



## Comparison of Serum Magnesium Level Among Patients with Chronic Kidney Diseases and Patients with Maintenance Hemodialysis

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### Abstract

**Background:** The worldwide incidence of Chronic Kidney Disease (CKD) is quickly expanding and has emerged as a major public health issue. According to studies, cardiovascular events account for more than half of all deaths in CKD patients. Serum magnesium protects the cardiovascular system in patients with CKD and Maintenance Hemodialysis (MHD). The aim of this study was to compare the Serum magnesium level among patients with chronic kidney diseases and patients with Maintenance Hemodialysis. **Material & Methods:** This was a cross-sectional study and was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka, Bangladesh during the period from July 2014 to June 2015. In our study, we took 50 diagnosed cases of CKD patients (Stage IV & V) and 50 CKD patients with MHD admitted to the Department of Nephrology, Dhaka Medical College Hospital. **Results:** In our study, we found the mean  $\pm$ SD age was  $43.86 \pm 9.21$ , and  $47.14 \pm 9.02$  in CKD, and CKD  $\bar{e}$  MHD respectively. BMI was almost similar in all groups. We found the mean  $\pm$  SD of serum magnesium was  $3.00 \pm 0.33$  mg/dl, and  $2.02 \pm 0.61$  mg/dl in CKD, CKD  $\bar{e}$  MHD respectively. Serum magnesium was significantly higher in CKD than in CKD with MHD patients. **Conclusions:** From the findings of our study, it is concluded that serum magnesium level is increased in patients with CKD (CKD Stage IV & V) than in patients with maintenance hemodialysis. Serum magnesium levels should be checked on a regular basis in CKD and MHD patients in order to prevent cardiovascular and cerebrovascular illness caused by hypomagnesemia.

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### INTRODUCTION

Chronic kidney disease (CKD) is widely acknowledged as a major public health issue around the world. It is distinguished by progressive worsening of renal function, which

eventually results in permanent loss of nephron number and function. This deterioration might occur over a period of months or years.<sup>[1]</sup> According to the definition by the National Kidney Foundation (NKF), CKD is defined as either kidney damage for

three months, as determined by structural or functional renal abnormalities, with or without decreased glomerular filtration rate (GFR) or  $GFR < 60 \text{ ml/min/1.73 m}^2$  for  $\geq 3$  months, with or without kidney damage.<sup>[2]</sup> Among several different diseases, high blood pressure and diabetes are the most common diseases that cause CKD. The incidence and prevalence of chronic kidney disease (CKD) are increasing worldwide.

In developing countries, the awareness and burden of CKD on society have been highlighted during the last decade. According to a study by Hasan et al., the incidence of CKD in Bangladesh is 19%.<sup>[3]</sup> The prevalence of CKD is increasing worldwide as a consequence of hypertension and diabetes mellitus.<sup>[4]</sup> The average worldwide prevalence of CKD was 7.2% in persons aged more than 30 years old.<sup>[5]</sup> The increase in the prevalence of CKD is an alarming condition. Because it is an irreversible condition and is associated with increased health hazards.<sup>[6]</sup> In Bangladesh, there are about 20 million people suffering from CKD.<sup>[7]</sup>

Magnesium is an intracellular cation that is essential for cellular physiology. Serum levels are frequently modestly elevated in chronic hemodialysis patients, and older data show that total body stores may be increased as well, based on bone biopsies in patients treated with greater dialysate magnesium levels than are now used. Several studies have demonstrated that magnesium, particularly magnesium carbonate, is an efficient phosphate binder and can reduce patients' calcium exposure.<sup>[8]</sup>

The kidney plays a critical role in magnesium homeostasis, and while renal magnesium handling is extremely flexible, this ability gets

worse when renal function drops dramatically. In moderate chronic kidney disease (CKD), increases in magnesium fractional excretion compensate for the reduction of GFR to preserve normal serum magnesium levels. However, when CKD progresses (creatinine clearance falls below 30 mL/min), this adaptive mechanism becomes insufficient, and overt hypermagnesaemia develops often in patients with creatinine levels below 10 mL/min. Dietary calcium and magnesium may affect each other's intestinal uptake, though data are ambiguous; similarly, the role of vitamin D on intestinal magnesium absorption is also unknown. The effect of different magnesium and calcium dialysate concentrations in dialysis patients has been studied in hemodialysis (HD) and peritoneal dialysis (PD). The results demonstrate that dialysate magnesium at 0.75 mmol/L is likely to cause mild hypermagnesaemia. The results for 0.5 mmol/L magnesium dialysate were less consistent, however, blood magnesium levels were usually normal to hypomagnesaemia when 0.2 and 0.25 mmol/L were utilized. While dialysate magnesium concentration is a primary driver of magnesium balance in HD or PD patients, other factors such as nutrition and drugs (e.g. laxatives or antacids) also play an essential role.<sup>[9]</sup>

Human bodies require magnesium to manage a variety of metabolic activities. The kidneys help the body systems to get rid of waste and control magnesium levels by determining how much magnesium to expel in urine. The function of the kidneys dictates how much magnesium the body requires.<sup>[10]</sup> In our study, we aimed to compare the Serum magnesium level among patients with chronic kidney

diseases and patients with Maintenance Hemodialysis.

## MATERIAL AND METHODS

This was a cross-sectional study and was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka, Bangladesh during the period from July 2014 to June 2015. In our study, we took 50 diagnosed cases of CKD patients (Stage IV & V) in group I and 50 CKD patients with MHD in group II admitted to the Department of Nephrology, Dhaka Medical College Hospital.

These are the following criteria to be eligible for enrollment as our study participants: a) Patients aged between 18 to 60 years; b) Patients diagnosed with CKD (Stage IV & V); c) CKD Patients on maintenance hemodialysis at least three months; d) Patients who were willing to participate were included in the study. And a) Patients with pregnancy; b) Patients taking magnesium influencing agents; c) Patients with very much critical condition; d) Patients with malignancy; e) Patients with any history acute illness (e.g., pancreatic diseases, ischemic heart disease etc.) were excluded from our study.

### Chronic kidney disease

Chronic kidney disease is either permanent kidney damage for  $\geq 3$  months, as defined by structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR) (which is manifested by pathological abnormalities or markers of kidney damage including abnormalities in the composition of blood or urine or abnormalities in imaging tests); or  $GFR < 60 \text{ ml/min/1.73m}^2$

$\text{m}^2$  for  $\geq 3$  months, with or without kidney damage.<sup>[11]</sup>

**Diagnosed cases of CKD patients (Stage IV & V):** Diagnosis was done in the Department of Nephrology, DMCH on the basis of-

1. Clinical history
2. Examination of the Patients
3. Laboratory investigations (Serum creatinine, blood urea etc.)
4. Ultrasonography

Staging was done by calculating eGFR.<sup>[12]</sup>

Stage IV:  $GFR: 15-29 \text{ ml/min/1.73m}^2$

Stage V:  $GFR: < 15 \text{ ml/min/1.73m}^2$

ESRD (End Stage Renal Disease): In this study, ESRD was considered when eGFR was found  $< 15 \text{ ml/min/1.73m}^2$  body surface area.<sup>[11]</sup>

Maintenance Hemodialysis: CKD patients on regular dialysis for 8-12 hrs/wk for at least 3 months.<sup>[11]</sup>

**Statistical Analysis:** All data were recorded systematically in preformed data collection form, and quantitative data was expressed as mean and standard deviation, and qualitative data was expressed as frequency distribution and percentage. The comparison was done by unpaired Student 't' test, Chi-square test, ANOVA test, and Pearson's Correlation coefficient Test. Statistical analysis was performed by using SPSS (Statistical Package for Social Sciences) for Windows version 10. A probability value  $< 0.05$  was considered as the level of significance. The study was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh.



## RESULTS

[Table 1] shows the general characteristics of the study subjects. The mean  $\pm$ SD age was 43.86  $\pm$ 9.21, and 47.14  $\pm$ 9.02 in CKD, and CKD  $\bar{e}$  MHD respectively. BMI was almost similar in all groups. Blood pressure was higher in CKD patients followed by CKD  $\bar{e}$  MHD. Study subjects were age and sex-matched.

[Table 2] shows serum magnesium in study subjects. We found the mean  $\pm$  SD of serum magnesium was 3.00  $\pm$  0.33 mg/dl, and 2.02 $\pm$  0.61 mg/dl in CKD, CKD  $\bar{e}$  MHD respectively.

Serum magnesium was significantly higher in CKD [3.00 $\pm$ 0.33] than CKD  $\bar{e}$  MHD [2.02 $\pm$ 0.61] patients.

[Table 3] shows the pattern of serum magnesium in different stages of CKD patients. Serum magnesium was significantly higher in stage V than that in stage IV.

[Table 4] shows the risk factors of the study subjects for CKD & CKD with MHD. In our study, we found HTN, DM, DM  $\bar{e}$  HTN, and dyslipidemia were similar in CKD and CKD  $\bar{e}$  MHD patients.

**Table 1:** General characteristics of the subjects of study groups.

Baseline characteristics	Group-I (n=50)	Group-II (n=50)	P-value
Age (mean $\pm$ SD)	43.86 $\pm$ 9.21	47.14 $\pm$ 9.02	0.075*
Range of age (18-60) yrs.	(25-60) yrs.	(21-60) yrs.	
Gender			0.395#
Male n (%)	32 (64.0)	37 (74.0)	
Female n (%)	18 (36.0)	13 (26.0)	
BMI (mean $\pm$ SD)	22.8 $\pm$ 1.7	23.3 $\pm$ 2.6	0.139*
Systolic BP (mmHg)	176 $\pm$ 29	154 $\pm$ 40	<0.001*
Diastolic BP (mmHg)	100 $\pm$ 10	90 $\pm$ 14	<0.001*

# Chi-square test was done to measure the level of significance; \*t-test was done to measure the level of significance

**Table 2:** Serum magnesium (mg/ dl) level in study subjects.

Serum magnesium level	Group-I (CKD) (n=50)	Group-II (CKD $\bar{e}$ MHD) (n=50)	P-value
S. Mg (mg/dl)	3.00 $\pm$ 0.33	2.02 $\pm$ 0.61	<0.001#

# ANOVA test was done to measure the level of significance

**Table 3:** Pattern of Serum magnesium in different stages of CKD patients

	Stage		P-value
	Stage-IV (Mean $\pm$ SD)	Stage-V (Mean $\pm$ SD)	
S. Mg (mg/dl)	2.79 $\pm$ 0.17	3.09 $\pm$ 0.35	0.003

t-test was done to measure the level of significance

**Table 4:** Distribution of study subjects according to risk factors for CKD & CKD with MHD.

Risk Factors	Group-I n (%)	Group-II n (%)	P-value
HTN	14 (28.0)	15 (30.0)	0.826
DM	18 (36.0)	18 (36.0)	1.000

DM & HTN	9 (18.0)	9 (18.0)	1.000
Dyslipidemia	32 (64.0)	34 (68.0)	0.673

Chi-square test was done to measure the level of significance

**Table 5:** Pattern of serum magnesium in CKD and CKD & MHD patients according to risk factors

Risk factors	Present (Mean ±SD)	Absent (Mean ±SD)	P-value
Hypertension	2.21 ± 0.86	2.63 ± 0.57	0.005
Diabetes mellitus	2.27 ± 0.78	2.64 ± 0.60	0.010
Dyslipidemia	2.46 ± 0.76	2.61 ± 0.51	0.285

[Table 5] shows the pattern of serum magnesium in CKD and CKD & MHD patients according to risk factors. Serum magnesium was significantly lower in HTN patients than that of non- HTN patients. Similarly, serum magnesium was significantly lower in DM patients than that of non-DM patients. However, there was no significant difference in serum magnesium between dyslipidemic and non-dyslipidemic patients.

## DISCUSSION

Chronic Kidney Disease (CKD) is increasing rapidly worldwide and has become a major health problem. Studies have shown that more than 50% of deaths in CKD patients are attributable to cardiovascular events. Serum magnesium has a protective role in the cardiovascular system in CKD and Dialysis patients.

A total number of 100 subjects of both sexes were selected with ages ranging from 18 to 60 years according to selection criteria. Among them, 50 CKD patients (stage IV & V) were included in the study group I, and 50 CKD patients with maintenance hemodialysis (MHD) were included in the study group II. The serum Magnesium of both groups was assessed and statistically compared among

groups to observe magnesium in CKD patients and patients with MHD and its relation with comorbidity.

In our study, serum creatinine level was estimated in the study groups for the determination of estimated GFR (eGFR). Staging of CKD was done based on eGFR. Lipid profile and fasting blood glucose were estimated in the study groups for determination of comorbidity.

In this study age and BMI was matched in between groups. Nakamura et al. (2008) also found similar results.<sup>[13]</sup>

In this study, S. Magnesium was significantly higher in CKD [3.00±0.33] than in CKD with MHD [2.02±0.61] patients. A similar type of observation was found by Cunningham, et al., (2013). Found in more advanced CKD (as creatinine clearance falls <30mL/min), this compensatory mechanism becomes inadequate such that overt hypermagnesaemia develops frequently in patients with creatinine clearances <10 mL/min.

In this study S. Magnesium in different stages of CKD patients. S. Magnesium was significantly higher in stage V (3.09±0.35) than that in stage IV (2.79±0.17). Cunningham et al.,

also found in healthy people, intestinal magnesium absorption and renal excretion are regulated so as to maintain magnesium balance in more advanced CKD (as creatinine clearance falls  $<30\text{mL}/\text{min}$ ), this compensatory mechanism becomes inadequate such that overt hypermagnesaemia develops frequently in patients with creatinine clearances  $<10\text{mL}/\text{min}$ .<sup>[9]</sup>

Magnesium is controlled in healthy people by glomerular filtration and renal tubular reabsorption in the kidneys.<sup>[14,15]</sup> Renal dysfunction can impair magnesium ion metabolism. Magnesium metabolism disorders can occur as renal failure progresses.<sup>[9,14,15]</sup> In recent years, there has been a greater focus on the magnesium metabolism of hemodialysis patients.<sup>[16,17,18,19,20]</sup> Serum magnesium content has been linked to mortality and CV events in hemodialysis and peritoneal dialysis patients in several studies.<sup>[17,18,19,20]</sup> Cunningham et al. discovered that the mean serum magnesium level in patients undergoing hemodialysis or peritoneal dialysis was 0.78-1.40 and 0.55-1.27 mmol/L, respectively, in a retrospective study.<sup>[9]</sup> The investigations reported by Cunningham et al. were based on small samples.<sup>[9]</sup> Epidemiological research, including large-sample studies in Japan and the United States, has reported blood magnesium concentrations in hemodialysis patients since 2014.<sup>[16,17]</sup> The average blood magnesium level in 142,555 hemodialysis patients in the Japanese study was 1.09 mmol/L.<sup>[16]</sup> The average blood magnesium concentration was 0.920.16 mmol/L in the study conducted in the United States.<sup>[17]</sup> Wu et al. reported the serum magnesium

concentration of 169 patients on maintenance hemodialysis in a research based on a Chinese population, and the average pre-dialysis serum magnesium concentration was 1.000.18 mmol/L.<sup>[21]</sup> In another study, the mean serum magnesium levels in 115 Chinese patients on dialysis was 0.95 mmol/L.<sup>[22]</sup>

In this study, we found that S. magnesium was gradually increased as per increment of the duration of H/D but there was no significant difference among the groups.

### Limitations of the study

Our study was a single centre study. We took a small sample size due to our short study period. Due to a lack of technological support, we only measured serum magnesium levels. After evaluating those patients, we did not follow up with them for a long term and have not known other possible interference that may happen in the long term with these patients.

### CONCLUSIONS

From the findings of our study, it is concluded that serum magnesium level is increased in patients with End Stage Renal Disease (CKD Stage IV & V) than in patients with maintenance hemodialysis. Serum magnesium levels should be checked on a regular basis in CKD and MHD patients in order to prevent cardiovascular and cerebrovascular illness caused by hypomagnesemia.

So further study with a prospective and longitudinal study design including a larger sample size needs to be done to evaluate the association of magnesium status with CKD.



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