Original Article

Association of Sertrailine and Escitalopram With Antidepressant Induced Hyponatremia Among Coronary Artery Disease Patients at a Tertiary Care Hospital of Rawalpindi

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ABSTRACT

Objective: To determine the association of sertraline and escitalopram with antidepressant-induced hyponatremia among coronary artery disease patients.

Study Design: Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the Armed Forces Institute of Mental Health Rawalpindi December 16 till March 15, 2026.

Methods: This study was conducted including 220 patients with coronary artery disease receiving sertraline or escitalopram. Demographic variables included age, gender, and socioeconomic status. Clinical variables included type and duration of coronary artery disease, comorbidities such as hypertension and diabetes, and concurrent medications.

Results: The mean age was 61.4 ± 10.8 years, and hyponatremia was observed in 26.4% of patients. Hyponatremia was more frequent with escitalopram compared to sertraline (65.5% vs 34.5%, p = 0.003). Patients with hyponatremia had lower serum sodium (131.1 ± 3.1 vs 139.2 ± 2.8 mEq/L; p <0.001) and higher creatinine levels (2.0 ± 0.9 vs 1.4 ± 0.6 mg/dL; p <0.001). Heart failure, diuretic use, high-dose SSRI therapy, and polypharmacy were significantly associated with hyponatremia (p <0.05). **Conclusion:** Antidepressant-induced hyponatremia is significantly associated with escitalopram use and multiple clinical risk factors in coronary artery disease patients. Regular monitoring and careful drug selection are essential to reduce complications

Key Words: Coronary artery disease; Hyponatremia; Sertraline; Escitalopram; SSRIs; Electrolyte imbalance

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INTRODUCTION

Depression is also an example of comorbidity in coronary cardiac patients with coronary artery disease (CAD), where a significant proportion of patients with cardiac diseases have depression that leads to worse clinical outcomes, morbidity and mortality[1]. It hurts in compliance to treatment, lifestyle change, and general quality of life among the cardiac patients[2].

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The most common example of such a drug is selective serotonin reuptake inhibitors (SSRIs), especially sertraline and escitalopram, which are recommended by their effectiveness and rather good cardiovascular safety record[3]. However, SSRIs are linked with unwanted effects, hyponatremia is one of them, and it is a clinically important condition[4]. The syndrome of inappropriate antidiuretic hormone secretion is the most widespread mediator of antidepressant-induced hyponatremia, which causes the dilutional sodium imbalance[5]. Though not severe in most cases, it may develop into severe problems like confusion, seizures, and risk of falls particularly in susceptible groups[6]. Elderly individuals, polypharmacy and regular taking of diuretics are specific risk factors to the patients with CAD[7]. This might result in further augmentation of the risk of hyponatremia and even make clinical management more challenging in such patients with the addition of SSRIs[8]. The symptoms of hyponatremia can be confused with symptoms of cardiac or depressive symptoms and, therefore, not recognized in time[9].

Sertraline and escitalopram are the most popular SSRIs, yet the relative risk of each of them triggering hyponatremia is still unclear[10]. There have been studies indicating differences in the risk of SSRIs and then there are those which show similarity in the safety profiles[11]. The lack of consistency also emphasizes the necessity to conduct additional assessment, especially among high-risk groups like CAD patients[12]. Data of the occurrence of antidepressant-induced hyponatremia in low- and middle-income countries such as Pakistan are scanty, even though there is an emerging trend of using SSIs in cardiac patients[13]. These factors can be localized, including comorbidities, medication habits, and access to healthcare and other relevant factors that might affect the presence and the rate of this complication[14]. This association is relevant to the safer prescribing and monitoring practices[15]. The patient at-risk can be identified at an early stage to reduce complications and enhance patient outcomes[16]. Thus, this research will evaluate the correlation between sertraline and escitalopram and antidepressant induced hyponatremia CAD patients in the tertiary care hospital of Rawalpindi.

METHODS

This cross-sectional analytical study was conducted at Armed Forces Institute of Mental Health Rawalpindi December 16 till March 15, 2026, including 220 patients diagnosed with coronary artery disease and receiving antidepressant therapy with either sertraline or escitalopram. Patients admitted to cardiology wards or attending outpatient services were enrolled consecutively during the study period to determine the association between specific SSRIs and antidepressant-induced hyponatremia.

Inclusion Criteria

- Patients aged ≥18 years with confirmed coronary artery disease
- Patients receiving sertraline or escitalopram for diagnosed depression
- Patients with baseline and follow-up serum sodium levels available
- Patients willing to participate and provide informed consent

Exclusion Criteria

- Patients with pre-existing hyponatremia prior to initiation of antidepressant therapy
- Patients with conditions known to cause hyponatremia (e.g., severe renal failure, liver cirrhosis, SIADH due to other causes)
- Patients on medications strongly associated with hyponatremia (e.g., carbamazepine, thiazide diuretics without adjustment)
- Patients with incomplete clinical or laboratory data

Data Collection: After institutional approval, data were collected using a structured proforma. Demographic variables included age, gender, and socioeconomic status. Clinical variables included type and duration of coronary artery disease, comorbidities such as hypertension and diabetes, and concurrent medications. Details of antidepressant therapy, including type (sertraline or escitalopram), dosage, and duration of use, were recorded. Laboratory data included baseline and follow-up serum sodium levels. Hyponatremia was defined as serum sodium level <135 mEq/L. Patients were categorized based on the presence or absence of hyponatremia following antidepressant use.

Statistical Analysis: Data were entered and analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentage. Comparison between sertraline and escitalopram groups regarding occurrence of hyponatremia was performed using chi-square test. Independent t-test was used for comparison of mean sodium levels where appropriate. A p-value of ≤0.05 was considered statistically significant.

RESULTS

The mean age was 61.4 ± 10.8 years, with higher age in patients with hyponatremia (65.2 ± 11.1 vs 59.8 ± 10.2 years; p = 0.002).

Table No. 1. Demographic and Clinical Characteristics of CAD Patients According to Hyponatremia (N = 220)

Variable	Category	Overall (N=220)	No Hyponatremia (n=162)	Hyponatremia (n=58)	p-value
Age (years)	Mean ± SD	61.4 ± 10.8	59.8 ± 10.2	65.2 ± 11.1	0.002
Age Group	≤60 years	104 (47.3%)	84 (51.9%)	20 (34.5%)	0.019
	>60 years	116 (52.7%)	78 (48.1%)	38 (65.5%)	0.019
Gender	Male	138 (62.7%)	104 (64.2%)	34 (58.6%)	0.442
	Female	82 (37.3%)	58 (35.8%)	24 (41.4%)	0.442
Hypertension	Present	148 (67.3%)	102 (63.0%)	46 (79.3%)	0.018
Diabetes Mellitus	Present	126 (57.3%)	88 (54.3%)	38 (65.5%)	0.124
Heart Failure	Present	72 (32.7%)	42 (25.9%)	30 (51.7%)	<0.001
Diuretic Use	Yes	94 (42.7%)	58 (35.8%)	36 (62.1%)	<0.001
Length of Stay (days)	Mean ± SD	7.9 ± 3.6	7.1 ± 3.2	9.8 ± 4.1	<0.001

A greater proportion of patients aged >60 years had hyponatremia (65.5% vs 48.1%) (p = 0.019). Hypertension (79.3% vs 63.0%; p = 0.018), heart failure (51.7% vs 25.9%; p <0.001), and diuretic use (62.1% vs 35.8%; p <0.001) were significantly more common in the hyponatremia group. These patients also had longer hospital stays (9.8 ± 4.1 vs 7.1 ± 3.2 days; p <0.001), while gender and diabetes showed no significant association.

Hyponatremia was significantly more frequent in patients receiving escitalopram compared to sertraline (65.5% vs 34.5%; p = 0.003). Longer antidepressant use (≥2 weeks) was associated with higher hyponatremia rates (75.9% vs 60.5%; p = 0.031). High-dose SSRI use was also more common in hyponatremic patients (41.4% vs 24.7%; p = 0.017). Additionally, polypharmacy (≥5 drugs) was significantly associated with hyponatremia (75.9% vs 56.8%; p = 0.009).

Table 2. Antidepressant Exposure and Hyponatremia (N = 220)

Variable	Category	Overall (N=220)	No Hyponatremia (n=162)	Hyponatremia (n=58)	p-value
Antidepressant	Sertraline	112 (50.9%)	92 (56.8%)	20 (34.5%)	0.003
	Escitalopram	108 (49.1%)	70 (43.2%)	38 (65.5%)	0.003
Duration of Use	<2 weeks	78 (35.5%)	64 (39.5%)	14 (24.1%)	0.031
	≥2 weeks	142 (64.5%)	98 (60.5%)	44 (75.9%)	0.031
Dose Category	Standard Dose	156 (70.9%)	122 (75.3%)	34 (58.6%)	0.017
	High Dose	64 (29.1%)	40 (24.7%)	24 (41.4%)	0.017
Polypharmacy	≥5 drugs	136 (61.8%)	92 (56.8%)	44 (75.9%)	0.009
	<5 drugs	84 (38.2%)	70 (43.2%)	14 (24.1%)	0.009

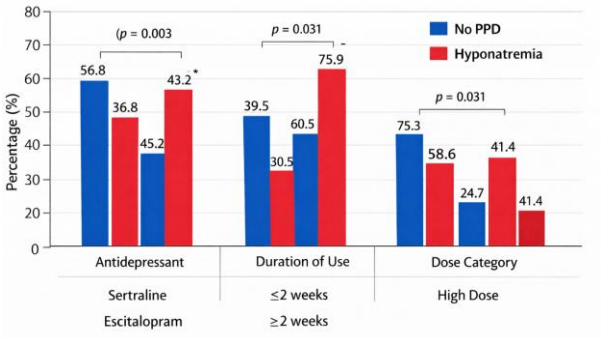

Figure 1. Antidepressant Exposure and Risk of Hyponatremia Among Coronary Artery Disease Patients (n = 220)

Patients with hyponatremia had significantly lower serum sodium levels (131.1 ± 3.1 vs 139.2 ± 2.8 mEq/L; p <0.001). They also showed lower potassium (3.9 ± 0.7 vs 4.3 ± 0.5 mEq/L; p = 0.001) and albumin levels (2.9 ± 0.6 vs 3.5 ± 0.5 g/dL; p <0.001). Conversely, creatinine (2.0 ± 0.9 vs 1.4 ± 0.6 mg/dL), blood urea (52.4 ± 17.1 vs 38.9 ± 13.7 mg/dL), and urine sodium (49.5 ± 13.8 vs 34.2 ± 10.4 mEq/L) were significantly higher in the hyponatremia group (p <0.001). Serum osmolality was also lower (272.3 ± 10.5 vs 286.1 ± 7.8 mOsm/kg; p <0.001).

Table No. 3. Laboratory Parameters in Patients With and Without Hyponatremia (N = 220)

Laboratory Parameter	Overall Mean ± SD	No Hyponatremia Mean ± SD	Hyponatremia Mean ± SD	p-value
Serum Sodium (mEq/L)	136.8 ± 4.2	139.2 ± 2.8	131.1 ± 3.1	<0.001
Serum Potassium (mEq/L)	4.2 ± 0.6	4.3 ± 0.5	3.9 ± 0.7	0.001
Serum Creatinine (mg/dL)	1.6 ± 0.8	1.4 ± 0.6	2.0 ± 0.9	<0.001
Blood Urea (mg/dL)	42.6 ± 15.3	38.9 ± 13.7	52.4 ± 17.1	<0.001
Serum Osmolality (mOsm/kg)	282.5 ± 9.4	286.1 ± 7.8	272.3 ± 10.5	<0.001
Urine Sodium (mEq/L)	38.7 ± 12.6	34.2 ± 10.4	49.5 ± 13.8	<0.001
Serum Albumin (g/dL)	3.3 ± 0.6	3.5 ± 0.5	2.9 ± 0.6	<0.001

On multivariate analysis, heart failure (OR = 2.94, p = 0.001), diuretic use (OR = 2.67, p = 0.003), escitalopram use (OR = 2.21, p = 0.013), high-dose SSRI (OR = 1.96, p = 0.036), and polypharmacy (OR = 2.15, p = 0.021) were independent predictors of hyponatremia. Age >60 years also showed a significant association (OR = 1.88, p = 0.042), while gender, hypertension, and duration of use were not statistically significant.

Table 4. Multivariate Analysis of Factors Associated with Hyponatremia (N = 220)

Variable	Adjusted OR	95% CI	p-value
Age >60 years	1.88	1.02 – 3.46	0.042
Female Gender	1.24	0.66 – 2.32	0.501
Hypertension	1.76	0.91 – 3.41	0.091
Heart Failure	2.94	1.54 – 5.61	0.001
Diuretic Use	2.67	1.41 – 5.05	0.003
Escitalopram Use	2.21	1.18 – 4.13	0.013
Duration ≥2 weeks	1.79	0.95 – 3.36	0.071
High Dose SSRI	1.96	1.04 – 3.69	0.036
Polypharmacy (≥5 drugs)	2.15	1.12 – 4.12	0.021

DISCUSSION

This research showed that there was a strong correlation between the use of SSRI and the antidepressant-induced hyponatremia in patients with coronary artery disease, where escitalopram was more prone to induce hyponatremia than sertraline. The prevalence of hyponatremia in the entire cohort points out its clinical importance in the patients with cardiac conditions who are under antidepressant therapy. The same results have been mentioned in the earlier-studies where the administration of SSRI was correlated with the risk of experiencing hyponatremia, especially in the circumstances of populations of patients with medical illnesses[17]. Advanced age was found as a significant risk factor and patients over 60 years demonstrated higher hyponatremia prevalence and a much higher means age in the hyponatremic group. This can be explained by the age-related alterations in renal functioning, greater susceptibility to antidiuretic hormone, and greater susceptibility to comorbid conditions. Other studies in the past have considered the advanced age as a persistent predictor of hyponatremia caused by SSRI[18]. Patients with hyponatremia had comorbid conditions, especially heart failure and hypertension. This close correlation with heart failure could be attributed to underlying fluid imbalance and neuro hormonal stimulation, which predisposes to sodium imbalances. Besides this, the use of diuretics was much greater in the hyponatremia group that further predisposed it by acting as a heightened loss of sodium and a loss of volume. Prior studies have reported similar associations between diuretics, heart failure and hyponatremia[19]. Escitalopram, relative to sertraline, had a greater percentage of hyponatremia, indicating that maybe there is a dissimilar risk pattern in SSRIs. The increased risk was also associated with longer duration of use and increased doses, which means that it is a dose- and exposure-dependent risk. Other studies have found similar results, with some SSRIs and higher dosage increased chances of hyponatremia[20].

Findings in this laboratory study were in line with the characteristics of dilutional hyponatremia that encompassed inadequately low serum sodium and osmolality in addition to an increase in the urine sodium levels that validated a mechanism of the inappropriate antidiuretic hormone secretion. High levels of creatinine and blood urea in the hyponatremia group also indicate poor renal functioning and fluid balance. This pattern of biochemical changes has been observed in earlier studies that examined the hyponatremia induced by the use of the SSRIs[21]. The multivariate analysis demonstrated that heart failure, diuretic use, escitalopram therapy, high-dose SSRI use, and polypharmacy were independent predictors of hyponatremia, which confirms the multifactorial nature of hyponatremia. Polypharmacy is a significant factor that implies possible interactions of drugs and cumulative effects on sodium balance. It has also been found that previous studies have highlighted the significance of various medications and comorbidities in the risk escalation of hyponatremia[22]. In general, the results suggest that patient factors, drug factors, and clinical factors combine to cause hyponatremia caused by antidepressants in CAD patients. The increased risk of escitalopram and the ability to alter it through dose and co-morbid drugs, highlights the importance of selecting and monitoring antidepressant therapy carefully. These findings are in line with the past studies and serve to underscore the need to regularly monitor the electrolytes in high-risk cardiac patients on SSRIs.

CONCLUSION

It is concluded that antidepressant-induced hyponatremia is a significant clinical concern among patients with coronary artery disease receiving SSRI therapy, with a higher association observed in those treated with escitalopram compared to sertraline. Advanced age, heart failure, diuretic use, high-dose antidepressant therapy, and polypharmacy were identified as important contributing factors. These findings highlight that hyponatremia is a multifactorial condition in CAD patients and emphasize the need for careful selection of antidepressants, dose optimization, and close monitoring of serum sodium levels, particularly in high-risk individuals, to prevent complications and improve clinical outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Jasim Tariq, Abid Aftab, Izzah Khalid
Drafting or Revising Critically:	Asif Azeem, Isbah Gul, Tariq Raheem
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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