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Article

# Cognition and Fall Assessment After Recovery from Syndrome of Inappropriate Anti-Diuresis

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**Abstract: Background/Objectives:** The syndrome of inappropriate antidiuresis (SIAD) is a common cause of hyponatremia, often leading to cognitive dysfunction, gait instability, and a greater risk of falls. While the treatment of symptomatic hyponatremia addresses the immediate electrolyte imbalance, the longer-term effects are not well understood. This study aimed to evaluate cognitive function and fall risk in patients 1–2 months after recovery from SIAD-related hyponatremia by comparing them with matched controls. **Methods:** This cross-sectional study included 40 patients who had recently recovered from SIAD-related hyponatremia and 40 age- and sex-matched controls. Cognitive function was assessed via the Mini-Cog and Trail Making Tests A and B, postural stability was assessed via the Timed Up and Go test, and functional independence was assessed via the Katz Index of Independence. Serum sodium levels were measured at discharge and during follow-up. Statistical analysis was conducted to compare outcomes between the two groups. **Results:** Patients who recovered from SIAD-related hyponatremia presented significant impairments in cognition and functional performance at the time of discharge, including lower Mini-Cog scores, prolonged Timed Up and Go times, and reduced Katz index scores. At the 1–2-month follow-up, these measures improved significantly ( $p < 0.001$ ), but patients still lagged behind controls, particularly in executive function, as seen in Trail Making Test B scores ( $239.6 \pm 106.3$  seconds vs.  $173.1 \pm 80.7$  seconds,  $p = 0.002$ ). **Conclusions:** Persistent deficits, particularly in executive function and mobility, highlight the importance of continued rehabilitation and monitoring to reduce fall risk and improve long-term outcomes. This study emphasizes the need for a multidisciplinary approach to care following recovery from SIAD.

**Keywords:** hyponatremia; postural stability; falls; mild cognitive impairment

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## 2. Introduction

The syndrome of inappropriate antidiuresis (SIAD) is a condition characterized by the excessive secretion of antidiuretic hormone (ADH), resulting in water retention and dilutional hyponatremia. Hyponatremia, defined as a serum sodium level less than 135 mEq/L, is the most common electrolyte disturbance observed in clinical practice. It affects a broad range of individuals but is particularly prevalent in hospitalized patients, elderly individuals, and those with chronic conditions such as heart failure, cirrhosis, and malignancies. [1,2] The consequences of hyponatremia can range from mild, nonspecific symptoms to severe neurological complications such as seizures and coma. [2,3]

Even mild and chronic hyponatremia has been shown to impair cognitive function, slow response times, and disrupt balance, increasing the risk of falls and fractures. [3,4] These effects are thought to stem from osmotic shifts in the brain, leading to cellular swelling and subsequent adaptive responses, including the loss of neuroactive osmolytes. [5] While acute hyponatremia is life-threatening and requires urgent correction, chronic hyponatremia often presents more subtly, with its long-term effects on brain function and mobility remaining underappreciated. [3]

Research has focused largely on the acute and chronic effects of untreated hyponatremia. However, there is limited understanding of the residual cognitive and physical impairments that may persist even after the biochemical correction of SIAD-related hyponatremia. [1,6] These residual effects could increase the risk of falls and hinder the recovery of normal functional independence, particularly in older adults.

This study aims to explore the cognitive and functional outcomes of patients recovering from SIAD-related hyponatremia, with a specific focus on their risk of falls and their ability to regain independence. By comparing these patients to age- and sex-matched controls, we seek to better understand the lingering effects of SIAD and the need for targeted interventions to optimize recovery. These findings could help bridge the gap between biochemical recovery and holistic rehabilitation, ensuring better long-term outcomes for these patients.

### 3. Materials and Methods

This study was a hospital-based cross-sectional analysis conducted over 21 months, from April 2023 to August 2024, at Kasturba Medical College teaching hospitals in Mangalore. The aim of this study was to evaluate cognitive function and postural stability in patients recovering from SIAD-related hyponatremia and compare them with those of age- and sex-matched controls.

Patients aged 18 years or older and patients diagnosed with SIAD-related hyponatremia during hospitalization for symptomatic hyponatremia, which was confirmed by clinical evaluation and biochemical test and whose sodium was corrected to normal levels ( $>135$  mEq/L) at discharge were included. Patients with preexisting conditions affecting cognition or mobility, including known dementia, prior stroke, head trauma, brain tumors, cirrhosis, heart failure, renal failure, hypothyroidism, or glucocorticoid deficiency, patients with using diuretics or medications known to influence serum sodium and patients unable to participate in follow-up assessments were excluded.

A total of 40 patients who recovered from SIAD-related hyponatremia were recruited as the test group, along with 40 age- and sex-matched controls without hyponatremia or SIAD. Convenience sampling was used to select participants who met the inclusion criteria. Cognition and postural stability were assessed via the following validated tools: Mini-Cog Test: To evaluate cognitive function, we focused on memory and executive function. [7] Timed up and go (TUG) test: To assess mobility and fall risk, the time taken to stand from a seated position, walk three metres, turn, and return was measured. [8] Katz Index of Independence in Activities of Daily Living: To evaluate functional independence in daily tasks such as bathing, dressing, and feeding. [9] Trail Making Tests A and B (TMTs A/B): To assess visual attention, processing speed, and task-switching abilities. [10]

Demographic data, comorbid conditions, and serum sodium levels were recorded. Baseline assessments were performed at discharge, with follow-up evaluations conducted 1–2 months later. The data are summarized and presented in the Supplementary Materials, including that requisite for diagnosis for SIAD-related hyponatremia.

Primary outcomes included cognitive function, postural stability, and functional independence, as measured by the above tests. Serum sodium levels were recorded at discharge and during follow-up. Comparisons between patients and controls were analyzed for significant differences. Descriptive statistics and summary measures such as the means, medians, standard deviations, and interquartile ranges were calculated for continuous variables, whereas categorical variables were expressed as percentages. Comparative independent t tests and Mann–Whitney U tests were used to compare the means of the cases and controls. Paired t tests were used to evaluate changes within groups over time. Logistic regression models adjusted for potential confounders were used to assess the associations

between hyponatremia and observed outcomes. Extra care was taken to prevent falls during the assessments, and no specific interventions were required beyond standard evaluation protocols. Ethical approval for the study was obtained from the institutional ethics committee, and written informed consent was obtained from all participants.

#### 4. Results

A total of 80 participants were divided equally into two groups: cases (patients with symptomatic SIAD-related hyponatremia) and controls (without hyponatremia). The participants were matched by age and sex to ensure demographic balance and minimize confounding effects. The mean age of the participants in the SIAD-related hyponatremia group was  $64.2 \pm 11.5$  years, which closely matched that of the controls ( $63.9 \pm 11.6$  years;  $p = 0.923$ ). The sex distribution was equal in both groups. The distributions were similar for diabetes mellitus, hypertension, chronic obstructive pulmonary disease, obstructive airway disease, and rheumatoid arthritis, with no statistically significant differences. The mean serum sodium level among patients at baseline was 116.4 mEq/L, and that at follow-up was 137.7 mEq/L. The mean serum sodium level among the controls at follow-up was 139.1 mEq/L. Descriptive statistics are depicted in Table 1.

**Table 1.** Descriptive statistics.

Variable	Cases		Controls
	At Discharge n=40	On Follow-Up n=40	On Follow-Up n=40
Age (mean (SD))	64.17 (11.49)		63.92 (11.65)
Gender- no. (%)			
Male	26 (65.0)		26 (65.0)
Female	14 (35.0)		14 (35.0)
Co-morbidities- no. (%)			
Diabetes	13 (32.5)		11 (27.5)
Hypertension	15 (37.5)		14 (35.0)
COPD	3 (7.5)		3 (7.5)
OAD	1 (2.5)		1 (2.5)
Rheumatoid Arthritis	1 (2.5)		1 (2.5)
Serum Sodium mEq/L (mean (SD))	116.45 (6.4)	137.65 (2.27)	139.12 (2.27)
Mini Cog scores- no. (%)			
0	12 (30.0)	3 (7.5)	-
1	1 (2.5)	-	-
2	2 (5.0)	2 (5.0)	1 (2.5)
3	15 (37.5)	16 (40.0)	7 (17.5)
5	10 (25.0)	19 (47.5)	32 (80)
Katz Index- no. (%)			
0	2 (5.0)	-	-
2	2 (5.0)	-	-
3	2 (5.0)	2 (5.0)	-
4	8 (20.0)	3 (7.5)	1 (2.5)
5	9 (22.5)	8 (20.0)	3 (7.5)

6	17 (42.5)	27 (67.5)	36 (90.0)
Time to Up and Go in seconds (mean (SD))	15.82 (4.89)	14.07 (4.99)	11.80 (3.76)
Trail Making Test A in seconds			
Mean (SD)	120.14 (62.15)	100.43 (57.48)	80.82 (52.41)
Median (IQR)	98 (29)	81 (35)	74 (52)
Trial Making Test B in seconds (mean (SD))	264.91 (102.10)	239.61 (106.28)	173.10(80.67)

COPD- Chronic Obstructive Pulmonary Disease, OAD- Obstructive Airway Disease

During follow-up, all patients had normalized serum sodium levels ( $>135$  mEq/L), with a mean level of  $137.7 \pm 2.3$  mEq/L. However, this value was slightly lower than the mean sodium level observed in the controls ( $139.1 \pm 2.3$  mEq/L). While sodium normalization was universally achieved, subtle differences in levels may reflect ongoing physiological recovery. At follow-up, patients who recovered from SIAD-related hyponatremia scored lower on the Mini-Cog test than did controls did, and the difference was statistically significant, with a p value of 0.002. While 47.5% of the patients achieved the maximum score of 5, indicating normal cognition, 7.5% displayed severe impairment (score of 0), which was not observed in any of the controls. These results suggest that although some recovery in cognitive function occurred, residual deficits remained in a subset of patients. The Katz index scores substantially improved from the time of discharge to follow-up ( $p < 0.001$ ). By the time of follow-up, 67.5% of patients achieved full independence (score of 6), compared with only 42.5% at discharge. However, this rate was still lower than the 90% independence rate observed in controls ( $p = 0.013$ ). Patients demonstrated notable improvements in mobility from discharge to follow-up, with average TUG times decreasing from  $15.82 \pm 4.89$  seconds to  $14.07 \pm 4.99$  seconds ( $p < 0.001$ ). However, they continued to underperform compared with the controls (mean  $11.8 \pm 3.77$  seconds,  $p = 0.012$ ). Furthermore, 15% of patients required more than 20 s to complete the test, a threshold associated with an increased risk of falls. These findings point to a reduction in fall risk over time, although residual mobility limitations persist compared with those of healthy controls. These significant recoveries in daily functioning but incomplete normalization compared with those of healthy peers. The TMT A scores showed considerable improvement, with mean completion times decreasing from  $120.14 \pm 62.15$  seconds at discharge to  $100.43 \pm 57.48$  seconds at follow-up ( $p < 0.001$ ). However, patients still performed slower than controls did ( $80.82 \pm 52.41$  seconds,  $p = 0.063$ ). The TMT B, which measures task switching and executive function, revealed more pronounced challenges. Patients recovering from hyponatremia took significantly longer to complete this test than controls did ( $239.6 \pm 106.3$  seconds vs.  $173.1 \pm 80.7$  seconds,  $p = 0.002$ ), indicating persistent deficits in higher-order cognitive processing and executive function despite normalized sodium levels. These are depicted in Table 2.

**Table 2.** Analysis cases vs controls.

Variable	Cases: Follow-Up n=40	Controls n=40	
Serum Sodium mEq/L (mean (SD))	137.65 (2.27)	139.12 (2.27)	p=0.998 (Student's t)
Mini Cog scores- no. (%)			
0	3 (7.5)	-	p=0.002* (Mann-Whitney U)
1	-	-	
2	2 (5.0)	1 (2.5)	
3	16 (40.0)	7 (17.5)	
5	19 (47.5)	32 (80)	

Katz Index- no. (%)			
0	-	-	p=0.013* (Mann-Whitney U)
2	-	-	
3	2 (5.0)	-	
4	3 (7.5)	1 (2.5)	
5	8 (20.0)	3 (7.5)	
6	27 (67.5)	36 (90.0)	
Time to Up and Go in seconds (mean (SD))	14.07 (4.99)	11.80 (3.76)	p=0.012* (Student's t)
Trail Making Test A in seconds (mean (SD))	100.43 (57.48)	80.82 (52.41)	p=0.063 (Mann-Whitney U)
Trial Making Test B in seconds (mean (SD))	239.61 (106.28)	173.10(80.67)	p=0.002* (Student's t)

\*p values of <0.05 were considered statistically significant

Patients who recovered from SIAD-related hyponatremia at the time of discharge and at follow-up demonstrated significant recovery across all measured domains. The Mini-Cog scores increased from 2.5 to 3.68 ( $p<0.001$ ), the TUG times decreased from 15.82 to 13.9 seconds ( $p<0.001$ ), and the Katz index scores improved from 4.73 to 5.5 ( $p<0.001$ ). These improvements indicate clear progress in cognitive function, mobility, and independence. These are depicted in Table 3.

**Table 3.** Analysis cases at discharge vs follow-up.

Variable	Cases: Discharge n=40	Cases: Follow-Up n=40	
Mini Cog scores- no. (%)			
0	12 (30.0)	3 (7.5)	p<0.001* (Wilcoxon W)
1	1 (2.5)	-	
2	2 (5.0)	2 (5.0)	
3	15 (37.5)	16 (40.0)	
5	10 (25.0)	19 (47.5)	
Katz Index- no. (%)			
0	2 (5.0)	-	p<0.001* (Wilcoxon W)
2	2 (5.0)	-	
3	2 (5.0)	2 (5.0)	
4	8 (20.0)	3 (7.5)	
5	9 (22.5)	8 (20.0)	
6	17 (42.5)	27 (67.5)	
Time to Up and Go in seconds (mean (SD))	15.82 (4.89)	14.07 (4.99)	p<0.001* (Student's t)
Trail Making Test A in seconds (mean (SD))	120.14 (62.15)	100.43 (57.48)	p<0.001* (Wilcoxon W)
Trial Making Test B in seconds (mean (SD))	264.91 (102.10)	239.61 (106.28)	p<0.001* (Student's t)

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*p values of <0.05 were considered statistically significant*

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Residual deficits in executive functions, cognition, mobility and independence, and increased fall risk among patients recovering from SIAD-related hyponatremia were the key observations. This underscores the need for targeted interventions to address residual challenges and support complete functional recovery.

## 5. Discussion

This study highlights the persistent cognitive and functional challenges faced by patients recovering from SIAD-related hyponatremia, even after normalization of serum sodium levels. While improvements were observed in cognitive function, mobility, and functional independence during follow-up, the lingering deficits compared with those in controls emphasize the importance of targeted interventions in these patients. A notable finding was the persistence of executive function impairment, as evidenced by prolonged Trail Making Test B completion times. This aligns with previous research indicating that hyponatremia disproportionately impacts higher-order cognitive functions, such as task switching and attention. [1,5,11] While Mini-Cog scores improved during follow-up, with 47.5% of patients achieving a perfect score of 5, residual cognitive deficits in 7.5% of patients (scoring 0) suggest incomplete recovery of neurocognitive function, echoing findings from earlier studies. [11] The Timed Up and Go test revealed significant improvements from discharge to follow-up. However, patients still performed worse than controls did, indicating a lingering increased fall risk. These findings are consistent with studies linking chronic hyponatremia to gait instability and delayed motor responses. [4,5,12] Continued mobility challenges highlight the necessity of post-discharge physiotherapy and balance training programs to mitigate fall risk. At follow-up, 67.5% of patients achieved full independence (Katz Index score of 6), whereas 42.5% achieved full independence at discharge. However, this percentage remained lower than the 90% independence rate observed in the controls. These findings emphasize that while recovery is achievable, it may be slower and incomplete in certain domains, particularly among older adults with preexisting vulnerabilities. [4] A positive finding was the 100% normalization of serum sodium levels at follow-up, reflecting effective management of SIAD-related hyponatremia. However, the slightly lower mean sodium levels in patients than in controls may reflect subtle differences in homeostatic regulation, potentially contributing to the observed functional deficits. [12] The persistent deficits observed in this study align with prior findings on the impact of hyponatremia on neurocognitive and motor functions. [4,5,11] However, the degree of improvement noted during follow-up underscores the potential for recovery with appropriate management. Unlike studies focusing solely on asymptomatic chronic hyponatremia, this study provides novel insights into the post-recovery phase of symptomatic SIAD-related hyponatremia.

This study builds on the literature by focusing not only on the acute effects of hyponatremia but also on its long-term impacts post-recovery. These findings highlight the need to incorporate neurocognitive and functional assessments into routine follow-up care for patients recovering from SIAD-related hyponatremia. Furthermore, this study contributes to the growing evidence linking chronic hyponatremia to delayed recovery in executive function and mobility, underscoring the need for multidisciplinary rehabilitation strategies. [13,14]

## 6. Conclusions

While recovery from SIAD-related hyponatremia leads to significant improvements in cognition, mobility, and functional independence, residual deficits remain, particularly in executive function and postural stability. These findings underscore the need for comprehensive post-discharge care, including cognitive training and fall prevention strategies. By addressing these lingering challenges, healthcare providers can improve the long-term outcomes and quality of life for these patients.

**Supplementary Materials:** The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

**Author Contributions:** Chakrapani M: Conceptualization, Resources, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Isha Bansal: Data Curation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; Koushik Ramachandra: Resources, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing.

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**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board All experiments were performed in accordance with relevant guidelines and regulations. The study protocol was reviewed and approved by the Institutional Ethics Committee of Kasturba Medical College, Mangalore (Reg. No. ECR/541/Inst/KA/2014/RR-20) with approval number IEC KMC MLR 04/2023/129.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

**Data Availability Statement:** All the data generated or analysed during this study are included in this article and its Supplementary Material files. Further inquiries can be directed to the corresponding author.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## Abbreviations

The following abbreviations are used in this manuscript:

ADH	Anti-Diuretic Hormone
SIAD	Syndrome of Inappropriate Anti Diuresis
TUG	Time to Up and Go
TMT	Trials Making Test

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