

SERUM MAGNESIUM IN CRITICALLY ILL PATIENTS AND ITS CORRELATION WITH OUTCOME

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ABSTRACT**BACKGROUND**

Hypomagnesaemia is an emerging electrolyte disturbance in hospitalised patients, especially in critically ill ones and it has been shown to predict mortality in intensive care units (ICUs). This study was aimed to find the impact of admission serum magnesium levels and patient outcome considering mortality, need and duration of ventilator support, length of stay in ICU and APACHE II score.

MATERIALS AND METHODS

The present one-year prospective study was conducted in ICU of Department of Medicine, SCB MCH, Cuttack. A total of 100 patients from December 2016 to November 2017 were included in the study. Patients were divided as hypomagnesaemics and normomagnesaemics basing on their serum magnesium values.

RESULTS

On admission 68 out of 100 (i.e. 68%) had normomagnesaemia, 28 out of 100 (i.e. 28%) had hypomagnesaemia and 4 out of 100 (4%) had hypermagnesaemia. The patient with hypomagnesaemia compared with patients of normomagnesaemia had higher mortality rate (64.28% vs. 22.06%), higher APACHE II score on admission (29.6 vs. 24.3), a more frequent hypoalbuminaemia and sepsis, and also more duration of hospital stay. There was low GCS (5 - 10) in 96.42% of patients with hypomagnesaemia, but only 45.58% of patients with normomagnesaemia.

CONCLUSION

The present study showed patients with hypomagnesaemia at admission are significantly at high risk of mortality, requirement of prolonged ventilator support and longer duration of ICU stay and also predict higher APACHE II score.

KEYWORDS

Hypomagnesaemia, Critically Ill Patients, Ventilator Support, APACHE II Score.

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BACKGROUND

Magnesium is a key mineral and is the second most abundant intracellular cation. It is a cofactor for various enzymes, is essential for maintenance of membrane potential and modification of vascular tone.¹ Magnesium is pivotal in the transfer, storage and utilisation of energy, as it regulates and catalyses > 300 enzyme systems.² It helps to maintain normal nerve and muscle function and supports a healthy immune system. In general, Mg deficiency has been associated with a number of clinical manifestations such as neuromuscular abnormalities, tetany, seizures, cardiac problems like atrial and ventricular arrhythmias, cardiac insufficiency, coronary spasm, torsades de pointes, sudden death, respiratory problems like respiratory muscle weakness and bronchospasm associated with electrolyte abnormalities including hypokalaemia, hypocalcaemia, hyponatraemia and hypophosphataemia.^{3,4,5}

Its deficiency results primarily from gastrointestinal or urinary Mg losses, but malnutrition and decreased dietary Mg intake may hasten the development of Mg depletion.⁶ Magnesium deficiency is common in critical illnesses and can be due to poor nutritional intake, protracted vomiting and diarrhoea, intake of drugs like diuretics, aminoglycosides, diuretic phase of acute renal failure, co-morbidities like diabetes mellitus and chronic alcoholism.^{6,7} Hypomagnesaemia in critically ill patients correlates with higher mortality rate and worse clinical outcome in the intensive care unit. The prevalence of hypomagnesaemia has a wide range (11% to 61%) and considerable controversy exists regarding its effects on morbidity and mortality.^{8,9} Hypomagnesaemia occur in 40% of hospitalised patients,¹⁰ approximately 60% of post-operative patients,¹¹ 65% of medical ICU patients¹² and upto 90% of surgical ICU patients.¹³ Hypomagnesaemia has been implicated in the development of cardiovascular dysfunction and the systemic inflammatory response syndrome in ICU patients.¹⁴ The severity of hypomagnesaemia can be assessed using subjective clinical evaluation and biochemical markers of organ dysfunction. Objective scoring systems, such as the Acute Physiologic and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores are also commonly used to assess severity of illness and to predict outcome in other groups of critically ill patients.^{15,16}

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The objective of the study was to study serum magnesium levels in critically ill patients and its correlation with outcome considering the parameters like mortality, need for ventilator support, duration of ventilator support, length of stay in ICU and APACHE II score.

MATERIALS AND METHODS

This study is a descriptive study and conducted in Department of Medicine of SCB Medical College and Hospital, Cuttack, from December 2016 to November 2017. After clearance from Institutional Ethics Committee (IEC), we included 100 adult critically ill patients admitted to medicine ICU. Written consent was obtained from each individual or from patient’s relatives participated in the study.

Patient Selection Criteria

All patients with APACHE II score of more than 20 or less than 6 admitted in ICU and patients of more than 18 years of age. Sample size was taken conveniently.

Exclusion Criteria

Patients who had received magnesium prior to admission. Patients receiving magnesium preparations at time of admission, who have received blood transfusion prior to ICU admission, patients with chronic alcoholism and patients receiving diuretics, aminoglycosides and pregnant women with eclamptic seizure and receiving MgSO₄, patients receiving cisplatin and amphotericin.

All patients underwent thorough clinical examination and laboratory investigations like complete blood counts, serum urea and creatinine, serum sodium and potassium, serum calcium, serum bilirubin, serum albumin, random blood glucose, arterial blood gases and serum magnesium.

Patients were divided into Three Groups based on their Serum Magnesium Concentration defined as below-

- Normal: 1.8 - 2.4 mg/dL.
- Low: < 1.8 mg/dL.
- High: > 2.4 mg/dL.

APACHE II score was calculated for each individual patient participated in the study.

Statistical Analysis

The observed data was statistically analysed by using IBM-compatible Statistical Package for the Social Sciences (SPSS) version 20.0. The qualitative data were expressed as numbers (%) and the comparison of continuous variables between the two groups were performed with the Student’s t-test and categorical variables were compared using the Chi-square test. A p-value of < 0.05 was considered significant and p-value of < 0.001 was considered highly significant, while p-value of > 0.05 was considered not significant.

RESULTS

A total of 100 patients admitted to intensive care units under the Department of Medicine from December 2016 to November 2017 were studied.

Patients were divided into two groups based on magnesium levels, that is magnesium levels < 1.8 (hypomagnesaemia) and > 1.8 (normomagnesaemia).

Hypermagnesaemia (> 2.4) patients were not taken into study, as the prevalence was not significant.

The data obtained was coded and entered into Microsoft Excel spread sheet. The data was analysed, and the final results and observations were tabulated as below.

Magnesium	No. of Patients	Percent
Hypomagnesaemia (< 1.8)	28	28
Normomagnesaemia (1.8 - 2.4)	68	68
Hypermagnesaemia (> 2.4)	4	4
Total	100	100

Table 1. Distribution of Magnesium Levels in Patients

Age Group (Years)	Serum Magnesium Levels (mg/dL)			
	< 1.8		> 1.8	
	No.	%	No.	%
40-45	1	3.57	8	11.76
45-60	12	42.86	37	54.42
>60	15	53.57	23	33.82
Total	28	100	68	100
				p= 0.15

Table 2. Age Distribution

In this study, among the patients with magnesium levels <1.8 mg/dL, 42.86% of patients were aged between 45 - 60 years as compared to 54.42% in patients with magnesium level > 1.8 mg/dL. The difference was statistically not significant (p= 0.15).

Sex	Serum Magnesium (mg/dL)			
	< 1.8		> 1.8	
	No.	%	No.	%
Male	16	57.14	41	60.29
Female	12	42.86	27	39.71

Table 3. Sex Distribution

P= 0.26

In the present study, among patients with magnesium value < 1.8 mg/dL, 57.14% were males and 42.86% were females, while in those with magnesium levels > 1.8 mg/dL, 60.29% were males and 39.71% were females. However, this difference was statistically not significant (p= 0.26).

APACHE II Score	Serum Magnesium (mg/dL)			
	< 1.8		> 1.8	
	No	%	No	%
21-25	2	7.14	54	79.41
26-30	20	71.43	11	16.17
>30	6	21.43	3	4.42
Total	28	100	68	100

Table 4. APACHE 2 Score

P= 0.01

In this study, 21.43% of patients with magnesium levels <1.8 mg/dL had APACHE II score of > 30 compared to 4.42% of patients with magnesium level > 1.8 mg/dL had APACHE II score > 30. This difference was statistically significant (p=0.01).

Outcome	Serum Magnesium (mg/dL)			
	< 1.8		>1.8	
	No.	%	No.	%
Improved	10	35.72	53	77.94
Death	18	64.28	15	22.06
Total	28	100	68	100

Table 5. Outcome

p= 0.01

In this study, 64.28% of patients with magnesium levels <1.8 mg/dL expired as compared to 22.06% of patients with magnesium level > 1.8 mg/dL. This difference was statistically significant (p= 0.01).

Score	Serum Magnesium (mg/dL)			
	< 1.8		> 1.8	
	No.	%	No.	%
11-15	0	0	35	51.47
5-10	27	96.42	31	45.58
<5	1	3.58	2	2.95
Total	28	100	68	100

Table 6. Glasgow Coma Score

p= 0.01

In the present study, at time of admission Glasgow coma score was 11 - 15 in nil patients with magnesium < 1.8 compared to 51.47% of patients with magnesium > 1.8 mg/dL. This difference was statistically significant (p= 0.01).

Ventilation	Serum Magnesium (mg/dL)			
	< 1.8		> 1.8	
	No	%	No	%
Yes	23	82.15	36	52.94
No	5	17.85	34	50.00
Total	28	100	68	100

Table 7. Requirement of Ventilation

p= 0.01

In this study 82.15% of patients with hypomagnesaemia (< 1.8) required ventilation, whereas 52.94% of normomagnesaemic (> 1.8) required ventilation. This difference is statistically significant (p= 0.01).

DISCUSSION

Magnesium is an important intracellular cation like potassium. It acts as a cofactor for adenosine triphosphate (ATP) reactions. Most of the studies done earlier as well the present study have made use of only total serum magnesium levels, whereas ionised magnesium levels should be measured ideally which gives a better idea of associations since it is the ionized magnesium which is metabolically active.

ICUs are the units with the highest mortality frequencies within hospital departments. Mortality rates in ICUs ranges between 16% and 67% depending on the patient groups followed up and their characteristics. Critically ill patients have a high prevalence of electrolyte disorders, because of the presence of multiple causative factors. Early diagnosis and treatment is necessary. Clinicians should be cautious about electrolyte homeostasis and the underlying

pathophysiology of electrolyte disorders to provide optimal therapy for patients.²⁰

Hypomagnesaemia is a common finding in critically ill patients. The prevalence of hypomagnesaemia in critically ill patients in different studies ranges from 20% to 65%. In the present study, 28% had hypomagnesaemia. Hypermagnesaemia is found less commonly than hypomagnesaemia. It is reported in the range of 4% to 14% in literature and in this study hypermagnesaemia was seen in 4% of patients.

The present one-year prospective study was conducted under the Department of Medicine, SCB MCH, Cuttack, on critically ill patients admitted to Medicine ICU. A total of 100 patients from December 2016 to November 2017, divided into two groups based on serum magnesium levels < 1.8 (hypomagnesaemia, n= 28) and 1.8 -2.4(normomagnesaemia, n= 68). Hypermagnesaemic (> 2.4) patients were not included in the study.

In the present study among the patients with hypomagnesaemia 57.14% were males and 42.86% were females, while in normomagnesaemia 60.29% were males and 39.71% were females. Though the prevalence of hypomagnesaemia was high in the male patients, but it was not true statistically (p= 0.25).

In the study, 53.57% of hypomagnesaemic patients were > 60 yrs. and 33.82% of normomagnesaemic patients were > 60 yrs. 42.86% of hypomagnesaemic patients were within 45-60 yrs. and 54.42% of normomagnesaemic patients were within 45-60 yrs. This association was not statistically significant.

Hypomagnesaemia patients have more severe organ dysfunction and higher APACHE II score than the other patients. This may be explained by a strong association of hypomagnesaemia with sepsis and septic shock, a common cause of death in ICU patients. In the present study, 21.43% of patients with hypomagnesaemia had APACHE II score >30, while 4.42% of patients with normomagnesaemia had score >30. Among hypomagnesaemic patients, 71.43% of patients had APACHE II score between 26 - 30 and 16.17% of normomagnesaemic patients had score in between 26 - 30. These findings suggest that patients with hypomagnesaemia may have significantly higher mortality risk based on APACHE II score at admission (p= 0.01). Kiran et al and Gupta et al found that patients with hypomagnesaemia had higher APACHE II score on admission. Demircan F et al could not find significant difference between the groups about APACHE II scores.

In this study, 64.28% of patients with hypomagnesaemia expired compared to 22.06% of patients with normal magnesium levels. This difference was statistically significant (p= 0.01) posing strong association between hypomagnesaemia and mortality. Rubiez et al reported nearly double mortality rates (46% vs. 25%) in hypomagnesaemic patients compared with those with normomagnesaemia. Gupta et al reported 56.25% vs. 21.62% mortality rates in hypomagnesaemic patients compared to normomagnesaemic patients. Kiran et al found 51.1% vs. 36.2% of mortality rates in hypomagnesaemic patients as compared to normomagnesaemic patients. Guerin et al⁹ had found no difference in mortality in ICU patients between hypomagnesaemic and normomagnesaemic groups (18% vs. 17%). Chernow et al,¹¹ Safavi et al and Broner et al did not

find any difference between hypomagnesaemic and normomagnesaemic patients in mortality.

Hypomagnesaemia is known to produce muscle weakness and respiratory failure, that is why hypomagnesaemia causes difficulty in weaning the ventilator, and thus the duration of ventilator support is prolonged. We also observed similar findings in our study ($p= 0.01$). In this study, 82.15% of patients with hypomagnesaemia needed ventilation and 52.94% of normomagnesaemic patients needed ventilation.

In this study, 96.42% of patients with hypomagnesaemia had GCS score between 5 - 10 and 45.58% of patients with hypermagnesaemia had GCS score between 5 - 10. This difference was statistically significant.

Magnesium is an important element in the regulation of various processes in the cell and cell membrane. It also has a role in protein and DNA synthesis, DNA and RNA transcription, translation of messenger RNA and the regulation of mitochondrial function. So early diagnosis and treatment of hypomagnesaemia in patients requiring ICU may be important and has been discussed several times.^{8,11} Moreover, it is comprehensible that hypomagnesaemia is associated with severity of illness or increased mortality.

Overall, hypomagnesaemia is a common electrolyte imbalance in the critically ill patients and is associated with higher mortality rate more frequent and more prolonged ventilator support. There early diagnosis and treatment of hypomagnesaemia is necessary. Monitoring of serum magnesium levels may have prognostic and perhaps therapeutic, implications and physicians should be alert to the high incidence of magnesium deficiency in critically ill patients.

CONCLUSION

Based on the present study it may be concluded that patients with hypomagnesaemia on admission are significantly at high risk of mortality, requirement of ventilation, prolonged ventilator support and longer duration of ICU stay. Further patients with lower levels of serum magnesium levels at admission predicts higher APACHE II score.

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