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The Effect of Magnesium Supplementation and Pregnancy Outcomes: Experimental Epidemiological Study

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ABSTRACT

The evidence that magnesium levels are related to pathological occurrences in pregnancy is increasing. This research was purpose to the effect of magnrsium suplemention ang pegnancy outcomes. The study was conducted in the maternal and child health polyclinic, Primary Health Care, Padang City, Indonesia from June 2019 - May 2020. It was experimental study with pre-test and post-test control group design carried out pregnant women. As much as 90 pregnant women were selected by convenience sampling method for the study, they are grouped as follows: Group-A (hypomagnesemia in intervention group), group-B (normal magnesium in intervention group), and group-C (normal magnesium in the control group). The intervention group with supplementation of magnesium 365 mg/ day during pregnancy starting at 22 weeks to 36 weeks. The control group received Fe tablet 180 mg/ day at the same time of the intervention group. In the third trimester of pregnancy blood samples were taken for examination of post-intervention magnesium in all groups. The effect of magnesium supplementation and pregnancy outcomes was tested using chi-square to determine the effect. Multiple logistic regression was tested to multivariate analysis. This study found that magnesium supplementation is associated with preeclampsia in pregnant women with hypomagnesemia in the interventional group (RR = 6.51 [95% CI 1.06-39.93]), and that magnesium supplementation on pregnant women with hypomagnesemia contributed to the prevention of preeclampsia 6.51 times. This study confirmed the effect of magnesium supplement among pregnant women with hypomagnesemia to prevent preeclampsia.

Keywords: *magnesium, pregnancy outcomes, hypomagnesemia, normal magnesium*

1. INTRODUCTION

Magnesium's beneficial influence on pregnancy has been studied for many years. Previous research has found an association between magnesium supplementation and pregnancy [1],[2]. Magnesium levels are being associated to pathological occurrences in pregnancy, according to new research. Hypomagnesemia has been associated with a higher risk of premature birth, spontaneous abortions, and cramping in the calf muscles [3].

A study found that higher magnesium consumption is related to a higher risk of preeclampsia [3]. According to this study, the magnesium level in healthy pregnant women review investigation on the effect of several dietary variables on the pregnancy-induced high blood pressure risk [4] found a connection between reduced magnesium consumption and an increased preeclampsia risk.

A sufficient magnesium intake appears to have a positive effect on maternal health throughout pregnancy. In pregnant women with gestational diabetes mellitus (GDM), a low post-partum magnesium level is an important variable of the development of later type 2 diabetes mellitus (T2DM) [5]. Another study found that low magnesium levels in the postpartum period are a

powerful factor of T2DM growth in women with a history of GDM [6]. Hypomagnesaemia has been associated to preterm labor in previous studies. In this study, prophylactic oral magnesium supplementation was indicated for women at increased risk of premature labor growth [7].

Due to a lack of data in this area in Indonesia, our research will look into whether research design dan sample is related to poor outcomes in the Indonesian pregnant women, and then explain a standard guideline for developing a magnesium supplementation intervention.

2. MATERIALS AND METHODS

2.1. Study Design and Research Sample

The study was conducted in the maternal and child health polyclinic, Primary Health Care, Padang City, Indonesia from June 2019 - May 2020. Pregnant women participated in an experimental study with a pre-test and post-test control group design. As much as 90 pregnant women were selected by convenience sampling method, they are grouped as follows: Group-A (hypomagnesemia in intervention group), group-B (normal magnesium in intervention group), and group-C (normal magnesium in the control group). A single live fetus, pregnant women aged 20-35 years, 22 weeks gestational age, never had a history of hypertension, kidney disease, a history of heart disease, diabetes mellitus, not suffering from severe anemia, no fetal anomalies, no smoking habits, no drinking habits, and patients who consume Fe tablets until the end of the pregnancy were all eligible participants.

2.2 Operational Definitions

Magnesium levels were assessed using Bioassay (Magnesium Kit), and magnesium status was determined using a spectrophotometric method, with measurement findings a) hypomagnesemia if serum magnesium levels were 1.9 mg/dl; b) normal if serum magnesium levels were 1.9 mg/dl.

2.3 Ethical Approval

The ethics committee of the Faculty of Medicine, Universitas Andalas, Padang, Indonesia granted ethical permission with No. 214/KEP/FK/2019. Participants written consent before involvement in the study.

2.4 Research Procedure

This study's techniques were divided into several steps: a) a screening of all patients undergoing antenatal care at Primary Health Care for screening samples that met the inclusion criteria; b) patients who met the criteria are given informed consent related to the study, which includes the purpose of the study, research procedures, benefits, rights and obligations, as well as research risks; c) data collection on the study sample (identity, age during pregnancy, gestational age, history of current pregnancy, and blood pressure) is done after the patient agrees to be a research sample; d) interviews were conducted using questionnaires, clinical and obstetric examinations, ultrasonography that was properly examined, and 2 cc venous blood samples taken for in-depth analysis; e) following the results, the samples are divided into three study groups: the intervention group with normal magnesium and hypomagnesemia status, the control group with normal magnesium status, and the intervention group with magnesium supplementation (365 mg/day, Bioelectra®) starting at 22 weeks and ending at 36 weeks. The control group received Fe tablets (180 mg/day) at the same time as the intervention group; g) blood samples were taken

2.5 Data Analysis

All quantitative data was analyzed with SPSS by SPSS 20.0. Then, for all relevant data, descriptive statistics were calculated. The impact of magnesium supplementation on pregnancy outcomes was examined using the chi-square method. Multivariate analysis was used to test multiple logistic regression. $P<0.05$ was used to indicate significance in all cases.

3. RESULTS

Table 1. Subject characteristics

Variables	Groups			p-value
	A (n=30)	B (n=30)	C (n=30)	
Age (years), mean±SD	28.10±4.58	29.30±4.40	28.57±4.17	0.568[a]
Age groups, f(%)				0.813[b]
> 30 years	8 (26.7)	10 (33.3)	10 (33.3)	
≤ 30 years	22 (73.3)	20 (66.7)	20 (66.7)	
Body mass index, f(%)				0.886 [b]
Underweight	2 (6.7)	1 (3.3)	1 (3.3)	
Normal	16 (53.3)	21 (70.0)	21 (70.0)	
Overweight	9 (30.0)	6 (20.0)	6 (20.0)	
Obesity	3 (10.0)	2 (6.7)	2 (6.7)	
Parity, f(%)				0.531[b]
Nulliparous	18 (60.0)	16 (53.3)	12 (40.0)	
Primiparous	7 (23.3)	10 (33.3)	13 (43.3)	
Multiparous	5 (16.7)	4 (13.3)	5 (16.7)	

*p<0.05 statistically significant
[a] one-way anova test
[b] chi-square test

Table 1 found there were no differences in age, BMI, or parity between hypomagnesemia, normal magnesium in interventional groups, and normal magnesium (p>0.05).

Magnesium supplementation and the outcome of pregnancy (Table 2-4).

Table 2. The effect of magnesium supplementation and pregnancy outcomes among hypomagnesemia in intervention group

Outcomes	Categorical	Group A		p value	RR (95% CI)
		Yes (f/%)	No (f/%)		
Preeclampsia	Yes	1 (3.3)	7 (11.7)	0.261	0.26 (0.03-2.23)
	No	29 (96.7)	53 (88.3)		
IUGR	Yes	5 (16.7)	5 (8.3)	0.292	2.20 (0.58-8.29)
	No	25 (83.3)	55 (91.7)		
Preterm	Yes	3 (10.0)	15 (25.0)	0.162	0.33 (0.09-1.26)
	No	27 (90.0)	45 (75.0)		
LBR	Yes	5 (16.7)	6 (10.0)	0.496	1.80 (0.50-6.46)
	No	25 (83.3)	54 (90.0)		
GDM	Yes	1 (3.3)	3 (5.0)	1.000	0.66 (0.06-6.58)
	No	29 (96.7)	57 (95.0)		
Cramps	Yes	3 (10.0)	11 (18.3)	0.370	0.495 (0.13-1.93)
	No	27 (90.0)	49 (81.7)		
Delivery	SC	11 (36.7)	19 (31.7)	0.813	1.25 (0.49-3.14)
	Normal	19 (63.3)	41 (68.3)		

Abbreviation: LBR, low birth weight; GDM, gestational diabetes mellitus; IUGR, intra uterine growth restiction; RR, relative risk; SC, sectio secarea; *p < 0.05, considered significant

Table 2 shows that the chi-square test did not reveal there is a significant or excellent effect of effect of magnesium supplementation on pregnancy outcomes in the intervention group with hypomagnesemia (sig >0.05).

Table 3. The effect of magnesium supplementation and pregnancy outcomes among normal magnesium in intervention group

Outcomes	Categorical	Group B		p value	RR (95% CI)
		Yes (f/%)	No (f/%)		
Preeclampsia	Yes	3 (10.0)	5 (8.3)	1.000	1.22 (0.27-5.49)
	No	27 (90.0)	55 (91.7)		
IUGR	Yes	4 (13.3)	6 (10.0)	0.726	1.39 (0.36-5.34)
	No	26 (86.7)	54 (90.0)		
Preterm	Yes	11 (36.7)	7 (11.7)	0.012*	4.38 (1.48-12.95)
	No	19 (63.3)	53 (88.3)		
LBR	Yes	5 (16.7)	6 (10.0)	0.496	1.80 (0.50-6.46)
	No	25 (83.3)	54 (90.0)		
GDM	Yes	2 (6.7)	2 (3.3)	0.598	2.07 (0.28-15.48)
	No	28 (93.3)	58 (96.7)		
Cramps	Yes	5 (16.7)	9 (15.0)	1.000	1.13 (0.34-3.74)
	No	25 (83.3)	51 (85.0)		
Delivery	SC	8 (26.7)	22 (36.7)	0.477	0.63 (0.24-1.65)
	Normal	22 (73.3)	38 (63.3)		

Abbreviation: LBR, low birth weight; GDM, gestational diabetes mellitus; IUGR, intra uterine growth restiction; RR, relative risk; SC, sectio secarea; *p < 0.05, considered significant

Table 3 found in the intervention group, there was no effect of magnesium supplementation on preeclampsia, intrauterine growth restriction, low birth weight, gestational diabetes mellitus, cramps, or type of delivery (p>0.05). Preterm labor is associated with magnesium supplementation (p<0.05).

Table 4. The effect of magnesium supplementation and pregnancy outcomes among normal magnesium in control group

Outcomes	Categorical	Group C		p value	RR (95% CI)
		Yes (f/%)	No (f/%)		
Preeclampsia	Yes	4 (13.3)	4 (6.7)	0.433	2.15 (0.49-9.29)
	No	26 (86.7)	56 (93.3)		
IUGR	Yes	1 (3.3)	9 (15.0)	0.155	0.19 (0.02-1.62)
	No	29 (96.7)	51 (85.0)		
Preterm	Yes	4 (13.3)	14 (23.3)	0.402	0.51 (0.15-1.69)
	No	26 (86.7)	46 (76.7)		
LBR	Yes	1 (33.3)	10 (16.7)	0.092	0.17 (0.02-1.42)
	No	29 (96.7)	50 (83.3)		
GDM	Yes	1 (3.3)	3 (5.0)	1.000	0.66 (0.07-6.58)
	No	29 (96.7)	57 (95.0)		
Cramps	Yes	6 (20.0)	8 (13.3)	0.538	1.63 (0.51-5.20)
	No	24 (80.0)	52 (86.7)		

Delivery	SC	11 (36.7)	19 (31.7)	0.813	1.25 (0.49-3.14)
	Normal	19 (63.3)	41 (68.3)		

Abbreviation: LBR, low birth weight; GDM, gestational diabetes mellitus; IUGR, intra uterine growth restiction; RR, relative risk; SC, sectio secarea; *p < 0.05, considered significant

Table 4 found in the control group, the hyphotesis test revealed no significant effect of magnesium supplementation on pregnancy outcomes (p>0.05).

The effect of magnesium supplementation and pregnancy outcome on hypomagnesemia in the control group was determined by multivariate analysis (Table 5).

Table 5. Multivariate analysis with multiple logistic regression to determine, pregnancy outcomes among hypomagnesemia in interventional group

Outcomes	B	S.E.	p-value	RR (95% CI)
Preeclampsia	1.873	0.926	0.043*	6.51 (1.06-39.93)*
IUGR	-0.871	4.857	1.000	0.02 (0.01-30.12)
Preterm	0.063	0.909	0.945	1.07 (0.18-6.32)
LBR	-18.040	4.529	1.000	0.14 (0.04-50.12)
GDM	1.578	1.354	0.244	4.85 (0.34-68.82)
Cramps	-0.884	1.329	0.506	0.41 (0.03-5.59)
Delivery	0.974	0.786	0.216	2.65 (0.57-12.36)

RR, relative risk; *p < 0.05, considered significant

Table 5 shows that magnesium supplementation is associated with preeclampsia in pregnant women with hypomagnesemia in the interventional group (RR = 6.51 [95% CI 1.06-39.93]), implying that magnesium supplementation on pregnant women with hypomagnesemia helped to prevent preeclampsia 6.51 times.

4. DISCUSSION

Magnesium supplementation is associated with preeclampsia in pregnant women with hypomagnesemia in the interventional group (RR = 6.51 [95% CI 1.06-39.93]), according to this study. lower plasma magnesium levels in healthy pregnant women and preeclampsia pregnant women compared to healthy non-pregnant women, according to previous research [3]. Lower magnesium levels in the erythrocyte membrane are also experienced by preeclampsia pregnant women. Several recent studies in various countries [8-10] have shown that preeclampsia pregnant women have lower plasma magnesium levels than normal pregnant women.

Another study found that pregnant women with preeclampsia have lower ionized magnesium levels in their brains. Furthermore, preeclampsia is associated with changes in magnesium content, according to molecular biology studies. In this study, researcher discovered significant changes in placental gene expression for numerous magnesium transporter systems in pregnant women with and without preeclampsia [11].

According to Shaykh et al, magnesium is essential for blood pressure control. Consumption of fruits and vegetables, which are high in potassium and magnesium, is linked to low blood pressure during pregnancy. Because magnesium plays a key part in the process of preeclampsia during pregnancy, 33% of patients with low magnesium levels will develop preeclampsia [12]. Magnesium shortage during pregnancy is linked to hypertension and preeclampsia [13].

Eclampsia is a complication of severe preeclampsia that might include or exclude organ failure. According to a study, a considerable

number of women with eclampsia have mild to severe hypertension prior to the onset of seizures. These findings suggest the use of magnesium sulfate as a preventive for all pregnant women with mild preeclampsia in order to lower the risk of developing eclampsia, which is the most common cause of mother and child mortality and morbidity [14-18].

Finally, it should be noted that study on the prevention of preeclampsia during pregnancy focuses mostly on high-risk pregnancies. According to the findings of our magnesium supplementation study, pregnant women with risk factors for preeclampsia may benefit from magnesium supplementation, but those without risk factors are less likely to benefit. As a result, it's plausible to assume that magnesium insufficiency is more common in pregnant women who are at risk.

5. CONCLUSION

This study proved the usefulness of magnesium supplementation in avoiding preeclampsia in pregnant women with hypomagnesemia. As a result, we can speculate that maternal hypomagnesaemia could be utilized to predict preeclampsia. This study implies that magnesium supplementation could be used as the basis for developing a future proposal for preventative magnesium supplementation among people at increased risk of developing preeclampsia.

AUTHOR'S CONTRIBUTION

IYD: conceptualization, methodology, formal analysis, visualisation, writing original draft.

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