International Journal Dental and Medical Sciences Research
Volume 6, Issue 3, May - June 2024 pp 327-332 www.ijdmsrjournal.com ISSN: 2582-6018

Study of serum magnesium level in Type 2 Diabetes patients, its correlation with glycemic status and diabetic complications in a tertiary hospital.

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Date of Submission: 15-06-2024 Date of Acceptance: 25-06-2024

ABSTRACT:
INTRODUCTION: Type 2 Diabetes Mellitus is an endocrinological disease associated with hyperglycaemia, insulin resistance and defective insulin secretion.Magnesium is an essential element involved in glucose homeostasis with frequently reported association. Hypomagnesemia may have negative impact on glucose homeostasis and insulin sensitivity in diabetes.
OBJECTIVES: The aim of the study was to evaluate serum levels of magnesium and HbA1c in diabetics and to assess the diabetic complications.
MATERIALS AND METHODS: Data collected from 100 patients attending General Medicine OPD and admitted in our hospital.An informed written consent was taken from the patient and cases meeting the selection criteria were included in the study. Baseline data with detailed medical history was collected, clinical examination was done. Serum magnesium, fasting blood sugar, postprandial blood sugar and HbA1c measured. Statistical analysis performed.
RESULTS: Study included 100 newly detected Type2 DM.Prevalence of hypomagnesemia in type 2 DM was 25% and magnesium deficiency was associated with diabetic retinopathy. No significant association exists between diabetic microangiopathies (nephropathy and neuropathy) and diabetic comorbidities- ischemic heart disease with magnesium.
CONCLUSION: Hypomagnesemia is prevalent in diabetic population and is associated with diabetic retinopathy. A periodical monitoring of serum magnesium levels is useful in diabetes management in clinical practice. Increasing dietary intake of magnesium rich food like spinach, figs, nuts and seafood must be initiated in case of low magnesium levels.

I. INTRODUCTION

Diabetes mellitus (DM) is considered as the most common non communicabledisease. Type 2 diabetes is a chronic disease characterized by a disorder of glucose metabolism associated with a reduced ability of tissues to respond to insulin (insulin resistance).Resulting chronic hyperglycaemia damages blood vessels and nerves throughout the body producing microvascular diseases including retinopathy, neuropathy and nephropathy. The risk for cardiovascular disease is considerably elevated in patients with type 2 diabetes compared to the general population.Globally, the number of people with diabetes is expected to rise from the current estimate of 220 million in 2010 to 300 million in 2025. Type 2 diabetes mellitus is the predominant form of diabetes worldwide accounting for 90% of cases globally!Therefore, type 2 diabetes represents a major public health problem causing high economic costs in industrialized countries. DM is an endocrine disease with high oxidative and metabolic stress. An important risk factor for development of microangiopathy in diabetes is elevated levels of HbA1c.HbAlc has special affinity for anoxia and playsa role in causation of micro and macroangiopathy.?DM leads to many complications and one of them is electrolyte imbalance which has been an ignored subject. In particular, diabetes has shown to be associated with abnormalities in the metabolism of zinc, chromium, copper, magnesium and manganese.

Magnesium is the second most abundant intracellular cation after potassium.Magnesium is essential for insulin secretion, insulin receptor interaction, post receptor events and normal carbohydrate utilization (by Mg dependent enzymes). Lowmagnesium status has repeatedly been demonstrated in patients with type 2 diabetes.Magnesium deficiency appears to have a negative impact on glucose homeostasis and insulin

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sensitivity in patients with type 2 diabetes and evolution of complications such as retinopathy, thrombosis, and nephropathy.The reasons why magnesium deficiency occurs in diabetes are not clear. They may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium compared to healthy individuals. Several studies have reported increased urinary magnesium excretion in type 1 and 2 diabetes. Studies show a correlation between glycaemic control and urinary magnesium loss. Low dietary intake may also contribute to low magnesium status in diabetics. Patients with type 2 diabetes are often overweight, and may consume a diet higher in fat and lower in magnesium density than non-diabetics.

Research has shown that magnesium is a clinically significant electrolyte, for a long-term global policy to lower the burden of diabetes mellitus.

II. MATERIALS AND METHODS

Sourceof data:

Patients who presented to OPD or admitted in Tertiary care centre were considered for the study. This study was done over a period of one year.

Study design:

An observational clinical study

Study population:

100 patients with newly detected Diabetes Mellitus were chosen based on random selection amongst out-patient and in patients in Tertiary care centre. These patients were grouped into 2 categories.

* Group 1: 50 patients with HbA1C >7% at the time of diagnosis of diabetes
* Group 2: 50 patients with HbA1C ≤ 7% at the time of diagnosis of diabetes

100 normal controls with HbA1c values <5.7% were randomly selected for thisstudy amongst those who presented to OPD in a tertiary Hospital for routine medical check-up.

Inclusion criteria:

* Patients willing to participate in the study.
* Age group: 30-70 years.
* Newly diagnosed Type 2 Diabetes Mellitus.

Exclusion criteria:

* Type 1 Diabetes
* Acute complications such as severe infection, major operations, trauma, GI disorders, cardio-respiratory distress, pregnant and breastfeeding individuals.
* Gestational diabetes, pancreatic diabetes
*Patients receiving magnesium supplements or magnesium containing antacids,taking supplements like antioxidants, minerals and vitamins.
*Patients on drugs affecting Magnesium levels.

Method collection of data:

200 subjects which included 100 newly detected diabetics and 100 normalcontrols were included in the study.

American Diabetes Association (ADA) criteria was used for the diagnosis ofdiabetes. Diagnosis was made on any one of the following:

* A haemoglobin A1c (HbAlc) level of 6.5% or higher, or
* A fasting plasma glucose (FPG) level of 126 mg/L (7 mmol/L) or higher; fasting is defined as no caloric intake for at least 8 hours, or
* A 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during a 75-goral glucose tolerance test, or
* A random plasma glucose of 200 mg/dL (11.1 mmol/L) or higher in a patient with classic symptoms of hyperglycaemia (ie, polyuria, polydipsia, polyphagia; weight loss) or hyperglycaemic crisis

The selected subjects were studied in detail with history and physicalexamination.

Statistical analysis: All values will be presented as Mean±SD.Comparison of mean values ofparameters of diabetic and control subjects was done by using Student's t test.

III. RESULTS

200 subjects were chosen for this study (119 men, 81 women, mean age49.68+12.21 years).100 patients with newly detected type-2 diabetes (52 men, 48 women, mean age52 years) comprised the study group. These patients were further grouped with regards to their HbA1C levels at the time of diagnosis.

* Group 1 - HbA1c>7%
* Group 2 - HbA1c≤7%

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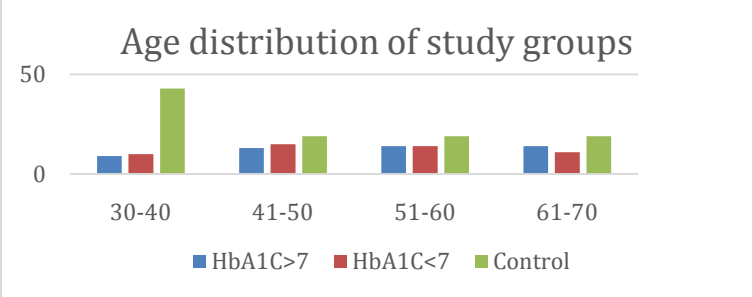
1. AGE DISTRIBUTION:

AGE IN YEARS	HbA1C >7%	HbA1C<7%	CONTROLS	TOTAL
30-40	9	10	43	62
41-50	13	15	19	47
51-60	14	14	19	47
61-70	14	11	19	44
Total	50	50	100	200
Mean	53.22	50.8	47.35	49.68



Patients were distributed across the age spectrum of 30 to 70 years.Mean age of the patients was 49.68 years. Most patients were in the age group of 30-40 years (31%).

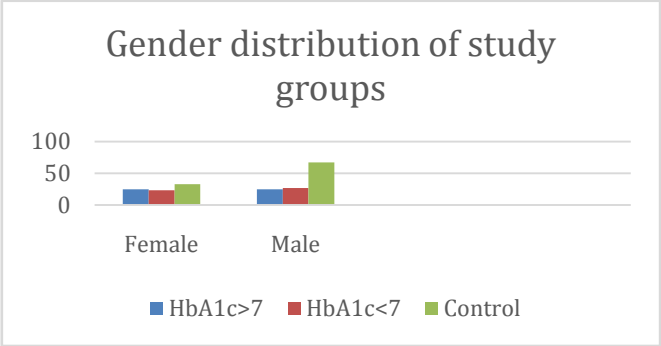
62 patients were in the age group between 30 and 40 years. 47 patients were in the age group between 41 and 50 years. 47 patients were in the age group between 51 and 60 years. 44 patients were in the age group between 61 and 70 years. The mean age of patients in the study was 49.68+12.21 years.

Among 50 patients in group 1 with HbA1C>7%, 9 patients were in the age group between 30 and 40 years. 13 patients were in the age group between 41 and 50 years. 14 patients were in the age group between 51 and 60 years. 14 patients were in the age group between 61 and 70 years. The mean age of patients in this group was53.22+11.91 years.

Among 50 patients in group 2 with HbA1C≤7%, 10 patients were in the age group between 12 and 40 years. 15 patients were in the age group between 41 and 50 years. 14 patients were in the age group between 51 and 60 years. 11 patients were in the age group between 61 and 70 years. The mean age of patients in this group was 50.8011.42 years. P value was 0.015 which was statistically significant. Student T test was used to analyse data.

2. GENDER DISTRIBUTION:

Gender	HbA1C>7	HbA1C<7	Control	Total
Female	25	23	33	81
Male	25	27	67	119
Total	50	50	100	200



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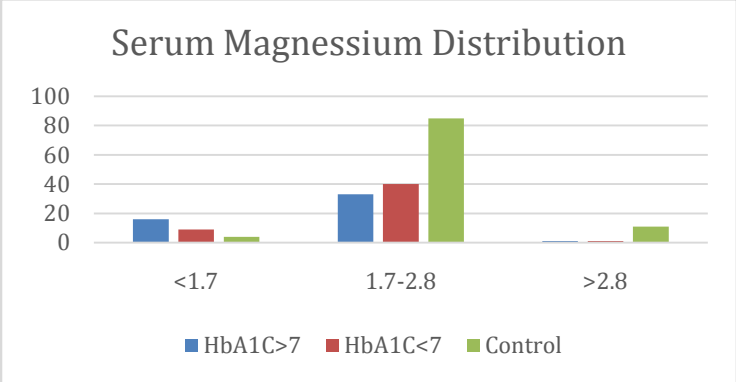
81 patients were females, while 119 were males in the study group. The mean age of patients in the study was 49.68+12.21 years. P value was 0.015 which was statistically significant.Amongst 50 patients in group 1 with HbA1C>7%, 25 patients were females and 25 patients were males. Amongst 50 patients in group 1 with HbA1C≤7%, 23 patientswere females and 27 patients were males. P value was 0.089 which suggests a trend in the direction of significance. Chi-Square Test was used to analyse data.

3. SERUM MAGNESIUM DISTRIBUTION:

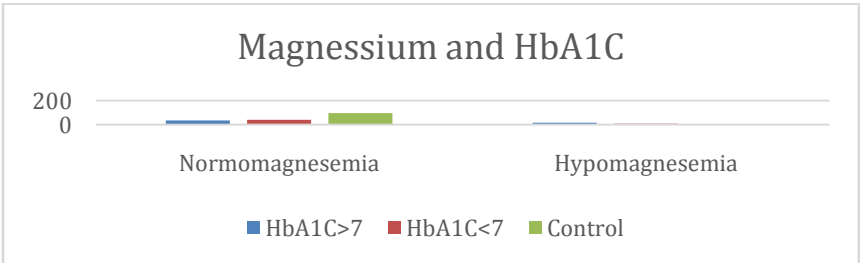
Serum Mg	HbA1C >7%	HbA1C <7%	Control	Total
<1.7	16	9	4	29
1.7-2.8	33	40	85	158
>2.8	1	1	11	13
Total	50	50	100	200



Hypomagnesemia (defined as fasting serum magnesium concentration< 1.7mg/di) was found in 4 patients in the controls. 9 out of 50 patients from Group 2 (HbAlc≤7) were found to have hypomagnesemia.While 16(32%) patients from Group 1 with HbAl>7 showed Mg values less than 1.7 mg/di.Hypomagnesemia was found in 14.5%(n=29) of the study population. Among the newly detected diabetes, 25%(n=25) were found to have low magnesium levels.13 patients in this study were found to have Serum Mg levels of more than 2.8mg/dl. P value was <0.001 which was highly significant. Fisher Exact Test method was used for analysis.

4. MAGNESIUM AND HbA1c :

Serum Mg	HbA1C >7%	HbA1C <7%	Control	Total
NormoMagnesemia	34	41	96	171
Hypomagnesemia	16	9	4	29
Total	50	50	100	200



In Group 1, 32% of the tested population was found to have hypomagnesemia which comprised of16 patients. In Group 2, 18% were found to be having hypomagnesemia (n=9).Among controls 4% had hypomagnesemia. Among newly detected diabetes theprevalence of hypomagnesemia was 25% in this study. P values was <0.001 and was found to be highly significant. Chi-square test was used for the data analysis.

IV. DISCUSSION

The main finding of our study was that Serum Mg levels were low in newlydetected type 2 DM.A number of studies recent and in the past have identified Magnesiumdeficiency in type 2 diabetes patients. In this study, 25% patients with newly detected type 2 DM were found to be having Serum Magnesium levels below the reference range,thereby confirming the general prevalence of hypomagnesemia status in type 2 DM in several studies.Marked magnesium deficiency has been reported in the previous studies in patients with type-2 diabetes.However, some clinicians have also reported normal and even high levels.In the present study, serum magnesium concentrations of 31 patients with type 2 diabetes, were below the reference range. This confirms the reported prevalence of low plasma magnesium status in type-2 diabetics in several studies, which ranged from 25 to 39%. Prevalence of hypomagnesemia in this study is comparable to a study by **Prabhu. G et al.** done in Rajah Muthiah Medical College and hospital which Showed a similar prevalence of 25% in type 2 diabetics in Chidambaram, India. Glycosylated hemoglobin (HbA1C) results from reaction between glucose and N-terminal valine of beta chain of b molecules by glycosylation of hemoglobin. When plasma glucose is consistently elevated, there is an increased glycosylation of hemoglobin. HbAC assays approximate with mean plasma glucose values over the previous 2 to 3 months. Higher percentages of HAIC indicate poor glycemic control in the previous months. In this study, newly detected diabetics were analysed for hypomagnesemia with reference to their HbAlc levels. HbAlc levels were used to indicate possible duration of diabetes before diagnosis.There are reports suggesting hypomagnesemia to be both a cause and result ofpoor glycemic control. Magnesium is a cofactor in both glucose transporting mechanisms of cell membrane and various enzymes that are important in carbohydrate oxidation.Multiple studies have shown that magnesium deficiency promotes insulin resistance. **Nadler et al. and Rude RK** have reported that insulin sensitivity decreases even in nondiabetic individuals after induction of magnesium deficiency. Likewise, elderly subjects were shown to have improved glucose tolerance when they received magnesium supplements.Thus, hypomagnesemia by itself results in poor glycemic control.

Sex, age and duration of diabetes were not the significant predictors of serum magnesium levels. **Yajnick et al. in 1984** reported that among diabetics, plasma magnesium concentration was directly related to age and men had significantly higher concentrations than women. In our study, patients with impaired renal functions wereexcluded. Our results confirm to the recent reports that have not shown any significantassociations between sex and age with serum magnesium levels.

A study done in Kota, Rajasthan in 2017 found a prevalence of hypomagnesemia in 34% of diabetics.There was also a significant note made of higher levels of FBS, PPBS and HbA1c in the diabetics with hypomagnesemia when compared to diabetics with normal magnesium levels. Similar findings are noted in this study where FBS and PPBS were found to be significant associations of hypomagnesemia.

V. LIMITATIONS OF OUR PRESENT STUDY:

Sample size does not reflect the true incidence and prevalence of the disease.Also since the study was done in a single centre, the study population may not be adequately represented. Other confounding variables like dietary patterns betweensubject groups were not taken into consideration

VI. CONCLUSION:

***** Prevalence of hypomagnesemia in type 2 diabetes was 25%.

* Youngest patient in our study was 30 years of age; mean age of patients in our study was 49.68 years.
* Prevalence of hypomagnesemia is significantly higher in patients with microvascular diabetic complications compared to diabetics with no complications.
* Subjects with a higher HbAlC% had higher prevalence of hypomagnesemia.This concurred with studies done before.

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