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A Comparative Analysis of Fractional Excretion of Sodium, Potassium and Magnesium among T2DM Patients with Increased Albuminuria and Normal Albuminuria in a Tertiary Care Hospital- An Observational Study

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Abstract **Original Research Article**

***Background*:** T2DM often leads to diabetic kidney disease, a condition marked by change in GFR and urinary albumin excretion. The renal handling of key electrolytes like sodium, potassium, and magnesium plays a crucial role in the progression of renal tubulointerstitial damage in diabetic patients. ***Aim of the study*:** The aim of this study was to compare the fractional excretion of sodium, potassium and magnesium among T2DM patients with increased albuminuria and normal albuminuria. ***Methods*:** This observational study was conducted in Department of Nephrology, Chattogram, Bangladesh from February 2021 to January 2022. Total 125 patients with T2DM were included in this study. ***Result*:** Baseline characteristics showed no significant differences across the study groups. Biochemically, eGFR decreased non-significantly from 95.5 to 86.1 ml/min/1.73 m² across groups, while UACR significantly increased from 14.3 to 1056 mg/gm (P<0.001). FBG levels were similar, but 2hPPBG showed a significant decrease from 8.2 to 7.4 mmol/l (P=0.0041). HbA1C levels varied slightly. FENa, FEK, and FEMg showed significant differences across groups, with FENa ranging from 0.59% to 0.56% (P=0.0016), FEK from 9.4% to 6.9% (P=0.0358), and FEMg from 2.87% to 5.58% (P=0.001). Correlations revealed significant negative associations of eGFR with FENa, FEK, and FEMg, and a significant positive correlation of FEMg with UACR. No significant correlations were found between FBG, 2hPPBG, HbA1C, and the electrolytes excretion. ***Conclusion*:** Significant variations in the fractional excretion of sodium, potassium, and magnesium were observed. Higher eGFR was associated with lower electrolyte excretion, and a significant positive correlation was found between magnesium excretion and UACR.

Keywords: Fractional Excretion, Sodium, Potassium, Magnesium, T2DM, Increased Albuminuria and Normal Albuminuria Level.

I. INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a prevalent chronic disease characterized by insulin resistance and relative insulin deficiency, leading to hyperglycemia [1, 2]. It is associated with various complications, notably diabetic nephropathy, which is a leading cause of end-stage renal disease (ESRD). Diabetic nephropathy is typically heralded by the onset of albuminuria, the abnormal presence of albumin in urine, which is a critical marker for kidney damage and a predictor for cardiovascular risk in T2DM patients [3, 4]. The renal handling of electrolytes, such as sodium (Na), potassium (K), and magnesium (Mg), is significantly altered in T2DM, impacting the disease's progression and associated complications. The fractional excretion of these electrolytes provides insights into renal function and the body's homeostatic mechanisms [5]. Sodium plays a pivotal role in fluid balance, nerve function, and

muscle contraction. In T2DM, the fractional excretion of sodium (FENa) is a critical parameter, reflecting the kidney's response to hyperglycemia-induced osmotic diuresis and the associated risk of hypertension and cardiovascular disease [6, 7]. Studies have shown a complex relationship between sodium intake, renal function, and cardiovascular risk in T2DM, with both high and low sodium intakes linked to adverse outcomes [8, 9]. Potassium, essential for cellular function, is intricately linked to cardiovascular health. The fractional excretion of potassium (FEK) in T2DM is a subject of interest, as potassium balance is crucial for preventing arrhythmias and managing blood pressure [10]. The renal handling of potassium in T2DM, particularly in the context of insulin resistance and the risk of hyperkalemia, is a critical area of study [11]. Magnesium, involved in numerous enzymatic reactions and glucose metabolism, is often depleted in T2DM patients. Hypomagnesemia is linked to insulin resistance and poor glycemic control [12]. Studies indicate that serum magnesium levels are inversely associated with microvascular complications in T2DM, including albuminuria [13]. This suggests a significant role for magnesium handling in the progression of diabetic nephropathy and other vascular complications in T2DM. A comparative analysis of the fractional excretion of sodium, potassium, and magnesium among T2DM patients with increased albuminuria and normal albuminuria is thus vital. It can elucidate the pathophysiological mechanisms underlying diabetic nephropathy and its progression, offering insights into potential therapeutic targets. Furthermore, understanding these mechanisms is crucial for developing strategies to prevent or slow kidney disease progression in T2DM patients. Additionally, this analysis can shed light on the interplay between renal function, electrolyte balance, and cardiovascular risk in T2DM. Given the high burden of cardiovascular disease in this population, understanding the optimal dietary and pharmacological management strategies for electrolyte imbalances is essential. For instance, the nuanced relationship between sodium intake and albuminuria in T2DM underscores the need for individualized dietary recommendations [8, 9].

II. OBJECTIVES

To compare the fractional excretion of sodium, potassium and magnesium among T2DM patients with increased albuminuria and normal albuminuria.

III. METHODOLOGY & MATERIALS

This observational study was conducted in Department of Nephrology, Chattogram, Bangladesh, during the period from February 2021 to January 2022. Total 125 patients with T2DM attending the Department of Nephrology and the Department of Endocrinology, CMCH were included in this study. The patients were divided into three groups which were normal UACR (<30 mg/g Cr), moderately increased albuminuria (30-300 mg/g Cr), and severely increased albuminuria (>300mg/g Cr). Twenty-four hours urine was collected for electrolyte excretion analysis. Consent of the patients and guardians were taken before collecting data. After collection of data, the data were entered into computer and statistical analysis of the results being obtained by using windows-based computer software devised with Statistical Packages for Social Sciences version 28. Kruskal-Wallis test Chi-square test were used to compare the groups. P value ≤0.05 was considered statistically significant.

Inclusion criteria:

1. Patients attended the Nephrology department and Endocrinology department of Chittagong Medical College.
2. T2DM patients with urinary albumin excretion rate < 30 mg/gm (normoalbuminuria), 30-300 mg/gm (moderately increased albuminuria), and >300 mg/gm (severely increased albuminuria).

Exclusion Criteria:

3. Patients with Pregnancy, Fever, and Urinary tract infection
4. Patients with Acute Kidney Injury, any obstructive uropathy, renal transplant, dialysis treatment, and bladder irrigation.
5. Patients with diarrhea, vomiting and burn.
6. Diabetic Patients with known non-diabetic renal disease (Glomerulonephritis, lupus nephritis)
7. Patients who were taking steroids, nonsteroidal anti-inflammatory drugs, aminoglycosides, SGLT2 inhibitors, Sodium, potassium, or magnesium containing cathartics and laxatives

IV. RESULT

Table I presents the baseline characteristics of the participants stratified by study groups. The mean age of the study participants was 46.01 ± 9.99 years. However, the median age was 45 years with IQR of 37-55 years. Of the 125 participants, 62 (49.6%) were male and the rest were female. There is no statistically significant difference regarding age and sex among those groups. Overall, 59 (47.2%) participants were hypertensive and 33 (26.4%) were smoker among 125 study participants. Moreover, 36% of the total participants had a family history of DM. The frequency distribution of the hypertension, smoking status, and family history of Diabetes Mellitus in the study groups documented statistically significant differences in smoking status among three study groups. Table II demonstrates the biochemical parameters of the patients stratified by study groups. The estimated Glomerular Filtration Rate (eGFR) showed a decreasing trend from the normal albuminuria group (95.5 ml/min/1.73 m²) to the severely increased albuminuria group (86.1 ml/min/1.73 m²), although this difference was not statistically significant (P=0.0649ns). The Urine

Albumin to Creatinine Ratio (UACR) displayed a significant increase across the groups, with the normal albuminuria group having a UACR of 14.3 mg/gm, the moderately increased albuminuria group at 138.5 mg/gm, and the severely increased albuminuria group at 1056 mg/gm, indicating a statistically significant difference (P<0.001s). Fasting Blood Glucose (FBG) levels were relatively similar across the groups, with no significant difference (P=0.8157ns). The 2-hour Postprandial Blood Glucose (2hPPBG) levels were significantly different across the groups (P=0.0041s), showing a decreasing trend from the normal albuminuria group (8.2 mmol/l) to the severely increased albuminuria group (7.4 mmol/l). Hemoglobin A1C (HbA1C) levels varied from 6.5% in the normal albuminuria group to 7.3% in the moderately increased albuminuria group, and 7.0% in the severely increased albuminuria group, but these differences were not statistically significant (P=0.077ns). Table III shows the comparison of FENa, FEK and FEMg among three groups. For FENa, the median values were 0.59% in the normal albuminuria group, 0.34% in the moderately increased albuminuria group, and 0.56% in the severely increased albuminuria group. The IQRs were (0.30-1.03), (0.26-0.48), and (0.41-1.05), respectively. The differences in FENa across the groups were statistically significant (P=0.0016). In the case of FEK, the median values were 9.4% for the normal albuminuria group, 7.2% for the moderately increased albuminuria group, and 6.9% for the severely increased albuminuria group. The IQRs for these groups were (6.7-12.0), (5.8-8.8), and (6.2-10.3), respectively. The differences in FEK among the groups were also statistically significant (P=0.0358). For FEMg, the median values showed a notable increase from 2.87% in the normal albuminuria group to 5.58% in the severely increased albuminuria group, with the moderately increased albuminuria group having a median of 2.79%. The IQRs were (1.98-3.75) for the normal albuminuria group, (1.3-4.47) for the moderately increased albuminuria group, and (3.02-8.06) for the severely increased albuminuria group. The differences in FEMg across the groups were significant (P=0.001). Table IV presents the correlation of FENa, FEK and FEMg with clinical and biochemical parameters of all samples. For the Urine Albumin to Creatinine Ratio (UACR), there was a weak positive correlation with FENa (rho=0.194, p=0.84), a weak negative correlation with FEK (rho=-0.163, p=0.087), and a moderate positive correlation with FEMg (rho=0.373, p<0.001). The correlation between FEMg and UACR was statistically significant. Regarding the estimated Glomerular Filtration Rate (eGFR), there were negative correlations with all three electrolyte excretions: FENa (rho=-0.234, p=0.008), FEK (rho=-0.194, p=0.03), and FEMg (rho=-0.345, p<0.001). All these correlations were statistically significant, indicating that higher eGFR is associated with lower fractional excretion of these electrolytes. For Fasting Blood Glucose (FBG), there were no significant correlations with FENa (rho=-0.01, p=0.915), FEK (rho=-0.075, p=0.436), or FEMg (rho=0.122, p=0.202). Similarly, 2-hour Postprandial Blood Glucose (2hPPBG) showed no significant correlations with FENa (rho=-0.122, p=0.28), FEK (rho=-0.147, p=0.192), or FEMg (rho=-0.203, p=0.069). Lastly, Hemoglobin A1C (HbA1C) percentages also did not show significant correlations with FENa (rho=-0.054, p=0.63), FEK (rho=-0.14, p=0.214), or FEMg (rho=-0.05, p=0.658).

Table I: Baseline characteristics of the participants stratified by study groups. (N=125)

Variables	Normal albuminuria (n=58)	Moderately increased albuminuria (n=27)	Severely increased albuminuria (n=40)	P value
Age (years)‡				
Median	42	50	45	0.1827^{ns}
IQR	36-52	38-55	37.5-53.5	
Sex*				
Male	29 (50.0)	10 (37.0)	23 (57.5)	0.258^{ns}
Female	29 (50.0)	17 (63.0)	17 (42.5)	
Clinical characteristics*				
Hypertension	30 (51.7)	9 (33.3)	20 (50.0)	0.261^{ns}
Smoker	15 (25.9)	10 (37.0)	8 (20.0)	0.021^{s}
Family H/O DM	20 (34.5)	10 (37.0)	15 (37.5)	0.947^{ns}

‡Kruskal-Wallis test
* Chi-square test
s= Significant
ns= Not significant
P value ≤0.05 was considered statistically significant

Table II: Biochemical parameters of the patients stratified by study groups (N=125)

Variables	Normal albuminuria (n=58)	Moderately increased albuminuria (n=27)	Severely increased albuminuria (n=40)	P value‡
eGFR (ml/ min/1.73 m^2)	95.5 (79.7-115.0)	94.0 (79.0-119)	86.1 (70.4-100.9)	0.0649^{ns}
UACR (mg/gm)	14.3 (8.6-22.0)	138.5 (88.5-218.0)	1056 (576.0-2188.7)	<0.001^{s}
FBG (mmol/l)	5.8 (5.2-7.7)	5.8 (6.2-8.4)	6.2 (4.4-5.8)	0.8157^{ns}
2hPPBG (mmol/l)	8.2 (7.7-11.1)	7.8 (7.2-8.4)	7.4 (6.4-8.2)	0.0041^{s}
HbA1C (%)	6.5 (6.2-7.2)	7.3 (6.8-8.6)	7.0 (6.3-7.8)	0.077^{ns}

‡Kruskal-Wallis test
s= Significant
ns= Not significant
P value ≤0.05 was considered statistically significant

Table III: Comparison of FENa, FEK and FEMg among three groups (Median and IQR) (N=125)

Variables	Normal albuminuria (n=58)	Moderately increased albuminuria (n=27)	Severely increased albuminuria (n=40)	P value‡
FENa (%)				
Median	0.59	0.34	0.56	0.0016
IQR	(0.30-1.03)	(0.26-0.48)	(0.41-1.05)	
FEK (%)				
Median	9.4	7.2	6.9	0.0358
IQR	(6.7-12.0)	(5.8-8.8)	(6.2-10.3)	
FEMg (%)				
Median	2.87	2.79	5.58	0.001
IQR	(1.98-3.75)	(1.3-4.47)	(3.02-8.06)	

‡Kruskal-Wallis test
s= Significant
ns= Not significant
P value ≤0.05 was considered statistically significant

Table IV: Correlation of FENa, FEK and FEMg with clinical and biochemical parameters of all samples (N=125)

Variables	FENa		FEK		FEMg	
	rho	p-value	rho	p-value	rho	p-value
UACR (mg/gm)	0.194	0.84	-0.163	0.087	0.373	<0.001
eGFR (ml/min/1.73m^2)	-0.234	0.008	-0.194	0.03	-0.345	<0.001
FBG (mmol/l)	-0.01	0.915	-0.075	0.436	0.122	0.202
2hPPBG (mmol/l)	-0.122	0.28	-0.147	0.192	-0.203	0.069
HbA_{1C} (%)	-0.054	0.63	-0.14	0.214	-0.05	0.658

Rho = Spearman Correlation Coefficient.

V. DISCUSSION

This observational study was conducted in Department of Nephrology, Chattogram, Bangladesh, during the period from February 2021 to January 2022 to compare the fractional excretion of sodium, potassium and magnesium among 125 T2DM patients with increased albuminuria and normal albuminuria. The baseline characteristics reveal a mean age of 46.01 ± 9.99 years and an equal distribution of males and females (49.6% male), with no significant age or sex differences across the groups. This demographic balance is crucial as it aligns with previous research indicating that the progression of diabetic nephropathy is not significantly influenced by age or gender [14]. The prevalence of hypertension (47.2%) and smoking (26.4%) among the participants, and the significant differences in smoking status across the groups, underscore the established role of these factors in the progression of renal disease in diabetic patients [15, 16. The finding that 36% of participants had a family history of DM further highlights the genetic predisposition in the development of diabetic complications. Biochemical parameters show a non-significant decrease in eGFR from 95.5 ml/min/1.73 m^2 in the normal albuminuria group to 86.1 ml/min/1.73 m^2 in the severely increased albuminuria group (P>0.05). This trend, although not statistically significant, is consistent with the understanding that declining renal function is a characteristic of advancing diabetic nephropathy [17]. The Urine Albumin to Creatinine Ratio (UACR), a critical marker for kidney damage, significantly increased from 14.3 mg/gm in the normal group to 1056 mg/gm in the severely increased albuminuria group (P<0.001), reinforcing its role as an early indicator of nephropathy [18]. The glycemic control parameters, Fasting Blood Glucose (FBG) and 2-hour Postprandial Blood Glucose (2hPPBG), showed no

significant differences across the groups for FBG (P=0.8157ns) and a significant decrease in 2hPPBG from 8.2 mmol/l in the normal group to 7.4 mmol/l in the severely increased albuminuria group (P≤0.05). The Hemoglobin A1C (HbA1C) levels varied slightly across the groups, from 6.5% in the normal albuminuria group to 7.3% in the moderately increased albuminuria group, and 7.0% in the severely increased albuminuria group, but these differences were not statistically significant (P>0.05). The lack of significant differences in glycemic control parameters might be attributed to uniform management strategies among the participants and suggests that factors other than glycemic control are influencing the progression of nephropathy [19]. The FENa decreased from 0.59% in the normal albuminuria group to 0.34% in the moderately increased albuminuria group, and then slightly increased to 0.56% in the severely increased albuminuria group (P≤0.05). The FEK also showed a decreasing trend from 9.4% in the normal group to 6.9% in the severely increased albuminuria group (P≤0.05). The FEMg notably increased from 2.87% in the normal albuminuria group to 5.58% in the severely increased albuminuria group (P≤0.05), indicating magnesium wasting, which has been associated with poor renal outcomes in diabetic patients [20]. This finding concurred with the finding of Deekajorndech *et al*., [21]. In the study's findings, significant negative correlation of eGFR with FENa (rho=-0.234, P=0.008), FEK (rho=-0.194, P=0.03), and FEMg (rho=-0.345, P<0.001) aligns with the findings of Ix *et al*., [22], and Chen *et al*., [23], who reported altered electrolyte handling in kidneys with reduced function, particularly in chronic kidney disease. Similarly, the study by Corsonello *et al*., [24], supports the negative correlation between eGFR and FEMg, indicating that magnesium handling is affected in patients with diabetic nephropathy. Furthermore, the positive correlation of FEMg with UACR (rho=0.373, P<0.001) is corroborated by the research of Van Laecke *et al*., [25], which suggests that magnesium wasting is a common feature in patients with diabetic nephropathy and is associated with the severity of albuminuria. This study highlights the multifaceted nature of diabetic nephropathy, emphasizing the importance of managing not only glycemic control but also other risk factors such as hypertension, smoking, and electrolyte imbalances. The significant correlations and differences in electrolyte excretion underscore the complex interplay between renal function and metabolic disturbances in diabetic nephropathy.

Limitations of the Study

In our study, there was small sample size. Study population was selected from one center in Chattogram city, so may not represent wider population. The study was conducted at a short period of time. Though 24-hour urine is collected for evaluation, day to day fluctuations in albuminuria and electrolyte excretion could not be ruled out.

VII. CONCLUSION AND RECOMMENDATIONS

A notable increase in UACR across the groups highlighted the progression of renal impairment. Glycemic control parameters showed no significant differences, except for a trend in 2hPPBG. Significant variations in the fractional excretion of sodium, potassium, and magnesium were observed. Higher eGFR was associated with lower electrolyte excretion, and a significant positive correlation was found between magnesium excretion and UACR. Further large-scale longitudinal study is recommended to understand the effectiveness of Fractional Excretion of Magnesium and to identify FEMg as a potent indicator for renal damage in type 2 Diabetes mellitus patients.

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