

Evaluation of Hyponatremia in Patients on Fluoxetine Therapy at a Psychiatry Outpatient Department in a Tertiary Care Hospital: A Cross-sectional Study

SA ABIRAMI BALAMBIKA¹, R NALINI², Y NISHA MAHESHWARI³, J EZHILRAMYA⁴

ABSTRACT

Introduction: Fluoxetine is a widely used Selective Serotonin Reuptake Inhibitor (SSRI) for various psychiatric illnesses. Identifying patients at increased risk of developing hyponatremia is essential for safe and successful treatment.

Aim: To estimate the prevalence of hyponatremia in patients on fluoxetine therapy attending the Psychiatry Outpatient Department (OPD) at a tertiary care hospital and to compare the changes in serum sodium levels between patients younger than 55 years and those older than 55 years on fluoxetine therapy.

Materials and Methods: The present cross-sectional study was conducted in the Outpatient Psychiatry Department of Tirunelveli Medical College and Hospital, Tirunelveli, Tamil Nadu, India over three months, from October 2022 to December 2022. It included patients on fluoxetine therapy for various psychiatric illnesses. The type and duration of psychiatric illness, detailed drug history, and any history suggestive of symptoms of hyponatremia were documented. Blood samples were collected for serum sodium level monitoring. Adverse drug reactions to fluoxetine were recorded and assessed for causality, severity, and preventability using the World Health Organisation (WHO)-Uppsala Monitoring Centre causality assessment scale, the modified Hartwig and Siegel scale, and the modified Schumock

and Thornton scale, respectively. Descriptive statistics were used to analyse baseline and demographic characteristics. The comparison of sodium levels between patients younger than 55 years and those older than 55 was performed using the Mann-Whitney U test.

Results: The mean age of the study participants being 41.03±13 years. The mean age of the males was 39±15.19 years, and that of the females was 42.05±12.29 years. A total of 30 participants were included in the study. Moderate depression was the most common condition for which fluoxetine was prescribed. Hyponatremia was present in 16.7% of the study participants. The median sodium level was 139±4.5 mEq/L in patients aged less than 55 years and 137±4 mEq/L in patients aged more than 55 years, with a p-value of 0.073. Among the reported adverse reactions, 64.5% were classified as possible, 67.74% as mild, and 58% as probably preventable.

Conclusion: Serum electrolyte monitoring is not routinely performed in all patients on fluoxetine. Therefore, relying solely on symptoms to detect hyponatremia may lead to underdiagnosis. Consequently, routine and frequent testing of serum sodium levels is recommended to prevent complications associated with hyponatremia.

Keywords: Adverse drug reactions, Causality assessment, Serotonin

INTRODUCTION

Psychiatric disorders constitute a wide spectrum ranging from sub-clinical states to very severe forms and are one of the leading causes of non fatal disease burden in India [1]. SSRIs are the most commonly prescribed drugs in a variety of psychiatric disorders, including depression, anxiety disorders, panic disorder, and Obsessive-Compulsive Disorder (OCD) [2]. Among the SSRIs, fluoxetine is a well-established antidepressant known for its tolerability and safety advantages over tricyclic agents [3]. It is well-tolerated, has better efficacy, fewer adverse effects, a longer half-life, good compliance, and a lower depression relapse rate after discontinuation, making it a preferred choice in elderly patients with depression. Serotonin-mediated effects on 5-HT (Hydroxytryptamine) and 5-HT_{1c} receptors have been shown to induce the release of the anti-diuretic hormone, resulting in impaired water excretion and consequent water retention, leading to hyponatremia [4,5]. Recent studies have reported that hyponatremia and Syndrome of Inappropriate Anti-diuretic Hormone (SIADH) are more frequent in fluoxetine users than in users of other SSRIs [6].

Hyponatremia is usually defined as a plasma sodium level below 135 mEq/L (normal range 135-145 mEq/L) and is one of the

most common electrolyte abnormalities encountered not only in hospitalised patients but also in routine psychiatric clinical practice [7]. It can lead to adverse sequelae such as drowsiness, confusion, seizures, and even death [8]. The incidence of hyponatremia in elderly patients treated with fluoxetine is 5/1000 per year, reaching a maximum of 8/1000 in elderly women [9]. Hyponatremia and SIADH can cause complications such as seizure, coma, and rarely death in fluoxetine users [10]. The risk of hyponatremia is much higher within the first 2-4 weeks of starting therapy, and this risk appears to diminish over time. By 3-6 months, the risk of hyponatremia is the same as for patients not taking antidepressants [11,12]. Identifying patients at increased risk for the development of hyponatremia is essential for the safe and successful treatment of psychiatric illnesses and for the prevention of treatment complications. There are not many studies on the occurrence of hyponatremia in present population [13,14]. Hence, the present study was conducted to evaluate hyponatremia in patients on fluoxetine therapy. The present study was aimed to estimate the prevalence of hyponatremia in patients on fluoxetine therapy attending the psychiatry Outpatient (OPD) at a tertiary care hospital and to compare the changes in serum sodium levels between patients younger than 55 years and those older than 55 years on fluoxetine therapy.

MATERIALS AND METHODS

The present cross-sectional study was conducted in the Outpatient Psychiatry Department of Tirunelveli Medical College and Hospital, Tirunelveli, Tamil Nadu, India over a period of three months, from October 2022 to December 2022. The study was carried out following approval from the Institutional Ethics Committee (Ref No: 20222404 dated 28.09.2022, Tirunelveli Medical College). Written informed consent was obtained from all study participants in the local vernacular language before inclusion in the study. The study was conducted in accordance with the Declaration of Helsinki. All patients who attended the psychiatric OPD during the study period and met the inclusion criteria were recruited.

Inclusion and Exclusion criteria: Patients attending the psychiatry OPD, aged over 18 years, of any gender, and on fluoxetine therapy for various psychiatric illnesses were included in the study. Pregnant and lactating women, as well as, patients on drugs known to cause hyponatremia, such as lithium, diuretics, carbamazepine, calcium channel blockers, Angiotensin Converting Enzyme (ACE) inhibitors, and laxatives, were excluded from the study.

Study Procedure

Patients of both genders who attended the Psychiatry OPD during the study period were selected by simple random sampling and enrolled in the study according to the inclusion criteria. Basic demographic details like age, gender, and occupation of the patients were recorded in their own language. The type and duration of psychiatric illness, detailed drug history, and history suggestive of symptoms like headache, irritability, dizziness, lethargy, muscle cramps, nausea, confusion, and seizures were inquired about, and blood samples were collected to compare serum sodium levels between individuals belonging to the age groups of less than 55 years and more than 55 years. The normal range of serum sodium levels is between 135 to 147 mEq/L [15]. The occupations of all the study participants were categorised based on the modified Kuppuswamy scale [16]. The WHO-UMC causality assessment was used to evaluate adverse events produced by fluoxetine therapy [17].

The severity of the reported Adverse Drug Reactions (ADRs) was assessed using the modified Hartwig and Siegel scale [18], which classifies ADRs into mild, moderate, and severe based on the clinical outcome. Here, a mild ADR is one where no change in treatment with the suspected drug is needed, and/or the suspected drug has to be held, discontinued, or needs to be changed, but no antidote or other treatment is required, and there is no increase in the length of stay. A moderate ADR is one that requires the treatment with the suspected drug to be held, discontinued, or changed without an increase in the length of hospital stay, or the ADR was the reason for hospitalisation for one day. A severe ADR is one that requires intensive medical care, causes permanent harm to the patient, or directly or indirectly leads to the patient's death. The preventability of the ADRs was measured using the modified Schumock and Thornton scale [19], a free scale with a questionnaire based on clinical circumstances that has three sections: definitely preventable, probably preventable, and not preventable.

STATISTICAL ANALYSIS

The data collected were statistically analysed using Statistical Package for Social Sciences (SPSS) software version 23.0. All the information was entered into a Microsoft excel sheet. Descriptive statistics were performed for baseline and demographic characteristics. Clinical diagnoses and the occurrence of hyponatremia were expressed in numbers and percentages. The Mann-Whitney U test, with a significance level of 0.05, was used to compare the median sodium levels between patients younger than 55 years and those older than 55 years. Adverse drug reactions were described using descriptive statistics, while their severity and preventability were expressed as percentages.

RESULTS

A total of 30 patients attending the psychiatry OPD who met the inclusion criteria were included in the study. Among them, 10 (33.3%) were males and 20 (66.7%) were females, with the mean age of the study participants being 41.03 ± 13 years. The mean age of the males was 39 ± 15.19 years, and that of the females was 42.05 ± 12.29 years. The majority of the study participants were in the age group of under 55 years (25 (83.3%)). The duration of fluoxetine therapy for various psychiatric illnesses ranged from two weeks to two years. The demographic details revealed that 14 (46.7%) of the study participants were housewives, followed by 5 (16.7%) who were private employees [Table/Fig-1].

Variables	n (%)
Study participants (n=30)	
Male	10 (33.3%)
Female	20 (66.7%)
Mean age of study participants (year\pmSD)	
Male	39 \pm 15.19
Female	42.05 \pm 12.29
Age of the participants	
<55-year-old	25 (83.3%)
>55-year-old	5 (16.7%)
Occupation	
Housewife	14 (46.7%)
Private employee	5 (16.7%)
Coolie	4 (13.3%)
Self employed	4 (13.3%)
Not employed	2 (6.7%)
Student	1 (3.3%)

[Table/Fig-1]: Demographic details of the patients.

'n' is number of patients and is expressed in percentage; \pm age expressed in; 'SD' is the Standard deviation

Among the 30 participants, the psychiatric illnesses for which fluoxetine was prescribed included moderate depression in 10 (33.3%) patients, followed by anxiety neurosis, paranoid schizophrenia, and mild depression in 4 (13.3%) patients each, obsessive-compulsive disorder and somatoform disorder in 3 (10%) patients each, and bipolar depression in 2 (6.6%) patients [Table/Fig-2]. Diazepam was the most frequently prescribed concomitant medication, taken by 15 (37.5%) patients [Table/Fig-3]. The table or figure shows the concomitant medications taken by the study participants.

Diagnosis	n (%)
Moderate depression	10 (33.3%)
Anxiety neurosis	4 (13.3%)
Mild depression	4 (13.3%)
Paranoid schizophrenia	4 (13.3%)
OCD	3 (10%)
Somatoform disorder	3 (10%)
Bipolar depression	2 (6.7%)

[Table/Fig-2]: Diagnosis of the study participants on fluoxetine therapy.

'n' is number of patients and is expressed in percentage

The prevalence of hyponatremia among the study participants was 5 (16.7%) patients. Among these, 3 (60%) patients were females and 2 (40%) patients were males. In the age group of less than 55 years, 4 (16.7%) patients had serum sodium levels below 135 mEq/L. Similarly, in the age group of more than 55 years, 1 (20%) patient had serum sodium levels below 135 mEq/L [Table/Fig-4]. The serum sodium levels ranged between 132 and 144 mEq/L in the age group of less than 55 years, while in the age group of more than 55 years, the levels ranged between 132 and 138 mEq/L.

Name of the medication	n (%)
Diazepam	15 (37.5%)
Vitamin B complex	7 (17.5%)
Risperidone	4 (10%)
Trihexyphenidyl	4 (10%)
Clonazepam	3 (7.5%)
Olanzapine	3 (7.5%)
Alprazolam	1 (2.5%)
Chlorpromazine	1 (2.5%)
Nitrazepam	1 (2.5%)
Amityptilline	1 (2.5%)

[Table/Fig-3]: Concomittant medications taken by the study participants. 'n' is number of medications and is expressed in percentage

Hyponatremia	n (%)
Age <55 years	4 (16.7%)
Age >55 years	1 (20%)
Male	2 (40%)
Female	3 (60%)

[Table/Fig-4]: Prevalence of hyponatremia among the study participants. 'n' is number of patients and is expressed in percentage

The median sodium value for the age group of less than 55 years was 139 ± 4.5 mEq/L, while for the age group of more than 55 years, it was 137 ± 4 mEq/L. The Mann-Whitney U test was used to compare the median sodium levels between the two age groups. At a 5% level of significance, there were no significant differences in the median sodium levels between the two age groups ($p=0.073 > 0.05$) [Table/Fig-5].

Variable	Age group		Mann-Whitney U statistic	p-value
	<55-year-old	>55-year-old		
Sodium level	139 (4.5)	137 (4)	30.50	0.073

[Table/Fig-5]: Median sodium levels of patients aged less than 55 years and patients aged more than 55 years. *IQR: Inter quartile range

A total of 31 Adverse Drug Reactions (ADRs) were recorded from 30 patients on fluoxetine therapy. The most common ADR reported was lethargy 5 (16.1%) occurrences, followed by headache, loss of appetite, myalgia, and fatigability. The least common adverse effects were sleepiness 2 (6.4%) occurrences and muscle cramps and irritability 1 (3.2%) occurrence each [Table/Fig-6].

Adverse drug reaction	Number of ADR	Percentage (%)
Lethargy	5	16.1
Headache	4	12.9
Loss of appetite	4	12.9
Myalgia	4	12.9
Fatigability	4	12.9
Dizziness	3	9.6
Nausea	3	9.6
Sleepiness	2	6.4
Muscle cramps	1	3.2
Irritability	1	3.2

[Table/Fig-6]: Adverse drug reactions profile of the study participants. ADR: Adverse drug reaction

According to the WHO UMC causality assessment of ADRs in patients on fluoxetine therapy, 20 (64.5%) occurrences of the ADRs were possible, 11 (35.5%) occurrences were probable, and none of the ADRs were certain [Table/Fig-7]. Based on the modified Hartwig and Siegel scale, 21 (67.74%) occurrences of the ADRs were mild,

10 (32.26%) occurrences were moderate, and there were no severe ADRs [Table/Fig-8]. According to the modified Schumock and Thornton scale, 18 (58%) occurrences of the ADRs were probably preventable, while 13 (42%) occurrences were not preventable [Table/Fig-9].

Causality	Frequency (n)	Percentage (%)
Possible	20	64.5
Probable	11	35.5
Certain	Nil	Nil

[Table/Fig-7]: WHO UMC causality assessment of adverse drug reactions. WHO UMC: World Health Organisation Uppsala Monitoring Centre 'n' is number of adverse drug reactions

Severity	Frequency (n)	Percentage (%)
Mild	21	67.74
Moderate	10	32.26
Severe	0	0

[Table/Fig-8]: Modified Hartwig and Siegel scale for assessing the severity of adverse drug reactions. 'n' is number of adverse drug reactions

ADR	Frequency (n)	Percentage (%)
Definitely preventable	Nil	Nil
Probably preventable	18	58
Not preventable	13	42

[Table/Fig-9]: Modified Schumock and Thornton scale for preventability of adverse drug reactions. 'n' is number of adverse drug reactions; ADR: Adverse drug reaction

DISCUSSION

Hyponatremia is a recognised complication of antidepressant medication due to the syndrome of inappropriate antidiuretic hormone secretion [19]. Among antidepressants, fluoxetine is the most frequently used SSRI because of its efficacy, better tolerability, and favourable adverse effect profile. Although hyponatremia is believed to develop primarily in elderly patients, it can also occur in younger patients, and age does not seem to be a significant risk factor for hyponatremia in this population according to a study by Siegler EL et al., [20]. Monitoring serum sodium levels helps in identifying patients at risk of developing hyponatremia. The present cross-sectional study was conducted in patients on fluoxetine therapy, and serum sodium values were measured in patients both younger and older than 55 years. Females constituted 66.7% of the study population, and a study by Malhotra S and Shah R, reveals that depression, anxiety, and unspecified psychiatric distress are more frequent in women [21].

In the study population, two-thirds of the participants were younger than 55 years, which is similar to the study by Gondek D et al., where middle-aged individuals are prone to psychological distress due to changes in the family environment, career, and increased responsibilities [22]. Housewives made up 46.7% of the study population, which aligns with the study by Fernandes MC et al., [23]. According to a study published in The Lancet by the India State-Level Disease Burden Initiative Mental Disorders Collaborators, the most common psychiatric illness is depression (33.8%), followed by anxiety disorders (19%), and the present study also showed a similar pattern [24]. In this study, diazepam was the most frequently prescribed concomitant medication. The study by Lemberger L et al., indicated that pharmacokinetic drug-drug interactions are minor and that dosage modification of either fluoxetine or diazepam was not necessary [25]. A study revealed that patients treated with SSRIs developed hyponatremia more frequently in the older population [26]. However, in the present study, hyponatremia was seen in both the under-55 years and over-55 years age groups. Studies have reported different frequencies of hyponatremia (25%

to 50%) among fluoxetine users, and most of these studies are retrospective. The majority of studies have been conducted in elderly patients [27]. Age-related susceptibility to hyponatremia may be due to physiological changes in renal and endocrine function. In a study by Liu BA et al., no association was found between the SSRI dose or the patient's age and the onset time of hyponatremia [28]. Various literature sources report symptoms such as headache, blurred vision, polydipsia, weakness, cramps, tremor, impaired gait, nausea, vomiting, seizures, confusion, and coma as indicative of hyponatremia. In the present study, adverse events reported included lethargy, headache, loss of appetite, myalgia, fatigability, dizziness, and nausea, which was similar to the studies by Zhang X and Li XY and Cipriani A et al., [29,30].

In a study by Edinoff AN et al., the most commonly reported side-effects of fluoxetine were sexual dysfunction, headache, and nausea [31]. Many symptoms suggestive of hyponatremia are nonspecific and can be difficult to distinguish from the symptoms or signs of the person's psychiatric illness, possibly leading to mismanagement [9]. The adverse drug reactions were analysed using the WHO UMC causality assessment, and 64.5% were possibly related to fluoxetine, similar to a study where 67% of the results were possible [32]. In the present study, most of the ADRs were mild (67.74%) and did not require discontinuation of drug therapy. A study by Sankhi S et al., showed that mild and moderate reactions accounted for 50.5% and 43.9%, respectively [33], while the study by Munoli S and Patil SB showed 78.96% as mild and 21.04% as moderate severity [34]. When assessing preventability using the Modified Schumock and Thornton scale, 58% of the ADRs were probably preventable, similar to the study by Venkatasubbaiah M et al., [35]. The strength of the study is that it presents evidence of hyponatremia in individuals younger than 55 years, although hyponatremia is traditionally associated with the elderly.

Limitation(s)

The limitation of the present study is that it is a cross-sectional study with a small sample size and a short duration, and baseline sodium values were not obtained. To overcome these limitations, it would be beneficial to conduct a multicentric, prospective study with a larger sample size over a longer duration. Additionally, measuring baseline serum sodium levels and monitoring serum sodium levels at frequent intervals would provide more comprehensive data.

CONCLUSION(S)

Monitoring of serum electrolytes is not routinely performed in all patients on fluoxetine. Therefore, relying solely on symptoms to detect hyponatremia may lead to underdiagnosis. As a result, routine and frequent testing of serum sodium levels is recommended. Active surveillance enables healthcare professionals to detect ADRs early and intervene in a timely manner, thereby providing maximum benefit to the patients.

Acknowledgement

Authors would like to thank colleagues of the faculties of the Department of Pharmacology and Psychiatry of Tirunelveli Medical College and Hospital, Tirunelveli, Tamil Nadu, India for their constant support. The authors would also like to thank the patients included in the present study.

REFERENCES

- Institute of Health Metrics and Evaluation. Global Health Data Exchange (GHDx). <http://ghdx.healthdata.org/gbd-results-tool?params=gbd-api-2019-permalink/d780dffbe8a381b25e1416884959e88b>.
- Blazer DG. Depression in late life: Review and commentary. *J Gerontol A Biol Sci Med Sci*. 2005;58(3):249-65.
- Upadhyay A, Jaber BL, Madias NE. Epidemiology of hyponatremia. *Semin Nephrol*. 2009;29(3):227-38.
- Gandhi S, Shariff SZ, Al-Jaishi A, Reiss JP, Mamdani MM, Hackam DG, et al. Second-generation antidepressants and hyponatremia risk: A population-based cohort study of older adults. *Am J Kidney Dis*. 2017;69(1):87-96.
- <https://emedicine.medscape.com/article/246650-overview>.
- Wilkinson TJ, Begg EJ, Winter AC, Sainsbury R. Incidence and risk factors for hyponatraemia following treatment with fluoxetine or paroxetine in elderly people. *Br J Clin Pharmacol*. 1999;47(2):211-17.
- Greenblatt HK, Greenblatt DJ. Antidepressant-associated hyponatremia in the elderly. *J Clin Psychopharmacol*. 2016;36(6):545-49.
- Mannesse CK, Jansen PA, Van Marum RJ, Sival RC, Kok RM, Haffmans PJ, et al. Characteristics, prevalence, risk factors, and underlying mechanism of hyponatremia in elderly patients treated with antidepressants: A cross-sectional study. *Maturitas*. 2013;76(4):357-63.
- Shakibaei F, Gholamrezaei A, Alikhani M, Taleizadeh K. Serum sodium changes in fluoxetine users at different age groups. *Iran J Psychiatry*. 2010;5(3):113.
- Lane RM. SSRIs and hyponatraemia. *Br J Clin Pract*. 1997;51(3):144-46.
- Coupland C, Dhiman P, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: Population based cohort study. *BMJ*. 2011;343:d4551.
- Leth-Møller KB, Hansen AH, Torstensson M, Andersen SE, Ødum L, Gislason G, et al. Antidepressants and the risk of hyponatremia: A Danish register-based population study. *BMJ Open*. 2016;6(5):e011200.
- Sarkar S, Roy UK, Biswas S, Mallick AK, Mandal P. Clinico-biochemical study of the safety and tolerability of Selective Serotonin Reuptake Inhibitors (SSRI) with special reference to SSRI-induced hyponatremia in humans and animals. *J Clin Diagn Res*. 2021;15(3):05-09.
- Nambiar VK, Parvathy J, Philip TM, Abhijith K, Sreeni S, Panicker NK, et al. Fluoxetine or Venlafaxine for early post stroke depression. *Neurology India*. 2022;70(6):2407.
- Serum Sodium: Reference Range, Interpretation, Collection and Panels. 2022 Oct 14.
- Ananthan VA. Modified Kuppuswamy scale for socioeconomic status of the Indian family-Update based on New CPI (IW) series from September 2020. *J Family Med Prim Care*. 2021;10(5):2048-49.
- https://who-umc.org/media/164200/who-umc-causality-assessment_new-logo.pdf. 2023 Oct 04.
- Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. *Am J Hosp Pharm*. 1992;49(9):2229-32.
- Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. *Hosp Pharm*. 1992;27(6):538.
- Siegler EL, Tamres D, Berlin JA, Allen-Taylor L, Strom BL. Risk factors for the development of hyponatremia in psychiatric inpatients. *Archives of Internal Medicine*. 1995;155(9):953-57.
- Malhotra S, Shah R. Women and mental health in India: An overview. *Indian J Psychiatry*. 2015;57(Suppl 2):S205.
- Gondek D, Bann D, Patalay P, Goodman A, McElroy E, Richards M, et al. Psychological distress from early adulthood to early old age: Evidence from the 1946, 1958 and 1970 British birth cohorts. *Psychological Medicine*. 2022;52(8):1471-80.
- Fernandes MC, Srinivasan K, Stein AL, Menezes G, Sumithra RS, Ramchandani PG. Assessing prenatal depression in the rural developing world: A comparison of two screening measures. *Arch Womens Ment Health*. 2011;14:209-16.
- Sagar R, Dandona R, Gururaj G, Dhaliwal RS, Singh A, Ferrari A, et al. The burden of mental disorders across the states of India: The Global Burden of Disease Study 1990-2017. *The Lancet Psychiatry*. 2020;7(2):148-61.
- Lemberger L, Rowe H, Bosomworth JC, Tenbarger JB, Bergstrom RF. The effect of fluoxetine on the pharmacokinetics and psychomotor responses of diazepam. *Clin Pharmacol Ther*. 1988;43(4):412-19.
- Rottmann CN. SSRIs and the syndrome of inappropriate antidiuretic hormone secretion: Close monitoring of serum sodium levels in high-risk patients taking SSRIs can prevent this condition and the resulting hyponatremia, which can be lethal. *AJN: Am J Nurs*. 2007;107(1):51-58.
- Sandhu HS, Gilles E, DeVita MV, Panagopoulos G, Michelis MF. Hyponatremia associated with large-bone fracture in elderly patients. *Int Urol Nephrol*. 2009;41(3):733-37.
- Liu BA, Mittmann N, Knowles SR, Shear NH. Hyponatremia and the syndrome of inappropriate secretion of antidiuretic hormone associated with the use of selective serotonin reuptake inhibitors: A review of spontaneous reports. *CMAJ: Can Med Assoc J*. 1996;155(5):519.
- Zhang X, Li XY. Prevalence of hyponatremia among older inpatients in a general hospital. *Eur Geriatr Med*. 2020;11(4):685-92.
- Cipriani A, Brambilla P, Furukawa TA, Geddes J, Gregis M, Hotopf M, et al. Fluoxetine versus other types of pharmacotherapy for depression. *Cochrane Database Syst Rev*. 2005;(4):CD004185.
- Edinoff AN, Akuly HA, Hanna TA, Ochoa CO, Patti SJ, Ghaffar YA, et al. Selective serotonin reuptake inhibitors and adverse effects: A narrative review. *Neurol Int*. 2021;13(3):387-401.
- Ambwani S, Dutta S, Mishra G, Lal H, Singh S, Charan J. Adverse drug reaction pattern of anti-depressant drugs prescribed in psychiatry out-patient department in a tertiary care hospital. *Cureus*. 2021;13(11): e19493.
- Sankhi S, Marasine NR, Sankhi S, Lamichhane R. Adverse drug reaction due to antidepressants among patients with depression in a private psychiatric hospital of Nepal. *Biomed Res Int*. 2020;2020:6682928.

[34] Munoli S, Patil SB. Adverse drug reaction monitoring of antipsychotic drugs and mood stabilizers in a teaching hospital. *Int J Pharmacol and Clin Sci.* 2016;5(4):118-21.

[35] Venkatasubbaiah M, Reddy PD, Satyanarayana SV. Analysis and reporting of adverse drug reactions at a tertiary care teaching hospital. *Alex J Med.* 2018;54(4):597-603.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Pharmacology, Government Medical College, Ramanathapuram, Tamil Nadu, India.
2. Associate Professor, Department of Pharmacology, Government Medical College, Tiruppur, Tamil Nadu, India.
3. Assistant Professor, Department of Pharmacology, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India.
4. Professor, Department of Pharmacology, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

R Nalini,
S2, Amazing Ark Apartment, 17th Cross Street, Maharajanagar, Palayamkottai,
Tirunelveli-627011, Tamil Nadu, India.
E-mail: nalluprabha@gmail.com

PLAGIARISM CHECKING METHODS: [\[Jain H et al.\]](#)

- Plagiarism X-checker: Jul 26, 2023
- Manual Googling: Sep 19, 2023
- iThenticate Software: Dec 23, 2023 (21%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 25, 2023**

Date of Peer Review: **Sep 11, 2023**

Date of Acceptance: **Dec 26, 2023**

Date of Publishing: **Feb 01, 2024**