

Serum Magnesium Levels in Patients with Diabetic Nephropathy

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ABSTRACT

Objective: To determine serum magnesium levels in patients with diabetic nephropathy.

Study Design: Cross sectional study.

Place and Duration of Study: Medicine Department, Combined Military Hospital, Kohat Pakistan, from Jun 2015 to Nov 2015.

Methodology: Forty-five patients fulfilling the inclusion/exclusion criteria were enrolled, to ascertain the serum magnesium levels in patients having diabetic nephropathy.

Results: Mean microalbuminuria was 37.51 ± 21.33 mg/L, while mean serum magnesium level was 1.36 ± 0.29 mg/dl. Mean serum magnesium level in patients with diabetic nephropathy was 1.27 ± 0.31 mg/dl, whereas mean serum magnesium level in patients without diabetic nephropathy was 1.50 ± 0.17 mg/dl. About of 67.9% of the patients with diabetic nephropathy had hypomagnesemia while 64.7% without diabetic nephropathy were found to have hypomagnesemia.

Conclusion: Serum magnesium levels in patients with diabetes mellitus were lower. Furthermore, serum magnesium levels in patients with diabetic nephropathy were also lower as compared to patients without diabetic nephropathy.

Keywords: Diabetes, Diabetic nephropathy, Hypomagnesemia.

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INTRODUCTION

Diabetes mellitus (DM) is a major health problem, and it's one of the important cause of morbidity and mortality.¹ In 2014, about four hundred and twenty two million people had DM. It is estimated to rise to six hundred and forty two million by 2035.² In Pakistan, around 13% of the population is suffering from DM.³ Diabetic nephropathy (DN) is one of the main causes of end-stage renal disease (ESRD). Risk factors for DN and its progression include longer duration of diabetes, poor control of blood sugar, hypertension (HTN) and albuminuria. Microalbuminuria leads to increased mortality in diabetic patients.⁴

Magnesium levels are low among patients type 2 diabetes,^{5,6} mainly because intracellular concentration of magnesium is regulated by insulin. Magnesium is the 4th most abundant cation in humans.⁷ It is present as free ion, complexed or bound to proteins. It plays an important role as a co-factor for reactions that require ATP and kinases. It also facilitates neuromuscular excitability, permeability of cell, and mitochondrial functions.² It is present in grains, nuts, and green leafy vegetables.⁸ Deficiency develops rapidly due to its poor absorption and rapid turnover.^{9,10}

Other factors include magnesium deficient diets, osmotic diuresis leading to excessive renal excretion, diuretics use causing magnesium wasting, and reduced reabsorption by renal tubules. Hypomagnesemia is associated with poor control of blood sugar and several long term diabetic complications.¹⁰ Several studies have shown that hypomagnesemia acts as a marker for the development of DN.¹¹

The rationale of study was that the serum magnesium levels are not routinely measured in diabetics. Low magnesium levels act as independent risk factor for DN. Therefore magnesium levels in patients with diabetes should be routinely measured, and magnesium supplementation should be advised to those found out to have low levels to prevent or slow down progression of DN.

METHODOLOGY

The cross sectional study was conducted at Department of Medicine, Combined Military Hospital, Kohat Pakistan, from June to November 2015. It was started after hospital ethical review committee's approval (Ltr no. A/28/76). Consent form was signed by all patients. All the data was entered in the proforma.

Inclusion Criteria: Patients with type 2 diabetes having FBS greater than or equal to 7.0mmol/L and HbA1c >6.5%, Both males and females with age range

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of 20-85 years, having duration of diabetes more than 5 years.

Exclusion Criteria: Patients with type 1 diabetes, patients with end stage renal disease or on drugs known to affect magnesium levels i.e. Aminoglycosides, Diuretics and Digoxin, or suffering from hypertension, haematuria, fever or urinary tract infection, thyroid or adrenal dysfunction, acute or chronic malabsorption states were excluded.

Total of forty five patients both male and female with type 2 DM having HbA1c more or equal to 6.5%, FBS more than or equal to 7.0mmol/L, random blood glucose concentration more or equal to 11.1mmol/L were enrolled from Out Patient department (OPD) of Combined Military Hospital(CMH) Kohat, Using consecutive, non-probability sampling technique. Sample size was calculated using WHO sample size calculator with these calculations (Level of confidence(%)=95, Population Mean=1.011, Standard Deviation=0.1711, Absolute precision=0.5). Serum Magnesium (by photometric xylidyl blue method), HbA1c (by immuno-inhibition method), microalbuminuria (24hrs urinary sample, by immunoturbidimetry method) and Fasting Blood Sugar (FBS by hexokinase method) were conducted in CMH, Kohat laboratory and verified by the Pathologist.

Data was entered and analysed by using SPSS version 16. Descriptive statistics were determined for qualitative as well as quantitative variables. For quantitative variables like serum magnesium, HbA1c, FBS, microalbuminuria (24hrs urinary sample), Mean±SD were calculated. For qualitative variables like gender and age frequency and percentages were calculated. Qualitative variables are presented as charts and tables. Independent sample t-test was used to compare quantitative variables like serum magnesium levels in patients with and without diabetic nephropathy. The *p*-value of ≤0.05 was considered significant.

RESULTS

Forty five patients meeting the inclusion/exclusion criteria were enrolled in the study and their serum magnesium levels were checked. Twenty five were males (55.6%) while 20 were females (44.4%). Mean age was 68.24±7.57 years. Mean microalbuminuria was 37.5±21.33 mg/L. Mean fasting plasma glucose was 8.77±1.42 mg/L.

Mean serum magnesium level was 1.36±0.29 mg/dl. Mean serum magnesium level in patients with diabetic nephropathy was 1.25±0.35 mg/dl, whereas mean serum magnesium level in patients without diabetic nephropathy was 1.50±0.17 mg/dl, *p*-value was

calculated as 0.009 showing a significant difference between the two groups (Table-I & II). The frequency of hypomagnesemia was 66.7% (30 out of 45 patients), while 33.3% (15 out of 45 patients) had normal magnesium levels (Figure-1).

Table-I: Mean Serum Magnesium in Patients with and without Diabetic Nephropathy (n=45)

| | Diabetic Nephropathy | n(%) | Mean±SD (mg/dl) |
|------------------|----------------------|------------|-----------------|
| Magnesium levels | Nephropathy | 28(66.67%) | 1.254±0.3512 |
| | No nephropathy | 17(33.33%) | 1.506±0.1784 |

Table-II: Mean Serum Magnesium in Patients with and without Nephropathy Independent samples test (n=45)

| Magnesium levels(mg/dl) | Patients with Diabetic Nephropathy | Patients without Diabetic Nephropathy | <i>p</i> -value |
|-------------------------|------------------------------------|---------------------------------------|-----------------|
| | 1.25±0.35mg/dl | 1.50±0.17mg/dl | 0.009 |

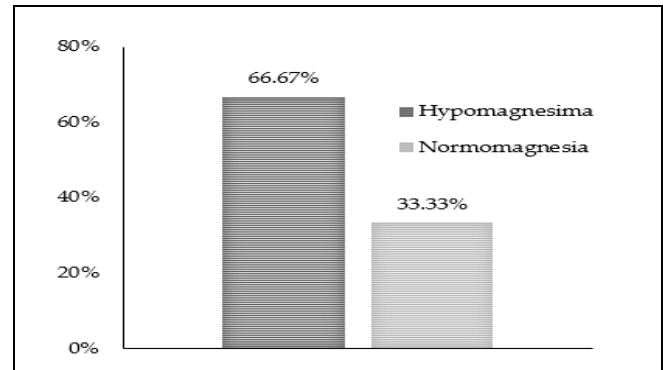


Figure-1: Percentage of Hypomagnesemia (n=45)

Mean microalbuminuria in patients having DN was 49.57±18.02 mg/L, while mean microalbuminuria in patients without nephropathy was 17.64±5.39 mg/L. 67.9% of the patients with DN had hypomagnesemia while 64.7% with no DN had hypomagnesemia (Figure-2). Gender wise distribution showed mean serum magnesium level in males and females was 1.44±0.26 and 1.23±0.34 mg/dl respectively, *p*-value was calculated as 0.031 showing a significant difference between the two groups (Table-III). Gender distribution showed that mean microalbuminuria in male and female patients was 29.08±13.71 and 48.0±24.6 mg/L respectively.

DISCUSSION

Diabetes mellitus (DM) is a major health problem, with a worldwide prevalence of over 250 million. 90-95% diabetics have type-2 diabetes. DM, along with its complications, is the 6th leading cause of death. In Pakistan, around 13% of the population is suffering from DM. Diabetic nephropathy (DN) is one of the main causes of end-stage renal disease (ESRD).^{11,12}

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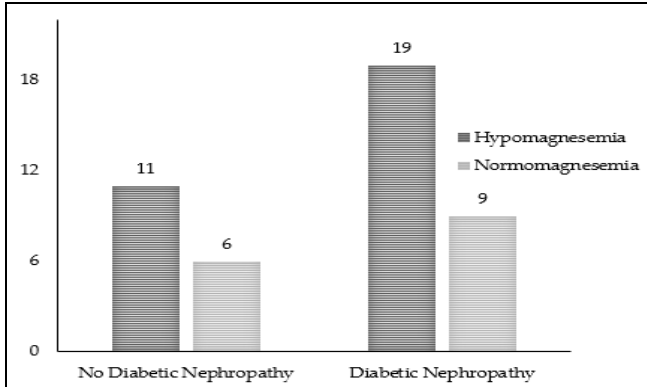


Figure-2: Frequency of hypomagnesemia in patients with and without nephropathy (n=45)

Table-III: Mean Serum Magnesium (Genderwise) Independent Samples Test (n=45)

| Magnesium levels(mg/dl) | Males | Females | p-value |
|-------------------------|-----------|-----------|---------|
| | 1.44±0.26 | 1.23±0.34 | 0.031 |

Magnesium being the 4th most abundant cation in humans, plays an important role as a co-factor for reactions that require ATP and kinases, as well as facilitates neuromuscular excitability, permeability of cell, and mitochondrial functions. Deficiency develops due to poor absorption and rapid turnover. Magnesium levels are low among type 2 diabetics, mainly because intracellular concentration of magnesium is regulated by insulin. Hypomagnesemia is associated with poor control of blood sugar and several long term diabetic complications. Serum magnesium levels are not routinely measured in diabetics. Low magnesium levels act as independent risk factor for DN. Therefore magnesium levels in diabetics should be routinely measured, and magnesium supplementation should be advised to those found out to have low levels to prevent or slow down progression of DN. Magnesium deficiency leads to various complications of DM including albuminuria. Therefore magnesium deficiency has specific role in the pathogenesis of DN, though its exact role is not clear.

Several studies have demonstrated that hypomagnesemia acts as a marker for the development of DN¹³⁻¹⁸. Results of our study showed that mean age in our patients was 68.24±7.57 years, mean microalbuminuria was 37.51±21.33 mg/L, mean microalbuminuria in patients having DN was 49.57±18.02 mg/L, while mean microalbuminuria in patients without nephropathy was 17.64±5.39 mg/L. Mean serum magnesium level was 1.36±0.29 mg/dl. The frequency of hypomagnesemia was 66.7% (30 out of 45 patients), while 33.3% (15 out of 45 patients) had normal serum magnesium levels. Mean serum magnesium level in

patients with DN was 1.27±0.31 mg/dl, whereas mean serum magnesium level in patients with no DN were 1.50±0.17 mg/dl, *p*-value was calculated as 0.001 showing a significant difference between the two groups. About of 67.9% of the patients having DN had hypomagnesemia while 64.7% without DN had hypomagnesemia.

As seen in our study, hypomagnesemia is quite common in patients suffering from DM (66.7%). The hypomagnesemia is severe in patients having diabetic complications. Serum magnesium levels were lower among patients with DN, as compared those without nephropathy. Hypomagnesemia leads to higher incidence of both microalbuminuria & macroalbuminuria.

In a similar study conducted by Farah Aziz Khan and others, it was shown that serum magnesium levels were significantly lower in patients with DN as compared to controls.¹² Corsonello *et al.* showed that serum magnesium is distinctly reduced in diabetic patients with microalbuminuria in contrast to those having no proteinuria.¹⁰ Magnesium supplementation provides renal protection in type-2 diabetics with nephropathy. Higher intake of Mg²⁺ significantly decreases the risk of developing type-2 diabetes.^{13,15}

The beneficial effect of Mg²⁺ on renal functions has been investigated in animal models. In one such study rats fed on a diet lacking magnesium had increased N-acetyl-β-d-glucosaminidase excretion in urine, implying that Mg²⁺ deficiency leads to renal tubular injury.¹⁶

Dewitte *et al.*¹⁷ showed that a significant negative correlation is found between serum magnesium levels and creatinine clearance in non diabetics, but not in those with DM. Pham *et al.*¹⁸ demonstrated in their study that the serum Mg²⁺ level and slope of the inverse serum creatinine showed a significant association in type-2 diabetics with normal renal functions.

The results of our study, were in conformity with the above quoted studies, thus justifying hypothesis of the study that "Serum magnesium levels are reduced in patients having diabetes mellitus and hypomagnesemia is associated with increased incidence and severity of diabetic nephropathy"

CONCLUSION

Serum magnesium levels are decreased in patients with DM. Amongst the diabetic patients, magnesium levels are lower in those with diabetic complications like DN. Serum magnesium levels in diabetics should be routinely checked to recognize patients at risk of nephropathy and magnesium supplementation should be given to those found out to be Mg²⁺ deficient, to prevent or retard the progression of DN.

Conflict of Interest: None.

Author's Contribution:

Following authors have made substantial contributions to the manuscript as under:

FT & RA: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

BA & NAS: Critical review, concept, drafting the manuscript, approval of the final version to be published.

LN & MN: Data acquisition, data analysis, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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