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Lack of association between dysnatremia and length of hospitalization in patients with COVID-19: Evidence from a retrospective analysis

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Abstract

Background: COVID-19 has substantially affected global health. Previous studies have associated sodium abnormalities (Dysnatremia), including hyponatremia and hypernatremia, with higher rates of ICU admission, mechanical ventilation, and complications that may impede recovery and prolong hospitalization. This study evaluated the association between sodium abnormalities and length of hospitalization among patients with COVID-19.

Methods: This retrospective study included patients with PCR-confirmed COVID-19 between 2019 and 2021. Data were collected through reviews of medical records and laboratory findings and through telephone interviews with patients. Data were analyzed using SPSS version 18. Descriptive statistics were used to summarize the data, and chi-square tests, t-tests/Mann-Whitney tests, and Pearson/Spearman correlations were applied as appropriate. Logistic regression was used to assess associations, with $P < 0.05$ considered statistically significant.

Results: The study included 129 participants, with a male-to-female ratio of 54.3% to 45.7%. Hyponatremia was present in 44.2% (n = 57) of patients, whereas hypernatremia was observed in 5.4% (n = 7). Overall, 50.4% (n = 65) of patients had normal serum sodium levels. Spearman correlation analysis showed no significant association between serum sodium levels and length of hospital stay ($P = 0.789$). Similarly, Kruskal-Wallis analyses showed no significant differences in hospitalization duration according to age group, sex, diuretic use, kidney disease, type of intravenous fluid, serum magnesium, albumin, blood sugar, ICU stay, or ward stay (All $P > 0.05$). Chi-square analysis also showed no significant association between serum sodium and patient outcomes ($P = 0.342$), and analyses stratified by outcome confirmed the absence of statistical significance (All $P > 0.05$).

Conclusion: Despite previous reports of an association between sodium disorders and morbidity and mortality in patients with COVID-19, this study found no significant relationship between these variables. Further research is needed to examine the potential effects of sodium abnormalities on outcomes in patients with COVID-19.

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Introduction

The emergence of COVID-19, caused by the novel coronavirus SARS-CoV-2, has created substantial challenges for global health systems (1,2). Given its wide range of clinical presentations, from asymptomatic infection to severe and fatal disease, understanding the relationship between sodium disorders and disease progression in patients with COVID-19 is important for optimizing treatment strategies and improving patient outcomes (3,4).

Laboratory findings in hospitalized patients with COVID-19 frequently include elevated leukocyte counts, increased inflammatory markers such as CRP and ESR, and elevated D-dimer levels (1). Leukopenia may also occur in some cases. Chest imaging typically shows ground-glass opacities in the lungs, contributing to the overall clinical presentation of this infectious disease (2). Given the novel nature of COVID-19, no definitive cure currently exists. Therefore, preventive measures such as vaccination, home quarantine, and public health interventions have been implemented worldwide to control disease transmission and reduce its effects on populations and healthcare systems (3). Electrolyte imbalances, including hyponatremia, hypernatremia, hypokalemia, hyperkalemia, and hypocalcemia, have been associated with higher mortality rates among patients with COVID-19. These disorders complicate treatment and may substantially impair recovery, prolong hospitalization, and increase the overall disease burden (4). This study focuses on sodium disorders, specifically hyponatremia and hypernatremia. Hyponatremia is defined as a plasma sodium level below 135 mmol/L, whereas hypernatremia is defined as a plasma sodium level above 145 mmol/L. These abnormalities may substantially affect patient outcomes and require careful clinical monitoring and management (5-7). Research indicates that patients with COVID-19 and hyponatremia or hypernatremia have longer hospital stays, higher rates of ICU admission and ventilation, and a greater risk of septic shock. These sodium abnormalities are also associated with increased mortality and complications, emphasizing the importance of monitoring and managing electrolyte imbalances in COVID-19 care (8,9). Recent systematic reviews and meta-analyses (10-13) have quantified the prevalence of hyponatremia among patients with COVID-19. A comprehensive meta-analysis (11) of 52 studies reported a pooled hyponatremia prevalence of 25.8% among hospitalized patients with COVID-19, demonstrating the high frequency of sodium abnormalities in this population. Because COVID-19 remains an evolving disease with many uncertainties regarding its pathogenesis and treatment, this study investigated its effects on sodium balance and the relationship between sodium abnormalities and COVID-19 disease progression. A better understanding of these factors may support strategies to maintain electrolyte homeostasis, shorten hospitalization, and prevent hospitalization-associated complications. This knowledge may ultimately help reduce mortality and adverse outcomes among patients

with COVID-19. The primary objective was to evaluate the association between sodium abnormalities, including hyponatremia and hypernatremia, and length of hospitalization in patients with PCR-confirmed COVID-19. The study also aimed to determine the prevalence of hyponatremia and hypernatremia among hospitalized patients with COVID-19 and examine whether the severity of these abnormalities was associated with adverse clinical outcomes, including intensive care unit admission and the need for mechanical ventilation.

Methods

This retrospective cohort study included patients with PCR-confirmed COVID-19 admitted to Sayad Shirazi Hospital in Gorgan, Iran. All included patients tested positive for SARS-CoV-2 using a real-time PCR assay. The retrospective cohort design enabled evaluation of clinical and laboratory data, including sodium levels, and their associations with hospitalization outcomes.

Data were collected retrospectively by reviewing the hospital medical records of all eligible patients diagnosed between 2019 and 2021. Patients were classified according to serum sodium status into dysnatremia (Hyponatremia or hypernatremia) and normonatremia groups. Clinical outcomes, including mortality, length of hospital stay, and disease course, were compared between the two groups. To minimize confounding, the groups were frequency-matched by age and sex. When necessary, telephone interviews were conducted in addition to the medical record review to obtain further clinical information, including disease symptoms, treatment adherence, and postdischarge outcomes. All participants were informed of the study objectives, and written informed consent was obtained. Participants were assured that their personal information would remain confidential throughout the study. Each patient was assigned a unique code to ensure anonymity, and no personal identifiers were recorded in the dataset. Confidentiality was strictly maintained during data collection, analysis, and publication.

The inclusion criteria comprised patients with PCR-confirmed COVID-19. The exclusion criteria included heart failure, hypothyroidism, or chronic kidney disease diagnosed within the 12 months before admission. Patients who had used thiazide diuretics within the three months before hospitalization were also excluded. Patients were classified on the basis of laboratory data. The case and control groups were matched by age and sex to assess mortality, hospitalization duration, and disease progression.

Statistical analysis

Data were analyzed using SPSS version 18. Descriptive statistics, including means, standard deviations, and frequencies, were used to summarize continuous and categorical variables. The chi-square test was used to compare categorical variables between groups, whereas the independent t-test or Mann-Whitney U test was used for continuous variables, depending on data normality. Pearson or Spearman correlation coefficients were used to evaluate relationships between continuous variables. Logistic regression analysis assessed associations between sodium abnormalities and clinical outcomes after adjustment for potential confounders such as age, sex, and comorbidities. A p-value of less than 0.05 was considered statistically significant. Statistical tests were selected according to the data type and distribution and the need to control for confounding factors, thereby supporting accurate interpretation of the results.

Results

A total of 129 patients with PCR-confirmed COVID-19 were included. Of these, 57 patients (44.2%) had hyponatremia, 7 patients (5.4%) had hypernatremia, and 65 patients (50.4%) had normal serum sodium levels. Serum sodium was measured at admission and periodically during hospitalization, allowing patients to be classified accurately into the respective groups.

Table 1 presents the association between sodium disorders and hospitalization duration, together with demographic and clinical variables. Spearman correlation analysis showed no significant relationship between serum sodium levels and length of hospital stay (P = 0.789). Kruskal-Wallis analyses showed no significant differences in hospitalization duration according to age group, sex, diuretic use, renal disease, type of intravenous fluid, magnesium level, albumin level, or blood sugar level (All P > 0.05).

Table 2 summarizes the correlations between sodium disorders and patient outcomes. Chi-square analysis showed no significant association between serum sodium levels and outcomes, including recovery, death, transfer to another center, or personal satisfaction (P = 0.342). Analyses stratified by outcome category confirmed the absence of statistically significant differences among sodium-status groups (All P > 0.05).

Regarding ICU stay, 98 patients (76%) were admitted for less than 4 days, whereas 31 patients (24%) stayed for 4 days or more; serum sodium levels were not significantly associated with ICU length of stay (P = 0.508). Similarly, ward length of stay did not differ significantly according to sodium status: 95 patients (73.6%) stayed for less than 7 days, and 34 patients (26.4%) stayed for 7 days or more (P = 0.278).

Overall, these findings indicate that sodium abnormalities were not significantly associated with prolonged hospitalization or adverse clinical outcomes in this cohort of patients with COVID-19.

Table 1. Association between sodium disorders and hospitalization duration in patients with COVID-19

Variables	Frequency	Percentage (%)	*P*-value
Serum Sodium Level			
Normal	65	50.4	0.854
Hyponatremia	57	44.2	
Hypernatremia	7	5.4	
Age Group			
Under 45 years	22	17.1	0.697
45-74 years	75	58.1	0.566
More than or Equal to 75 years	32	24.8	0.705
Gender			
Male	70	54.3	0.885
Female	59	45.7	0.447
Diuretic Use			
Yes	12	9.3	0.733
No	117	90.7	0.777
Renal Disease			
Yes	16	12.4	0.668
No	113	87.6	0.928
Type of Serum			
Normal saline	60	46.5	0.707
Half saline	64	49.6	0.839
Ringer's solution	5	3.9	0.374
Magnesium Level			
Normal	124	96.1	0.157
Abnormal	5	3.9	0.903
Albumin Level			
Normal	92	71.3	0.545
Abnormal	37	28.7	0.753
Blood Sugar Level			
Normal	111	86	0.978
Abnormal	18	14	0.209
Length of stay in ICU			
Less than 4 days	98	76	0.508
4 days or more	31	24	0.611
Length of Hospitalization in the Ward			
Less than 7 days	95	73.6	0.278
7 days or more	34	26.4	0.931
Outcome of Patients			
Recovery	37	28.68	0.315
Death	84	65.11	0.662
Transfer to Another Center	5	3.87	0.949
Personal Satisfaction	3	2.32	-

Table 2. Correlation between sodium disorders and patient outcomes

Outcome of Patients	Serum Sodium Level						*P*-Value
	Normal		Hyponatremia		Hypernatremia		
	Frequency	Percent	Frequency	Percent	Frequency	Percent	
Recovery	21	16.27	14	10.85	2	1.55	0.342
Death	39	30.23	41	31.78	4	3.10	
Transfer to Another Center	2	1.55	2	1.55	1	0.77	
Personal Satisfaction	3	2.32	-	-	-	-	

Discussion

COVID-19 has placed a substantial burden on healthcare systems worldwide, with more than one million deaths since its emergence. Electrolyte imbalances, including sodium disorders such as hyponatremia and hypernatremia, have been associated with higher disease-related mortality and complication rates and therefore require close monitoring and management (9,14). This retrospective study examined the effect of sodium disorders on hospitalization duration among patients with COVID-19 at Sayad Shirazi Hospital in Gorgan from 2019 to 2021. The analysis included 129 hospitalized patients and was designed to improve understanding of the relationship between electrolyte imbalances and outcomes in patients with COVID-19.

This study found no statistically significant relationship between serum sodium levels and hospitalization duration among patients with COVID-19 (P = 0.789). Similarly, the qualitative serum sodium category (Normal, hyponatremia, or hypernatremia) was not significantly associated with hospitalization duration (P = 0.854). In contrast, a 2021 Italian study by Andrea Berni et al. found that hyponatremia at admission was associated with greater requirements for noninvasive ventilation and ICU transfer (P = 0.001 and P =0.007). Moreover, patients with hyponatremia were 2.7 times more likely to die than those with normal sodium levels or hypernatremia (15). These contrasting findings indicate that further research is needed to clarify the relationship between sodium abnormalities and the progression and outcomes of COVID-19.

In our study, 41 of the 57 patients with hyponatremia (71.9%) died during hospitalization, accounting for 48.8% of all deaths. Although mortality was numerically higher among patients with hyponatremia, the association between hyponatremia and mortality was not statistically significant (P = 0.342). These findings should therefore be interpreted cautiously, and larger prospective studies are needed to clarify the relationship between hyponatremia and mortality among patients with COVID-19. The findings are consistent with a 2021 Italian study by Martino et al., which reported a worse prognosis among patients with combined serum sodium abnormalities than among those with hyponatremia or hypernatremia alone. This cohort also had longer hospital stays (P = 0.031), a greater need for mechanical ventilation (P = 0.028), and higher rates of ICU transfer (P = 0.001) (16). Similarly, a 2020 Turkish study by Tezkan et al. found that electrolyte disturbances, particularly hyponatremia, were associated with poor outcomes among patients with COVID-19. Hyponatremia was present in 35.8% of participants, whereas no cases of hypernatremia were reported. In the present study, hyponatremia was found in 44.18% of patients and hypernatremia in 5.42%. Tezkan's study also showed that electrolyte disorders, including abnormalities in sodium, calcium, potassium, and chlorine, were associated with higher rates of ICU admission, a greater need for mechanical ventilation, and longer hospitalization (P < 0.001) (17). Collectively, these studies suggest that electrolyte imbalances, particularly sodium disorders, may predict adverse outcomes among patients with COVID-19.

Although the present study found no significant association between serum sodium levels and hospitalization duration, previous research has demonstrated the substantial effects of hyponatremia on patient prognosis and outcomes. These findings are consistent with a 2019 study by Frontera et al. in New York, which showed that patients with moderate-to-severe hyponatremia (Sodium levels below 130) were more likely to require mechanical ventilation (P = 0.001). The risk of encephalopathy was also estimated to be eight times greater among patients with hyponatremia than among those with hypernatremia. The study further reported a 38% increase in mortality associated with greater hyponatremia severity. However, hospitalization duration was not significantly correlated with hyponatremia severity (P = 0.381), consistent with the present findings (18).

In this study, serum sodium levels were not significantly associated with length of hospital stay or other clinical outcomes among patients with COVID-19. These findings contrast with several previous reports that identified hyponatremia as a common electrolyte disturbance in COVID-19 and associated it with higher risks of ICU admission, mechanical ventilation, and mortality. The absence of a significant relationship in our cohort may reflect differences in patient characteristics, sample size, or management protocols at our center. Strict exclusion criteria, including preexisting heart failure, kidney disease, hypothyroidism, and recent thiazide use, may also have limited variation in sodium disturbances and reduced their effects on outcomes. Our findings suggest that although sodium abnormalities are clinically important, their effects on hospitalization duration and immediate patient outcomes may be less pronounced in certain populations or under specific management strategies. Larger multicenter studies are needed to clarify the prognostic significance of sodium disorders in COVID-19 and reconcile these discrepancies with the previous literature.

These results support close monitoring and management of sodium abnormalities among patients with COVID-19. Further research is needed to develop targeted interventions and establish optimal electrolyte-management strategies for this population. A systematic review and meta-analysis by Rizki Akbar et al. (10) further supports the adverse effects of hyponatremia on outcomes among patients with COVID-19 and concluded that hyponatremia is associated with a poor prognosis. This observation is consistent with the present study, in which a considerable proportion of patients with hyponatremia (71.92%) died. The association between hyponatremia and adverse outcomes among patients with COVID-19 demonstrates the importance of electrolyte monitoring and management. Additional research should investigate the underlying mechanisms and develop targeted interventions to improve outcomes and reduce mortality.

Additional factors that contribute to electrolyte imbalances among patients with COVID-19 include malnutrition and inadequate oral intake, adverse medication effects, endocrine dysfunction caused by inflammation or direct viral effects, and impaired renal function, including acute kidney injury. Comprehensive monitoring and management strategies are needed to address these multifactorial disturbances.

Several limitations should be considered when interpreting these findings. First, the retrospective design may introduce bias and confounding that could affect the observed associations between sodium disorders and COVID-19 outcomes. Second, the relatively small sample may limit generalizability and reduce the statistical power to detect subtle but clinically important associations. Third, because this was a single-center study, the population may not reflect broader demographic or clinical diversity, and site-specific practices may have influenced the findings. Unmeasured or unadjusted confounders, including disease severity and specific treatments, may also have affected the observed relationships between sodium abnormalities and patient outcomes. Finally, although this study focused on sodium disorders, other electrolyte abnormalities may contribute to the progression and outcomes of COVID-19. Larger multicenter studies that comprehensively assess electrolyte disturbances are needed to address these limitations and provide stronger evidence regarding the clinical significance of sodium disorders among patients with COVID-19.

Future research should include multicenter studies involving patients from diverse backgrounds to improve the generalizability of the findings. Larger sample sizes are needed to increase statistical reliability and identify subtle relationships between sodium disorders and COVID-19 outcomes. Research should also examine electrolytes other than sodium, including potassium, magnesium, and calcium, to clarify how combined abnormalities may affect disease progression. Prospective studies could follow patients over time, reduce potential bias, and evaluate whether correcting these abnormalities improves recovery and overall outcomes.

Despite the absence of a significant association between sodium abnormalities and short-term hospitalization outcomes in this study, continuous monitoring of electrolyte levels remains important for patients with COVID-19. Prompt identification and management of sodium and other electrolyte abnormalities may prevent complications, support recovery, and improve patient safety. Clinicians should remain vigilant, particularly when treating patients with severe disease or multiple comorbidities, and use individualized strategies to correct electrolyte disturbances when necessary.

Conclusion

In this study, sodium abnormalities were not significantly associated with length of hospital stay or key clinical outcomes among patients with COVID-19. Although previous studies have linked dysnatremia to adverse outcomes, our findings suggest that sodium abnormalities may have a limited effect on immediate hospitalization outcomes under the management protocols used in this cohort. These results support individualized patient monitoring and suggest that routine correction of mild sodium disturbances may not substantially alter short-term clinical outcomes. Larger multicenter studies involving more diverse populations are needed to clarify the prognostic role of sodium disorders in COVID-19 and guide evidence-based management.

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Ethical Statement

The research was conducted in accordance with the principles of the Declaration of Helsinki. The institutional ethics committee of Golestan University of Medical Sciences approved all study protocols. All procedures complied with the standards of Golestan University of Medical Sciences. The study was approved in accordance with the ethics committee guidelines of the Faculty of Medicine, Golestan University (IR.GOUMS.REC.1400.419).

Conflicts of Interest

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Amirhossein Parmah, Taraneh Esmaeili, Majid Dastorani, Saeid Amirkhanlou. Data curation: Amirhossein Parmah. Formal analysis: Taraneh Esmaeili, Majid Dastorani. Investigation: Amirhossein Parmah. Methodology: Saeid Amirkhanlou. Project administration: Saeid Amirkhanlou. Supervision: Saeid Amirkhanlou. Validation: Majid Dastorani, Saeid Amirkhanlou. Visualization: Taraneh Esmaeili, Majid Dastorani, Saeid Amirkhanlou. Writing-Original draft: Ebrahim Kouhsari, Amirhossein Parmah, Taraneh Esmaeili, Majid Dastorani, Saeid Amirkhanlou. Writing-Review and Editing: Majid Dastorani, Ebrahim Kouhsari, Saeid Amirkhanlou. All authors read and approved the final version of the manuscript.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request and in accordance with ethical guidelines.

Use of Artificial Intelligence

ChatGPT (OpenAI; GPT-6) was used to assist in language editing, improve clarity, and refine the scientific presentation of the manuscript. The authors reviewed and approved the final content and take full responsibility for the manuscript.

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