

Serum and Urinary Magnesium Levels in Adult Type 2 Diabetes Mellitus Patients in Oredo Local Government, Benin City, EDO State Nigeria

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Abstract: The global burden of diabetes mellitus is increasing worldwide. Prevalence world wide and in Nigeria is increasing. Micronutrients have been investigated both as potential preventive and therapeutic agents amongst which magnesium is important.

Aim: To evaluate the serum and urinary magnesium levels in type 2 diabetes mellitus patients and its association with C reactive protein and glycated haemoglobin.

Materials and methods: This was a cross sectional study, conducted in the state specialist Hospital, Benin City, Edo State, Nigeria.

Forty-six type 2 diabetes mellitus patients, both male and female within the age range of 30-85 years were recruited for the study, after meeting the inclusion criteria. Twenty age and gender matched healthy subjects were selected as controls. Fasting plasma glucose, glycated haemoglobin, C-Reactive protein, were assayed. Serum and urinary magnesium was assayed by the calmagite dye method.

Results: There was a significant difference between means of glycated haemoglobin, C-reactive protein of the subjects ($8.3 \pm 2.1\%$, 17.9 ± 1.3 mg/L) and controls ($4.5 \pm 1.1\%$, 10.3 ± 2 mg/L) $P < 0.05$. A statistically significant difference was observed between mean serum magnesium of subjects (0.8 ± 0.2 mmol/L) and control (1.3 ± 0.2 mmol/L) $P < 0.05$. Urinary magnesium was significantly lower in the subjects (1.5 ± 0.4 mmol/L) than in the controls (2.2 ± 0.7 mmol/L) $P < 0.05$. Prevalence of hypomagnesaemia was 4.3%. Serum magnesium showed a significant negative correlation with C Reactive protein $r = -.444$, $P < 0.05$.

Conclusion: The serum magnesium deficit and hypomagnesaemia observed amongst the subjects, coupled with the negative correlation of serum magnesium with C-reactive protein may be suggestive of possible roles that magnesium deficit and hypomagnesaemia may play, both in pathogenesis and development of complications in type 2 diabetes mellitus.

Keywords: Type 2 diabetes mellitus, Serum magnesium, C reactive protein.

I. Introduction

Micronutrients have been investigated as potential preventive and therapeutic agents for type 2 diabetes mellitus and common complications of diabetes¹. It has been shown to be associated with abnormalities in the metabolism of the magnesium, zinc, chromium, copper, manganese². Amongst them, magnesium has been investigated as a clinically significant electrolyte, for a long term policy, to lower the burden of diabetes mellitus with new findings and researches³, with the recommendations made by the international expert committee for the diagnosis and treatment of diabetes mellitus⁴.

Magnesium is an essential element involved in glucose homeostasis. It is a cofactor for various enzymes in carbohydrate metabolism⁵. It is also involved in multiple levels in insulin secretion, binding and activity^{5,6}.

Reduced magnesium levels has been reported in type 2 Diabetes mellitus^{6,7,8}.

Hypomagnesaemia may have negative impact on glucose haemostasis and insulin sensitivity in type 2 diabetes mellitus⁹. Reduced intracellular magnesium concentration results in a defective tyrosine-kinase activity, postreceptorial impairment in insulin action and worsening of insulin resistance in diabetic patients¹⁰. A low magnesium intake and an increased magnesium urinary loss appears to be the most important mechanism that may favour magnesium depletion in patients with type 2 diabetes mellitus¹⁰. Low dietary magnesium has been related to the development of type 2 diabetes and metabolic syndrome¹⁰. Some studies have been done in Nigeria on micronutrients in type 2 diabetes mellitus patients^{1,11}, which have revealed altered metabolism of some of these micronutrients.

The aim of this study was to evaluate serum and urinary magnesium in type 2 diabetes mellitus patients in Benin City, Edo State, Nigeria, its association with C reactive protein and glycated haemoglobin and possible association with pathogenesis and development of complications in diabetics.

II. Materials and Methods

This was a cross-sectional study carried out in the state specialist Hospital, Benin City, Edo State, Nigeria, over a three months period. Forty-six type 2 diabetic patients, both male and female in the age range 38

and 83 years were recruited for the study. They were already diagnosed as type 2 diabetes mellitus patients, and attending the outpatient clinic of the hospital. They have been diabetic for a mean duration of 5 years and three months. They were recruited consecutively as they presented in the clinic, after obtaining their informed consent. Structured questionnaires were administered to the subjects to obtain socio-demographic data and medical history which included duration of disease, type of medications they were on, history suggestive of complications. General physical examination was performed on the patients, and parameters such as height and weight were measured with a stadiometer and weighing scale respectively. Blood pressure was measured with a sphygmomanometer. Twenty age and gender matched apparently healthy subjects were recruited as controls.

Inclusion criteria: Type 2 diabetes mellitus patients diagnosed according to the World Health Organization criteria.

Exclusion Criteria:

Patients with recent infections and infectious diseases, immunological disorders, smokers, malignancy, other inflammatory disorders were excluded from the study.

Sample collection:

8ml of overnight fasting blood sample was collected from the antecubital vein aseptically and dispensed into plain bottle for serum magnesium and C reactive protein estimation, ethylenediaminetetraacetate (EDTA) bottle for glycated haemoglobin, fluoride oxalate bottle for glucose assay. Urine was collected in a universal bottle for urine magnesium assay. Samples in the EDTA bottle were refrigerated immediately at 4⁰c, while that in the fluoride oxalate bottle were centrifuged at 3000 rpm for 5 minutes, and plasma separated into clean plain tubes and stored in an ultradfrizer at - 80⁰c until time of analysis. Samples in plain bottle was allowed to clot and then centrifuged for 5 minutes, serum was separated and stored in clean plain tubes until time of analysis.

Biochemical Assay:

Glycated haemoglobin was estimated with the boronate affinity method using the in-2-it Biorad system. Serum and urinary magnesium was assayed using the photometric calmagite dye method. Glucose and C reactive protein were assayed by the Glucose oxidase and latex based immunoturbidometric method.

Statistical analysis:

This was done using the SPSS version 17, means of variables are reported as mean ± standard deviation. Test of significant difference between means of variables was determined using the student "T" test and ANOVA. A value of ≤ 0.05 was considered significant. Pearson's correlation was used to determine correlation between variables.

III. Results

A total of 46 subjects participated in the study, of which 38.1% were males and 61.9% females, in the age range of 38 to 83 years. Mean age was 58.3± 1.2 years.

Mean fasting plasma glucose, glycated haemoglobin and body mass index and C reactive protein was 7.9 + 0.4mmol/L, 8.3 ± 2.1% and 27.6 ± 6.5 kg/m², 17.9 ± 1.3mg/L respectively (Table 1).

Serum magnesium in the subject and controls was 0.82 ± 0.2 mmol/L and 1.3 ± 0.2mmol/L respectively. Difference was statistically significant P<0.05 (Table 1) Urinary magnesium of subjects and controls was 1.5 ± 0.4mmol/L and 2.2± 0.7mmol/L respectively. (Table 1). Difference was statistically significant P<0.05

CRP showed a significant negative correlation with serum magnesium r = - .444, P< 0.05 (Table 2) (Fig. 1). Glycated haemoglobin correlated negatively with serum magnesium, but this was not statistically significant. r=-.222 P> 0.05. Prevalence of hypomagnesaemia (serum magnesium <0.6mmol/L) was 4.3%.

IV. Discussion

Diabetes has become a disease of global concern. Approaches to treatment and prevention requires constant updates and review, with a view of providing patients with optimal care.

Mean fasting plasma glucose, Glycated haemoglobin, C reactive protein in the subjects was significantly higher than in the controls. Similar observations have been reported by other authors^{12,13} and shows the derangements that occur in these parameters in type 2 diabetic mellitus patients.

Mean serum magnesium in this study was 0.8 ± 0.2 mmol/L. This is similar to the values reported by Seyum Berhane and co authors¹⁴, in their study in a diabetic population in Ethiopia. Other authors^{11, 15,16} have also reported these low normal serum magnesium values amongst diabetics.

Serum magnesium in the subjects was significantly lower than in the controls. Several studies have reported similar observations^{17,18,19}. Hussein F and co authors in their study, on type 2 diabetic patients in Pakistan⁷, reported that serum magnesium and zinc levels were significantly lower than in control subjects. Nsonwu AC and co authors²⁰ in Calabar, Nigeria also reported similar findings amongst diabetics studied. Also prevalence of hypomagnesaemia (serum magnesium <0.61mml/L) was 4.3%. Seyoum Berhane¹⁴ in Ethiopia reported a much higher value of 65%. It can be inferred from these findings that hypomagnesaemia and/or magnesium deficit seems to be a common finding amongst diabetics. The cause of hypomagnesaemia in

diabetics is multifactorial²¹, ranging from the osmotic actions of glycosuria and hyperglycemia, to reduced net tubular absorption of magnesium. Magnesium deficit including hypomagnesaemia and/or reduced dietary intake have been associated with increased risk of developing glucose intolerance and diabetes²¹, while magnesium intake is associated with a significant decline in the incidence of type 2 diabetes mellitus.²²

Deficient dietary intake may be a contributory factor to the findings of low serum magnesium compared with controls, and hypomagnesaemia in our study. The diet largely consumed in the urban population, where this study was carried out, maybe deficient in these micronutrients. Factors such as food processing, storage, preservation and mode of transportation, are all factors that affect the quality of food being consumed, apart from the nutrient deficient soil in which crops are grown. All these may play a role in the deficient dietary intake. Also lifestyle and social habits where consumption of grains, nuts, cereals may have been overtaken by consumption of fast foods may also be contributory.

Serum urinary magnesium was significantly higher in the subjects than in controls. Nsonwu A.C.²⁰ reported similar findings. This further highlights the fact that tubular absorption of magnesium is reduced in diabetics, and this causes magnesium loss in urine.

Serum magnesium showed a negative correlation with glycated haemoglobin, which was not statistically significant. However, Mohanty and coauthors⁵, Seedahmed JE²³ in their studies reported a significant negative correlation between serum magnesium and glycated haemoglobin. The finding seems to vary in different population, though hyperglycemia is known to cause tubular dysfunction.

A statistically significant negative correlation was observed between serum magnesium and C reactive protein. As magnesium levels reduced, C-reactive protein levels increased. Baig MSA et al⁹ reported similar findings amongst diabetics with or without complication in India. C Reactive protein is a marker of inflammation, and increasing serum CRP with reducing serum magnesium, could mean that serum magnesium deficit and/or hypomagnesaemia promotes inflammatory activities. Studies have shown that hypomagnesaemia has been associated with inflammation²¹. It has been reported to trigger the development of a proinflammatory state, by causing excessive production and release of interleukins, and elevating concentrations of neuropeptides that trigger activation of low grade chronic inflammation^{18,19}. C reactive protein is a measure of inflammation and is associated with cardiovascular risk in type 2 diabetes mellitus²⁴.

The low serum magnesium and 4.3% prevalence of hypomagnesaemia, and its association with increased levels of C reactive protein observed in the subjects studied, indicate that serum magnesium deficit is a challenge that needs to be tackled amongst diabetics. Both preventive and therapeutic measures are advocated. Preventive measures such as intake of diet rich in micronutrients especially magnesium, such as local Nigerian diet like guinea corn, semovita, millets, and fruits like banana, watermelon, pawpaw along with oral supplements by at risk individuals viz those in pre diabetic state, people with positive family history of diabetes.

Therapeutic measures in ensuring patients who are already diagnosed as diabetic and show magnesium deficit or hypomagnesaemia are treated with oral supplements, diet rich in micronutrients, along with other therapy, to prevent development of complications.

V. Conclusion

The Significantly low serum magnesium compared with controls and hypomagnesaemia in 4.3 % of subjects observed in this study, and its association with significantly raised C reactive protein, rising with reducing levels of magnesium, suggests that magnesium deficit and hypomagnesaemia may play a role both in the pathogenesis of type 2 diabetes mellitus, and the development of complications. Magnesium as both a preventive and therapeutic supplement is advocated.

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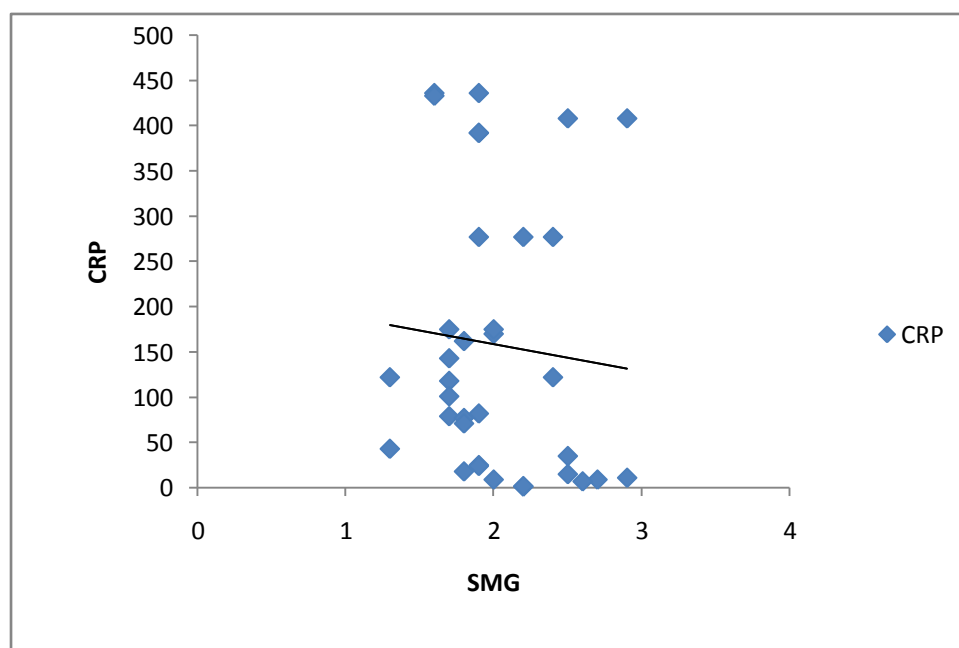
Table 1: Dermographic Characteristics and parameters in the subjects and control

Parameter	Subjects	Control	P value
Age (years)	58.3 ±1.2	56.1 ± 1.1	0.32
Male population (%)	38.1	40	
Female population (%)	61.9	60	
Body mass index (kg/m ²)	27.6 ±6.5	23.2±1	.063
Fasting plasma glucose (mmol/L)	7.9 ± 0.4	4.5 ± 1.1	0.001
Glycated haemoglobin (%)	4.5 + 1.0	8.3 ± 2.1	0.000
Serum magnesium (mmol/L)	0.8 ± 0.2	1.3 ± 0.2	<.001
Urine magnesium (mmol/l)	1.5 ± 0.4	2.2 ± 0.7	.001
C reactive protein (mg/L)	17.9 ± 1.3	10.3 ± 2.0	.005

Table 2: Correlation between Serum magnesium, glycated haemoglobin and C Reactive protein.

	Pearson's correlation (r)	P value
Glycated Haemoglobin	-. 222	.538
C Reactive Protein	-. 444	.003

Figure 1



Correlation between serum magnesium and C reactive protein in the subjects.