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Magnesium levels and mortality relationship in patients with *Acinetobacter baumannii* detected in the Intensive Care Unit

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Abstract. – OBJECTIVE: Acinetobacter baumannii (*A. baumannii*) causes serious nosocomial infections, especially in Intensive Care Units (ICU). Studies have shown that magnesium (Mg) levels change in sepsis. This study aimed to investigate the effect of Mg levels on mortality in patients with *A. baumannii* sepsis in the ICU.

PATIENTS AND METHODS: 140 patients who were hospitalized in the tertiary ICU between January 2018 and March 2020 and who were found to have *A. baumannii* sepsis in their culture follow-ups were included in the study. Demographic information of the patients, Mg levels during hospitalization and follow-up, and various data in the ICU were recorded.

RESULTS: The factors that predicted one-month mortality were old age, APACHE II score, CCIS, *A. baumannii* detection in the early stages of ICU admission, and high Mg level on day *A. baumannii* was detected, and the lowest Mg level after *A. baumannii* was detected in the early period. According to the multivariate logistic regression analysis, age increase [OR (95% CI): 1.062 (1.009-1.117)], APACHE II increase [OR (95% CI): 1.251 (1.141-1.372)], and early detection of *A. baumannii* during ICU admission [OR (95% CI): 0.902 (0.845-0.962)] were found to be factors that increase one-month mortality.

CONCLUSIONS: Hypermagnesemia in patients with *A. baumannii* indicates longer-term mortality, while a rapid decrease in Mg levels is a predictor of early mortality. Keeping Mg levels of patients within the reference range with frequent Mg measurement reduces mortality. Knowing colonized patients during admission to the ICU may be useful as an indicator of *A. baumannii* infection development and mortality risk.

Key Words:
Acinetobacter baumannii, Hypermagnesemia, Hypomagnesemia, Intensive care, Sepsis.

Introduction

Acinetobacter baumannii (*A. baumannii*) is one of the most important pathogens responsible for serious hospital infections in various hospital units, especially in intensive care units (ICUs)[1]. *A. baumannii*, which can cause sepsis and septic shock, is a common cause of hospital-acquired pneumonia and has a high mortality rate compared to other hospital infections. A study by Park et al[2] found that mechanical ventilation is a risk factor for *A. baumannii*, and mortality is higher in this group of patients. Hypomagnesemia is common in critically ill patients in ICUs and has been shown[3] to be significantly associated with increased mechanical ventilation requirements, prolonged ICU stay, and increased mortality.

Magnesium (Mg) level is a critical factor in immunological competence[4]. Hypomagnesemia has been associated[3] with sepsis and increased mortality in critically ill patients. In a study[5] evaluating sepsis patients, a significant decrease in Mg serum concentrations was observed in patients with acute bacterial infections (bronchopneumonia and urinary tract infections). In a cohort study of patients with community-acquired pneumonia, abnormal Mg levels at admission were associated with an increase in 30-day mortality compared to normal levels[6]. A study investigating risk factors in patients with severe pneumonia found that *A. baumannii* was the most common pathogen with a rate of 18.4%, and hypomagnesemia was identified as a risk factor, emphasizing the importance of Mg concentration in diagnosis[7].

The aim of this study is to investigate the effect of changes in Mg levels after the identification of *A. baumannii* in patients with *A. baumannii* sepsis in the ICU on mortality.

Patients and Methods

A total of 140 adult patients who had been admitted to the tertiary adult intensive care unit

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of Ankara Atatürk Sanatorium Training and Research Hospital and diagnosed with sepsis based on sepsis criteria (vital signs, physical examination findings, laboratory values, and SOFA score) between January 2018 and March 2020, and in whom *A. baumannii* was detected in culture follow-ups, were included in the study. After approval of the study protocol by our institution's Ethics Committee (2012-KAEK-15/2590), the patients' demographic characteristics, clinical care information, laboratory values, treatments administered, and outcomes were retrospectively examined.

The Mg levels monitored during ICU admission of patients, Mg levels measured on the day *A. baumannii* was detected, and the lowest and highest Mg levels after the detection of *A. baumannii* were recorded. The day of *A. baumannii* onset in the ICU, the day of the lowest and highest Mg levels after the onset of *A. baumannii*, and whether there were any renal function abnormalities during this time were evaluated using glomerular filtration rate (GFR) monitoring.

Patients' age, sex, underlying diseases, Charlson comorbidity index (CCI), Acute Physiology and Chronic Health Evaluation Score (APACHE-II), mechanical ventilation requirement and duration, nutrition support provided (oral, enteral, and parenteral), 1-week and 30-day mortality status, the location of culture where *A. baumannii* was detected (blood, catheter, urine, endotracheal aspirate culture), culture antibiogram, ICU length of stay, and length of hospital stay were recorded.

Antibiotic treatment was given to the patients according to the culture antibiogram. Antibiotic doses were adjusted according to daily kidney function tests.

As nutritional status may change during prolonged hospitalization, the nutrition support received by the patients on the day *A. baumannii* was detected was taken into account.

Sepsis patients with other infections besides *A. baumannii*, patients with documented hypomagnesemia who received Mg supplementation before admission to the ICU, and patients with incomplete data on Mg levels were excluded from the study.

Statistical Analysis

The data analyses were performed using SPSS for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). The normality of the distribution of continuous variables was determined using the Kolmogorov-Smirnov test. The homogeneity of variances was evaluated using Levene's test. Skewed continuous data were described as median (interquartile range), while categorical data were described as the number of cases (%). The Mann-Whitney U test was used to compare variables that were not normally distributed between two independent groups, while Pearson's Chi-square test or Fisher's exact test were used to compare categorical variables. The degree of correlation between variables was evaluated using Spearman correlation analysis. A p-value <.05 was considered statistically significant for all analyses.

Results

A retrospective study was conducted on 140 patients followed up with a diagnosis of *A. baumannii* sepsis in the adult tertiary general intensive care unit. The mean age of the patients was 67.50±16.04, with 85 (60.7%) male and 55 (39.3%) female patients. The mean APACHE-II score of the patients was 21.50±7.06, the mean CCI score was 5±2.17, the mean length of stay in the hospital was 27±21.8, the mean length of stay in the ICU was 16±12.3, and the mean duration of mechanical ventilation in patients receiving invasive respiratory support was 6.5±11.97. Nutritional support was recorded as follows: 20 (14.3%) patients received oral nutrition, 76 (54.3%) received enteral support, and 44 (31.4%) received total parenteral nutrition.

When examining the culture location for growth, *A. baumannii* was detected in the highest percentage (91.4%) in endotracheal aspirate cultures (ETA), and in 2.9% of blood, catheter, and wound cultures. As the most commonly used antibiotics for patients with *A. baumannii* were colistin, meropenem, tigecycline, and amikacin, the susceptibility of these four antibiotics was evaluated in the antibiogram of patients with *A. baumannii* growth. The resistance rates were 56.4% for amikacin, 20.7% for colistin, 87.9% for meropenem, and 32.9% for tigecycline. With regard to mortality, 14 patients (10%) died within one week of detection of *A. baumannii*, while 77 patients (55%) died within one month.

A Spearman correlation analysis was conducted to examine the relationship between the Mg value measured during admission to the ICU and the variables measured, as shown in Table I. The analysis revealed a low positive statistical correlation between the Mg value at admission and the CCI score (r=0.230, p=.006). According to the statistical results, it can be said that patients with a high CCI score had a high Mg value at admission, while those with a low CCI score had a low Mg value at admission.

Table I. Analysis of ICU admission Mg^{-1} value.

(n: 140)		Mg admission
Age	*r*	.105
	p	.218
APACHE-II	*r*	-.003
	p	.974
CCI	*r*	**.230**
	p	**.006**
Hospital length of stay	*r*	.043
	p	.614
ICU length of stay	*r*	.037
	p	.667
MV duration	*r*	.007
	p	.938

Spearman correlation analysis. Mg: Magnesium, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CCI: Charlson Comorbidity Index, ICU: Intensive Care Unit, MV: Mechanical Ventilation.

In order to examine the relationship between the variables (Table II) and one-week mortality, a Chi-square analysis was applied. The results showed that the rate of amikacin-sensitive patients was statistically significantly higher in those who experienced one-week mortality compared to those who did not (p=.027).

To examine the relationship between one-week mortality and other variables, the Mann-Whitney U test was performed (Table III), and it was found that the APACHE II score was statistically significantly higher in patients with one-week mortality compared to those without (p=.004). Hospital stay (p<.001), ICU stay (p<.001), and MV duration (p=.044) were lower in patients with one-week mortality compared to those without. One-week mortality was statistically significantly associated with *A. baumannii* detection in the early days of ICU admission (p=.001) and the lowest Mg value after *A. baumannii* detection in earlier periods (p<.001).

To investigate the relationship between variables and one-month mortality, Chi-square analysis was applied for gender, antibiotic susceptibilities, reproductive site, and nutritional status (Table IV). It was found that there was a statistically significant difference in terms of nutrition between those who experienced one-month mortality and those who did not (p<.001). Patients who were fed through parenteral support had a higher one-month mortality rate compared to those who were fed enterally, while no mortality was observed in patients who were orally fed.

The Mann-Whitney U test was applied to examine the relationship between one-month mortality and other variables (Table V). The results showed that age, APACHE II, and CCI scores were significantly higher in patients who developed one-month mortality compared to those

Table II. Effect of variables on one-week mortality-I.

		One-week mortality				
		Yes (n: 14)		No (n: 126)		
		N	%	N	%	*p*
Gender	Male	10	(71.4%)	75	(59.5%)	.387
	Female	4	(28.6%)	51	(40.5%)	
Location of infection	ETA	14	(100.0%)	114	(90.5%)	.999
	Blood	-	4	(3.2%)		
	Catheter	-	4	(3.2%)		
	Wound	-	4	(3.2%)		
Amikacin	Sensitive	10	(71.4%)	51	(40.5%)	**.027**
	Resistant	4	(28.6%)	75	(59.5%)	
Colistin	Sensitive	14	(100.0%)	97	(77.0%)	.074
	Resistant	-	29	(23.0%)		
Meropenem	Sensitive	-	17	(13.5%)	.218	
	Resistant	14	(100.0%)	109	(86.5%)	
Tigecycline	Sensitive	12	(85.7%)	82	(65.1%)	.144
	Resistant	2	(14.3%)	44	(34.9%)	
Nutrition	Oral	-	20	(15.9%)	.054	
	Enteral	6	(42.9%)	70	(55.6%)	
	Parenteral	8	(57.1%)	36	(28.6%)	

ETA: Endotracheal aspirate. Categorical variables are expressed as either frequency (percentage). Categorical variables were compared using Pearson's Chi-square test or fisher exact test. Statistically significant *p*-values are in bold.

Table III. Effect of variables on one-week mortality-II.

	One-week mortality				
	Yes (n: 14)		No (n: 126)		
	Median	(IQR)	Median	(IQR)	*p*
Age (yr)	70.00	(15.00)	67.00	(23.00)	.667
APACHE-II	31.00	(14.00)	21.00	(10.00)	**.004**
CCI	5.00	(4.00)	5.00	(3.00)	.365
Hospital length of stay (day)	6.00	(17.00)	28.00	(26.00)	**< .001**
ICU length of stay (day)	5.00	(3.00)	17.00	(20.00)	**< .001**
MV duration (day)	3.00	(4.00)	8.00	(19.00)	**.044**
Number of days *A. baumannii* was detected	3.00	(2.00)	9.00	(12.00)	**.001**
Mg (mg/dl)					
Admission	1.90	(0.30)	2.00	(0.50)	.059
Detection of *A. baumannii*	1.70	(0.40)	1.80	(0.60)	.278
Lowest Mg after *A. baumannii*	1.70	(0.20)	1.60	(0.40)	.211
Highest Mg after *A. baumannii*	2.10	(0.60)	2.00	(0.60)	.867
Day of lowest Mg after *A. baumanni*i	1.00	(1.00)	7.00	(10.00)	**< .001**
Day of highest Mg after *A. baumannii*	3.00	(2.00)	5.00	(7.00)	.083
GFR at lowest Mg	89.00	(52.00)	81.00	(67.20)	.487
GFR at highest Mg	63.00	(43.00)	50.00	(80.00)	.923

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CCI: Charlson Comorbidity Index, ICU: Intensive Care Unit, MV: Mechanical Ventilation, *A. baumannii*: *Acinetobacter Baumannii*, Mg: Magnesium, GFR: glomerular filtration rate. Continuous variables are expressed as median (interquartile range). Continuous variables were compared with Mann- Whitney U test. Statistically significant *p*-values are in bold.

Table IV. The effect of variables on one-month mortality-I.

		One-month mortality				
		Yes (n: 77)		No (n: 63)		
		N	%	N	%	*p*
Gender	Male	44	(57.1%)	41	(65.1%)	.339
	Female	33	(42.9%)	22	(34.9%)	
Location of infection	ETA	67	(87.0%)	61	(96.8%)	.077
	Blood	4	(5.2%)	-		
	Catheter	2	(2.6%)	2	(3.2%)	
	Wound	4	(5.2%)	-		
Amikacin	Sensitive	36	(46.8%)	25	(39.7%)	.401
	Resistant	41	(53.2%)	38	(60.3%)	
Colistin	Sensitive	57	(74.0%)	54	(85.7%)	.090
	Resistant	20	(26.0%)	9	(14.3%)	
Meropenem	Sensitive	6	(7.8%)	11	(17.5%)	.081
	Resistant	71	(92.2%)	52	(82.5%)	
Tigecycline	Sensitive	53	(68.8%)	41	(65.1%)	.638
	Resistant	24	(31.2%)	22	(34.9%)	
Nutrition	Oral	-		20	(31.7%)	**<.001**
	Enteral	45	(58.4%)	31	(49.2%)	
	Parenteral	32	(41.6%)	12	(19.0%)	

ETA: Endotracheal aspirate. Categorical variables are expressed as either frequency (percentage). Categorical variables were compared using Pearson's Chi-square test or Fisher exact test. Statistically significant *p*-values are in bold.

Table V. Effect of variables on 1-month mortality-II.

	One-Month mortality				
	Yes (n: 77)		No (n: 63)		
	Median	(IQR)	Median	(IQR)	*p*
Age (yr)	76.00	(23.00)	61.00	(15.00)	**< .001**
APACHE-II	26.00	(10.00)	17.00	(5.00)	**< .001**
CCI	6.00	(3.00)	5.00	(3.00)	**< .001**
Hospital length of stay (day)	22.00	(16.00)	39.00	(28.00)	**< .001**
ICU length of stay (day)	17.00	(18.00)	10.00	(23.00)	.459
MVDuration (day)	10.00	(15.00)	3.00	(18.00)	**.022**
Number of days *A.baumannii* was detected	5.00	(7.0)	13.00	(18.00)	**.002**
Mg (mg/dl)					
Admission	2.00	(0.50)	2.00	(0.50)	.838
Detection of *A. baumannii*	1.90	(0.50)	1.70	(0.40)	**.001**
Lowest Mg after *A. baumannii*	1.70	(0.40)	1.50	(0.50)	**.002**
Highest Mg after *A. baumannii*	2.10	(0.60)	2.00	(0.50)	.320
Day of lowest Mg after *A. baumannii*	6.00	(6.00)	6.00	(12.00)	.056
Day of highest Mg after *A. baumannii*	4.00	(7.00)	5.00	(8.00)	.446
GFR at lowest Mg	75.00	(59.00)	97.00	(58.00)	**.005**
GFR at highest Mg	40.00	(66.00)	85.00	(80.00)	**< .001**

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, CCI: Charlson Comorbidity Index, ICU: Intensive Care Unit, MV: Mechanical Ventilation, *A. baumannii*: *Acinetobacter Baumannii*, Mg: Magnesium, GFR: glomerular filtration rate. Continuous variables are expressed as median (interquartile range). Continuous variables were compared with Mann-Whitney U test. Statistically significant *p*-values are in bold.

who did not (p<.001). In addition, MV duration (p=.022), Mg level at *A. baumannii* detection (p=.001), and lowest Mg level after *A. baumannii* detection (p=.002) were also significantly higher in patients who developed one-month mortality. Patients with shorter hospital stays (p<.001) and those in the earlier stages of *A. baumannii* ICU stay (p=.002) had a higher risk of one-month mortality. The GFR values were significantly lower in patients with one-month mortality compared to those without at their lowest Mg level (p=.005) and highest Mg level (p<.001).

The graph in Figure 1 illustrates the relationship between Mg levels at admission to the ICU

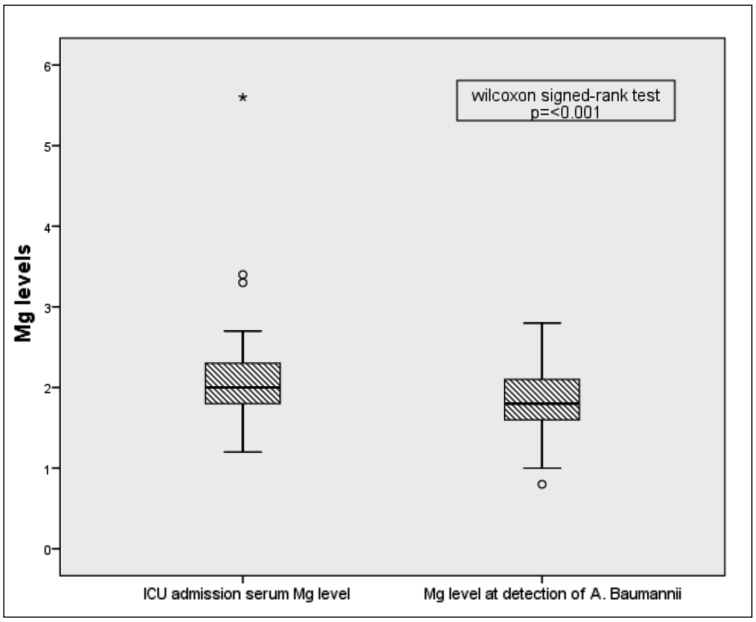

Figure 1. Distribution of Mg levels at ICU admission and on the day of *A. baumannii* detection (grayscale). Outlier ○, extreme outliers*.

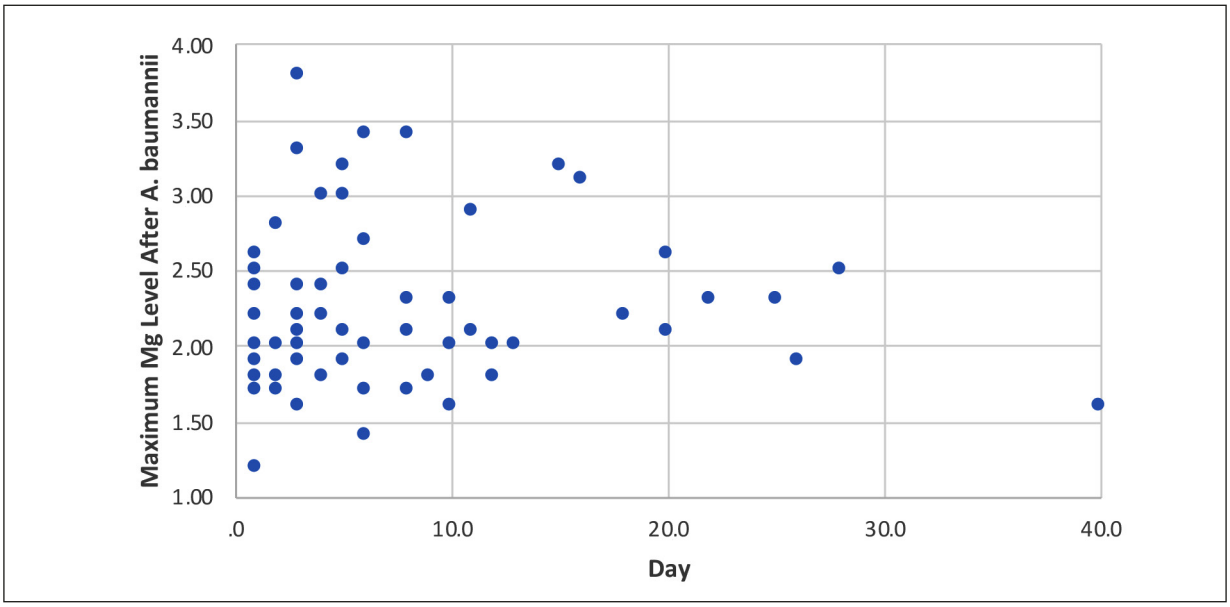

Figure 2. Distribution of maximum Mg levels observed after *A. baumannii* detection, respectively (grayscale).

and Mg levels on the day *A. baumannii* was detected. The decrease in Mg levels in the graph indicates a decline in Mg levels after the detection of *A. baumannii*. According to the Wilcoxon signed rank test, there was a statistically significant difference between the Mg level measured at admission to the ICU and the Mg level measured on the day *A. baumannii* was detected ($p \leq 0.001$). This graph shows that Mg levels decreased after the detection of *A. baumannii*.

Figure 2 illustrates the distribution of maximum Mg levels during ICU stay, while Figure 3 illustrates the distribution of minimum Mg levels during ICU stay after *A. baumannii* detection.

In Table VI, a univariate logistic regression analysis was applied for factors thought to be

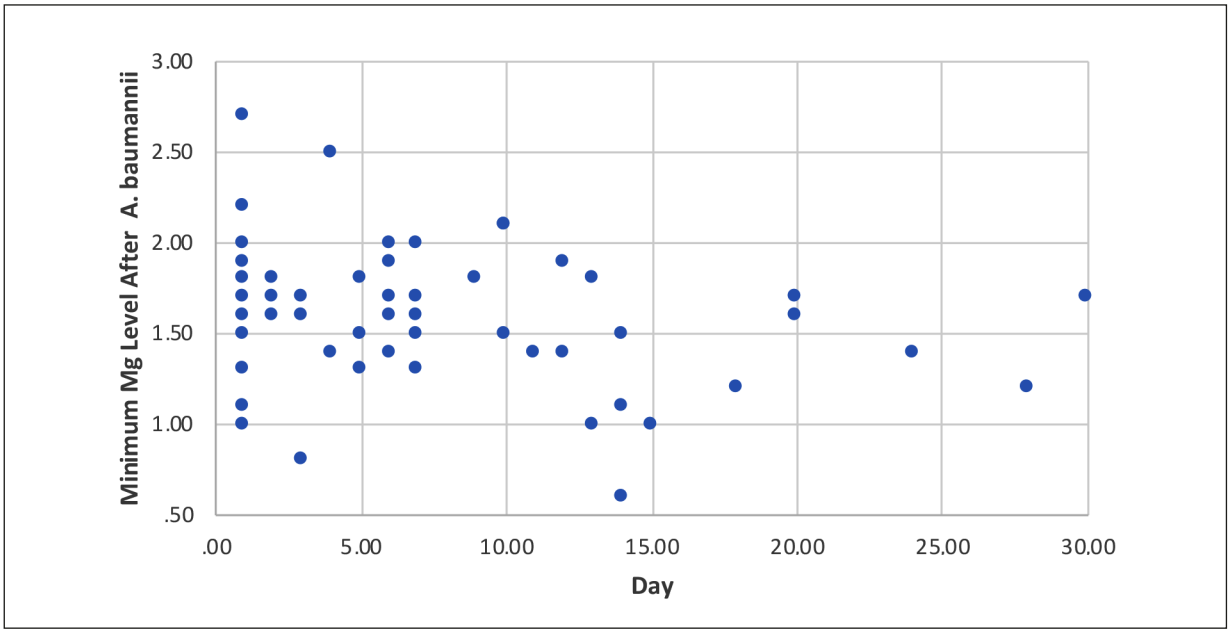

Figure 3. Distribution of minimum Mg levels observed after *A. baumannii* detection, respectively (grayscale).

Table VI. Univariate and multivariate logistic regression analysis for factors thought to be effective in predicting 1-month mortality.

	Univariate logistic regression					Multivariate logistic regression				
				95% C.I. for OR					95% C.I. for OR	
	Wald	*p*	OR	Lower	Upper	Wald	*p*	OR	Lower	Upper
Age	18.929	**< .001**	1.063	1.034	1.093	5.296	**.021**	1.062	1.009	1.117
Gender (male)	0.912	.339	1.398	0.703	2.778					
Location of infection (ETA)	3.639	.056	4.522	0.959	21.605					
Amikacin (sensitive)	0.703	.402	0.749	0.382	1.471					
Colistin (sensitive)	2.811	.094	2.105	0.882	5.027					
Meropenem (sensitive)	2.894	.089	2.503	0.870	7.204					
Tigecycline (sensitive)	0.221	.638	0.844	0.416	1.713					
APACHE II	28.851	**< .001**	1.219	1.134	1.310	22.561	**< .001**	1.251	1.141	1.372
CCIS	11.226	**.001**	1.355	1.134	1.618	0.026	.872	1.026	0.751	1.402
ICU length of stay	0.320	.571	0.992	0.966	1.020					
MV duration	0.186	.666	1.006	0.978	1.035					
Number of days *A. baumannii* was detected	11.923	**.001**	0.930	0.893	0.969	9.863	**.002**	0.902	0.845	0.962
Mg admission	1.402	.236	0.681	0.360	1.287					
Mg at the time *A. baumannii* was detected	7.628	**.006**	3.644	1.456	9.121	0.459	.498	1.639	0.392	6.845
Lowest Mg after *A. baumannii*	8.192	**.004**	4.472	1.603	12.473	0.339	.560	1.212	0.635	2.311
How many days after the detection of A. baumannii was the lowest Mg observed in the ICU	9.195	**.002**	0.916	0.866	0.970	0.494	.482	0.969	0.888	1.058
Highest Mg after *A. baumannii*	0.625	.429	1.304	0.675	2.518					
How many days after the detection of *A. baumannii* was the highest Mg observed in the ICU	0.745	.388	0.981	0.938	1.025					
Constant						12.323	.001	0.001		

Wald: test statistics, OR: odds radio, CI: Confidence interval. Statistically significant *p*-values are in bold. APACHE II: Acute Physiology and Chronic Health Evaluation-II, CCIS: Charlson Comorbidity IndexSCore, ICU: Intensive Care Unit, MV: mechanical ventilation.

effective in predicting one-month mortality. The data that were found to be significant in the statistical analysis were evaluated for univariate logistic regression analysis. A single-variable logistic regression analysis revealed that age, APACHE II, CCIS, the number of days from admission to the ICU for *A. baumannii*, the day when *A. baumannii* was detected, and the lowest Mg level and the number of days after *A. baumannii* detection may be factors that affect the prediction of 1-month mortality. The variables with a *p*-value below .05 in the single-variable logistic regression analysis were included in the multivariable logistic regression analysis using the enter method. According to the results, an increase in age [OR (95% CI): 1.062 (1.009-1.117)], an increase in APACHE II [OR (95% CI): 1.251 (1.141-1.372)], and a decrease in the number of days from *A. baumannii* isolation in the ICU [OR (95% CI): 0.902 (0.845-0.962)] were evaluated as factors that increase the 1-month mortality.

Discussion

This study examines the relationship between mortality and Mg levels in 140 patients admitted to the ICU due to *A. baumannii* sepsis. The mortality rate was 10% (14 patients) within one week from detecting *A. baumannii*, and 55% (77 patients) within one month. It was found that old age, high APACHE-II score, and early detection of *A. baumannii* during ICU admission are factors that increase the one-month mortality rate. A high Mg level was also observed on day *A. baumannii* was detected, and the occurrence of the lowest Mg level in the early period after *A. baumannii* also affected mortality.

There are numerous studies[8-10] in the literature that examine the relationship between *A. baumannii* infection and severity scores frequently used in ICUs, such as APACHE-II and CCIS, as well as the relationship between these scores and Mg levels. Chen et al[8] demonstrated that the APACHE-II score at the onset of *A. baumannii* bacteremia is a reliable parameter in predicting mortality. Martín-Aspas et al[9] found that the presence of chronic disease and high CCIS levels affect mortality in patients with both *A. baumannii* colonization and infection. The relationship between CCIS and mortality has also been shown in other studies[10]. It has been observed[11] that patients with high APACHE-II scores at admission to the ICU developed more hypomagnesemia during ICU follow-up. When the relationship between CCIS and Mg levels was examined, CCIS was found to be significantly higher in the hypermagnesemia group[12]. In this study, a positive statistical relationship was found between Mg levels and CCIS, and high initial admission Mg levels were observed in patients with high CCIS. It was found that high APACHE-II and CCIS scores are effective factors in predicting one-month mortality in *A. baumannii* patients, which is consistent with the literature.

A. baumannii has been reported[2] to be the most common nosocomial pathogen among gram-negative bacilli, with 92.7% being nosocomial- and 7.3% community-acquired. Rehospitalization and mortality rates are significantly higher in these patients depending on comorbidities and disease severity[13]. The high mortality and morbidity in resistant *A. baumannii* infections have been attributed[14] to increased hospital stays, readmission rates, and reinfection rates. Readmissions are quite common in infections caused by multi-drug resistant (MDR) pathogens[15]. In a 5-year study[16] conducted at the University of Maryland in the United States, patients colonized with MDR *A. baumannii* at admission to the ICU were found to have a 15-fold greater likelihood of developing subsequent infection, and a significant positive relationship was observed between mortality and MDR *A. baumannii* colonization. Patients who developed *A. baumannii* infection during follow-up were reported to be older with a history of antibiotic use before admission to the ICU and at least one previous hospitalization. Latibeaudiere et al[17] reported a prevalence of 14% for carbapenem-resistant *A. baumannii* among 364 trauma patients admitted to the ICU, and an 8.4-fold increased risk of developing infection during ICU follow-up. The ideal antibiotic choice is based not only on the pathogen itself but also on the location of the pathogen and the concentration of the antibiotic in that area. Many factors, including lipophilicity, pH, protein binding, alveolar-capillary membrane, and bronchial inflammation, can affect the penetration of antibiotics into the epithelial lining fluid[18].

Compared to colonized patients, the time to death in infected patients was almost significantly shorter[19]. In our study, 1-week and 1-month mortality were found to be higher in patients with *A. baumannii* detected in the early days of ICU admission. As *A. baumannii* is a hospital-acquired infection, a history of hospitalization prior to ICU admission is quite common. We believe that early

deaths may be due to sepsis in patients who are already colonized. Delayed results of admission cultures may have caused a delay in intervention. Knowing patients who are colonized at admission to the ICU would be useful as an indicator of the risk of developing *Acinetobacter* infections and dying during hospitalization. Active surveillance can guide empirical antibiotic selection and facilitate infection control practices.

Disruption of the balance in the inflammatory response leads to the transformation of colonizing bacteria into infection and sepsis[20]. Acute kidney failure and electrolyte disorders are frequently observed in sepsis. There are many studies in the literature[3,21,22], particularly on sepsis and hypomagnesemia. A sudden decrease in Mg levels increases mortality. Magnesium deficiency causes a systemic stress response by activating neuroendocrinological pathways and also causes an overreaction to immune stress. Oxidative stress occurs as a result of the inflammatory response[23]. In experimental studies conducted by Watanabe et al[24] on mice, it was shown that cardiac tolerance against hypoxia was significantly reduced in animals with Mg deficiency, and even small Mg changes had significant effects on mechanical and electrical activities in heart cells. In this study, higher 1-week mortality was found in those with lower Mg levels after *A. baumannii* in the early days. As the decrease in Mg levels after *A. baumannii* can affect early mortality, it is necessary to support it with Mg supplements.

When examining the literature, in addition to studies investigating the relationship between hypomagnesemia and mortality, there are also numerous studies demonstrating the effect of hypermagnesemia on mortality. In a study[25] conducted in Switzerland that screened 22.239 emergency department patients, a significant relationship was found between hypermagnesemia and in-hospital mortality when examining Mg levels at admission to the emergency department. In a prospective study[26] examining changes in total serum Mg and ionized serum Mg^{+2}, ionized hypermagnesemia was found to be associated with higher mortality, while no relationship was found between hypomagnesemia and mortality. In our study, we also found that high Mg levels on the day *A. baumannii* was detected were associated with 1-month mortality. This may be due to renal dysfunction associated with sepsis.

Serum Mg levels increase in chronic kidney disease. In addition, low Mg levels have been associated with cardiovascular disease and death in end-stage kidney disease. In dialysis patients, low Mg levels may reflect poor nutritional status and be a result of systemic inflammation[27]. When looking at the Mg level at the time of hospital admission, both hypomagnesemia and hypermagnesemia are associated with increased risk for in-hospital adverse events[28]. Additionally, renal failure is one of the indicators of mortality associated with *A. baumannii* infection[29]. In this study, it was found that in individuals with low GFR values on the day when the lowest and highest Mg levels were detected after *A. baumannii* infection, one-month mortality was high.

Patients with *A. baumannii* sepsis requiring mechanical ventilation have a significantly higher mortality rate[2]. Enteral or parenteral nutrition is started for patients who are intubated and placed on mechanical ventilation support, as they cannot be orally fed. Hypomagnesemia has been found[30] more frequently in patients receiving parenteral nutrition compared to those fed orally. In this study, prolonged use of mechanical ventilation was found to be an independent risk factor for one-month mortality. Additionally, it was observed that Mg levels were lower in parenterally-fed patients compared to enterally-fed patients. One-month mortality was higher in parenterally-fed patients, while no mortality was observed in orally-fed patients. Patients with *A. baumannii* sepsis are generally older with high comorbidities and have previously been hospitalized, so hypomagnesemia may have been observed due to oral intake disorder.

Limitations

There are some limitations to our study. One of the limitations of our study is the single-center retrospective design and the inability to control all possible confounders. Moreover, Mg levels in the ward were not measured for patients admitted from the ward to the ICU, so it is not known whether there was an increase or decrease in Mg levels in colonized patients upon admission to the ICU. Information on colonization status, previous hospitalization history, and pre-ICU antibiotic use history could not be obtained. Empirical treatment started for patients may have affected one-week mortality. Information on the amount and rate of Mg supplementation given to patients with hypomagnesemia during ICU follow-up could not be obtained. Total serum Mg levels were measured in our hospital, but ionized Mg levels were not measured, so it was not possible to distinguish between intracellular Mg transport

or Mg loss. There are not many studies related to our study in the literature, so prospective studies are necessary to confirm our data.

Conclusions

High levels of Mg on the day *A. baumannii* is detected are associated with increased one-month mortality, while the lowest Mg levels after *A. baumannii* infection are associated with a high one-week mortality in early stages. This indicates that hypermagnesemia in patients with *A. baumannii* results in longer-term mortality, while a rapid drop in Mg levels is a predictor of early mortality. Antibiotics used after *A. baumannii* infection may worsen renal function in patients with borderline kidney function, leading to increased hypermagnesemia and long-term mortality. We believe that frequent monitoring of Mg levels and keeping them within reference range with Mg supplements could reduce mortality in patients with *A. baumannii*. Furthermore, in early-stage ICU patients with *A. Baumannii,* the high mortality rate is generally attributed to the high risk of sepsis-related mortality in patients who were colonized before being admitted to the ICU. Identifying patients with colonization during ICU admission could be useful as an indicator of increased risk of developing *Acinetobacter* infection and mortality during hospitalization.

Conflict of Interest
The authors declare that they have no conflict of interest to declare.

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Authors' Contribution
The planning of the study, the preparation of the patient follow-up form, the scanning and analysis of the data, the statistical evaluation, the interpretation of the findings, the writing of the study, the revisions, the verification and approval of the version of the article were performed by both authors.

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Availability of Data and Materials
All data generated or analyzed during this study are included in this published article.

Informed Consent
Informed consent was obtained from all individual participants included in the study.

Ethics Approval
The study was carried out with the permission of Research Ethics Committee of Health Sciences University Ankara Ataturk Sanatorium Traning and Research Hospital (approval date and number: 23.11.2022, 2012-KAEK-15/2590).

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