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Research Article

Relationship Between Magnesium Levels and Mortality in Intensive Care Patients

Yoğun Bakım Hastalarında Magnezyum Düzeyi ve Mortalite İlişkisi

Ayşe Nur TAŞKAPILI[1], Bilge Banu TAŞDEMİR MECİT[1], Kamil TAŞKAPILI[1*]

[1]Afyonkarahisar Health Sciences University, Department of Anesthesiology and Reanimation, Afyonkarahisar, Turkey

drkamiltaskapili@gmail.com

*Sorumlu Yazar / Corresponding Author

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Abstract
This study aimed to investigate the relationship between serum magnesium levels at the time of admission to the intensive care unit and mortality in patients monitored in the intensive care unit. A total of 204 patients aged 18 years and older, who were followed for more than 24 hours in the Anaesthesiology and Resuscitation intensive care unit of our hospital between 01.11.2021 and 01.11.2022, were included in the study. Patients whose data could not be obtained were excluded from the study. The demographic and clinical characteristics, laboratory data, APACHE II and SOFA scores, mechanical ventilator requirements, and mortality rates of the patients were compared according to their Mg levels measured upon admission to the intensive care unit. Patients were divided into five groups according to their magnesium levels: Group 1 (<1.8 mg/dL), Group 2 (1.8-<2 mg/dL), Group 3 (2-<2.2 mg/dL), Group 4 (2.2-<2.4 mg/dL) and Group 5 (≥2.4 mg/dL). The mechanical ventilation requirements and mortality rates of patients were found to be higher in the group with the highest magnesium levels (≥2.4 mg/dL) compared to the other groups (p=0.02, p=0.008). When the patients' SOFA and APACHE II scores were examined between groups, there was a statistically significant difference (p=0.001, p=0.034), and SOFA and APACHE II scores were higher in the hypermagnesaemic (≥2.4 mg/dL) group. Therefore, monitoring magnesium levels is important in critically ill patients. Prospective studies could be conducted in larger study groups on this topic.
Keywords: Hypermagnesemia, Hypomagnesemia, Mortality.

Özet
Bu çalışmada yoğun bakım ünitesinde takip edilen hastalarda yoğun bakıma kabul sırasındaki serum magnezyum düzeyleri ile mortalite arasındaki ilişkinin araştırılmasını amaçladık. Hastanemiz Anesteziyoloji ve Reanimasyon yoğun bakım ünitesinde 01.11.2021 ve 01.11.2022 tarihleri arasında, 24 saatten daha uzun süre takip edilen, 18 yaş üstü toplam 204 hasta çalışmaya dahil edildi. Verilerine ulaşılamayan hastalar çalışma dışı bırakıldı. Hastaların demografik ve klinik özellikleri, laboratuvar verileri, APACHE II ve SOFA skorları, mekanik ventilatör ihtiyaçları ve mortaliteleri; yoğun bakım ünitesine kabulleri sırasında ölçülen Mg düzeylerine göre karşılaştırıldı. Hastalar magnezyum düzeylerine göre beş gruba ayrıldı: Grup 1 (<1.8 mg/dL), Grup 2 (1.8-<2 mg/dL), Grup 3 (2-<2.2 mg/dL), Grup 4 (2.2-<2.4 mg/dL) ve Grup 5 (≥2.4 mg/dL). Hastaların mekanik ventilasyon ihtiyaçları ve mortalite oranları, magnezyum düzeyi en yüksek seyreden grupta (≥2.4 mg/dL) diğer gruplara göre daha yüksek bulundu (p=0,02, p=0,008). Hastaların SOFA ve APACHE II skorları gruplar arası incelendiğinde istatiksel olarak anlamlı fark mevcuttu (p=0.001, p=0.034) ve hipermagnezemik (≥2,4 mg/dL) grupta SOFA ve APACHE II skorları daha yüksek bulundu. Bu yüzden kritik hastalarda magnezyum takibi önemlidir. Bu konuyla ilgili daha geniş çalışma gruplarında prospektif çalışmalar yapılabilir.
Anahtar Kelimeler: Hipermagnezemi, Hipomagnezemi, Mortalite.

Introduction

Intensive care units (ICUs) are clinical units where patients requiring advanced monitoring and treatment due to critical illness are monitored, and where mortality rates are high. In these patients, metabolic and electrolyte balance can undergo rapid changes throughout the course of the disease, and these changes can have a significant impact on clinical outcomes (1). Magnesium (Mg) is the fourth most abundant element in the body and the second most abundant cation in intracellular fluid. Mg is essential for cellular energy production and the activation of numerous enzymes (2). Consequently, the effects of changes in Mg levels on clinical outcomes in critically ill patients have been studied for a long time. Hypomagnesaemia plays a role in the pathophysiology of many diseases. Mg deficiency creates a systemic stress response through the activation of neuroendocrine pathways (3). Hypermagnesemia can occur in conditions such as sepsis, renal failure, and aggressive magnesium replacement therapy, and can potentially lead to serious clinical complications (4).

Clearly establishing the relationship between serum magnesium levels and mortality in intensive care patients is important both to increase the effectiveness of electrolyte management and to contribute to prognostic assessments. This study aims to evaluate the relationship between Mg levels and mortality in the ICU and to provide new data to the existing literature. In our study, we aimed to retrospectively evaluate the relationship between hypomagnesaemia and hypermagnesaemia occurring during the follow-up of critically ill patients and their intensive care admission pathologies, chronic diseases, length of stay in intensive care, duration of mechanical ventilation, and mortality.

Material and Method

This clinical study was conducted at the Department of Anaesthesiology and Reanimation, Afyonkarahisar Health Sciences University Hospital, following ethical committee approval (decision date and number: 04/11/2022, 2022/14). All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and the 2013 Helsinki Declaration and subsequent amendments or comparable ethical standards. The medical records of patients admitted to the Anaesthesiology and Resuscitation Intensive Care Unit of Afyonkarahisar Health Sciences University Hospital between November 2021 and November 2022 and followed up for more than 24 hours were retrospectively reviewed. A total of 204 patients with fully accessible data were included in the study. Patients whose data could not be accessed were excluded from the study.

Patients monitored in the intensive care unit were divided into five groups based on their serum total Mg levels. Group 1 (<1.8 mg/dL), Group 2 (1.8- <2 mg/dL), Group 3 (2- <2.2 mg/dL), Group 4 (2.2- <2.4 mg/dL) and Group 5 (≥2.4 mg/dL). The threshold for hypomagnesemia was determined to be <1.8 mg/dL and for hypermagnesemia ≥2.4 mg/dL; these determinations are consistent with previous studies investigating magnesium disorders in an intensive care unit setting (5). The patients' admission serum total Mg values were compared with their demographic findings (age, gender), comorbidities, creatinine levels and reasons for admission to intensive care. In addition, APACHE II scores, SOFA scores, length of stay in intensive care, mechanical ventilator (MV) support requirements, and mortality rates were evaluated.

Statistical Analysis

IBM SPSS Statistics version 20 was used for statistical analysis. Data were expressed as ratios, medians (min-max), and means ± SD. The normality of variables was determined using visual (histograms and probability plots) and analytical methods (Kolmogorov-Smirnov test). The Kruskal-Wallis and ANOVA tests were used to compare continuous variables in groups, and the Chi-square test was used to compare categorical variables. Where there were significant differences between groups (SOFA, APACHE II), pairwise post-hoc comparisons were performed. In multivariate analysis, age, APACHE II, SOFA, Mg and creatinine variables were examined using logistic regression analysis to predict mortality. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 204 patients admitted to the Anaesthesiology and Resuscitation intensive care unit between 1 November 2021 and 1 November 2022 were compared based on their serum total Mg values upon admission. The patients' admission Mg levels were 1.93±0.37 mg/dl. The median age of the patients was 49.50, and 63.7%

were male and 36.3% were female. Looking at the distribution of chronic diseases among the patients, 53.4% had no chronic disease, 10.8% had cardiac disease, 8.8% had neurological disease, 6.9% had malignancy, 7.4% had lung disease, 6.4% had hypertension, 5.4% had diabetes, and 1% had renal disease. When we divided the patients into groups according to their Mg levels, there were no significant differences between the groups in terms of age, gender, and chronic disease (p=0.174, p=0.177, p=0.202).

The most common reason for admission to intensive care was trauma (51.5%), followed by postoperative admission (17.6%), post-arrest patients (15.2%), intoxications (8.8%), patients admitted due to general deterioration (4.9%), lung diseases (1.5%), and acute kidney injury (0.5%). When we divided the groups according to Mg levels, there was no significant difference between the groups in terms of admission reasons (p=0.332). Subgroup analysis was performed because trauma patients constituted a significant portion of the study population in terms of reasons for admission (51.5%). Subgroup analysis revealed that the impact of hypermagnesemia was particularly pronounced in trauma patients. In this group, patients with Mg>2.4 mg/dL exhibited a strikingly higher mortality rate (85.7%) compared to those in other magnesium categories (p=0.020). Conversely, in non-trauma patients, magnesium levels did not show a statistically significant association with mortality (p=0.269), suggesting that the prognostic value of admission magnesium may vary depending on the patient's primary pathology.

Table 1 compares patients' creatinine levels, MV requirements, MV and intensive care admission durations, and mortality rates. The median creatinine levels of the patients was 0.89 and no statistically significant difference was found according to Mg values (Table 1).

Table 1. Comparison of Clinical Characteristics, Severity Scores, and Outcomes According to Serum Magnesium Levels at Intensive Care Unit Admission

	Mg<1.8 mg/dl N=75	**Mg 1.8-<2 mg/dl N=55**	**Mg 2-<2.2 mg/dl N=39**	**Mg 2.2<2.4 mg/dl N=19**	**Mg≥2.4 mg/dl N=16**	**Total N=204**	**P**
MV, Yes/No, n (%)	54 (72) / 21 (28)	31 (56.4) / 24 (43.6)	26 (66.7) / 13 (33.3)	13 (68.4) / 6 (31.6)	**16 (100) / 0**	140 (68.6) / 64 (31.4)	**0.02***
MV duration, days	3 (0-480)	1 (0-390)	2 (0-41)	1 (0-300)	3 (1-27)	1 (0-480)	0.129#
Length of stay in intensive care, days	8 (1-480)	5 (1-390)	7 (1-59)	6 (1-400)	3.5 (1-30)	6.5 (1-480)	0.062#
Outcome: Death/discharge, N (%)	34 (45.3) / 41 (54.7)	19 (34.5) / 36 (65.5)	12 (30.8) / 27 (69.2)	9 (47.4) / 10 (52.6)	**13 (81.2) / 3 (18.8)**	87 (42.6) / 117 (57.4)	**0.008***
Creatinine levels	0.88 (0.12-6.71)	0.81 (0.26-7.17)	0.89 (0.26-2.90)	0.93 (0.13-3.96)	1.82 (0.46-3.87)	0.89 (0.12-7.17)	0.151#
SOFA score	7 (0-17)	4 (0-15)	6 (0-14)	8 (0-17)	12 (4-16)	7 (0-17)	**0.001#**
APACHE score	18 (0-49)	14 (0-44)	17 (0-39)	10 (5-48)	26.5 (12-39)	17 (0-49)	**0.034#**

Data are expressed as number of patients (%), mean ± SD (standard deviation), median (minimum-maximum). *Chi-Square, #Kruskal Wallis. MV; mechanical ventilation, Mg; magnesium. †: A secondary analysis was performed by excluding Group 5 (≥2.4 mg/dL) to determine the influence of the hypermagnesemic group on the overall statistical significance. Upon exclusion of Group 5, no significant differences were observed between the remaining four groups regarding both mechanical ventilation requirements (p=0.316*) and mortality rates (p=0.338*), indicating that the observed clinical significance was primarily driven by the hypermagnesemic group.

While 68.6% of patients required MV, 31.4% did not, and this difference was statistically significant when compared according to Mg levels (p=0.02, Table 1). Patients in the group with the highest Mg levels had a greater need for MV compared to the other groups (p=0.02). This result was attributed to the fact that no significant difference was observed when the other groups were compared in terms of their need for MV after the group with Mg ≥2.4 mg/dl was excluded (p=0.316, Table 1). The median MV duration for patients was 1 day, and no significant difference was found between groups (p=0.129, Table 1). The median intensive care unit stay duration for patients was 6.5 days, and no significant difference was found between groups (p=0.062, Table 1). While 42.6% of patients died, 57.4% were discharged, and this difference was statistically significant when compared according to Mg levels (p=0.008, Table 1). Patients in the group with the highest Mg levels had a higher mortality rate than the other groups (p=0.008). This result was attributed to the fact that after excluding the group with Mg ≥ 2.4 mg/dl, no significant difference was observed in mortality among the other groups (p=0.338, Table 1).

When the SOFA and APACHE II scores of patients were examined between groups, statistically significant differences were observed (p=0.001, p=0.034, Table 1). When pairwise post-

hoc comparisons were performed between groups for SOFA scores, significant differences were observed between groups 2-5 (p<0.001), groups 3-5 (p<0.001), groups 1-5 (p<0.001), and groups 4-5 (p=0.027) (Table 2).

When we performed pairwise post-hoc comparisons between groups for APACHE II scores, significant differences were observed between groups 2-5 (p=0.002), group 3-5 (p=0.007), group 4-5 (p=0.026), and group 1-5 (p=0.023) showed significant differences (Table 3).

According to the logistic regression analysis performed in Table 4, the effect of age, APACHE II, SOFA, Mg, and creatinine values on mortality was examined. Accordingly, age, APACHE and SOFA scores (p=0.006, p=0.001, p<0.001, respectively) were found to be significant predictors of mortality, while Mg and creatinine levels were not significant predictors on their own (p=0.635, p=0.523, respectively).

Table 2. Post-hoc Comparison Results of SOFA Scores Between Groups

Groups	**Group 3-2**	**Group 3-1**	**Group 3-4**	**Group 3-5**	**Group 2-1**	**Group 2-4**	**Group 2-5**	**Group 1-4**	**Group 1-5**	**Group 4-5**
p	0.900	0.297	0.115	**<0.001**	0.312	0.119	**<0.001**	0.360	**<0.001**	**0.027**

Group 1; Mg<1.8 mg/dl, Group 2; Mg 1.8-<2 mg/dl, Group 3; Mg 2-<2.2 mg/dl, Group 4; Mg 2.2-<2.4 mg/dl, Group 5; Mg≥2.4 mg/dl

Table 3. Post-hoc Comparison Results of APACHE II Scores Between Groups

Groups	**Group 2-3**	**Group 2-4**	**Group 2-1**	**Group 2-5**	**Group 3-4**	**Group 3-1**	**Group 3-5**	**Group 4-1**	**Group 4-5**	**Group 1-5**
p	0.738	0.650	0.162	0.002	0.856	0.367	0.007	0.627	0.026	0.023

Group 1; Mg<1.8 mg/dl, Group 2; Mg 1.8-<2 mg/dl, Group 3; Mg 2-<2.2 mg/dl, Group 4; Mg 2.2-<2.4 mg/dl, Group 5; Mg ≥2.4 mg/dl

Table 4. Multivariable Logistic Regression Analysis of Factors Associated with Mortality in Critically Ill Patients.

Risk Factor	**RR (95% confidence interval)**	**P**
Age	0.967 (0.944-0.990)	0.006
APACHE score	0.915 (0.866-967)	0.001
SOFA score	0.674 (0.579-0.784)	0.000
Magnesium level	0.749 (0.227-2.475)	0.635
Creatinine level	0.828 (0.464-1.478)	0.523

RR: Estimated relative risk, shown as the odds ratio and 95% confidence interval

Discussion

In this retrospective study, the relationship between serum total Mg levels measured upon admission to the intensive care unit and mortality was evaluated, revealing a significant increase in mortality, particularly in patients with Mg ≥2.4 mg/dL. The significantly higher need for mechanical ventilation in the same group suggests that Mg balance may affect not only mortality but also the need for respiratory support. However, although mortality rates were high in the hypomagnesaemic group, the statistically significant difference was more pronounced in the hypermagnesaemic group.

The marked differences in APACHE II and SOFA scores according to Mg levels in our study suggest that Mg disturbances may be an indicator of disease severity. The highest scores in the hypermagnesium group are consistent with increased mortality. Conditions commonly encountered in intensive care patients, such as sepsis, renal dysfunction, tissue damage, and metabolic stress, can elevate Mg levels and are also associated with poor clinical outcomes.

When planning our study, considering that Mg has many structural and functional roles in the body, we aimed to investigate the effects of Mg monitoring, in addition to other electrolyte imbalances, on patient prognosis and follow-up in intensive care patients, if not done. Studies in the literature have also shown that both hypomagnesaemia and hypermagnesaemia increase mortality, the need for mechanical ventilation, and intensive care prognosis scores.

The relationship between hypomagnesaemia and mortality has been extensively studied in the literature. In a systematic review by Upala and colleagues, it was demonstrated that hypomagnesaemia significantly increases the risk of mortality in critically ill patients (6). Similarly, the study by Solanki and colleagues reported that low Mg levels in intensive care patients were associated with increased APACHE II scores, prolonged MV duration, and increased mortality (7). These findings suggest that Mg deficiency may affect clinical outcomes in critically ill patients through mechanisms such as systemic stress response, inflammation, cardiac conduction disturbances, and respiratory muscle dysfunction. Studies on the addition of Mg to daily treatment in intensive care patients also exist. One of the main reasons for this increased interest among intensive care clinicians is the high incidence of

hypomagnesaemia reported in patients admitted to the ICU, with magnesium deficiency reported in 20 to 61 per cent of intensive care patients (8).

In the study conducted by Cırık and colleagues, a strong association between hypermagnesaemia and high mortality in intensive care patients was demonstrated, similar to our study (9). Hypermagnesaemia is recognised as a strong independent risk factor for mortality in critically ill patients (10). Teeranan and colleagues conducted a study investigating the relationship between Mg levels and mortality in patients diagnosed with coronary insufficiency and found that patients with hypermagnesemia had high cardiovascular mortality rates. This result demonstrates the importance of the relationship between Mg and cardiac dysfunction, which is frequently seen in critically ill patients (11). There were also studies in the literature showing that hypermagnesemia increased the SOFA score in intensive care patients (12,13). In our study, the mortality rate was quite high at 81.2% in the group with Mg ≥2.4 mg/dL, which is consistent with these findings in the literature. Additionally, a striking finding from the subgroup analysis of trauma patients admitted to intensive care was that the mortality rate was significantly higher (85.7%) in trauma patients with hypermagnesaemia (≥2.4 mg/dL).

On the other hand, some studies have suggested that Mg levels may not be directly related to mortality. Huijgen and colleagues demonstrated that serum total and ionised Mg levels in intensive care patients may have limited predictive power for mortality (14). A more recent study confirmed the growing scientific interest in this topic by reporting that Mg disorders are associated with intensive care mortality (15).

Stanojević and colleagues emphasised that measuring only serum total Mg in critically ill patients may not fully reflect the true Mg status and that ionised Mg may be more clinically valuable (16). In our study, we measured serum total magnesium levels. However, it is important to note that total magnesium does not always accurately reflect the biologically active, ionized fraction, especially in critically ill patients who often present with hypoalbuminemia and acid-base disturbances. The lack of ionized magnesium measurement in our study remains a limitation, as total magnesium levels may mask an underlying functional deficiency or excess. In some studies, Mg has been measured in peripheral blood cells (red and mononuclear blood cells), muscles, and bones (17).

Considering the effects of Mg on various physiological systems, the findings of our study are biologically significant. Mg plays a decisive role in energy production, cellular stability, cardiac conduction, neuromuscular activity, and inflammatory response. Hypomagnesaemia may increase the risk of haemodynamic instability and arrhythmia by increasing catecholamine release, while hypermagnesaemia may increase mortality due to conditions such as respiratory depression, AV block, and muscle weakness. These pathophysiological mechanisms are consistent with the increase in mortality and ventilation requirements observed in our study.

Among the strengths of our study are its larger sample size compared to many studies in the literature (n=204), the detailed examination of Mg levels in five separate categories, and the evaluation of important clinical outcomes such as APACHE II score, SOFA score, MV requirement, MV duration, and mortality. However, the study also has some limitations. The retrospective design limits the establishment of cause-and-effect relationships. The single-centre nature of the study limits its generalisability. The fact that only serum total Mg levels were measured limits the biological accuracy of the Mg assessment. Another limitation is that detailed control of factors such as Mg replacement protocols and medication use could not be performed. Furthermore, our study did not account for all potential clinical factors that could influence serum magnesium levels, such as the use of magnesium-containing medications (e.g., laxatives, antacids), magnesium replacement protocols, or the presence of metabolic acidosis, which can cause transcellular magnesium shifts. The retrospective nature of the data collection limited our ability to control for these confounding variables. Consequently, the observed hypermagnesemia could partly reflect these clinical conditions or therapeutic interventions rather than being a purely primary metabolic state. Since the aim of the study was to examine the relationship between serum total magnesium levels and mortality upon admission to the intensive care unit, the lack of repeated value analysis is a significant limitation. A single, static measurement does not account for dynamic changes in magnesium levels that may occur during the patient's clinical course due to treatment, fluid resuscitation, or progressive organ dysfunction. Future prospective studies using serial magnesium measurements will provide a more comprehensive understanding of its prognostic value over time.

Conclusion

We cannot correlate intensive care mortality with Mg alone. With this study, we wanted to draw attention to the importance of Mg. Mg levels may be an indicator of adverse outcomes in intensive care patients. We recommend close monitoring of serum Mg levels.

In conclusion, our study suggests that hypermagnesemia at the time of intensive care unit admission is associated with increased mortality, MV requirements and higher disease severity scores. Rather than being a direct cause of death, elevated magnesium levels may serve as a significant clinical marker reflecting the severity of the patient's underlying condition and overall prognosis.

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Conflict of interest statement

Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics Committee Approval

Afyonkarahisar Health Sciences University Clinical Research Ethics Committee, 04/11/2022, 2022/14, 2011-KAEK-2.

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