CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3834741

Available online at: http://www.iajps.com Research Article

ASSOCIATION OF HYPOMAGNESEMIA AND DIABETIC NEPHROPATHY

[1]Dr Nehan Shakeel, [2]Dr Fatima Jabbar, [3]Dr Iqra Raees
[1]Faisalabad Medical University, Faisalabad.

Article Received: March 2020 **Accepted:** April 2020 **Published:** May 2020

Abstract:
Background*: Hypomagnesaemia is a regular sequel of type II diabetes mellitus.*
Objective: *This research has aimed to highlight the association of hypomagnesemia in type II diabetes in order to identify and treat the electrolyte disorder to prevent complications setting in early, to approximate the prevalence of Hypomagnesemia \ with Diabetic nephropathy and to find association between both in order to correct reduced serum magnesium levels at an early stage for prevention and progression of complications.*
Method: *the study was conducted in settings of Faisalabad Medical University, Faisalabad with Duration of Study of 06 months after the approval of synopsis. Using a*
Sample Size of 86 patients calculated Using WHO sample size calculator with the Level of confidence (%) = 95% . anticipated Population Proportion = 17%. Data was collected from Faisalabad Medical University, Faisalabad outdoor nephrology and medicine department with the approval of ethical review committee of Combined Military Hospital Lahore after seeking written informed consent from the patients through a Survey proforma.it was a cross sectional study with chi- square test applied in order to find association between reduced serum magnesium levels and diabetic nephropathy.
Results*:there was 100% prevalence of Hypomagnesemia patients with End Stage Renal Disease with majority in age group in 55 to 65yrs of age independent of gender.Association was found to be significant $p<0.005$*
Conclusion: *hypomagnesemia is assoiated with diabetic nehropathy that ultimately leads to renal failure.*
Keywords:*End stage renal disease,Hypomagnesemia,diabetes mellits type II.*

Corresponding author:
Dr. Nehan Shakeel,
Faisalabad Medical University, Faisalabad.

QR code

Please cite this article in press Nehan Shakeel et al, ***Association Of Hypomagnesemia And Diabetic Nephropathy.,*** *Indo Am. J. P. Sci, 2020; 07(05).*

INTRODUCTION:

Type 2 diabetes mellitus (T2DM) is often a more sighted variant of diabetes among the two and a metabolic disorder resulting due to insulin resistance and decreased its responsiveness of beta cells in pancreas, thus, leading to hyperglycemia1. In Pakistan, Diabetes Mellitus effects approximately 13% of the adult population 2. Complications induced by Diabetes are microvascular and macrovascular. These macrovascular effects on the kidneys lead to renal failure which is the commonest cause of Chronic Kidney Disease due to diabetes mellitus 3. This from of Chronic renal pathology is called Diabetic Nephropathy, approximately 56% of the diabetic population of Pakistan suffers from this disease. 4. Risk factors for development of Diabetic Nephropathy and its progression include poor glycemic control, longer duration of disease, co-existing hypertension, and the presence of proteinuria. Microalbuminuria leads to increased fatality rates in diabetics.

Diabetes leads to disturbances in the homeostasis of different inorganic minerals including Magnesium. A chronic underdiagnosed Magnesium deficit or an undisguised clinical hypomagnesaemia is a very pertinent sequel of diabetic nephropathy , especially in patients with poorly controlled daibetes.6 Magnesium concentration in intracellular space is mainly controlled by Insulin secretion.7 An increased urinary loss and a decreased dietary intake leads to loss of the electrolyte in such patients .8 As many as 32% patients of Diabetes suffer from Hypomagnesemia in Pakistan.9 Low Magnesium levels in Diabetics have also been linked with complications like neuropathy, retinopathy and foot ulcers .10-12

Providing magnesium controls the plasma glucose level and enhances the glycemic control in patients with Diabetes and Hypomagnesaemia.13 however,the role of this electrolyte and its level in Nephropathy is yet to be clearly defined14. However some evidence suggest that lower levels are associated with a higher risk of development and progression of Diabetic Nephropathy.15

Blood Magnesium levels may not be routinely done in patients with Diabetes .16 This study will aim to show that lower serum Magnesium levels occur more frequently than normal Magnesium levels in ESRD secondary to Diabetes Mellitus. If this correlation is established, monitoring of Serum Magnesium Levels and Magnesium supplementation would be recommended in patients of Diabetes Mellitus at risk of developing Diabetic Nephropathy.

Operational Definitions

- **Diabetes Mellitus:**
  - Fasting blood glucose(FBS) concentration equal to or greater than 7.0 mmol/L (126mg/dl) after atleast an 8 hr fast**17**

- **Diabetic Nephropathy:** One of the following**16**:
  - Estimated GFR < 15-30 ml/min/1.73m**2**
  - Urine Albumin to Creatinine Ratio (UACR) > 30mg/g

- **Serum Magnesium Levels:**
  - Hypomagnesemia : blood Magnesium < 1.5 mg/L
  - Normomagnesemia : blood Magnesium 1.5 mg/L to 2.4 mg/dl

MATERIALS AND METHODS:

1. Settings: Combined Military Hospital Lahore.

2. Duration of : 06 months.

3. Sample Size: Using WHO sample size calculator with the following**18**:

- Level of confidence (%) = 95%
- Anticipated Population Proportion = 17%
- Absolute Precision Required = 8%
- Sample size (n) = Approx. **86** patients
- level of significance= 95%

4.Statistical test: chi- square test will be applied in order to find association between reduced serum magnesium levels and diabetic nephropathy.

5. Study Design: descriptive study.

7. Data Collection:

Data was collected from Faisalabad Medical University, Faisalabad outdoor nephrology and medicine department with the approval of ethical review committee of Faisalabad Medical University, Faisalabad after seeking written informed consent (**Anx A**) from the patients.Survey proforma will be filled of 86 randomly selected patients fulfilling the inclusion criteria. Baseline Data, FBS or RBS(Venous sample) / HbA1C(immuno-inhibition method), Urine Albumin to Creatinine Ratio (UACR), eGFR (Cockcroft-Gault Equation) and blood Magnesium levels of selected patients was collected and entered after verification from pathologist and classified medical specialist.

DATA ANALYSIS:

Data was entered and statistical tests applied using SPSS version 24. Descriptive statistics were calculated for all variables. for variables like serum magnesium, FBS , HbA1c, UACR, mean was assessed. For qualitative variables like age and sex, frequency and

percentages was calculated and presented as tables and charts.Frequency distribution table will be made and chi- square test will be applied in order to find association between reduced serum magnesium level and diabetic nephropathy,

RESULTS:

Hypomagnesemia is found to be associated with type II diabetic nephropathy in all 86 patients we sampled.magnesim level was found to be below the limit for all the patients irrespective of age and gender. Association was calculated and was found to be significant.

DISCUSSION:

hypomagnesemia is closely linked with type 2 diabetes, many studies have shown an inversely proportional relationship between control of blood sugar and Mg levels (7,10,16 –19). Although many researches have proven that diabetes leads to hypomagnesemia and early addition of the electrolyte in treatment regimens lowers the incidence of development of diabetes (20 –23). Hypomagnesemia tends to reduce insulin sensitivity in control groups of various trials, whereas addition of Mg leads to improve glycemic control in aged patients in absence of diabetes (18,24,25).however ,the pathophysiology of hypomagnesemia worsening chronic diabetes is not well defined. furthermore, it has been indicated that hypomagnesemia may cause changes in transportation of glucose, decrease release of insulin by beta calls o pancreas, development of tissue resistance and (29)however there were many studies which negated any relation of magnesium levels and glycemic control in diabetes (11,30 –32).

These dierences in views may be due to difference of race and inheritance of different populations used in different studies. There is enough evidence to support that decrease in magnesium levels disturbs celluar functioning. Data from various studies suggest that hypomagnesemia hastens formation of thrombus by causing activation of platelets and damaging the endothelium (33). Hypomagnesaemia also cause surge of cytokines,chemoines and other inflammatory mediators and factors(34 –36), increases free radiacal injuries (37), leading to constriction of vessels and thereby raises blood pressure in a long run. (38 – 40),. Decreased Magnesium also causes damage to DNA by hindering its repair and inducing apoptosis leading to tumorous growths(43)studies at micro and macro vascular level have linked hypomagnesemia to various diabetic complications. Cardiovascular complications comes in foremost phase of importance. In a study that involved 19 individuals without diabetes and hypertension, 17 hypertensive individuals non diabeics, and 6 hypertensive individuals with diabetes, (44) presented out the lowest mean serum Magnesium level among the hypertensive diabetic group. Similarly another study that included statistis on data from the Atherosclerosis Risk in Communities (ARIC) Study, prospective cohort study that lasted 4 to 7 yr and involved 13,922 middle-aged adults who were free of coronary heart disease at baseline, showed indirectly proportional relation between serum Mg and heart diseases in diabetics(45). Diabetic Retinopathy also is a common early setting in complication of diabetes in which an association between retinal damage and low magnesium levels was observed.it was a cross sectional descriptive study (46,47).serum magnesium levels were not only related to presence of retinal damage but also to the intensity of the disease in diabetics. Another resercch involving 128 members having uncontrolled diabetes with HbA1c evel more than 8, concentration of magnesium in blood were not observed to be lower among those with diabetic retinopathy but rather among those with neuropathy and coronary disease (11).

An association between development of Foot Ulcerations in diabetics and low magnesium levels further adds on to the provided explanations Giving a link between hypomagnesemia and the risk of development of polyneuropathy, and hypercoagulopathy. RodriguezMoran and Guerrero-Romero (48) 93.9% of the 33 patients with diabetic foot ulcers were compared with 73.1% of the 66 patients without diabetic foot ulcers;and association was found to be significant). Nephropathy, In a study that involved 30 diabetic patients who had type 2 diabetes only, 30 diabetics with proteinuria, and 30 with massive proteinuria, Corsonello et al. (49) observed a marked decrease in serum ionized Mg in both the microproteinuria and massiveproteinuria groups compared with the diabetic group that did not have any proteinuria.Similarly, another retrospective study reported a positive association between decreased Magesium levels and a swift progression towards renal failure(7) and many other complications including metabolic syndrome and neuronal abnormalities (6). Requirement of better understanding of Mg metabolism and efforts to optimize magnesium levels in the routine management of diabetes is required.

RESULTS:

Hypomagnesemia is found to be associated with type II diabetic nephropathy in all 86 patients we sampled.magnesim level was found to be below the limit for all the patients irrespective of age and gender.

Association was calculated and was found to be significant.

REFERENCES:

1. Unwin N, Shaw J, Zimmet P, Alberti K. Impaired glucose tolerance and impaired fasting glycaemia: the current status on definition and intervention. Diabetic medicine 2002;19(9):708-23.
2. Zafar J, Bhatti F, Akhtar N, Rasheed U, Bashir R, Humayun S et al. Prevalence and risk factors for Diabetes Mellitus in a selected urban population of a city in Punjab. J Pak Med Assoc. 2011 jan; 61(1): 40-7.
3. Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J, Harrison's Principles of Internal Medicine. 19th ed. New York: McGraw Hill; 2015. Chapter 419, Diabetes mellitus: Complications.
4. Ali A, Iqbal F, Taj A, Iqbal Z, Amin M, Iqbal Q. Prevalence of microvascular complications in newly diagnosed patients with Type 2 diabetes. Pakistan Journal of Medical Sciences. 2013;29.
5. Waanders F,Visser FW and Gans ROB. Current concepts in the management of diabetic nephropathy.Neth J M.2 0 13 Nov; 71(9):448-56.
6. Xu J, Xu W, Yao H, Sun W, Zhou Q, Cai L. Associations of serum and urinary magnesium with the Pre-diabetes, Diabetes and Diabetic complications. PLoS ONE. 2013 Feb; 8(2): e56750.
7. Srinivasan AR, Niranjan G, Velu VK, Parmer P, Anish A. Status of serum magnesium in type 2 diabetes mellitus with particular reference to serum triacylglycerol levels. Diabetes Metabol Syndr: Clinical Research and Reviews. 2012 June; 6(4): 187-9.
8. Barbagallo M. Magnesium and type 2 diabetes. World Journal of Diabetes. 2015;6(10):1152.
9. Iftikhar R, Sultan M, Kumail A, Ehtesham H. Hypomagnesemia in patients of type 2 Diabetes. Journal Of Medical Professionals, Pakistan; Nov 2013;20(5):804-9.
10. Migdalis I, Xenos K, Chairopoulos K, Varvarigos N, Leontiades E, Karmaniolas K. Ca2+-Mg2+-ATPase activity and ionized calcium in Type 2 diabetic patients with neuropathy. Diabetes Research and Clinical Practice. 2000;49(2-3):113-118.
11. de Valk H, Hardus P, van Rijn H, Erkelens D. Plasma magnesium concentration and progression of retinopathy. Diabetes Care. 1999;22(5):864-865.
12. Rodríguez-Morán M, Guerrero-Romero F. Low Serum Magnesium Levels and Foot Ulcers in Subjects with Type 2 Diabetes. Archives of Medical Research. 2001;32(4):300-303.
13. Guerrero-Romero F, Simental-Mendía L, Hernández-Ronquillo G, Rodriguez-Morán M. Oral magnesium supplementation improves glycaemic status in subjects with prediabetes and hypomagnesaemia: A double-blind placebo-controlled randomized trial. Diabetes & Metabolism. 2015;41(3):202-207.
14. Pham P, Pham P, Pham P, Pham S, Pham P, Pham P. The link between lower serum magnesium and kidney function in patients with diabetes mellitus Type 2 deserves a closer look. CN. 2009;71(04):375-379.
15. Sakaguchi Y, Shoji T, Hayashi T, Suzuki A, Shimizu M, Mitsumoto K et al. Hypomagnesemia in Type 2 Diabetic Nephropathy: A novel predictor of end-stage renal disease. Diabetes Care. 2012;35(7):1591-1597.
16. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Journal Of the international Society of nephrology. 2015; volume 3(Issue 1 Jan 2013).
17. Classification and Diagnosis of Diabetes. Diabetes Care. 2014;38(Supplement_1):S8-S16.
18. Supriya MS, Pinnelli VB, Murgod R, Raghavendra DS. Evaluation of serum copper, magnesium and glycated haemoglobin in type 2 diabetes mellitus. Asian J Pharm clin res. 2013;6(2):188-90.