Research Paper

Prevalence of Hyponatremia and its Association with Variabilities Related to Urinary Tract Infection in Fevered Hospitalized Patients with Urinary Tract Infection at Allameh Bohlol Gonabadi Hospital in Gonabad City in Iran

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ABSTRACT

Aims Urinary tract infection (UTI) is the most common urinary system disease, which is considered a contributing factor to renal failure. The present study aimed to evaluate the significance of hyponatremia in the diagnosis and treatment of hospitalized patients with UTI at Allameh Bohlol Gonabadi Hospital in Gonabad City, Iran.

Materials & Methods This cross-sectional study was conducted on 384 collected samples from patients diagnosed with UTI from 2013 to 2017. Demographic and clinical data of the patients were recorded using a checklist. The samples were divided into two groups: hyponatremia and non-hyponatremia, and variables including leukocyte count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and duration of fever were examined. After sample collection, the data were analyzed using the SPSS (version 20) software and Chi-squared and Mann-Whitney statistical tests.

Findings In this study, 384 individuals with febrile UTI were examined, of which 71.6% were female and 28.4% were male. Hyponatremia was present in 57.6% of individuals with UTI. No significant correlation was found between age, gender, and hyponatremia (P=0.189 and P=0.238, respectively). Patients with hyponatremia had increased leukocyte count, elevated ESR, and positive CRP. A significant association was observed between hyponatremia and CRP, ESR, leukocyte count, and duration of fever (P<0.001).

Conclusion The results demonstrated that hyponatremia may serve as a marker in the diagnosis of febrile renal infections, and its presence at the time of diagnosis suggests a likelihood of pyelonephritis and severe inflammation.

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Derafshi R, et al. Prevalence of Hyponatremia and Association with Variabilities Related to Urinary Tract Infection in Fevered Hospitalized Patients with Urinary Tract Infection at Allameh Bohlol Gonabadi Hospital in Gonabad City in Iran. Intern Med Today. 2023; 29(2): 116-121.

مقاله پژوهشی

بررسی شیوع هیپوناترمی و ارتباط آن با متغیّرهای مرتبط با عفونت ادراری در بیماران مبتلا به عفونت ادراری تب‌دار بستری در بیمارستان علّامه بهلول گنابادی شهر گناباد

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چکیده

هدف عفونت مجاری ادراری شـایع‌ترین بیماری دسـتگاه ادراری این بیماری به‌عنوان عاملی برای نارسـایی کلیه در نظر گرفته می‌شـود. این مطالعه به‌منظور ارزیابی اهمیت هیپوناترمی در تشـخیص و درمان بیماران مبتلا به عفونت ادراری بسـتری در بیمارسـتان علامه بهلول گنابادی انجام شده است.

مواد و روش‌ها مطالعه حاضر یک مطالعه مقطعی اسـت که بر روی ۳۸۴ نمونه جمع‌آوری‌شده از بیماران با تشخیص عفونت ادراری در طی سال‌های ۱۳۹۲-۱۳۹۶ انجام شد. اطلاعات دموگرافیک و بالینی بیماران با اسـتفاده از چک‌لیست ثبت گردید. نمونه‌ها به دو گروه هیپوناترمی و غیرهیپوناترمی تقسیم می‌شوند و در هر گروه متغیّرهای لکوسیتوز، CRP، ESR و طول مدت تب بررسی می‌گردند. پس از جمع‌آوری نمونه‌ها، داده‌ها با اسـتفاده از نرم‌افزار SPSS نسـخه ۲۰ و آزمون‌های آماری chi-squared و Mann-Whitney تجزیه‌وتحلیل شدند.

یافته‌ها در این مطالعه تعداد ۳۸۴ بیمار بسـتری مبتلا به عفونت ادراری تب‌دار بررسـی شـدند که ۷۱/۶ درصد افراد موردمطالعه زن و ۲۸/۴ درصد مرد بودند. ۵۷/۶ درصد افراد دارای عفونت ادراری، هایپوناترمی داشتند. بین متغیّرهای سن و جنس با هایپوناترمی ارتباط معنی‌داری مشـاهده نشـد (به ترتیب ۰/۱۸۹=p و ۰/۲۳۸=p). در این مطالعه، بیماران دارای هیپوناترمی، دارای لکوسـیتوز، ESR افزایش‌یافته و CRP مثبت بودند و بین هایپوناترمی و CRP، ESR، لکوسـیتوز و طول مدت تب ارتباط معنی‌داری مشـاهده شـد (۰/۰۰۱>p).

نتیجه گیری نتایج این مطالعه نشـان داد بین هیپوناترمی با لکوسـیتوز،CRP و ESR در بیماران مبتلا به عفونت ادراری ارتباط آماری معنی‌داری وجود داشت و می‌توان هیپوناترمی را به‌عنوان یک مارکر تشخیصی در عفونت‌های ادراری در نظر گرفت.

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Introduction

Urinary tract infection (UTI) is the most common urinary tract disease. This disease is considered a cause of kidney failure. Since most of the clinical symptoms in these patients are vague, a lack of diagnosis and treatment in the long term causes complications, such as high blood pressure, kidney failure, and Gastroesophageal reflux. Therefore, timely diagnosis and correct treatment of this disease should be considered important, and special attention should be paid to prevent related complications. Pyelonephritis is an upper UTI, a potentially fatal infection that often leads to scarring of the kidney tissue and can lead to high blood pressure and even kidney failure. In young children, due to the non-specificity of the symptoms of kidney involvement and the unreliability of common laboratory indicators, such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and leukocyte count, distinguishing acute pyelonephritis from lower UTI is a diagnostic problem [1]. Compared to adults, children are more at risk of acute kidney injury and scarring in the kidneys after UTIs [2,3]. During the acute phase of the disease, it is challenging to distinguish lower UTI from acute pyelonephritis. Hyponatremia (reduction of serum sodium level) is an electrolyte disorder that occurs as a result of the imbalance between water and sodium in the body and is defined by a serum sodium level of less than 135 meq/L. Although most patients with hyponatremia are asymptomatic, it can lead to some medical emergencies, such as convulsions, coma, respiratory arrest, and permanent brain damage, thus worsening the prognosis of the disease. On the other hand, hypertonic saline is an effective and potential treatment for hyponatremia. This condition occurs not only in chronic diseases but also in some acute diseases [4-6]. Hyponatremia can be seen as a result of using cytotoxic drugs, children's respiratory infections, meningitis, heart infarction, and Kawasaki disease [7-11]. Regarding hyponatremia and its prevalence in hospitalized patients, there are different statistics, such that Mokhtari et al. reported the prevalence of hyponatremia at 60.5% in the ICU of Imam Hossein Hospital in Tehran, Iran, and 18.5% in the pediatric department of Beharloo Hospital in Tehran [10, 12]; they indicated obvious differences. Different mechanisms have been named to cause hyponatremia. The first mechanism is the inappropriate secretion of antidiuretic hormone (ADH) due to cytokines, such as interleukin-1-β (IL-1β), IL-6, and tumor necrosis factor (TNF), which reduce the formation and function of sodium channels and sodium/potassium pumps [13, 14]. The second mechanism of dysfunction is due to severe inflammation in the proximal tubule and collecting ducts.

The third mechanism is pseudo hypoaldosteronism (PHA) in children with acute pyelonephritis, which is due to tubular unresponsiveness to aldosterone [14-16]. In fact, PHA can be observed alone in both pyelonephritis and obstructive uropathy. As a result of the presence of an anomaly in the kidney, an increase in intratubular pressure causes secondary PHA [11, 16]. Some investigations have demonstrated that people with fevered diseases like pneumonia, meningitis, encephalitis, or Kawasaki disease had hyponatremia at the beginning of hospitalization [17]. However, there are few studies on the association between urinary infection and hyponatremia, and the relationship between bacterial infections and electrolyte disorders, such as hyponatremia, is not fully known. Therefore, the present study aimed to evaluate the importance of hyponatremia in patients with UTI hospitalized in Allameh Bohlol Gonabadi Hospital in Ghonabad City, Iran.

Materials and Methods

This cross-sectional study included 384 hospitalized patients suffering from UTI at Allameh Bahloul Hospital in Gonabad City from 2013 to 2017. Patients had a fever above 37.5°C and a positive result in urine culture, with no history of heart, kidney, or liver diseases and no severe vomiting or chronic diarrhea. The sample size was calculated using previous studies with 95% confidence and a 5% error margin. Demographic and clinical information of patients was recorded using a checklist. The samples were divided into two groups: hyponatremia and non-hyponatremia, and leukocyte count, CRP, ESR, and duration of fever variables were analyzed in each group. In this investigation, the nurse measured the patient's body temperature every six hours using a mercury thermometer in the axillary position, which was measured for 3-5 min and recorded in the patient's file. After collecting the samples, the data were analyzed using the SPSS (version 20) software, as well as chi-squared and Mann-Whitney statistical tests. All patient information was coded and remained confidential.

Results

This study examined 384 samples collected from hospitalized patients whose urine cultures were positive. The majority of participants were women (71.6%), and the average age and standard deviation of the studied population were 40.20 and 32.14 years, respectively. The lowest sodium level was 106, and its highest level was 158, with an average of 134.44 (meq/L). Among the studied population, the average WBC level was 10.49 ($\times 10^3$ µl), with a minimum of 2.4 and a maximum of 76 ($\times 10^3$ µl). The minimum duration of fever in the examined patients was 2 h, and the maximum was 26 h, with an average of 11.17 h.

Among the studied subjects, 194 (50.50%) had high ESR, and 190 (49.50%) had normal ESR. Additionally, 242 (63%) had positive CRP, while 142 (37%) had a normal range of this factor. A total of 221 (57.6%) of the subjects had hyponatremia, and 163 (42.40%) did not have hyponatremia. In this study, there was a statistically significant relationship between hyponatremia and

leukocyte count (P=0.001), CRP (P=0.001), and ESR (P<0.001) in patients with UTI (Table 1).

Moreover, a significant relationship was observed between hyponatremia and duration of fever in patients with UTI (P<0.001). However, there was no statistically significant relationship between hyponatremia and gender (P=0.189) or age (P=0.238) in patients with UTI (Table 2).

Table 1. Relationship of hyponatremia with leukocyte, CRP, ESR, and gender in patients with UTI

		Hyponatremia		P-value Chi-Squared
		Yes Frequency (%)	No Frequency (%)	
CRP	Positive	181 (81.9)	61 (37.4)	0.001
	Negative	40 (18.1)	102 (62.6)	
ESR	High	138 (62.4)	56 (34.4)	<0.001
	Normal	83 (37.6)	107 (65.6)	
Leukocyte	Yes	98 (44.3)	46 (28.2)	0.001
	No	123 (55.7)	117 (71.8)	
Gender	Male	57 (52.3)	52 (47.7)	0.189
	Female	164 (59.6)	111 (40.4)	

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Table 2. Relationship between age and duration of fever with hyponatremia in patients with UTI

	Hyponatremia		P-value Mann-Whitney
	Yes	No	
Age (Year) Mean±SD	44.37±32.80	41.6±31.24	0.238
Length of Fever (Hour) Mean±SD	13.56±5.74	7.95±3.54	<0.001

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Discussion

Urinary tract infections in hospitalized patients are one of the factors contributing to morbidity and mortality. Approximately 8.3 million visits to physicians are made annually in the United States due to these infections, and 150 million patients with infections are diagnosed worldwide. Among hospitalized patients, UTIs are the most common form of hospital infections, and in special care units, their rate reaches 25%, accounting for 30% of total hospital infections [18, 19].

In the present study, 384 people with fevered UTI were investigated; 71.6% of the studied individuals were women, and 28.4% were men, with ages ranging from newborn to 98 years old. The average age was 40.20 years, and 57.6% of people with UTI had hyponatremia. Among those with hyponatremia, 52.3% were men, and 59.6% were women. Among non-hyponatremic individuals, 47.7% were men and 40.4% were women. In another study, 2.8% of children with UTI had hyponatremia, which was not related to urinary tract abnormalities [20]. In the present work, there was no significant relationship between age and gender variables with hyponatremia. In Mazzoni et al.'s study, a significant relationship was found between gender and age variables with hyponatremia, indicating that

patients with hyponatremia were significantly younger than those without this condition [21]. The average duration of fever among hyponatremic subjects was 13.56±5.74 h, while among non-hyponatremic subjects, it was 7.95±3.54 h, demonstrating a relationship between hyponatremia and duration of fever, consistent with the study by Kompani et al. [22]. Meanwhile, in the study by Hasegawa et al., no significant relationship was found between hyponatremia and the severity of UTI in children [17]. In the study by Park et al., the serum sodium level was reported to be significantly lower. Additionally, serum sodium had an inverse relationship with the number of white blood cells and ESR. Their study indicated that hyponatremia and high levels of CRP can be used as two independent factors in predicting the occurrence of kidney damage [4]. In another study examining hyponatremia in children with respiratory infections, male gender and increased CRP levels were identified as independent risk factors for developing hyponatremia [23].

These results are similar to the findings of the present research, as patients with hyponatremia had elevated leukocyte counts, high ESR, and positive CRP. Among those with hyponatremia, 44.3% had leukocytes, and among non-hyponatremic subjects, 28.2% had leukocytes. A total of 63% of the studied subjects had

positive CRP. Among those with hyponatremia, 81.9% had positive CRP, and among non-hyponatremic individuals, 37.4% had positive CRP. In total, 50.5% of the studied subjects had high ESR. Among those with hyponatremia, 62.4% had high ESR, and 37.6% had a normal range of this factor. Among non-hyponatremic individuals, 34.4% had high ESR, and this factor was in the normal range for 65.6% of the subjects.

Hyponatremia in infections is related to various factors, including the infection itself, kidney damage, drug use, malnutrition, or critical body conditions related to various diseases. Understanding the predisposing factors of hyponatremia is essential for proper diagnosis and treatment. It should be emphasized that most infection-related deaths occur due to respiratory or circulatory failure, not neurologic damage associated with hyponatremia. Therefore, large-scale prospective trials are needed to prove the causal relationship between hyponatremia and the worsening of the patient's infectious conditions. Until then, in patients with infections, hyponatremia should be interpreted as an indirect marker of disease severity, a potential direct marker of other comorbidities, or a predictor of poor prognosis in these conditions. A low serum sodium level is a significant predictor of more severe disease, as reflected by a higher CRP, a more extended hospital stay, and a higher rate of renal parenchymal involvement.

Conclusion

The results of this study showed that there was a statistically significant relationship between hyponatremia and leukocyte count, CRP, and ESR in patients with UTI.

Therefore, hyponatremia can be considered a diagnostic marker in UTI.

Ethical Considerations

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