International Journal of Integrated Health Sciences (IIJHS)
ISSN Print: 2302-1381; ISSN Online: 2338-4506

Original Article

# Serum Magnesium Levels in Patients Admitted with Septic Shock and Its Correlation with Outcome

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**Article History**

Received: December 11, 2023
Accepted: March 07, 2024
Published: April 15, 2024

**DOI:** 10.15850/ijihs.v12.n1.3699
**IJIHS. 2024;12(1):10–16**

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## Abstract

**Objective:** To evaluate the initial serum magnesium levels of critically ill septic shock patients upon admission to the intensive care unit (ICU) and correlate these levels with the patients' requirements and outcomes, including ventilator support, length of stay in the ICU, occurrence of cardiac arrhythmias, and mortality rates.

**Methods:** This was an observational study involving 60 patients who were admitted to the medical Intensive Care Unit (ICU) for septic shock. Serum magnesium levels were measured upon admission to the ICU. A comparison was made between patients with normal and abnormal magnesium levels at the time of admission to evaluate the need for vasopressor support, the average duration of assisted ventilation and dialysis, the incidence of arrhythmia, the average length of ICU stay, and mortality rates.

**Results:** Out of the 60 cases studied, there were 42 males (70.00%) and 18 females (30.00%), resulting in a M:F ratio of 1:0.42. The mean age of both male and female patients was found to be comparable. The need for assisted ventilation and renal replacement therapy was found to be comparable in patients with normal and abnormal serum magnesium levels. The number of days for which assisted ventilation was required, the incidence of arrhythmia, the mean duration of ICU and hospital stay, and mortality were significantly higher in patients with abnormal magnesium levels at the time of ICU admission ($P<0.05$).

**Conclusion:** Abnormal serum magnesium levels are associated with increased morbidity and mortality in critically ill septic shock patients admitted to the ICU.

**Keywords:** Arrhythmias, hypomagnesemia, mortality, septic shock

## Introduction

Critical illnesses, such as septic shock, often manifest as complex physiological derangements that go beyond the primary insult. In critically ill patients, various factors contribute to the delicate balance of homeostasis and electrolyte imbalances, which significantly influence the final outcome. Disruptions in electrolyte levels are common during times of severe physiological stress and can have profound consequences.[1] Critical illnesses usually provoke a cascade of physiological responses that impact multiple organ systems. Electrolyte imbalances frequently occur as the body tries to cope with the stress of the disease. Maintaining appropriate levels of sodium, potassium, calcium, and magnesium is important for vital physiological functions, such as cellular membrane stability, nerve conduction, and muscle contraction. The dysregulation of these electrolytes can worsen the severity of critical illness and have a negative impact on the final outcome.[2]

In critical care medicine, patients often have a range of electrolyte imbalances. Hyponatremia and hypernatremia are common disturbances

that can occur due to changes in fluid balance and hormone secretion. Potassium imbalances, particularly hypokalemia, can be caused by factors such as renal dysfunction or medications. Calcium dysregulation, which is frequently observed in sepsis, can result in cardiovascular instability. Amongst these imbalances, magnesium disturbances are increasingly being recognized as significant factors contributing to the clinical condition of patients.[3]

Magnesium, an intracellular cation, plays a crucial role in enzymatic reactions, neuromuscular transmission, and cardiovascular stability. In critically ill patients, serum magnesium levels can change dynamically due to various factors. Sepsis is associated with an increase in pro-inflammatory cytokines and oxidative stress, resulting in a higher demand for magnesium.[4] Concurrent Additionally, factors such as gastrointestinal losses, renal dysfunction, and therapeutic interventions can further disrupt magnesium homeostasis. Therefore, Understanding the etiopathogenesis of magnesium imbalances in critical illness is imperative for devising targeted interventions.[5]

The crucial importance of serum magnesium as a prognostic marker has garnered interest among researchers. Magnesium plays a vital role in cellular function, myocardial stability, and vascular tone, and has been found to affect the outcomes of patients admitted to the ICU.[6] However, limited research has focused on the intricate interplay between magnesium status at admission and the subsequent clinical trajectory in septic shock patients. Therefore, understanding how magnesium levels influence outcomes in this specific subset of critically ill patients having septic shock is crucial for refining treatment strategies and optimizing patient care.[8]

This prospective observational study aims to analyze the impact of serum magnesium abnormalities, specifically hypomagnesemia and hypermagnesemia, on the outcomes of patients diagnosed with septic shock and admitted to the medical ICU.

## Methods

This is a prospective observational study conducted in the department of general medicine at the Regional Institute of Medical Sciences in Imphal, India. Since the study was purely observational and no ethical issues were involved, no ethical clearance was required. The study duration was one year, from January 2023 to December 2023.

The inclusion criteria for the study were patients above 18 years of age admitted to the medical ICU with a diagnosis of septic shock, as defined by Sepsis III. This includes the clinical diagnosis of sepsis with significant hypotension requiring vasopressors to maintain a mean arterial pressure above 65 mm Hg and a serum lactate level greater than 2 mmol/L (18 mg/dL) after adequate volume resuscitation. Informed and written consent was obtained from the patients' relatives.

The following patients were excluded from the study: those under 18 years of age, patients or relatives who refused consent, patients who received any form of magnesium therapy within 3 days of admission to the NICU, patients on drugs known to affect magnesium levels such as diuretics, gentamicin, cisplatin, and cyclosporine, and patients with end-stage renal disease.

The sample size was calculated using the formula

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

using OPENEPI software, based on pilot studies conducted on the topic of electrolyte imbalance in septic shock. With 90% power and a 95% confidence interval assumed, a determination of 50 patients was made, resulting in the inclusion of 60 patients in this study.

The demographic details of patients, including age, gender, and occupation, were noted. A thorough history was taken regarding the duration of illness, signs and symptoms, and the presence of any localizing signs. A comprehensive clinical examination, including a systemic examination, was performed. Hemodynamic parameters, such as pulse rate, respiratory rate, mean arterial pressure, and SpO2, were recorded for all cases. Routine blood investigations, including a complete blood count, renal function test (blood urea, serum creatinine), hepatic function test, and electrolytes (serum sodium, potassium, magnesium, and calcium), were conducted at the time of admission to the ICU. The patients were comprehensively evaluated using the SOFA (Sequential Organ Failure Assessment) score,[9] which consists of three key components: altered mental status, hypotension, and an increased respiratory rate, as well as the APACHE II (Acute Physiology and Chronic Health Evaluation) score[10], a scoring system that considers various physiological parameters, including vital signs, laboratory values, and age. Patients were divided into

three groups based on their serum magnesium level at the time of admission to the ICU: normal (1.6 to 2.5 mg/dL), increased (serum magnesium >2.5 mg/dL), or decreased (serum magnesium <1.6 mg/dL). Patients were compared in terms of outcome, including vasopressor-free days, ventilator-free days, incidence of QTc prolongation, incidence of arrhythmia, length of ICU stay, length of hospitalization, and mortality rates, between the three groups. Statistical analysis was performed using SPSS version 21.0 software. Quantitative data was presented as mean and standard deviation. Unpaired t-tests were used for quantitative data, and Chi-square tests were used for qualitative data. A p-value <0.05 was considered statistically significant.

## Results

Out of 60 patients diagnosed with septic shock according to sepsis III criteria, there were 42 (70.00%) males and 18 (30.00%) females, resulting in a male-to-female ratio of 1:0.42. The most common age group was between 41-50 years (46.67%), followed by above 50 years (30.00%) and 31-40 years (16.67%). Only 4 patients (6.67%) were under 30 years old. The mean age of male patients (48.24 +/- 11.28 years) was comparable to that of female patients (46.92 +/- 12.84 years) (P=0.6917) (Table 1).

The analysis of risk factors showed that out of 60 patients, 18 (30.00%) had type II diabetes mellitus, 9 (15.00%) had some form of immunosuppression such as HIV, were on immunosuppressive therapy, or were on long-term steroid therapy. Additionally, 4 (6.67%) patients had burns, and 2 (6.67%) patients had a history of undergoing abdominal surgeries (Fig. 1).

Out of 60 cases, 38 (63.33%) had a normal magnesium level (1.6 to 2.5 mg/dL), while 14 (23.33%) patients had hypomagnesemia (<1.6 mg/dL), and the remaining 8 (13.33%) patients were found to have hypermagnesemia (>2.5 mg/dL). The analysis of patients with normal and abnormal magnesium levels at the time of admission was based on APACHE II and SOFA scores. The mean APACHE II score in patients with normal magnesium levels was 13.12±4.12, while in patients with abnormal magnesium levels, it was 15.82 +/- 5.34. The mean SOFA score in patients with normal magnesium levels was 6.14 ± 2.98, and in patients with abnormal magnesium levels, it was 8.40 +/- 3.12. Both the APACHE II and SOFA scores were higher in patients with abnormal magnesium levels, and the difference was statistically significant (P<0.05) (Table 2).

Out of the patients who had normal magnesium levels at the time of admission to the ICU, 7 (18.42%) required some form of assisted ventilation, while 31 (81.58%) patients did not require assisted ventilation. Among the 22 patients with abnormal magnesium levels, 5 (22.73%) required assisted ventilation.

Moreover, out of the patients who had normal magnesium levels at the time of admission to the ICU, 6 (15.79%) required dialysis, whereas 32 (84.21%) patients did not require any renal replacement therapy. Among the 22 patients with abnormal magnesium levels, 4 (18.18%) required dialysis. It was observed that the need for assisted ventilation, as well as renal replacement therapy, was comparable in patients with both normal and abnormal serum magnesium levels (Table 3).

The analysis of patients regarding the number of days for which vasopressors were required showed that patients with normal magnesium levels required vasopressor support for an average of 5.12 +/- 2.98 days, while patients with abnormal magnesium levels required support for an average of 6.36

**Table 1 Age Distribution of the Cases with Sepsis**

| | Male | | Female | |
|---|---|---|---|---|
| | No of patients | Percentage | No of patients | Percentage |
| <30 years | 3 | 5.00% | 1 | 1.67% |
| 31–40 years | 9 | 15.00% | 1 | 1.67% |
| 41–50 years | 19 | 31.67% | 9 | 15.00% |
| Above 50 years | 11 | 18.33% | 7 | 11.67% |
| Total | 42 | 70.00% | 18 | 30.00% |
| Mean Age | 48.24 +/- 11.28 years | | 46.92 +/- 12.84 years | |

p=0.6917 (Not Significant)

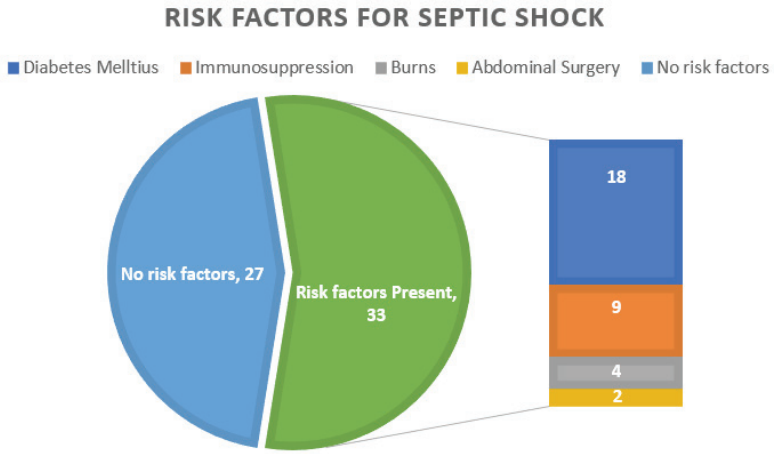


**Fig. 1 Analysis of Risk Factors for Septic Shock in Studied Cases**

**Table 2 Mean APACHE II and SOFA Score in Studied Cases**

| APACHE II and SOFA Scores | Patients with Normal Magnesium Levels (1.6 to 2.5 mg/dL) (n=38) | Patients with Hypomagnesemia or Hypermagnesemia (< 1.6 or >2.5 mg/dl) (n=22) | Significance |
|---|---|---|---|
| Mean APACHE II score | 13.12±4.12 | 15.82 +/- 5.34 | 0.032 significant |
| Mean SOFA score | 6.14 ± 2.98 | 8.40 +/- 3.12 | 0.007 significant |

+/- 3.12 days. The number of days for which assisted ventilation was required in patients with normal and abnormal magnesium levels were 2.12 +/- 1.48 and 3.12 +/- 1.62, respectively. Renal replacement therapy was required for 1.12 +/- 0.98 days in patients with normal magnesium levels and 1.46 +/- 1.10 days in patients with abnormal magnesium levels. In the normal magnesium level group, 4 (10.53%) patients had some form of arrhythmia during their ICU stay, while in the abnormal magnesium level group, 8 (36.36%) patients experienced some or the other form of arrhythmia. Mean ICU stay as well as mean hospital stay were longer in patients with abnormal magnesium levels at the time of

**Table 3 Serum Magnesium Level and Need of Assisted Ventilation and Dialysis**

| Assisted Ventilation and Dialysis | Assisted Ventilation | | Renal replacement therapy/Dialysis | |
|---|---|---|---|---|
| | Required | Not Required | Required | Not Required |
| Patients with normal magnesium levels (1.6 to 2.5 mg/dL) (n=38) | 7 (18.42%) | 31 (81.58%) | 6 (22.73%) | 32 (84.21%%) |
| Patients with abnormal magnesium levels (< 1.6 or >2.5 mg/dL) (n=22) | 5 (22.73%) | 17 (77.27%) | 4 (18.18%) | 17 (81.82%) |
| p-value | p=0.744 (not significant) | | p=0.5109 (not significant) | |

**Table 4 Comparison of Patients on Various Parameters During ICU Stay**

| Assisted Ventilation, Renal Replacement Therapy and Comparison of Hospital Stay in Patients | | Normal Magnesium Level (1.6 to 2.5 mg/dL) (n=38) | Hypomagnesemia or Hypermagnesemia (< 1.6 or >2.5 mg/dL) (n=22) | p-value |
|---|---|---|---|---|
| Number of days for which vasopressor was required | | 5.12 +/- 2.98 | 6.36 +/- 3.12 | p=0.1322 not significant |
| Number of days for which assisted ventilation was required | | 2.12 +/- 1.48 | 3.12 +/- 1.62 | p=0.017 significant |
| Number of days for which renal replacement therapy was required | | 1.12 +/- 0.98 | 1.46 +/- 1.10 | p=0.220 not significant |
| QTc prolongation/Arrythmia | Yes | 34 | 14 | p=0.0221 significant |
| | No | 4 | 8 | |
| Mean duration of ICU stay | | 7.12 +/- 2.34 | 9.64 +/- 3.62 | 0.001 significant |
| Mean duration of hospital stay | | 11.32 +/- 4.40 | 14.40 +/- 5.12 | 0.01 significant |

admission to the ICU, and this difference was found to be statistically significant ($p<0.05$) (Table 4).

Finally, the analysis of mortality in the studied cases showed that out of the 38 patients with normal magnesium levels, 5 (13.16%) patients expired. On the other hand, out of the 22 patients with abnormal magnesium levels, 9 (40.91%) patients succumbed to complications of septic shock (Table 5).

## Discussion

Electrolyte imbalance is common in critically ill patients due to a complex interplay of a number of factors inherent to critical illnesses. The physiological stress caused by severe illness, combined with systemic inflammatory responses, often disrupts the equilibrium of electrolytes. Other factors that contribute to these imbalances include altered renal function, fluid resuscitation, and medications administered during intensive care management. Additionally, the nature of critical illness requires close monitoring and aggressive interventions, which can unintentionally impact electrolyte homeostasis. Understanding relationship between the severity of illness and electrolyte derangements is important for planning therapeutic strategies effectively, thereby optimizing patient outcomes.[11]

In this study, it was found that 38 (63.33%) participants had a normal magnesium level (1.6 to 2.5 mg/dL), while 14 (23.33%) patients had hypomagnesemia (<1.6 mg/dL), and the remaining 8 (13.33%) patients had hypermagnesemia (>2.5 mg/dL) upon admission to the ICU. Overall, abnormal magnesium levels were observed in 22 (36.67%) patients. Charles BS *et al* conducted a study to assess the levels of magnesium in critically ill patients upon their admission to the ICU. The purpose of the study was to

**Table 5 Mortality in Patients With Normal and Abnormal Serum Magnesium Levels**

| Mortality in studied cases | Normal Magnesium Level (1.6 to 2.5 mg/dL) (n=38) | | Hypomagnesemia or Hypermagnesemia (< 1.6 or >2.5 mg/dL) (n=22) | |
|---|---|---|---|---|
| Recovered | 33 | 86.84% | 13 | 59.09% |
| Expired | 5 | 13.16% | 9 | 40.91% |
| Total | 38 | 100.00% | 22 | 100.00 % |

p=0.0249: significant

determine if systematically correcting low magnesium levels had an impact on patient outcomes.[12] The study found that the incidence of hypomagnesemia was 23.96%. Correcting serum magnesium levels resulted in a decrease in the mean duration of ICU stay (p=0.78), the percentage of patients requiring mechanical ventilation (52.08% vs. 65.625%), and the duration of mechanical ventilation (p=0.04). Mortality was higher in the comparison group (p=0.01). Based on these findings, the authors concluded that screening for and correcting magnesium levels in critically ill patients leads to reduced morbidity and mortality. Similar incidences of abnormalities in magnesium levels were also reported by Hansen *et al.*[13] and Pannem *et al*.[14]

In this study, patients with abnormal magnesium levels required vasopressor support for a longer period compared to patients with normal magnesium levels. However, the difference was not statistically significant. Similarly, patients with abnormal magnesium levels experienced a prolonged need for assisted ventilation (which was significantly higher in the abnormal magnesium level group) and renal replacement therapy (with no statistically significant difference) compared to their counterparts with normal magnesium levels. The incidence of arrhythmias during ICU stay was significantly higher in the abnormal magnesium level group. Importantly, patients with abnormal magnesium levels at ICU admission exhibited a significant increase in both the mean duration of ICU stay and hospital stay.

Solanki *et al*.[15] conducted a study to analyze serum magnesium levels in critically ill patients.In this study, 246 critically ill patients admitted to the ICU were examined, and their serum total magnesium levels were measured upon ICU admission. The primary outcome assessed was ICU mortality, while secondary outcomes included the necessity and duration of ventilator support, length of ICU stay, and the occurrence of cardiac arrhythmias. The findings indicated that patients with hypomagnesemia experienced significantly higher rates of ICU mortality compared to those with normal magnesium levels. Additionally, hypomagnesemia was linked to a greater requirement for ventilator support, extended ICU stays, elevated APACHE II scores, QTc prolongation, and a higher frequency of cardiac arrhythmias compared to patients with normal magnesium levels. Hypomagnesemia was identified as an independent and statistically significant predictor of ICU mortality. The study concluded that low magnesium levels were correlated with an increased mortality rate, prolonged ventilator support and ICU stay, and higher APACHE II scores among critically ill patients. Similar outcomes were also reported by other authors, such as Gonuguntla *et al.*[16] and Velissaris *et al*.[17]

Finally, the analysis comparing mortality outcomes showed that out of 38 patients with normal magnesium levels, 5 (13.16%) patients expired. In contrast, out of 22 patients, 9 (40.91%) patients succumbed to complications of septic shock. Patients with abnormal serum magnesium levels were found to have a significantly higher risk of mortality compared to patients with normal serum magnesium levels. Zafar *et al* conducted a study to investigate the mortality pattern in critically ill patients and their serum magnesium levels.[18] The study included 70 patients admitted to the ICU. Among these critically ill patients, 50 patients (71.43%) had normal magnesium levels, 17 patients (24.29%) had hypomagnesemia, and 3 patients had hypermagnesemia. The differences in ICU stay duration, Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores, and the presence of co-morbidities between the groups were not statistically significant (p>0.05 for ICU stay, p=0.34 for APACHE-II scores, and p=0.360 for co-morbidity). Hypomagnesemia patients often had co-existing electrolyte imbalances.

The most common electrolyte imbalances observed in patients included hypokalemia (58.82%), hyponatremia (47.05%), hypocalcemia (70.58%), and hypophosphatemia (29.41%). A significant portion of the hypomagnesemia patients (76.47%) were taking medications known to lower magnesium levels, compared to 46% of those with normal magnesium levels (p= 0.030). The mortality rate was significantly higher in the hypomagnesemia group (74.47%) compared to the normomagnesemia group (36%), with a P-value of 0.004.

Similar high mortality rates have been reported in critically ill patients with abnormal magnesium levels by Upala *et al*.[19] Abnormal magnesium levels at the time of admission to the ICU are associated with an increased need for assisted ventilation, a higher incidence of arrhythmia, a longer mean duration of ICU and hospital stay, as well as increased mortality rates. This study highlights the importance of monitoring magnesium levels in critically ill patients admitted to the ICU.

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