Original Article

DOI: 10.7860/JCDR/2018/28073.11329

# Role of Hypomagnesaemia in Acute Kidney Injury

Internal Medicine Section

VENTAKARAKESH CHINTALA[1], VENKATARAYA M PRABHU[2], MANASWITHA BOYANAGARI[3], AJAY N BHAT[4]

## ABSTRACT

**Introduction:** Acute Kidney Injury (AKI) is a common problem with various causes and consequences like electrolyte disturbances in the form of hypocalcaemia, hypokalemia, hyperkalemia depending on the phase. Serum magnesium concentration of <1.5 meq/L is defined as hypomagnesaemia and is one of the common electrolyte abnormality. Serum magnesium levels are not routinely done in AKI cases.

**Aim:** The aim of our study was to assess the role of hypomagnesaemia as a risk factor for non recovery of AKI.

**Materials and Methods:** A cross-sectional study was conducted between July 2014 and August 2015 with a sample of 100 patients. The decrease in magnesium <1.5 meq/L was defined as hypomagnesaemia. AKI was defined as per KDIGO criteria. Day 1, day 3 and day 6 magnesium levels were measured.

**Results:** Prevalence of hypomagnesaemia was 69%, 43% and 27% on day 1, day 3 and day 6 respectively. It was observed that hypomagnesaemia on day 1 was significantly associated with recovery of AKI (p=0.004).

**Conclusion:** Prevalence of hypomagnesaemia was significantly higher in AKI patients and hypomagnesaemia on day 1 was associated with recovery. However, magnesium levels on day 3 and day 6 had no significant correlation with the renal function in AKI.

**Keywords:** Electrolyte abnormality, Renal failure, Serum magnesium

## INTRODUCTION

Hypomagnesaemia is seen in >12% of inpatients in the hospital. It varies in frequency from 60-65% in ICU patients [1,2]. The various factors responsible for hypomagnesaemia are impaired nutrition, the decrease in albumin, gastrointestinal losses due to diseases like diarrhoea, sepsis, blood pressure, genetic disorders such as Bartter, Gitelman syndrome, familial hypomagnesaemia, and uncontrolled diabetes mellitus [2]. Use of medications like proton pump inhibitors, diuretics, amino glycosides and administration of gentamicin in an increasing manner causes a rapid and reversible decrease in absorption of magnesium in rats [3]. Cisplatin decreases gastrointestinal magnesium reabsorption in addition to renal magnesium wasting [4]. In alcoholics, alcohol induced reversible tubular dysfunction contribute to magnesium wasting in addition to dietary deficiency, pancreatitis and diabetes [5]. Post-transplant patients develop hypomagnesaemia due to renal magnesium wasting primarily by treatment with calcineurin inhibitors [6]. Hypomagnesaemia is an important risk factor for new onset diabetes mellitus after transplantation [7-9]. It is difficult to attribute a particular clinical feature specifically to hypomagnesaemia. Hypomagnesaemia manifests the symptoms of neuromuscular and cardiovascular diseases such as tetany, seizures, athetoid, choreiform movements, widening of QRS complex, prolongation of P-R interval besides hypocalcaemia. Hypomagnesaemia alters the Glomerular Filtration Rate (GFR) and the blood flow to the kidney and increases renal injury caused by post ischaemic insult [10]. Serum magnesium levels are not routinely examined in AKI cases. Hypomagnesaemia has a detrimental effect in AKI, and supplementation of magnesium in ischaemic renal injury in an animal model showed an increase in renal blood supply and GFR [11]. The aim of the study was to assess the role of hypomagnesaemia in AKI by assessing the prevalence of hypomagnesaemia and further to evaluate its role as a risk factor for non recovery of AKI.

## MATERIALS AND METHODS

A cross-sectional study was conducted with 100 patients admitted in KMC group of hospitals between July 2014 and August 2015. Written informed consent was taken from all patients included in the study. All patients more than 18 years of age and diagnosed of AKI as per KDIGO criteria were included [6]. Patients with multiorgan dysfunction and those who were on the ventilator, postrenal (obstructive uropathy), and toxin induced (drug), hypokalemia, hypocalcaemia and diabetics were excluded. AKI is defined as increase in serum creatinine level x 3.0, decrease in GFR by 75%, or serum creatinine level ≥4 mg/dL with acute increase of >0.5 mg/dL; UO <0.3 mL/kg/hour for 24 hours, or anuria for 12 hours. Patients whose creatinine was normalised at the end of follow up of study (<1.2 mg/dL) were considered under the recovery. Patients whose creatinine level was not normalised at the end of follow up were considered to be non recovered. Serum magnesium levels were measured on day of admission, day 3 and day 6 and clinical features of hypomagnesaemia were observed. Magnesium <1.5 mg/dL was considered as hypomagnesaemia. Magnesium levels were measured using colorimetric method by COBAS 601/501 analyser.

## STATISTICAL ANALYSIS

Data were analysed by Statistical Package of Social Science (SPSS) version 17.0 and the mean and proportion values of various variables were calculated accordingly using Chi-square test. A p-value less than 0.05 were considered as statistically significant.

## RESULTS

In total 140 cases, 40 cases were excluded out of which 10 were due to obstructive uropathy, 10 were on the ventilator, 10 were suffering from multiorgan dysfunction syndrome. Ten patients were treated with 3 sessions of dialysis. Majority of the patients were

males (n=73, 73.0%). Most of the patients belonged to the age group 41 years and above (n=54, 54.0%) [Table/Fig-1]. Symptomatic treatment was given in 100 patients and they recovered. No specific drugs were given including nephrotoxic drugs. Prevalence of hypomagnesaemia was 69%, 43%, and 27% on day 1, day 3, and day 6 respectively. Out of n=69 patients with hypomagnesaemia on day 1, n=60 patients recovered. Hypomagnesaemia at day 1 was significantly (p=0.004) associated with recovery from AKI. Out of 43 patients with hypomagnesaemia on day 3, 38 recovered and 5 did not recover. These observations were significant (p=0.001). On Day 6, out of 27 patients with hypomagnesaemia, 23 recovered and 4 were non recovered (p=0.001). In patients who have recovered, day 1, mean magnesium levels in recovery and non recovery were 1.29 and 1.79 meq/L respectively which is highly significant (p=0.001) [Table/Fig-2]. Out of 31 patients with serum magnesium levels >1.5 meq/L, on day 1, 12 were non recovered (38.7%, p=0.004) showing an association with non recovery of AKI. Serum magnesium levels >1.5 meq/L on day 3 was not significantly (p=0.133) associated with non recovery of AKI. Out of 57 patients with serum magnesium levels >1.5 meq/L, 15 were non recovered and 42 were recovered (26.3% vs. 73.7%). Among patients with serum magnesium levels >1.5 meq/L on D6, out of 73, 17 were non recovered and 56 were recovered (23.3% vs. 76.7%, p=0.356). In patients who recovered, mean day 1 serum creatinine was 4.1 mg/dL with a standard deviation of 1.62. In patients who have non recovered, mean day 1 serum creatinine was 6.2 with a standard deviation of 2.4. These values are significant (p<0.001) [Table/Fig-3].

| Characteristics | Sex and age distribution | Frequency | Percentage |
|---|---|---|---|
| Gender | Male | 73 | 73.0 |
| | Female | 27 | 27.0 |
| Total | | 100 | 100.0 |
| Age (years) | ≤20 | 3 | 3.0 |
| | 21-40 | 43 | 43.0 |
| | ≥41 | 54 | 54.0 |
| Total | | 100 | 100.0 |

**[Table/Fig-1]:** Demographic details of the study population.

| Magnesium levels | Number | | Mean | p-value |
|---|---|---|---|---|
| Day 1 Magnesium levels | Recovery | 82 | 1.29 | 0.001 |
| | Non recovery | 18 | 1.79 | |
| Day 3 Magnesium levels | Recovery | 82 | 1.59 | 0.002 |
| | Non recovery | 18 | 1.92 | |
| Day 6 Magnesium levels | Recovery | 82 | 1.79 | 0.273 |
| | Non recovery | 18 | 1.89 | |

**[Table/Fig-2]:** Chi-square test result showing the day 1, day 3 and day 6 mean magnesium levels and its correlation with recovery and non recovery AKI.

| Recovery status | Number | Mean | p-value |
|---|---|---|---|
| Recovered | 82 | 4.1195 | <0.001 |
| Non recovered | 18 | 6.2611 | |
| Total | 100 | 4.5050 | |

**[Table/Fig-3]:** Chi-square test result showing mean serum creatinine on day 1 in patients of recovery and non recovery from AKI.

## DISCUSSION

Though the present study aimed to assess the prevalence of hypomagnesaemia in AKI and association of serum magnesium levels in non recovery of AKI. We found that the prevalence of hypomagnesaemia was 69% on day 1, 43% on day 3, 27% on day 6 respectively. Hypomagnesaemia at day 1 in this study was significantly associated with recovery (n=60, p=0.004). Hypomagnesaemia is a frequent electrolyte abnormality found in inpatients in a hospital, especially in the seriously ill patients. Hypomagnesaemia has high risk of cardiovascular disease in CKD and non CKD patients [12,13]. Several hypotheses were formulated to explain the association between hypomagnesaemia and impaired AKI recovery. Magnesium relaxes smooth muscle by competing with calcium transport in cell membrane [14]. Cyclosporine and angiotensin II induced contraction in mesangial cells was inhibited by magnesium [15]. In zidovudine treated rats decreased magnesium levels have detrimental effect on GFR and renal blood flow [16]. Magnesium acts as renal vasodilator by acting as $Ca^{2+}$ channel antagonist and also by stimulating release of NO [17]. Magnesium increases RBC deformability, decreases platelet aggregation, has anti-inflammatory action and maintains endothelial cell integrity [18]. Prevalence of hypomagnesaemia varies from 11-65% in different studies [19]. Prevalence was more in ICU patients with sepsis, hypotension, usage of drugs like diuretics and aminoglycosides [2]. Magnesium levels >1.5 meq/L were significantly associated with the non recovery of AKI patients (12 out of 31, p=0.004) on day 1. Studies done previously demonstrated significant association between hypomagnesaemia and AKI non recovery [13,20]. Study done by Alves SC et al., demonstrated that decrease in magnesium levels was significantly associated with the delayed recovery of renal function in AKI patients especially who were seriously ill [20]. In the same study, it was found out that prevalence of hypomagnesaemia was significantly higher in those who had delayed recovery compared with those who recovered from AKI (70% vs. 31%, p=0.003). A study done by Satish R and Gokulnath G showed that decrease in magnesium levels was observed in 62% of patients who were recovering from acute renal failure [21]. About 74% of them had clinical features of hypomagnesaemia and 15 symptomatic patients received intravenous correction. In our study, none of the patients required intravenous magnesium correction. In contrary to the above discussed studies, our observations suggest that patients who were recovered from AKI were more in hypomagnesaemia and normal magnesium levels compared on day 1, 3 and day 6. In patients who were recovered day 1, mean magnesium levels were statistically significant (p=0.001).

## LIMITATION

The study was done on small sample in a single centre; thus, bias due to non identified centre characteristics was possible and there was also lack of correlation between various causes of AKI and severity of hypomagnesaemia.

## CONCLUSION

Hypomagnesaemia was associated with recovery from AKI (day 1). At the same time magnesium levels >1.5 meq/L on day 1 was also significantly associated with the non recovery of AKI. A greater association with non recovery of AKI was found to be with hypomagnesaemia particularly on day 1 warranting large scale studies to determine the exact role of magnesium in non recovery from AKI.

## REFERENCES

[1] Slatopolsky E, Hruska KA. Disorders of phosphorus, calcium and magnesium metabolism in 'Diseases of the kidney and urinary tract'. In: Schrier RW, 2001. pp. 2649-60.
[2] Tong GM, Rude RK. Magnesium deficiency in critical illness. J Intensive Care Med. 2005;20:03-17.
[3] Foster JE, Harpur ES, Garland HO. An investigation of the acute effect of gentamicin on the renal handling of electrolytes in the rat. J Pharmacol Exp Ther. 1992;261:38.
[4] Lajer H, Kristensen M, Hansen HH, Christensen S, Jonassen T, Daugaard G. Magnesium and potassium homeostasis during cisplatin treatment. Cancer Chemother Pharmacol. 2005;55:231.
[5] De Marchi S, Cecchin E, Basile A, Bertotti A, Nardini R, Bartoli E. Renal tubular dysfunction in chronic alcohol abuse--effects of abstinence. N Engl J Med. 1993;329:1927.
[6] Ramos EL, Barri YM, Kubilis P, Peterson JC, Pfaff WW, Howard RJ, et al. Hypomagnesaemia in renal transplant patients: improvement over time and association with hypertension and cyclosporine levels. Clin Transplant. 1995;9:185.

[7] Van Laecke S, Van Biesen W, Verbeke F, De Bacquer D, Peeters P, Vanholder R. Post transplantation hypomagnesaemia and its relation with immunosuppression as predictors of new-onset diabetes after transplantation. Am J Transplant. 2009;9:2140.
[8] Huang JW, Famure O, Li Y, Kim SJ. Hypomagnesaemia and the risk of new-onset diabetes mellitus after kidney transplantation. J Am Soc Nephrol. 2016;27:1793.
[9] Vallee BL, Wacker WE, Ulmer DD. The magnesium-deficiency tetany syndrome in man. N Engl J Med. 1960;262:155.
[10] Campos SB, Silva JC, Seguro AC. Hypomagnesaemia potentiates postischemic acute renal failure. J Am Soc Nephrol. 2001;12:A4057.
[11] De Araujo M, Andrade L, Coimbra TM, Rodrigues AC Jr, Seguro AC. Magnesium supplementation combined with N-acetylcysteine protects against postischemic acute renal failure. J Am Soc Nephrol. 2005;16:3339-49.
[12] Al-Ghamdi SM, Cameron EC, Sutton RA. Magnesium deficiency: pathophysiologic and clinical overview. Am J Kidney Dis. 1994;24:737.
[13] Quamme GA. Renal magnesium handling: new insights in understanding old problems. Kidney Int. 1997;52:1180.
[14] Wong ET, Rude RK, Singer FR, Shaw ST Jr. A high prevalence of hypomagnesaemia and hypermagnesemia in hospitalized patients. Am J Clin Pathol. 1983;79:348.
[15] Chernow B, Bamberger S, Stoiko M, Vadnais M, Mills S, Hoellerich V, et al. Hypomagnesaemia in patients in postoperative intensive care. Chest. 1989;95:391.
[16] DeRouffignac C, Quamme G. Renal magnesium handling and its hormonal control. Physiol Rev. 1994;74:305.
[17] Chubanov V, Waldegger S, Mederos Y Schnitzler M, Vitzthum H, Sassen MC, Seyberth HW, et al. Disruption of TRPM6/TRPM7 complex formation by a mutation in the TRPM6 gene causes hypomagnesaemia with secondary hypocalcemia. Proc Natl Acad Sci USA. 2004;101:2894.
[18] Voets T, Nilius B, Hoefs S, van der Kemp AW, Droogmans G, Bindels RJ, et al. TRPM6 forms the $Mg^{2+}$ influx channel involved in intestinal and renal $Mg^{2+}$ absorption. J Biol Chem. 2004;279:19.
[19] Kroenke K, Wood DR, Hanley JF. The value of serum magnesium determination in hypertensive patients receiving diuretics. Arch Intern Med. 1987;147:1553.
[20] Alves SC, Tomasi CD, Constantino L, Giombelli V, Candal R, Bristot Mde L, et al. Hypomagnesaemia as a risk factor for the non-recovery of the renal function in critically ill patients with acute kidney injury. Nephro Dial Transplant. 2013;28:910-16.
[21] Satish R, Gokulnath G. Serum magnesium in recovering acute renal failure. Indian J Nephrol. 2008;18:101-04.

**PARTICULARS OF CONTRIBUTORS:**
1. Junior Resident, Department of General Medicine, Kasturba Medical College, Mangaluru, Karnataka, India.
2. Professor and Dean, Department of General Medicine, Kasturba Medical College, Mangaluru, Karnataka, India.
3. Research Assistant, Department of General Medicine, Kasturba Medical College, Mangaluru, Karnataka, India.
4. Assistant Professor, Department of General Medicine, Kasturba Medical College, Mangaluru, Karnataka, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Ajay N Bhat,
Assistant Professor, Department of General Medicine, Kasturba Medical College, Mangaluru-575001, Karnataka, India.
E-mail: ajaybhatmj53363@yahoo.co.in

**FINANCIAL OR OTHER COMPETING INTERESTS:** None.

Date of Submission: **Mar 19, 2017**
Date of Peer Review: **Jun 14, 2017**
Date of Acceptance: **Jan 18, 2018**
Date of Publishing: **Mar 01, 2018**