SERUM MAGNESIUM LEVELS IN DIABETIC RETINOPATHY

Naveed Ahmed Shah, Muhammad Amir, Lubna Noreen*, Jamil Ahmed Shah, Rubina Habib***, Naveed Khan,
Yasser Nadeem**

Combined Military Hospital Lahore Pakistan, *Armed Forces Institute of Dentistry/National University of Medical Sciences (NUMS)
Rawalpindi Pakistan, **Fauji Foundation Hospital Rawalpindi Pakistan, ***Combined Military Hospital Quetta/ National University of
Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the serum magnesium levels in patients with diabetic retinopathy.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Department of Medicine, Combined Military Hospital Lahore, Six months from Nov 2014 to May 2015.

Patients and Methods: A total of 50 cases of type 2 Diabetes Mellitus were included in the study. Serum magnesium levels, fasting blood sugar and HbA1c were recorded in all patients. Retinopathy was confirmed by direct Ophthalmoscopy.

Results: In our study, out of 50 cases, 30% (n=15) were between 20-40 years of age while 70% (n=35) were between 41-65 years of age. Mean ± SD was calculated as 46.12 ± 7.76 years. Forty-six percent (n=23) were males and 54% (n=27) were females. Mean fasting blood sugar was calculated as 8.06 ± 0.49 mmol/L. Mean HbA1C was calculated as 7.11± 0.30 while mean serum magnesium levels were calculated as 1.15 ± 0.15 mg/dl.

Conclusion: Mean magnesium levels in patients with diabetic retinopathy were significantly lower than the magnesium levels that were taken as the reference suggesting a possible role of hypomagnesaemia in increasing the risk of retinopathy amongst patients with diabetes.

Keywords: Diabetes, Retinopathy, Serum Magnesium.

INTRODUCTION

Diabetes mellitus is one of the major health concerns in the world. Almost 250 million people suffer from it worldwide[1]. Ninty to ninty five percent of diagnosed cases of diabetes belong to type 2 diabetes[2]. In Pakistan also, its prevalence is increasing, with more than 13% of the population suffering from it[3]. Retinopathy, a complication of diabetes, is one of the leading causes of blindness in the world[2]. With different treatment modalities, its incidence can be decreased upto 90%[2]. Magnesium is the fourth most abundant cation in our body[4]. It is an important component of many foods such as grains, nuts and green leafy vegetables[4]. It is a critical co-factor in more than 300 enzymatic reactions, especially those related to energy metabolism[5]. Its deficiency is easily developed as it has poor absorption and

Correspondence: Dr Naveed Ahmed Shah, House No. 11, Street No 1-A, Sector D, DHA-II Islamabad Pakistan

Email:naveedahmedshah5@gmail.com

has a rapid turnover[6]. Magnesium levels are reported to be low at an increased frequency among patients with type 2 Diabetes[2]. This is mainly because insulin regulates the intra cellular magnesium concentration[7]. Various other causes include diets low in magnesium, osmotic diuresis leading to high renal excretion of magnesium, rampant use of diuretics causing magnesium wasting, diabetic autonomic neuro-pathies and reduced tubular reabsorption[8]. Thus hypomagnesaemia has been associated with poor glycemic control as well as with various long term complications of diabetes[8]. A study by Kundu *et al* labels hypomagnesaemia as a marker for risk of development of retinopathy in diabetic patients with mean magnesium levels of 1.30 ± 0.39 in patients with diabetic retinopathy[2]. Xu J observed association of magnesium levels and diabetic complications in Chinese population[4]. A similar association was previously revealed by Dasgupta A[8]. Thus low magnesium levels in diabetic patients can be used as a predictor of

development of diabetic complications. Investigations for magnesium levels are not carried out routinely. Our study was designed to estimate serum magnesium levels in type 2 Diabetes Mellitus with retinopathy so that magnesium levels can be used to prevent microvascular complications.

PATIENTS AND METHODS

This descriptive cross sectional study was carried out in Department of Medicine, Combined Military Hospital Lahore from Nov 2014 to May 2015. Using WHO calculator, sample sizewas calculated as follows :

- Level of confidence (%) = 95

- Population mean = 1.382

- Standard deviation = 0.392

- Absolute precision = 0.195

- Sample size = n = Approx 50 patients

A total of 50 cases with type 2 Diabetes Mellitus having HbA1c >6.5% and fasting blood sugar ≥7.0 mmol/L with retinopathy between 20-65 years, both males and females were enrolled in the study using consecutive, non-probability sampling technique. Study was started after taking approval from ethical review committee of the institute. Consent form was signed by each patient. All the data and procedures were entered in the proforma by the researcher. Patients diagnosed with type 1 Diabetes Mellitus or Gestational Diabetes, patients on drugs known to affect magnesium levels (like Aminoglycosides, Amphotericin B, Cyclosporine, Diuretics, Digoxin and Cetuximab), patients with serum creatinine >1.5 mg/dl were excluded from the study. Patients with acute or chronic malabsorption states, thyroid or adrenal dysfunction, recent metabolic acidosis, pregnancy, lactation or sepsis and history of alcohol intake or vitamin or mineral supplements in recent past were also excluded from the study. Blood samples were collected for Serum magnesium levels, HbA1c and fasting blood glucose levels. The levels of Serum Magnesium were determined using photometric xylidyl blue method and HbA1c was determined using the standard immunoinhibition method. The biochemical levels were measured at CMH Lahore laboratory and verified by Pathologist. Direct Ophthalmoscopy was used for diagnosing retinopathy. A diagnosis of retinopathy was made if patient had microaneurysm, dot and blot haemorrhages, flame shaped haemorrhages, cotton wool spots, hard exudates or neovascularization on direct ophthalmoscopy. Statistical analysis were performed using SPSS version 22. Continuous data (like serum magnesium, FBS and HbA1c) was expressed as mean ± standard deviation (SD), and categorical data (like age, gender) as percentage (%). Distribution of the study variables were assessed using histograms. Univariate tests of the differences were carried out between age groups and gender using the independent samples. Independent t-test was performed for comparing continuous variables. Confounding variableslike age and genderwere controlled by stratification. A p-value <0.05 was considered significant.

RESULTS

We studied 50 Pakistani men and women fulfilling the inclusion/exclusion criteria to determine mean magnesium levels in diabetic patients with retinopathy. Clinical characteristics of the participants showed that out of 50 participants, 30% were between 20-40 years of age while 70% were between 41-65 years of age. Mean age of the participants was 46.12 ± 7.76 years. Results are presented intable-I. The proportion of male and female participants was approximately equal. Results showed that 46% were male and 54% were females (table-II). Results from the analysis of biochemical measures revealed that mean fasting blood sugar and HbA1c was higher in these participants (table-III). Fasting blood sugar was 8.06 ± 0.49 mmol/L while the mean HbA1C was calculated as 7.11 ± 0.30. On the other hand, the mean serum magnesium levels were calculated as 1.15 ± 0.15 mg/dl (table-III) which was much lower than the normal serum magnesium levels (reference range = 1.6-2.6 mg/dl). Mean serum magnesium levels

were similar amongst the participants aged 20-40 years and 41-65 years (1.15 ± 0.14 vs. 1.15 ± 0.16 respectively, *p*-value=1, table-IV). There was no difference in mean serum magnesium levels between males and females. The mean serum magnesium levels were calculated as 1.13 ± 0.16 in male and 1.17 ± 0.15 in females (*p*-value=0.895) (table-V).

association between diabetes mellitus and hypomagnesaemia is compelling for its wide ranging impact on diabetic control and complications. Magnesium depletion has been linked to the development of retinopathy. Although it is generally believed that strict metabolic control delays the development of late complications in diabetes mellitus, it has not been demonstrated

Table-I: Age Distribution of participants with diabetic retinopathy (n=50).

Age (years)	No. of patients	Percentage (%)
20-40	15	30
41-65	35	70
Total	50	100
Mean ± SD	46.12 ± 7.76	

Table-II: Gender distribution of particpants with diabetic retinopathy (n=50).

Gender	No. of patients	Percentage (%)
Male	23	46
Female	27	54
Total	50	100

Table-III: levels of Biochemeical Parameters amongst Patients with Diabetic Retinopathy(n=50).

	Mean	SD
Fasting blood sugar (mmol/L)	8.06	0.49
HbA1c (%)	7.11	0.30
Serum magnesium (Magnesium/dl)	1.15	0.15

Table-IV: Comparison of mean serum magnesium levels between the two age groups (n=50)

Age (in years)	Serum magnesium (Magnesium/dl)	
	Mean	SD
20-40	1.15	0.14
41-65	1.15	0.16

p-value=1

Table-V: Comparison of mean serum magnesium levels between males and females (n=50).

Gender	Serum magnesium (Magnesium/dl)	
	Mean	SD
Male	1.13	0.16
Female	1.17	0.15

p-value=0.895

DISCUSSION

Magnesium is a cofactor in more than 300 cellular enzymatic systems and has a key role in cellular metabolism. The recognition that Magnesium deficiency or excess may be associated with significant clinical consequences has resulted in an increased interest in the utility of serum Magnesium measurement. The

conclusively that such controls holds back the development of diabetic retinopathy. We planned this study with the view to prove that estimation of magnesium levels in type 2 diabetes is significant to prevent retinopathy and that this test should be made a routine and Magnesium supplements should be given to prevent microvascular injury. In other words, diabetic

patients with hypomagnesaemia should have close ophthalmologic follow up and should receive Magnesium supplements. Our study reported significantly low levels of serum magnesium in patients who developed diabetic retinopathy. These findings were comparable to the published research that identified hypomagnesaemia as a risk factor for development and progression of retinopathy in patients with type 2 diabetes. The exact cause of hypomagnesaemia is not known. However some studies suggest that an increased urinary loss of magnesium may contribute to hypomagnesaemia in patients with type 2 diabetes. On the other hand, some research studies revealed that hyperglycemia causes depression in the net tubular reabsorption of magnesium leading to hypomagnesaemia. The findings of our study were in agreement with a study by Kundu *et al* which labelledhypomagnesaemia as a marker for risk of developing retinopathy in diabetic patients, with mean magnesium levels of 1.30 ± 0.39 in patients with diabetic retinopathy[2]. Xu J observed association of magnesium levels and diabetic complications in Chinese population[4]. A similar association was previously revealed by Dasgupta A[8]. Hatwal *et al* studied the association of hypomagnesaemia with diabetic retinopathy and found that serum magnesium levels were significantly lower in diabetic retinopathy than in those without diabetic retinopathy. Ishrath Kareem *et al* found that serum magnesium levels in patients with diabetic retinopathy were significantly lower compared to patients without retinopathy[9] Sharma *et al* also found that serum magnesium levels were significantly lower in patients with diabetic retinopathy when compared to diabetic patients without retinopathy[10]. Dipankar Kundu and others[11] carried out a study to see the correlation between serum magnesium levels, glycosylated hemoglobin and urinary total protein levels in diabetic patients with retinopathy and concluded that hypomagnesaemia and albuminuria individually or in conjunction serve as indicators for dysglycemia and could be used as

marker for the risk of development of diabetic retinopathy.

Haddad and others[12] assessed magnesium level in relation to the stages of diabetic retinopathy and recorded that among the 136 patients with diabetes mellitus, 94 patients had diabetic retinopathy and 42 had no retinopathy. There was a significant statistical differences (*p*-value <0.05) between diabetic retinopathy and control groups in serum magnesium levels, 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 serum magnesium level (1.35 Magnesium/dl). They concluded that serum magnesium levels were decreased in patients with diabetic retinopathy with lowest level being observed in patients with advanced retinopathy and maculopathy. Valk *et al*[13] who observed a significant association between plasma Magnesium concentration and the development of background retinopathy but did not state the association with the severity of retinopathy. However, in light of the current study and other studies, it is clarified that diabetic patients with hypomagnesaemia should have close ophthalmologic follow up and should receive Magnesium supplements. The limitation of our study was that, we did not include any control group, which could enable us for more accurate comparison, however, in coming trials it may be done for validation of our results.

CONCLUSION

We concluded that mean magnesium levels in patients with diabetic retinopathy were significantly lower than the magnesium levels taken as reference, suggesting a possible role of hypomagnesaemia in increasing the risk of retinopathy amongst patients with diabetes. Hypomagnesaemia in patients with diabetes should have close ophthalmologic follow up and should receive Magnesium supplements.

CONFLICT OF INTEREST

This study has no conflict of interest to declare on any author.

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