ORIGINAL RESEARCH PAPER

General Medicine

STUDY OF SERUM MAGNESIUM LEVEL IN TYPE 2 DIABETES MELLITUS PATIENTS AND ITS RELATION WITH GLYCEMIC CONTROL OF PATIENTS.

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ABSTRACT

INTRODUCTION: Diabetes is an iceberg disease, the prevalence of diabetes in adults was around 4% worldwide.The recent WHO report suggests that over 19% of worlds diabetic population currently resides in India.Patient with longer duration of diabetes had higher mean HbA1c values and lower mean magnesium values. Hypomagnesemia may lead to the induction of pro inflammatory and profibrogenic response, cause induction or augmentation of vasoconstriction and hypertension.Patient with longer duration of diabetes had higher mean HbA1c values and lower mean magnesium values.

OBJECTIVE: To study the distribution of serum magnesium level in relation to HbA1c level, FBS, duration of diabetes and demographic profile of patients.

MATERIALS AND METHODS: This cross sectional analytical study was carried out in our institution for duration of 1 year.Total of 500 subjects were enrolled in the study.Detailed clinical and demographic profile including duration of diabetes and patients were investigated for HbA1c level,FBS. The data were analysed using SPSS Version 16.

RESULT: Prevalence of hypomagnesemia in type 2 diabetes was 33% with serum magnesium level 1.31 ± 0.087 mg/dl. Hypomagnesemia has significant association with glycemic control which was reflected in uncontrolled fasting blood sugar (FBS >126 mg%) (p value 0.001) and HbA1c >7% (p value 0.0001).It has significant reverse correlation with duration of diabetes(p value = 0.0004)

CONCLUSION: Our study showed significant correlation between hypomagnesimia and uncontrolled glycemic status and duration of diabetes that will indicate magnesium plays an important role in glucose metabolism.

INTRODUCTION:

Diabetes is an iceberg disease, the prevalence of diabetes in adults was around 4% worldwide. The recent WHO report suggests that over 19% of worlds diabetic population currently resides in India [1] The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 415 million in 2017. Based on current trends, the IDF projects that 642 million individuals will have diabetes by the year 2040. [2] Hyperglycemia in diabetes results from defects in insulin secretion, insulin action, or, most commonly both.The chronic hyperglycemia and attendant metabolic deregulation of diabetes mellitus may be associated with secondary damage in multiple organ systems especially kidneys, eyes, peripheral nerves and blood vessels. [3] Magnesium is the fourth most abundant mineral in the body and the most abundant intracellular divalent cation, with essential roles in many physiological functions [4].magnesium modulates glucose transport through the membrane and is cofactor in several enzymatic reactions involving glucose oxidation, its deficiency may increase insulin resistance. [5]There is one study found better control of. Diabetes with increasing dose of magnesium supplementation in diabetes [5]. In another study in 1998 found that the serum magnesium levels were significantly lower in participants with cardiovascular disease, hypertension and diabetes than in those free of these disease.Normal magnesium level ranges from 1.5-2.5 mg/dl, less than 1.5 mg/dl considered as hypomagnesemia. [6] Magnesium is a cofactor in the glucose transporting mechanism of the cell membrane and various enzymes in carbohydrate oxidation.Cellular magnesium seems to play an important role in glucose metabolism as it is a critical cofactor for the activities of various enzymes involved in glucose oxidation and may play a role in the release of insulin. [7]

MATERIALS AND METHODS:

This cross sectional analytical study was carried out in our institution for duration of 1 year.Total of 500 subjects were enrolled in the study.Informed Patient Consent was obtained before clinical examination.Thorough history taking and clinical examination were done. Patient's proforma was maintained which included all demographic particulars, past medical, surgical, drug, personal and family history.HbA1c was measured by High Performance Liquid Chromatography.Plasma glucose estimation (FBS and PPBS) was carried out by the glucose oxidase method in the auto analyser. Serum magnesium was estimated by xylidyl blue, colorimetric method. The patients were grouped as hypomagnesemia of diabetic patients and normomagnesemia of diabetic patients based on their serum magnesium level.

SELECTION CRITERIA
INCLUSION CRITERIA:
- All Type 2 Diabetes Mellitus patients
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EXCLUSION CRITERIA:
- Patients suffering from Type 1 diabetes
- Alcoholism
- Chronic diarrhoea
- Malabsorption syndrome
- Patients on diuretics
- Nephrotoxic drugs
- Patients with renal failure
- Patients suffering from thyroid-related disorders

STATISTICAL ANALYSIS:
Statistical evaluation was performed by statistical package for social sciences (SPSS) version 16 for windows statistics program using the Unpaired t test/single factor ANOVA and categorical variables were analysed with chi squared test and Fisher Exact Test.Correlations of hypomagnesemia with HbA1C,FBS and were obtained using Pearson's formula.Arithmetic mean and standard deviation was calculated from our data.A P value <0.05 was considered

statistically significant.

OBSERVATION AND RESULTS:
Among the 500 diabetic patients enrolled in the study, we divided them in two groups on the bases of serum magnesium level hypomagnesemic group (mg level <1.5 mg/dl) and normomagnesemic group (mg level > 1.5 mg/dl).As shown in table no.1,Mean value of serum magnesium level in hypomagnesemic group was 1.31± 0.087 mg/dl and 2.61±0.26 mg/dl in normomagnesemic group. Prevalence of hypomagnesemia in type 2 diabetes was 33%.

As shown in table no.2, in our study 290 (58%) were male patients and 210 (42%) were female patients, 248(49.6%) patients were rural and 252(50.4%) patients were urban.We divided patients on the basis of age in two groups 35-55 Yrs with Mean age 49±4.52 and 55-75 yrs with Mean age 61±4.52. Mean duration of diabetes in hypomagnesemic patients was 7.26± 2.13years. Mean BMI in Hypomagnesemic group was 25.79±0.96 and normomagnesemic group was25.38±0.88. On the basis of treatment mode, two groups were formed one group was taking OHA only and another group taken OHA+Insulin, 322 patients were taking OHA only and 178 patients were taking OHA+Insulin.In our study 50.96% patients were found with FBS(> 126 mg/dl) and 53% patients were found with HbA1c level >7%.

As shown in table no.3, gender, demographic distribution and age of patients were have no significant correlation with hypomagnesemia, and BMI and mode of treatment also not affected serum magnesium level.

But hypomagnesemia was stastically significantly associated with parameters of uncontrolled diabetes like HbA1C level and FBS of patients. Hypomagnesemia was present in 4.76% of cases with <7% HbA1c level and 53.44% of cases with >7% HbA1c level. This was statistically significant (p value = 0.0001).Out of the 500 patients, 200 patients were with controlled FBS and mean 113±7.41, 300 patients were with uncontrolled FBS and mean 152±18.60.

Hypomagnesemia was present in 3.68% of cases with controlled FBS and in 50.96% of cases with uncontrolled FBS. This was statistically significant (p value = 0.001).Duration of diabetes was 7.2±2.13 years in hypomagnesemia cases and 4.5±1.66 years in cases with normal magnesium values. This difference was statistically significant(p=0.0004), so duration of diabetes was inversely proportional to serum magnesium level.

TABLE NO.1 PREVALENCE OF HYPOMAGNESEMIA

	PREVALENCE	MEAN SERUM MAGNESIUM LEVEL (mg/dl)
HYPOMAGNESEMIA(S.mg <1.5 mg/dl)	165 (33%)	1.31± 0.087
NORMOMAGNESEMIA(S.mg >1.5 mg/dl)	335	2.61±0.26

TABLE NO.2 CHARACTERISTICS OF PATIENTS

CHARACTERISTIC	NUMBER		%
Number of subjects		500	
Males		290	58%
Females		210	42%
Rural		248	49.6%
Urban		252	50.4%
Age groups			
35-55 Yrs (Mean age 49±4.52)		227	
55-75 yrs (Mean age 61±4.52)		273	
BMI in hypomagnesemic patients	25.79±0.96		
BMI in normomagnesemic patients	25.38±0.88		
Mean duration of DM	7.26± 2.13		
Medication	OHA 322		64.4%
	OHA + I 178		35.6%
HbA1C level	< 7% 210		42%
	> 7 % 290		58%
FBS	< 126 (113±7.41) 200		40%
	> 126(152±18.60) 300		60%

TABLE NO.3 CORRELATION OF SERUM MAGNESIUM LEVEL AND DIFFERENT PARAMETERS

	CASES	HYPOMAGNESEMIA		NORMOMAGNESEMIA		P VALUE
GENDER AND SERUM MAGNESIUM IN DIABETES MELLITUS						
MALES	290	93	(32.06%)	197	(67.94%)	0.602
FEMALES	210	72	(34.28%)	138	(65.72%)	
DEMOGRAPHIC DISTRIBUTION AND SERUM MAGNESIUM LEVEL						
RURAL	248	77	31.04%	171	68.96%	0.310
URBAN	252	88	35.31%	163	64.69%	
AGE & SERUM MAGNESIUM IN TYPE 2 DM						
35-55 Yrs	227	79	34.80%	148	65.2%	0.430
55-75 yrs	273	86	31.50%	187	68.5%	
BMI AND HYPOMAGNESEMIA						
		25.79±0.96	25.38±0.88			0.09
DURATION OF DIABETES AND MAGNESIUM						
	Mean	7.26	4.5			*0.0004*
	SD	2.13	1.66			

HYPOMAGNESEMIA AND MODE OF TREATMENT						
OHA	322	107	(33.2%)	215	(66.8%)	0.88
OHA+I	178	58	(32%)	120	(68%)	
HbA1c AND SERUM MAGNESIUM LEVEL						
<7 %	210	10	4.76%	200	95.24%	*0.0001*
>7 %	290	155	53.44%	135	46.56%	
SERUM MAGNESIUM & FASTING BLOOD SUGAR						
(<126mg/dl)	200	7	(3.68%)	183	(96.31%)	*0.001*
(>126 mg/dl)	300	158	(50.96%)	152	(49.0%)	

DISCUSSION:

In our study, we have observed distribution of serum magnesium level in controlled and uncontrolled diabetic patients and with duration of diabetes.And also studied correlation with other demographic parameters of patients. gender, demographic distribution and age of patients were have no significant correlation with hypomagnesemia, and BMI and mode of treatment also not affected serum magnesium level.A recent study **Prabhu G et al (2015)** [8] reported that there is no relation between age, sex of patient and serum magnesium level. Our results confirm to the recent reports that have not shown any significant associations between sex and age.**Halder et al in 2016** [9] found in study same results like our study that low magnesium level was seen in mean BMI 24.25±2.87 and normomagnesemia seen in mean BMI 25.08±2.82. In present study 500 patients we have investigated and were found prevalence of low serum magnesium concentrations in type 2 diabetes patients was 165 (33%). Similarly Marked magnesium deficiency has been reported by **Walti MK et al (2003)** [10] in patients with type-2 diabetes that is 13.5% to 47.7% The prevalence of hypomagnesaemia among patients with type 2 diabetes treated at the NCDEG in 2014 was found to be 19%[11].**Odussan O et al in 2017** [12] found (27%) of patients who had DM have hypomagnesemia which was significantly more than 12% of control. Duration of diabetes was 7.26±2.13 years in hypomagnesemia cases and 4.5±1.66 years in cases with normal magnesium values, was statistically significant relationship (P value = 0.0004).Similarly **Dana Hyassat et al (2014)** [11] found hypomagnesaemia was significantly associated with increasing duration of diabetes, patients who had diabetes between 5-9 years or ≥ 10 years had 24% and 23% prevalence of hypomagnesaemia, respectively; while those who had their diabetes < 5 years had a prevalence rate of only 12%.

in our study out of 500 cases 210 (42%) were found with HbA1c level <7% and 290 (48%) were found with HbA1c level >7% and prevalence of hypomagnesima was (4.76% v/s 53.44%) respectively in both group, that is statistically significant (p value = **0.0001).**

Dana Hyassat et al (2014) [11] observed that Hypoma gnesaemia existed in 13% of patients with HbA1c < 7, 25% of those with HbA1c between 7-7.9%, 19% of those with HbA1c between 8-8.9% and 22% of those with HbA1c ≥ 9%.

Similarly **Dasgupta et a(2012)** [13] reported Mean HbA1c was 11.9% in the hypomagnesemic patients compared with 9.8% in controls (P =0.0016) similar to our result. In the present study out of the 500 cases 200 patients found with controlled FBS (<126mg/dl) and 300 patients with uncontrolled FBS (>126mg/dl) and prevalence of hypomagnesemia was (3.68%v/s 50.96%) respectively in both groups revealed statistically significant ('P' value =0.0001) correlation between low serum magnesium levels and fasting blood sugar.**Kauser et al (2014)** [14] reported The mean FBS levels among cases and controls were 230.1 mg/dl and 99.42 mg/dl respectively. There was significant difference between levels of serum magnesium among diabetics and controls. The mean serum magnesium levels in cases and controls were 1.67 mg/dl and 2.03 mg/dl respectively.

Intracellular Mg2+ regulates glucokinase, KATP channels, and L-type Ca2+ channels in pancreatic -cells, preceding insulin secretion. Moreover, insulin receptor autophosphorylation is dependent on intracellular Mg2+ concentrations, making Mg2+ a direct factor in the development of insulin resistance. Conversely, insulin is an important regulator of Mg2+ homeostasis. In the kidney, insulin activates the renal Mg2+ channel transient receptor potential melastatin type 6 that determines the final urinary Mg2+ excretion. Consequently, patients with T2DM and hypomagnesemia enter a vicious circle in which hypomagnesemia causes insulin resistance and insulin resistance reduces serum Mg2+ concentrations. [15]

CONCLUSION:

Our study showed significantly lower serum magnesium values in poor glycemic control patients, so may be hypomagnesemia itself a cause of insulin resistance and other metabolic derangements of diabetes mellitus.

LIMITATIONS:

The major limitation of the study was that it was conducted in small population that may not represent the entire population. The follow up of the cases was not possible to determine the prognostic significance of our findings. Moreover, it could have been possible to correlate and check the reversibility of hypomagnesemia with glycaemic control over a period of time.

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