



Study of Serum Magnesium levels in diabetic patients with and without retinopathy.

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ABSTRACT... Objectives: The aim of our study is to evaluate the possible association of serum magnesium in diabetic patients with and without retinopathy. **Study Design:** Cross-sectional observational. **Setting:** Bahawal Victoria Hospital, Bahawalpur. **Period:** September, 2018 to May, 2019. **Material & Methods:** A total of 258 subjects were enrolled in the study. They were divided in 3 groups, which comprised of 208 diabetic patients; 92 with retinopathy, 116 without retinopathy and the control group comprised of 50 healthy individuals. Both cases and controls were subjected to blood tests for the estimation of biochemical parameters. **Results:** A considerable decrease was observed in the serum magnesium level of diabetics in comparison with the healthy participants. The mean serum magnesium levels amongst the groups were 1.5 ± 0.2 mg/dl and 2.4 ± 0.3 mg/dl respectively ($p < 0.001$). There was also a marked variation in serum levels of magnesium among diabetic retinopathy patients and diabetics without complications i.e. 1.3 ± 0.1 mg/dl and 1.69 ± 0.1 mg/dl respectively ($p < 0.001$). **Conclusion:** Patients suffering from diabetic retinopathy displayed significantly lower serum magnesium levels in contrast to the control group and diabetics without retinopathy.

Key words: Complication, Diabetes Mellitus, Diabetic Retinopathy, Hypomagnesaemia, Serum Level.

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INTRODUCTION

The contributions of micronutrients as potential preventive and therapeutic agents are being investigated in patients of Diabetes Mellitus and their micro vascular and macro vascular complications.¹ Diabetic patients have found to suffer from abnormalities in their zinc, chromium, copper, magnesium and manganese levels.² The role of magnesium nowadays is of great scholarly and clinical interest in Diabetes Mellitus.

Magnesium, being the fourth most abundant cation in the human body, plays a significant part in the cellular metabolism and serves as a cofactor in the glucose transporting process of cell membranes of almost 300 cellular enzymatic systems.^{3,4} The recognition that change in the magnesium levels may result in significant clinical consequences has heightened interest in the utility of serum magnesium measurement. Hypomagnesemia is a common feature in

diabetic patients.⁵ The possible reason for this deficiency may be the necessity of magnesium for insulin receptor interaction, its secretion, post receptor events like tyrosine kinase mediated phosphorylation and carbohydrate utilization.^{1,6} If any of these functions are compromised, it leads to insulin resistance. This is contributed by a) Hyperglycemia, which leads to a further decrease in cellular Mg levels, independent of insulin levels, b) increase urinary Mg loss due to osmotic diuresis c) use of hypolipidemic agents and diuretics increasing urinary Mg loss.^{6,7}

Patients suffering from diabetes exhibit lower serum Mg levels in comparison to non-diabetics. Hypomagnesaemia has been reported in 13.5 to 47.7% of regularly visiting type 2 diabetics while these figures add up to 2.5 to 15% in non-diabetics.^{8,9}

Magnesium depletion can lead to the development

of retinopathy.^{3,4} Diabetic retinopathy is known to be one of the major causes of vision loss worldwide.¹⁰ Although the exact mechanism of microvascular changes and their progression is yet to be fully comprehended, it is most likely that decrease in serum magnesium inhibits the function of prostacyclin receptors producing an imbalance between thromboxane effect and prostacyclin. It has a marked atherogenic potential and is responsible for the microvascular complications.^{11,12}

Despite the fact that sufficient literature is available which links hypomagnesemia to diabetic complications; clinicians pay little attention to this matter. The association between hypomagnesaemia and diabetes mellitus can prove significantly beneficial in diabetic control and preventing complications. The main objective of this study was to estimate the prevalence of hypomagnesaemia in diabetics and to correlate the serum magnesium concentrations with retinopathy. As minimal work has been done on this domain in our setup, the findings of our study will benefit in better management of diabetic patients in the future.

MATERIAL & METHODS

Patients

Observational cross-sectional study was carried out in the Diabetic Clinic, Bahawal Victoria Hospital, Bahawalpur over a period of eight months from September, 2018 to May, 2019. Permission was taken from the ethical committee of the institute and an informed verbal consent was taken from cases and controls before commencing the study.

258 subjects were included in the study. They were further divided into the following groups:

Group I (Controls)

50 age and gender-matched healthy individuals.

Group II (Cases)

92 diabetic patients without retinopathy.

Group III (Cases)

116 diabetic patients with retinopathy.

Inclusion Criteria

Type 2 diabetic patients in the age group of 46 – 65 years, with and without retinopathy were selected.

Exclusion Criteria

Patients taking diuretics, magnesium containing antacids, magnesium supplementation or any other drugs known to affect magnesium levels.

Patients with renal failure, chronic diarrhea, malabsorption syndrome, liver diseases, tuberculosis, adrenal and thyroid dysfunction, pregnancy, lactation and sepsis.

METHODS

A detailed history was taken, together with the duration of diabetes and treatment mode. All symptoms suggestive of diabetic retinopathy were obtained as per the proforma, followed by a physical examination. As per WHO criteria, biochemical investigations were used to verify the diagnosis of type 2 diabetes mellitus.

Screening for retinopathy was done through the use of direct and indirect ophthalmoscopy and fundus photography, which was performed by an ophthalmologist, in all the cases of diabetes mellitus enrolled in the study.

Fasting venous blood samples were collected from cases and controls for the measurement of serum magnesium levels and blood glucose. The serum was separated by centrifugation and stored at 4°C.

Hexokinase/G6PDH enzymatic method was used for measuring blood glucose.

Fasting blood glucose level of <100 mg/dL was taken to be as normal glucose tolerance, 100-125 mg/dL as impaired glucose tolerance and >126 mg/dL as abnormal glucose tolerance.

HbA1c estimation was done by Turbidimetric Immuno-inhibition method.

HbA1c of <5.6% was taken as normal glucose tolerance, 5.7-6.4% as impaired glucose tolerance

and >6.5% as abnormal glucose tolerance.

Serum Magnesium was estimated by Xylidyl Blue, Colourimetric method. The serum magnesium level <1.8 mg/dL indicated hypomagnesaemia where normal range is 1.8-2.6 mg/dL.

All assays were run on Beckman Coulter AU2700 fully automated analyzer.

Statistical Analysis

Analysis of the data was done by SPSS version 24.0 whereas graphs and tables were generated by Microsoft Word and Excel. Chi-square and Student t-test (independent two-tailed) were used as the test of significance. Probability of P < 0.05 was considered significant.

RESULTS

Our study consisted of 92 diabetics with retinopathy, 116 diabetics without any complications and 50 healthy subjects. The purpose was to investigate the changes in the levels of serum magnesium. The average age

of the subjects in these groups was 52.6±7.6, 46.1±10.2 and 61.1±9.8 respectively. The gender distribution was almost equal among all groups. However, there was male preponderance in Group II.

All diabetic patients with retinopathy (Group III) have higher mean values of Blood Sugar (fasting), HbA1c and total urine proteins as compared to diabetic patients without retinopathy (Group II) and healthy controls (Group I). (Table-I)

Mean value of serum magnesium was found to be lower in cases with diabetic retinopathy (Group III), 1.3±0.1mg/dl, when compared with both the diabetic cases without retinopathy (Group II), 1.6±0.1mg/dl, and healthy controls (Group I), 2.4±0.3 mg/dl and was statistically significant (Figure-1).

Sr. Magnesium levels were negative correlated to HbA1c levels (r=-0.71, P < 0.01) and it had greater statistical significance in patients with diabetic retinopathy (Figure-2).

		Group 1 Controls N=50 (Mean±SD)	Group 2 Cases without retinopathy N=116 (Mean±SD)	Group 3 Cases with retinopathy N=92 (Mean±SD)
Age		52.6±7.6	46.1±10.2	61.1±9.8
Sex	Male	28	71	43
	Female	22	45	49
Duration		-	9.5±3.1	14.1±7.8
FBS (mg/dl)		93.5±8.5	168±15.2	220±19.4
HbA1c (%)		5.3±1.2	8.1±1.1	9.8±1.4
Mg (mg/dl)		2.4±0.3	1.6±0.1	1.3±0.1
Urine proteins total (mg/day)		40.5±4.6	302.4±26.2	421.1±31.2

Table-I. Demographic and laboratory features of the study groups:

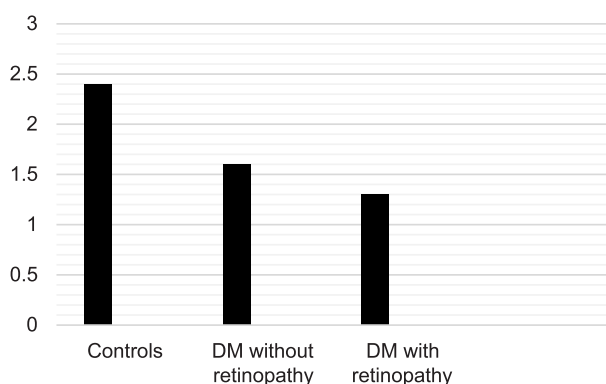


Figure-1. Serum Magnesium levels of the study groups.

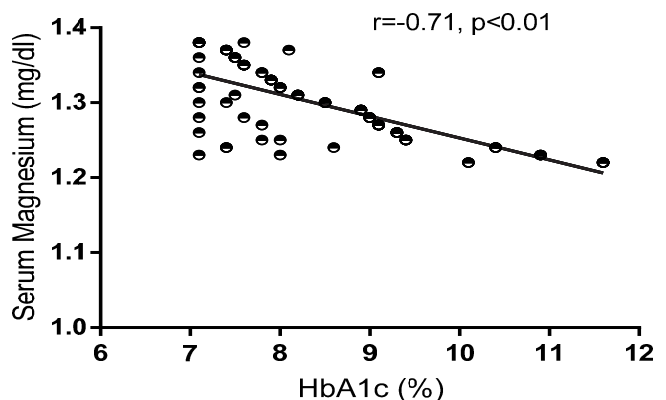


Figure-2. Correlation between serum magnesium and HbA1c in cases with diabetic retinopathy

DISCUSSION

This study included 208 diabetic patients; 92 with retinopathy and 116 without retinopathy, and 50 non-diabetics. Serum magnesium levels were determined in all the subjects.

In our study the diabetic patients ranged from 46 to 65 years of age. The mean age in cases and controls was 52.6 and 52.7 years respectively.

Maximum patients (56%) with diabetes mellitus were males and 44% were females. Sapuro et al¹ also reported that the prevalence of hypomagnesemia was more in males than in females. However, Ozawa et al found a higher incidence of diabetic retinopathy in females.¹³

In the present study, mean duration of diabetes in patients without retinopathy is 9.5 ± 3.1 years and with retinopathy is 14.1 ± 7.8 years. There is a substantial difference in the prevalence of hypomagnesaemia in accordance with the duration of disease ($p < 0.01$). The level of serum magnesium decreases as the duration of diabetes increases. These results are in conflict with other studies suggesting no association between the levels of serum magnesium and duration of diabetes.^{1,14,15}

Our study showed statistically significant negative correlation in serum Mg level and HbA1c ($P < 0.001$). It was similar to the results of two studies which concluded that hypomagnesemia was associated with poor glycemic control.^{15,16} The mean HbA1c level was higher in diabetic patients with retinopathy as compared to the patients without retinopathy ($P < 0.001$), which clearly shows that poorly controlled diabetes mellitus with higher HbA1c is associated with more micro vascular complications. A high affinity of HbA1c for oxygen may be related to tissue anoxia and diabetic retinopathy consequently.¹⁷

In this study, we found that the serum Mg level is significantly low in diabetic patients than in the healthy controls and hypomagnesemia is more prevalent in diabetics, as it was detected in all cases of this study. None of the healthy control had magnesium deficiency.

This is supported by many previous studies which have shown that the mean serum Mg levels are lower in both type 1 and type 2 diabetic patients, prediabetes and metabolic syndrome, compared with nondiabetic controls^{5-7,9} and in patients with diabetic complications.^{11,14} The prevalence of hypomagnesemia was high in the patients with diabetic retinopathy in the current study, as 90 (98%) of 92 patients with retinopathy had hypomagnesemia. It also showed that the serum Mg levels were a little higher in patients without retinopathy than in those with retinopathy (1.6 ± 0.1 vs. 1.3 ± 0.1 , respectively); and the difference was statistically significant.

These results are supported by various previous studies which found that diabetic patients with retinopathy had significantly lower serum magnesium than the patients without retinopathy.^{8,12,18,19} Baig et al^{4,14} found similar results and suggested that proposed mechanism of development of retinopathy and other microvascular complications of diabetes were due to hypomagnesemia. Diabetic patients without retinopathy had lower levels of sr. magnesium in present study. The patients who had retinopathy had the lowest levels of sr. magnesium. Therefore, not only in the present study but also in available literature, hypomagnesemia is suggested as a possible risk factor for diabetic retinopathy.^{4,20}

The urinary total protein was significantly higher in diabetic patients with retinopathy in contrast to the diabetics without retinopathy and healthy controls. Our results are in accordance with Rao et al²¹ which also indicate decreased urinary total proteins in patients with diabetic retinopathy. An inverse association was present between serum magnesium levels and urinary total proteins. Patients with retinopathy, suffering from diabetes mellitus type 2, had low serum magnesium levels and high levels of urinary proteins. These findings are in agreement with various studies conducted in the past.^{17,21}

CONCLUSION

It can be concluded that estimation of the serum magnesium level may lead to an early






recognition of complications like retinopathy in diabetic patients and provide hope for a timely intervention. However, more studies on serum magnesium levels and oral supplementation should be encouraged, to prevent chronic complications in diabetic patients.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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3	Hashim Raza	Research conception & Data acquisition.	
4	Saleha Zafar	Data analysis & interpretation.	
5	Sami Ahmad	Data acquisition & manuscript preparation.	
6	Riaz Ahmed Javed	Reserach conception & Design.	