# **Original Research Article**

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# An observational study on effects of hypomagnesemia among critically ill patients at a tertiary care hospital

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## **ABSTRACT**

**Background:** Magnesium is the fourth abundant cation in the human body and second most abundant intracellular cation after potassium and also serving as cofactor in more than 300 enzymatic reactions. Magnesium deficiency is the most commonly overlooked condition in critically ill patients and associated with other coexisting electrolyte abnormalities. The aim of the present study was to evaluate serum magnesium levels in critically ill patients and to correlate with patient outcome and other parameters like length of stay in ICU, ventilator support, APACHE-II score and duration and mortality.

**Methods:** A two years observational study after ethical committee approval was conducted at a tertiary care hospital among critically ill patients admitted in ICU. Serum magnesium levels and other relevant investigations were performed within 24 hours of admission. Patients management and progress were followed till the outcome. The data was analysed by using SPSS software version 16.0 for windows.

**Results:** Total of 150 patients with 102 males and 48 females were enrolled. 97 cases (64.7%) of hypomagnesemia were observed and 11 cases of hypermagnesemia and 42 cases with normal serum magnesium levels were observed. Hypomagnesemia cases were compared with normal cases and found that: Hypomagnesemia cases had higher mortality rate, higher APACHE II score, more length of hospital stay and ventilator duration. Significant association was identified with diabetes and chronic alcoholism (p valve <0.05).

**Conclusions:** Monitoring of magnesium levels in critically ill patients has several prognostic and therapeutic implications and should be recommended as a regular parameter as it is commonly out looked condition. Statistically significant association of hypomagnesaemia was found with hypocalcaemia, hypoalbuminaemia, septicaemia, diabetes and chronic alcoholism. Higher APACHE II score is associated with higher mortality and more length of stay in ICU among the cases of hypomagnesaemia.

Keywords: APACHE II score, Chronic alcoholism, Critically ill, Hypomagnesemia

#### INTRODUCTION

Magnesium is the fourth abundant cation in the human body and second most abundant intracellular cation after potassium and also serving as cofactor in more than 300 enzymatic reactions. Magnesium maintains neuromuscular excitability and it's important in maintenance of cardiac function. Magnesium deficiency is the most commonly overlooked condition in critically

ill patients and associated with other coexisting electrolyte abnormalities commonly confused with hypokalemia. Various studies have reported the incidence of hypomagnesemia as 65% in critically ill patients. The incidence of hypomagnesemia is reported as 2% in general population, 10-20% in hospitalized patients, 50-60% in ICU patients, and 25% among out patients with diabetes and alcoholism. Hypomagnesemia can induce fatal complications which include coronary artery spasm,

ventricular arrhythmias' and sudden cardiac death. Magnesium monitoring among critically ill patients have prognostic and therapeutic implications as they are predisposed to symptomatic and asymptomatic magnesium deficiency which may lead to the development of neurotoxicity, psychiatric problems and leading to increased morbidity and mortality.<sup>3</sup>

The aetiology of magnesium deficiency is multifactorial and may be related to drugs (diuretics), renal and gastrointestinal loss, co-morbidities like diabetes mellitus, chronic alcoholism and metabolic disorders (Barters syndrome). Hence a high index of suspicion is warranted in critically ill patients to define the cause of hypomagnesemia. Results of several studies like Leicester Intravenous magnesium intervention trial (LIMIT-2) have stated a reduction in mortality with reduced incidence of heart failure and arrhythmias' among critically ill patients with hypomagnesemia.<sup>4</sup>

Hypomagnesemia is associated with increased stay in the ICU and has a devastating effect among critically ill patients requiring mechanical ventilation or prolonging the duration of mechanical ventilation and causing a difficulty in weaning the ventilator support. Despite the fact that serum levels of magnesium represent only 0.3% of total body magnesium content and that serum Mg<sup>+</sup> do not correlate with other tissue pools. The total serum Mg<sup>+</sup> ion concentration is still used as standard for evaluating magnesium status in patients.

The aim of the present study was to evaluate serum magnesium levels in critically ill patients and to correlate with patient outcome and other parameters like length of stay in ICU, ventilator support, APACHE-II score and duration and mortality.

## **METHODS**

A prospective observational study was conducted at a tertiary care hospital of south India for a period of two years from January 2015 to December 2016. The study was approved by the Institutional ethical committee and the guidelines of the committee were followed in designing the study protocol.

All the cases admitted in the ICU (intensive care unit) of the hospital with variable medical and surgical conditions were included in the study. The study details were clearly explained to the cases included in the study. Written informed consent was obtained from all the cases who consented for participation in the study. All the cases admitted in the ICU were scored on the day of admission based on acute physiology and chronic health evaluation (APACHE-II) scoring system which includes acute physiology score, Glasgow coma scale, points assigned to age with chronic disease and chronic health condition score. The socio demographic data, medication history, clinical history, diagnosis and co-morbid conditions were noted in the study designed protocol.

#### Inclusion criteria

- All the cases above 18 years of age irrespective of the sex
- And with a score of above 18 were included in the study.

## Exclusion criteria

- Cases on magnesium lowering drugs
- Already known cases of hypomagnesemia, who received magnesium supplements
- Or calcium infusions and cases not consenting were excluded from the study.

The length of stay in the ICU, development of new complications, mechanical ventilation and its duration and the outcome parameter which are discharge, transfer to the ward, death or discharge against advice were noted for every case enrolled in the study. Additional laboratory investigations which included biochemical, microbiological and radiological investigations (CT, MRI) were performed as per the management protocol. The study didn't interfere with the management of the cases in the ICU.

About 5ml of venous blood was drawn from the cases on the day of admission in ICU and serum magnesium levels were assayed in the central laboratory of the hospital by calmagite calorimetric method. Magnesium combines with calmagite in an alkaline medium to form a red coloured complex. Interference of proteins and calcium is eliminated by using chelating agents. Intensity of colour formed is directly proportional to the amount of magnesium present in the sample. The normal range of magnesium being 1.7-2.7mg/dL and the cases were grouped as hypomagnesemic (<1.7mg/dL) and hypermagnesemia (>2.7mg/dL).

## Statistical analysis

Quantitative data is represented as mean±standard deviation. Association between variables was assessed by chi-Square test. Differences were considered statistically significant if p <0.05. The data was analyzed by using SPSS software version 16.0 for windows.

#### **RESULTS**

In the present prospective observational study, a total of 150 patients were enrolled who fulfilled the inclusion criteria in the study. Males were predominant with 102 cases (68%) and females 48 (32%) (Figure 1). Of the 150 cases admitted in the intensive care unit, 42 (28%) of the cases had normal serum magnesium levels, 97 with hypomagnesemia (64.7%) and 11 cases with hypermagnesaemia (7.3%). The lowest serum magnesium value recorded in the study was 1mg/dl while the highest value was 3.7mg/dl with a total mean of 2.126mg/dl. In the present study the % of cases with hypermagnesaemia

was only 7.3% which was not statistically significant (p value >0.05) hence hypermagnesaemia is not considered in further discussion. The range of duration of stay in ICU of all the cases varied from 1day to 38days with a mean of 8.18days. The mean duration of stay of cases of normal serum magnesium levels was 6.23±2.6days, while in cases of hypomagnesemia it was 8.26±2.89days and among cases of hypermagnesaemia it was 5.24±2.1days. The difference was statistically not significant (p value >0.05). Majority of the cases in the study were in the age group of 30-40 years (52/150, 34.67%) followed in order by 41-50 (25.33%), >50years (21.33%) and 18-29years (18.67%). The mean age of the patients in the study was 32.12±8.1years. Of the 97 cases of hypomagnesemia, 58 (59.79%) were males and 39 (40.21%) were females.

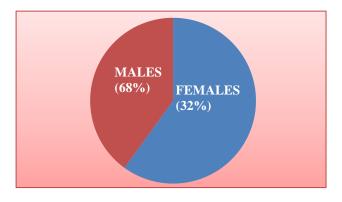


Figure 1: Gender distribution of cases in the study.

The mean APACHE II score of total 150 cases in the study was 23.14±2.08, mean APACHE II score in patients recovered and discharged was 20.12±1.4, in cases of death was 25.48±3.4, and in cases of discharge

against medical advice was 26.48±3.2 and discharge on was  $18.26\pm1.0$ . While in cases Hypomagnesemia APACHE II score was 25.24±2.9 and in cases with death as outcome in Hypomagnesemia the score was  $28.24 \pm 6.4$  and among cases Hypermagnesaemia the score was 24.26±4.9. In present study, hypomagnesemia was associated with increased mortality and higher APACHE II score and was found statistically significant (p value <0.05). In the present study, 68 cases of 150 required ventilator support (45.33%), whereas in cases of hypomagnesemia, 50 of 97 (51.55%) required ventilator support, 10 cases of 42 cases (23.80%) with normal serum magnesium levels and 4 of 11 cases of hypermagnesaemia (36.36%) required ventilator support. Highly statistical significance was associated with hypomagnesemia (p value <0.001). Patients with hypomagnesemia required ventilator support. The mean duration of cases in the study with ventilator support was 4.12±1.4days, while in cases of hypomagnesemia the mean duration was 5.32±2.9days and in normal magnesium levels was 3.11±1.8days and in of hypermagnesaemia was  $3.87 \pm 2.5 days$ . Hypomagnesemic patients required ventilator support for greater number of days compared with other cases of normomagnesemic and hypermagnesemic cases (p value <0.05). Hypomagnesemia patients comprised mostly of multi-organ dysfunction (45.36%), respiratory failure (28.87%), sepsis (19.59%) and cardiac complications (6.19%). The mortality rate among cases of hypomagnesemia was 48 out of 97 (49.48%), whereas in cases of hypermagnesaemia it was only 1 out of 11 cases and in cases with normal magnesium levels it was 10 of 42 (10.30%). Statistically significant association was observed with hypomagnesemia and mortality rate (p value < 0.05).

Table 1: Results of study with significance factors with hypo and normomagnesaemia.

	Hypomagnesemia	Normomagnesaemia	Significance
Prevalence	97/150 (64.7%)	42/150 (28%)	Yes (p value < 0.05)
Mortality rate	48/97 (49.48%)	10/42 (23.80%)	Yes (p value < 0.05)
Ventilator support	50/97 (51.54%)	10/42 (23.80%)	Yes (p value < 0.05)
MICU stay (days)	8.26±2.89	6.23±2.6	No (p value >0.05)
Duration of ventilator (days)	5.32±2.9	3.11±1.8	No (p value >0.05)
APACHE-II score	25.24±2.9	22.24±2.4	Yes (p value < 0.05)
Hypocalcaemia	54/97 (55.97%)	12/42 (28.57%)	Yes (p value < 0.05)
Hypoalbuminaemia	87/97 (89.69%)	19/42 (45.23%)	Yes (p value < 0.05)
Diabetes mellitus	67/97, (69.07%)	22/42 (52.38%)	Yes (p value < 0.05)

Hypocalcaemia was of observed in cases hypomagnesemia 3 of (55.67%),cases 12 hypermagnesaemia (27.27%)and cases of The normomagnesaemia (28.57%). of incidence hypocalcaemia was significantly higher in cases of hypomagnesemia and was found statistically significant (p value <0.05). Hypoalbuminaemia was observed in 87 cases of 150 (58%), of which 68 were hypomagnesemic (78.16%), 19 cases were with normal serum magnesium levels (21.84%). Significant association was observed between Hypoalbuminaemia and cases of hypomagnesemia (p value <0.05) 63 cases had normal albumin levels of which 29 had hypomagnesemia (46.03%) and 34 had normal magnesium levels and

hypermagnesaemia. The incidence of hypomagnesemia was higher among cases of hypoalbuminaemia (Table 1).

The occurrence of sepsis was more common among patients with hypomagnesemia (19/97, 19.59%) when compared with cases of normomagnesemic and hypermagnesemic cases in the study and was found statistically significant (p value <0.05). Other significant factors associated with hypomagnesemia were diabetes mellitus and chronic alcoholism. Hypomagnesemia was observed in 67 cases of diabetes mellitus (67/97, 69.07%) and 34 cases of chronic alcoholics (37/97, 38.14%). Other associated electrolyte abnormalities were hyponatremia, hypokalemia and hypophosphatemia. No significant association was observed with other abnormalities like smoking.

#### **DISCUSSION**

Magnesium is second most common intracellular cation which plays a crucial role in homeostasis. It acts as cofactor in most of the adenosine triphosphate (ATP) reactions. Hypomagnesemia is multi factorial in critically ill patients and may be associated with other electrolyte disturbances and is most commonly overlooked condition. Hypermagnesaemia is less common and mostly due to renal failure or iatrogenic.

The prevalence of hypomagnesemia among critically ill patients mentioned in various studies range from 14% to 70% and is variable from place to place and region to region and is mostly dependable upon the clinical condition of the patient. In present study, the prevalence observed was 65% which concurs with the findings universally mentioned in various studies. However, in the present study total serum magnesium was estimated where ionized magnesium is ideal as it is the metabolically active form.

The prevalence of hypermagnesaemia in present study was 7.3% which is in the range mentioned in various studies globally.7 Few studies which have measured ionized magnesium states that the prevalence of hypomagnesemia was less than when measured with total serum magnesium levels as mentioned in the reports of Deheinzelin D et al.<sup>8</sup> The relationship between mortality and hypomagnesemia is variable from study to study, in our study the mortality was 49.48% among the cases of hypomagnesemia and was found to be statistically significant. Findings of our study concurs with the study of Safavi M et al.9 However reports of Chernow et al, Soliman HM et al, mentioned less rate of mortality in their studies which deviates from the findings of our study. 10,11 These higher rates of mortality can be explained by higher incidence of associated electrolyte abnormalities, arrhythmias and sepsis and shock which was noticed among the patients of present study. A study by Guerin et al, reported that there was no association between hypomagnesemia and mortality in cases of ICU.4

In present study, authors observed that cases of hypomagnesemia required ventilator support for longer days and were difficult to wean because of muscle weakness produced by the condition and also few cases of ICU were on respiratory failure. In the current study supplementation of magnesium caused improvement in muscle weakness and the same was not observed in cases with normal or elevated magnesium levels. Findings of present study concurs with the findings of Fiaccordori et al.12 APACHE II score was higher in cases of hypomagnesemia when compared with normo and hypermagnesaemic patients in our study and higher score was associated with higher mortality in present study. The APACHE II score of hypomagnesemia cases in our study was 25.24±2.9 and was similar to the findings of Honarmand et al.<sup>13</sup> however few studies mentioned no significant association between hypomagnesemia and APACHE II score in their study which is against the finding in present study.

Magnesium plays an important role in sepsis as its deficiency is associated with increased release of cytokines and endothelin. Sepsis is an independent risk factor for development of hypomagnesemia in cases of ICU and strongly associated with increased mortality among cases with septic shock. In the present study sepsis was associated twice commonly and was found to be a statistically significant factor in cases of hypomagnesemia. Similar observations were reported by Malpuech et al, in their study. 14 The present study reports increased association of hypomagnesemia with diabetes and hypertension which was similar to the findings of Limave et al. and Safavi et al. 9,15 Chronic alcoholism was found as significant associated factor in cases with reduced magnesium levels. Magnesium depletion in cases of hypomagnesemia may be due to multiple factors which may be poor nutrition, renal tubular dysfunction, pancreatitis, intracellular shift in alcohol withdrawal syndrome. Rivlin RS, reported similar findings in his study.16

Hypomagnesemia is associated with other electrolyte abnormalities which are hypokalemia, hyponatremia and hypophosphatemia. These are considered as predictors of hypomagnesemia. In the present study hypokalemia was observed in 42% of cases and hypocalcaemia in 26% of cases of present study. Similar findings were also observed in many experimental and observational studies globally. Hypoalbuminaemia was a significant associated factor among critically ill patients with reduced and normal magnesium levels. This factor is a strong predictor in development of renal failure and mortality in cases of hypomagnesemia.

# CONCLUSION

To conclude, monitoring of magnesium levels in critically ill patients has several prognostic and therapeutic implications and should be recommended as a regular parameter as it is commonly out looked condition.

Statistically significant association of hypomagnesemia was found with hypocalcaemia, hypoalbuminaemia, septicaemia, diabetes and chronic alcoholism. Higher APACHE II score is associated with higher mortality and more length of stay in ICU among the cases of hypomagnesemia. The potential benefit of magnesium supplementation among the cases of hypomagnesemia whether aids in recovery is still to ascertain.

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Institutional Ethics Committee

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