Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

A study to assess serum magnesium level in type 2 DM

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Received Date: 19/09/2023 ***Acceptance Date: 03/10/2023***

Abstract
Background: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia. Diabetes is considered a lifestyle disease and diet plays an important role in the development of DM and its associated complications. It is claimed that there is an inverse relationship between Mg intake and incidence of diabetes mellitus (DM)2. Mg deficiency is common in diabetic patients. Magnesium deficiency may lead to decreased synthesis of glutathione thereby enhancing the process of lipid peroxidation. The free radical mediated lipid peroxidation (oxidative stress) has also been implicated in the pathogenesis of diabetes mellitus. **Methodology**- The study was conducted on 70 patients of type 2 diabetes mellitus admitted to GIMS, Kalaburagi between January 2020 and December 2021. Also 70 non diabetic patients admitted during the same period were included in the study under the control group. Patients were considered to be diabetic based on WHO criteria for diagnosis of diabetes mellitus. All the necessary investigations were done. Estimation of serum magnesium was done and the results were interpreted. **Results**- The mean serum magnesium was 1.65 mg/dl and 1.99 mg/dl in diabetics and control respectively. The mean serum magnesium level in patients on OHA was 1.99 mg/dl on insulin was 1.59 mg/dl and in patients on both OHA and insulin was 1.26 mg/dl. The serum magnesium in patients who had diabetes under control was 1.75 mg/dl and that in whom it was uncontrolled was 1.23 mg/dl. **Conclusion**- Hypomagnesemia is a factor in type 2 diabetes mellitus patients leading to various complications. Hence, it is worthwhile estimating magnesium levels in type 2 diabetes mellitus patients and probably correlates their relationship with various complications.

Keywords-Diabetes, magnesium, DM, Hypomagnesemia, deficiency
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Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia. Type 2 diabetes mellitus (T2DM) constitutes 90% of all DM cases and is characterized by progressive insulin secretory defect associated with insulin resistance.[1] It is a growing public health burden across the world, particularly in the developing countries. Indians have a high ethnic and genetic susceptibility for the disease and also have lower threshold limits for the environmental risk factors. Indians develop T2DM at a younger age is a matter to be concerned compared with western populations. They also develop diabetes with minor weight gain.[2] Diabetes is considered a lifestyle disease and diet plays an important role in the development of DM and its associated complications. These complications can be either microvascular (retinopathy, neuropathy, nephropathy) or macro vascular (coronary heart disease, peripheral arterial disease, cerebrovascular disease) or both.[3] Although the clinical manifestations of diabetes complications are varying, but some common pathophysiological characteristics exist in these syndromes, trace elements are one of the

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

important factors.[4] There are various studies to substantiate on the potential prevention or treatment of trace elements for types 1 and 2 diabetes mellitus and their common complications.[5]

Magnesium ion is the second most important intracellular cation, after potassium ion and is the fourth most abundant cation in the human body and plays a key role in many fundamental biological processes, including energy metabolism and DNA synthesis. [6] Magnesium is mainly absorbed in the small intestine and is excreted through the kidney.[7] Kidney can help the plasma magnesium concentration to maintain a normal level at 1.7– 2.4 mg/dl.[5] The normal reference range for Mg2+ in the serum is 0.76–1.15 mmol/L. Magnesium deficiency (Mg D) is a condition where the serum concentration of Mg2+ in the body is less than 0.75 mmol/L (1.8 mg/dL).[8] Patients are considered frankly hypomagnesemia with serum Mg2+ concentrations are less than 0.61 mmol/L (1.5 mg/dL).[6] Magnesium modulates glucose transport through the membrane and it is a cofactor in several enzymatic reactions involving glucose oxidation.[9] Its deficiency has been implicated in insulin resistance, carbohydrate intolerance, dyslipidaemia, and complications of diabetes. [3] It is claimed that there is an inverse relationship between Mg intake and incidence of diabetes mellitus (DM)2. Mg deficiency is common in diabetic patients. The incidence of hypomagnesemia varies between 11 and 47.7%3-7. Compared with the control group, incidence of hypomagnesemia in newly diagnosed diabetes is 10.5-fold and in patients with previously diagnosed diabetes is 8.5-fold more common.[10] Microalbuminuria (MA) was first described in diabetic patients in 1982. It was shown to be associated with increased risk of cardiovascular morbidity and mortality in diabetic patients. At the same time, it is accepted as an indicator for the presence of diabetic retinopathy/ neuropathy, cardiovascular and peripheral vascular disease and increased mortality. The presence of MA and overt proteinuria in non-insulin dependent diabetes mellitus (NIDDM) is an indicator of poor glycemic control as well as poor glycemic control; insulin resistance and low Mg level strongly associated with increased the prevalence of MA13.[10] An important study by Kao *et al.* shows that the relationship between magnesium and glucose metabolism is obvious. Magnesium deficiency may lead to decreased synthesis of glutathione thereby enhancing the process of lipid peroxidation. The free radical mediated lipid peroxidation (oxidative stress) has also been implicated in the pathogenesis of diabetes mellitus, mainly through the role of magnesium in mediating the effects of glutathione on peripheral insulin action.[11]

The above study was conducted to assess the serum magnesium levels in type 2 Diabetes Mellitus patients.

Materials And Methods

Study place- The study was conducted at the Gulbarga Institute of medical Sciences Hospital, Kalaburagi from January 2020 and December 2021.

Study design- Comparitive study.

Inclusion criteria- Patients having urine sugar positive, fasting blood sugar >126 mg/dl, ready to give informed consent for participation.

Exclusion Criteria-Patients who were diabetics, who had associated hypertension, gastrointestinal disorders, impaired renal function, alcoholism pancreatitis, other endocrinal disorders and those on diuretic therapy, aminoglycosides and iatrogenic administration and those who refused to give informed consent.

Sample size- 70 patients of type 2 diabetes mellitus. Also 70 non diabetic patients admitted duringthe same period were included under the control group.

Data analysis- Data was analyzed using the Microsoft SPSS 18. Version and Systat 10.0 were used for the analysis of the data. Microsoft word and Excel have been used to generate tables .

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Ethical considerations- The Institutional Ethics Committee permission was taken before beginning the study.

Patients were considered to be diabetic based on WHO criteria for diagnosis of diabetes mellitus which is as follows-

- Symptoms of diabetes mellitus plus a random glucose concentration > 200 mg/dl (11.1mmol/l). The classic symptoms of DM include polyuria, polydipsia, and unexplained weight loss.
- Fasting blood glucose >126mg/dl(7.0mmol/l). Fasting is defined as no caloric intake for at least 8 hours.
- 2-hour post prandial glucose >200mg/dl. Among diabetics, the above criteria were considered to be included for the study.

Those patients who had persistent FBS levels >126 mg% in spite of therapy during hospital stay were grouped as uncontrolled diabetics. Estimation of serum magnesium was done by Colorimetric method using calmagite dye.

Test procedure:

Pipette into test tubes	**Blank**	**Standard**	**Test**
Magnesium working reagent	1.0 ml	1.oml	1.0ml
Standard	-	10µL	-
Distilled water	10µL	-	-
Sample	-	-	10µL
Mix and incubate at room temperature (22-28 C) for 10 min. read the absorbance of the test (AT), standard (AS) and blank (AB) against distilled water at 530 nm.			

Calculations

Magnesium concentration (mEq/lit) =

Interfering substances:

Hemolyzed, grossly icteric or lipemic specimens are unsuitable for this method.

Linearity

4 mEq/L (4.86 mg/dl)

Normal values-

Adults- 1.3-2.5 mEq/L

Children-1.4- 1.9 mEq/L

New born-1.5-2.3 mEq/L

Results

Table 1: Age distribution of cases & controls

Age in years	**Cases**		**Controls**	
	Number	%	Number	%
□ 40	3	4.28	3	4.28
41-50	29	41.42	29	41.42
51-60	15	21.42	15	21.42
61-70	6	8.57	6	8.57
71-80	16	22.85	16	22.85
≥ 81	1	1.42	1	1.42
Total	70	100	70	100
Mean □ SD	55.90□12.90		56.60□13.25	

The mean age of the diabetics was 55.90□12.90 years whereas it was 56.60□13.25 years

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respectively. Among the cases the sex distribution was same i.e., 63% and 37% males and females respectively and among the controls sex distribution was 39% and 61% respectively. The maximum number of patients was in the age group of 41-50 i.e., 43%.

Table 2: Mean Pattern of FBS and S. creatinine

FBS/S. Creatinine (Mean □ SD)	**Cases**	**Controls**	**P value**	
FBS (mg/dl)	230.74□91.59	99.23□10.12	P<0.0001	Student t=11.94,
Serum Creatinine (mg/dl)	0.90□0.36	0.93□0.16	0.525	t=0.63
Range	0.20-1.50	0.70-1.30		
95% CI	0.81-0.98	0.89-0.97		

There was no significant difference between cases and controls with respect to serum creatinine levels. The mean serum creatinine levels among cases and controls were 0.90mg/dl and 0.93 mg/dl respectively. The mean FBS levels among cases and controls were 230.74 mg/dl and 99.23 mg/dl respectively.

Table 3: Effect of DM on Serum magnesium

Serum Magnesium	**Cases**	**Controls**
Range (Min-Max)	1.0-2.50	1.50-2.60
Mean □ SD	1.65□0.38	1.99□0.24
95% CI	1.57-1.75	1.93-2.05
Significance	Student t=6.227, P<0.001	

Table 4: Comparison of serum Magnesium levels between cases and Controls

Serum Magnesium	**Cases (n=50)**		**Controls (n=50)**	
	Number	%	Number	%
□ 1.0	3	4.3	-	-
1.0-1.50	24	34.3	2	2.9
1.50-2.00	31	44.3	45	64.3
2.00-2.50	12	7.1	21	30.0
>2.50	-	-	2	2.9

There is significant difference between levels of serum magnesium levels among diabetics and controls. The mean serum magnesium levels in cases and controls are 1.65 mg/dl and1.99 mg/dl respectively. **Cases are 21.34 times more likely to have serum magnesium**<1.50mg/dl when compared to controls with p<0.001**.**

Table 5: Effect of level of Control of DM on Serum magnesium

Serum Magnesium	**Controlled (n=57)**	**Not-Controlled (n=13)**
Range (Min-Max)	1.20-2.50	1.00-1.60
Mean □ SD	1.75□0.34	1.23□0.19
95% CI	1.66-1.85	1.11-1.35

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Significance	Student t=5.36, P<0.001

There was significant difference between magnesium levels among controlled and uncontrolled diabetics. The mean serum magnesium levels among controlled and uncontrolled diabetics were 1.75 mg/dl and 1.23 mg/dl respectively.

Table 6: Effect of type of treatment on Serum magnesium

Serum Magnesium	**Insulin (n=47)**	**OHA (n=23)**
Range (Min-Max)	1.0-2.20	1.60-2.50
Mean □ SD	1.49□0.29	1.99□0.31
95% CI	1.41-1.58	1.86-2.13
Significance	Student t=6.5, P<0.001	

Of the total of 70 diabetic patients 33(47%) were on insulin alone, 23(33%) were on OHA'S and 14(20%) were on combination of OHA'S and insulin. The mean serum magnesium levels in the OHA group and insulin group were 1.99 mg/dl and 1.49mg/dl respectively. The serum magnesium levels were significantly lower in the insulin treated group compared to the OHA treated group.

Discussion

The present study included 70 type 2 diabetic patients and 70 control subjects. Serum magnesium levels were determined in all these subjects.

The present study had diabetic patients ranging from 38-81 years. The average age of controls in the present study was 56.60 years while in the study of C.S. Yajnik *et al.* was 46.5 years. The mean age of diabetics in the present study was 55.9 years as against 54.7 in study of C.S. Yajnik *et al.*[4] The mean age of patients on insulin was 52.73 years and 45.9 years in the present and the study conducted by C.S. Yajnik *et al.* respectively and the mean age of non-insulin treated diabetics was 61.1 years and 59.7 years respectively in the present study and the study of C.S. Yajnik *et al.*[4]

A.P. Jain, N.N. Gupta and Abhay Kumar[12] (1976) selected 85 cases, which included 20 comparable healthy adults and 65 diabetics of whom 50 diabetics were without apparent renal involvement. They have studied simultaneously the intracellular (erythrocytic), extracellular (serum) and urinary magnesium levels in controls and diabetics. An attempt to compare the findings in these groups and in controlled and uncontrolled diabetics: those getting insulin with the group not getting insulin was made. In the diabetic group low serum, normal erythrocyte and high urinary magnesium levels were recorded in comparison to controls (2.03□0.25 v/s 2.07□0.27 in controls and 1.67□0.37 v/s 1.8□0.22 in diabetics).

On establishing the relationship between magnesium levels and the state of control of diabetes, it was observed that in poorly controlled diabetic's serum and urinary magnesium levels were respectively lower and higher than that of poorly controlled (1.75□0.34v/s1.85□0.08 in fairly controlled and 1.25□0.19 v/s 1.68□0.12 in poorly controlled) with no significant difference in erythrocytic magnesium levels.

The diabetics getting insulin therapy had lower serum and higher urinary magnesium levels than those getting OHA'S (1.50□0.27 v/s 1.59□0.13 in the insulin treated and 2.02□0.29 v/s 1.90□0.18 in the OHA treated subjects). The present study compared similar parameters that was done by A.P. Jain, N.N. Gupta and Abhay Kumar [12] and found variations similar to that study.

Nadler JL, Malayan S, Luong H, Shaw S, Natrajan RD and Rude RK (1992)[13] evaluated intracellular (erythrocytic) Mg^{2+} concentration in 20 type 2 diabetics. In addition, effects of

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 10, 2023

intravenous 3-h drip or 8 weeks of oral magnesium supplementation on intracellular Mg^{2+} concentration levels and platelet reactivity was studied. The results showed intracellular Mg^{2+} concentration of diabetic patients was significantly reduced compared with values in non-diabetic control subjects. Serum magnesium levels were also reduced in the diabetic patients compared control subjects (2.03□0.25 v/s 2.31□0.12 in controls and 1.67□0.37 v/s 1.94□0.05 in diabetics). Oral magnesium supplementation for 8 weeks (400mg/day) restored RBC magnesium concentration to normal without significantly changing serum magnesium concentration. Both intravenous and oral magnesium supplementation markedly reduced platelet reactivity in response to the thromboxane A2 analog, U46619.

The present study correlated with the study done by Nadler JL, Malayan S, Luong H, Shaw S, Natrajan RD and Rude RK[13] with respect to the comparison of serum magnesium in diabetics and controls. However, the present study did not include evaluating the effects of oral or IV magnesium supplementation.

Nagase N[14] (1996) studied the interrelationships between hypertension, ischemic heart disease and diabetes mellitus and diabetes mellitus in the diabetic subjects without ischemic heart disease or with ischemic heart disease and subjects with ischemic heart disease which were not complicated with diabetes mellitus.

Their results showed serum magnesium levels of diabetes mellitus (1.90□0.37) was significantly lower than that of normal controls (2.30□0.32). They also concluded that serum magnesium level of poorly controlled diabetic patients is lower than that of well controlled diabetic patients. These results suggested that magnesium deficient state is one of the causes of insulin resistance. The present study did not evaluate the interrelations between hypertension, ischemic heart disease. However, the magnesium levels of diabetics as compared to controls and the comparison of serum magnesium levels between well controlled and poorly controlleddiabetics had a positive correlation with the present study.

Garland H O [15] in his study speculated on a potential link between magnesium deficit of diabetes and several diabetic complications including cardiovascular problems and retinopathy.[33]

Rude R K[16] suggested repletion of the deficiency or prophylactic supplementation with oral magnesium may help avoid or ameliorate such complications as arrhythmias, hypertension and sudden cardiac death and may improve the course of diabetic condition.

However, in the present study, the complications of diabetes in relation to hypomagnesemia were not studied. Also, magnesium supplementation and its effects towards magnesium levels or metabolic control was not done in this study which can be taken as limitations of the present study. There was no scope for follow up in the present study. Hence change in magnesium states with respect to improvement or worsening of diabetic state in the long run was not studied. This study focuses on estimating magnesium levels in type 2 diabetics at a given point (during admission) but not on therapeutically correcting hypomagnesemia or otherwise (not correcting) in the future course of the disease and its outcome.

Conclusion

Serum magnesium levels were lower in type 2 diabetic patients when compared to controls. Levels of serum magnesium in uncontrolled type 2 diabetic patients were further lower than those in whom diabetes was under control. Hypomagnesemia is a factor in type 2 diabetes mellitus patients leading to various complications. Hence, it is worthwhile estimating magnesium levels in type 2 diabetes mellitus patients and probably correlates their relationship with various complications.

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