JEIMP
E-ISSN: 2980-0617

The Journal of
European Internal Medicine Professionals

JEIMP
The Science

Original Article

Magnesium Deficiency and Mortaliy in ICU Patients

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doi 10.5281/zenodo.13315541

J Eur Int Prof. Year; 2024, Volume: 2, Issuse: 3 *Submitted at*: 23.04.2024, *Accepted at*: 12.08.2024, *Published at*: 19.08.2024

JEIMP belongs to "*The Foundation for the Management of Chronic Diseases*" and is supervised by the MKD Digital Publishing. www.jeimp.com and digitalmkd.com

Abstract

Background: Magnesium plays a critical role in numerous physiological processes, including electrolyte balance, cellular function, and modulation of oxidative stress and inflammation. Hypomagnesemia is prevalent among intensive care unit (ICU) patients and has been associated with adverse outcomes. This study aims to investigate the prevalence of hypomagnesemia in a Turkish ICU cohort and its association with all-cause mortality.

Methods: This retrospective single-center study was conducted at Karabuk State Hospital, Department of ICU from January 2018 to June 2018. Data were extracted from local hospital software. Adult patients (>17 years) with longer than 24 hours of ICU stay were included. Demographic, clinical, and laboratory data were collected, including serum magnesium, C-reactive protein (CRP), albumin, and creatinine levels. Hypomagnesemia was defined as serum magnesium levels <1.7 mg/dL. Statistical analyses were performed using SPSS version 21.

Results: A total of 119 patients were included, with a mean age of 69.63±14.02 years. Hypomagnesemia was observed in 68.0% of patients upon ICU admission. Survivors (n=82) were younger than nonsurvivors (n=37) (p=0.003). Lower magnesium (p=0.023) and albumin (p=0.023) levels and higher CRP levels (p=0.043) were noted in nonsurvivors. The presence of acute kidney injury (AKI) and heart failure (HF) was significantly higher in nonsurvivors (p<0.001). Univariate analysis showed that only AKI had a significant impact on mortality (p=0.012, OR=1.689).

Conclusion: Hypomagnesemia is highly prevalent among ICU patients and is associated with increased mortality, particularly in the presence of AKI. These findings highlight the importance of monitoring and managing magnesium levels in ICU patients to improve outcomes. Further research with larger, multicenter trials is needed to establish definitive guidelines for magnesium supplementation in critically ill patients.

Keywords: Hypomagnesemia, intensive care unit, mortality, acute kidney injury

INTRODUCTION

Magnesium plays a crucial role in maintaining human health by participating in hundreds of enzymatic reactions. Its ionized form is crucial for various physiological processes, including electrolyte balance, membrane integrity, cellular division, and the initiation of nerve impulses (1). Magnesium's role in modulating oxidative stress and inflammation further underscores its importance in critical care settings (2,3). Identifying hypomagnesemia in intensive care unit (ICU) patients holds significant clinical importance, as it has been suggested the replecament of magnesium may provide crucial benefits in ICU patients (2-4).

Previous studies have reported hypomagnesemia incidence around 50 to 65% in ICU patients (5). Magnesium deficiency may result from various clinical conditions such as diabetes mellitus, renal diseases, metabolic alkalosis, drug-induced causes (intensive diuretic use, aminoglycosides, etc.), gastrointestinal disorders, and malnutrition (6,7). Additionally, magnesium depletion brings with hypokalemia which may exacerbate the risk of cardiovascular mortality and morbidity (8,9). Recent research also highlights the relationship between hypomagnesemia and systemic inflammatory response syndrome (SIRS), where low magnesium levels correlate with increased inflammatory markers and worse clinical outcomes (10).

Hypomagnesemia has been associated with an increased need for mechanical ventilation, prolonged ICU stays, and heightened mortality rates (10,11). Notably, critically ill patients with low magnesium levels tend to have a more severe disease course, necessitating more intensive therapeutic interventions and demonstrating poorer prognoses (12,13).

In this study, we aimed to investigate the prevalence of hypomagnesemia during ICU stay in a Turkish cohort and its association with all-cause mortality. Understanding the incidence and implications of hypomagnesemia in this specific population may help refine management strategies and improve patient outcomes in critical care settings.

METHODS

This retrospective single-center study was conducted at Karabuk State Hospital, Department of Internal Medicine ICU. Patients who were accepted for general ICU stay between January 2018 and June 2018 were enrolled in the study. Data were obtained from local hospital software system. This study was conducted in agreement with the Declaration of Helsinki-Ethical principle for Human researches.The consent form is not available since the study is retrospective.

All adults (>17 years old) patients who survived more than 24 hours in the ICU were enrolled. Cases who were transferred to our ICU from external ICUs were excluded. Patients who had been admitted to ICU following elective and emergency surgery were excluded. Patients with lacking data were also excluded.

The demographic and clinical features of the individuals were noted upon admission to the ICU. Age, sex, comorbidities, reasons for ICU admission, and the patient's intubation status during their initial admission were investigated. Laboratory studies included serum magnesium, potassium, C-reactive protein, albumin, and creatinine levels. The presence of acute kidney injury was assessed by monitoring daily changes in creatinine levels. Additionally, data on ICU length of stay, time to intubation (or extubation, if the patient was initially intubated), survival rates, mortality rates, and response to cardiopulmonary resuscitation were recorded. Hypomagnesemia was defined as serum magnesium level <1.7 mg/dL.

STATISTICAL ANALYSIS

The analyses were conducted using the SPSS version 21 for Windows (Released 2012; IBM Corp., Armonk, New York, United States). Numerical variables were summarized using mean values and standard deviations (± SD). To compare parametric variables between two independent groups – those who survived and those who did not – the Independent Samples T-Test was employed. This test assesses whether the means of these two groups are statistically different from each other, facilitating the examination of continuous variables like magnesium and CRP levels. The Kolmogorov-Smirnov Test was used to evaluate the distribution of variables to determine if they follow a normal distribution. For the comparison of categorical variables, such as the presence of comorbidities and gender distribution, the Chi-square test was applied. When the assumptions for parametric tests were not met, the Wilcoxon test, a non-parametric alternative, was used for comparing paired samples. This test helped to evaluate differences in variables like ICU stay length between the two groups without assuming a normal distribution. To explore relationships between continuous variables, correlation coefficients were calculated. The univariate analysis method was used to identify individual factors that could impact patient outcomes. Variables such as age, sex, CRP, serum albumin, and baseline magnesium levels were analyzed to determine their effect on mortality, with the significance of each factor assessed through p-values. Throughout the analysis, a significance level of p<0.05 was considered to denote statistical significance. Correlation graphes were designed by using chatGPT 4.0.

RESULTS

A total of 119 individuals, 59 (49.6%) male and 60 (50.4%) female, with a mean of 69.63±14.02 age were included in the study. Eighty-two patients were discharged or transferred to various inpatient services while 37 died. Survivors were younger than deceased individuals (66.18± 9.65 vs 74.25±16.80, p=0.003). Eighty-one (68.0%) individuals had hypomagnesemia at admission to ICU. The basic features of the individuals were given in the **Table 1**.

In the death group, the lower magnesium and albumin

Table 1. The demographical and clinical features of the patients in the ICU

Parameter	Mean ± SD, n (%)
Baseline_Mg	1.61 ± 0.51
K, mEq/L	4.18 ± 0.68
CRP, mg/dl	12.51 (0.1- 137.5)
Albumin, gr/dL	2.79 ± 0.84
Hospital stay, day	23.18 ± 13.94
Male/female, n(%)	59 (49.58%)/60 (50.42%)
Death/Survivor, yes/no (%)	37(30.1%)/82(66.7%)
Comorbidities at admission	
• DM, yes/no (%)	74 (63.24%) / 45 (36.76%)
• HT, yes/no (%)	91 (76.47%) / 28 (23.53%)
• HF, yes/no (%)	53 (44.53 %) / 66 (55.47%)
• CKD, yes/no (%)	75 (63.03%) / 44 (36.97%)
• Infection, yes/no (%)	75 (63.03%) / 44 (36.97%)
• AKI, yes/no (%)	80 (67.22%) / 39 (32.78%)

DM; diabetes mellitus, HT; hypertension, HF; heart failure, CKD; chronic kidney disease, AKI; acute kidney injury

Table 2. Comparison of discharged and deceased patients in terms of laboratory, Average staying period in intensive care unit, gender and comorbidities.

Variable	Deaths, n=37	Survivors, n=82	p-value
Baseline_Mg	1.46 ± 0.56	1.64 ± 0.49	0.023
K, mEq/L	4.01 ± 0.77	4.20 ± 0.65	0.061
CRP, mg/dl	26.54 ± 12.69	19.67 ± 12.70	0.043
Albumin, gr/dL	2.80 ± 0.80	3.28 ± 0.86	0.023
ICU stay, day	22.19 ± 13.57	23.63 ± 14.25	0.604
Sex	Male: 20 (54.05%), Female: 17 (45.95%)	Male: 39 (47.56%), Female: 43 (52.44%)	0.647
DM	Yes: 25 (67.56%), No: 12 (32.44%)	Yes: 49 (59.76%), No: 33 (40.24%)	0.072
HT	Yes: 31 (83.78%), No: 6 (16.22%)	Yes: 60 (73.17%), No: 22 (26.83%)	0.303
HF	Yes: 23 (62.16%), No: 14 (37.84%)	Yes: 30 (36.59%), No: 52 (63.41%)	<0.001
CKD	Yes: 20 (54.05%), No: 17 (45.95%)	Yes: 55 (67.07%), No: 27 (32.93%)	0.247
Infection	Yes: 27 (72.91%), No: 10 (17.09%)	Yes: 53 (64.63%), No: 29 (35.37%)	0.737
AKI	Yes: 30 (81.08 %), No: 7 (18.92%)	Yes: 40 (48.78%), No: 42 (51.22%)	<0.001

CRP, c-reactive protein, DM; diabetes mellitus, HT; hypertension, HF; heart failure, CKD; chronic kidney disease, AKI; acute kidney injury

levels and higher CRP levels were observed compared to the survivors group ($p<0.05$) (**Table 2**). While the length of ICU stay and the presence of comorbidities including diabetes, hypertension, and CKD, rates were not significantly different between the groups ($p>0.05$), AKI and HF prevalence was higher in the death group ($p<0.001$). The majority of the deaths occured within the first month of ICU stay and more than half of those died within 20 days of ICU admission (**Graph 1**).

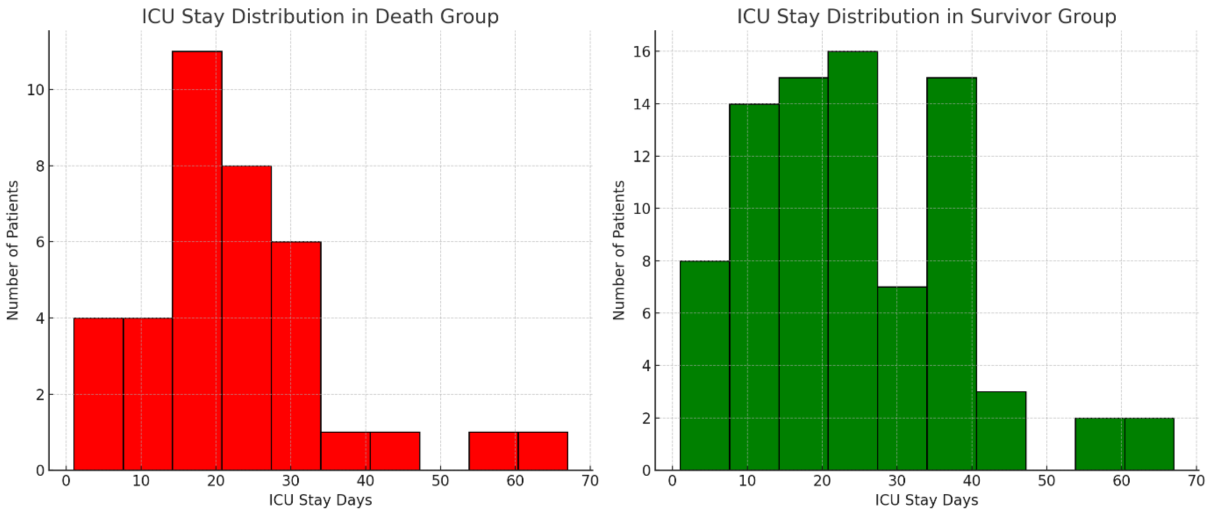
Hypomagnesemia was associated with longer ICU stay in death group while there was no correlation between ICU admission serum magnesium and ICU stay (**Graph 2 and 3**).

Univariate analysis demonstrated age, sex, CRP, serum albumin, and baseline magnesium levels at admission to ICU had no impact on death ($p>0.05$) (**Table 3**). However, AKI strongly had impact on mortality ($p=0.012$ and OR=1.689).

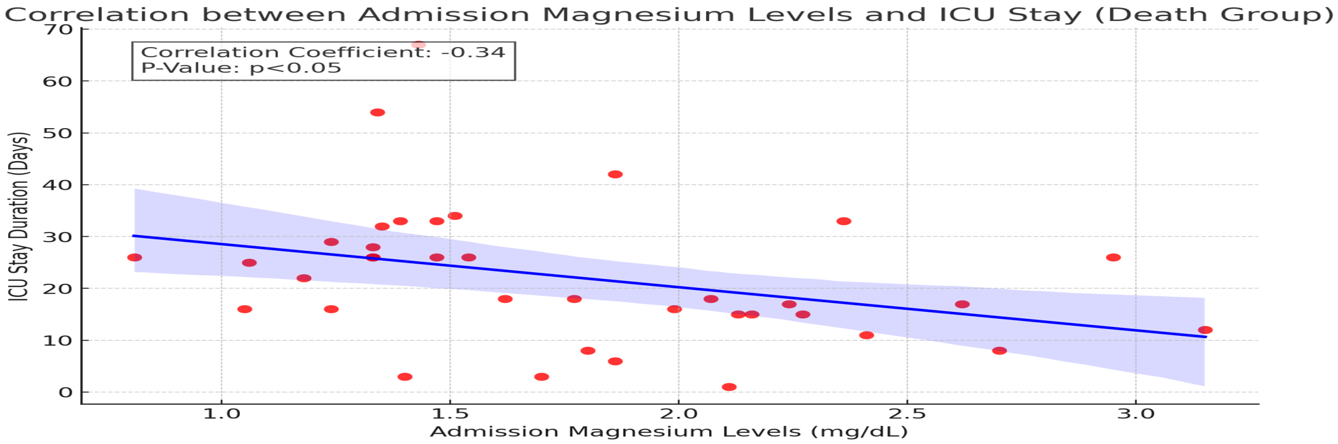
The correlation analysis between CRP, albumin, and baseline magnesium levels indicates that none of the relationships are statistically significant ($p>0.05$) (**Table 4**). Specifically, the correlation between CRP and Albumin has a coefficient of 0.16 with a p-value greater than 0.05 ($p>0.05$), suggesting that CRP and Albumin levels do not have a significant linear relationship. Similarly, the correlation between albumin and admission magnesium yields a coefficient of 0.08 and a p-value greater than 0.05 ($p>0.05$), indicating no significant relationship between these two variables. Lastly, the relationship between asmission magnesium and CRP also shows a correlation coefficient of 0.08 with a p-value greater than 0.05 ($p>0.05$), demonstrating that these variables do not significantly correlate. Overall, these findings suggest that CRP, albumin, and admission magnesium levels are not significantly interrelated in this context.

DISCUSSION

This study demonstrated the high prevalence of hypomagnesemia in ICU patients, especially among deceased patients and its association with AKI. Another



Graph 1. The graph demonstrates that; whereas ICU stay duration seems shorter than nonsurvivor, in the death group, a substantial part of the cases died in the early period of the ICU stay.



Graph 2. The graph shows that lower magnesium levels at admission might be linked to longer ICU stays for patients who did not survive.

Table 3. Age, sex, CRP, serum albumin, and baseline magnesium levels at admission to ICU impact on death.

Variable	Coefficient	P-Value	Odds Ratio
Age, years	-0.0029	0.834	0.993
Sex, male vs female	-0.2861	0.472	0.750
CRP, mg/dl	0.0211	0.106	1.029
Albumin, gr/dL	0.0266	0.910	1.021
Baseline Mg, mg/dL	-0.2956	0.454	0.740
HF, yes vs no	0.0356	0.085	0.071
AKI, yes vs no	0.2651	0.012	1.689

CRP; c-reactive protein, HF; heart failure, AKI; acute kidney injury Mg; magnesium

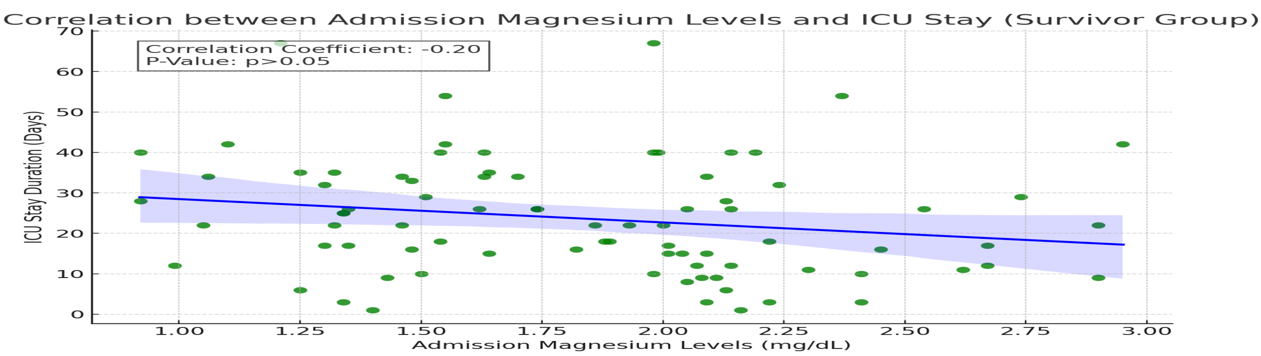
striking finding of the study is that AKI was the strongest factor that impacted mortality in ICU patients. Hypomagnesemia was associated with prolonged ICU stay and represents a specific clinical presentation that requires rigorous assessment and follow-up in the ICU.

The prevalence of hypomagnesemia in ICU patients may vary considerably depending on the design of the studies (5,13). This wide range highlights the variability depending on the patient population, the criteria used for defining hypomagnesemia, and the specific conditions of the ICU setting. Hypomagnesemia is often associated with a higher risk of morbidity and mortality, increased need for ventilatory support, and longer ICU stays (5,14). In this study, the prevalence of hypomagnesemia was 68%. Magnesium levels at admission to the ICU were lower in nonsurvivors compared to survivors. The length of stay in the ICU was similar between the two groups. This outcome may be attributed to some patients with severe hypomagnesemia dying early, while the remaining patients stayed in the ICU for an extended period, in nonsurvivors.

Previous studies demonstrated that comorbidities such as DM, HT, HF, and CKD affect two-fifths of intensive care unit admissions and have highly variable effects on subsequent outcomes (15,16). In this study, comorbidities rates were higher compared to previous studies, however, the study population was relatively older. Comorbidity rates were higher among nonsurvivors in this study, however, only HF and AKI reached a statistical significance level. Univariate analysis confirmed the impact of AKI on mortality,

Table 4. Correlation between CRP, serum albumin, and baseline magnesium

Variable Pair	Correlation Coefficient	P-Value
CRP and Albumin	0.158	0.087
Albumin and baseline magnesium	0.081	0.383
Baseline magnesium and CRP	0.077	0.402



Graph 3. The grapgh demonstrates a slight tendency for higher magnesium levels to be associated with shorter ICU stays among survivors.

similar to previous studies (17-19). Older age, higher prevalence of comorbidity can be cause of longer ICU stay, however, they have no impact on mortality. There can be more powerful contributors to mortality such as AKI.

Lower albumin levels were observed in the nonsurvivor group, a finding consistent with studies by Turcato et al. and Yu et al. that highlight hypoalbuminemia as a marker of poor prognosis in ICU patients (20,21). However, in univariate analysis, neither albumin nor magnesium had an impact on mortality. The interaction between serum albumin, magnesium, and other mortality-related risk factors may have collectively influenced patient outcomes instead of individual effects. Previous studies reported that while albumin infusion cannot decrease the mortality rate in most cases, magnesium replacement may provide some benefits in ICU admissions (4,21,22). Beside a review by Panahi et al. suggests that while magnesium plays a role in critical illness, the evidence for routine supplementation remains inconclusive. Further, Saglietti et al. emphasize the need for more controlled trials to establish definitive guidelines on magnesium management in the ICU (4).

Another key point was that serum magnesium level at admission to ICU did not correlate with ICU stay duration. It seems like various confounding factors; such as AKI and infections may cause prolongation in ICU stay, rather than hypomagnesemia. However, the higher mortality rate of hypomagnesemia observed in the deceased group indicates its clinical importance in the ICU.

Limitations of the Study

The retrospective nature of the study may introduce biases related to the accuracy and completeness of the recorded data. Being conducted at a single center limits the generalizability of our findings. Variations in ICU management practices across different hospitals might affect the outcomes. The relatively small sample size may limit the statistical power of our analyses, particularly in subgroup comparisons. We did not account for the potential effects of magnesium supplementation during ICU stays, which could influence the observed outcomes. Unmeasured confounding factors, such as nutritional status or specific treatment protocols, could also impact the relationship between magnesium levels and patient outcomes.

CONCLUSION

Our study underscores the significant association between hypomagnesemia and increased mortality in ICU patients in a small Turkish population. These findings support the findings of the previous literature and provide the importance of monitoring and managing magnesium levels to potentially improve outcomes in critical care settings. Future research should focus on large-scale, multicenter trials to further elucidate the role of magnesium supplementation and its impact on clinical outcomes in critically ill patients.

DECLERATIONS

Ethics Committee Approval: Karabuk State Hospital, Ethical Committee for Scientific Human Research; 2024/1867.

Financial Disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions: M.P.; Data collection, project design, writing, submission, and analysis of the final version. The other researchers contributed equally to project design, writing, submission, and analysis of the final version of the manuscript. All authors read and approved the final manuscript.

Conflict of interest: None

Informed consent form: Not available

Funding source: No funding was received for the research

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