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A STUDY ON EFFECTS OF HYPOMAGNESEMIA AMONG CRITICALLY III PATIENTS ADMITTED TO INTENSIVE CARE UNIT

Internal Medicine

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ABSTRACT

BACKGROUND: Hypomagnesemia is one of the common electrolyte disorders found in critically ill patients, but mostly remains under diagnosed . Our aim is to study prevalence and effects of hypomagnesemia among critically ill patients admitted to intensive care unit and to correlate with patient outcome and other parameters like length of stay in ICU, ventilator support and duration, mortality. **METHODS:** This cross-sectional study was conducted at Tripura Medical College and DR. BRAM Teaching hospital, over a period of 6 months duration from 1st June 2022 to 30th November 2022. 102 Critically ill patients of age more than 18 years admitted to ICU fulfilling the criteria were included in the study. Demographic data , medical history, length of ICU stay, requirement of ventilatory support and mortality was recorded for each patient. The severity scoring system used was Acute Physiology and Chronic Health Evaluation-II (APACHE-II). Serum magnesium levels along with other relevant investigations were done within first 24 h of hospital admission. **RESULTS:** Among 102 patients, the mean age was 52.5 ± 13.7 years. 66 (64.7%) were male and 36 (35.3%) were females. The mean APACHE-II score was 21.9 ± 1.8. Prevalence of hypomagnesaemia in the present study was 36.3 % , whereas 63.7% had normomagnesemia. Majority of patients with hypomagnesemia had sepsis (51%). When hypomagnesemia was compared with normomagnesemia group, patients with hypomagnesemia had higher APACHE II score (23.1 ± 1.7 vs 21.2 ± 1.5), more frequently had sepsis (51% vs 20%), higher ICU stay (10.3 ± 2.5 vs 8.7 ± 2.1), more frequent need for ventilatory support (54% vs 27%), higher mortality (41% vs 12%), and the association was statistically significant. However, no significant difference was found in the duration of ventilation between the two groups. **CONCLUSION:** This study has found high prevalence of hypomagnesemia in critically ill patients. Hypomagnesemia was associated with higher APACHE II score on admission, increased duration of ICU stays, increased need of ventilator support and higher mortality. Hence, monitoring of magnesium levels should be recommended in critically ill patients as it has several prognostic and therapeutic implications.

KEYWORDS

APACHE II score, Hypomagnesemia, Critically ill patients

INTRODUCTION

Magnesium (Mg) is an essential for life and plays a key role in the human body's various biochemical and physiological processes. A healthy individual need to ingest about 0.15-0.2 mmoL/kg/day to maintain a normal magnesium status.[1]

Hypomagnesemia is a common, often overlooked electrolyte imbalance in critically ill patients.[2] Many factors contribute to hypomagnesemia in critically ill patients such as impaired GI absorption, nasogastric suction, poor content of magnesium in feeding, drugs like diuretics, aminoglycosides, amphotericin-B which causes renal wasting of magnesium.[3]

Magnesium deficiency is known to be associated with a number of electrolyte abnormalities e.g., hypokalaemia, hypocalcaemia, hyponatremia and hypophosphatemia. It is also associated with a lot of clinical manifestations such as atrial and ventricular arrhythmias, cardiac insufficiency, coronary vasospasm, sudden death, skeletal and respiratory muscle weakness, bronchospasm, tetany, seizures and other neuromuscular abnormalities.[4]

The incidence of hypomagnesemia is reported as 2% in general population, 10-20% in hospitalized patients, 50-60% in ICU patients, and 30-80% in persons with alcoholism, and 25% in out patients with diabetes.[5]

Hypomagnesemia is associated with increased stay in ICU and have a detrimental effect among critically ill patients requiring mechanical ventilation. It can prolong the duration of mechanical ventilation and causes difficulty in weaning the ventilator support. Thus, there should be a high index of suspicion to look for hypomagnesemia in all critically ill patient and define the cause for better patient outcome.

As there is a paucity of such data for our state, the present study have been designed to explore the spectrum of magnesium deficiency and its influence on the outcome of critically ill patients.

AIM AND OBJECTIVES

- To estimate the prevalence of hypomagnesemia among critically ill patients.
- To study the conditions predisposing to hypomagnesemia.
- To compare the outcomes between hypomagnesemia and normomagnesemia in terms of duration of ICU stay, requirement for ventilator support and mortality.

MATERIAL & METHODS

It was a Cross Sectional Study was conducted over a period of 6 months duration from 1st June 2022 to 30th November 2022 in Tripura Medical College and Dr BRAM Teaching Hospital , Tripura. The study was done on 102 patients admitted to Intensive care unit (ICU) of Tripura Medical College and DR. BRAM Teaching hospital fulfilling the criteria and written informed consent were obtained in all cases.

Inclusion Criteria

- Cases above 18 years of age.
- APACHE-II score above 18 will be included in the study.

Exclusion Criteria

- Already known cases of hypomagnesemia, who received magnesium supplements.
- Cases on magnesium lowering drugs or calcium infusions.
- Patients not willing to give consent.

Demographic data (age and sex), medical history, medications administrated and length of ICU stay of each patient was recorded. The severity scoring system used was Acute Physiology and Chronic Health Evaluation-II (APACHE-II).[6]

5 ml of venous blood was drawn from the patients on the day of admission in ICU and serum magnesium levels was assessed in the central laboratory of the hospital by Xylidyl blue colorimetric method . Magnesium ions reacts with Xylidyl blue in alkaline medium to form purple coloured complex . The intensity of the purple colour is directly proportional to the concentration of magnesium in the specimen.

Normal range for magnesium concentration in our laboratory was 1.7-2.6 mg/dl. Serum magnesium level of <1.7 mg/dl were regarded as hypomagnesemia. Subjects were divided into normomagnesemia and hypomagnesemia groups and compared for various parameters like conditions predisposing to hypomagnesemia, duration of ICU stays, requirement for ventilator support, duration of ventilator support and mortality.

Additional laboratory investigations which included biochemical analysis like serum potassium, serum calcium, serum sodium, liver function test, liver function test , lipid profile and microbiological and radiological investigations (CT, MRI) were performed as per the management protocol.

Statistical Analysis

Collected data were entered into Microsoft excel and analysed using SPSS software version 22. The quantitative variables were expressed as mean ± standard deviation; qualitative variables were presented as frequency and percentage. The Mann-Whitney U test was applied for the comparing the mean values, Chi-square test for the comparison of frequencies and correlation. The p-value <0.05 was considered statistically significant.

RESULTS

In the present study, a total of 102 patients were enrolled who fulfilled the inclusion criteria in the study. Mean age of the study population was 52.5 ± 13.7. Majority (57%) of the patients were in the age group above 50 years. Minimum age was 23 years and maximum age was 81. Males were predominant with 66 (64.7%) and females 36 (35.3%). Among 102 patients, 35.3% patients were smokers and 33.3% were alcoholic. Hypertension was observed in 47% of the patients and 40.1 % had diabetes. (Table 1).

Table 1 : Demographic Profile Of The Study Population.

		Number (n)	Percentage (%)
AGE (years)	18-29 years	7	7 %
	30-50 years	37	36%
	>50 years	58	57 %
Gender	Male	66	64.7 %
	Female	36	35.3 %
Smoker	Yes	36	35.3 %
	No	66	64.7 %
Alcoholic	Yes	34	33.3 %
	No	68	66.7 %
Hypertension	Yes	48	47 %
	No	54	53%
Diabetes	Yes	41	40.2 %
	No	61	59.8 %

Amongst the cases, 37 (36.3%) had hypomagnesemia, and 65 (63.7%) had normomagnesemia (Figure 1). There were no cases of hypermagnesemia. The lowest serum magnesium value recorded in the study was 1 mg/dl while the highest value was 2.6 mg/dl with a total mean of 1.8 ± 0.4 mg/dl.

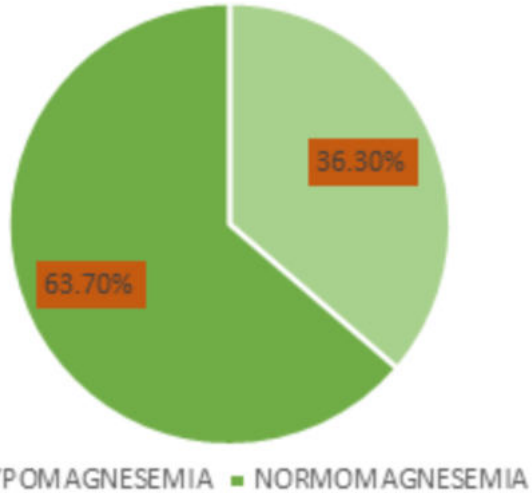

Figure 1: Magnitude of magnesium disturbances

Mean serum magnesium level in subjects with normomagnesemia was 2.14 ± 0.22 mg / dL and in subjects with hypomagnesaemia it was 1.32 ± 0.18 mg / dL, and the difference was statistically significant (p =0.00).

In our study, majority 32 (31.4%) had sepsis, 12 (11.8%) had chronic liver disease , 12 (11.8%) had chronic obstructive pulmonary disease, 11 (10.8%) had pneumonia, 10 (9.8%) had cerebrovascular accident, 10 (9.8%) had acute coronary syndrome, 7 (6.9%) had alcohol intoxication, 5 (4.8%) had meningoencephalitis, 3 (2.9%) had status epilepticus (Table 2).

Table 2: Clinical Diagnosis At Admission.

Clinical diagnosis	Number of patients (n)	Percentage (%)
Sepsis	32	31.4 %
Chronic liver disease	12	11.8 %
COPD	12	11.8 %
Pneumonia	11	10.8 %
Acute coronary syndrome	10	9.8 %
Cerebrovascular accident	10	9.8 %
Alcohol Intoxication	7	6.9 %
Meningoencephalitis	5	4.8 %
Status Epilepticus	3	2.9 %
Total	102	100%

Among conditions predisposing to hypomagnesemia, majority had Sepsis 19 (51%), 6 (16%) had chronic obstructive pulmonary disease, 4 (11%) had chronic liver disease, 3 (9%) had Cerebrovascular accident, 2 (5%) had alcohol intoxication , 2 (5%) had acute coronary syndrome, 1 (3%) had pneumonia (Table 3). Majority of the patient with hypomagnesemia had sepsis (51%) compared to compared to patients with normomagnesemia (20%), and the association was statistically significant (p = 0.01).

Table 3: Conditions Predisposing To Hypomagnesemia

Clinical diagnosis	Number (n)	Percentage (%)
Sepsis	19	51 %
COPD	6	16 %
Chronic liver disease	4	11 %
Cerebrovascular accident	3	9 %
Alcohol intoxication	2	5 %
Acute coronary syndrome	2	5 %
Pneumonia	1	3 %
Total	37	100 %

Hypocalcaemia was observed in 20 cases of hypomagnesemia (54 %) and 24 cases of normomagnesemia (37%), and the association was statistically insignificant (p value= 0.09). Hypoalbuminemia was observed in 24 cases of hypomagnesemia (65%) and 19 cases of with normomagnesemia (46%). Significant association was observed between hypoalbuminemia and cases of hypomagnesemia (p value =0.04) (Table 4).

Table 4 : Comparison Between Normomagnesemia And Hypomagnesemia Patients.

Parameters	Hypomagnesemia (n=37)	Normomagnesemia (n=65)	p-value*
Serum Magnesium (Mean ± SD)	1.32 ± 0.18	2.14 ± 0.22	<0.001
APACHE II score (Mean ± SD)	23.1 ± 1.7	21.2 ± 1.5	<0.001
Serum Sodium (Mean ± SD)	131.2 ± 11.2	135.8 ± 5.5	0.007
Serum Potassium (Mean ± SD)	3.5 ± 0.6	4.3 ± 4.9	0.339
Hypocalcemia (%)	20 (54%)	24 (37%)	0.093
Hypoalbuminemia (%)	24 (65%)	30 (46%)	0.041
ICU stay in days (Mean ± SD)	10.3 ± 2.5	8.7 ± 2.1	<0.001
Requirement of ventilator (%)	20 (54%)	18 (27%)	0.005
Days in ventilator (Mean ±SD)	2.9 ± 3.6	1.8 ± 2.9	0.098
Mortality (%)	15 (41%)	8 (12%)	0.015
Sepsis (%)	19 (51%)	13 (20%)	0.018
Diabetes mellitus (%)	18 (48.65%)	23 (35.38%)	0.193

*P value < 0.05 taken as significant.

The mean APACHE II score of total 102 cases in the study was 21.9 ± 1.8. The mean APACHE II score in cases with normomagnesemia was (21.2 ± 1.5) which was significantly lesser than Subjects with hypomagnesaemia (23.1 ± 1.7), hypomagnesemia was associated with higher APACHE II score and the difference was found to be statistically significant (p value =0.00) (Table 4) .

The range of duration of stay in ICU of all the cases varied from 4 day to 15 days with a mean of 9.3 ± 2.3 days. The mean duration of stay of cases of normal serum magnesium levels was 8.7 ± 2.1 days, while in cases of hypomagnesemia it was 10.3 ± 2.5 days , the difference was statistically significant (p value <0.001) (Table 4).

In the present study, 38 (37.3%) required ventilator support. Among cases with hypomagnesemia, 20 (54%) required ventilator support, whereas among cases with normomagnesemia, 18 (27%) required ventilator support, the difference was statistically significant association (p value =0.00) (Table 4).

Patients with hypomagnesemia needed mechanical ventilator support for 2.9 ± 3.6 days while normomagnesemia group needed ventilator support only 1.8±2.9 days. The difference is not statistically significant (p value = 0.09). The mortality rate among cases of hypomagnesemia was 15 (41%), whereas in cases of normomagnesemia it was only 8(12%). Statistically significant association was observed with hypomagnesemia and mortality rate (p value = 0.01) (Figure 2).

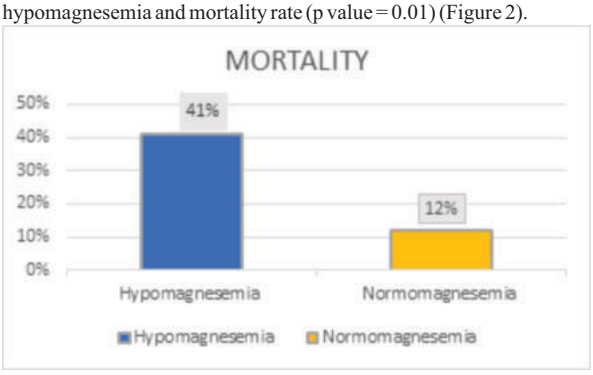

Figure 2: Magnesium and mortality

The occurrence of sepsis was more common among patients with hypomagnesemia (51%) when compared with cases of normomagnesemia (20%) , and the difference was found statistically significant (p value <0.05). No significant association was observed with hyponatremia, hypokalaemia, diabetes.

DISCUSSION

Magnesium is the second most common intracellular cation. Hypomagnesemia is multi factorial in critically ill patients and may be associated with other electrolyte disturbances, neuromuscular hyper excitability, respiratory muscle weakness and intractable arrhythmias.

Hypomagnesemia is a common finding in critically ill patients. The prevalence of hypomagnesemia in critically ill patients in different studies range from 20% to 65% and showed that these patients may have significantly higher morbidity and mortality.[5]

In this study, out of 102 patients, the mean age was 52.5 ± 13.7. Majority (57%) of the patients were above 50 years Majority (57%) of the patients were in the age group above 50 years , which was quite similar to the study by Gholyaf et al[7]. In this current study, majority (64.7%) were males and 35.3% were females, similar to study by Pannem RB et al [8], 68 % were males.

In our study, Prevalence of hypomagnesaemia was 36.3%. This was quite similar to the study by Bharath M.S et al [9] ,the prevalence of hypomagnesaemia was 37 %, Kiran HS et al [10](30 %), Kumar S et al [11] (25%), Islam MM et al [12] (38%).Several other studies found higher prevalence like Pannem RB et al [8] (64.7%), Singh H et al.[13] (60.2%). However, in the present study total serum magnesium was estimated whereas ionized magnesium is ideal as it is the metabolically active form. In contrast, in studies by Huijigen et al [14] and Soliman et al [15], the prevalence of hypomagnesaemia was much lower (14 % and 18 % respectively) where ionized magnesium was measured as it is a better index of intracellular magnesium as compared to serum magnesium.

In present study, 47 % had hypertension and around 40.1 % had Diabetes. In this study, there was no significant association of diabetes with hypomagnesemia (p value= 0.19). However, in study by Pannem RB et al [8] found significant association between hypomagnesemia and diabetes (p value < 0.05). This relation of hypomagnesaemia with diabetes mellitus may be due to increased renal losses of magnesium that accompany glycosuria. There is also a strong relationship between hypomagnesemia and insulin resistance.

Hypalbuminaemia was a significant associated factor among critically ill patients with hypomagnesemia, similar findings were observed in study by Pannem RB et al[8]. In this study hypokalaemia, hypocalcaemia was not significantly associated with hypomagnesaemia, however study by Limaye et al [16] have shown significant association of hypokalaemia with hypomagnesemia.

Among the conditions predisposing to hypomagnesemia, majority had sepsis 51% where as among patients with normomagnesemia, 20% had sepsis, which ultimately indicates that the hypomagnesemia patients are more prone to develop sepsis and the association was found to be statistically significant (p value = 0.01). Similar results was found by Limaye et al[16], which showed sepsis more common in patients with hypomagnesemia compared to normomagnesemia (69 % vs 28%).Magnesium plays an important role in sepsis. Hypomagnesemia is associated with increased release of endothelin, proinflammatory cytokines with increase lethality associated with endotoxin challenge. 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.[15]

APACHE II Score is one of the various ICU scoring systems available to prognosticate the patient's condition. The mean APACHE score in subjects with hypomagnesaemia was (23.1 ± 1.7) which was significantly higher than patients with normomagnesemia (21.2 ± 1.5), and was similar to findings by Singh H et al [13]and Kiran HS et al [10]. Hypomagnesaemia was associated with a higher APACHE II score.

In our study, we found that patients admitted with hypomagnesaemia their length of stay in ICU was prolonged compared to normomagnesemic individuals (10.3 ± 2.5 vs 8.7 ± 2.1), which is similar to study by Singh H et al [14](8.49 ± 5.19 vs 7.40 ± 4.73). In the study carried out by Soliman et al[16] there was no difference in the length of ICU stay.

In present study, hypomagnesemic patients required ventilator support for longer days compared to normomagnesemic patients (54% vs 27%), and the association was statistically significant. Pannem RB et al[10] had also found similar results. The duration of mechanical ventilation among patients with hypomagnesaemia was (2.9 ± 3.6 days) which was significantly more than patients with normomagnesemia (1.8±2.9 days), but was statistically insignificant Similar results was found in study by Pannem RB et al[8]. However, Safavi et al[17] found that in patients with hypomagnesemia the duration of mechanical ventilation was longer (7.2 vs 4.7 days, p<0.01). In the current study, it has been seen that patients with hypomagnesaemia needed ventilatory support more frequently and for a longer duration. Hypomagnesaemia leads to muscle weakness and respiratory failure, causing difficulty in weaning the patient from the ventilator.

Mortality was another important outcome in this study. Mortality among hypomagnesmic patients were significantly higher as compared to normomagnesemic patients (41% vs 12%),and the association was statistically significant. Higher mortality among patients with hypomagnesaemia was also found in studies by Singh H et al[13] (33.9%), Kumar MA et al[18] (64.8%). The mortality in patients with hypomagnesaemia was attributed to be secondary to more causes like electrolyte imbalance, cardiac arrhythmias, sepsis and septicaemia.

CONCLUSION

This study highlights the spectrum of magnesium disturbances on admission in critically ill patients admitted to ICU under Department of General Medicine of TMC & Dr BRAM teaching hospital. High prevalence of hypomagnesemia in critically ill patients was observed in our study. Hypomagnesemia was associated with higher APACHE II score on admission, increased duration of ICU stay, more frequent and more prolonged ventilator support , higher mortality, septicaemia. Early diagnosis of hypomagnesemia in critically ill patients is must to avoid adverse outcomes. Further studies are needed to assess the benefit of magnesium supplementation to prevent or correct hypomagnesaemia in critically ill patients.

LIMITATIONS

As the study population was small, the present results might not be a

representative of a general population.

Serum magnesium levels were recorded within first 24 h of admission. Follow-up magnesium levels were not done.

This was a descriptive non interventional study.

A large multicentric, randomized, double-blind, interventional, trial for magnesium supplementation in critically ill patients with Hypomagnesaemia is needed in future to evolve consensus / guidelines for treatment of Hypomagnesaemia in critically ill patients.

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