospital, USU Hospital, Pirngadi General Hospital Medan, and Sundari General Hospital since July 2019 with 50 samples, which were divided by the same number into 2 groups (preeclampsia and normal pregnancy).

The characteristics of the study subjects by age in the two groups showed similar findings, namely, the entire sample of the preeclampsia group and 96.0% of the control group were aged 20-35 y, while only 1 sample from the control group was 38 y old. The proportion of primigravida was more prevalent in the preeclampsia group (88.0%), while multigravida was more prevalent in the control group (64.0%).

In this study a significant difference was found between the serum Mg levels of the preeclampsia group and the control group, with an average Mg of the preeclampsia group of 1,39 mEq/l (SD±0,35), lower than the control group of 1,53 mEq/l (SD±0,17).

Abdellah in her research tried to find out whether there was a significant difference in serum magnesium levels between preeclampsia pregnant women and other normal pregnant women. Of 149 pregnant women, Mg levels were lower in the preeclampsia group (1.44±0.09 mEq/l) than in the control group (1.53±0.09 mEq/l) (p = 0.03). Decreased magnesium levels during pregnancy can be a risk factor for predictors of preeclampsia and supplementation of these minerals in the diet is considered to be able to prevent the occurrence of preeclampsia [17, 18].

Another study found that mean serum Mg levels in preeclamptic pregnant women were lower than other normotensive pregnant women, which were 1.53±0.16 mEq/l and 1.34±0.09 mEq/l (p<0.05). There is a hemodilution effect caused by the hormone estrogen and an increasing number of mineral requirements by infants who are developing intrauterine so that it certainly reduces serum magnesium levels in pregnant women; in the case of preeclampsia, Mg excretion in urine also increases so that it can reduce Mg levels even more [19].

Contrary to what is generally concluded, Golmohammad *et al.* they did not find a significant difference of serum Mg levels in each of 52 preeclampsia pregnant women and 52 other normal pregnant women, namely 1.56±0.21 mEq/l and 1.56±0.19 mEq/l respectively [20].

The analysis in this study showed that there were significant differences between serum Mg levels in preeclampsia patients before and after MgSO<sub>4</sub> administration. The average Mg level in preeclampsia patients before MgSO<sub>4</sub> administration was 1,39 mEq/l (SD±0,28). The lowest Mg level before administration of MgSO<sub>4</sub> in the sample was 1,00 mEq/l, while the highest was 2,02 mEq/l. After the administration of MgSO<sub>4</sub>, the average Mg level became 4,90 mEq/l (SD±0,37), with the lowest serum Mg level of the patient being 4,19 mEq/l and the highest 5,94 mEq/l. MgSO<sub>4</sub> maintenance dose is given because in this condition the excretion of Mg by the kidneys increases, so that therapeutic Mg levels can be maintained 4.8-8.4 mg/dl (3.94–6,91 mEq/l) so that the patient does not experience seizures.

MgSO<sub>4</sub> has been used extensively in the management of preeclampsia, especially as a therapy in preventing seizures with one of the goals of administration as an effort to prevent disease progression to eclampsia. Clinical and empirical evidence has shown support for the effectiveness of MgSO<sub>4</sub>. Euser and Cipolla stated that the compound works through several channels. One of them is

working as a vasodilator against peripheral and cerebrovascular vessels, thereby reducing vascular resistance and/or decreasing vasoconstriction. In addition, MgSO<sub>4</sub> can also protect the blood-brain barrier and limit the formation of cerebral edema, or can work as a central anticonvulsant [21, 22].

Pascoal *et al.* found a significantly increased serum Mg level with the administration of MgSO<sub>4</sub>. In that study, researchers compared the administration of a 1 g/h MgSO<sub>4</sub> dose to 2 g/h. In both cases, MgSO<sub>4</sub> administration resulted in Mg serum having a significant increase in levels. Although serum Mg levels were higher in the 2 g/h group, researchers found no statistically significant difference in effectiveness between the two doses of increasing serum Mg levels [23].

A Study by Easterling *et al.* also showed similar results, it is a specific increase in serum Mg levels after administration of MgSO<sub>4</sub>. In that study, the main finding was that serial bolus MgSO<sub>4</sub> administration showed a higher increase in serum Mg concentration compared with continuous infusion (p = 0.02) [24].

Imaralu *et al.* found that Mg levels in preeclampsia patients had low levels before giving MgSO<sub>4</sub> (1,61±0,23 mEq/l), even lower levels were found in eclampsia patients (p<0.001). After the administration of MgSO<sub>4</sub> to patients, the average serum Mg level increased significantly to 4,45±0,47 mEq/l. The author also concluded that low serum Mg levels before or during treatment was a risk factor for convulsions [25].

In this study, several side effects were found from the increase in serum Mg levels after the administration of MgSO<sub>4</sub> in preeclampsia patients. There are 3 forms of side effects, namely flushing, nausea, and headache. The highest incidence of side effects was flushing (76.0%) which occurred in patients with preeclampsia, with an average serum Mg level of 4,87 mEq/l, whereas 8.0% of the sample experienced nausea (mean Mg of serum 5,31 mEq/l). 4.0% of patients with a serum Mg level of 5,94 mEq/l had headaches.

Smith *et al.* in his article found the incidence of loss of patellar reflexes in 9556 preeclampsia-eclampsia women who treated with MgSO<sub>4</sub> by 1.6% (0-57%), while respiratory depression (0-8.2%). Only one maternal death was reported as a result of MgSO<sub>4</sub> (serum magnesium level: 24 mEq/l) from 24 studies collected. When compared to the total population and accumulation of previous studies, the incidence is relatively small and the amount does not exceed the percentage [26].

Magnesium toxicity can also occur due to human error, as reported by Kumar in his case report. The errors referred to here can be caused by lack of understanding regarding the safe dosage range of the MgSO<sub>4</sub> regimen, the appearance of drugs that are similar to other drugs, mislabelling of drugs, or even miscommunication between medical personnel.

Kumar found a case of a 28-year-old primigravida woman with a dichorionic diamniotic multiple pregnancy accompanied by severe preeclampsia (urine protein increases to 6 g in 24 h). The MgSO<sub>4</sub> treatment protocol given with serum magnesium levels before therapy was 2.80 mEq/l and increased to 3.94 mEq/l the following morning. Both babies were successfully delivered via spontaneous vaginal delivery. The uterus contracts after misoprostol was given, even though it contains blood clots. Upon further observation, the patient complained of shortness of breath; 92% oxygen saturation and sensorium dropped to somnolen [20].

After passing through several stages of examination, it was found that serum magnesium levels were in the toxic range of 17.2 mEq/l; this underlies the occurrence of respiratory depression and

neurological deficits. This rapid increase in magnesium levels is most likely due to a drug error: it was found that there was a misinterpretation of the oxytocin and magnesium sulfate infusion packaging so that the patient was given 40 g MgSO<sub>4</sub> IV. A secondary magnesium sulfate toxicity diagnosis was made in this patient. The American Journal of Maternal Child Nursing 2004 also reported cases of MgSO<sub>4</sub> overdose; many are caused by unintentional rapid infusion of MgSO<sub>4</sub>. Hypermagnesemia, although rare, is most often an iatrogenic case due to an overdose of MgSO<sub>4</sub> and even though the renal physiology is normal, hypermagnesemia is clinically significant. Manifestations caused by dose-dependent, in the form of loss of patellar reflexion, weakness of diaphragmatic muscles and other respiratory muscles that trigger respiratory depression, hypotension, complete heart block, even asystole [20].

#### CONCLUSION

In this study it was found that preeclampsia was more experienced by women aged 20-35 y with primigravida status. Serum Mg levels in preeclampsia patients are significantly lower than in women with normal pregnancies. MgSO<sub>4</sub> administration provides a significant increase in serum Mg levels in preeclampsia women. The most common side effect of increasing serum Mg levels after administration of MgSO<sub>4</sub> is flushing, followed by nausea and headache. Patients with the highest serum Mg levels have side effects in the form of headaches.

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#### AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

#### CONFLICTS OF INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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