Association of Fractional Excretion of Uric Acid in Patients Presenting with Hyponatremia

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Hyponatremia, fractional excretion of uric acid (FEUA), Fractional excretion of sodium (FENa), SIADH

ABSTRACT
Hyponatremia is a prevalent electrolyte imbalance observed in hospitalized patients, with the syndrome of inappropriate antidiuresis (SIADH) being the most common underlying cause. Accurate clinical assessment of a patient's volume status, which is crucial for diagnosing hyponatremia, is often challenging and imprecise. In this study a total of 83 patients with hyponatremia are studied. This study aims to evaluate various diagnostic tools to enhance the accuracy of differential diagnosis for hyponatremia. Additionally, it seeks to investigate the diagnostic potential of fractional excretion of uric acid (FEUA) over fractional excretion of sodium (FENa) in patients presenting with hyponatremia

1. Introduction

When the serum sodium level drops below 135 MEq/L, it is known as hyponatremia. Serum osmolality decreases in true hyponatremia, which may be further subdivided into euvolemic, hypovolemic, and hypervolemic forms (7). In euvolemic hyponatremia, (U-Na > 20meq/l with SIADH) the amount of sodium remains the same but total body water increases. In the case of hypervolemic the U-Na < 20meq/l, and in the case of hypovolemic hyponatremia U-Na > 20meq/l (8).
Hyponatremia due to decreased effective arterial blood volume (EABV) follows hyponatremia caused by syndrome of inappropriate antidiuretic hormone secretion (SIADH), the most prevalent cause of hyponatremia. The diagnostic value and reference standard for distinguishing between euvolemic hyponatremia in SIAD (U-Na>30mmol/liter) and decreased EABV in hypovolemic and hypervolemic disorders (U-Na<30mmol/liter) is the sodium (Na) concentration as determined from spot urine (urinary N-excretion [U-Na] or fractional urine Na excretion [FE-Na]). Because diuretic treatment inhibits Na reabsorption and increases renal Na excretion (20), the U-Na and FE-Na are not very useful as diagnostic tools. What is meant by "fractional excretion of uric acid" is the proportion of urate that is filtered out in urine by the glomeruli. A dependable way to detect hyponatremia instances based on volume status is by examining the fractional urine excretion of uric acid (FeUa), even when diuretics are used. Elevated FeUa levels exhibit high sensitivity and specificity, effectively pinpointing hyponatremic patients experiencing volume expansion attributed to the syndrome of inappropriate antidiuretic hormone (SIADH)

Aim:

- To assess the correlation between hyponatremia and fractional uric acid excretion in patients.

Objective:

- In order to diagnose and categorize hyponatremia, it is necessary to analyze the following indicators: urine osmolality, urinary salt concentration, FENA, and FEUA.
- In order to find out how well FEUA can diagnose euvolemic hyponatremia.
- For the purpose of establishing whether FEUA has higher specificity than FENA in identifying cases of euvolemic hyponatremia.

Inclusion criteria:

1. Subjects aged >18 years with serum sodium <135 meq/I.

Exclusion criteria:

1. Individuals suffering from congestive heart failure are not eligible.

2. Patients who are suffering from hypothyroidism are also excluded.
3. Patients with liver failure are not included in this study.
4. After receiving clearance from the Institutional Ethics Committee (IHEC) and obtaining informed consent from every patient, the current research was conducted.

2. Methodology

A total of 83 adults were included in this research who had hyponatremia (< 135 mEq/L), urine osmolality >100 mOsm/kg, and serum osmolality <280 mOsm/kg.Hydrochlorothiazide, metolazone, indapamide, furosemide, and potassium canrenoate are examples of oral diuretics that patients were required to take for at least three months.
The information was gathered at a pre-study meeting in the form of a proforma. Two liters of isotonic saline were given over the course of 24 hours as a fluid challenge test in situations where the results were ambiguous. Along with spot urine samples, blood samples were taken in the morning to assess sodium (Na), potassium (K), uric acid (UA), glucose, blood urea nitrogen (BUN), and creatinine levels. The laboratory tests were performed one day after the last oral dosage of the diuretic drugs.
From these numbers, we were able to determine the fractional excretion of potassium (FEK), uric acid (FEUA), and sodium (FENa). The formula is used to compute the values:

1. FRACTIONAL EXCRETION OF SODIUM:

- FENA = 100 × urinary sodium × plasma creatinine

  Plasma sodium × urinary creatinine

2. FRACTIONAL EXCRETION OF URIC ACID:

- FEUA = 100 × urine uric acid × plasma creatinine

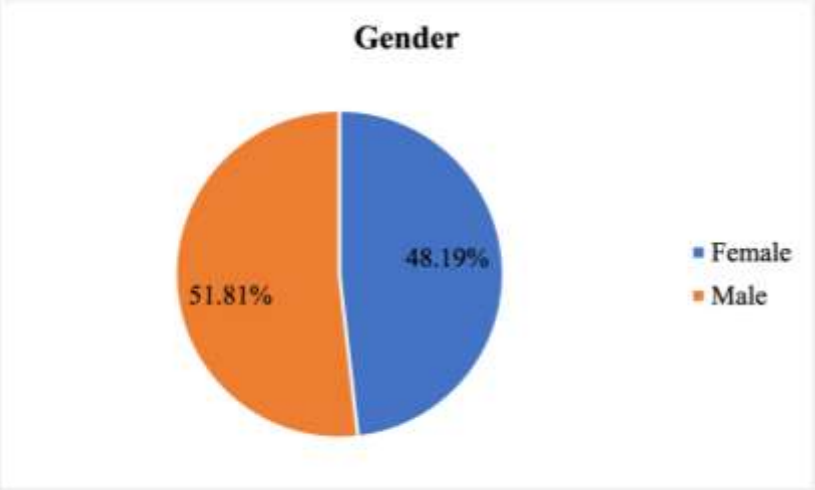
  Plasma uric acid x urine creatinine

To conduct the statistical study, STATA 11.2 was used. Hyponatremia, SIADH, diuretics, urine sodium, FENA, and FEUA are among the demographic information examined. When looking at the mean and standard deviation of the FENA and FEUA, we used the non-parametric Mann-Whitney t-test to see whether there was a significant difference. To examine the link between age distribution and hypernatremia, gender and hyponatremia, hyponatremia severity and vomiting, loose stools, etc., the chi-square test or distribution-free test was used. All of these metrics are shown as percentages and frequencies. A p-value less than 0.05 is deemed to have statistical significance.

3. Results

Table 1: Shows the demographic breakdown of the research participants

Variables	**No of cases**	**Percentage**
Age (Mean ± SD)	60.36 ± 9.54	
Gender		
Female	**40**	**48.19%**
Male	**43**	**51.81%**
Total	**83**	**100.00%**

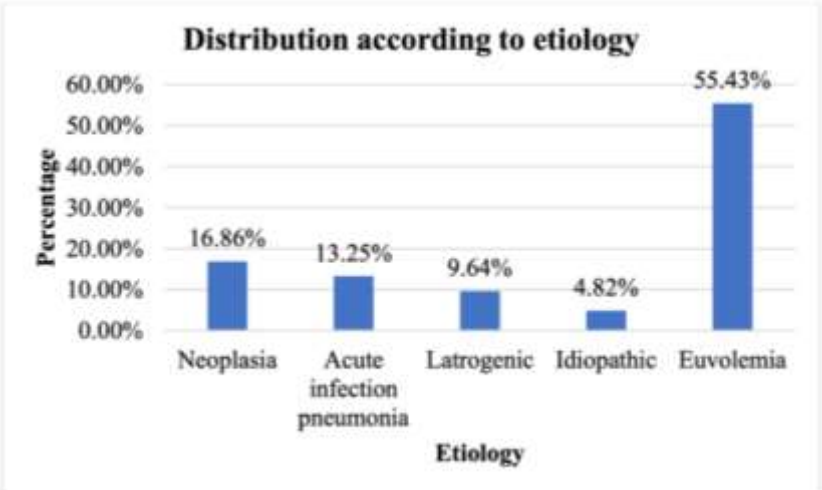


Graph-1: Gender distribution in the study group

In a study investigating the association of fractional excretion of uric acid (FEUA) in patients presenting with hypernatremia, demographic data revealed a total of 83 cases with a mean age of 60.36 years (±9.54 SD). The gender distribution among the patients showed that 48.19% were female and 51.81% were male.

Table 2: Distribution according to etiology

Etiology SIAD	No of cases	Percentage
Neoplasia	14	16.86%
Acute infection pneumonia	11	13.25%
Latrogenic	8	9.64%
Idiopathic	4	4.82%
Euvolemia	46	55.42%



Graph 2: Distribution according to etiology

The distribution of etiologies among patients with hypernatremia and associated fractional excretion of uric acid (FEUA) varied significantly in the study. Euvolemia accounted for the largest proportion at 55.42%, comprising 46 cases. Neoplasia followed with 16.86%, representing 14 cases. Acute infection pneumonia constituted 13.25% with 11 cases, while iatrogenic causes contributed 9.64%, totaling 8 cases. Idiopathic cases were the smallest category at 4.82%, with 4 cases identified.

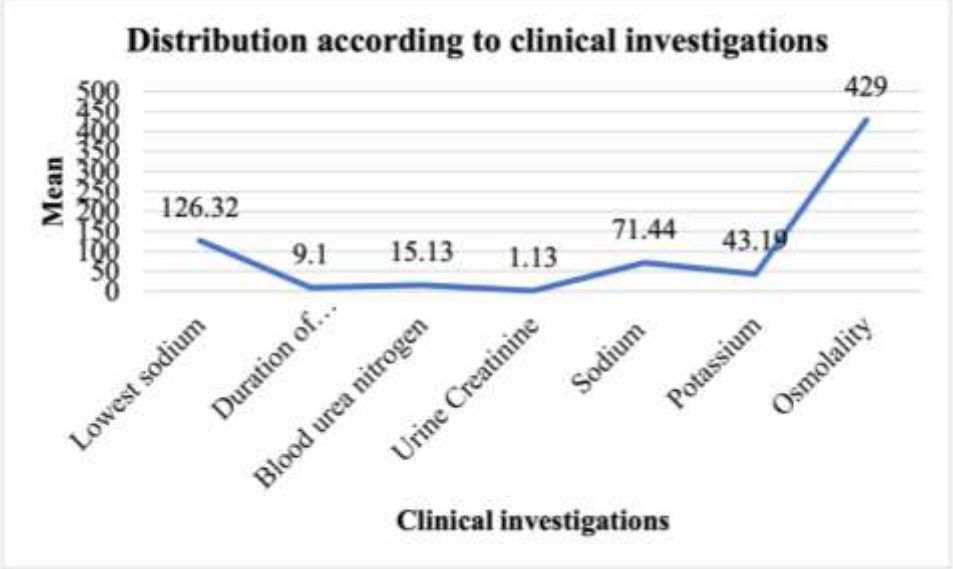
Table 3: Distribution according to current diuretic therapy

	No of cases	**Percentage**
Current diuretic thearapy	31	37.35%

In the study, 37.35% of patients with hypernatremia were currently receiving diuretic therapy.

Table 4: Distribution according to clinical investigations

Clinical investigations	**Mean ± SD**
Lowest sodium	126.32 ± 0.12
Duration of hyponatrimia	9.1 ± 1.70
Blood urea nitrogen	15.13 ± 2.39
Urine Creatinine	1.13 ± 0.09
Sodium	71.44 ± 3.22
Potassium	43.19 ± 3.50
Osmolality	429 ± 30



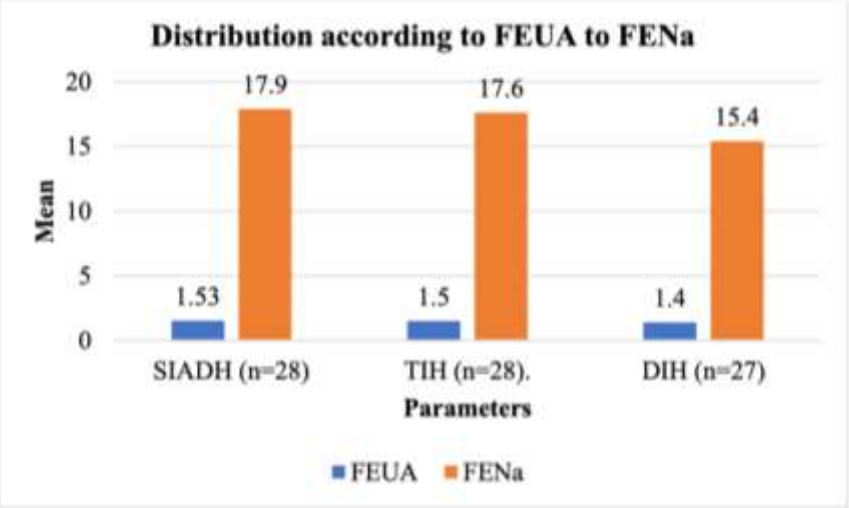
Graph 3: Distribution according to clinical investigations

In the study of hypernatremia patients, clinical investigations revealed distinct mean values for various parameters. These included the lowest sodium level, which was measured at 126.32 ± 0.12 mmol/L, indicating minimal variability observed. The duration of hyponatremia averaged 9.1 ± 1.70 days, reflecting the period over which sodium levels were monitored. Blood urea nitrogen levels were recorded at 15.13 ± 2.39 mmol/L, while urine creatinine levels were measured at 1.13 ± 0.09 mmol/L. Sodium and potassium concentrations showed distinct averages, with sodium at 71.44 ± 3.22 mmol/L and potassium at 43.19 ± 3.50 mmol/L. Osmolality, which measured solute concentration, averaged 429 ± 30 mOsm/kg.

Table 5: Distribution as a function of sodium and uric acid fractional excretion.

Sr. No.	Parameter	SIDAH (n=28) **Mean ± SD**	TIH (n=28) **Mean ± SD**	DIH (n=28) **Mean ± SD**	**p-value**
1	FEUA	1.53 (0.6)	1.5 (0.6)	1.4 (0.7)	NS
2	FENa	17.9	17.9	15.4	0.05

The table shows the distribution of fractional excretion of uric acid (FEUA) and fractional excretion of sodium (FENa) among three types of hyponatremia: SIADH, TIH, and DIH. The mean FEUA values were 1.53 ± 0.6 for SIADH, 1.5 ± 0.6 for TIH, and 1.4 ± 0.7 for DIH. The p-value for FEUA is not significant (NS), indicating no significant difference between the types of hyponatremia. In contrast, the mean FENa was 17.9 for both SIADH and TIH, while DIH had a lower mean FENa of 15.4. When comparing DIH to SIADH and TIH, we find that DIH has lower FENa levels (p = 0.05), suggesting a statistically significant difference. Thus, FEUA levels are consistent across all types, but FENa varies significantly, highlighting DIH as having lower sodium excretion compared to SIADH and TIH.

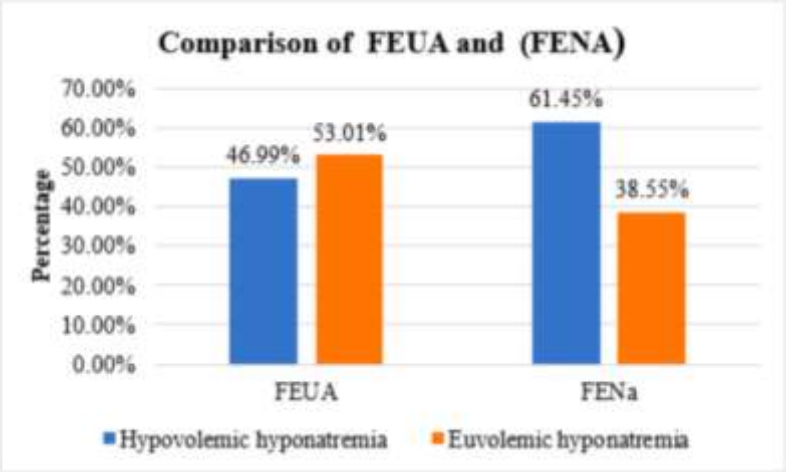


Graph 4: Distribution according to FEUA to FENa.

Table 6: Comparison of fractional sodium and uric acid excretion rates.

Hyponatremia	FEUA		FENa		P-value
	No of cases	Percentage	No of cases	Percentage	
Hypovolemic hyponatremia	39	46.99%	51	61.45%	0.05
Euvolemic hyponatremia	44	53.01%	32	38.55%	
Total	83	100.00%	83	100.00%	

In Table 6, we can see how hypovolemic and euvolemic hyponatremia compare in terms of fractional excretion of uric acid (FEUA) and sodium (FENa). Among the 83 total cases, hypovolemic hyponatremia accounted for 39 cases (46.99%) with a mean FENa of 51 cases (61.45%). In contrast, euvolemic hyponatremia comprised 44 cases (53.01%) with a mean FENa of 32 cases (38.55%). Cases with hypovolemic hyponatremia have a greater FENa than euvolemic hyponatremia, as shown by the statistically significant difference between the two groups (p-value = 0.05). There was no p-value provided for FEUA, so the statistical significance for FEUA is not determined. Overall, this analysis highlights a significant difference in sodium excretion between the two types of hyponatremia.



Graph 5: Comparison of the fractional excretion of sodium (FENa) and uric acid (FEUA)

4. Conclusion

Hyponatremia is a commonly observed issue in clinical practice and significantly contributes to patient morbidity and mortality. Identifying the underlying cause and providing suitable treatment can greatly enhance patient outcomes. Clinicians must be well-versed in the latest treatment guidelines and understand the proper use of vaptans to ensure accurate diagnosis and effective management of this condition.

However, Fractional excretion of uric acid (FE-UA) provides a highly specific means to diagnose the syndrome of inappropriate antidiuretic hormone secretion (SIADH). When FE- UA is combined with urinary sodium (U-Na) levels, it significantly enhances the diagnostic accuracy for hyponatremic patients, irrespective of whether they are receiving diuretic therapy.

The complexity of this condition can be better understood by applying fundamental physiological principles to the various subtle variations observed. By adopting this approach, we aim to demystify hyponatremia and prevent misdiagnosis and improper treatment of the diverse array of diseases associated with it. This includes exploring related to conditions such as renal salt wasting (RSW) that can occur even in the absence of hyponatremia.

In conclusion, incorporating the assessment of fractional excretion of uric acid (FEUA) into the evaluation of hyponatremia offers crucial diagnostic insights and enhances patient care. Understanding how uric acid excretion (E-UA) correlates with hyponatremia allows clinicians to personalize treatment strategies according to the specific pathophysiological mechanisms involved. Therefore, this approach aims to optimize therapeutic interventions, leading to improved clinical outcomes for patients.

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