

## Original Research Article

# Study of effect of serum magnesium concentration on clinical outcome of critically sick patients in medical intensive care unit

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## ABSTRACT

**Background:** Deficiency of magnesium is common and often ignored. It is associated with cardiac irregularity, cardiac insufficiency, seizure and electrolyte imbalance. As this element has multiple functions in our body it is important in the pathophysiology of several critical illnesses in intensive care unit (ICU). Hence the present study was undertaken to determine the usefulness of admission serum magnesium levels with regards to patient outcome considering mortality, need and duration of ventilator support, and acute physiologic assessment and chronic health evaluation 2 (APACHE 2) score.

**Methods:** Demographic data such as age and sex were recorded. Patients were assessed for presenting complaints, history of other diseases and habits through an interview with the patients or care giver. These findings were recorded on a predesigned proforma patients was followed up for the outcomes such as mortality, need of ventilator support, duration of ICU stay and APACHE 2 score.

**Results:** Regarding comparison between outcome of patients between two groups, 44% patients with magnesium level <1.7 mg/dl have improved and 72% patient didn't improve. 44% patients with magnesium level >1.7 mg/dl have improved and 28% patient didn't improve.

**Conclusions:** From present observational study we can conclude that hypomagnesaemia is more common in patients more than 50 years of age and with male predominance. Pneumonia with septicaemia and cerebrovascular accident (CVA) was commonly associated with hypomagnesaemia. In present study we have observed that hypomagnesaemia is associated with high APACHE 2 score, poor outcome and more requirement of ventilatory support.

**Keywords:** Serum magnesium concentration, Outcome, Critically sick patients

## INTRODUCTION

Magnesium is eighth common element on the earth crust, fourth most common cation in our body and second most common intracellular after potassium.<sup>1,2</sup> Magnesium has numerous function in our body, act as counter ion for the energy-rich adenosine triphosphate (ATP) and nuclear acid, cofactor in many enzymes, essential for calcium homeostasis, nerve conduction, skeletal muscle activity, and maintenance of calcium and potassium homeostasis.<sup>3,4</sup> Deficiency of magnesium is common and often ignored. It is associated with cardiac irregularity, cardiac

insufficiency, seizure and electrolyte imbalance. As this element has multiple functions in our body it is important in the pathophysiology of several critical illnesses in intensive care unit (ICU). It has been reported that magnesium deficiency is common in critically ill patients and is associated with increased mortality and poor clinical outcome.<sup>5</sup> The prevalence of hypoglycemia has wide range and there is variability in the report of various literatures. Zafar et al have reported that out of 70 critically ill-patients, 50 patients (71.43%) were normomagnesemic, 17 patients (24.29%) were hypomagnesemic and three patients were hypermagnesemic. Hypomagnesemia is a

significant electrolyte abnormality in critically ill-patients. Critically ill hypomagnesemic patients have higher mortality than the normomagnesemic patients.<sup>1,7</sup> Hypomagnesemia occurred in 42% of patients with hypokalemia, 29% of patients with hypophosphatemia, 27% of patients with hyponatremia, and 22% of patients with hypocalcemia. Whang et al has reported that hypomagnesemia occurred in 42% of patients with hypokalemia, 29% of patients with hypophosphatemia, 27% of patients with hyponatremia, and 22% of patients with hypocalcemia.<sup>8</sup> Wong et al has reported that hypomagnesemia (less than 1.2 mEq/l) was present in 68 patients or 11.0%, and hypermagnesemia (greater than 1.9 mEq/l) occurred in 58 patients or 9.3%.<sup>9</sup> Limaye et al has reported that hypomagnesemia was associated with a higher mortality rate in critically ill patients. The need for ventilatory support was significantly higher in hypomagnesemic patients. Hypomagnesemic patients required ventilator support for longer duration.<sup>10</sup>

However there is a paucity of data evaluating serum magnesium at admission as a predictor of morbidity or mortality especially in Indian context.

Hence the present study was undertaken to determine the usefulness of admission serum magnesium levels with regards to patient outcome considering mortality, need and duration of ventilator support, and acute physiologic assessment and chronic health evaluation 2 (APACHE 2) score.

## **METHODS**

### ***Place of study***

Present study has been conducted in the department of general medicine, Rangaraya Medical College, Kakinada, Andhra Pradesh, India.

### ***Duration of study***

The study has been conducted from November 2018 to July 2020.

### ***Type of study***

This is a prospective observational study.

### ***Ethics***

Present study is approved by institutional ethics committee. A written informed consent was obtained from all patients before enrolling them for study.

### ***Selection of patients***

Patients admitted in intensive care unit in the department of general medicine, Rangaraya Medical College,

Kakinada, Andhra Pradesh, India were selected for study based on inclusion and exclusion criteria.

### ***Selection criteria***

#### ***Inclusion***

All patients with APACHE 2 score of more than 20 or less than 6 admitted in ICU, and patients aged more than 18 years were included.

#### ***Exclusion***

Patients who had received magnesium prior to admission, patients receiving magnesium preparations at time of admission, patients who have received blood transfusions prior to ICU admission, patients with chronic alcoholism, patients receiving diuretics, aminoglycosides, pregnant women with eclamptic seizures, receiving MgSO<sub>4</sub>, and patients receiving cisplatin and amphotericin were excluded.

### ***Method of collection data***

Demographic data such as age and sex were recorded. Patients were assessed for presenting complaints, history of other diseases and habits through an interview with the patients or care giver. Further these patients underwent a thorough clinical examination for vitals (pulse rate blood pressure and respiratory rate) and other clinical signs including Glasgow coma score (GCS) followed by systemic examination. These findings were recorded on a predesigned proforma (Annexure-II) patients was followed up for the outcomes such as mortality, need of ventilator support, duration of ICU stay and APACHE 2 score.

### ***Investigations***

The selected patients underwent the following investigations: haemoglobin, total white blood cell (WBC) count, haematocrit, platelet count, blood urea nitrogen (BUN), serum creatinine, serum sodium, serum potassium, serum calcium, serum bilirubin, serum albumin, arterial blood gases and serum magnesium.

#### ***Estimation of serum magnesium***

At time of admission to medical ICU, serum magnesium levels were tested. Calmagite dye method for quantitative estimation of serum magnesium.

Subsequently patients were divided into three groups based their serum magnesium concentrations defined as follows: normal 1.7 to 2.4 mg/dl, low <1.7 mg/dl, and high >2.4 mg/dl.

#### ***Outcome variables***

Patients were assessed for the following parameters.

### APACHE 2 score

APACHE 2 is a severity of disease classification system one of several ICU scoring systems. It is applied within 24 hours of admission of a patient an ICU. An integer score from 0 to 71 is computed based on several measurements. Higher scores correspond to more severe disease and a higher risk of death. APACHE 2 score was calculated for each patient at admission to medical ICU.

### Chronic health points

If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows: for non-operative/emergency postoperative patients-5 points, and for elective postoperative patients-2 points.

### Ventilator support

Ventilator support was assessed as number patients requiring ventilation and duration of ventilation support in days.

### Length of stay in ICU

Length of stay in ICU was noted.

### Mortality

Patients were evaluated for the outcome and evaluated as improved or expired.

### Sample size

Sample size was calculated to be 100 by considering prevalence 27% from previous study and using formulae given.

$$n = Z^2 P(1 - P) / d^2$$

Where n is the sample size, Z is the statistic corresponding to level of confidence, and P is expected prevalence. They were divided in to two groups.

### Statistical analysis

Data were recorded in excel sheet and statistical Analysis was done with software statistical package for the social sciences (SPSS)-14 version. Qualitative data were calculated as percentage and proportions. Quantitative data were expressed as mean  $\pm$  standard deviation (SD). Chi square test was used to compare the qualitative variable.

## RESULTS

In present prospective observational study 100 patients admitted in the medical intensive care unit with various

critical medical conditions were enrolled for this study. These patients were divided in two groups based on serum magnesium concentration below 1.7 mg/dl and above 1.7 mg/dl

**Table 1: Clinicodemographic profile of patients with hypomagnesaemia and normal magnesium level.**

Variables	Serum magnesium concentration (mg/dl)		
	Below 1.7	Above 1.7	P value
<b>Age of the patients (mean=58.22<math>\pm</math>18.46)</b>			
Less than 25	9	6	0.015
26 to 50	12	28	
More than 51	29	16	
<b>Sex</b>			
Male	32	36	0.39
Female	18	14	
<b>Fever (%)</b>	30 (60)	38 (76)	
<b>Breathlessness (%)</b>	26 (52)	12 (24)	
<b>Altered consciousness (%)</b>	30 (60)	20 (40)	
<b>Decrease urine output (%)</b>	14 (28)	4 (8)	
<b>Pain abdomen (%)</b>	16 (32)	9 (18)	

Regarding clinicodemographic profile of the patients, there were statistically significant differences between two groups regarding age. In hypomagnesaemia group most of the patients were more than 51 years of age and in normomagnesaemia most of the patients were between 26 to 50 years of age. Both groups were comparable to each other regarding sex distribution.

Regarding clinical presentation, fever was common in both group (60% patients in >1.7 mg/dl group and 76% in <1.7 mg/dl group. Breathlessness, Altered consciousness, Decrease urine output and pain abdomen was more common in >1.7 mg/dl group.

In present study, 20% patients with magnesium level <1.7 mg/dl were diagnosed to have pneumonia with septicaemia, 8% acute exacerbation of COPD, 8% acute myocardial infarction, 10% have acute pulmonary oedema, 4% patient have RVF, 20% patients have CVA, meningitis and liver abscess was present in 8% patients, urinary tract infection (UTI) with septicaemia, malaria and dengue haemorrhagic fever was present in 4% patients each.

Similarly, 16% patients with magnesium level >1.7 mg/dl were diagnosed to have pneumonia with septicaemia, 4% acute exacerbation of COPD, 6% acute myocardial infarction, 6% have acute pulmonary oedema, 2% patient have RVF, 8% patients have CVA, meningitis was present in 12% patients, liver abscess was present in 16% patients. UTI with septicaemia, malaria was present in 12% patients

each. Dengue haemorrhagic fever was present in 6% patients.

**Table 2: Relation between diagnosis of patients and magnesium level.**

Variables	Serum magnesium concentration (mg/dl) (%)	
	Below 1.7	Above 1.7
Pneumonia with septicemia	10 (20)	8 (16)
Acute exacerbation of COPD	4 (8)	2 (4)
Acute myocardial infarction	4 (8)	3 (6)
Acute pulmonary oedema	5 (10)	3 (6)
RVF	2 (4)	1 (2)
CVA	10 (20)	4 (8)
Meningitis	4 (8)	6 (12)
Liver abscess	4 (8)	8 (16)
UTI with septicemia	2 (4)	6 (12)
Malaria	2 (4)	6 (12)
Dengue haemorrhagic fever	2 (4)	3 (6)

**Table 3: Relation between clinical outcome of patients and magnesium level.**

Variables	Serum magnesium concentration (mg/dl) (%)		P value
	Below 1.7	Above 1.7	
<b>Glasgow coma scale</b>			
Less than 5	1 (2)	4 (8)	0.438
5 to 10	18 (36)	12 (24)	
11 to 15	31 (62)	34 (34)	
<b>APACHE II score</b>			
21 to 25	24 (48)	36 (72)	0.02
26 to 30	18 (36)	12 (24)	
More than 30	8 (16)	2 (4)	
<b>Outcome</b>			
Improved	22 (44)	36 (72)	0.004
Expired	28 (56)	14 (28)	
<b>Ventilation</b>			
Required	40 (80)	26 (52)	0.003
Not required	10 (10)	24 (48)	

Both groups were comparable to each other regarding GCS ( $p=0.438$ ). Most of the patients in both groups have GCS score was in between 11 to 15 at the time of admission. In present study, 48% patients with magnesium level  $<1.7$  mg/dl have APACHE 2 score between 21 to 25, APACHE 2 score was between 26 to 30 in 18 (36%) and above 30 in 8 (16%) patients. Similarly 72% patients with magnesium level  $>1.7$  mg/dl have APACHE 2 score between 21 to 25, APACHE 2 score was between 26 to 30 in 12 (24%) and

above 30 in 2 (4%) patients. This finding is significant statistically.

Regarding comparison between outcome of patients between two groups, 44% patients with magnesium level  $<1.7$  mg/dl have improved and 72% patient didn't improve. 44% patients with magnesium level  $>1.7$  mg/dl have improved and 28% patient didn't improve. This finding is significant statistically.

Regarding comparison between requirement of ventilation between two groups, 80% patients with magnesium level  $<1.7$  mg/dl have required ventilation and 10% patient didn't required ventilation. 52% patients with magnesium level  $>1.7$  mg/dl have required ventilation and 48% patient didn't required ventilation. This finding is significant statistically.

## DISCUSSION

Present study was undertaken to determine the usefulness of admission serum magnesium levels with regards to patient outcome considering mortality, need and duration of ventilator support, and APACHE 2 score.

In the present study 50% critically ill patient have magnesium level below normal, Karnik et al has reported that the prevalence of hypomagnesemia in critically ill patients in different studies ranges from 20% to 65%, this finding support our study.<sup>11</sup> The mean age of the patient was  $58.22 \pm 18.46$  years with male predominance. This finding is supported by the work of Hansen et al and Velissaris et al.<sup>7,12</sup> Fever was common in both group (60% patients in  $>1.7$  mg/dl group and 76% in  $<1.7$  mg/dl group. Breathlessness, altered consciousness, decrease urine output and pain abdomen was more common in  $>1.7$  mg/dl group. This finding is supported by work of Chernow et al and Upala et al.<sup>13,14</sup> Pneumonia with septicemia and CVA was commonly associated with hypomagnesaemia. This finding corroborates with study of Bharath et al.<sup>15,16</sup>

In present study we have observed that hypomagnesaemia is associated with high APACHE 2 score, poor outcome and more requirement of ventilatory support. Jiang et al from their meta-analysis concluded that collectively, our data indicated that hypomagnesaemia appears associated with greater risk of mortality, sepsis, mechanical ventilation, and the length of ICU stay in patients admitted to ICU. The role of magnesium therapy for improving outcomes in critically ill patients is needed to further study, this statement corroborates with our study.<sup>17</sup>

Pannem et al has concluded that higher APACHE 2 score is associated with higher mortality and more length of stay in ICU among the cases of hypomagnesaemia this finding corroborates with our study.<sup>18</sup>

Soliman et al has reported that development of ionized hypomagnesaemia during an ICU stay is associated with a worse prognosis. It is often associated with the use of

diuretics and the development of sepsis. Monitoring of ionized magnesium levels may have prognostic, and perhaps therapeutic, implications. This finding corroborates with our study.<sup>19</sup> Kumar et al has reported that hypomagnesaemia was associated with a slightly higher mortality rate. Requirement and duration of ventilatory support were also higher, although not statistically significant. This finding corroborates with our study 3.

### Limitations

Sample size is major limitation for us.

### CONCLUSION

From present observational study we can conclude that hypomagnesaemia is more common in patients more than 50 years of age and with male predominance. Pneumonia with septicemia and CVA was commonly associated with hypomagnesaemia. In present study we have observed that hypomagnesaemia is associated with high APACHE 2 score, poor outcome and more requirement of ventilatory support.

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