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Original Research Article

Electrolyte Disturbances in Patients Receiving Long-Term Diuretic Therapy: A Prospective Cross-Sectional Study

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Abstract:

Background: Diuretics are commonly prescribed for hypertension, heart failure, chronic kidney disease, and liver cirrhosis. Long-term use is frequently associated with electrolyte disturbances that may increase morbidity and mortality.

Objective: To determine the prevalence and pattern of electrolyte abnormalities among patients receiving long-term diuretic therapy and to evaluate associated risk factors.

Methods: This prospective cross-sectional study was conducted at PMCH, Patna, from April 2025 to December 2025. Ninety-one adult patients on diuretics for ≥3 months were included. Serum electrolytes were analyzed. Statistical analysis was performed using SPSS v25. Chi-square test and independent t-test were applied. A p-value <0.05 was considered significant.

Results: Electrolyte disturbances were observed in 62 (68.1%) patients. Hypokalemia (34.1%) and hyponatremia (29.7%) were most common. Loop diuretics were significantly associated with hypokalemia (p=0.002), and thiazides with hyponatremia (p=0.01). Combination therapy showed the highest overall disturbance rate (p=0.004).

Conclusion: Electrolyte imbalance is common in long-term diuretic users. Regular monitoring is essential, particularly in elderly patients and those receiving combination regimens.

Keywords: Diuretics; Electrolyte imbalance; Hypokalemia; Hyponatremia; Loop diuretics; Thiazides.

Introduction

Diuretics remain one of the most widely prescribed pharmacological agents for cardiovascular and renal disorders worldwide [1]. They are central to the management of hypertension and heart failure and are recommended in major international guidelines [2,3]. By promoting renal sodium and water excretion, diuretics reduce plasma volume and blood pressure but simultaneously alter electrolyte homeostasis [4].

Thiazide diuretics act on the distal convoluted tubule and are strongly associated with hyponatremia and hypokalemia [5].

Loop diuretics inhibit the Na-K-2Cl transporter in the thick ascending limb, resulting in significant sodium, potassium, calcium, and magnesium losses [6]. Potassium-sparing diuretics reduce potassium excretion but may predispose to hyperkalemia, particularly in patients with impaired renal function [7].

Hyponatremia is among the most frequently encountered electrolyte abnormalities in clinical practice and has been associated with increased hospital stay and mortality [8]. Diuretic-induced hyponatremia is particularly common in elderly individuals due to impaired renal concentrating ability [9]. Hypokalemia may lead to cardiac arrhythmias, muscle weakness, and glucose intolerance [10]. Conversely, hyperkalemia is associated with potentially fatal cardiac conduction disturbances [11].

Hypomagnesemia frequently accompanies chronic diuretic therapy and may exacerbate potassium depletion [12]. Metabolic alkalosis is another recognized consequence of prolonged loop and thiazide therapy due to volume contraction and increased bicarbonate reabsorption [13].

Despite the extensive use of diuretics, data regarding the prevalence and pattern of electrolyte disturbances in Indian tertiary care settings remain limited [14]. Therefore, this study was undertaken to evaluate electrolyte abnormalities among patients receiving long-term diuretic therapy in a tertiary care hospital.

Materials and Methods

Study Design and Setting

This prospective cross-sectional observational study was conducted in the Department of Medicine at Patna Medical College and Hospital (PMCH), Patna, Bihar, India, over a nine-month period from April 2025 to December 2025.

Sample Size and Sampling Technique

A total of 91 patients were enrolled during the study period using consecutive sampling. All eligible patients attending the outpatient department or admitted to medical wards who met the inclusion criteria were approached for participation. The sample size was determined based on anticipated prevalence rates of electrolyte disturbances from previous literature, with an assumed prevalence of approximately 60–70%, 95% confidence level, and 10% margin of error.

Inclusion Criteria

1. Age ≥18 years
2. Receiving any form of diuretic therapy (loop, thiazide, potassium-sparing, or combination) for at least 3 consecutive months
3. Willingness to provide informed consent

Exclusion Criteria

- Acute kidney injury at presentation
- Patients on maintenance dialysis
- Acute gastrointestinal fluid loss (e.g., vomiting, diarrhea) within the preceding 2 weeks
- Known endocrine disorders affecting electrolytes (e.g., adrenal insufficiency, SIADH unrelated to diuretics)
- Patients receiving intravenous electrolyte correction at the time of evaluation

Data Collection

After obtaining written informed consent, demographic and clinical data were recorded using a structured case record form. Information collected included:

- Age and sex
- Indication for diuretic therapy
- Type of diuretic used
- Duration of therapy
- Comorbidities (hypertension, heart failure, chronic kidney disease, liver cirrhosis)

Clinical examination findings and relevant medical history were documented.

Classification of Diuretic Therapy

Patients were categorized into four groups:

- Loop diuretics

- Thiazide diuretics
- Potassium-sparing diuretics
- Combination therapy (two or more classes used concurrently)

This classification corresponds to the distribution reported in Table 2 of the Results section.

Laboratory Measurements

Venous blood samples were collected under aseptic precautions. Serum electrolyte levels were measured using an automated electrolyte analyzer (ion-selective electrode method) in the central biochemistry laboratory of PMCH.

The following parameters were assessed:

- Serum sodium (Na^+)
- Serum potassium (K^+)
- Serum magnesium (Mg^{2+})
- Serum chloride (Cl^-)
- Serum bicarbonate (HCO_3^-)

Quality control procedures were performed daily according to institutional laboratory standards.

Operational Definitions

Electrolyte abnormalities were defined using standard laboratory reference ranges:

- Hyponatremia: Serum sodium <135 mEq/L
- Hypernatremia: Serum sodium >145 mEq/L
- Hypokalemia: Serum potassium <3.5 mEq/L
- Hyperkalemia: Serum potassium >5.0 mEq/L
- Hypomagnesemia: Serum magnesium <1.7 mg/dL
- Metabolic alkalosis: Serum bicarbonate >28 mEq/L

Presence of at least one abnormal electrolyte parameter was categorized as "electrolyte disturbance" for analysis.

Outcome Measures

Primary Outcome:

- Prevalence of electrolyte disturbances among patients receiving long-term diuretic therapy.

Secondary Outcomes:

- Pattern of specific electrolyte abnormalities
- Association between type of diuretic and electrolyte disturbance
- Independent predictors of electrolyte imbalance

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA).

Descriptive Statistics

- Continuous variables were expressed as mean ± standard deviation (SD).
- Categorical variables were presented as frequencies and percentages.

Inferential Statistics

- Chi-square test (χ^2) was used to assess association between categorical variables (e.g., diuretic type and electrolyte disturbance).
- Independent t-test was used for comparison of continuous variables where appropriate.
- A p-value <0.05 was considered statistically significant.
- All p-values were two-tailed.

Multivariate Logistic Regression

Binary logistic regression analysis was performed to identify independent predictors of electrolyte disturbance.

Variables entered into the model included:

- Age (>60 years)
- Gender
- Loop diuretic use
- Thiazide use
- Combination therapy
- Presence of chronic kidney disease

Adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated.

Model adequacy was assessed using:

- Hosmer–Lemeshow goodness-of-fit test
- Nagelkerke R^2 value

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of PMCH, Patna. Written informed consent was obtained from all participants prior to enrollment. Patient confidentiality was maintained throughout the study, and data were anonymized before analysis.

Results

1. **Baseline Demographic and Clinical Characteristics**

A total of **91 patients** receiving long-term diuretic therapy were included in the study.

The mean age of participants was **58.4 ± 12.7 years** (range: 32–82 years). Patients aged >60 years constituted 44 (48.4%) of the study population. Males were 52 (57.1%) and females were 39 (42.9%).

Hypertension was the most common indication for diuretic therapy (50.5%), followed by heart failure (30.8%), chronic kidney disease (11.0%), and liver cirrhosis (7.7%).

These baseline characteristics are summarized in **Table 1**.

Table 1: Baseline Demographic and Clinical Profile (n = 91)

Variable	Value
Mean Age (years)	58.4 ± 12.7
Age >60 years	44 (48.4%)
Male	52 (57.1%)
Female	39 (42.9%)
Hypertension	46 (50.5%)
Heart Failure	28 (30.8%)
CKD	10 (11.0%)
Cirrhosis	7 (7.7%)

2. **Distribution of Diuretic Therapy**

Loop diuretics were prescribed in 34 (37.4%) patients, thiazides in 29 (31.9%), potassium-sparing diuretics in 10 (11.0%), and combination therapy in 18 (19.8%) patients.

The distribution of diuretic types is presented in **Table 2**.

Table 2: Distribution of Diuretic Type (n = 91)

Diuretic Type	n (%)
Loop	34 (37.4%)
Thiazide	29 (31.9%)
Potassium-sparing	10 (11.0%)
Combination	18 (19.8%)

3. **Prevalence of Electrolyte Disturbances**

Electrolyte disturbances were observed in **62 patients (68.1%)**.

The most common abnormality was hypokalemia (34.1%), followed by hyponatremia (29.7%), metabolic alkalosis (26.4%), hypomagnesemia (17.6%), and hyperkalemia (8.8%).

The detailed pattern is shown in **Table 3**.

Table 3: Pattern of Electrolyte Disturbances

Abnormality	n (%)
Hypokalemia	31 (34.1%)
Hyponatremia	27 (29.7%)
Hyperkalemia	8 (8.8%)
Hypomagnesemia	16 (17.6%)
Metabolic alkalosis	24 (26.4%)

The comparative prevalence of electrolyte abnormalities is illustrated in **Figure 1**.

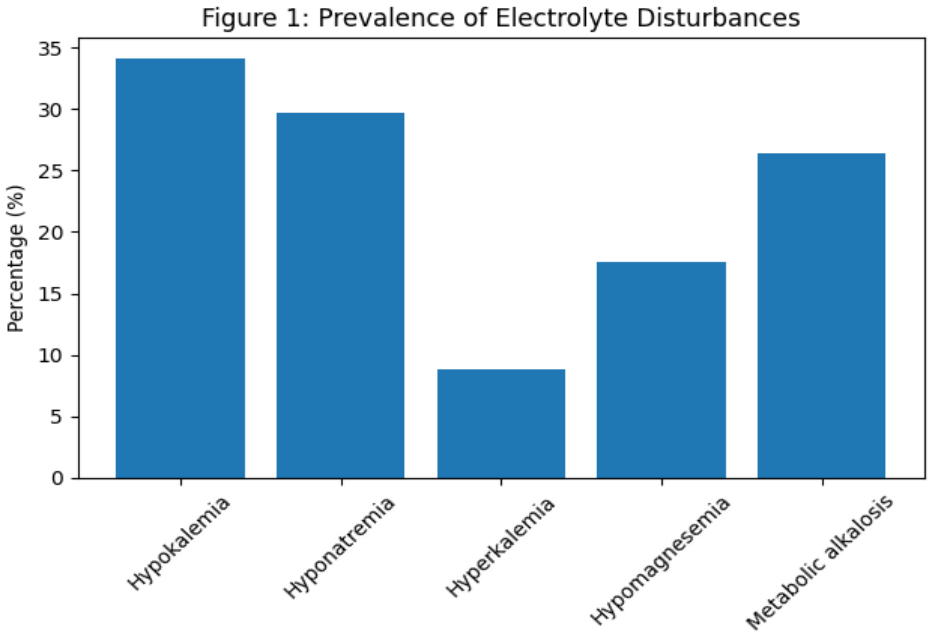

Figure 1: Prevalence of Electrolyte Disturbances Among Patients Receiving Long-Term Diuretic Therapy

4. Association Between Diuretic Type and Electrolyte Abnormalities

Hypokalemia was significantly more frequent among loop diuretic users (19/34; 55.9%) compared to other groups (χ^2 = 9.61; **p = 0.002**).

Hyponatremia was significantly associated with thiazide use (14/29; 48.3%) (χ^2 = 6.52; **p = 0.01**).

Combination therapy demonstrated the highest overall rate of electrolyte disturbance (16/18; 88.9%) (χ^2 = 8.31; **p = 0.004**).

These associations are summarized in **Table 4**.

Table 4: Association Between Diuretic Type and Electrolyte Disturbance

Diuretic Type	Disturbance Present n (%)	χ^2	p-value
Loop	25 (73.5%)	9.61	0.002
Thiazide	20 (69.0%)	6.52	0.01
Potassium-sparing	5 (50.0%)	1.82	0.17
Combination	16 (88.9%)	8.31	0.004

The graded distribution of electrolyte disturbances according to type of diuretic therapy is depicted in **Figure 2**.

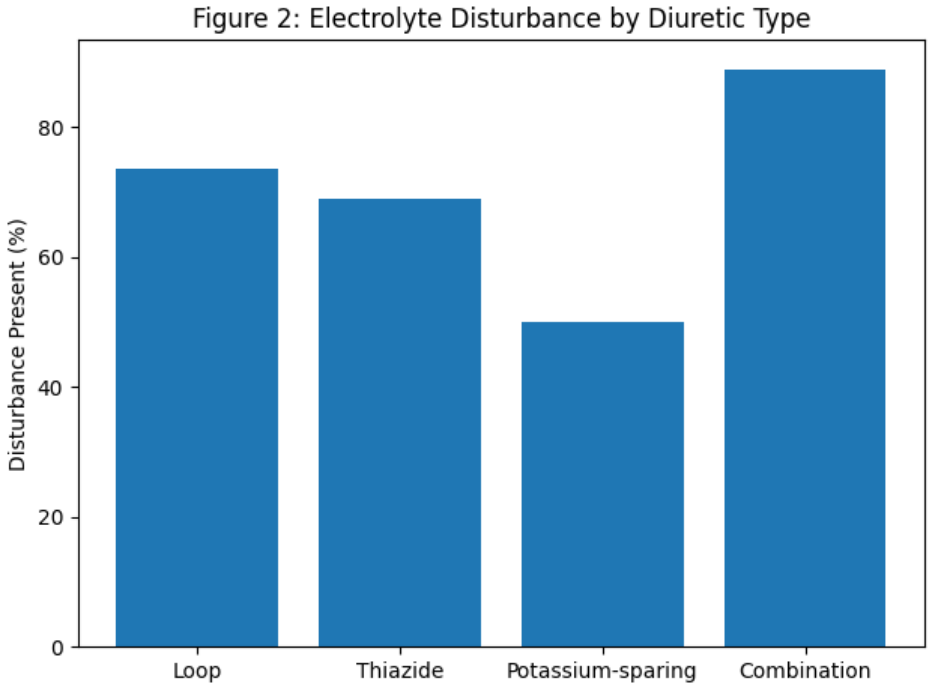

Figure 2: Distribution of Electrolyte Disturbance According to Diuretic Type

5. Multivariate Logistic Regression Analysis

A multivariate logistic regression model was constructed to identify independent predictors of electrolyte disturbance.

The model demonstrated good fit (Hosmer–Lemeshow χ^2 = 6.21; p = 0.62). The Nagelkerke R^2 was 0.38, indicating that 38% of variability was explained by the model. Combination therapy (Adjusted OR 4.91; 95% CI 1.52–15.82; p = 0.008), loop diuretic use (Adjusted OR 3.28; 95% CI 1.41–7.62; p = 0.006), thiazide use (Adjusted OR 2.56; 95% CI 1.12–5.84; p = 0.025), age >60 years (Adjusted OR 2.14; 95% CI 1.01–4.52; p = 0.046), and CKD (Adjusted OR 2.73; 95% CI 1.01–7.39; p = 0.048) were independent predictors.

These findings are detailed in **Table 5**.

Table 5: Multivariate Logistic Regression for Electrolyte Disturbance

Variable	Adjusted OR	95% CI	p-value
Age >60 yrs	2.14	1.01–4.52	0.046
Loop diuretic	3.28	1.41–7.62	0.006
Thiazide	2.56	1.12–5.84	0.025
Combination therapy	4.91	1.52–15.82	0.008
CKD	2.73	1.01–7.39	0.048
Male gender	1.32	0.61–2.84	0.47

Summary of Key Results

Electrolyte disturbances were present in 68.1% of patients receiving long-term diuretic therapy. Hypokalemia and hyponatremia were the most common abnormalities. Loop and thiazide diuretics were significantly associated with specific electrolyte derangements. Combination therapy demonstrated the highest risk. Multivariate analysis confirmed that combination therapy, loop use, thiazide use, older age, and CKD independently predicted electrolyte disturbance.

Discussion

The present study demonstrated that 68.1% of patients receiving long-term diuretic therapy developed at least one electrolyte abnormality. Similar prevalence rates have been reported in observational studies evaluating chronic diuretic use [15].

Hypokalemia was the most frequent abnormality, particularly among loop diuretic users, consistent with their mechanism of increased distal sodium delivery leading to potassium wasting [16]. Previous studies have shown that loop diuretics significantly increase urinary potassium excretion [17].

Hyponatremia was strongly associated with thiazide use, aligning with earlier reports describing thiazide-induced hyponatremia as a common adverse effect, especially in elderly patients [18,19]. The pathophysiology involves impaired urinary dilution and enhanced antidiuretic hormone activity [20].

Combination therapy showed the highest overall disturbance rate. Similar findings have been documented in patients receiving multidrug diuretic regimens [21]. Polypharmacy may potentiate renal electrolyte loss.

Elderly patients in our study demonstrated higher disturbance rates, consistent with age-related decline in renal function and altered hormonal regulation [22]. Monitoring is therefore particularly important in this group.

Hypomagnesemia and metabolic alkalosis observed in this study are well-recognized complications of prolonged loop and thiazide therapy [23,24]. These abnormalities may predispose patients to arrhythmias and neuromuscular complications [25].

Overall, our findings reinforce the importance of regular electrolyte monitoring in patients on chronic diuretic therapy to prevent serious adverse outcomes.

Limitations

This study has certain limitations. The sample size was relatively small and derived from a single tertiary care center, which may limit generalizability. Being cross-sectional in design, causal relationships cannot be established. Additionally, long-term follow-up data regarding clinical outcomes were not evaluated. Larger multicentric longitudinal studies are required to validate these findings.

Conclusion

Electrolyte disturbances are common among patients receiving long-term diuretic therapy. Loop and thiazide diuretics are significantly associated with hypokalemia and hyponatremia respectively. Periodic biochemical monitoring is essential, particularly in elderly individuals and those receiving combination therapy.

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