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RESEARCH ARTICLE

Relationship between Serum Magnesium Status and the Incidence of Preeclampsia at 8 Padang Primary Health Care

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Abstract

Introduction*: Preeclampsia is one of the main causes of maternal morbidity and mortality, with its etiology and pathophysiology not fully understood. Several studies have shown that magnesium plays an important role in preeclampsia. Magnesium plays a role in modulating endothelial function. Decreased serum magnesium levels in pregnancy can trigger endothelial dysfunction that has an impact on the occurrence of preeclampsia.*

Objective*: Determine the relationship between serum magnesium status with incidence of preeclampsia in pregnant women at 8 Padang Primary Health Care.*

Method*: An observational analytic with cross-sectional design. Sampling was carried out using total sampling technique from research master data at 8 Padang Primary Health Care for period June 2019 – May 2020. The total sample was 45 pregnant women who met the inclusion and exclusion criteria. Data were analyzed using Fisher's.*

Result*: The serum magnesium status of pregnant women in the 8 Padang Primary Health Care was dominated by normal serum magnesium status (91.1%) and only 8.9% of pregnant women had preeclampsia. Fisher's test showed that there was a significant relationship between serum magnesium status and the incidence of preeclampsia (p-value = 0,034).*

Conclusion*: There is a significant relationship between serum magnesium status and preeclampsia (with overlook the factors of previous preeclampsia history, family history of preeclampsia, and magnesium intake during pregnancy). Hypomagnesemia status in pregnant women can exacerbate the occurrence of preeclampsia.*

Keywords: *Serum magnesium status, pregnant women, preeclampsia.*

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INTRODUCTION

Maternal mortality is a global health problem that is an indicator of the success of maternal health efforts, as well as describing the degree of public health[1]. WHO data in 2015, MMR in the world was 219/100.000 live births and in 2017 it fell to 211/100.000 live births. The MMR in Indonesia in 2017 was 177/100.000 live births, and is one of the highest among ASEAN countries. This figure is still far from the target of the third SDG's point, which is 70/100.000 live births in 2030[2]. In West Sumatra, the MMR in 2019 was 109/100.000 live births, and in Padang City in the same year it was 101/100.000 live births. In 2014-2017 the number of maternal deaths in the city of Padang was stagnant at 16-20 cases/year[3].

Maternal death is a complex event caused by various causes. In 2019, 25.3% of maternal deaths in Indonesia were caused by hypertension in pregnancy, including preeclampsia[1]. Preeclampsia is a pregnancy-specific syndrome characterized by hypertension and proteinuria that occurs after the 20th week of gestation[4]. The incidence of preeclampsia in Indonesia is estimated at 128.273 cases/year or 5.3% of the entire population giving birth.[5] in the city of Padang in 2014, preeclampsia became the main cause of maternal death (31.25%)[6].

There are several theories of the etiology of preeclampsia, namely trophoblast invasion abnormalities, immunological intolerance, maladaptation to cardiovascular changes, genetic factors, and nutritional factors. And there are a number of risk factors for preeclampsia: multiple pregnancies, age > 35 years, nullipara, and micronutrient deficiencies[4]. Several studies have stated that one of the risks of preeclampsia is associated with a decrease in serum magnesium levels[7].

Magnesium plays an important role in more than 300 types of enzyme systems in the body. Magnesium plays a role in blood pressure regulation by inhibiting Angiotensin II and Endothelin-1, as well as inhibiting blood vessel constriction so that it can reduce peripheral resistance which ultimately has an impact on lowering blood pressure[8]. Magnesium also plays an important role in reducing oxidative stress and can improve endothelial function.

Research conducted by Enaruna (2013) concluded that the incidence of preeclampsia is associated with hypomagnesemia and is 22 and 47 times more likely to cause preeclampsia than

age and BMI[7]. Devita & Vitri's research (2016) also found a relationship between serum magnesium levels and the incidence of preeclampsia[9]. However, another study conducted by Darkwa (2017), found no difference in serum magnesium levels between preeclampsia and normal pregnant women[10].

Therefore, researchers are interested in knowing the relationship between serum magnesium status and the incidence of preeclampsia at 8 Padang City Primary Health Care. The research was conducted at the Primary Health Care in Padang because there had never been any related research conducted at the Padang City Primary Health Care before. While, the Primary Health Care is the first line for promotive and preventive stage in preeclampsia. By knowing the relationship between serum magnesium status and the incidence of preeclampsia, it is hoped that it will help in the development of strategies and interventions for preeclampsia.

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METHODS

This study is an observational analytic study with a cross sectional design which was carried out in March 2020 – December 2021. The study population was master data on pregnant women at 8 Primary Health Care in Padang that met the inclusion criteria and there were no exclusion criteria, the period June 2019 – May 2020. The inclusion criteria are: (1) Age 20-35 years, (2) Checking serum magnesium levels in the third trimester, and (3) Have complete master data research. Meanwhile, the exclusion criteria are: (1) Nullipara, (2) Pre-pregnancy BMI ≥ 30 kg/m^2, (3) Pregnancy with a history of hypertension, diabetes mellitus, kidney disease, or heart disease, (4) Multiple pregnancy, and (5) Have a smoking habit and alcohol consumption. Sampling was done by total sampling.

The research variable consisted of the independent variable, namely serum magnesium status, and the dependent variable, namely the incidence of preeclampsia. Serum magnesium status was measured using the Magnesium Kit with a spectrophotometric method and grouped into two measurement results a) hypomagnesemia, if serum magnesium level < 1.9 mg/dl; b) normal, if the serum magnesium level is ≥ 1.9 mg/dl. Preeclampsia is determined based on blood pressure. If systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg measured on 2 measurements with 4 hours intervals at gestational age > 20 weeks with previously normal blood pressure, with or without proteinuria, then it is classified as preeclampsia.

Data were analyzed univariately to see the distribution of frequency and central tendency (mean, standard deviation), and bivariate analysis using Fisher's Exact Test and said to be significant if $p < 0.05$. This research has been approved by the ethics committee of the Faculty of Medicine, Andalas University, with No: 95/UN.162/KEP-FK/2021.

RESULTS AND DISCUSSION

The research was conducted by taking data from the master research data for pregnant women at 8 Primary Health Care in Padang. The data obtained amounted to 85 people. Of these, 45

people met the inclusion and exclusion criteria. The characteristics of the subjects assessed in this study consisted of the age of pregnant women, gestational age, parity, and pre-pregnancy BMI, which can be seen in Table 1.

Based on Table 1, it is known that the average age of pregnant women is 28.6 ± 2.9 years, and the average gestational age is 37.5 ± 1.5 weeks. Gestational age was dominated by term pregnancies (71.1%), and parity was dominated by primparas (82.2%). The average pre pregnancy BMI was 23.3 ± 2.7 kg/m^2 with more than half of the study subjects (71.1%) belonging to the normal BMI group.

Based on Table 2, it is known that from 45 pregnant women, 4 subjects (8.9%) belonged to the category of hypomagnesemia and 41 subjects (91.1%) belonged to normal serum magnesium status.

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Table 3 shows that 41 subjects (91.1%) did not have preeclampsia, and 4 subjects (8.9%) had preeclampsia.

Based on Table 4, it is known that from 4 hypomagnesemia subjects, 2 subjects (50%) had preeclampsia and 2 subjects (50%) did not have preeclampsia. The Fisher's Exact Test results from the table above obtained a p-value of 0.034 (p-value < 0.05) which indicates that there is a significant relationship between serum magnesium status and the incidence of preeclampsia at the Primary Health Care in Padang.

DISCUSSION

In this study, the average age of pregnant women was 28.6 ± 2.9 years with an age range of 20–35 years. The age of 20–35 years is a safe and ideal age for pregnancy and childbirth, because at that age a woman's reproduction has developed and functions optimally, so she is ready to accept and undergo pregnancy and childbirth. Meanwhile, age < 20 or > 35 years is a risk factor for preeclampsia. This is associated with the occurrence of placental failure and degenerative processes that affect blood pressure[11].

The mean gestational age was 37.5 ± 1.5 weeks and most were at term (71.1%). Maternal parity in this study was dominated by primiparas (82.2%), while multiparas were 17.8%. In this study, nulliparous pregnant women were excluded because nullipara was a risk factors for preeclampsia. This situation is associated with the occurrence of immunological intolerance[4].

The average pre-pregnancy BMI was 23.3 ± 2.7 kg/m^2, with the highest group being in the normal BMI group (71.1%). Obese pregnant women (BMI > 30 kg/m^2) were not included in the study because obesity is associated with an increased risk of preeclampsia[12]. Obesity can affect the occurrence of preeclampsia through the mechanism of hyperleptinemia, inflammatory reactions, or an increase in free radicals which leads to endothelial dysfunction and causes an increase in maternal blood pressure[13,14].

Serum Magnesium Status

The results of the study were dominated by normal serum magnesium status (91.1%) and only 8.9% were categorized as hypomagnesemia. The results of this study are supported by the research of Tabrizi & Pakdel (2014) which showed that 87% of pregnant women had normal serum magnesium status, and 13% had hypomagnesemia status[15]. Nabouli's research (2016) also found 91.9% of pregnant women had normal magnesium status, and 8.1% with hypomagnesemia[16]. Meanwhile, research by Eltayeb (2018) and Okunade (2014) found a higher percentage of hypomagnesemia than this study, namely 57.2% and 36%[17,18]. This difference in the prevalence of hypomagnesemia can be caused by variations in the study population, differences in food intake, and differences in laboratory parameters used.

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Magnesium is mostly stored in bones, muscles, and soft tissues, with 0.3% of total body magnesium found in serum. Although it does not describe the total body magnesium level, currently in clinical practice, serum magnesium is the most commonly used test to assess magnesium status[8].

In pregnancy, hypomagnesemia is generally caused by low magnesium intake, inadequate gastrointestinal absorption, or increased renal excretion[19]. Research by Rosanoff (2012) shows that more than 50% of women of reproductive age consume less magnesium than the recommended amount (310 mg/day)[20]. Inadequate absorption can be caused by chronic diarrhea, pancreatic insufficiency, chronic alcoholism, celiac disease, inflammatory bowel disease, and short bowel syndrome. Consumption of foods high in salt, sugar, coffee, soft drinks, and alcohol can also reduce and inhibit the absorption of magnesium in the body[21]. In addition, pregnant women also experience an increase in urinary magnesium excretion by 25% due to an increase in the glomerular filtration rate in the second and third trimesters of pregnancy[22].

Preeclampsia Incidence

In this study, the incidence of preeclampsia was 8.9%. Not much different from the Pare study (2014) which found the incidence of preeclampsia with a percentage of 9%[23]. Mayrink's research (2019) also found that the prevalence of preeclampsia was almost the same, namely 7.5%[13]. Arwan's research (2017) found a lower preeclampsia rate, namely 5.3% of all mothers giving birth[14]. This difference in the prevalence of preeclampsia can be influenced by differences in the number and characteristics of the sample, especially differences in the determination of inclusion and exclusion criteria due to the many risk factors that can cause preeclampsia.

The incidence of preeclampsia is associated with failure of spiral artery remodeling which can lead to failure of placentation and impaired endothelial function or the occurrence of endothelial dysfunction[24]. Preeclampsia is also influenced by many risk factors including maternal age, history of childbirth, history of preeclampsia, multiple pregnancies, and pre-existing health problems such as obesity, hypertension, diabetes mellitus, autoimmune disorders, kidney disease, and heart disease[4].

Pregnant women age < 20 years or > 35 years have a 1.2–3-fold risk of developing preeclampsia compared to those aged 20-35 years. Nullipara 2.91–3 times more likely than multipara, multiple pregnancy 2.93 times more likely than singleton pregnancy and pre-pregnancy BMI > 30 kg/m^2 has a 2–4-fold higher risk of developing preeclampsia[12,25]. In multiple pregnancies, there is an increase in placental mass which causes an increase in sFlt-1 levels that contribute to preeclampsia[26]. Ayunani's research (2019) confirmed that chronic hypertension is one of the highest risk factors for preeclampsia (OR=9.74)[27]. The presence of dominant risk factors in the study is thought to have an effect on differences in the prevalence of preeclampsia.

Relationship between Serum Magnesium Status and the Incidence of Preeclampsia

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Based on the results of statistical analysis using the Fisher's Exact Test, a p-value of 0.034 was obtained, which indicated that there was a significant relationship between serum magnesium status and the incidence of preeclampsia in pregnant women. The results of this study are similar to the research conducted by Devita & Vitri (2016) at RSUP Dr. M. Djamil Padang, it was found that there was a relationship between serum magnesium levels and the incidence of preeclampsia (p = 0.002)[9]. Enaruna's study (2013) on 160 pregnant women in Nigeria found a significant relationship between hypomagnesemia and the incidence of preeclampsia (p = 0.011) with an OR of 22[7]. The Cabarkapa study (2018) on 403 pregnant women in Serbia also found that serum magnesium was significantly higher low in women with preeclampsia (p < 0.001) and can be used to predict the incidence of preeclampsia[28].

However, research by Darkwa (2017) and Vafaei (2015) found that there was no significant difference between preeclamptic pregnant women and controls in terms of serum magnesium levels[10,29]. Differences in the results of this study may be caused by variations in the study populations and differences in food intake of the population studied.

Shaikh's research (2012) states that hypomagnesemia has a significant relationship with the incidence of preeclampsia, IUGR, preterm labor, and muscle cramps[30]. Magnesium plays an important role in blood pressure regulation by modulating tone and influencing vascular contractility[8]. Magnesium reduces vascular tone by increasing the release of Nitric Oxide (NO), which is a powerful vasodilator. Magnesium also increases the release of prostacyclin which synergistically with NO can inhibit platelet aggregation[24].

Kostov's research (2018) linked hypomagnesemia with decreased NO concentrations, impaired prostacyclin production and increased levels of Endotelin-1 (ET-1). Increased ET-1 causes vasoconstriction and pro-inflammation by activating platelets and free radicals in the blood vessel wall that contribute to endothelial dysfunction[31]. Hypomagnesemia also increases the vasoconstrictive effect of Angiotensin II which triggers the release of aldosterone, causing an increase in vascular resistance which results in an increase in blood pressure[8].

Magnesium deficiency significantly increases the production of TNF-α and IL-1. Increased levels of TNF-α reduce the ability of the endothelium to produce NO. Hypomagnesemia also causes a decrease in the expression and activation of the enzyme superoxide dismutase which causes an increase in lipid peroxides and triggers an increase in blood pressure, thus leading to preeclampsia[24,31].

CONCLUSION

There is a significant relationship between serum magnesium status and the incidence of preeclampsia (excluding factors such as previous history of preeclampsia, family history of preeclampsia, and magnesium intake during pregnancy). Hypomagnesemia status in pregnant women can exacerbate the occurrence of preeclampsia.

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