Serum magnesium levels patients with Type 2 diabetes mellitus: comparisons between good and poor glycaemic control

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ABSTRACT

Introduction: Magnesium is a major determinant of insulin and glucose metabolism. The lower the magnesium, the greater the amount of insulin required to metabolise the same amount of glucose load, indicating insulin insensitivity. Many studies have reported hypomagnesaemia in diabetes mellitus and its relation to poor glycaemic control. This study provides overview regarding the level of serum magnesium among patients with type 2 diabetes mellitus in the Hospital University Science Malaysia (HUSM) and correlates the level with diabetic control as measured by Hb_{A1c}. **Materials and Methods:** A comparative cross sectional study was conducted among 75 good control ($Hb_{A1c} \leq 7.0\%$ in two consecutive reading or one $\leq 6.5\%$) and 75 poor glycaemic control (two $Hb_{A1c} > 7.0\%$ readings or one $\geq 6.5\%$ reading over the study period) who attended the Out-Patient Department Clinic and Medical Specialist Clinic HUSM, Kelantan. The patient had been called for sampling of serum magnesium level within three weeks of last the Hb_{A1c} result. **Results:** The proportion of hypomagnesaemia was 8.6% and seen mostly among the poor glycaemic control group. The mean serum magnesium level in good glycaemic control patients (0.94 ± 0.10 mmol/L) was significantly higher than the poor glycaemic control group (0.88 ± 0.10 mmol/L, $p<0.05$). Significant but weak inverse correlation were observed between serum magnesium levels and Hb_{A1c} in both groups (r=-0.22 and $p=0.004$ in poor control group, r= -0.26 and $p=0.020$ in good control group). **Conclusion:** Subjects with poor glycaemic control had significantly lower magnesium level than good glycaemic control. There was significant correlation between serum magnesium level and glycaemic control.

Keywords: Glycaemic control, hypomagnesaemia, hypermagnesaemia, diabetes mellitus

INTRODUCTION

Type 2 diabetes has been associated with hypomagnesaemia compared to non-diabetic subjects. [1] Hypomagnesaemia may be a con-

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sequence of insulin resistance and may worsen insulin resistance, a condition that often precedes the development of frank diabetes, [2] and may alter the entry of glucose into cells. [3] Possible causes of hypomagnesaemia in diabetes mellitus include poor oral magnesium intake, renal magnesium loss, poor gas-

trointestinal absorption of magnesium as a result of autonomic dysfunction, oesophageal dysfunction and diabetic gastroparesis. [4] In patient with diabetes mellitus with decreased serum magnesium level, oral supplementation with magnesium (50 ml $MgCl_2$ solution) for 16 weeks have been shown to increase the serum magnesium level. [5] Currently there is no reported data on serum magnesium level and its influence on diabetes control among Malaysian patient population with diabetes mellitus. This study reports on our findings on serum magnesium level in among our diabetic patients and correlation with diabetic or glycaemic control.

MATERIALS AND METHODS

A comparative cross-sectional study was conducted among patients with good and poor glycaemic control respectively seen at the Out Patient Department Clinic and Medical Specialist Clinic, Hospital University Science Malaysia (HUSM). Good glycaemic control was defined as Hb_{A1c} value <7.0% for at least two consecutive measurements or Hb_{A1c} <6.5% for single measurement within the study period. Poor control was defined as Hb_{A1c} value >7.0% for at least two consecutive measurements or Hb_{A1c} >6.5% for single measurement within the study period.

Patients' Hb_{A1c} results were traced from the endocrine laboratory within the study period. A total of 392 patients with poor glycaemic control and 86 patients with good glycaemic control were identified. Based on sample size calculation, the minimum sample required for our study was n = 75 per group. The sampling interval, k^{th} = N/n were used for systematic random sampling of the subjects. We randomly chose a starting point

between number one and five and then subsequently selected every fifth patient on the list until we obtained the desired sample size.

All patients with good glycaemic control who fulfilled the criteria were included. Out of 86 good glycaemic control patients, 75 patients who fulfilled the study criteria consented to participate in the study. All patients were recalled for blood sampling (serum magnesium) within three weeks of the last Hb_{A1c} result. Serum magnesium was analysed by colourimetric method and Hb_{A1c} was measured by the HPLC Biorad variant II Turbo. The inclusion and exclusion criteria are shown in Table 1.

The data was analysed using the Statistical Package for Social Science (SPSS) version 18.0. Comparison of mean age, body mass index (BMI) and duration of diabetes mellitus between the groups were analysed using the independent t-test. Comparisons of gender were made using the Chi-Square test and comparison of race between the groups were made using the Fisher's Exact test. Correlation between serum magnesium level and Hb_{A1c} were analysed using Pearson correlation. A *p* value of <0.05 was taken as significant for all analysis.

Table 1: The inclusion and exclusion criteria for the study.

Inclusion criteria	Exclusion criteria
Patients diagnosed with type 2 diabetes mellitus.	Elderly (more than 65 years of age)
Patient's age 30-65 years old	Patient who are active athletes
Patient's with Hb_{A1c} result	Patient on loop diuretics
	Patient on oral contraceptive therapy
	Patient on hormone replacement therapy
	Patient who are chronic alcoholism

RESULTS

This study included 80 female and 70 male patients with diabetes mellitus. There was no significant differences in the glycaemic control between the male and female patients. A majority of the patients were Malays, reflecting the population demographic of patients seen in the centre. A majority of the patients were obese and there was no significant difference in the BMI between the two groups. The duration of underlying diabetes mellitus in the good control group was significantly shorter than those in the poor controlled groups. The demographic details of patients included in this study are shown in Table 2.

Out of 150 patients, 8.6% had low serum magnesium level (<0.8 mmol/L). Of the patients with hypomagnesaemia, 94.4% were in the poor control group (*p*<0.001). Most of the patients with good and poor glycaemic control had serum magnesium levels within the normal range (0.80 to 1.05 mmol/L). However, the mean serum level were significantly different between good and poor glycaemic control (Figure 1). There were no significant differences between those categorised as having hypo– or hypermagnesaemia.
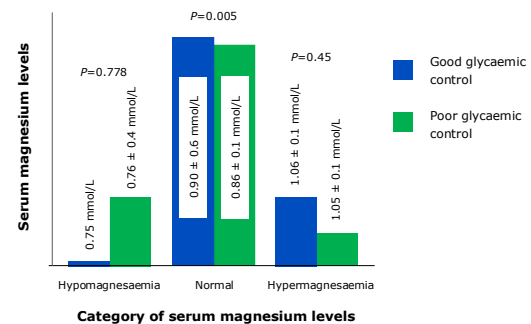

**Fig. 1: Serum magnesium level in good and poor control diabetes.**

Twenty-five patients had hypermagneseamia, and a majority (n=17, 68%) was in the good control group. The mean serum magnesium level in those with good control was significantly higher (0.94 ± 0.10 mmol/L) compared to those with poor glycaemic control (0.88 ± 0.10 mmol/L, *p*<0.05).

The correlation between serum magnesium with Hb_{A1c} was significant in both the good control and poor control diabetes (r=-0.22 and *p*=0.004 in poor control group, r=-0.26 and *p*=0.020 in good control group) (Figures 2a and 2b).

Table 2: Demographic of overall and the different groups of patients included in the study.

Parameters	Total subjects (n=150)	Good control (n=75)	Poor control (n=75)	P-value
Age (years)	54.31 ± 8.50	55.6 ± 8.01	53.1 ± 8.74	0.690
Sex				*0.304
Male	70 (47.8)	36 (48.0)	34 (43.8)	
Female	80 (52.2)	35 (52.0)	45 (56.2)	
Race				**0.210
Malay	132 (88.4)	62 (88.0)	70 (88.8)	
Chinese	16 (10.3)	8 (10.7)	8 (10.0)	
Indian	2 (1.3)	1 (1.3)	1 (1.2)	
BMI (Kg/m^2)	27.49 ± 4.90	27.19 ± 4.99	27.7 ± 4.90	0.465
Duration (years)	8.71 ± 5.81	7.57 ± 4.84	9.8 ± 6.44	0.017

All result analysed by Independent t-test except race and sex
All result are expressed as Mean ± SD; Race and sex are expressed as number of subject(%)
* Pearson Chi-Square test, p< 0.05 value is taken as significant at 95% confidence interval
** Fisher's Exact test, p< 0.05 value is taken as significant at 95% confidence interval
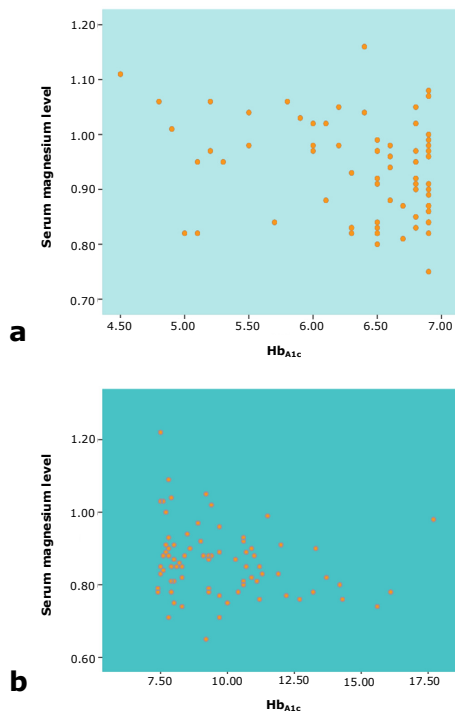
Figs. 2: a) Correlation between serum magnesium level and Hb$_{A1c}$ in good glycaemic control, and b) correlation between serum magnesium level and Hb$_{A1c}$ in poor glycaemic control.

DISCUSSION

Insulin is the most important factor that controls the level of plasma and intracellular magnesium. Insulin modulate the shift of magnesium from extracellular to intracellular space. Intracellular magnesium is a critical cofactor for many enzymes involved in carbohydrate metabolic pathway. It also play an important role as part of the activated Mg-ATP complex required for all of the rate limiting enzymatic glycolysis and regulation of enzymatic activities involved in phosphorylation reaction. Many studies have found low intracellular and extracellular magnesium in type 2 diabetic patient and this correlated with glycaemic control.

Our observations showed the propor-

tion of hypomagnesaemia among our patients was 8.6% and was mainly among those with poor glycaemic control (94.4%). The proportion of hypomagnesaemia in our study was lower compared to other studies. Hypomagnesaemia has been reported to occur in 13.5% to 47.7% of patients with type 2 diabetes compared with 2.5 to 15.0% in the control (non-diabetic) subjects. [6] However the proportion of hypomagnesaemia among our diabetic patients was higher compared to the rate reported for the general population which was estimated to be around 2% in one study. [7] Hypomagnesaemia has also been reported to be common among critically ill patients (~ 52%), [8] as compared with 26% in all hospitalised patients. [9]

Our study also found that the mean serum magnesium level among those with good glycaemic control (0.94 ± 0.10 mmol/L) was significantly higher than those with poor control (0.88 ± 0.10 mmol/L). Many previous studies had only compared serum magnesium levels between patients with diabetes and controls (non-diabetic). The mean serum magnesium level among all patients with type 2 diabetic in our study was 0.90 ± 0.1 mmol/L, and this is higher compared to the levels found for in other studies. One possible reason for the better serum magnesium status among our patients compared to other places is probably dietary related. The magnesium content in the diets among Kelantanese is generally high. Green leafy vegetables, nuts and whole seeds are among food that have high level of magnesium. In Kelantan, vegetables are typically consumed uncooked with either hot sauces and anchovy sauce. However, our study did not evaluate magnesium intake.

A cross sectional study (N=159) from Ethiopia showed the prevalence of hypomagnesaemia to be 65.0% among patients with diabetes mellitus. [10] In Ethiopia, a large portion of the population is malnourished. A diet containing low magnesium would therefore probably be the major contributing factor. A study from the United Kingdom showed the prevalence of hypomagnesaemia in unselected diabetic patients to be 25.0%. [11] The magnesium level in this study was measured using atomic absorption spectrophotometry whereas in our study, we measured the serum magnesium using colourimetry, a method which is the most widely used. The wide range in the reported incidence of hypomagnesaemia may also reflect the differences in the definition of hypomagnesaemia (reference range) apart from the different methods used.

A study from India reported that patient with diabetic retinopathy (Hb_{A1c} of 10.48 ± 1.82%) had lower (0.60 mmol/L or 1.20 mg%) magnesium level compared to those without retinopathy (Hb_{A1c} 7.62 ± 0.69% and serum magnesium level of 1.07 mmol/L (2.13 ± 0.32 mg%). [12] This study concluded that the hypomagnesaemia was a contributing factor to high Hb_{A1c} level in patients with diabetic retinopathy. [12] This study supported the finding of higher incidence of hypomagnesaemia among poor diabetic patients seen in our study.

A case control study by Kao *et al.* [13] showed that among individuals with serum magnesium levels of 0.95 mmol/L or greater, the adjusted relative odds for incident type 2 diabetes was significantly lower compared to those with low magnesium levels. The mean

± SD of serum magnesium among good diabetic control in our study was 0.94 ± 0.10 mmol/L. Therefore this probably suggest that the serum magnesium level should be kept between 0.94 mmol/L and 0.95 mmol/L for optimal or good control of diabetes.

Out of a total of 150 patients, 25 had hypermagnesaemia and a majority (n=17, 68%) were in the good control group. Hypermagnesaemia found in our study may be due to different definition of high magnesium. Some laboratory uses the range of 0.75 mmol/L to 1.25 mmol/L (1.50-2.50mg/dl) for normal range of serum magnesium whereas our laboratory reference range is between 0.80 mmol/L and 1.05 mmol/L for normal level.

We also found significant inverse correlation between the serum magnesium level and glycaemic control; low levels with poor glycaemic control. However the correlation was weak. The possible reasons for this weak correlation included small sample size which might have contributed to the small range of measured Hb_{A1c}. Our study of negative correlation have also been reported in other studies, in both types 1 and 2 diabetes mellitus.

A study looking at youths with type 1 diabetes mellitus showed lower levels of serum total magnesium in subjects with poor glycemic control (0.79 ± 0.09) compared to those with good control (0.82 ± 0.09 mmol/L, $p = 0.002$), (adjusted r2 0.17, $p=0.004$). [14] An older study showed significant inverse correlation between the Hb_{A1c} level with the concentrations of magnesium in muscle (r=-0.62, $p<0.001$), plasma (r=-0.62, $p<0.001$), and mononuclear cells (r=-0.47, $p<0.05$) from 25

subjects with type I diabetes mellitus. Intracellular magnesium level may provide a better correlation with Hb_{A1c} compared to serum total magnesium measurement.

A study looking at Sudanese with type 2 diabetes reported a strong inverse correlation between plasma magnesium level and Hb_{A1c} (r=-0.71, _p_<0.001). [16] The serum magnesium level in this study was almost similar to our study for poor control groups (1.8 ± 0.2 mg/dl or 0.74mmol/L) and good control group (2.3 ± 0.1 mg/dl or 0.95 mmol/L). However, the duration of the diabetes among their study subjects were much longer (up to 20 years) as compared with our study a mean duration of 9.8 ± 6.44 years (poor control groups).

Correlation of serum magnesium level with Hb_{A1c} is not only related to glycaemic control, but probably also related to the duration of diabetes. The modest correlation in our study was perhaps due to the shorter mean duration of diabetes in our study subjects. The sample size was small to cover the whole reportable range of Hb_{A1c} and should include the patient with longer duration.

In conclusion, almost on in tenth of our patients with diabetes mellitus had hypomagnesaemia. Subjects with poor glycaemic control had significantly lower serum magnesium level than those with good glycaemic control. Although weak, there was a significant correlation between serum magnesium level and glycaemic control. This study support the current recommendation of the American Diabetes Association (ADA) that only diabetic patients at high risk of hypomagnesaemia (poor diabetic control) should have

serum magnesium assessed and oral magnesium supplementation will be given only if hypomagnesaemia can be proved. [17] Further studies on the role of magnesium supplementation in type 2 diabetic patients in our population are recommended.

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