

## ORIGINAL ARTICLE

# Estimation of Serum Magnesium Level in Patients of Type-II Diabetes Mellitus and Diabetic Nephropathy

ALI RAZA MEMON<sup>1</sup>, SHIRJEEL HUSSAIN<sup>2</sup>, SINDHU LAGHARI<sup>3</sup>, FOZIA SHAIKH<sup>4</sup>, ABDUL SATTAR<sup>5</sup>, SYEDA NARGIS FATIMA<sup>6</sup>

<sup>1</sup>Assistant Professor Biochemistry Department Liaquat University of Medical & Health Sciences, Jamshoro

<sup>2</sup>Assistant Professor General Medicine Department Liaquat College of Medicine and Dentistry, Karachi

<sup>3</sup>Research Associate Medical Research Centre Liaquat University of Medical & Health Sciences, Jamshoro

<sup>4,5</sup>Lecturer Department of Biochemistry Liaquat University of Medical & Health Sciences, Jamshoro

<sup>6</sup>Assistant Professor Physiology Department Liaquat College of Medicine and Dentistry, Karachi

Corresponding Author: Ali Raza Memon, Email: [raza.memon@lumhs.edu.pk](mailto:raza.memon@lumhs.edu.pk)

## ABSTRACT

**Aims & Objective:** This study was conducted to estimate the serum magnesium level in patients of type-II diabetes mellitus and diabetic nephropathy.

**Methodology:** This case control study was conducted at LUMHS Jamshoro Sindh Pakistan. Total 120 subjects were selected for this research divided in to three groups, control and two case study groups for the period of six months July 2020 to December 2020. FBS, HbA1c%, serum creatinine, serum magnesium levels were estimated from all subjects. The statistical analysis was done by SPSS version 21 by applied ANOVA test to compare the parameters in different groups.

**Results:** Serum Magnesium level was significantly ( $p < 0.05$ ) decline in group C patients of diabetic nephropathy with poor glycemic control as compared to control or diabetic patients without complications.

**Conclusion:** Estimation of serum magnesium level in the diabetic patients can be use for the early predictor tool to know the expansion of diabetic complications.

**Keywords:** Type-2 Diabetes Mellitus, Diabetic Nephropathy, Serum Magnesium

## INTRODUCTION

The poor glycemic control of diabetes mellitus can lead chronic loss of kidney function leading to diabetic nephropathy.<sup>1</sup> More than 30% patients of type-I & II diabetes mellitus are affected with nephropathy.<sup>2</sup> The chronic kidney disease and end stage renal disease (ESRD) are also caused by diabetic nephropathy.<sup>3,4</sup> More than one third diabetic population all over the world also suffered from ESRD due to diabetic nephropathy.<sup>5</sup> The earliest pathology in diabetic nephropathy is constriction of efferent arterioles and dilation of afferent arterioles, which can lead to hypertension and hyperfiltration of glomeruli capillaries.<sup>6</sup> Urine albumin and serum creatinine are the main biochemical parameters for assessment of renal function in diabetic nephropathy.<sup>7</sup> When micro albuminuria (UAE > 20 g/min and 199 g/min) and macro albuminuria (UAE > 200 g/min) occur, diabetic nephropathy should be investigated.<sup>8</sup> Increasing prevalence rate of type-II diabetes mellitus all over the world can lead to increase the incidence of end stage renal disease.<sup>5</sup> Magnesium is one of the important intracellular cation and main cofactor in different metabolic ATPase dependent reactions of carbohydrate metabolism.<sup>9,10</sup> Magnesium plays important role in release of insulin.<sup>11</sup> Depletion of magnesium can affect insulin sensitivity.<sup>11</sup> Hyperglycemia causes increased magnesium loss in the kidneys, resulting in hypomagnesaemia in diabetics.<sup>12</sup> Depletion of magnesium also take part in development of diabetic complications like nephropathy, retinopathy.<sup>13</sup> The goal of this study is to evaluate the status of serum magnesium levels in diabetics without nephropathy, diabetics with nephropathy and in control patients.

## METHODOLOGY

This case control study was conducted for period of six months from July to December 2020 at Liaquat University

of Medical & Health Sciences Jamshoro, Sindh. Diabetic patients were recruited from diabetic OPD and diabetic nephropathy patients collected from diabetic OPD and nephrology unit. Total 120 subjects were selected with their own consent and permission and divided in to three groups, group A contained 40 normal subjects selected as control, group B 40 diabetic patients without diabetic complications and group C 40 diabetic patients with diabetic nephropathy. The patients with both genders of type-II diabetes mellitus with history of diabetes from last five years with age 40 to 60 years were included while patients of type-I diabetes and type-II diabetes below age 40 or above 60 years, patients of hypertension, retinopathy, liver disorders, patients having history of usage of diuretic drugs, alcohol were excluded from this study. The overnight fasting sample was taken from each subject under aseptic measurements 5ml of blood sample collected 1ml separated in fluoride containing gel tube while remaining sample in plain test tube and sample was centrifuged at 4000rpm for 5 to 10 min. Urine sample was collected in sterile urine bottles. Fasting Blood glucose level was measured by Glucose Oxidase Method while HbA1c% measured on Cobas auto analyzer, serum magnesium estimated by Kit Method while Urine albumin level measured by Immunoturbidimetric method.<sup>14</sup> The data was statistical analyzed by SPSS version 21 by applied ANOVA test to compare parameters with in three groups.

## RESULTS

The results of this study shows there is statistically significance raised fasting blood sugar levels, HbA1c%, serum creatinine, albumin in urine in diabetic as well diabetic with nephropathy group. Serum magnesium levels statistically significant decline ( $p < 0.05$ ) in diabetic nephropathy group.

Table 1: Mean &amp; S,D with Significant Values of all Parameters under Study

Parameters	Group A	Group B	Group C
FBS (mg/dl)	77 ± 11	134 ± 14 *	199 ± 26**
HbA1c%	5.2 ± 0.3	7.7 ± 1.3 *	11.5 ± 2.1**
S.Creatinine (mg/dl)	0.6 ± 0.2	1.1 ± 0.3	3.4 ± 1.6*
Micro albumin (Urine)	21.8 ± 4.99	51.7 ± 15.3	87.13 ± 25.37*
S.Mg <sup>++</sup> (mg/dl)	1.9 ± 0.1	1.2 ± 0.3*	0.8 ± 0.7 *

(\* = p &lt; 0.05 / \*\* = p &lt; 0.001)

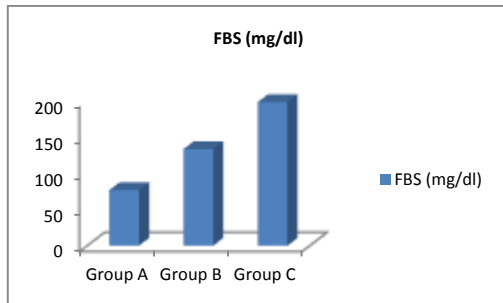


Figure 1: Fasting Blood Glucose Level

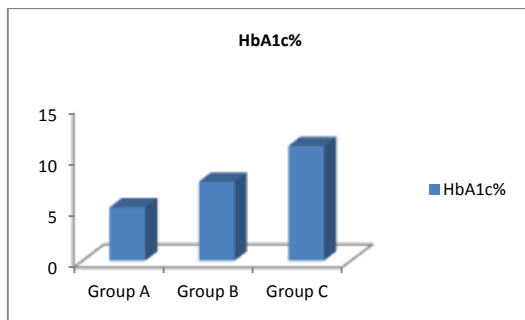


Figure 2: HbA1c%

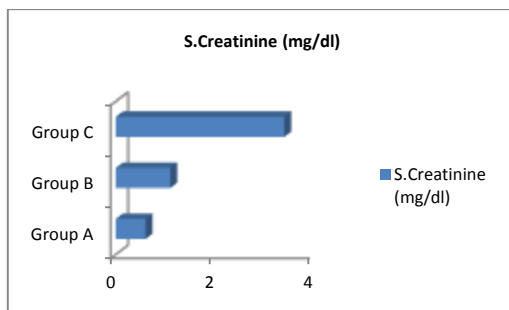


Figure 3: Serum Creatinine Levels

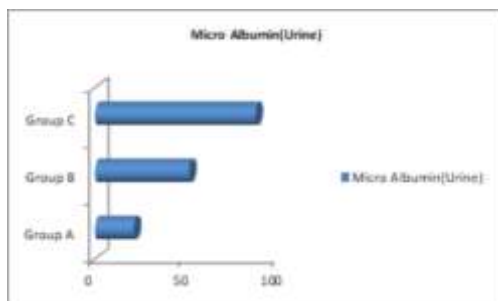


Figure 4: Micro Albumin Levels in Urine

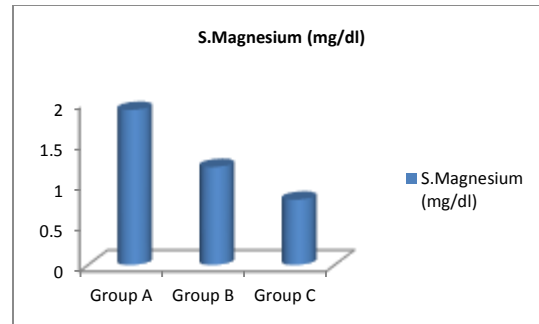


Figure 5: Serum Magnesium Levels

## DISCUSSION

Magnesium is the intracellular cation that plays vital role as cofactor to regulate the functions of different enzymes of carbohydrate metabolism which are the energy dependent or energy yielding enzymes.<sup>15</sup> Magnesium plays important role in the secretion and regulation of insulin from pancreas.<sup>16</sup> Hypomagnesaemia can lead to decrease secretion of insulin or disturb the proper actions of insulin so it leads hyperglycemia because magnesium depletion can interrupt the function of Kinases enzyme family and it may cause the development of oxidative stress and formation of free radicals.<sup>17,18</sup> When oxidative stress persists in diabetic population, that will lead to development of complications like, angina, myocardial infarction, nephropathy and retinopathy.<sup>19</sup> In diabetic nephropathy magnesium depletion more markedly observed due to impaired absorption, excessive loss in urine due to hyperglycemia, osmotic diuresis, and defective reabsorption of magnesium from renal tubules.<sup>20,21</sup>

Our findings are consistent with those of Matsuo S, et al (2009)<sup>22</sup>, who found that serum magnesium levels fall in diabetics, whereas serum creatinine levels rise dramatically in diabetic nephropathy. The findings of this investigation, which were backed up by Dewitte et al (2004)<sup>23</sup> and Schwarz S et al (2006)<sup>24</sup>, suggested a link between serum magnesium and diabetic nephropathy. Why the impact of hypomagnesaemia on renal outcome differed between type 2 diabetic nephropathy and nondiabetic CKD is unknown. Mg shortage has been linked to the development of diabetic problems due to disruption of cell membrane transport and consequent myo-inositol depletion within the cell.<sup>25</sup> Mg deficiency is, in fact, associated with various type 2 diabetes complications including albuminuria.<sup>26</sup>

Therefore, it is plausible that Mg deficiency has specific pathogenic significance in type 2 diabetic nephropathy; however, the exact role of Mg deficiency in type 2 diabetic nephropathy warrants further investigation.

From above discussion it is also proven that magnesium is considered as biomarker before the development of ESRD.

## CONCLUSION

This study concluded that serum magnesium level is significantly decline in poor glycemic control with diabetic complication like diabetic nephropathy. Estimation of serum magnesium level in the diabetic patients can be the early predictor tool for indication the expansion of diabetic complications.

## REFERENCES

1. Gil CL, Hooker E, Larrivée B. Diabetic kidney disease, endothelial damage, and podocyte-endothelial crosstalk. *Kidney Medicine*. 2021 Jan 1;3(1):105-15.
2. Kuniss N, Freyer M, Müller N, Kielstein V, Müller UA. Expectations and fear of diabetes-related long-term complications in people with type 2 diabetes at primary care level. *Actadiabetologica*. 2019 Jan 28;56(1):33-8.
3. Sagoo MK, Gnudi L. Diabetic nephropathy: an overview. *Diabetic Nephropathy*. 2020:3-7.
4. Warren AM, Knudsen ST, Cooper ME. Diabetic nephropathy: an insight into molecular mechanisms and emerging therapies. Expert opinion on therapeutic targets. 2019 Jul 3;23(7):579-91.
5. Chen HY, Pan HC, Chen YC, Chen YC, Lin YH, Yang SH, Chen JL, Wu HT. Traditional Chinese medicine use is associated with lower end-stage renal disease and mortality rates among patients with diabetic nephropathy: a population-based cohort study. *BMC complementary and alternative medicine*. 2019 Dec;19(1):1-3.
6. Ohishi M. Hypertension with diabetes mellitus: physiology and pathology. *Hypertension research*. 2018 Jun;41(6):389-93.
7. Chen L, Xiang E, Li C, Han B, Zhang Q, Rao W, Xiao C, Wu D. Umbilical cord-derived mesenchymal stem cells ameliorate nephrocyte injury and proteinuria in a diabetic nephropathy rat model. *Journal of diabetes research*. 2020 Apr 29;2020.
8. Siddharthan R. A Study on Prevalence and Risk Factors of Diabetic Nephropathy in Newly Detected Type 2 Diabetes Mellitus Patients (Doctoral dissertation, Chengalpattu Medical College and Hospital, Chengalpattu). 2020.
9. Al Alawi AM, Majoni SW, Falhammar H. Magnesium and human health: perspectives and research directions. *International journal of endocrinology*. 2018 Apr 16; 2018.
10. Ashok V, Padmini PJ. Study of Serum Magnesium Levels and Its Relation to Glycemic Control in Patients with Type 2 Diabetes Mellitus. *Journal of Stress Physiology & Biochemistry*. 2020; 16(4).
11. Feng J, Wang H, Jing Z, Wang Y, Cheng Y, Wang W, Sun W. Role of magnesium in type 2 diabetes mellitus. *Biological trace element research*. 2020 Jul; 196 (1):74-85.
12. Garnier AS, Duveau A, Planchais M, Subra JF, Sayegh J, Augusto JF. Serum magnesium after kidney transplantation: a systematic review. *Nutrients*. 2018 Jun;10(6):729.
13. Kebir NE, Zahzeh T, Khaled MB, Diaf M. Magnesium, A Key Element for The Management of Hypertension, Cardiovascular Complications, Retinopathy, and Diabetic Foot in Diabetes. *Egyptian Academic Journal of Biological Sciences. C, Physiology and Molecular Biology*. 2021 Nov 7;13(2):177-88.
14. Cassol JP, Scolari R, Moresco RN. Impact of albumin carbamylation on immunoturbidimetric measurement of urinary albumin. *Analytical Biochemistry*. 2021 Feb 1; 614: 114047.
15. Kostov K. Effects of magnesium deficiency on mechanisms of insulin resistance in type 2 diabetes: focusing on the processes of insulin secretion and signaling. *International journal of molecular sciences*. 2019 Jan; 20(6):1351.
16. Dubey P, Thakur V, Chattopadhyay M. Role of minerals and trace elements in diabetes and insulin resistance. *Nutrients*. 2020 Jun; 12(6):1864.
17. Kostov K. Effects of magnesium deficiency on mechanisms of insulin resistance in type 2 diabetes: focusing on the processes of insulin secretion and signaling. *International journal of molecular sciences*. 2019 Jan; 20(6):1351.
18. Chiruvella V, Annamaraju P, Guddati AK. Management of nephrotoxicity of chemotherapy and targeted agents: 2020. *American Journal of Cancer Research*. 2020;10(12):4151.
19. Oguntibeju OO. Type 2 diabetes mellitus, oxidative stress and inflammation: examining the links. *International journal of physiology, pathophysiology and pharmacology*. 2019;11(3):45.
20. Yamada S, Inaba M. Potassium Metabolism and Management in Patients with CKD. *Nutrients* 2021, 13, 1751. Extension of Healthy Life Span of Dialysis Patients in the Era of a 100-Year Life. 2021:111.
21. Spires D, Manis AD, Staruschenko A. Ion channels and transporters in diabetic kidney disease. *Current topics in membranes*. 2019 Jan 1;83:353-96.
22. Matsuo S, Imai E, Horio M, et al. Collaborators developing the Japanese equation for estimated GFR Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis* 2009;53:982–992.
23. Dewitte K, Dhondt A, Giri M, et al. Differences in serum ionized and total magnesium values during chronic renal failure between nondiabetic and diabetic patients: a cross-sectional study. *Diabetes Care* 2004;27:2503–2505.
24. Schwarz S, Trivedi BK, Kalantar-Zadeh K, Kovesdy CP. Association of disorders in mineral metabolism with progression of chronic kidney disease. *Clin J Am SocNephrol* 2006;1:825–831.
25. Grafton G, Bunce CM, Sheppard MC, Brown G, Baxter MA. Effect of Mg<sup>2+</sup> on Na(+)-dependent inositol transport. Role for Mg<sup>2+</sup> in etiology of diabetic complications. *Diabetes* 1992;41:35–39.
26. Migdalis IN, Xenos K, Chairopoulos K, Varvarigos N, Leontiades E, Karmaniolas K. Ca(2+)-Mg(2+)-ATPase activity and ionized calcium in Type 2 diabetic patients with neuropathy. *Diabetes Res ClinPract* 2000;49:113–118.