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# A Study of Hypomagnesemia in Patients Admitted in Medical ICU and Its Correlation with Final Outcome

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## ABSTRACT

**Introduction:** Magnesium is the second most common intracellular cation found in the body that is required as cofactor in numerous enzymatic reactions, smooth functioning of cardiac and neurological systems. Magnesium deficiency is often overlooked in critically ill patients and is linked with risk of electrolyte imbalance, difficulty weaning off ventilator, sudden cardiac deaths and poorer outcome.

**Objective**- To assess prevalence of magnesium deficiency in critically ill patients admitted to Medical ICU and its association with requirement & duration of mechanical ventilation, ICU stay, APACHE-II & mortality.

**Methods-** Prospective descriptive study was conducted on 69 critically ill patients admitted in medical ICU. After taking informed consent serum magnesium level of patients were collected and entered in spreadsheet and final analysis was done with help of Open EPI and SPSS software.

**Results-**It was concluded that patients having hypomagnesemia were at increased risk of electrolyte abnormalities, longer ventilatory support, longer hospital and ultimately poorer outcome stay as compared to patients with normal magnesium levels.

**Conclusion-** Magnesium remains an important but often side-lined cation in critically ill patients. However, Hypomagnesemia is a repeated finding seen in critically ill patients and is significantly associated with a higher mortality rate and frequent need for mechanical ventilation.

## INTRODUCTION

Magnesium is the fourth most plentiful cation in the human body [1][2] and additional only to the intracellular cation after potassium and turns as a cofactor in over three hundred enzymatic reactions. Magnesium is essential for maintaining neuromuscular [3][4] and heart functions. Magnesium deficiency is a condition that is often overlooked in critically ill patients [5] and is associated with other electrolyte abnormalities like hypokalemia. Hypomagnesemia can cause fatal complications including coronary artery spasm, ventricular arrhythmias, and sudden cardiac death. [6-8] Magnesium monitoring among critically ill patients has predictive and therapeutic effects as they are associated with significant magnesium and asymptomatic deficiency that can lead to the development of neurotoxicity, psychiatric disorders and increased morbidity and mortality.

The etiology of magnesium deficiency has many compo-

nents and associated with drugs induced, kidney and stomach loss, Diabetes, alcoholism, and some metabolic disorders. [9] Even though serum magnesium levels represent only 0.3% of the total magnesium content in the body, the amount of serum $Mg^{+2}$ ion concentration is still used as a measure of magnesium status in patients.

## AIMS AND OBJECTIVES

Aim of this study is to Assess the prevalence of magnesium deficiency in critically sick patient, to quantify the serum magnesium levels and its correlation with requirement & duration of mechanical ventilation, ICU stay, APACHE-II score and ultimately outcome.

## METHODS

This Prospective descriptive study was conducted on 69 patients admitted in Medical ICU in Surat Municipal Institute of Medical Education and Research (SMIMER) Hospital, Surat, Gujarat, from year February 2020 to August 2021. Patients admitted consecutively to the ICU were screened by the investigator for the satisfaction of the eligibility criteria of the patient.

Patients over 18 years suffering from various medical conditions directly admitted to ICU were included in the study after obtaining informed written consent of patient or patients' legal guardian. Patients having age <18 years, patient with any known case of Chronic kidney disease, Chronic alcoholic, Drugs affecting serum magnesium level, Chronic diarrhea and patients who had received magnesium prior to transfer to hospital, patients not willing to participate were excluded from the study. Approval for this study was taken in institutional ethical committee. Informed written consent of all the participants was taken. All necessary confidentiality of participants was maintained. A separate consent for blood sampling was also taken.

Patients who being treated for severe infections such as complicated malaria, urinary tract infections, cellulites, meningitis, pneumonia, and tuberculosis; hepatic failure due to acute viral hepatitis or cirrhosis; acute renal failure due to hypovolemia, infections; respiratory failure due to chronic obstructive pulmonary disease, interstitial lung disease, and ARDS; and congestive cardiac failure due to ischemic heart disease or valvular heart disease; cerebrovascular accident secondary to cerebral infarct or hemorrhage; poisonings including organophosphate compounds, acute pancreatitis, Guillain-Barre syndrome, malignancy, status epilepticus and diabetic ketoacidosis were included in the study.

A blood sample was taken to determine the serum total magnesium level and any other hematological abnormalities that the patient had on admission to the ICU. Each patient's medical history and clinical findings were meticulously recorded. Every patient underwent additional hematological and biochemical tests that were required. Detail history, examination, and investigations as per proforma were done for each participant.

APACHE severity [10] of the patient's sickness was scored at the time of admission to the ICU. The study had no effect on the ICU's patient handling. The level of magnesium in the blood was measured using a colorimetric technique. The findings were recorded in the Patient's proforma. The patient was given appropriate treatment for Hypomagnesemia & any other abnormalities detected by consultants of the respective treating unit. Outcome of the patients with Hypomagnesemia was monitored according to duration of stay in ICU, duration of ventilatory support and mortality. Patients were followed till discharge from ICU/ death in the hospital from the hospital. Data was entered in MS EXCEL spread sheet and was analyzed with the help of Open EPI and SPSS software. Statistical analysis was done by appropriate statistical method.

## RESULTS

In Table 1, it was observed that incidence of critical illness patients in ICU among patients was major in age group 21-30 years 20 (28.99%) followed by age group 31-40 years 18 (26.09%). The calculated mean age was 34.71 ± 14.65 years.

Table 2 shows Apache-II score was found as 31 (44.93%) patients higher in 11-15 score followed by 23 (33.34%) patients 16-20 score. In addition, mean Apache II score was found as 15.52 ± 4.23. Table 3 shows comparison of ICU stay vs Hospital stay which was found 6.55 ± 2.56 days and 13.36 ± 5.82 days respectively. Moreover, the mortality rate was 24 (34.79%) patients while 45 (65.21%) patients survived.

**TABLE 1. Age and gender wise distribution**

| Variables | Patients (n=69) |
|---|---|
| **Age in years** | |
| 18-20 | 11 (15.94%) |
| 21-30 | 20 (28.99%) |
| 31-40 | 18 (26.09%) |
| 41-50 | 9 (13.04%) |
| 51-60 | 4 (5.80%) |
| >60 | 7 (10.14%) |
| Mean Age (yrs) | 34.71 ± 14.65 |
| **Gender** | |
| Male | 42 (60.87%) |
| Female | 27 (39.13%) |

**TABLE 2. APACHE score wise distribution.**

| Apache Score | Patients (n=69) (%) |
|---|---|
| ≤10 | 7 (10.14%) |
| 11-15 | 31 (44.93%) |
| 16-20 | 23 (33.34%) |
| >20 | 8 (11.59%) |
| Mean ± SD | 15.52 ± 4.23 |

**Table 3. Outcome wise distribution**

| Outcome | Patients(n=69) |
|---|---|
| Ventilation Stay (days) | 3.71 ± 1.18 |
| ICU Stay (days) | 6.55 ± 2.56 |
| Hospital Stay (days) | 13.36 ± 5.82 |
| Survive | 45 (65.21%) |
| Death | 24 (34.79%) |

Table 4 shows comparison between the two group of Hypomagnesemia and Normal magnesium have found that Hypernatremia (41.02% vs 13.33%), Hypokalemia (35.89% vs 6.66%), Hypocalcemia (71.79% vs 16.66%), Hypoalbuminemia (79.87% vs 30%) were statistically significant and were frequently present in Hypomagnesemia group. In addition, ventilation stay, Mortality rate and Diabetes mellitus were present frequently in hypomagnesemia group compared to normal magnesium group which was statistically significant. (p<0.001).

**Table 4. Correlation with hypomagnesaemia with other parameters**

| Variables | Hypomagnesemia (n=39) | Normal magnesium(n=30) | P value** |
|---|---|---|---|
| Age (years) | 35.24 ± 12.60 | 34.91 ± 16.91 | 0.9264 |
| Gender | | | |
| Male | 25 (67.57%) | 17 (53.13%) | 0.2202 |
| Female | 12 (32.43%) | 15 (46.87%) | |
| Hypernatremia | 16 (41.02%) | 4 (13.33%) | **<0.001** |
| Hypokalaemia | 14 (35.89%) | 2 (6.66%) | **<0.001** |
| Hypocalcaemia | 28 (71.79%) | 5(16.66%) | **<0.001** |
| Hypoalbuminemia | 31 (79.87%) | 9 (30%) | **<0.001** |
| DM | 19 (48.71%) | 7 (23.33%) | **0.0246** |
| Apache II Score | 16.10 ± 4.58 | 14.84 ± 3.74 | 0.2196 |
| Ventilation Stay (days) | 3.92 ± 1.22 | 3.23 ± 1.10 | **0.0178** |
| ICU Stay (days) | 6.89 ± 2.76 | 6.15 ± 2.28 | 0.2334 |
| Hospital Stay (days) | 13.81 ± 6.02 | 12.84 ± 5.63 | 0.4940 |
| Death | 18 (46.15%) | 6 (26.6%) | **<0.001** |

** Chi-square test

## DISCUSSION

The second most frequent intracellular cation is magnesium. It is essential for maintaining homeostasis. Because the magnesium-ATP complex is attached to the enzymes and hydrolysed by them, magnesium is the cofactor for most ATP processes. Magnesium deficiency in critically ill patients is caused by a variety of factors, including impaired GI absorption, nasogastric suction, low magnesium content in feeding formulae or TPN solutions, and the administration of drugs such as aminoglycosides, diuretics, and Amphotericin-B, which cause magnesium wasting through the kidney.

The three major factors that affect magnesium requirements, particularly in the study, are as follows: (1) dietary factors like poor intake, and intake of refined processed food, excess fibre and excess sugar; (2) host factors like anabolism or catabolism, ischemia, chronic disease, decreased intestinal absorption, increased renal excretion, hormonal, enzyme, vitamin imbalance, and alcohol consumption; and (3) environmental factors like stress due to provoked and psychological diseases and also medications like cardiac medications, diuretics, antibiotics, and purgatives.

Prevalence of Hypomagnesemia was studied in different studies and showed Kumar S et al [11] was 59.30%, Chaudhari S et al [12] 43%. While in study conducted by Ugaragol PG et al [13] Prevalence of Hypomagnesemia was 55.3%, Limaye CS et al [14] was 52% and Sudha R et al [15] was 45%. While in study conducted by Pannem RB et al [16] prevalence was highest 64.7%.

The range of hypomagnesemia varies between 40 %- 70 %. In our study, the prevalence of hypomagnesemia was 56.52%. Various studies with prevalence of hypomagnesemia is shown in above table. The total serum magnesium was tested in most of the investigations, whereas RBC magnesium was assessed in a few others. Ionized magnesium, on the other hand, has only been measured in a few investigations. The prevalence of hypomagnesemia was found to be quite low in those investigations. Studies that looked at ionised magnesium levels found a lower prevalence than those that looked at serum magnesium levels.

**Correlation of magnesium with other parameters**

In the present study, when compared Hypomagnesemia vs Normal magnesium levels, it was found that Hypernatremia (41.02% vs 13.33%), Hypokalaemia (35.89% vs 6.66%)), Hypocalcaemia (71.79% vs 16.66%), Hypoalbuminemia (79.87% vs 30%) were statistically significant. (p<0.05).

Zafar MSH et al [17] have accompanying outcomes were the electrolyte abnormalities such as hypokalaemia (58.82%), hyponatremia (47.05%), hypocalcaemia (70.58%) and hypophosphatemia (29.41%). Between hypomagnesemia and normomagnesemia patients, there

was a highly significant difference in death. In addition, Similar study by Sudha R et al [15] have found that Hypocalcaemia (33% vs 3%), Hypokalaemia (20% vs 6.25%), Hyponatremia (40% vs 12.5%), Hypoalbuminemia (50% vs 31%) statistically significant between hypomagnesemia and normal magnesium patients.

It has been noted that the APACHE score on admission varies dramatically depending on the magnesium level. Patients who acquire ionised hypomagnesemia during their ICU stay have a higher APACHE score at the time of admission. However, in the current study no correlation was found between APACHE II score and level of magnesium (p=0.2126). This is parallel with the results of Kumar S et al [11], Sudha R et al [15], Zafar MSH et al [17] and Chaudhari S et al [12] found no kind of variance in APACHE II score between the hypomagnesemia and normal magnesium group.

Muscle weakness and respiratory failure are known side effects of hypomagnesemia. It's one of the reasons why weaning the patient off the ventilator is so tough. Magnesium supplementation reduces respiratory muscle weakness in hypomagnesaemia patients. Hypomagnesaemia patients have been found to require ventilator assistance more frequently and for a longer period than individuals with normal magnesium. The length of patients on breathing assistance device in our study ranged from 2 to 6 days, with an average of 3.71 days. Hypomagnesemia was shown to be strongly linked to the use of a ventilator (p=0.0178). The studies conducted by Kumar S et al [11], Charles BS et al [18], Sudha R et al [18], and Pannem RB et al [16] were statistically significant between hypomagnesaemia with normal magnesium level respectively ($p<0.05$)

The association between hypomagnesemia and mortality rate varies depending on different studies. Patients with hypomagnesemia had a greater mortality rate than those with normomagnesemia in the studies done by Chaudhari S et al [12] (39% vs 25%), Limaye CS et al [14] (57.7% vs 31.7%) and Pannem RB et al [16] (49.48% vs 23.80%). Similar results were seen in our present study (46.15% vs 26.6%).

The increased risk of electrolyte abnormalities, particularly hypokalaemia, and cardiac arrhythmias in hypomagnesemia patients explains the higher fatality rates. Hypomagnesemia has a significant relationship to septicaemia and septic shock, which is a usual cause of death in ICU patients. Muscle weakness and respiratory failure can be caused by hypomagnesemia. It is one of the issues preventing the patient from being weaned off the ventilator. In this study, there was no difference in the length of ICU stay between the two groups. However, the patients who established hypomagnesemia during their ICU stay had higher length of stay in ICU. They also originate that the length of stay in ICU is a distinct risk factor for developing hypomagnesemia.

Many factors contribute to hypomagnesaemia in an ICU patient, including impaired GI absorption, nasogastric suction, low Mg content in feeding formulae or total parenteral nutrition solutions, routine use of proton pump inhibitors, and administration of drugs such as diuretics, aminoglycosides, and Amphotericin B, which cause wasting of Mg through kidney. Even patients with "normal" magnesium levels at admission may have low serum Mg within a few days in the ICU, implying that routine serum magnesium test should be done at least at varied intervals during the ICU stay, not just at the time of admission.

## CONCLUSION

Magnesium remains an important but often side-lined cation in the critically ill patient. However, Hypomagnesemia is a repeated finding seen in critically ill patients and is significantly associated with a higher mortality rate and more frequent need for mechanical ventilation. It is also associated with other electrolyte abnormalities like hypokalemia, hypocalcemia and hyponatremia when compared to patients with normal magnesium levels. These findings may be helpful to monitor the level of magnesium as a marker of mortality in critically ill patients.

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