RESEARCH ARTICLE

ASSOCIATION OF SERUM MAGNESIUM LEVELS WITH GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Hypomagnesemia is one of the conditions that can accelerate diabetes complications in patients with type 2 diabetes mellitus (T2DM) by altered insulin function and secretion. Hypomagnesemia has been linked to poor glycemic control due to increased insulin resistance and impaired of insulin secretion. **Objective:** The aim of this study is to analyze the association between serum magnesium levels and glycemic control in patients with T2DM who treated with metformin or pioglitazone. **Methods:** Serum magnesium levels and HbA1c were examined from a total of 41 patients with T2DM treated with metformin $\geq$ 750 mg/day for at least 3 weeks or pioglitazone $\geq$ 15 mg/day for at least 4 weeks with a body mass index (BMI) of < 30 kg/m^2. An examination of HbA1c was analyzed using *Variant and D10* with *National Glychohaemoglobin Standardization Program* (NGSP) certification. The serum magnesium level was analyzed using *Roche/Hitachi Cobas C 311/501 System*. **Results:** The mean value of serum magnesium levels was 2.04±0.19 mg/dl and the mean of HbA1c was 7.44±1, 57%. There was significant negative correlation between serum magnesium levels with HbA1c (r-0.449, p-value 0.003). Low serum magnesium levels was correlated with poor glycemic control. **Conclusion:** Serum magnesium levels in patients with T2DM treated with metformin or pioglitazone was inversely correlated to glycemic control. Serum magnesium levels monitoring is important to reduce the risk of diabetes-related complications.

Citation: Sony Wibisono Mudjanarko and Huwainan Nisa Nasution, **2020.** "Association of serum magnesium levels with glycemic control in patients with type 2 diabetes mellitus", *International Journal of Current Research*, 12, (01), 9531-9533.

INTRODUCTION

The prevalence of type 2 diabetes mellitus (T2DM) has been increasing exponentially with high rates of diabetes-related morbidity and mortality due to complications (Bergman *et al.,* 2012). Hypomagnesemia is one of the conditions that can accelerate complication in patients with T2DM (Chhabra *et al.,* 2017). The prevalence of hypomagnesemia in patients with type 2 diabetes varies between 25-39% (Gunther, 2010). Several studies have shown that hypomagnesemia is significantly associated with poor glycemic control and increased incidence of diabetes-related complications within a certain period of time (Sales *et al.,* 2011; Dasgupta *et al.,* 2012; Gupta *et al.,* 2014; Sadiq and Nawaz, 2014; Rao and Shariff, 2015). Magnesium plays an important role in carbohydrate metabolism as a critical cofactor for the mechanism of glucose transport in membrane cells and the activities of various enzymatic reactions involved in carbohydrate oxidation (Hans *et al.,* 2002). Magnesium deficiency has been associated with worsening of plasma glycemic control due to an impairment of both, insulin secretion and insulin action (Chhabra *et al.,* 2017; Gommers *et al.,* 2016).

MATERIALS AND METHODS

It is an observational analytic study with cross-sectional design conducted at Private Practice of Internists of Metabolic and Diabetes Endocrinology Consultants in Surabaya, Indonesia. The study was approved by the Committee of the Health Research Ethics of the Faculty of Medicine, Airlangga University, Surabaya. The inclusion criteria were patients with T2DM, more than 18 years, use of metformin $\geq$ 750 mg/day for at least 3 weeks or pioglitazone $\geq$ 15 mg/day for at least 4 weeks and the body mass index (BMI) < 30 Kg/m^2. The exclusion criteria included impaired renal function with serum creatinine > 1.2 mg/dl for women and > 1.5 mg/dl for men, pregnant or lactating women, acute infections or inflammation, gastrointestinal and chronic liver diseases, history of drinking alcohol or smoking, taking proton pump inhibitors, diuretics, aminoglycoside drugs, amphotericin B, vitamin and mineral supplementation, steroids and history of getting therapy of cetuximab, erlotinib, cisplatin, carboplatin, cyclosporine or tacrolimus. The examinations of HbA1c and serum magnesium levels were done. HbA1c was analyzed using *Variant and D10* with *National Glychohaemoglobin Standardization Program* (NGSP) certification. The serum magnesium level was

analyzed using *Roche/Hitachi Cobas C 311/501 System*. All data were analyzed using *SPSS version 20.0 software*. Bivariate analysis of correlations among the variables was performed by Rank Spearman test. The results were presented in a correlation coefficient (r-value), and the significant p-value was < 0.05 and the confidence interval was 95%.

RESULTS

The study involved 41 subjects of patients with T2DM who had met the inclusion and exclusion criteria. The characteristics of the subjects are presented in Table 1. The mean of serum magnesium levels was 2.04±0.19 mg/dl. The mean of HbA1c was 7.44±1.57%. Bivariate analysis by using with Rank Spearman test related to the association of serum magnesium levels with HbA1c. Serum magnesium levels had a significant association with HbA1c with p-value 0.003 and correlation coefficient -0.449. These data are shown in Table 2. Figure 1 shows a graph of the correlation between serum magnesium level and HbA1c.

Table 1. Characteristics of study participants

Characteristics	n = 41
Female, n (%)	30 (73.2%)
Age (years), mean (SD)	60.3 (11.5)
Duration of type 2 DM (years), mean (SD)	11.8 (10.11)
Dyslipidemia, n (%)	25 (65.9)
Use of statin, n (%)	27 (65.9)
Use of antihypertensive, n (%)	5 (12.2)
Use of insulin, n (%)	13 (31.7)
IMT (Kg/m^2), mean (SD)	25.4 (2.8)
Fasting plasma glucose (mg/dl), mean (SD)	131.8 (40.95)
Postprandial plasma glucose (mg/dl), mean (SD)	185 (78.43)
HbA1c (%), mean (SD)	7.44 (1.57)
Total cholesterol (mg/dl), mean (SD)	167.41 (37.90)
Triglyceride (mg/dl), mean (SD)	127.9 (52.9)
LDL (mg/dl), mean (SD)	95.94 (34.08)
HDL (mg/dl), mean (SD)	47.64 (15.41)
Serum creatinine (mg/dl), mean (SD)	0.79 (0.18)
eGFR (ml/minute), mean (SD)	86.8 (17.62)
Serum magnesium (mg/dl), mean (SD)	2.04 (0.19)

Table 2. Association of serum magnesium levels with fasting plasma glucose

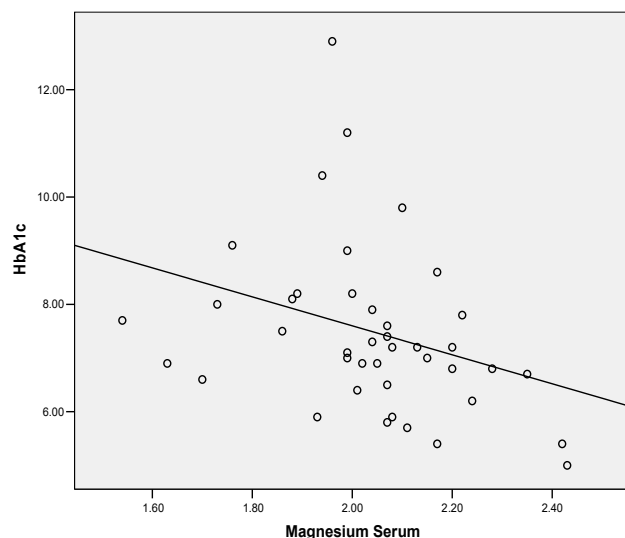| Independent variable	Dependent variable	r-value	p-value
Serum magnesium	HbA1c	-0.449	0.003

Figure 1. Graph of correlation of serum magnesium levels with HbA1c

DISCUSSION

The characteristics of the subjects were dominated by women. It is different from Pokharel *et al.* (2017) in Nepal and Gupta *et al.* (2014) in India which the subjects were mostly men. This result is in line with previous data in Indonesia taken from Riskesdas 2013 indicated that the prevalence of diabetes was higher in women (Gupta *et al.*, 2014; Pokharel *et al.*, 2017). The mean of age was 60 years and the dominant age group was 46-60 years (46.3%). A different result was shown by Gupta *et al.* (2014) in which dominated by the age group of 34-45 years. The study is in line with the previous study of Riskesdas 2013 which dominated by the age group of 45-64 years. The mean of serum magnesium levels in this study was 2.04±0.19 mg/dl. A similar result was shown by Tarigan *et al.* (2015) in Jakarta which the serum magnesium levels < 1.7 mg/dl was 13.2% and ≥ 1.7 mg/dl was 86.8%, mostly in normomagnesemia group (Tarigan *et al.*, 2015). This study also in line with Pokharel *et al.* (2017) with the mean serum magnesium levels was 2.10±0.16 mg/dl (Pokharel *et al.*, 2017). The different results were shown in the previous studies in India by Gupta *et al.* (2014) with the mean of serum magnesium levels were 1.2 mg/dl (Gupta *et al.*, 2014). The mean HbA1c shown in this study was 7.44±1.57%. Different results were shown by Pokharel *et al.* (2017) and Gupta *et al.* (2014) with an average of 8.4±1.2% and 8.2±0.45%. The different result probably caused by this study was conducted in a private clinic and the majority of subjects has been well-controlled (82.9%). The second reason was the subjects has been treated with metformin or pioglitazone resulted in lower HbA1c. In this study, the serum magnesium levels had a significant negative correlation to HbA1c with r-0.449 and p-value 0.003. It is similar to Gupta *et al.* (2014) with r-0.29; p <0.0001 and Pokharel *et al.* (2017) with r-0.299; p <0.001. Low serum magnesium levels in patients with T2DM is associated with poor glycemic control. The variation in the study may be due to several factors including different research design, the use of metformin or pioglitazone, and other confounding factors such as diet, physical activities, and dyslipidemia. The limitations and weaknesses of this study were uncontrolled confounding variables such as diet, physical activity, and dyslipidemia and unprovided overall antidiabetic drug equation.

Conclusion

Serum magnesium levels in patients with T2DM treated with metformin or pioglitazone was inversely correlated to glycemic control. Serum magnesium levels monitoring is important to reduce the risk of diabetes-related complications.

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