A comparative study of serum magnesium in type 2 diabetes mellitus with and without retinopathy and healthy controls and its correlation with glycemic status

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Abstract

Background: Type 2 diabetes mellitus(DM) is a disease of impaired carbohydrate metabolism. The onset of uncontrolled hyperglycemia causes various microvascular complications such as retinopathy and nephropathy. The present study aimed to see the effect of serum magnesium on glycemic control in the presence of retinopathy and to show their role in pathogenesis.

Objectives: The study was designed to estimate and compare serum magnesium levels in cases of type 2 diabetes mellitus with and without retinopathy and healthy controls. A correlation of serum magnesium was done with glycosylated hemoglobin in diabetics with retinopathy and without retinopathy.

Materials and methods: It was a case control study. The study included 60 cases of clinically diagnosed type 2 DM with retinopathy, 60 cases of type 2 DM without retinopathy and 60 matched healthy controls. Venous blood sample was analyzed for fasting blood sugar(FBS), post prandial blood sugar (PPBS), serum magnesium and glycosylated hemoglobin(HbA1c) in both cases and controls. Statistical analysis was done using student 't' test. Pearson's correlation was performed to establish the relationship between study variables.

Results: There was significantly decreased levels of serum magnesium (p<0.001) in cases of retinopathy as compared to the controls. There was highly significant negative correlation between serum magnesium and glycosylated hemoglobin (HbA$_1$c) in cases of DM with retinopathy.

Conclusion: The severity of diabetic retinopathy in the study group was influenced by factors such as good glycemic control and hypomagnesemia. These parameters could be used as a supportive diagnostic tool in type 2 DM.

Key words: Diabetic retinopathy, Type 2 DM, Magnesium, glycosylated hemoglobin

Introduction

Type II Diabetes Mellitus (DM) is a metabolic disorder primarily characterized by hyperglycemia. It is caused by insulin resistance and/or relative insulin deficiency[1]. Chronic hyperglycemia is a major initiator of microvascular complications, including nephropathy, retinopathy and neuropathy[2]. Diabetic retinopathy is one of the dangerous complication of DM and also is a leading cause of acquired blindness in adults. Several risk factors are related to the development and progression of retinopathy such as the duration of DM, poor glycemic control, dyslipidemia, hypertension and hypomagnesemia[3,4].

Many hypothesis have been proposed to explain the pathogenesis of type 2 DM and its complications that connects the disease to a state of subclinical chronic inflammation[5]. Metabolically triggered inflammation has been proposed to be a key step in the pathogenesis of type 2 DM[6]. Apart from this, the metabolism of several minerals has been reported to alter in DM and these elements might have specific roles in the pathogenesis and progression of this disease. Of these minerals, magnesium is the important one. Magnesium is the fourth most abundant caution in the body and second in the intracellular environment. It takes part in more than 300 enzymatic reactions. Magnesium is a cofactor in phosphorylation of glucose, and it helps in carbohydrate metabolism[7].

Studies on this parameter have been done in other areas but very few in our locality. Hence, we conducted this study with following aims-

1) To estimate serum magnesium levels in cases of type 2 DM with and without retinopathy and to compare it with healthy controls.
2) To correlate serum magnesium levels with HbA1c in patients with type 2 DM with retinopathy.

Materials and methods

Study participants: This was a case control study. The study was carried out on 60 cases of clinically diagnosed type 2 diabetes mellitus with retinopathy, 60

cases of type 2 diabetes mellitus without retinopathy attending the Opthalmology OPD at SNMC and HSK hospital , Navanagar, Bagalkot. Sixty (60) age and sex matched healthy subjects were taken as controls. The study was conducted over a period of one year from Jan 2013 to Dec 2013. Ethical clearance was obtained from the institute's ethical clearance committee. Informed consent was taken from the cases and controls after explaining the procedure. Diabetes Mellitus was diagnosed as per the WHO diagnostic criteria[8]. Retinopathy was diagnosed by fundus examination under mydraisis of both eyes using opthalmoscope and 90 D lens[9].

Patients of DM with other microvascular complications, individuals with severe inflammatory diseases, infections, cardiac, hepatic or renal diseases were excluded from the study. Patients on diuretics, individuals receiving magnesium supplements, individuals taking drugs that affect blood glucose levels, pregnant and lactating women were also excluded.

Based on the analysis of medical history, clinical examination and investigation results, the patients were grouped into type 2 DM with and without retinopathy.

Biochemical analysis: A sample of 3 ml venous blood was collected in both fasting and post prandial state under aseptic precautions. It was allowed to clot and serum was separated by centrifugation.
The following parameters were studied.

1. FBS and PPBS –Glucose oxidase peroxidase method[10,11]. (kits supplied by Erba Diagnostics)
2. Serum Magnesium-Xylidyl Blue method[12,13]. (Kit by Raichem Diagnostics). All the parameters were read using semi auto analyser (STAT FAX 3300).
3. HbA1c was estimated by Nycocard reader II[14].

Data was expressed in terms of mean ± SD. Chi-square test was applied to estimate the difference between the two groups of population. Unpaired 't'-test was used to study the changes in serum magnesium levels between the study groups. Pearson correlation between the study variables was performed to establish the relationship between study variables. p value <0.05 was considered statistically significant.

Results

This was a comparative case control study conducted on 60 cases of type 2 DM (n=60) with retinopathy, 60 cases of type 2 DM without retinopathy (n=60) and 60 healthy controls (n=60). Serum magnesium was estimated, analyzed and correlated with HbA1c. The results were expressed as mean ± standard deviation.

The age distribution of cases and controls is depicted in **Table 1.** The mean age (in years) of cases with retinopathy was 54.00±10.15, cases without retinopathy was 50.88±10.11 and that of controls was 52.60±8.13 and was statistically non-significant.

Table 2 shows the gender distribution. Out of 60 cases of retinopathy, 31(52%) were males and 29(48%) were females. Out of 60 controls, 30(45 %) were males and 30(45%) were females and it was not statistically significant (p=0.38).

The mean serum magnesium (mg/dL) in cases of retinopathy was 1.970 ± 0.41, in cases without retinopathy was 2.07± 0.45 and in controls was 2.79 ± 0.47 and was highly significant (p < 0.0001) **(Table 3, Fig. 1).**

Serum magnesium and HbA1c: There was negative correlation between serum magnesium and HbA1c. r = - 0.51, p < 0.0001 and was highly significant **(Fig. 3).**

Table 1: Age distribution of cases and controls

Age in years	Diabetic with retinopathy		Diabetic without retinopathy		Controls	
	N	%	N	%	N	%
≤ 35	1	2	0	0	0	0
36-45	17	28	23	39	17	28
46-55	17	28	17	28	22	37
56-65	18	30	17	28	20	33
≥ 66	7	12	3	5	1	2
Total	60	100	60	100	60	100

Table 2: Gender distribution of cases and controls

Gender	Diabetic with retinopathy -n (%)	Diabetic without retinopathy -n (%)	Controls - n (%)
Male	31(52)	33(55)	30(45)
Female	29(48)	27(45)	30(45)

X^2= 4.165   p= 0.38, Not significant

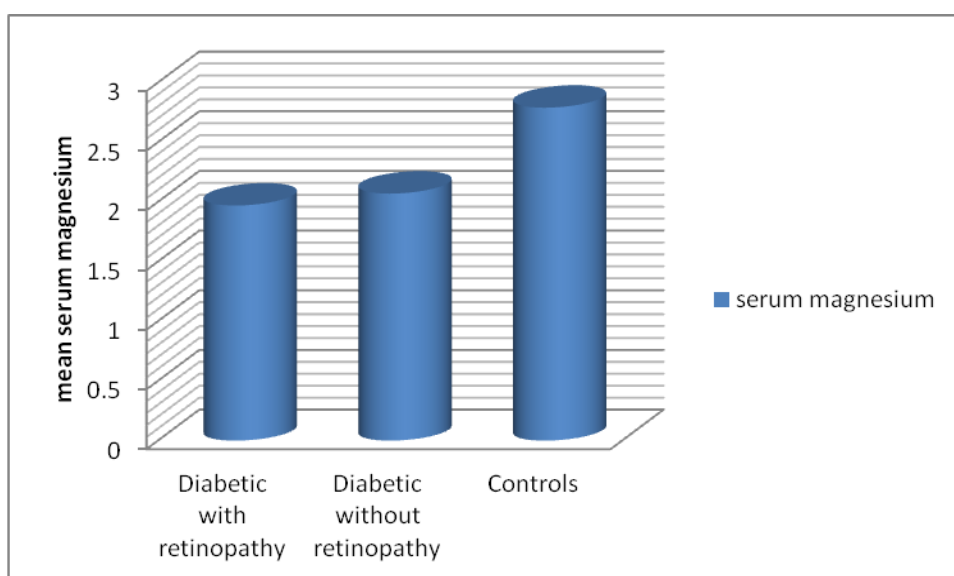**Table 3: Comparison of serum magnesium (mg/dl) levels between control and diabetic retinopathy**

	DM with retinopathy	DM without retinopathy	Controls
Serum magnesium(mgdL)	1.970 ± 0.41	2.07± 0.45	2.79± 0.47

DM-Diabetes Mellitus

Table 4: Comparison of FBS, PPBS, and HbA1c in study groups

Study variables	Cases with retinopathy	Cases without retinopathy	Controls	p value
FBS(mg/dL)	196.50 ± 66.5	187.48 ± 67.9	93.46 ± 13.72	0.001
PPBS(mg/dL)	297.90 ± 80.32	280.90 ± 84.23	122.18 ± 10.20	0.001
HbA1c	8.6 ± 1.3	8.2 ± 1.02	5.30 ± 0.63	0.001

FBS-Fasting Blood Sugar, PPBS- Post Prandial Blood Sugar, HbA1c-Glycosylated hemoglobin

Fig. 1: Comparision of serum magnesium in between the groups
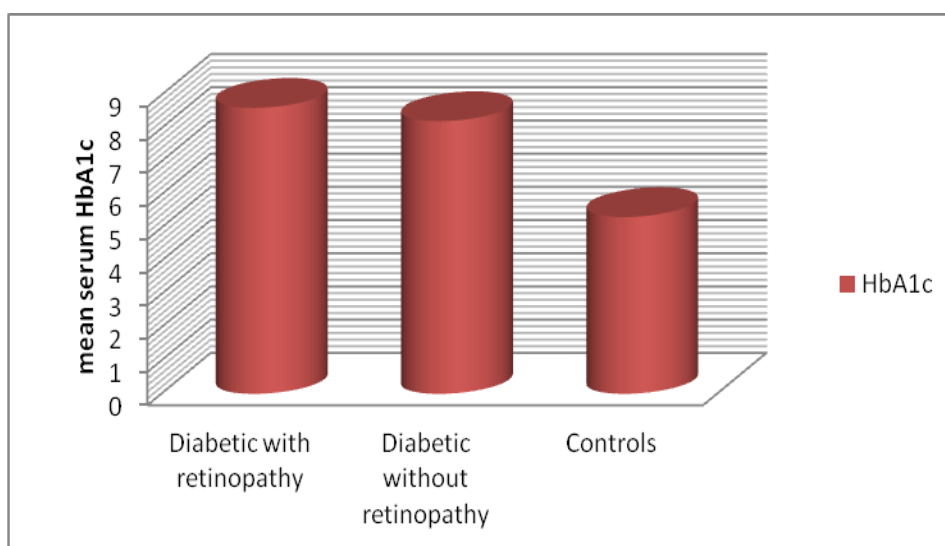
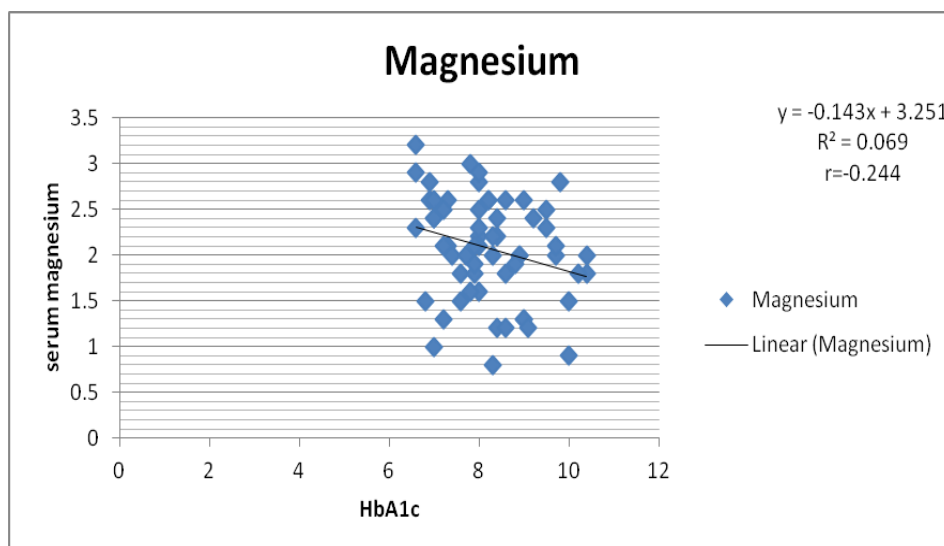**Fig. 2: Comparison of HbA1c levels between groups**

Fig. 3: Correlation between HbA1c and magnesium in cases of diabetic retinopathy

Discussion

Diabetes mellitus is an endocrinological disease having high metabolic and oxidative stress. Diabetic retinopathy is a important microvascular complication of uncontrolled diabetes mellitus and is one of the leading causes of acquired blindness. Findings show that oxidative stress has the greatest role in development of the complications. Many risk factors have been related to the development and progression of retinopathy in diabetic patients.

Many trace elements are important for human metabolic function. Numerous studies have demonstrated the essential roles of elements such as magnesium in carbohydrate metabolism[15]. In view of this, the present study had been taken up to assess clinical utility of serum magnesium as a promising biochemical marker, which is inexpensive and can be of some diagnostic and prognostic significance.

In this case control study, we have compared serum magnesium in 60 cases of DM with retinopathy, 60 cases of DM without retinopathy and 60 matched healthy controls. The significance of this parameter between the groups, its diagnostic value and correlation with HbA1c is analysed and discussed.

In our study, the mean FBS (mg/dl) values were 196.56 ± 66.53 in cases of DM with retinopathy, 187.48 ± 67.90 in cases of DM without retinopathy and 93.46 ± 13.7 in controls respectively which is statistically highly significant (p<0.001). FBS values were higher than the cut off value of 110mg/dL in cases which correlated well with the clinical diagnosis. Similarly the mean PPBS (mg/dL) values were 297.94 ± 80.32 in cases of diabetic retinopathy, 280.92 ± 84.24 in cases of DM without retinopathy and 122.18 ± 10.20 in controls respectively which is statistically highly significant (p<0.001). PPBS values were higher than the cut off value of 200 mg/dL in cases which correlated well with the clinical diagnosis.

In our study the mean HbA1c values were 8.6 ± 1.31 in cases of diabetic retinopathy, 8.22 ± 1.02 in cases of DM without retinopathy and 5.5 ± 0.63 **(Fig. 2)** in controls respectively which is statistically highly significant (p<0.001). The values in this study are in accordance with several other studies[16,17].

Serum magnesium: In our study there were statistically decreased levels of serum magnesium in cases (p < 0.0001). Similar results were seen in many other studies[15,18,19,20,21]. Hence hypomagnesemia acts as a possible risk factor in the development and progression of diabetic retinopathy. The exact cause of diabetic hypomagnesaemia is still unknown but an increased urinary loss of magnesium may contribute to it. Two factors may work together in this respect namely, the osmotic action of glucosuria and the hyperglycemia per se, the latter being known to depress the net tubular reabsorption of magnesium in normal man. Other studies have documented that the oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 DM[19,20,21].

In the current study, we found highly significant negative correlation between serum magnesium and HbA1c levels(r= -0.24, p<0.0001). This result is supported by previous studies[22,23] who found significantly elevated HbA1c levels and serum magnesium.

Conclusion

Serum magnesium levels were significantly decreased in cases of diabetic retinopathy thus suggesting the role of inflammation, oxidative stress in the development of complications of DM. Hypomagnesaemia correlated significantly with HbA1c. Estimation of serum magnesium, HbA1c can help us predict the onset and progression of diabetic retinopathy and hence

they should be a part of the screening panel in the risk detection and progression of diabetic complications.

Increasing magnesium intake may be important for improving insulin sensitivity, reducing systemic inflammation and decreasing diabetes risk.

Magnesium supplementation in addition to other nutritional treatment, may prove beneficial in delaying the further progress of diabetic retinopathy and other complications. Further studies on a larger sample are needed to substantiate our findings before firm conclusion can be drawn on the utility of these parameters for the diagnostic assessment of diabetic complications such as retinopathy.

Acknowledgement

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