

Evaluation of hypomagnesaemia in diabetic patients with nephropathy in a reference clinical laboratory: A comparative cross sectional study

Sumaiya Qamar, Muhammad Anwar, Zujaja Hina Haroon, Afshan Bibi, Muhammad Usman Munir, Sobia Irum Kirmani

Abstract

Serum Magnesium plays a significant role in different diabetic complications. This comparative cross sectional study was conducted to evaluate serum magnesium levels in patients with Type 2 Diabetes Mellitus (T2DM) with and without nephropathy. A total of 182 diabetic patients (91 with nephropathy and 91 without nephropathy) were included. Odds ratio were calculated and Mann Whitney U test was used to compare quantitative variables; $p < 0.05$ was considered significant. The results showed that 64/91 (70.3%) patients with nephropathy had hypomagnesaemia as compared to 21/91 (23.07%) patients without nephropathy. The risk of hypomagnesaemia was higher in patients with nephropathy than without nephropathy (Odds ratio 2.7 vs 0.34). Median magnesium levels (1.73 mg/dl) were lower in patients with nephropathy as compared to patients without nephropathy (2.09 mg/dl), $p < 0.01$. It is concluded that magnesium levels were significantly lower in patients with diabetic nephropathy as compared to without nephropathy.

Keywords: Hypomagnesaemia, Nephropathy, Type 2 Diabetes Mellitus.

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Introduction

Diabetes is one of the challenges of 21st century across the globe including Pakistan. It is a chronic metabolic disease that results in increased glucose levels in the body.¹ In the UK, it is estimated that the prevalence of type 2 Diabetes Mellitus (T2DM) will increase to 54% between the year 2015–2030 and mortality will also increase by 38% annually.² There will be 20% increase in adults who have diabetes in developed countries and 69% increase in developing countries between the year 2010–2030.³ The chance to develop Chronic Kidney Disease (CKD) will increase two-folds in T2DM patients as compared to non-diabetic people.⁴ According to the United States (US)

Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology, National University of Medical Sciences, Rawalpindi, Pakistan.

Correspondence: Muhammad Anwar. e-mail: cphanwar09@yahoo.com
ORCID ID. 0000-0002-4028-1332

National Health and Nutrition Examination Survey (NHANES) 2009 to 2014, the occurrence of CKD was estimated to be 26.2% among diabetic adults.⁵ Magnesium (Mg) and other trace elements enhance the action of insulin by activating insulin receptor sites, regulating co-factors involved in the glucose metabolism, and increasing insulin sensitivity. Hypomagnesaemia has been reported to occur in 13.5–47.7% of patients with T2DM.⁶ Prevalence of hypomagnesaemia was 52% in T2DM patients with diabetic nephropathy (DN) as compared to only 22% in patients without DN with a statistical difference of ($p < 0.00$).⁷ Prevalence of T2DM and burden of DN in these patients is very high. The disease burden of DN in Pakistan is about 31%.⁸

To the best of our knowledge no such study has been done in the local population. The aim of this study was to evaluate the serum Mg levels and risk of hypomagnesaemia in T2DM patients with and without DN and assess the association of DN with serum magnesium levels.

Patients, Methods and Results

A comparative cross-sectional study was conducted at the Department of Chemical Pathology and Endocrinology, Armed Force Institute of Pathology, from July to December 2021. After formal approval of the Institutional Ethical Review board, a total of 182 T2DM (91 with DN and 91 without DN) patients were included in the study. Patients with thyroid disorders, liver cirrhosis, Cushing syndrome, Addison's disease, acromegaly, malabsorption, chronic pancreatitis, and chronic kidney disease due to any other reason were excluded. Blood samples were taken in a plain tube for estimation of serum Mg, urea, and creatinine, and in Potassium EDTA tube for HbA1c estimation. Fresh urine samples were obtained in a clean, puncture proof container for albumin to creatinine ratio estimation. Serum Mg, urea, creatinine and urine creatinine were measured by spectrophotometric methods and urinary Albumin was measured by immunoturbidimetry method on automated chemistry analyser. HbA1c was measured on SEBIA by capillary electrophoresis. eGFR was calculated by CKD-EPI calculator. Data was analysed by SPSS version 23. Mann Whitney U test was used to compare the median and IQR of age, HbA1c, Mg, urea, creatinine, and eGFR between the two groups. Odds ratios with 95% confidence interval were

calculated for risk of hypomagnesaemia in DN patients, non-DN patients, male and female subjects. Spearman correlation was used to assess the correlation between the magnesium levels and ACR. $p < 0.05$ was considered statistically significant.

Among the 182 participants, 100 (55%) were males and 82 (45%) were females. On the basis of urinary ACR, selected individuals were divided in two equal groups 91 (50%) with DN ($ACR \geq 30$ mg/g) and 91 (50%) without DN ($ACR < 30$ mg/g) after being adjusted for age and gender. The mean

Table-1: Comparison of Medians and IQR of age, HbA1c, Magnesium, Urea and Creatinine between patients with DN and without DN by Mann Whitney U test.

Parameter	Unit	Nephropathy (n=91) Median (IQR)	Non-nephropathy (n=91) Median (IQR)	p-value
Age	Years	61 (17)	58 (15)	0.115
HbA1c	%	8.4 (2.3)	8.0 (2.6)	0.373
Magnesium	mmol/l	0.71 (0.19)	0.86 (0.11)	0.000
	mg/dl	1.73 (0.46)	2.09 (0.27)	
Urea	mmol/l	6.4 (4.4)	5.4 (2.4)	0.000
	mg/dl	17.93 (12.32)	15.13 (6.72)	
Creatinine	μ mol/l	108 (42)	99 (27)	0.011
	mg/dl	1.22 (0.48)	1.12 (0.31)	
eGFR	(mil/min)	56(32)	69(26)	0.001

Note: DN= Diabetic Nephropathy, HbA1c= Glycosylated Hemoglobin, IQR= Interquartile range.

Table-2: Odds ratios for risk estimation of hypomagnesaemia in DN and Non-DN patients with 95% confidence interval.

	DN Present n (%)	DN not present n (%)
Hypomagnesaemia present	64 (70.3)	21 (23.07)
Hypomagnesaemia not present	27 (29.67)	70 (76.93)
Total	91	91
Odd ratio	2.7 (1.9-3.8)	0.34 (0.23-0.50)

Note: DN= Diabetic Nephropathy.

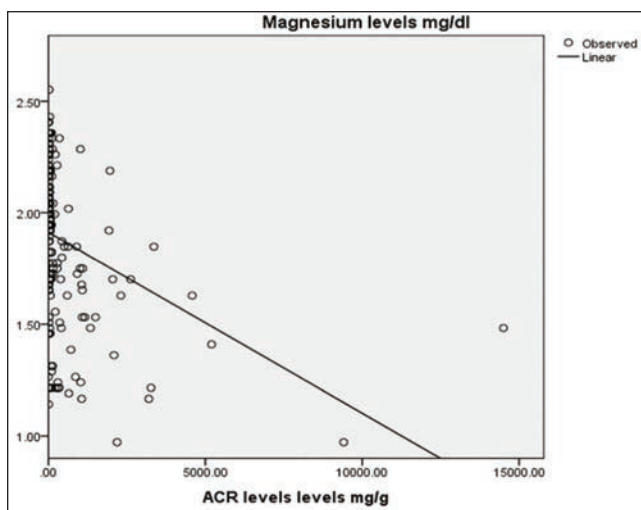


Figure: Scatter plot showing the correlation between Mg levels and ACR. ACR= Albumin to creatinine ratio, Mg= Magnesium.

age of the patients with DN was 60 ± 2 years; whereas in patients without DN it was 58 ± 2 years. Data normality was checked by Shapiro-Wilk test which showed non-parametric distribution ($p < 0.05$). Significant difference was observed in median and IQR of Mg, urea, creatinine, and eGFR between the two groups ($p < 0.05$) when compared by Mann Whitney U test. No significant difference was observed in the median and IQR of age ($p = 0.115$) and HbA1c ($p = 0.373$) as shown in Table-1.

In patients with DN, 64 (70.3%) individuals had hypomagnesaemia as compared to 21 (23.07%) patients without DN. Odds ratio with 95% confidence interval for risk of hypomagnesaemia was higher 2.7 (1.9-3.8) in patients with DN than without DN 0.34 (0.23-0.50) as shown in Table-2.

DN and hypomagnesaemia were more prevalent in females. Out of 82 female patients 48 (58.5%) had DN and 46 (56.1%) had hypomagnesaemia, while out of 100 male patients 43 (43%) had DN and 39 (39%) had hypomagnesaemia. Odds ratio for hypomagnesaemia were 0.730 (0.553-0.962) and 1.458 (1.054-2.018) for males and females, respectively.

The linear regression plot showed that Mg levels decreased as the value of ACR increased. Spearman correlation coefficient demonstrated negative correlation between Mg and ACR ($r = -0.46$, $p = 0.00$), respectively as shown in figure.

Discussion

Magnesium (Mg) is an important mineral, regulating many vital functions in the body. In this cross-sectional study, Mg levels in T2DM patients with and without DN were compared. Mg levels were significantly lower in diabetic nephropathic patients. Bherwani et al observed the association between Mg level and DN ($n = 100$). They reported that there was significantly higher prevalence of DN in patients with hypomagnesaemia as concluded in our study.⁷ Enikuomehin et al ($n = 400$) reported the association of gender with different diabetic complications and concluded that both genders have equal chance to develop diabetic complications except diabetic retinopathy ($p = 0.027$).⁹ The current study showed that females have increased chances of developing DN. Hajar Saeed et al in 2018 ($n = 100$) noted the correlation between Mg and HbA1c and reported that there was no significant association between them ($p = 0.46$) which supports our study ($p = 0.37$).¹⁰ Christine Maric-Bilkan in 2017 highlighted the gender difference among different diabetic complications and noted that diabetic men living in the US are more prone to develop DN as compared to women. These results were not in agreement with our study.¹¹

Conclusion

It was concluded that serum Mg levels were lower and the risk of Hypomagnesaemia was higher in diabetic patients with nephropathy. Serum Mg showed significant correlation with ACR and it can be used as a marker of DN, especially where ACR assay is not available. Moreover, Mg supplements may improve overall wellbeing and reduce complications in patients with T2DM.

Limitations: This was a cross sectional study with small sample size. Multicentre longitudinal studies on larger sample size may be needed to establish the role of Mg in the diagnosis and pathogenesis of diabetic complications, especially DN.

Disclaimer: None.

Conflict of Interest: None.

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