

SERUM MAGNESIUM AND SEVERITY OF DIABETIC RETINOPATHY

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ABSTRACT

Background: Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20–74 years. Magnesium deficiency is a possible metabolic factor involved in the pathogenesis of diabetic micro - and macro - vascular complications.

Aim: To assess magnesium level in relation to the stages of diabetic retinopathy.

Methods: The study enrolled 136 diabetic patients consulting Ophthalmology Outpatient Department. The ophthalmologist assigned the patients into 5 categories; background, preproliferative, proliferative, advanced and maculopathy. Serum magnesium, random blood glucose and glycated hemoglobin were determined.

Results: Among the 136 patients with diabetes mellitus, 94 patients had diabetic retinopathy and 42 had no retinopathy. There is a significant statistical differences (P-value <0.05) between diabetic retinopathy and control groups in serum magnesium, random blood glucose, glycated hemoglobin and duration of diabetes. It had been found that serum magnesium remained statistically significant among the groups of patients with different stages of retinopathy. Patients with maculopathy had the lowest value for the serum magnesium level (1.35 mg/dl)

Conclusions: Serum magnesium level decreased in patients with diabetic retinopathy with lowest level being observed in patients with advanced retinopathy and maculopathy.

INTRODUCTION

Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20-74 years.^[1] During the first two decades of the disease, nearly all patients with type 1 diabetes and > 60% of patients with type 2 diabetes have retinopathy.^[1] Diabetic patients had been found to have a lower mean plasma magnesium concentration than non diabetic control subject.^[2,3] Magnesium (Mg) deficiency is a possible metabolic factor involved in the pathogenesis of diabetic micro - and macro – vascular complications.^[4,5] Magnesium depletion has been linked to the development of retinopathy.^[6,7] In this study, we tried to assess magnesium level in association with the stages of diabetic retinopathy.

PATIENTS AND METHODS

The Study was carried out in the ophthalmology outpatient clinic, Basrah General Hospital. It enrolled 136 diabetic patients consulting Ophthalmology Outpatient Department. Indirect fundus bimirscopy was done for retinal examination after full pupillary dilatation with topical tropicamide 1% drop. The ophthalmologist assigned the patients into 5 categories depend on internationally accepted classification based on the presence of microaneurysm, oedema, exudates and new vessel formation; background, preproliferative,

proliferative, advanced and maculopathy.^[8] Venous blood samples were collected for estimation of serum magnesium and random blood glucose and glycated hemoglobin (HbA1c). Serum magnesium was determined using magnesium liquor kit supplied by Human Company, Germany, in which magnesium ion in alkaline medium forms a colored complex with Xylidyl Blue. The absorbance increased in proportion to the magnesium concentration in the sample.

Blood glucose was determined using glucose kit (Gluko-PAP) supplied by RANDOX Laboratories Ltd., United Kingdom in which glucose was determined after enzymatic oxidation in the presence of glucose oxidase.

HbA1c was measured using Bio-Rad VARIANT Hemoglobin A1c Program utilizes principles of ion-exchange High-Performance Liquid Chromatography (HPLC) for the automatic and accurate separation of HbA1c.

Statistical analysis were made using analysis of variance (ANOVA), Student's t test, P-value <0.05 was considered statistically significant. All data was analyzed with SPSS software (statistical Package for Social Sciences, version 15.0 for windows XP; SPSS, Inc, Chicago).

RESULTS

Among the 136 patients with diabetes mellitus, 94 patients had diabetic retinopathy and 42 had

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no retinopathy. (Table-1), shows a comparison between patients with diabetic retinopathy and those without in regard to age, blood glucose level, glycated hemoglobin (HbA1c), serum magnesium and duration of diabetes mellitus. There is a significant statistical differences (P-value <0.05) between diabetic retinopathy and control groups in serum magnesium, blood

glucose, glycated hemoglobin (HbA1c) and duration of diabetes. However, there is no difference in age between the two groups. The lowest concentration of serum magnesium was found in the group of diabetic retinopathy and in those had the longest duration of diabetes (Table-1).

Table 1. Comparison between diabetic retinopathy and control groups.

	Diabetic retinopathy N=94	No retinopathy N=42	P-value*
Age	52.7 (± 1.1)	51.9 (±1.4)	0.691
Random Blood glucose (mg/dl)	252.1 (± 64.2)	215 (± 72)	0.013
Serum magnesium (mg/dl)	1.54 (±0.21)	1.92 (±0.25)	0.001
Duration of DM (years)	12.5 (±8.1)	6.8 (±3.3)	0.023
Hb A1c (%)	9.3 (±1.5)	7.4(±0.79)	0.001

Data are expressed as mean ± SD.

*P< 0.05 was considered statistically significant

Patients with diabetic retinopathy were classified into 5 groups; background, preproliferative, proliferative, advanced and maculopathy. Then the studied parameters were compared among different groups. It had been found that serum magnesium, remained

statistically significant among the groups of patients with different stages of retinopathy (P-value <0.05) while blood glucose level and glycated hemoglobin (HbA1c) showed no significant difference between the groups (Table-2).

Table 2. Comparison of serum magnesium, blood glucose in diabetic patients with retinopathy.

	Background	Pre proliferative	Proliferative	Advanced	Maculopathy	P-value*
	n=12	n=8	n=30	n=16	n=28	
Random Blood Glucose (mg/dl)	277(±37.3)	185(±40.2)	254.6(±84.9)	259.6(±37.2)	258.2(±50.8)	0.095
Hb A1c (%)	10.1(±1.05)	7.8(±0.89)	9.4(±2.0)	9.5(±1.02)	9.3(±1.28)	0.090
Serum magnesium (mg/dl)	1.72(±0.10)	1.65 (±0.09)	1.61(±0.17)	1.54(±0.15)	1.35(±0.19)	0.001

Data are expressed as mean ± SD.

*P< 0.05 was considered statistically significant

As shown with table 2, patients with maculopathy had the lowest value for the serum magnesium level (1.35 mg/dl).

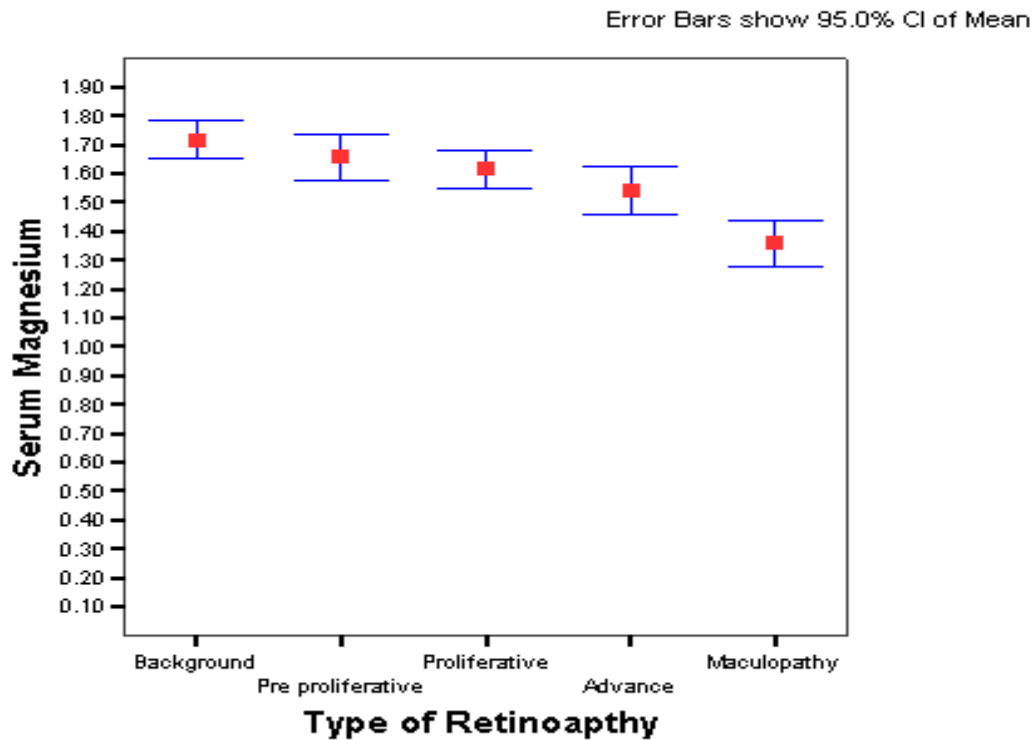


Fig 1. Serum Magnesium among patients with different stages of diabetic retinopathy.

DISCUSSION

Magnesium (Mg), is one of the most abundant intracellular ions with an essential role in fundamental biological reactions. Magnesium activates more than 300 enzymes in the body^[9] and is a critical cofactor of many enzymes in carbohydrate metabolism. Cellular magnesium deficiency can alter the activity of membrane bound sodium-potassium ATPase.^[9] Diabetes mellitus (DM), characterized by metabolic disorders related to high levels of serum glucose, is probably the most common disease associated with Mg depletion in intra and extra cellular compartments.^[10,11] Hypomagnesemia has been related, as a cause, to insulin resistance, also being a consequence of hyperglycemia, and when it is chronic, it leads to the development of macro and microvascular complications of diabetes, that worsens the deficiency of Mg.^[12] Hypomagnesemia, defined by low serum Mg concentrations, has been reported to occur in 13.5% to 47.7% of non hospitalized patients with type 2 diabetes compared with 2.5% to 15% among normal

subject.^[13] In diabetes, there is a direct relationship between serum magnesium level and cellular glucose disposal that is independent of insulin secretion. This change in glucose disposal has been shown to be related to increased sensitivity of the tissues to insulin in presence of adequate magnesium levels.^[14] Our observation revealed lower serum magnesium in patients with diabetic retinopathy in comparison to control group. These observations are similar to results of other workers.^[15] The results of the presented study showed that there were significant differences in the level of serum magnesium among different stages of retinopathy. These differences correlate negatively with advancing stages of retinopathy i.e. the more advanced the stage of retinopathy, the lower is the serum magnesium concentration. These findings are consistent with the study of Valk et al^[16] who observed a significant association between plasma Mg concentration and the development of background retinopathy but did not state the

association with the severity of retinopathy. Consequently hypomagnesemia seem to be as a possible risk factor in the development and progress of diabetic retinopathy. Hypomagnesemia was more pronounced in case of advanced retinopathy and diabetic maculopathy. These might be related to the mechanism of maculopathy which depends on leakage of microaneurysm that increases with increasing endothelial cell damage. Low Mg levels may promote endothelial cell dysfunction and thrombogenesis via increased platelet aggregation and vascular calcifications.^[17] Low Mg levels may also lead to induction of pro-inflammatory and pro-fibrogenic response^[18,19] and to reduction of protective enzymes against oxidative stress.^[20] Moreover, because Mg is crucial in DNA synthesis and repair.^[21] it is possible that Mg deficiency may interfere with normal cell growth and regulation of apoptosis. We, therefore, conclude that serum magnesium level decreased in patients with diabetic retinopathy with lowest level being observed in patients with advanced retinopathy and maculopathy.

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