Original Article

Study Of Serum Magnesium Level In Type 2 Diabetes Mellitus In Tertiary Care Centre Of South Gujarat

Dr. Rushangi Vasava*, Dr. Mohita Shah*, Dr. Prafful Kothari**, Dr. Ashokkumar Choudhary ***

*Resident Doctor, **Assistant Professor, ***Additional Professor, Department Of General Medicine, Surat Municipal Institute Of Medical Education And Research, Surat, Gujarat

Abstract: Background: 1) To estimate Serum Magnesium Level in patients with Type 2 Diabetes Mellitus 2) To determine association between Serum Magnesium Level with micro vascular complications like retinopathy, nephropathy and neuropathy. Materials and Methods: A cross-sectional study was carried out on 100 patients above the age of 18 years presenting with Type2 diabetes mellitus admitted in medicine department of Surat tertiary care center. Results: 1)Mean FBS and HbA1C was high in patients of low serum magnesium level as compared to patients of normal serum magnesium level which is statistically significant 2)Statistically significant association observed between low serum magnesium level and diabetic retinopathy, neuropathy and nephropathy. Conclusion: There is an association between serum concentration of magnesium and type 2 DM as well as its micro vascular complication like diabetic nephropathy, diabetic retinopathy and diabetic neuropathy. There is a strong negative correlation between serum concentration of magnesium and duration of diabetes. No significant association exists between serum magnesium concentration and other factors like age, sex, mode of treatment, ischemic heart disease and hypertension. More the level of fasting blood sugar and HbA1c, lower is the serum magnesium level.
[Vasava R Natl J Integr Res Med, 2021; 12(5): 1-6]
Key Words: Diabetes Mellitus, Magnesium, HbA1C, Metformin

Author for correspondence: Dr. Prafful Kothari, Assistant Professor, Department Of General Medicine, Surat Municipal Institute Of Medical Education And Research, Surat, Gujarat
E-Mail: drpraffulkothari@yahoo.in

Introduction: Type 2 diabetes mellitus (type 2 DM) is a non-autoimmune, complex, heterogeneous and polygenic metabolic disease in which body fails to produce enough insulin, characterized by abnormal glucose homeostasis[1].It is the predominant form of Diabetes, accounting for 90% cases globally, is a worldwide health crisis, WHO predicts an incidence of 300 million by 2025[2]. W.H.O has declared India as the global capital of diabetes As per International Diabetes Federation (IDF) the number of diabetes is said to raise from 40.9 million to 69.9 million by the year 2025 in India.

Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with Type 2 diabetes. Magnesium deficiency can lead to development of complications such as retinopathy, thrombosis and hypertension. Several studies have shown that high prevalence of low serum magnesium concentrations in Type 2 diabetes when compared to healthy controls. Magnesium deficiency may result in failure to inhibit entry of calcium into myocardial cells, failure to extrude calcium from the cells, formation of crystals in mitochondria and failure of sarcoplasmic reticulum to sequester excess calcium[3]. Many studies have shown that both mean plasma and intracellular free magnesium levels are lower in patients with diabetes than in the general population. This magnesium deficiency, which may take the form of a chronic latent magnesium deficit rather than clinical hypomagnesaemia, may have clinical importance because the magnesium ion is a crucial cofactor for many enzymatic reactions involved in metabolic processes. Many studies show that mean plasma levels are lower in patients with both type 1 and type 2 diabetes compared with non-diabetic control subjects. The concentration of intracellular free magnesium in erythrocytes is a more sensitive marker in people with diabetes and insulin resistance than are plasma levels of magnesium.

Decreased levels of free intracellular magnesium in erythrocytes have been reported in the majority of patients with type 2 diabetes. Resnick and associates suggest that extracellular and intracellular magnesium deficiency is typical in chronic, stable, mild type 2 diabetes and may be a strong predisposing factor for the development of the excess cardiovascular morbidity associated

with diabetes. These investigators showed that the levels of serum ionized magnesium and erythrocyte intracellular free magnesium were significantly lower in 22 untreated patients with type 2 diabetes and mild hyperglycemia than they were in 30 healthy control subjects(P <0.01).Serum total magnesium was not reduced[4].

It is observed that low serum magnesium concentration and poor magnesium status are common in Type 2 diabetes mellitus. Preventing hypomagnesaemia in diabetes by supplementing magnesium may be helpful in increasing insulin sensitivity and delaying the development of late diabetic complications. Therefore, the aim of the study is to compare the serum magnesium concentrations in patients with Type 2 diabetes and non-diabetic controls to assess its impact on complications.

Material & Methods: Source Of Data: Patients with type 2 diabetes admitted in Surat tertiary care Centre, who satisfied the inclusion criteria and consented to participate in the study were included. Period Of Study: MARCH 2019-JULY 2020. Type Of Study: Cross sectional study. 100 patients were randomly selected. 100 patients of type 2 DM were included in the study. Detailed history – including age, duration of diabetes, treatment mode, symptoms suggestive of diabetic neuropathy, nephropathy, retinopathy associated diseases such as hypertension and ischemic heart disease as obtained as per the proforma.

Detailed physical and neurological examination was done. Retinopathy was assessed by direct ophthalmoscopy. Samples were collected for estimation of fasting blood glucose and magnesium level. Postprandial blood sugar was measured two hours after a standard meal.

Clinical Central nervous examination was done on selected patients by experience neurologist with symptoms & signs suggestive of neuropathy.

Blood urea, serum creatinine and 24-hour urinary albumin were estimated. Serum magnesium was estimated by Calmagite dye method.. HbA1C measurement was done by a modified calorimetric method.

Calmagite Dye Method – Test Principle: Under alkaline conditions, magnesium combines with Calmagite dye to form a red color which is read spectrophotometrically at 530 nm. Formation of color is dependent on magnesium levels. To eliminate the interference of calcium during estimation, EDTA is included in the reagent. Cyanide reduces heavy metal interference. Surfactant reduces protein interference.

Table 1: Test Procedure

In Test Tubes	Blank	Standard	Test
Calmagite	1 ml	1 ml	1ml
Standard Sample	-	10 ml	-
Patient's Sample	-	-	10 ml
Distilled Water	10 ml	-	-

These test tubes are incubated at room temperature (22-28°C). The Absorbance (A) of Test (T), Standard (S) and Blank (B) are read at 530nm spectrophotometer. Magnesium concentration is calculated by the following formula. Magnesium concentration (mEq/L) = (AT -AB / AS -AB) x 2. Serum magnesium concentration is expressed in mg/dl by linearity of 1 mEq/L=1.2mg/dl. According to magnesium levels patients were classified into:

- Normal, 1.7 to 2.4mg/dl (Normomagnesemia),
- Low <1.7mg/dl (Hypomagnesemia),
- High > 2.4mg/dl (Hypermagnesemia).

Patients were also categorized based on duration of diabetes, mode of treatment, presence/absence of retinopathy, neuropathy and nephropathy, and glycemic control (FBS and HbA1C).

Cases with diabetic retinopathy were further divided into

- Non-proliferative diabetic retinopathy.
- Proliferative diabetic retinopathy.

Diabetic nephropathy was graded depending on 24-hour urinary excretion of albumin as follows:

- No nephropathy < 30mg/24hour
- Micro albuminuria 30 – 299 mg/24hour
- Macro albuminuria (clinical proteinuria) ≥ 300 mg/24hour.

Statistical Analysis: The statistical analysis was done by SPSS 15 software.MS Word and Excel were used to generate tables and charts. Following tests were used: 1. Chi square test, 2. Independent t test, 3. Diagrammatic

representation, 4. Mean ± standard deviation, Statistical results were considered significant at P<0.05.

Results: Age Distribution: Patients were distributed across the age spectrum of 43 to 78 years. Mean age 56.8 years. Most patients (n=40) were present in 51-60 group. Youngest patient was 43 years old. The average duration of diabetes in study population was 8.9 years (range 2-23 years).

Table 2: Serum Magnesium And Duration Of Diabetes

Sr. No	Duration (Years)	Normal Serum Magnesium Group (N=65)	Low Serum Magnesium Group (N=35)	Pearson's Correlation Coefficient RHO	P Value For RHO
1	Below 6yrs	43 (66.1%)	3 (8.6%)		
2	6 To 10yrs	12 (18.5%)	12 (34.3%)		
3	11 To 15yrs	2 (3.08%)	10 (61.6%)	-0.528	<0.01
4	16 To 20yrs	4 (6.2%)	9 (25.7%)		
5	21yrs & Above	4 (6.2%)	1 (2.9%)		

Gender Distribution According Various Age Groups: The mean age value of Male groups and Female groups were 56.9 and 56.0. So there was no statistically significant association observed in gender distribution in various age groups (P value >0.05).

Association Between Age And Serum Magnesium Level: The mean age value of low serum magnesium groups and normal serum magnesium groups were 59 and 56. So there was no statistically significant association observed between age and serum magnesium level (P value >0.05).

Table 3: Serum Magnesium Level And Mode Of Diabetic Treatment

Serum Magnesium	Treatment	
	OHA(N=60)	OHA+INSULIN(N=40)
Mean	1.94	2.03
Mean ± SD	1.94 ± 0.5	2.03 ± 0.37
P value	0.55	

Association Between Gender And Serum Magnesium Level: In our study, low serum magnesium level was found in 35 patients out of 100 patients in whom 19 (54.2%) patients were female and 16 (45.7%) patients were male. 65 patients were having normal serum magnesium level out of 100 patients in whom 29 (44.6%) patients were female and 36(55.4%) patients were male. There was no correlation found between low serum magnesium level in men and women (p value >0.05).

Table 4: Serum Magnesium Level And Fasting Blood Sugar Level

| No	FBS	Normal Serum Magnesium Group (N=65)	Low Serum Magnesium Group (N=65)
1	<90	7 (107%)	2 (5.7%)
2	91-100	12 (18.4%)	0
3	101-110	11 (16.9%)	8 (17.8%)
4	111-120	16 (24.6%)	2 (5.7%)
5	121-130	14 (21.5%)	3 (8.6%)
6	>131	5 (7.7%)	20 (57.1%)

Association Between Level Of Serum Magnesium Andduration Of Diabetes: Statistically significant negative correlation was found between level of serum magnesium level and duration of diabetes indicating that serum magnesium level decreases with duration of diabetes.

Association Between Serum Magnesium Level And Mode Of Diabetic Treatment: Of the 100 diabetic patients, 60 (60%) were on oral hypoglycemic agents (OHAs), 40 (40%) were on both OHAs and insulin. The mean serum magnesium levels in the OHA group and OHA

with insulin treated group were 1.94 and 2.03 mg/dl. The serum magnesium levels were found within normal limit in OHA alone and OHA with insulin treated patients (P >0.05).

Association Between Serum Magnesium Level And Fasting Blood Sugar Level (FBS): It was observed that mean FBS was high in patients of low serum magnesium levels as compared to patients with normal serum magnesium level which is statistically significant (P<0.05).

Image 1: Association Between Level Of Serum Magnesium And HbA1c
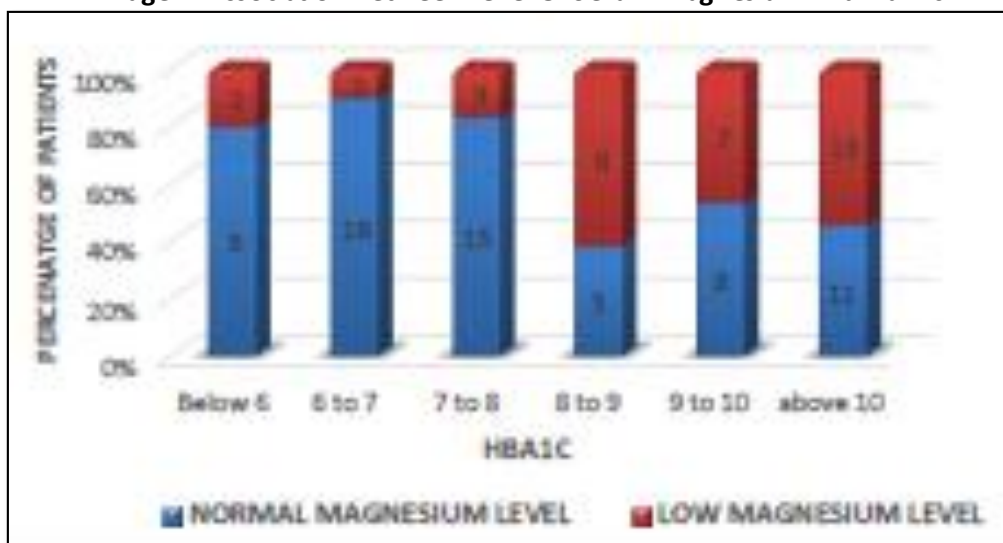
Association Between Serum Magnesium Level And Microvascular Complications Of Type 2 Dm:

Diabetic Retinopathy: In the current study, out of 100 patients, 40 (40%) patients were having diabetic retinopathy and 60 (60%) patients were not having diabetic retinopathy. Out of 40 patients of diabetic retinopathy, 22 (55%) patients were having low serum magnesium level & 18 (45%) patients were having normal serum magnesium level. Out of 60 patients of not having diabetic retinopathy, 13 (21.7%) patients were having low serum magnesium level & 47 (78.3%) patients were having normal magnesium level. Statistically Significant association observed between low serum magnesium level and diabetic retinopathy (p value <0.05).

Diabetic Neuropathy: In present study, out of 100 patients, 13 (13%) patients were having diabetic neuropathy, and 87 (87%) patients were not having diabetic neuropathy. Out of 13 patients of diabetic neuropathy, 9 (69.23%) patients were having low serum magnesium level & 4 (30.77%) patients were having normal serum magnesium level. Out of 87 patients not having diabetic

neuropathy, 26 (29.89%) patients were having low serum magnesium level & 61 (70.11%) patients were having normal magnesium level. Statistically significant association observed

between low serum magnesium level and diabetic neuropathy (p value <0.05).

Diabetic Nephropathy: In present study, out of 100 patients, 35 (35%) patients were having diabetic nephropathy, and 65 (65%) patients were not having diabetic nephropathy. Out of 35 patients of diabetic nephropathy,33 (94.28%) patients were having low serum magnesium level & 2 (5.71%) patients were having normal serum magnesium level. Out of 65 patients not having diabetic nephropathy, 2 (3.07%) patients were having low serum magnesium level& 63 (96.92%) patients were having normal serum magnesium level. Statistically significant association was observed between low serum magnesium level and diabetic nephropathy (p value <0.05).

Discussion: In our study included 100 diabetic patients in whom 35(35%) patients were having low serum magnesium level and 65(65%) patients were having normal serum magnesium level. Proportion of low serum magnesium level in Type 2 DM in current study was similar to other study like Nadler et al. & Walti MK et al. 67 reported a 37.6% proportion of low serum magnesium level in T2DM versus 10.9% in non diabetic controls in Zurich, Switzerland.

1. Age: In our study, mean age of the study population was 56.8 (± 8.1) years. In similar study

done by Arpaci, D et al. mean age of study population of type 2 DM was 55.6 ± 10.4 years.

2. Comparison Of Association Between Serum Magnesium Level And Gender In Type 2 Dm In Two Study: There was no significant association between serum magnesium level and gender (p value >0.05). This is accordance with wahid A et al study.

3. Association Between Serum Magnesium Level And Age: In our study, the mean age value of low serum magnesium groups and normal serum magnesium groups were 59 and 56. There was no significant association between serum magnesium level and age. This is accordance with wahid et al study.

4. Association Between Serum Magnesium Level And Mode Of Diabetic Treatment: In present study, of the 100 diabetic patients, 60 (60%) were on oral hypoglycemic agents (OHAs), 40 (40%) were on both OHAs and insulin. The mean serum magnesium levels in the OHA group and OHA+ insulin group were 1.94 and 2.03 mg/dl. The serum magnesium levels were found within normal limit in OHA alone and OHA with insulin treated patients. (P >0.05) There was no statistical significance association between level of serum magnesium and mode of diabetic treatment (p value >0.05). this study finding is accordance with Nawal SK, Srivastava C study[5].

5. Association & Correlation Between Level Of Serum Magnesium And Duration Of Diabetes: In our study, the mean value of duration of DM (years) were 12.91 and 6.80 in low serum magnesium groups and normal serum magnesium groups respectively.

Statistically significant negative correlation was found between level of serum magnesium and duration of diabetes indicating that serum magnesium decreases with duration of diabetes. This is in accordance with Arpaci, D et al. study.

6. Association Between Serum Magnesium Level And Biochemical Parameters (FBS And HbA1c): In our study, the mean values of FBS were 131 ± 21.77 and 111.52 ± 15.77 respectively in low serum magnesium and normal serum magnesium group. The mean FBS value was high in patients who were having low serum concentration of magnesium compared to normal, which was statistically significant (p value <0.05). These

result were almost similar with the study done by Wahid A et al.68. In our study the mean values of HbA1C were 9.5 ± 1.96 and 7.9 ± 1.7 respectively in low serum magnesium and normal serum magnesium group.

The mean HbA1C was high in patients who were having low serum concentration of magnesium compared to normal, which is statistically significant (p value <0.05). These values were almost similar with the study done by Wahid A et al [6] andDasgupta, et al[7].

7. Comparison Of Association Between Serum Magnesium Level And Microvascular Complication In Type 2 Dm In Various Study: In our study, there was statistically significant association between diabetic retinopathy and low serum magnesium level. This is in accordance with Joy SS et al.[71] and Ishrath Kareem et al study. In present study, there was statistically significant association between diabetic neuropathy and low serum magnesium level. This is in accordance with Joy SS et al. study. In our study, there was statistically significant association between diabetic nephropathy and low serum magnesium level. This is in accordance with Corsonello, et al74 study and Bherwani, S.et al study.

Conclusion: There is an association between serum concentration of magnesium and type 2 DM as well as its micro vascular complication like diabetic nephropathy, diabetic retinopathy and diabetic neuropathy. There is a strong negative correlation between serum concentration of magnesium and duration of diabetes. No significant association exists between serum magnesium concentration and other factors like age, sex, mode of treatment, ischemic heart disease and hypertension. More the level of fasting blood sugar and HbA1c, lower is the serum magnesium level.

References:
1. Chrisopter, J. and Hupfeld, C., Courtney, H. and Olefsky, J.M. (2010) Type 2 Diabetes Mellitus: Etiology, Pathogenesis and Natural History. In: Jameson, J.L. and De Groot, L.J., Eds., Endocrinology Adult and Paediatric, Volume 1, 6th Edition, Saunders Elseveir, Philadelphia, 765
2. Buse, J.B., Polonsky, K.S. and Charles (2007) Type2 Diabetes Mellitus. In: Kronenberg, H.M., Melmed, S., et al., Eds., Williams

Texbook of Endorinology, 11th Edition, Saunders Elsevier Publication, Philadelphia, 1329.

3. Bursch GE, Gibbs TD. Importance of magnesium deficiency in cardiovascular disease. Am Heart J 1977;94:649-654.

4. Resnick LM, Altura BT, Gupta RK, Larsh JH,Alderman MH, Altura BM. Intracellular and extracellular magnesium depletion in type 2 diabetes mellitus. Diabetologia 1993;36:767-770.

5. Nawal SK, Srivastava C. Study of Magnesium Level as an Indicator of Diabetic Complications. Int J Med Res Rev 2015;3(7):726-732.doi:10.17511/ijmrr.2015. i7.137

6. Wahid A, Verma GC, Meena CP, Pathan AR. Study of serum magnesium level in patients with type 2 diabetes mellitus and it's correlation with glycosylated hemoglobin and diabetic complications. Int J Adv Med 2017; 4:311-6.

7. Dasgupta A, Sarma D, Saikia UK. Hypomagnesemia in type 2 diabetes mellitus. Indian J EndocrMetab 2012;16:1000-3.