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ORIGINAL ARTICLE

Prevalence, Risk Factors and Impact of Proteinuria-Associated Hypomagnesemia in Chronic Kidney Disease Patients: A Cross Sectional Study

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ABSTRACT

Background and Aim: Chronic kidney disease (CKD) patients who have hypomagnesemia are at greater risk of mortality and progression. A limited amount of data is available on the prevalence of hypomagnesemia in kidney-related risk factors and chronic kidney disease patients. The present study aimed to assess the Proteinuria-associated hypomagnesemia in chronic renal disease patients: prevalence, risk factors, and effect.

Patients and Method: This cross-sectional study was carried out on 128 chronic kidney disease patients in the Medicine Department of Shifa International Hospital, Rawalpindi from January 2022 to August 2022. Patients were categorized into two groups based on estimated glomerular filtration rate (eGFR) are as follows: group-I composed of Proteinuric and group-II non-proteinuric. Prior to study conduction, the ethical committee approved the protocol. Patients with prior history of ileostomy, malignancy, chronic diarrhea, colostomy, and using magnesium based medications were excluded. Detailed history, physical examination, and investigations such as serum total magnesium level (mg/dl), serum sodium level (mg/dl), serum creatinine (mg/dl), and total cholesterol and triglycerides (mg/dl) were recorded. Hypomagnesemia was defined as a serum magnesium level < 1.8 mg/dL.

Results: Of the total 128 CKD patients, there were 66 (51.6%) male and 62 (48.4%) females. Group I and II had 64 patients each. The overall mean age of group-I and group-II was 48.82±12.52 and 48.21±10.64 years respectively. The prevalence of hypomagnesemia (<1.8 mg/dL) in the proteinuric group was 20 (31.3%). Diabetic patients are more susceptible to hypomagnesemia. The incidence of diabetic, hypertensive, and both diabetic and hypertensive was 12 (60%), 3 (15%), and 5 (25%) respectively among 20 hypomagnesemia. Hypomagnesemia patients had higher CRP (46 mg/L), UACR (2064 mg/g), lower serum potassium (56.4%), lower mean hemoglobin levels (10.2 g/dL), and lower serum sodium (34.9%) as compared to normomagnesemic patients 12 mg/L, 810 mg/g, 24.8%, 11.25 g/dL, and 8.6% respectively.

Conclusion: The present study found that there is an independent association between hypomagnesemia and proteinuria in non-dialysis CKD patients. Anemia and hyperparathyroidism are risk factors for inflammation and anemia in CKD patients pre-dialysis. Dietary magnesium supplementation and hypomagnesemia correction may retard proteinuria and CKD progression in CKD patients.

Keywords: Chronic kidney disease, Proteinuria-associated hypomagnesemia, Risk factors

INTRODUCTION

Patients with chronic kidney disease (CKD) who have hypomagnesemia are at greater risk of mortality and progression. A vital component of the cell's metabolic mechanism, the second most prevalent intracellular electrolyte is magnesium [1]. In addition, magnesium is essential for bone and mineral metabolism [2, 3]. Hormones do not appear to control magnesium. Renal excretion and intestinal absorption are significantly associated with magnesium balance regularization. Magnesium homeostasis is maintained by the kidney's essential role but abnormalities in their levels such as hypermagnesemia and hypomagnesemia are mostly common in chronic kidney disease patients [4]. Medication is the prime reason for hypomagnesemia induction in CKD patients [5]. These medications include calcineurin inhibitor, proton pump inhibitor, and diuretics. Other diseases such as volume expansion and diabetes could cause hypomagnesemia [5, 6]. Numerous studies evaluated the hypomagnesemia in CKD, non-CKD, and ESRD patients and has been associated with increased cardiovascular mortality [7, 8]. Hypomagnesemia has also been related to a rapid decrease rate of eGFR, however this has yet to be proven [9].

The estimated Glomerular Filtration Rate (eGFR) decreasing rate in chronic kidney disease patients is responsible for hypermagnesemia. With decreasing renal function, plasma magnesium levels increase based on the primary magnesium regulatory system controlled by urinary excretion [10]. In the initial stages of CKD, an increase in partial magnesium excretion compensates for the renal function loss, and within normal limits of serum magnesium levels [11]. In the late stages of CKD, impaired tubular reabsorption leads to an increase in the fraction excretion of fltered magnesium [12]. The association between hypermagnesemia and mortality is murkier. Numerous studies have found that minor increases in serum magnesium levels are connected with an increase in survival [13]. There has been no research that investigates the associations between hypermagnesemia and CKD development. Therefore, the present study aimed to determine the Proteinuria-associated hypomagnesemia in chronic renal disease patients: prevalence, risk factors, and consequences.

METHODOLOGY

This cross-sectional study was carried out on 128 chronic kidney disease patients in the Medicine Department of Shifa International Hospital, Rawalpindi from January 2022 to August 2022. Patients were categorized into two groups based on estimated glomerular filtration rate (eGFR) are as follows: group-I composed of Proteinuric and group-II non-proteinuric. Prior to study conduction, the ethical committee approved the protocol. Patients with prior history of ileostomy, malignancy, chronic diarrhea, colostomy, and using magnesium based medications were excluded. Detailed history, physical examination, and investigations such as serum total magnesium level (mg/dl), serum sodium level (mg/dl), serum creatinine (mg/dl), and total cholesterol and triglycerides (mg/dl) were recorded. Hypomagnesemia was defined as a serum magnesium level < 1.8 mg/dL. For 3 months, CKD was defined as the existence of kidney disease or a glomerular filtration rate (GFR) of 60 mL/min/1.73m2. The eGFR was calculated. Both gender participants over the age of 18 were included. Individuals

having a history of persistent diarrhoea, ileostomy, or colostomy, patients with cancer, patients on magnesium-based drugs, and patients who refused to participate were excluded. Patients underwent a detailed history, a comprehensive physical examination, and investigations to ensure they met inclusion and exclusion criteria.

RESULTS

Of the total 128 CKD patients, there were 66 (51.6%) male and 62 (48.4%) females. Group I and II had 64 patients each. The overall mean age of group-I and group-II was 48.82±12.52 and 48.21±10.64 years respectively. The prevalence of hypomagnesemia (<1.8 mg/dL) in the proteinuric group was 20 (31.3%). Diabetic patients are more susceptible to hypomagnesemia. The incidence of diabetic, hypertensive, and both diabetic and hypertensive was 12 (60%), 3 (15%), and 5 (25%) respectively among 20 hypomagnesemia. Hypomagnesemia patients had higher CRP (46 mg/L), UACR (2064 mg/g), lower serum potassium (56.4%), lower mean hemoglobin levels (10.2 g/dL), and lower serum sodium (34.9%) as compared to normo-magnesemic patients 12 mg/L, 810 mg/g, 24.8%, 11.25 g/dL, and 8.6% respectively. Hypomagnesemia related independent determinants were determined by multivariate regression analysis. These independent predictors were sodium, UACR, serum potassium, and CRP etc. Figure-1 depicts the gender's distribution. The incidence of diabetes, hypertension, and both are shown in Figure-2. Comorbidities in both groups are compared in Figure-3. Different serum electrolytes compared in both groups are shown in Table-I. Association of laboratory data and magnesium level are compared and shown in Table-II.

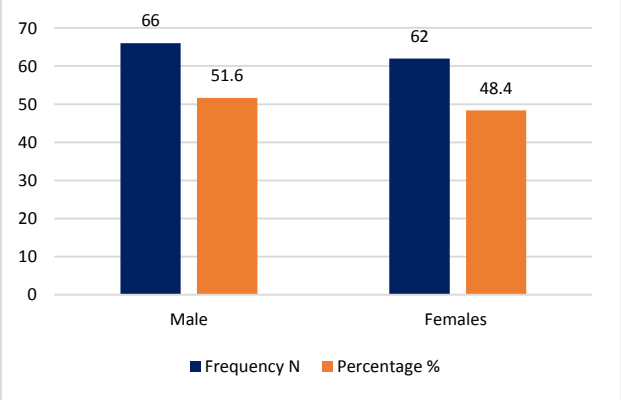

Figure-1: Gender's distribution

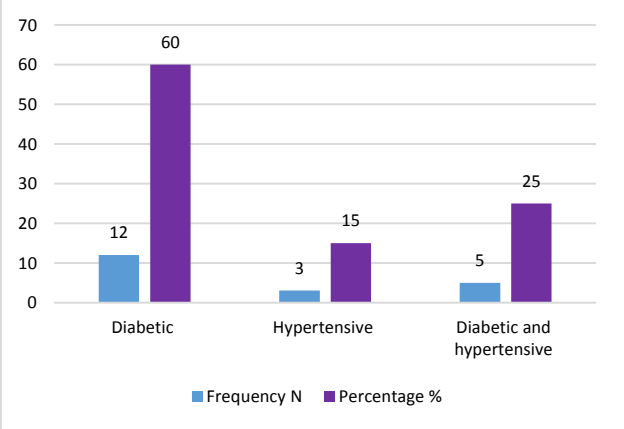

Figure-2: Incidence of diabetes, hypertension, and both in Proteinuric group (n=20/64).

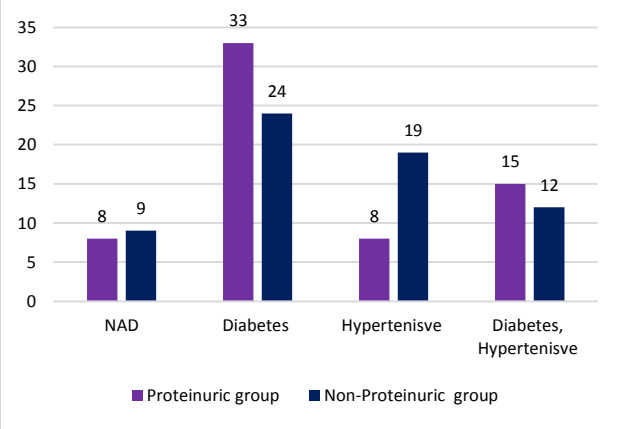

Figure-3: Comparison of different comorbidities in both groups

Table-1: Different serum electrolytes compared in both groups

Variables	Proteinuric group N (%)	Non-proteinuric group N (%)	P-value
Magnesium level Normal Hypo	 48 (64) 16 (25)	 64 (100) 0 (0)	<0.001
Calcium level Normal Hypo	 30 (46.9) 34 (53.1)	 16 (25) 48 (75)	0.021
Potassium level Normal Hypo	 41 (64.1) 23 (35.9)	 64 (100) 0 (0)	<0.001
Sodium Level Normal Hypo	 53 (82.8) 11 (16.2)	 54 (84.4) 10 (15.6)	

Table-2: Comparing the association of laboratory data and magnesium level for both groups

Variables	Proteinuric group	Non-proteinuric group	P-value
Hemoglobin (g/dL)	10.2	11.25	0.036
CRP (mg/L)	46	12	<0.001
UACR (mg/g)	2064	810	<0.001
Serum potassium	56.4	24.8	0.031
Serum sodium	34.9	8.6	0.031
eGFR	25.9	24.02	0.41
Creatinine	2.52	2.76	0.342
Total Cholesterol	225.61	219.54	0.552

DISCUSSION

The current study focused on the prevalence, risk factors, and effect of proteinuria-related hypomagnesemia in chronic renal disease patients and found that in non-dialysis CKD patients, there is an independent relationship between hypomagnesemia and proteinuria. Pre-dialysis anaemia and hyperparathyroidism are risk factors for inflammation and anaemia in CKD patients. In CKD patients, dietary magnesium supplementation and hypomagnesemia correction may slow proteinuria and CKD development. In the proteinuric group, the frequency of hypomagnesemia (1.8 mg/dL) was 20 (31.3%). Hypomagnesemia is more common in diabetic people. The prevalence of diabetic, hypertensive, and both diabetic and hypertension patients among 20 hypomagnesemia patients was 12 (60%), 3 (15%), and 5 (25%), respectively. Magnesium is essential for several cellular processes, including storage, use, and energy transport, carbohydrate, protein, and lipid metabolism; parathyroid hormone (PTH) secretion control, and appropriate cell membrane function [14].

Systemically, the variations in peripheral vascular resistance and lower blood pressure are caused by magnesium. Hypomagnesemia is associated with metabolic derangement such as dyslipidemia, diabetes, vascular calcification, and pathophysiology of hypertension which are cardiovascular disease

risk factors that in turn cause morbidity and mortality in the majority of CKD cases [15, 16]. However, in comparison to the widespread interest in calcium and phosphate metabolism disorders and vascular/valvular calcification, magnesium metabolism is frequently overlooked and remains one of the less well known clinical issues faced by nephrologists [17, 18].

Magnesium homeostasis and excretion in CKD patients has received little attention. Despite the gap, in cases where GFR falls below 20-30 mL/min, there are increase in serum magnesium levels; however, variations in serum magnesium levels in patients with CKD stages 1-3, GFR > 30 mL/min is yet to be determined [19].

The present study reported that the incidence of hypomagnesemia was 31.3% in proteinuric group patients. Fang et al [20] conducted their study on 5000 patients and found that hypomagnesemia was the most prevalent electrolyte abnormality which had a similar incidence among chronic kidney disease patients [21]. Ellison et al [22] investigated 100 chronic kidney disease patients and found that hypomagnesemia was present in 6% of the proteinuric group patients. In the present study, the magnesium levels are found significantly lower in proteinuric groups as compared to non-proteinuric groups. This is consistent with the findings of Blaine et al., who evaluated diabetic individuals with proteinuria and discovered a significant reduction in serum ionized magnesium compared to those with norm albuminuria [23].

The serum magnesium level was shown to be inversely associated with the UACR level. This is consistent with the findings of William et al. [24] and Fan et al. [25], who discovered that proteinuria in diabetic patients showed a substantial decrease in ionized magnesium serum when associated to the non-proteinuria group. The osmotic diuresis might explain the association between proteinuria and hypomagnesemia, which results in excretion of urine magnesium increased by the kidney.

In our study, individuals with anemia was most prevalent in hypomagnesemia as compared to those with normal blood magnesium levels in the proteinuric group. These findings matched with Sakaguchi et al [26]'s large cohort research that revealed the hypomagnesemia patients were more susceptible to anemia as compared to the normomagnesemia patients. Blood magnesium is required for several critical enzymes involved in energy metabolism and the synthesis of cellular and nuclear proteins, hypomagnesemia may result in a decrease in energy production and, as a result, a decrease in hemoglobin synthesis [27].

CONCLUSION

The present study found that there is an independent association between hypomagnesemia and proteinuria in non-dialysis CKD patients. Anemia and hyperparathyroidism are risk factors for inflammation and anemia in CKD patients pre-dialysis. Dietary magnesium supplementation and hypomagnesemia correction may retard proteinuria and CKD progression in CKD patients.

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