Original Article

Hypomagnesemia in Critically Ill Patients

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ABSTRACT

Background : Magnesium (Mg) is essential for normal cellular functions and is the second most abundant intracellular cation after potassium. In general, Mg deficiency has been associated with a number of clinical manifestations. 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.

Aims and Objectives : To study serum magnesium level in critically ill patients and to correlate it with Length of stay in MICU, Need for ventilatory support, Duration of ventilatory support, APACHE II score and mortality.

Results : In the present study 44% of patients were hypomagnesemic as compared to 56% of patients who were normomagnesemic. The patient with hypomagnesemia had longer duration of hospital stay (3.52 ± 1.60 vs 2.51 ± 0.87) more frequent need for ventilatory support (60.46% vs 39.53%) had higher mortality (60% vs 40%) higher APACHEII score and higher frequency of sepsis (62.96% vs 37.03%) compared to patients with normal magnesium. Serum hypokalemia was present in 55.17% of patients with hypomagnesemia and hypocalcemia was present in all the patients with hypomagnesemia. Hypertension (60% vs 40%), Diabetes mellitus (64.51% vs 58.06%) was significantly higher in hypomagnesemic than normomagnesemics.

Conclusion : Patients with hypomagnesemia on admission are significantly at high risk of mortality, requirement of ventilation, prolonged ventilatory support and longer duration of hospital stay and higher APACHE II score. So it is recommended to do serum magnesium level on admission in patient admitted in intensive care units.

Key words : Hypomagnecemia, Critically ill patients, APACHE II score.

Introduction :

Magnesium (Mg) is essential for normal cellular functions and is the second most abundant intracellular cation after potassium. It serves as a co-factor for several enzymes required for electrolyte homeostasis and is also necessary for membrane stability, cell division and generation of action potentials.[1] Magnesium is pivotal in the transfer, storage, and utilization of energy as it regulates and catalyzes > 300 enzyme systems.[2] In general, Mg deficiency has been associated with a number of clinical manifestations such as atrial and ventricular arrhythmias, cardiac insufficiency, coronary spasm, sudden death, skeletal and respiratory muscle weakness, bronchospasm, tetany, seizures and other neuromuscular abnormalities and a number of electrolyte abnormalities, including hypokalemia, hypocalcemia, hyponatremia and hypophosphatemia.[3-5] Magnesium deficiency is common in critical illnesses[6], and correlates with higher mortality rate and worse clinical outcome in the intensive care unit patients.[6] Hypomagnesemia is often overlooked, although it carries prognostic significance. The Prevalence of hypomagnesemia (measuring total serum magnesium) has a wide range (11% to 61%) and considerable controversy exists regarding its effects on morbidity and mortality.[1] 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 ventilatory support, length of stay in ICU and APACHE II Score.

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Methodology :

A Prospective observational study was conducted for a period of three year at tertiary care hospital

after clearance from Institutional Ethics Committee. The patients with APACHE II score more than 20 admitted in ICU were enrolled after taking written informed consent. 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 and pretested proforma. A blood sample was collected for estimation of serum total magnesium level by CALMAGITE METHODE on admission. Other haematological biochemical and radiological investigation were performed as indicated in every patient. Patients were followed up for the outcomes such as mortality, need of ventilator support, duration of ICU stay and APACHE II Score.

Statistical Analysis :

The data obtained was coded and entered into Microsoft Excel Worksheet. The categorical data like sex, presenting complaint and ventilatory support was expressed as actual numbers and percentage and comparison was done using Pearson's chi-square test. The continuous data like age, temperature, pulse rate was expressed as mean ± standard deviation (SD) and comparison was done by unpaired student 't' test. A probability value ('p' value) of less than or equal to 0.05 was considered as statistically significant.

Statistical software STATA version 13.1 was used for statistical analysis.

Results :

Total 100 patients included in the study were analysed in two groups based on serum magnesium level that is, serum magnesium < 1.5 mg/dl were considered hypomagnesemic and serum magnesium = 1.5 mg/dl were considered normomagnesemic.

In the present study 44% of patients were hypomagnesemic as compared to 56% of patients who were normomagnesemic Mean age of the cases inhypomagnesemic gr was 50.40 + 16.35 vs 42.39 + 13.89 in normomagnesemic group. Among patients with hypomagnesemia 72.22% of patients were aged more than 60 years as compare to 27.77% in patients with normomagnesemia. This difference was statistically significant (p=0.0008). ***(Table 1)***

The mean duration of hospital stay in patients with hypomagnesemia was significantly high (3.52 ± 1.60 days) compared to normomagnesemic patients (2.51 ± 0.87) (p=0.0001). ***(Table 1)***

Significantly higher number of patients with hypomagnesemia required ventilation (60.46%) compared to patient with normomagnesemia (39.53%) (p<0.004). Mean days of ventilation among patients with hypomagnesemia was also significantly high (3.12 ± 1.42) compared to normomagnesemic patients (2.16 ± 0.70) (p=0.004). ***(Table 1)***

All the patients with APACHE II score of > 30 were having serum hypomagnesemia as compared with none of the patient with normomagnesemia had APACHE II score > 30. This difference was statistically significant (p=0.0001). ***(Table 1)***

Mortality was 60% in patients with hypomagnesium levels as compared to 40% of patients with normomagnesemia. This difference was statistically significant (p=0.001). ***(Table 1)***

Pre-existing risk factors like hypertension & Diabetes Mellitus were significantly more hypomagnesemia group as compared to Normomagnesemia group (Hypertension 60% vs 40% & DM 64.51% vs 58.06%) (p=0.035 & p=0.001).

At time of admission 55.5% of patients with Glasgow coma score between 5-10 had low serum magnesium as compared to 44.4% of patients with normal serum magnesium. This difference was statistically significant (p=0.024). ***(Table 1)***

ARDS was observed significantly more (87.5%) in patients with hypomagnesium compared to 12.5% in patients with normal serum magnesium level. Next common complication observed was sepsis ie in 62.96% of patients with low serum magnesium compared with 37.03% patients with normal serum

magnesium. ***(Table1)***

Similarly multiorgan dysfunction was seen in 66.66% patients with hypomagnesemia compared with 33.33% of patients with normal serum magnesium .

When electrolytes were estimated, hypokalemia was seen predominantly in 55.17% of patients with hypomagnesemia and next common was Hypocalcemia which was seen in all the cases with hypomagnesemia compared with 54.16% with normal serum magnesium. ***(Table 1)***

Reported incidence of hypomagnesemia in critically ill patients in previous studies[10,11] is 56% and 52%, While in the present study it was 44% which is slightly less than others.

Mean age of the patients with hypomagnesemia, 60.27+0.82 vs 58.84+0.86 of normomagnesemia is reported in one of the studies[1]. In the present study mean age of the patients with hypomagnesemia was 50.40+16.35 vs 42.39+13.89 yrs. innormomagnesemic group which was statistically significant.

Table 1 : **Results of present study. In Two different groups**

Parameters	Serum Magnesium		p-value
	<1.5	**= 1.5**	
Age in years	50.40 ± 16.35	42.39 ± 13.89	S
Mortality rate	30/44 (60%)	20/56 (40%)	S
Prevalence	44/100 (44%)	56/100 (56%)	
GCS	10.38 ± 1.50	11.10 ± 1.50	S
APACHE-II	25.02 ± 3.28	22.25 ± 1.66	S
Serum sodium	134.63 ± 10.3	135.17 ± 9.34	NS
Hypokalemia	3.66 ± 1.11	4.16 ± 0.93	S
Sr. Calcium	6.65 ± 1.05	7.26 ± 0.89	S
Duration of ICU(days)	3.52 ± 1.60	2.51 ± 0.87	S
Duration of ventilatory support (days)	3.12 ± 1.42	2.16 ± 0.70	S
Need for ventilation	26/44(60.4%)	17/56(39.5%)	S

S = Statistically significant. NS = Statistically not significant

Discussion :

Magnesium plays an important role in homeostasis and is a cofactor for most of ATP reactions. Hypomagnesemia is an emerging electrolyte disturbance in hospitalized patients especially in the critically ill ones. Many factors contributes to hypomagnesemia like impaired GI absorption, nasogastric suction poor intake and drugs causing increase renal loss. Most of the studies measured total serum magnesium however RBC MAGNESIUM is a better index of intracellular magnesium. Its prevalence has a wide range (11% to 61%) and considerable controversy exists regarding its effects on morbidity and mortality.[7-9]

No statistically significant difference was observed between hypomagnesemia & gender in the present study. In contrast **Safavi M** *et al.*[12] reported 51% of the patients with hypomagnesemia were males and 49% were females with male to female ratio of almost 1:1.

Hypomagnesemia is known to cause muscle weakness and respiratory failure. It is one of the factors causing difficulty in weaning the patient from the ventilator.[13] A strong association was observed between severity of Hypomagnesemia and need of mechanical ventilation for longer duration prolonged hospital stay also.[13,14]

In the present study 26 (60.46%) patients with Hypomagnesemia required ventilation as compared to 17 (39.53%) patients with normal magnesium levels. The mean duration of ventilation in patients with hypomagnesemia was also significantly high (3.12 + 1.42 days) compared to (2.16 + 0.70 days) in cases with normal magnesium & mean duration of hospital stay was also significantly more in hpomagnesemic patients. Similar kind of results are reported by **Demircan F** *et al*[14]

Hypomagnesemic patients have more severe organ dysfunction and higher APACHE II score than the other patients. This may be explained by a strong association of hypomagnesemia with sepsis and septic shock, a common cause of death in the ICU patients. Cases with hypomagnesemia may have significantly higher mortality risk based on APACHE II score at admission. In most of the previous studies higher mortality was reported in critically ill cases with hypomagnesemia with high APACHE II score.[12,14,15] The present study could find similar results.

Rubeizet *et al*.[16] reported nearly double mortality rate (46% vs 25%) in hypomagnesemic patients compared to those with normomagnesemia. In contrast, **Guerin** *et al*.[9] found no significant difference between hypomagnesemic and normomagnesemic patients in ICU mortality (18% vs 17%) but noted higher mortality in hypermagnesemic patients.

The disparity in rates of mortality among the hypomagnesemics could be attributed to the various other factors such as age, history and clinical presentation at admission.

Hypomagnesemia has been known to be associated with diabetes mellitus, insulin resistance and hypertension. Hypomagnesemia is due to increase renal loss of magnesium that accompanies glycosuria. Magnesium supplementation is associated with decreased insulin requirements and better control of blood sugar[17-18] Amomgst pre-existing risk factors Hypertension and DM did not show any significant association with Hypomagnesemia.

Magnesium plays an important role in sepsis. Hypomagnesemia is associated with increase release of endothel in and proinflammatory cytokines. In the present study sepsis was observed in 62.96% of cases with Hypomagnesemia while multiorgan dysfunction in 66.66% cases suggesting that ARDS with sepsis and multiorgan failure are commonly associated with serum hypomagnesemia. Similar kind of results are reported by various authors in their studies previously.[14,19]

Zafar, Mir Sadaqat Hassan *et al.*[19] found that Hypomagnesemic patients mostly comprised of multiorgan dysfunction (41.17%), respiratory failure (17.64%) and septicemia (11.76%) where asnormomagnesemic patients had mostly septicemia (20%), post-operative course (16%), respiratory failure (14%), renal failure (10%) and acute myocardial infarction (10%).

Hypomagnesemia is commonly associated with other electrolyte abnormalities. Like Hypokalemia & hypophosphatemia, hypocalcemia and hyponatremia. **Whang** *et al.*[20] in his study on critically ill cases with hypomagnesemia reported hypokalemia in 42%, hypophosphatemia 29%, hyponatremia 27% cases and 22% patients hadhypocalcemia. In the study by **Limaye** *et al.*[10], half of the patients (48%) with hypokalemia had low serum magnesium levels. **Zafar, Mir Sadaqat Hassan** *et al.*[19] found that associated electrolyte abnormalities in hypomagnesemic patients were hypokalemia (58.82%), hyponatremia (47.05%), hypocalcemia (70.58%) and hypophosphatemia (29.41%).

In our study, hypokalemia was seen in 55.17% of patients with hypomagnesemia and Hypocalcemia was seen in all the cases with hypomagnesemia compared with 54.16% with normal serum magnesium. This incidence was slightly more as compared to others.

Hypokalemia, hypocalcemia, hypophosphatemia are said to be the predictors of hypomagnesemia. Hypokalemia seen in hypomagnesemic patients is relatively refractory to potassium supplementation until magnesium deficiency is corrected.[20-21] This is

due to defective membrane ATPase activity and also because the renal potassium loss is increased in presence of hypomagnesemia..

Overall, hypomagnesemia is a common electrolyte imbalance in the critically ill patients and is associated with higher mortality rate, more frequent and prolongedventilatory support. Therefore, early diagnosis and treatment of hypomagnesaemia is necessary.

Conclusion :

Hypomagnesemia is a common electrolyte imbalance in critically ill patients. Patients with hypomagnesemia on admission are significantly at high risk of mortality, requirement of ventilation, prolonged ventilatory support and longer duration of hospital stay. It may be the result of underlying disease, diuretics or sepsis.

Implication of the study :

Additional studies are required to address the current approach to magnesium imbalance in critically ill patients, as well as the association of hypomagnesemia with morbidity and mortality, and the effect of the correction of this electrolyte disorder. It seemed that correction of hypomagnesemia decreases hypomagnesemia associated morbidity, therefore early diagnosis and treatment of hypomagnesemia is necessary. Monitoring of serum magnesium level may have prognostic, and perhaps, therapeutic implications and we physicians should be alert to the high incidence of magnesium deficiency in critically ill patients

Conflicts of Interest : None reported by authors.

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