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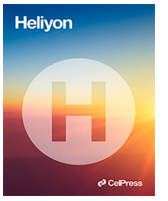

Research article

The relationship between potassium levels and 28-day mortality in sepsis patients: Secondary data analysis using the MIMIC-IV database

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ABSTRACT

Objective: The goal of the research is to investigate the link between serum potassium levels and death after 28 days in sepsis patients, utilizing an extensive sample of patients from the multi-center Medical Information Mart for Intensive Care IV (MIMIC-IV) database. Current research on serum potassium levels and 28-day mortality in sepsis patients is questionable. This study adds to the growing body of evidence linking serum potassium levels to the 28-day possibility of death in patients with sepsis.

Methods: We collected 349,08 patients with sepsis from the retrospective cohort MIMIC-IV database, using serum potassium level on the first day of admission to the intensive care unit as the exposure variable and mortality at 28 days as the outcome variable. And controlled for confounding characteristics including gender, age, ethnicity, and vital signs during admission.

Results: Serum potassium has a U-shaped connection with 28-day mortality in patients suffering from sepsis. The turning point was 4.10 mmol/L (95 % confidence interval: 4.03 to 4.22). Serum potassium and 28-day mortality were negatively linked on the inflection point's left side (OR: 0.72; 95 % CI: 0.63 to 0.83, $P < 0.0001$); on the opposing side of the point of inflexion, serum potassium was enthusiastically attached to 28-day mortality. (OR: 1.13; 95 % CI: 1.06 to 1.21, $P < 0.0001$).

Conclusion: The research conducted found that too high or too low potassium levels were linked to a 28-day risk of mortality in humans with sepsis.

1. Introduction

According to the most recent definition, sepsis occurs when the host immune system fails to respond to an infection, resulting in various potentially lethal organ dysfunctions [1]. Sepsis has become one of the most common causes of mortality in hospitalized patients worldwide, and its prevalence is rising [2]. Epidemiological data show that sepsis and its consequences kill approximately 1

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million hospitalized people each year in the United States, with a death rate of 20 % [3]. According to a recent research report that examined adult ambulatory data from seven countries with a high-income level, 19.4 million individuals are diagnosed with sepsis each year, with approximately 5.3 million dying as a result [4]. One of the primary reasons for this might be the lack of adequately effective models for predicting sepsis prognosis; hence, developing strong predictive models is critical for increasing the survival of patients with sepsis. However, developing strong predictive models requires a thorough understanding of the association between the model's predictors and the results. Potassium is the exposure variable addressed in this study.

Potassium is the main mineral in the human body; it is an essential intracellular cation found in all cells and is vital for maintaining normal cell function [5]. Disorders of potassium metabolism manifest as hypokalemia or hyperkalemia [6]. Previous research has indicated that hypokalemia and hyperkalemia are associated with unfavourable outcomes in heart failure, chronic renal disease, and

Table 1
Baseline characteristic of participants.

Potassiummean quartile	Q1 (2.20–3.80)	Q2 (3.85–4.20)	Q3 (4.20–4.55)	Q4 (4.60–9.2)	P-value
N	8282	8895	8240	9491	
Age at admission, median (Q1, Q3), year	66.31 (54.06–78.15)	67.54 (56.33–78.53)	69.02 (58.82–79.18)	68.85 (58.49–79.26)	<0.001
Gender, No (%)					<0.001
Female	4026 (48.61 %)	5085 (57.17 %)	5012 (60.83 %)	6005 (63.27 %)	
Male	4256 (51.39 %)	3810 (42.83 %)	3228 (39.17 %)	3486 (36.73 %)	
White, No (%)					<0.001
Yes	5526 (66.72 %)	6120 (68.80 %)	5734 (69.59 %)	6214 (65.47 %)	
Others	2756 (33.28 %)	2775 (31.20 %)	2506 (30.41 %)	3277 (34.53 %)	
Heartrate, mean ± SD, times	105.75 ± 23.97	103.92 ± 24.43	102.74 ± 23.97	103.50 ± 25.45	<0.001
Respiratory rate, mean ± SD, times	27.23 ± 9.50	26.37 ± 9.58	26.29 ± 9.66	26.90 ± 9.81	<0.001
Temp, mean ± SD, degrees	36.96 ± 1.31	36.80 ± 1.26	36.70 ± 1.24	36.65 ± 1.25	<0.001
SOFA, mean ± SD, score	6.18 ± 3.54	6.12 ± 3.52	6.31 ± 3.62	7.53 ± 4.00	<0.001
Charlson comorbidity index, mean ± SD, rate	5.68 ± 2.92	5.80 ± 2.89	6.13 ± 2.87	6.80 ± 2.94	<0.001
The use of dexamethasone, No (%)					<0.001
Yes	1060 (12.80 %)	1056 (11.87 %)	864 (10.49 %)	834 (8.79 %)	
No	7222 (87.20 %)	7839 (88.13 %)	7376 (89.51 %)	8657 (91.21 %)	
The use of methylprednisolone, No (%)					<0.001
Yes	1298 (15.67 %)	1454 (16.35 %)	1370 (16.63 %)	2015 (21.23 %)	
No	6984 (84.33 %)	7441 (83.65 %)	6870 (83.37 %)	7476 (78.77 %)	
The use of cortisone, No (%)					0.948
Yes	169 (2.04 %)	180 (2.02 %)	176 (2.14 %)	200 (2.11 %)	
No	8113 (97.96 %)	8715 (97.98 %)	8064 (97.86 %)	9291 (97.89 %)	
The use of dopamine, No (%)					<0.001
Yes	456 (5.51 %)	538 (6.05 %)	560 (6.80 %)	903 (9.51 %)	
No	7826 (94.49 %)	8357 (93.95 %)	7680 (93.20 %)	8588 (90.49 %)	
The use of dobutamine, No (%)					<0.001
Yes	283 (3.42 %)	331 (3.72 %)	334 (4.05 %)	549 (5.78 %)	
No	7999 (96.58 %)	8564 (96.28 %)	7906 (95.95 %)	8942 (94.22 %)	
The use of norepinephrine					<0.001
Yes	2554 (30.84 %)	2606 (29.30 %)	2398 (29.10 %)	3507 (36.95 %)	
No	5728 (69.16 %)	6289 (70.70 %)	5842 (70.90 %)	5984 (63.05 %)	
The use of carbapenem antibiotics, No (%)					<0.001
Yes	1899 (22.93 %)	1736 (19.52 %)	1593 (19.33 %)	2214 (23.33 %)	
No	6383 (77.07 %)	7159 (80.48 %)	6647 (80.67 %)	7277 (76.67 %)	
The use of cephalosporin antibiotics, No (%)					<0.001
Yes	657 (7.93 %)	721 (8.11 %)	749 (9.09 %)	896 (9.44 %)	
No	7625 (92.07 %)	8174 (91.89 %)	7491 (90.91 %)	8595 (90.56 %)	
The use of penicillin antibiotics, No (%)					<0.001
Yes	4703 (56.79 %)	4476 (50.32 %)	3817 (46.32 %)	5065 (53.37 %)	
No	3579 (43.21 %)	4419 (49.68 %)	4423 (53.68 %)	4426 (46.63 %)	
The use of vancomycin antibiotics, No (%)					<0.001
Yes	6860 (82.83 %)	6955 (78.19 %)	6489 (78.75 %)	8080 (85.13 %)	
No	1422 (17.17 %)	1940 (21.81 %)	1751 (21.25 %)	1411 (14.87 %)	
The use of IVIG, No (%)					0.063
Yes	242 (2.92 %)	218 (2.45 %)	190 (2.31 %)	233 (2.45 %)	
No	8040 (97.08 %)	8677 (97.55 %)	8050 (97.69 %)	9258 (97.55 %)	
The use of mechanical ventilation, No (%)					<0.001
Yes	3205 (38.70 %)	3960 (44.52 %)	3837 (46.57 %)	4359 (45.93 %)	
No	5077 (61.30 %)	4935 (55.48 %)	4403 (53.43 %)	5132 (54.07 %)	
The use of continuous renal replacement therapy					<0.001
Yes	268 (3.24 %)	306 (3.44 %)	364 (4.42 %)	837 (8.82 %)	
No	8014 (96.76 %)	8589 (96.56 %)	7876 (95.58 %)	8654 (91.18 %)	
28-day mortality, No (%)					<0.001
Yes	1301 (15.71 %)	1216 (13.67 %)	1205 (14.62 %)	1958 (20.63 %)	
No	6981 (84.29 %)	7679 (86.33 %)	7035 (85.38 %)	7533 (79.37 %)	

SOFA, sequential organ failure detection score; IVIG, intravenous immunoglobulin.

diabetes mellitus, as well as an association between serum potassium and mortality rates [7,8]. However, the association between serum potassium levels and poor sepsis outcomes remains controversial. Wu et al. reported that serum potassium is one of the most frequent factors predicting in-hospital mortality in patients with sepsis [9]. A study on American veterans with sepsis showed that potassium levels were a predictor of the risk of death [10]. Ahmad et al. reported no association between electrolyte imbalance and mortality in neonates [11]. However, these studies had limited sample sizes and significant discrepancies in the populations studied and the research methodologies.

This investigation aimed to examine the correlation between potassium levels and the 28-day probability of mortality from sepsis, utilizing a large number of participants in the Medical Information Mart for Intensive Care IV (MIMIC-IV) sepsis database and numerous factors. A substantial sample volume will provide more consistent and precise data, allowing us to more thoroughly comprehend the relationship between serum potassium levels and the probability of death from sepsis after 28 days from admission to the intensive care unit (ICU).

2. Patients and methods

2.1. Methods

Data used in this study were obtained from the MIMIC-IV database. From 2008 to 2019, clinical data were collected from patients who visited the Beth Israel Deaconess Medical Center. Chen Lu was authorised to collect data from this database (Record ID: 50668217). This study complied with the Observational Research Routine Health Data (RECORD) declaration guidelines.

2.2. Patients

We extracted information from 35,010 patients identified as having sepsis from the database using the International Classification of Diseases (ICD)-9 and ICD-10 codes [ICD-9 codes (99591–99592) or ICD-10 codes (R652, R6520, and R6521)]. Patient data were retrieved from 2008 to 2019. The outcome variable was death within 28 days following admission to the ICU (dichotomous variable, Y = 1, death; Y = 0, survival). Serum potassium was the variable related to exposure (preserved as an ongoing variable), and a connection between the result and exposure variables was analysed. The time for obtaining serum potassium levels was the first day of admission to the ICU. Patients lacking exposure variable information were excluded from the study.

Our selected covariates included, among others, demographic factors: age (years), sex (male or female), ethnicity, vital signs, Charlson comorbidity index, Sequential Organ Failure Assessment (SOFA) score, use of mechanical ventilation and continuation of renal replacement therapy, glucocorticoids (dexamethasone, methylprednisolone, cortisone), vasoactive drugs (dopamine, dobutamine, norepinephrine), use of immunoglobulin and antibiotics (cephalosporins, carbapenems, vancomycins, penicillin). We selected these factors based on our research and clinical experience [12–16].

2.3. Missing data explanation

Because the missing rate for each variable in the study was less than 5 %, serial interpolation was not used to handle missing data. (0–4.1 %).

2.4. Statistical analysis

Rates are used to show categorical variables. The median (minimum, maximum) or mean and standard deviation (Gaussian distribution) were used to illustrate continuous variables. A breakdown of the baseline patient data in the four groups was documented because this was a retrospective cohort study. Consequently, the exposure variables were categorised into four (quartiles) groups. The means and proportions of the groups were compared statistically using the Kruskal–Wallis H (skewed distribution) test, chi-square test (categorical variables), and one-way analysis of variance (Gaussian distribution). Binary logistic regression models with single and multiple variables were used to investigate the relationship between serum potassium levels and the probability of mortality within 28 days of ICU admission. Model 1 had no adjustments (no variables were modified). Model 2 was slightly adjusted (for population variables). Model 3 was a fully adjusted model (that accounts for all factors in Table 1). Estimated odds ratios (OR) and 95 % confidence intervals (CIs) were calculated. Additionally, serum potassium was converted into a categorical variable (quartile) to determine whether the results were reliable when potassium was used as a continuous or categorical variable.

Although serum potassium level is a continuous variable, nonlinear connections are possible. We utilised a generalised additive model (GAM) and smoothed curve fitting to examine the association between serum potassium levels and 28-day mortality from sepsis owing to the inability of the binary logistic regression model to deal with nonlinear correlations. The GAM is a generalization of linear regression, allowing for nonlinear relationships between the response and explanatory variables. In the GAM, the linear predictor is specified as the sum of the smooth functions of each explanatory variable rather than a simple linear combination. If the connection was not linear, the inflexion point values were generated using a recursive procedure, and the OR values on both sides of the inflexion point and the 95 % CI were calculated using a two-piecewise linear model. The two-piecewise linear model is a semi-parametric regression model. It divides the range of predictor variable values into two intervals and establishes separate linear regression models for these intervals. Using two simple linear models can approximate the shape of a complex nonlinear function without needing to specify the exact form of the function. Thus, it can better fit nonlinear data using two linear segments. Compared with fully

parametric models, it is more flexible, and the calculation is simpler and more direct.

The statistical packages R (http://www.R-project.org, The R Foundation) and Empower Stats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA) were used for the analyses, and P values less than 0.05 (two-sided) were considered statistically significant.

3. Results

3.1. Patient selection procedure

The MIMIC-IV database, containing 377,207 sepsis cases, was used in this investigation. A total of 34,908 patients with sepsis satisfied the nadir criteria and were included in the final study after excluding 342,197 patients without sepsis and 102 patients with missing potassium data (Fig. 1).

3.2. Patient baseline characteristics

The baseline patient characteristics are shown in Table 1. Serum potassium was classified into four groups (Q1–Q4) using quadratic grouping. After sorting into several categories, it was possible to see how each variable was distributed throughout the various groupings. The average age of the patients was 66.67 ± 16.01 years. Mortality occurred at an average rate of 16.27 % (56,80/34,908) at 28 days. When cortisone and immunoglobulin were used, we found no statistically significant changes in the distribution of various potassium subgroups (all P values > 0.05). Compared with the Q4 cohort, the Q1, Q2, and Q3 groups had a greater percentage of men, higher temperatures, and a higher frequency of vancomycin antibiotic use. The Charlson comorbidity index and SOFA scores were much lower in the Q1, Q2, and Q3 groups than in the Q4 group. Dexamethasone, dobutamine, methylprednisolone, norepinephrine, carbapenems, cephalosporins, and penicillin were used less frequently, and the proportion of patients requiring mechanical breathing and continuous renal replacement treatment was significantly lower in the Q1, Q2, and Q3 groups than in the Q4 group.

3.3. Univariate and multivariate analyses of potassium

Table 2 shows the serum potassium levels and mortality at 28 days in people with sepsis after controlling for many factors. When serum potassium was employed as a continuous variable, the OR values in the non-adjusted, adjusted I, and adjusted II groups, with p-values larger than 0.05, were 1.32, 1.32, and 1.01, respectively. This suggests that serum potassium was not significantly associated with sepsis. No significant relationship was observed between serum potassium levels and the probability of mortality in patients after 28 days. For the sensitivity analysis, we converted serum potassium into categorical variables and derived the p-values. The adjusted II findings demonstrated that using serum potassium as a continuous variable produced the same results as using potassium as a variable that can be categorised (Table 2).

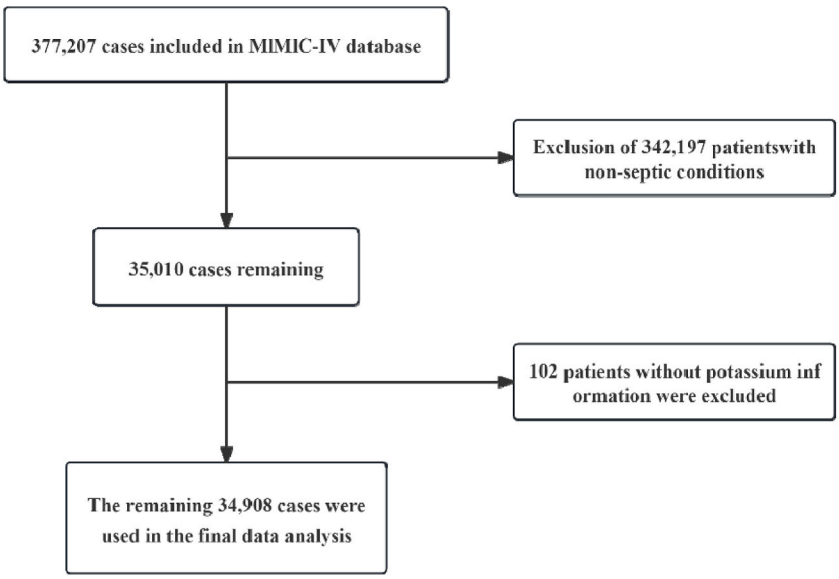

Fig. 1. The flowchart of study. In figure, we showed the procedures of subjects selection. Shows the study flowchart, which illustrates how we screened the study subjects from the MIMIC-IV database.

Table 2
Potassium with 28-day mortality after univariate and multivariate logistic regression analysis.

Exposure	Non-adjusted	Adjust I	Adjust II
Potassiummean	1.32 (1.27, 1.38) <0.0001	1.32 (1.27, 1.38) <0.0001	1.02 (0.97, 1.07) 0.5035
Potassiummean four groups			
Q1	1.0	1.0	1.0
Q2	0.85 (0.78, 0.92) 0.0002	0.83 (0.76, 0.91) <0.0001	0.84 (0.76, 0.92) 0.0003
Q3	0.92 (0.84, 1.00) 0.0519	0.89 (0.81, 0.97) 0.0069	0.86 (0.78, 0.95) 0.0020
Q4	1.39 (1.29, 1.51) <0.0001	1.38 (1.27, 1.49) <0.0001	0.93 (0.85, 1.01) 0.0980
P for trend	<0.0001	<0.0001	0.2889

Adjust I, adjusted for demographic characteristics only; Adjust II, adjusted for all covariates presented in Table 1.

3.4. Nonlinear correlation results

The results shown in Fig. 2 and Table 3 suggest that the association between baseline serum potassium levels and the risk of 28-day mortality in patients with sepsis was U-shaped. When the association of potassium with the risk of 28-day mortality was fitted using a standard logistic regression model, the effect size (OR) was 1.01, with a 95 % CI of 0.96–1.06 and a P value of 0.6803, indicating that the effect size of the model was not significant. However, the results changed significantly when a two-piecewise linear model was used for fitting. The break point of the model was 4.10 (95 % CI, 4.03–4.22). Within the range of 2.20–4.10, the effect size (OR) was 0.72, with a 95 % CI of 0.63–0.83 and a P value less than 0.0001, indicating that within this range, for every 1 mmol/L increase in potassium, the risk of death in critically ill patients decreased by 17 %. Within the range of 4.10–9.2, the effect size (OR) was 1.13, with a 95 % CI of 1.06–1.21 and a P value of 0.0002, indicating that within this range, for every 1 mmol/L increase in potassium, the risk of death increased by 13 % and was statistically significant. The P value of the log-likelihood ratio test was less than 0.001, indicating that the two-piecewise linear model was a better fit for the data than the standard logistic regression model.

4. Discussion

Based on a large multicentre sepsis cohort, this study explored the association between serum potassium and the 28-day risk of mortality in patients with sepsis. A U-shaped link was discovered between serum potassium and the probability of mortality at 28 days with sepsis after a retrospective examination of data from a substantial number of patients with sepsis (N = 34,908). This indicates that low and high serum potassium concentrations are associated with an increased risk of fatality from sepsis.

Our results are comparable to those reported by Wu et al. and Sutton et al. The study by Wu et al. was divided into two phases: rule discovery and rule analysis. Researchers used the MIMIC III database to simulate in-hospital mortality events in 2021 ICU patients diagnosed with sepsis. The RuleFit approach was used during the rule discovery phase to mine several hidden rules that could predict individual in-hospital mortality events. The investigators used survival and decomposition analyses during the rule analysis phase to

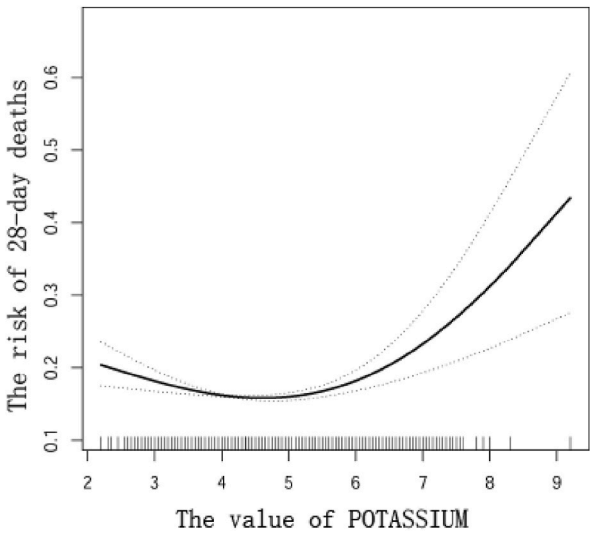

Fig. 2. The nonlinear relationship among potassium and sepsis mortality at 28 days. The relationship between the value of potassium and the risk of 28-day deaths. The x-axis represents the value of potassium, ranging from 2 to 9. The y-axis represents the risk of 28-day deaths, ranging from 0.1 to 0.6. There are three lines in the figure, each representing different datasets or conditions: The solid line represents the average relationship between the value of potassium and the risk of 28-day deaths. The upper dotted line represents the upper limit of the risk of 28-day deaths as the value of potassium increases. The lower dotted line represents the lower limit of the risk of 28-day deaths as the value of potassium increases.

Table 3
Non-Linear relationships addressing.

Models	OR, 95%CI, P value
Fitting model by standard logistic regression model	1.01 (0.96, 1.06) 0.6803
Fitting model using two-piecewise linear model	
Inflection point	4.10 (4.03, 4.22)
2.20 to 4.10	0.72 (0.63, 0.83) <0.0001
4.10 to 9.2	1.13 (1.06, 1.21) 0.0002
Log-likelihood ratio tests	<0.001

Adjust the strategy to be the same as the Adjust II model.

test and demonstrate the risk-prediction abilities of these rules. Serum potassium levels were eventually discovered to be one of the most common indicators of sepsis in in-hospital deaths [9]. Sutton et al. conducted a retrospective cohort study of 9386 patients hospitalized with sepsis, and the findings revealed that potassium levels were linked to a greater risk of hospitalisation and overall death using a multivariate-adjusted Cox proportional risk model and propensity score analysis [10]. These findings align with ours. The distinction was that we used a larger sample size and more covariate data.

However, the findings of Ahmad et al. are conflicting. In an observational study, Ahmad discovered that most cases of newborn sepsis involve electrolyte abnormalities, with hyperkalaemia being the most prevalent. However, no significant relationship was identified between electrolyte imbalance and death [11]. We assume that the following reasons are primarily responsible for the differences in results: (1) Differences in sample size: the larger sample size and wider distribution interval of serum potassium values in this study made it easier to find the true association between serum potassium and 28-day mortality. We used a more rational algorithm to process the data accurately (discovery of a U-shaped relationship). (2) We used a more reasonable approach to analyse the data more accurately (a U-shaped link was discovered). (3) We adjusted for different variables than in previous studies, we adjusted for confounding factors reported in the literature that may affect sepsis prognosis, the nonlinear link between potassium and 28-day mortality in sepsis was further investigated. (4) Our study included adult patients, whereas the previous study included only newborns.

Potassium is a key electrolyte for maintaining cell membrane potential and conducting nerve impulses [17]. Serum potassium levels that are too high (hyperkalaemia) or too low (hypokalaemia) can affect the normal functions of the heart, muscles, and nervous system [18]. The U-shaped association between the serum potassium levels measured on the first day of ICU admission and the 28-day risk of death may reflect the effects of sepsis on multiple body systems and the importance of electrolyte balance in maintaining physiological stability. High baseline potassium levels may indicate impaired cardiac function, renal insufficiency, or a more severe inflammatory response. In contrast, low baseline potassium levels may result from malnutrition, gastrointestinal potassium loss, or certain medications [19,20]. These electrolyte imbalances can interfere with normal physiological and metabolic processes, leading to multiorgan dysfunction and an increased risk of death [21,22]. Therefore, baseline potassium levels may be a prognostic marker for patients with sepsis, reflecting the severity of the disease and the patients response to therapy. Close monitoring and management of electrolyte levels, even during the early stages of sepsis, are essential to improve patient prognosis. Our study also demonstrates important clinical value. The normal standard for potassium in the United States is 3.5–5.0 mmol/L. However, it is unknown whether this standard is used in critically ill patients with sepsis who are in a state of severe stress and whose physiological function has been significantly altered. In contrast, the present study, based on data from a large multicentre sample, found that patients with sepsis had the lowest risk of death when blood potassium was in the range of 4.03–4.22 mmol/L. Although further studies are needed to validate this finding, it may be useful for clinicians to consider this when developing treatment strategies and assessing the risk of disease severity in patients.

The main advantages of this study are as follows: (1) A larger sample size was used, so it has a higher statistical efficacy; (2) a generalised summation model and a two-piecewise linear model were also used, and the advanced algorithm can better determine the true association between serum potassium and mortality at 28 days in individuals with sepsis; and (3) a large number of sensitivity analyses were used, so the results have better robustness.

However, this study has significant shortcomings. First, because our study population was primarily from the United States, whether our findings can be applied to other nations must be evaluated in larger worldwide investigations. Second, because this was an observational study, confounding was unavoidable. Nonetheless, we rigorously adjusted for confounders and used a sensitivity analysis to assess the reliability of the results. Third, based on the inherent limitations of observational research, we identified correlations rather than causal relationships. Fourth, although we were able to consider measurable confounders, we were unable to do so for unmeasurable ones. Further clinical studies with larger populations and stronger levels of support are required to confirm our results. Finally, the time interval between the measurement of potassium levels and the diagnosis of sepsis was not available in the database, although potassium levels were recorded on the first day of ICU admission. In addition, we could not determine whether treatment relevant to the severity of sepsis had been administered at the time of serum potassium measurement (although in clinical scenarios, treatment should have been followed or synchronised with serum potassium measurement).

5. Conclusion

A U-shaped association was observed between serum potassium levels and 28-day mortality in septic patients. Lower or higher serum potassium levels were associated with increased risk of 28-day mortality in septic patients.

Ethics and informed consent statement

The MIMIC-IV database, which has become open online, was used in this investigation. The database was authorized by the institutional review boards of Beth Israel Deaconess Medical Center (2001-P-001699/14) in Boston, Massachusetts, and the Massachusetts Institute of Technology (0403000206). This study also passed the IRB examination of Guizhou Medical University Hospital. Because the data is accessible to the public and the patient's identity is unidentified, patient informed permission was canceled.

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Data accessibility

All of the data available in our articles has been saved in the MIMIC-IV database, which is freely accessible for analysis and downloading.

CRediT authorship contribution statement

Juan Tang: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Formal analysis, Data curation, Conceptualization. **Peiling Zhao:** Writing – original draft, Formal analysis, Data curation. **Yi Li:** Project administration, Conceptualization. **Shaowen Liu:** Visualization, Methodology. **Lu Chen:** Funding acquisition, Formal analysis, Data curation. **Yu Chen:** Validation, Conceptualization. **Rui Chen:** Software, Investigation, Formal analysis. **Yong Shen:** Software, Data curation. **Yongmei Liu:** Writing – review & editing, Writing – original draft.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Yongmei Liu reports financial support was provided by the Affiliated Hospital of Guizhou Medical University Doctoral Start-up Funding. Yu Chen reports financial support was provided by the 2021 hospital-level clinical research project of the Affliated Hospital of Guizhou Medical University. Lu Chen reports financial support was provided by the Science and Technology Fund Project of Guizhou Provincial Health Commission. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] M. Singer, C.S. Deutschman, C.W. Seymour, M. Shankar-Hari, D. Annane, M. Bauer, R. Bellomo, G.R. Bernard, J.-D. Chiche, C.M. Coopersmith, R.S. Hotchkiss, M.M. Levy, J.C. Marshall, G.S. Martin, S.M. Opal, G.D. Rubenfeld, T. van der Poll, J.-L. Vincent, D.C. Angus, The third international consensus definitions for sepsis and septic shock (Sepsis-3), JAMA 315 (2016) 801–810.
[2] J.A. Kempker, G.S. Martin, The changing epidemiology and definitions of sepsis, Clin. Chest Med. 37 (2016) 165–179.
[3] N. Zhang, Y. Liu, C. Yang, P. Zeng, T. Gong, L. Tao, X. Li, Association between smoking and risk of death in patients with sepsis: a systematic review and meta-analysis, Tob. Induc. Dis. 20 (2022) 65.
[4] K.E. Rudd, S.C. Johnson, K.M. Agesa, K.A. Shackelford, D. Tsoi, D.R. Kievlan, D.V. Colombara, K.S. Ikuta, N. Kissoon, S. Finfer, C. Fleischmann-Struzek, F. R. Machado, K.K. Reinhart, K. Rowan, C.W. Seymour, R.S. Watson, T.E. West, F. Marinho, S.I. Hay, R. Lozano, A.D. Lopez, D.C. Angus, C.J.L. Murray, M. Naghavi, Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study, Lancet 395 (2020) 200–211.
[5] Y. Chen, Y. Sang, S.H. Ballew, A. Tin, A.R. Chang, K. Matsushita, J. Coresh, K. Kalantar-Zadeh, M.Z. Molnar, M.E. Grams, Race, serum potassium, and associations with ESRD and mortality, Am. J. Kidney Dis. 70 (2017) 244–251.
[6] A.J. Viera, N. Wouk, Potassium disorders: hypokalemia and hyperkalemia, Am. Fam. Physician 92 (2015) 487–495.
[7] E. Kardalas, S.A. Paschou, P. Anagnostis, G. Muscogiuri, G. Siasos, A. Vryonidou, Hypokalemia: a clinical update, Endocr. Connect. 7 (2018) R135–R146.
[8] L. Coregliano-Ring, K. Goia-Nishide, É.B. Rangel, Hypokalemia in diabetes mellitus setting, Medicina (Kaunas) 58 (2022).
[9] Y. Wu, S. Huang, X. Chang, Understanding the complexity of sepsis mortality prediction via rule discovery and analysis: a pilot study, BMC Med. Inf. Decis. Making 21 (2021) 334.
[10] S.S. Sutton, J. Magagnoli, T.H. Cummings, J.W. Hardin, Melatonin use and the risk of 30-day mortality among US veterans with sepsis: a retrospective study, J. Pineal Res. 73 (2022) e12811.
[11] M.S. Ahmad, D. Ahmad, N. Medhat, S.A.H. Zaidi, H. Farooq, S.A. Tabraiz, Electrolyte abnormalities in neonates with probable and culture-proven sepsis and its association with neonatal mortality, J. Coll. Phys. Surg. Pak. 28 (2018) 206–209.
[12] X. Li, H. Shen, T. Zhou, X. Cao, Y. Chen, Y. Liang, T. Lu, J. He, Z. Dou, C. Liu, Y. Tang, Z. Zhu, Does an increase in serum FGF21 level predict 28-day mortality of critical patients with sepsis and ARDS? Respir. Res. 22 (2021) 182.

[13] S. Ge, S. Lin, L. Zhang, M. Zeng, The association of red blood cell distribution width to platelet count ratio and 28-day mortality of patients with sepsis: a retrospective cohort study, Therapeut. Clin. Risk Manag. 16 (2020).
[14] E. Karakike, E. Kyriazopoulou, I. Tsangaris, C. Routsi, J.-L. Vincent, E.J. Giamarellos-Bourboulis, The early change of SOFA score as a prognostic marker of 28-day sepsis mortality: analysis through a derivation and a validation cohort, Crit. Care 23 (2019) 387.
[15] J.H. Kim, D.-H. Jang, Y.H. Jo, G.J. Suh, W.Y. Kwon, J.H. Lee, J. Shin, I. Park, C.U. Lee, S.-M. Lee, Serum total carbon dioxide as a prognostic factor for 28-day mortality in patients with sepsis, Am. J. Emerg. Med. 44 (2021) 277–283.
[16] H. Tai, Z. Zhu, H. Mei, W. Sun, W. Zhang, Albumin-to-Fibrinogen ratio independently predicts 28-day mortality in patients with peritonitis-induced sepsis, Mediat. Inflamm. 2020 (2020) 7280708.
[17] Z. Xia, X. Huang, K. Chen, H. Wang, J. Xiao, K. He, R. Huang, X. Duan, H. Liu, J. Zhang, G. Xiang, Proapoptotic role of potassium ions in liver cells, BioMed Res. Int. 2016 (2016) 1729135.
[18] O. Vardeny, B. Claggett, I. Anand, P. Rossignol, A.S. Desai, F. Zannad, B. Pitt, S.D. Solomon, Incidence, predictors, and outcomes related to hypo- and hyperkalemia in patients with severe heart failure treated with a mineralocorticoid receptor antagonist, Circ. Heart Fail. 7 (2014) 573–579.
[19] M.J. Kim, C. Valerio, G.K. Knobloch, Potassium disorders: hypokalemia and hyperkalemia, Am. Fam. Physician 107 (2023) 59–70.
[20] A.R. Rodan, Potassium: friend or foe? Pediatr. Nephrol. 32 (2017) 1109–1121.
[21] J. Tromp, J.M. Ter Maaten, K. Damman, C.M. O'Connor, M. Metra, H.C. Dittrich, P. Ponikowski, J.R. Teerlink, G. Cotter, B. Davison, J.G. Cleland, M.M. Givertz, D.M. Bloomfield, M.H. van der Wal, T. Jaarsma, D.J. van Veldhuisen, H.L. Hillege, A.A. Voors, P. van der Meer, Serum potassium levels and outcome in acute heart failure (data from the PROTECT and COACH trials), Am. J. Cardiol. 119 (2017) 290–296.
[22] L.J. Engelhardt, F. Balzer, M.C. Müller, J.J. Grunow, C.D. Spies, K.B. Christopher, S. Weber-Carstens, T. Wollersheim, Association between potassium concentrations, variability and supplementation, and in-hospital mortality in ICU patients: a retrospective analysis, Ann. Intensive Care 9 (2019) 100.