



## LITERATURE REVIEW

# THE ROLE OF MAGNESIUM SUPPLEMENTS ON HYPERTENSION IN PREGNANCY AND PREECLAMPSIA

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### Abstract

**Objective:** This article aims to discuss the effects of magnesium supplementation on clinical outcomes of pregnancy and highlights the benefits of magnesium supplementation in reducing the risk of hypertension in pregnancy and preeclampsia. **Method:** In this systematic review article, the author conducted a literature search using certain keywords and selected articles that were published from 2013-2023, can be accessed in full-text in pdf format, and are in Indonesian or English. The methods used were in accordance with the reporting guidelines provided in the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). **Results:** After carefully searching the database and eliminating articles that were not related to the topic, 6 articles were obtained for review. Hypertension in pregnancy and preeclampsia are serious health problems that can harm both mother and baby. Magnesium supplements have been studied as a way to reduce the risk of hypertension in pregnancy and preeclampsia. **Conclusion:** Magnesium supplements may help reduce the risk of hypertension in pregnancy and preeclampsia.

**keywords:** Preeclampsia; Magnesium supplements; Pregnancy



## INTRODUCTION

Hypertension in pregnancy is a major problem in the health of pregnant women because it has high mortality and morbidity rates.<sup>1</sup> According to *World Health Organization* (WHO), the incidence of preeclampsia ranges from 2% to 10% of all pregnancies in the world with 1.8% - 16.7% of the incidence reported in developing countries.<sup>2</sup> In Indonesia, preeclampsia is the second leading cause of death among pregnant women with an incidence of around 24% of total pregnancies.<sup>3</sup>

Hypertension in pregnancy is defined by *International Society for the Study of Hypertension in Pregnancy* (ISSHP) as systolic blood pressure  $\geq 140$  mmHg or diastolic  $\geq 90$  mmHg at a gestational age of more than 20 weeks.<sup>4</sup> Hypertension in pregnancy and preeclampsia have an impact on maternal and fetal health in the short and long term. Preeclampsia can increase the risk of long-term *hypertension*, cardiovascular disease mortality, and maternal stroke. Preeclampsia can also increase the risk of occurrence *Intra-uterine growth restriction* (IUGR), preterm birth, oligohydramnios, placental abruption, fetal distress, and fetal death.<sup>4</sup>

The cause of preeclampsia is still uncertain, but the most widely believed theory is that there is an abnormality in the placental implantation process which disrupts the process of remodeling the spiral arteries, resulting in placental hypoxia.<sup>5</sup> The difference in incidence in developing and developed countries shows the role of environmental factors in the occurrence of preeclampsia. Another theory related to gene variations and nutritional factors is the administration of vitamins C and E, L-Arginine, calcium and magnesium as non-pharmacological interventions in preeclampsia.<sup>6</sup>

Magnesium (Mg) has an important role in regulating vasomotor tone and cardiac excitability. Magnesium intake for women is recommended to be 280 mg/day, while magnesium intake during pregnancy is 350 mg/day. This amount is needed to maintain the function of more than 300 enzymes that use ATP.<sup>7</sup> The most common causes of magnesium deficiency are insufficient intake or impaired absorption, increased excretion, or increased magnesium requirements such as during pregnancy. Magnesium deficiency during pregnancy is associated with an increased risk of preeclampsia.<sup>8</sup>

There are several studies that explain that magnesium supplementation during pregnancy can prevent pregnancy complications. However, the limited literature regarding the role of magnesium supplementation in hypertension during pregnancy and preeclampsia makes the author want to write this literature review article.

## METHOD



The literature sources used come from national and international journal websites such as Google Scholar, Science Direct, Elsevier, PubMed, and StatPearls. Search using keywords: *Preeclampsia, Magnesium supplementation, hypertension in pregnancy, Oral magnesium, Pregnancy outcome, Prevention (AND, OR)*. The selection criteria for literature selection use literature published from 2013-2023, which can be accessed online full-text in pdf format, and in Indonesian or English. The methods used in this systematic review are reported in accordance with the reporting guidelines provided in *Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)*.

## RESULTS AND DISCUSSION

On **Figure 1**, After carefully searching the database and eliminating articles that were not related to the topic, 6 articles were obtained for review, namely: 2 original *article* regarding the effects of magnesium supplementation on clinical outcomes of pregnancy, 1 original *article* regarding magnesium supplementation and blood pressure in pregnancy, 2 original *article* regarding the effects of magnesium supplementation and preeclampsia, and 1 systematic review of magnesium supplementation in pregnancy.

### The role of magnesium in pregnancy

Magnesium is one of the essential minerals needed during pregnancy. Magnesium is useful for maintaining the function of various enzymes and acts as a cofactor in more than 600 enzyme reactions.<sup>14</sup> Magnesium plays a role in energy metabolism, nucleic acid and protein synthesis, bone formation, and neuromuscular signaling.<sup>15</sup> Magnesium levels have a significant effect on cardiac excitability, contractility, and reactivity. Magnesium also causes relaxation of vascular muscles. During pregnancy, physiologically magnesium levels will decrease. Decreased magnesium levels in pregnancy are still not well understood. Serum magnesium decreases during pregnancy due to hemodilution, which is a natural process that occurs during pregnancy, where the body produces more blood to support fetal growth.<sup>16</sup> In addition, maternal hypomagnesemia is associated with a decreased renal *clearance* and increased mineral consumption by the fetus.<sup>17</sup>

Several studies show that low magnesium levels are associated with preeclampsia, as well as being associated with preterm birth, gestational diabetes, restricted fetal growth, or low birth weight.<sup>8,13</sup> Hypomagnesemia during pregnancy can interfere with fetal growth and development and can cause premature labor. Preterm labor is caused by uterine hyperexcitability caused by chronic hypomagnesemia in the mother and further aggravated by stressful situations in the mother. Magnesium deficiency during the gestational period can have major impacts on the mother, fetus and child that may last throughout life. The consequences of primary magnesium deficiency in the mother are not limited to the prenatal and perinatal periods. Low magnesium levels during pregnancy may have important consequences throughout life, with hypomagnesemia representing an important factor in the



broad spectrum of fetal programming theories regarding diseases that emerge later in life, in childhood, or in adulthood.<sup>18</sup>

### **Magnesium and hypertension in pregnancy**

Magnesium supplementation is a therapeutic option for preventing eclampsia and its use is preferred over phenytoin and diazepam. Magnesium was associated with a 59% reduction in the risk of eclampsia and a 36% reduction in abruption. Magnesium is recommended in women with severe preeclampsia.<sup>19</sup> Magnesium plays a role in inhibiting calcium channels thereby preventing an increase in intracellular calcium concentration which causes vasodilation. In addition to improving blood flow, the vasodilatory effects of magnesium have been shown to prevent preeclampsia by selectively dilating cerebral blood vessels and eliminating cerebral spasms associated with preeclampsia.<sup>20</sup> Atiba et al, in their study there were 27 of 28 patients with severe systolic hypertension ( $\geq 160$  mmHg) had low magnesium levels ( $< 0.63$  mmol/l), while 9 patients with mild systolic hypertension (140-159 mmHg) had low magnesium levels, but this was not statistically significant ( $P > 0.05$ ).<sup>13</sup>

Several studies show that the risk of hypertension in pregnancy is related to changes in magnesium homeostasis. Meta-analysis study *Cochrane* shows that the efficiency of magnesium supplementation has not been proven in preventing hypertension in pregnancy, but there are several studies that suggest magnesium supplementation.<sup>12</sup>

Research by Ika Yulia et al found the benefits of magnesium supplementation in preventing preeclampsia in pregnant women with hypomagnesemia so that the incidence of hypomagnesemia in women can be used to predict preeclampsia.<sup>9</sup> Rylander et al in their review of magnesium and blood pressure in pregnancy, showed the influence of magnesium supplementation on blood pressure regulation during pregnancy. Magnesium plays a role in the pathophysiology of pre-eclampsia and magnesium sulfate supplementation is recommended for the treatment of pre-eclampsia. Magnesium sulfate has been shown to have vasodilatory effects through inhibition of angiotensin II and endothelin I and may also have an immunomodulatory role.<sup>16</sup>

Therefore, magnesium supplementation is beneficial in pregnant women with hypomagnesemia. The recommended magnesium intake during pregnancy is 350 mg/day. Based on the Regulation of the Minister of Health of the Republic of Indonesia No. 75 of 2013 concerning the recommended nutritional adequacy rate (RDA) for pregnant women, the recommendation for magnesium intake is +40 mg in the 1st, 2nd and 3rd trimesters with the RDA for women of reproductive age being 310–320 mg.

In a clinical study conducted by Maria B et al, as many as 199 pregnant women met the inclusion criteria, then the magnesium supplementation and placebo interventions were administered randomly. As a result, 25% of mothers who were given magnesium supplementation experienced an increase in diastolic blood pressure  $< 15$  mmHg compared to the placebo group ( $P$  value  $< 0.05$ ). However, the number of mothers diagnosed with



hypertension in pregnancy and preeclampsia was evenly distributed between the groups with magnesium supplementation and placebo.<sup>10</sup> In addition, an experimental study by Ika et al in Padang, Indonesia, of 90 mothers divided into intervention groups with hypomagnesemia, normal magnesium, and a control group with normal magnesium, found that magnesium supplementation was associated with preeclampsia in pregnant women with hypomagnesemia (RR = 6.51 [95% CI 1.06 – 39.93]). Thus, it is reasonable to assume that magnesium insufficiency is a frequent maternal risk of preeclampsia.<sup>9</sup> In a clinical study conducted by Elaheh Z et al in Iran, using the same method without hypomagnesemia, magnesium had a beneficial effect in the group given oral supplementation. This was proven to reduce the rate of preeclampsia (P = 0.018) and this research is in line with research by Bullarbo et al, that magnesium supplementation can prevent an increase in diastolic blood pressure during the final week of pregnancy.<sup>8</sup> Several studies studying the role of magnesium supplements in preeclampsia and hypertension in pregnancy have been concluded in **Table 1**.

According to Shaykh et al, magnesium plays an important role in blood pressure control. Consumption of fruits and vegetables rich in potassium and magnesium is associated with lower blood pressure during pregnancy. This is because magnesium plays an important role during pregnancy, and 33% of patients with low magnesium levels are likely to develop preeclampsia.<sup>9</sup> Magnesium deficiency during pregnancy is associated with hypertension and preeclampsia.<sup>21</sup> Magnesium is an important element to prevent various diseases during pregnancy and unwanted complications. Moreover, magnesium has various physiological benefits. Many studies have been conducted to assess the effects of magnesium supplementation on preventing preeclampsia and hypertension in pregnancy.<sup>8,22,23</sup>

Hypermagnesemia usually occurs in preeclamptic women after magnesium supplementation therapy.<sup>16</sup> Hypermagnesemia can have a negative impact on the mother and indirectly harm the fetus. Several studies have shown that the fatal oral dose of magnesium for humans ranges from 0.5 to 5 g/kg in adults. Symptoms can vary from mild to severe depending on age, gender, health condition and various internal and external factors.<sup>24</sup> Toxicity studies on a single dose of magnesium sulfate with intravenous administration carried out on rats and dogs showed that the LD50 value was 206 mg/kg for males and 174 mg/kg for females.<sup>25</sup>

## CONCLUSION

Magnesium supplementation has been proven to prevent the incidence of



hypertension in pregnancy and preeclampsia, especially in mothers with hypomagnesemia. In addition, magnesium insufficiency has been proven to be associated with the incidence of preeclampsia. Although magnesium supplementation may not be necessary for pregnant women with their first pregnancy who do not have risk factors for hypertension in pregnancy or preeclampsia because magnesium is found in many food sources, magnesium absorption can be influenced by many factors, even though magnesium needs in pregnant women tend to increase. With the many physiological effects obtained from magnesium supplementation, there is no harm in pregnant women taking oral magnesium supplementation.

Copy and write down the source of funds (grants) or other financial support along with the grant number and URL of the funder's website (if any).

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