



## Hypomagnesemia is a risk factor for metabolic syndrome and type 2 diabetes mellitus in native Balinese

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### Abstract

**Objective:** To determine the prevalence of hypomagnesemia and the risk of hypomagnesemia on metabolic syndrome and type 2 diabetes mellitus events in native Balinese.

**Methods:** A cross-sectional population-based study was conducted in 111 subjects among native Balinese. Chi-square test was used to determine the prevalence risk (OR) of hypomagnesemia for metabolic syndrome and diabetes.

**Results:** Prevalence of hypomagnesemia was 17.1%. The prevalence of hypomagnesemia was higher in subjects with metabolic syndrome and type 2 diabetes mellitus than those without (34.7% vs. 12.5%,  $P = 0.025$ ; and 60.0% vs. 15.1%,  $P = 0.035$ ). Hypomagnesemia was a risk factor for metabolic syndrome (OR = 3.7; 95% CI, 1.28-10.83) and type 2 diabetes mellitus (OR = 8.4; 95% CI, 1.30-54.50).

**Conclusion:** The prevalence of hypomagnesemia is very high among native Balinese and hypomagnesemia is an important risk factor for metabolic syndrome and type 2 diabetes mellitus events in the population.

**Keywords:** Hypomagnesemia, Metabolic syndrome, Type 2 diabetes mellitus

### Introduction

Magnesium (Mg), one of the micronutrients, has a critical role in glucose homeostasis and insulin action [1]. Mg is a cofactor for many enzymes in glucose metabolism. Mg is a cofactor for all ATP transfer reactions, indicating that Mg plays a critical role in phosphorylation of insulin receptor. Depletion of intracellular Mg might cause functional defect of tyrosine kinase at insulin receptor, leading to decreased insulin capability to stimulate glucose uptake in insulin sensitive tissues [2]. Although there are many studies demonstrating association between hypomagnesemia with insulin resistance and type

2 diabetes mellitus (DM), this ion is often overlooked and not managed. Mg function in biological process has always been ignored to a point where Mg is said to be a forgotten ion [3,4].

Pedawa is a village located at mountainous areas where most of the residents (native Balinese) are farmers. High risk of low Mg intake could result from the soil, thus increasing risk of Mg deficiency among the population.

The objective of this study was to explore the prevalence of hypomagnesemia and risk of hypomagnesemia for metabolic syn-

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drome and type 2 DM events in native Balinese.

### Methods

A cross-sectional study was conducted among native Balinese in Pedawa village. Due to any reasons, only 111 out of 300 targeted subjects (a follow-up study after over 5 years from the first study) over 18 years were recruited by stratified random sampling. Subjects with chronic diarrhea, chronic kidney diseases, alcoholism, on medications such as diuretics, aminoglycosides, amphotericine, cyclosporine, cisplatin, insulin antagonists such as corticosteroids, pregnant women, and children or young adolescents in growth period were excluded from this study. The authors received consent from all participants.

Hypomagnesemia is defined as serum Mg level lower than mean  $-1$  SD of the Mg levels in all subjects. Diagnosis of DM was established using the ADA (2012) criteria [5]. Diagnosis of metabolic syndrome was defined by the criteria of A Joint Interim Statement of the IDF Task Force on Epidemiology and Prevention; NIH; AHA; WHF; IAS; and IASO (2009) [6]. Data were analyzed by chi-square test to determine the difference prevalence and odds ratios (prevalence risk or risk estimate).

### Results

Of the 111 subjects, 45 were male and 66 were female, with age between 27-100 years old. Mean Mg level was  $2.02 \pm 0.15$  mg/dL. By defined criteria, 17.1% (19/111) of subjects had hypomagnesemia (Mg level  $<1.87$  mg/dL). By age, the elderly (aged  $\geq 60$  years old)

had higher prevalence of hypomagnesemia compared to the younger group (34.5% vs. 11%;  $P = 0.004$ ).

Prevalence of metabolic syndrome was 20.7%. Prevalence of hypomagnesemia was higher in subjects with metabolic syndrome than those without (34.8% vs. 12.5%,  $P = 0.025$ ; OR = 3.7, 95% CI, 1.28-10.83). Prevalence of type 2 DM was 4.5%. Prevalence of hypomagnesemia was higher in subjects with type 2 DM than non-diabetic subjects (60% vs. 15.1%,  $P = 0.0035$ ; OR = 8.43, 95% CI, 1.30-54.55) (Table 1).

### Discussion

By cut-off point 1.87 mg/dL, hypomagnesemia was found very high in Balinese residents at Pedawa village (17.1%). Studies revealed that prevalence of hypomagnesemia in general population (Mg level was measured by different tools, and definition of hypomagnesemia was also different) was 2.5%-15%. Study of 16,000 subjects in Germany found that prevalence of hypomagnesemia was 14.5% [7].

Mechanism of how hypomagnesemia causes insulin resistance and type 2 DM is not fully understood. There was a strong independent association between serum Mg levels and prevalence of metabolic syndrome (OR = 6.8; 95%

CI, 4.2-10.9) [8]. Compared with those in the lowest quartile of Mg intake, multivariable-adjusted hazard ratio of metabolic syndrome for participants in the highest quartile among young adults was 0.7% (95% CI, 0.50-0.91;  $P < 0.01$ ), suggesting that young adults with higher Mg intake have lower risk of development of metabolic syndrome [9]. Women in the highest quintile of Mg intake had 27% lower risk of metabolic syndrome compared with those in the lowest quintile of intake (OR = 0.73; 95% CI, 0.60-0.88) [10]. Serum ionized Mg levels were significantly reduced in patients with low HDL cholesterol, high triglycerides, high waist circumference, and high blood pressure. After adjusting for potential confounders, plasma triglycerides (OR = 4.7; 95% CI, 2.56-8.67), waist circumference (OR = 2.21; 95% CI, 1.21-4.04), were independently associated with hypomagnesemia [11].

Diabetic subjects have higher incidence of hypomagnesemia compared to non-diabetic patients. Incidence of hypomagnesemia is estimated 13.5%-47.7% among diabetic outpatients, and 2.5%-15% in non-diabetic outpatients [12,13]. Prevalence of hypomagnesemia in diabetic outpatients were 38% in Switzerland, 25%-39% in US, and 73.1% in Mexico [14].

Hypomagnesemia is an important

Table 1. Hypomagnesemia in subjects with metabolic syndrome and type 2 DM

	Metabolic Syndrome		DM		
	Yes(n=23)	No(n=88)	Yes(n=5)	No(n=106)	
Hypomagnesemia	Yes	8 (34.8%)	11(12.5%)	3 (60.0%)	16 (15.1%)
	No	15 (65.2%)	77 (87.5%)	2 (40.0%)	90 (84.9%)
Fisher's exact test	P = 0.025		P = 0.035		
Risk estimate (OR)	3.7		8.4		
95 % CI	1.28 – 10.83		1.30 – 54.55		



risk factor for metabolic syndrome (OR = 3.7; 95% CI, 1.28-10.83; P = 0.0025) and type 2 DM (OR = 8.43; 95% CI, 1.30-54.55; P = 0.0035) in native Balinese. Subjects with hypomagnesemia have risk close to 4 times of metabolic syndrome and more than 8 times of type 2 DM events. Future studies with large sample size are needed to further confirm the conclusions of the current study.

### Conflict of interest

The authors declare no conflict of interest relevant to this article.

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### . COCHRANE UPDATES & NICE GUIDELINES .

#### STABLE ANGINA

This quality standard defines clinical best practice within this topic area. It provides specific, concise quality statements, measures and audience descriptors to provide the public, health and social care professionals, commissioners and service providers with definitions of high-quality care.

This quality standard covers care of adults (18 years and older) presenting with stable chest pain or those diagnosed with stable angina due to atherosclerotic disease. It does not cover people with acute coronary syndrome, chest pain or discomfort of unknown cause, angina-type pain that is likely to be due to non-cardiac disease or angina-type pain associated with other types of heart disease. It addresses the diagnosis of stable angina, medical management, revascularisation and re-evaluation of refractory symptoms.

(Source: NICE Quality Standards, QS21, August 2012; available at <http://guidance.nice.org.uk/QS21>)