OPEN ACCESS Freely available online

Journal of Psychiatry

Research Article

Hyponatremia in Patients with Mental Disorders

Vasileiadis Panagiotis[1], Mavridis Giorgos[1], Fryda Chrysothemis[2*], Vasileiadis Ilias[3], Mykoniati Sofia[4]

[1]*Internal Medicine Department, General Hospital "G. Papanikolaou- Psychiatric Hospital Thessaloniki", Organic Unit of Psychiatric Hospital, Thessaloniki, Greece*

[2]*General Hospital "G. Papanikolaou- Psychiatric Hospital Thessaloniki", Organic Unit of Psychiatric Hospital, Thessaloniki, Greece*

[3]*University of Thessaly, Greece*

[4]*Internal Medicine Department, Hospital of Jura, Delemont, Switzerland*

INTRODUCTION

Hyponatremia is a potentially dangerous phenomenon that commonly implicates the treatment of psychiatric patients. It is defined as a plasma sodium level below 135 mmol/L, and appears with symptoms such as lethargy, restlessness, disorientation and seizures. The prevalence of hyponatremia in patients with mental disorder ranges from 0.04% (1) to 6.49% (2). Differential diagnoses for hyponatremia are disorders related to renal losses (use of thiazides, loop diuretics, osmotic diuresis, salt losing nephropathies, renal failure), gastrointestinal and third place losses, edematous conditions, antidiuretic hormone (ADH) excess (syndrome of inappropriate ADH secretion-SIADH, mineralocorticoid deficiency, hypothyroidism), primary polydipsia, reset osmostat syndrome, hyperglycemia and hyperlipidemia in form of pseudohyponatremia (3)

Obsessive compulsive disorders, delusional thoughts, xerostomia associated with anticholinergic side effects as well as SIADH syndrome are conditions related to hyponatremia in patients with mental disorder Psychogenic (primary) polydipsia is a disorder with a significant morbidity and mortality affecting 6% to 20% of patients with mental disorder (4-6). Psychogenic polydipsia is relatively common in this population, with a study supporting that up to 70% of institutionalized patients with schizophrenia consume greater than average amounts of water (7). Nevertheless, only one-fifth to one-third of polydipsic patients will experience symptomatic hyponatraemia (8). The syndrome of psychosis, intermittent hyponatremia, and polydipsia (PIP syndrome) is manifest clinically as polydipsia and intermittent hyponatremia and its pathophysiology is based on defects on thirst regulation, inappropriate arginine vasopressin (AVP) secretion and excessive response to AVP by the renal tubes. There are studies that correlate nicotine and caffeine abuse, treatment with anticholinergic or certain psychotropic medications, substance abuse, concurrent diagnoses of schizophrenia and alcohol abuse with PIP syndrome (9).

Hyponatremia has been associated with a wide range of psychiatric medication. During treatment with SSRIs, it can affect 0.5 to 25% of patients (10). Especially fluoxetine but also sertraline, paroxetine (11), citalopram and fluvoxamine have been reported for possible correlation with hyponatremia (12-15). There are also case reports that implicate escitalopram, with hyponatremia and SIADH (12,13-17). SSRIs combined with diuretics and angiotensin converting enzyme (ACE) inhibitors, induce a 10-fold risk increase of hyponatremia comparing to use of SSRIs alone (1). Among patients treated with SSRIs, women of age greater than 65 years, with history of pneumonia, low body weight, low baseline sodium and concurrent use of diuretics are more possible to suffer from hyponatremia (18).

Regarding the rest psychiatric medication, tricyclic antidepressants, monoamine oxidase inhibitors (19), duloxetine (20), desvenlafaxine (21), bupropion (22,23), mirtazapine (24), carbamazepine, oxcarbazepine(19), trazodone(25), sodium valproat (19) , typical (19) and atypical antipsychotic agents (25,26) including quetiapine (27) and aripiprazole (28,29), have also been reported to implicate SIADH and hyponatremia. Venlafaxine is also accused to induce hyponatremia (19, 30-32) and when combined with SSRIs it is 5.6 times more likely to cause this electrolyte imbalance(33).

In general, older age, use of diuretics (30) and generally co-medications known to induce hyponatremia, severe physical illness (34), female gender (12,13,34), low bodyweight (35), higher dose of SSRIs (36) and diagnosis of a mood disorder (25) are assumed to be risk factors for the development of hyponatremia in patients with mental disorder.

In our study we aimed to investigate the prevalence of hyponatremia in inpatients with mental disorders and the

Correspondence to: Fryda Chrysothemis, General Hospital "G. Papanikolaou- Psychiatric Hospital Thessaloniki", Organic Unit of Psychiatric Hospital, Thessaloniki, Greece, Tel: 306942559029; E-mail: xrisfry@gmail.com

Received: October 28, 2019; **Accepted:** August 25, 2021; **Published:** September 06, 2021

Citation: Panagiotis V, Giorgos M, Chrysothemis F, Ilias V, Sofia M (2021) Hyponatremia in Patients with Mental Disorders. J Psychiatry. 24:p623.

possible correlations between demographical features, medications and hyponatremia in this group of patients.

MATERIALS AND METHODS

Data was collected from the medical records of patients that were admitted in the Internal Medicine Department of Psychiatric Hospital of Thessaloniki from May 2012 to June 2016 through an observational retrospective study. Patients had given a blood sample for a complete blood count at their admission to the internal medicine department.

From the initial population of inpatients, the following patients were excluded: patients without a psychiatric diagnosis, patients with hypervolemic hyponatremia such as cirrhosis and patients with hypothyroidism and TSH> 4,1mIU/L. Incidents of pseudohyponatremia due to hyperglycemia, were corrected according to the type that a serum glucose increase of 100mg/dL, causes a serum sodium reduction of 1,6 mEq/L. The remaining population included 501 patients. Patients with sodium serum levels ≤ 135 mEq/L, were considered to have hyponatremia.

Statistical analysis was conducted using SPSS 21.0. Variables that were studied were age, BMI, gender, smoking, educational level, marital status, ethnicity, comorbidities, reason of admission to internal medicine department, psychiatric diagnosis, laboratory data and psychiatric, antihypertensive, hypolipidemic and hypoglycemic medication. Univariate level associations between the different socio-demographic, clinical, laboratory and pharmacological variables were made with t-tests, Chi-Square tests, or Fisher's Exact test, as appropriate. P-values less than 0.05 were considered statistically significant.

The anonymity of the patients was maintained and only medical personnel conducted the study after the approval of the Psychiatric Hospital Ethics Committee (protocol number: 197-26/9/2016).

RESULTS

The population that satisfied the study criteria included 501 patients. Among them, 108 patients had hyponatremia (21.6%). Among patients with mental disorder and hyponatremia, 78.7% were male and 21.3% female. They had a mean age of 59 years and a mean BMI of 26.6 kg/m2. Regarding their educational level, 3.7% of patients with hyponatremia were illiterate and 38% of them had attended the elementary school. Only 13.9% were married and 86.1% were unmarried/widowed or divorced. The majority of the patients were smokers (72.6%) and hypertension was detected in 39.6% of the patients (Table 1).

Table 1: Demographical characteristics and comorbidities.

	Percentage
Male	78.7%
Female	21.3%
Smokers	72.5%
Hypertension	39.6%
Hyperlipidemia	16.2%
Coronary artery disease	10.2%
Diabetes Melitus 2	15.2%
Illiterate educational level	3.7%
Elementary school	38%
High school	6.5%
College/ University	2.8%
Greek nationality	91.7%
Non-greek nationality	8.3%
Married	13.9%
Unmarried/widowed/divorced	86.1%

Patients with hyponatremia, as presented in Table 2, had an elevated mean erethrocyte sedimentation rate (37mm/h), elevated blood glucose levels (122.4 mg/dl). Hct, Hb, WBCs, Urea, creatinine, SGOT, SGPT, cholesterol, triglycerides, HDL, LDL, HbA1c were within the normal range.

Table 2: Laboratory results of patients with hyponatremia.

	Mean
Hct (%)	36.6
Hb (g/dl)	12.5
WBCs	9,259
ESR(erethrocyte sedimentation rate, mm/h)	37
Glucose (mg/dl)	122.4
Urea (mg/dl)	37
Creatinine (mg/dl)	1
SGOT (U/L)	35.7
SGPT (U/L)	31.4
Cholesterole (mg/dl)	167
Triglycerides (mg/dl)	115.9
HDL (mg/dl)	49.5
LDL (mg/dl)	98.1

HbA1c (%)	6.5

Psychotic patients accounted for 58.4% of total population. Nevertheless, patients with psychosis accounted for 77.6% of patients with hyponatremia. Among hyponatremic patients, 37.4% of them had schizophrenia and 40.2% other types of psychosis. Among the rest of the population with hyponatremia, 13.1% of patients had mood disorders (5.6% and 7.5% for depression and bipolar disorder respectively), 3.7% had a personality disorder, 3.7% suffered from organic psychosyndrome and 1.9% of them from alcohol related disorders (Table 3).

Table 3: Distribution of psychiatric diagnoses in total population and in population with hyponatremia.

Mental disorder	Total population		Hyponatremic patients	
Psychosis		58.4%		77.6%
-Schizophrenia	22.6%		37.4%	
-Other Psychoses	35.8%		40.2%	
Mood disorders		18.9%		13.1%
-Depression	12.6%		5.6%	
-Bipolar Disorder	6.3%		7.5%	
Personality disorders		3.5%		3.7%
Alcoholism		14.8%		1.9%
Organic psychosyndrome		3.7%		3.7%
Other		0.8%		0%
Total		100%		100%

Among the patients with hyponatremia, 24.1% were admitted to the Internal Medicine department due to electrolyte imbalances and 15.7% specifically for hyponatremia. The rest of them were admitted with a number of different diagnoses (data not shown).

In order to study the correlation between medication and hyponatremia, we estimated the percentage of hyponatremia among population taking each drug. Drugs that were studied, were benzodiazepines, SSRIs, SNRIs, atypical and typical antipsychotics, anticonvulsants as well as antihypertensive, hypoglycemic and hypolipidemic agents and others (Tables 4, 5).

Table 4: Psychiatric drug distribution in patients with hyponatremia.

Psychiatric medication (number of patients taking the drug in total population)	Frequency in patients with hyponatremia	P-value	Odds ratio/ 95% Confidence Interval
SNRIs (n=12)	25%	0.72	0.82[0.218,3.084]
SSRIs (n=97)	26.8%	0.17	0.69 [0.41,1.15]
BENZODIAZEPINES (n=162)	30.2%	0.02	0.486 [0.31,0.752]
ATYPICAL ANTIPSYCHOTICS (n=249)	34.1%	0.00	0.194 [0.11,0.32]
TYPICAL ANTIPSYCHOTICS (n=51)	27.5%	0.28	0.69 [0.36, 1.34]
ANTICONVULSANTS (n=80)	33.8%	0.007	0.46 [0.27,0.78]
OTHERS (n=143)	7%	0.000	5 [2,53, 9.92]
SNRIs			
Duloxetine (n=10)	20%	1	1.1 [0.23, 5.26]
Venlafaxine (n=2)	50%	0.38	0.27 [0.01, 4.4]
SSRIs			
Citalopram (n=28)	28.6%	0.34	0.67 [0.28, 1.56]
Escitalopram (n=33)	9.1%	0.081	2.8 [0.86, 9.67]
Fluoxetine (n=13)	30.8%	0.49	0.6 [0.18, 2]
Sertraline (n=16)	25%	0.75	0.81 [0.25, 2.5]
Paroxetine (n=7)	100%	0.000	0.93 [0.89, 0.98]
BENZODIAZEPINES			
Bromazepam (n=9)	44.4%	0.1	0.33 [0.08, 1.27]

Alprazolam (n=13)	7.7%	0.31	3.37 [0.43, 26.21]
Clonazepam (n=6)	33.3%	0.61	0.54 [0.098, 3]
Lorazepam (n=95)	32.6%	0.005	0.48 [0.29, 0.79]
Chlorodiazepoxide (n=3)	0%	1	1 [0.99, 1]
Diazepam (n=44)	25%	0.566	0.8 [0.39, 1.65]
ATYPICAL ANTIPSYCHOTICS			
Olanzapine (n=73)	31.5%	0.031	0.53 [0.31, 0.93]
Clozapine (n=24)	41.7%	0.021	0.36 [0.15, 0.84]
Quetiapine (n=93)	35.5%	0.001	0.41 [0.25, 0.67]
Risperidone (n=70)	27.1%	0.21	0.69 [0.39, 1.24]
Ziprasidone (n=2)	50%	0.38	0.27 [0.01, 4.4]
Paliperidone (n=6)	66.7%	0.022	0.13 [0.02, 0.73]
Amisulpride (n=29)	37.9%	0.036	0.42 [0.19, 0.92]
Aripiprazole (n=3)	33.3%	0.51	0.54 [0.04, 6]
TYPICAL ANTIPSYCHOTICS			
Haloperidol (n=127)	22.8%	0.7	0.9 [0.55, 1.46]
Chloropromazine (n=2)	0%	1	1 [0.99, 1]
Levomepromazine (n=35)	31.4%	0.14	0.57 [0.27, 1.21]
Zuclopenthixole (n=6)	0%	0.34	1 [1,1]
Perphenazine (n=8)	25%	0.68	0.82 [0.16, 4.13]
Trifluoperazine (n=2)	50%	0.38	0.99 [0.97, 1]
ANTICONVULSANTS			
Carbamazepine (n=2)	100%	0.046	0.98 [0.95, 1]
Oxcarbamazepine (n=10)	50%	0.043	0.26 [0.07, 0.93]
Valproic Sodium (n=59)	33.9%	0.018	0.48 [0.26, 0.87]
Lamotrigine (n=6)	16.7%	1	1.37 [0.15, 11.92]
Topiramate(n=19)	15.8%	0.77	1.48 [0.42, 5.19]
OTHERS			
Lithium (n=4)	0%	0.58	1 [1,1]
Hydroxizine (n=2)	0%	1	1 [0.99, 1]
Donepezil (n=5)	20%	1	1.1 [0.12, 9.94]
Biperiden (n=157)	27.4%	0.035	0.61 [0.39, 0.96]
Mirtazapine (n=24)	16.7%	0.79	1.34 [0.46, 4.16]
Amitryptiline (n=11)	18.2%	1	1.24 [0.26, 5.83]
Buspirone (n=3)	33.3%	0.51	0.54 [0.04, 6.09]

Table 5: Non psychiatric drug distribution in hyponatremic patients.

Angiotensin II receptor blockers (n=63)	17.5%	0.51	1.34 [0.67, 2.67]
Angiotensin converting enzyme inhibitors (n=29)	34.5%	0.1	0.49 [0.22, 1.1]
Calcium channel blockers			
Amlodipine (n=45)	35.6%	0.022	0.45 [0.23, 0.87]
Barnidipine (n=6)	66.7%	0.022	0.13 [0.02, 0.73]
Felodipine (n=2)	0%	1	1 [0.98, 1]
Verapamil (n=3)	33.3%	0.51	0.54 [0.04, 6]
HYPOLIPIDEMIC AGENTS			

Paravastatin (n=9)	11.1%	0.69	2.22 [0.27, 17.9]
Simvastatin (n=33)	12.1%	0.19	2 [0.71, 6]
Atorvastatin (n=47)	17%	0.57	1.37 [0.62, 3]
Rosuvastatin (n=2)	50%	0.38	0.27 [0.01, 4.4]
Fenofibrate (n=10)	30%	0.45	0.63 [0.16, 2.49]
Ezetimibe (n=2)	0%	1	1 [0.99, 1]
HYPOGLYCEMIC AGENTS			
Metformin (n=68)	11.8%	0.039	2.25 [1, 4.86]
Insulin (n=10)	20%	1	1.1 [0.23, 5.26]
Sitaglipitin (n=20)	15%	0.58	1.58 [0.45, 5.5]
Vidaglipitn(n=14)	28.6%	0.51	0.67 [0.2, 2.2]
Linagliptin (n=2)	50%	0.38	0.27 [0.01, 4.4]
Gliclazide (n=2)	0%	1	1 [0.99, 1]

Benzodiazepines, atypical antipsychotics and anticonvulsants in general were found to cause hyponatremia in statistical significant percentages of 30.2% (X2(1,n=501)=10.69, p=0.02, OR= 0.48, CI[0.31,0.752]), 34.1% (X2(1,n=501)=46.32, p=0, OR= 0.194, CI[0.11, 0.32]), and 33.8% (X2(1,n=501)=8.37, p=0.007, OR= 0.46, CI[0.27, 0.78]) respectively.

Benzodiazepines that were studied were bromazepam, alprazolam, clonazepam, lorazepam, chlorodiazepoxide and diazepam. Only lorazepam was found to be a statistically significant cause of hyponatremia with a percentage of 32.6% and X2(1,n=501)=8.503, p=0.005, OR= 0.48, CI[0.29, 0.79]. That meant that of the 95 patients that took lorazepam, 32.6% of them were found to have hyponatremia.

Among SNRIs, duloxetine and venlafaxine were studied, but niether of them showed a statistically significant correlation with hyponatremia.

SSRIs that were studied were citalopram, escitalopram, fluoxetine, sertraline and paroxetine. Only paroxetine had a statistically significant correlation with hyponatremia. All 7 patients that took paroxetine had hyponatremia. (X2(1,n=501)=25.83, p=0, OR= 0.93, CI[0.89,0.98]).

Atypical antipsychotics that were studied were olanzapine, clozapine, quetiapine, risperidone, ziprasidone, paliperidone, amisulpride and aripiprazole. Of all patients that took olanzapine, 31.5% were found to have hypontremia (X2(1,n=501)=5, p=0.031, OR= 0.53, CI[0.31,0.93]). Prevalence of hyponatremia among patients taking clozapine was 41.7% (X2(1,n=501)=6.02, p=0.02, OR= 0.36, CI[0.15,0.84]), taking quetiapine 35.5% (X2(1,n=501)=13.09, p=0.001, OR= 0.41, CI[0.25,0.67]), taking paliperidone 66.7% (X2(1,n=501)=7.3, p=0.02, OR= 0.13, CI[0.02, 0.73]) and taking amisulpride 37.9% X2(1,n=501)=4.88, p=0.036, OR= 0.42, CI[0.19, 0.92]).

Among typical antipsychotics that were studied, such as haloperidol, chloropromazine, zuclopenthixole, perphenazine, trifluoperazine, none of them was found to have a statistically significant correlation with hyponatremia.

Anticonvulsants that were studied were carbamazepine, oxcarbazepine, valproic sodium, lamotrigine and topiramate. Statistically significant results were found for carbamazepine - both patients that took the agent had hyponatremia, (X2(1,n=501)=7.3, p=0.046, OR= 0.98, CI[0.95,1]), oxcarbamazepine (prevelance of hyponatremia 50%, X2(1,n=501)=4.88, p=0.043, OR= 0.26, CI[0.07,0.93]) and valproic sodium (prevalence 33.9%, X2(1,n=501)=6.02, p=0.018, OR= 0.48, CI[0.26,0.87]).

Other agents that were studied were lithium, hydroxyzine, donepezil, biperiden, mirtazapine, amitryptiline and buspirone. Among them only biperiden showed a statistically significant correlation with hyponatremia, with prevalence of 27.4% (X2(1,n=501)=4.59, p=0.035, OR= 0.61, CI[0.39,0.96]).

Regarding antihypertensive medication, among aldosterone antagonists, central acting a2 adrenergic agonists, diuretics, b-blockers, angiotensin II receptor blockers, angiotensin converting enzyme inhibitors and calcium channel blockers, only the latter had a statistically significant correlation with hyponatremia, with prevalence 36.8% (X2(1,n=501)=8.88, p=0.006, OR= 0.41, CI[0.23,0.75]). Among calcium chanel blockers, amlodipine and barnidipine had statistically significant results with percentages of hyponatremia 35.6% (X2(1,n=501)=5.73, p=0.022, OR= 0.45, CI[0.23, 0.87]), and 66.7% (X2(1,n=501)=7.3, p=0.022, OR= 0.13, CI[0.02,0.73) respectively.

Hypolipidemic agents such as paravastatin, simvastatin, atorvastatin, rosvastatin, fenofibrate and ezetimibe did not show statistically significant results.

Finally, among hypoglycemic agents that were studied, such as metformin, insulin, sidagliptin, vidagliptin, linagliptin and gliclazide, only metformin showed statistically significant results with percentage of 11.8% (X2(1,n=501)=4.46, p=0.039, OR= 2.25, CI[1,4.86])

DISCUSSION

In a population of patients with mental disorder that were eligible for our study, the prevalence of hyponatremia was 21.6%. This is a very high percentage compared to other studies, whereas the highest percentage was 6.49% in a population of 1000 inpatients with mental disorder (2).

According to our findings, psychotic patients had a greater tendency to show hyponatremia, since they accounted for 77.6% of patients with hyponatremia, with 37.4% of them having schizophrenia and 40.2% other types of psychosis. Regarding mood disorders, the prevalence of hyponatremia was 13.1% with 5.6% of them having depression and 7.5% bipolar disorder. On the contrary, Lange-Asschenfeldt et al. in 2013, in a large retrospective study of 7113 inpatients with mental disorder, found that mood disorders are associated with more severe hyponatremia (25).

The positive association between most of SSRIs and hyponatremia, indicated by multiple studies (12-17), was not confirmed by our findings, neither by Lange-Asschenfeldt et al. in 2013. More specifically, in our study, among SSRIs only paroxetine was found to have a statistically significant correlation with hyponatremia, since all 7 patients who took it had hyponatremia.

In our study, most of atypical antipsychotics, as confirmed by various studies and case reports (25-29) correlated with hyponatremia. Olanzapine 31.5%, clozapine 41.7%, quetiapine 41.7%, paliperidone 66.7% and amisulpride 37.9%. On the contrary, none of the typical antipsychotics, as supported by Liamis et al. 2008 in a review of drug induced hyponatremia, had a statistically significant association with hyponatremia in our study.

Finally, among classes of antihypertensive medication, only calcium channel blockers were found to have a positive correlation with hyponatremia and specifically amlodipine (35.6%) and barnidipine (66.7%) in contrast with other studies that indicate diuretics (25,30) and angiotensin converting enzyme inhibitors (25) as a risk factor for hyponatremia.

The 27.4% of patients who took biperiden and had hyponatremia is not considered to be assessable due to the supplementary use of the drug for the extrapyramidal effects of antipsychotics. Among benzodiazepines, patients who were under treatment with lorazepam, had hyponatremia in a percentage of 32.6%. Among anticonvulsants, carbamazepine, oxcarbazepine and valproic sodium were also found to cause hyponatremia in significant degree. Nevertheless, due to the rare use of the above drugs as a monotherapy in inpatients with mental disorder, these results were not considered assessable, too.

Furthermore, a limitation of our study was that drugs could not be associated with hyponatremia as monotherapy, as they were a multiple drug medication.

CONCLUSION

In our study we found a high prevalence of hyponatremia in inpatients with mental disorder. Male gender, smokers, elevated ESR as well as the presence of psychosis seemed to be risk factors for hyponatremia in inpatients with mental disorder. Most of atypical antipsychotics and anticonvulsants, only paroxetine amongst SSRIs and calcium channel blockers were included in medication accused for hyponatremia. Close monitoring of inpatients with mental disorder with symptoms of polydipsia, timely change of medication implicating hyponatremia, regular laboratory and clinical revaluation of patients with low plasma sodium levels could improve the diagnosis and outcome of hyponatremia that so commonly implicates the treatment of patients with mental disorder.

REFERENCES

1. Letmaier M, Painold A, Holl AK, Vergin H, Engel R, Konstantinidis A, Kasper S, Grohmann R. Hyponatraemia during psychopharmacological treatment: results of a drug surveillance programme, Int J Neuropsychopharmacol. 2012; 15(6): 739-48.
2. Manu P, Ray K, Rein JL, De Hert M, Kane JM, Correll CU. Medical outcome of psychiatric inpatients with admission hyponatremia. Psychiatry Res. 2012; 198(1): 24-7.
3. Milionis H, Liamis G, Elisaf M. The hyponatremic patient: a systematic approach to laboratory diagnosis. CMAJ. 2002; 166(8): 1056-1062.
4. Dundas B, Harris M, Narasimhan M. Psychogenic polydipsia review: etiology, differential, and treatment. Current Psychiatry Reports. 2007; 9(3): 236–241.
5. Verghese C, De Leon J, Joslassen RC. Problems and progress in the diagnosis and treatment of polydipsia and hyponatremia. Schizophrenia Bulletin. 1996; 22(3): 455–464.
6. De Leon J, Gill M, McCauley M, Polydipsia--a study in a long-term psychiatric unit. Eur Arch Psychiatry Clin Neurosci. 2003; 253(1): 37-9.
7. Vieweg WVR, Wilkinson EC, David JJ, Rowe WT, Hobbs WB, Spradlin, WW. The use of demeclocycline in the treatment of patients with psychosis, intermittent hyponatremia, and polydipsia (PIP syndrome). Psychiatric Quarterly. 1988; 59: 62-68
8. De Leon J, Verghese C, Tracy JI, Josiassen RC, Simpson GM. Polydipsia and water intoxication in psychiatric patients: a review of the epidemiological literature. Biological Psychiatry. 1994; 35(6): 408–419.
9. Leadbetter RA, Shutty MS Jr, Higgins PB, Pavalonis D. Multidisciplinary approach to psychosis, intermittent hyponatremia, and polydipsia. Schizophr Bull. 1994; 20(2): 375-85.
10. Grover S, Biswas P, Bhateja G, Kulhara P. Escitalopram-associated hyponatremia. Psychiatry Clin Neurosci. 2007; 61(1): 132-143.
11. Fabian TJ, Amico JA, Kroboth PD, Mulsant BH, Corey SE, Begley AE, Bensasi SG, Weber E, Dew MA, Reynolds CF 3rd, Pollock BG Paroxetine-induced hyponatremia in older adults: a 12-week prospective study. Arch Intern Med. 2004; 164(3): 327-32.
12. Giorlando F, Teister J, Dodd S, Udina M, Berk M. Hyponatraemia: an audit of aged psychiatry patients taking SSRIs and SNRIs. Curr Drug Saf. 2013; 8(3): 175-180.
13. Romero S, Pintor L, Serra M, Plana T, Navarro V, Gastó C, Goldstein B. Syndrome of inappropriate secretion of antidiuretic hormone due to citalopram and venlafaxine. Gen Hosp Psychiatry. 2007; 29(1): 81-4.
14. Odeh M, Beny A, Oliven A. Severe symptomatic hyponatremia during citalopram therapy. Am J Med Sci. 2001; 321: 159–160.
15. Liu B, Mittman N, Knowles SR, Shear NH. Hyponatremia and syndrome of inappropriate secretion of antidiuretic hormone associated with the use of selective serotonin re uptake inhibitors: A review of spontaneous reports. Can Med Assoc. J. 1996; 155: 519–527.
16. Nahshoni E, Weizman A, Shefat D, Pik N. A case of hyponatremia associated with escitalopram. J Clin Psychiatry. 2004; 65: 1722.
17. CNS Spectr. 2006; 11(6): 429-32.

18. Jacob S, Spinler SA, Hyponatremia associated with selective serotonin-reuptake inhibitors in older adults. Ann Pharmacother. 2006; 40(9): 1618–1622.
19. Liamis G, Milionis H, Elisaf M. Review of drug induced hypontremia. Am J Kidney Dis. 2008; 52:144-153
20. Choi JS, Lee HW, Lee JY, Jung HY. Rapid-onset hyponatremia induced by duloxetine in a middle-aged male with depression and somatic symptoms. Psychiatry Investig. 2012; 9(1): 83-4.
21. Lee G, Leung J, Syndrome of inappropriate secretion of antidiuretic hormone due to desvenlafaxine. Gen Hosp Psychiatry. 2013; 35(5): 574.e1-3.
22. Kate N, Grover S, Kumar S, Modi M. Bupropion-induced hyponatremia. Gen Hosp Psychiatry. 2013; 35(6): 681.e11-2.
23. Wiggins A, Balasubramanian T, Ferraro A. Hyponatraemia and confusion in a 70-year-old female when bupropion was added to dothiepin and escitalopram. Australas Psychiatry. 2015; 23(5): 507-9.
24. Ghosh A, Hegde A, Grover S. Mirtazapine-associated hyponatremia presenting as delirium. Indian J Pharmacol. 2014; 46(4): 448-9.
25. Lange-Asschenfeldt C, Kojda G, Cordes J, Hellen F, Gillmann A, Grohmann R, Supprian T. Epidemiology, symptoms, and treatment characteristics of hyponatremic psychiatric inpatients. J Clin Psychopharmacol. 2013; 33(6): 799-805.
26. Gandhi S, McArthur E, Reiss JP, Mamdani MM, Hackam DG, Weir MA, Garg AX. Atypical antipsychotic medications and hyponatremia in older adults: a population-based cohort study. Can J Kidney Health Dis. 2016; 11(3): 21.
27. Koufakis T. Quetiapine-Induced Syndrome of Inappropriate Secretion of Antidiuretic Hormone. Case Rep Psychiatry. 2016; 2016: 4803132.
28. Lecamwasam DL, Alexander J. Aripiprazole associated hyponatraemia. Aust N Z J Psychiatry. 2011; 45(8): 686-7.
29. Behere RV, Venkatasubramanian G, Naveen MN, Gangadhar BN. Aripiprazole-induced hyponatremia: a case report. J Clin Psychiatry. 2007; 68(4): 640-1.
30. De Picker L, Van Den Eede F, Dumont G, Moorkens G, Sabbe BG. Antidepressants and the risk of hyponatremia: a class-by-class review of literature. Psychosomatics. 2014; 55(6): 536-47.
31. 31. Javed Q, Alam F, Krishna S. Reversible hyponatraemia with venlafaxine in a young patient. BMJ Case Rep. 2009; 07: 2009-2084.
32. Roxanas M, Hibbert E, Field M. Venlafaxine hyponatraemia: incidence, mechanism and management. Aust N Z J Psychiatry. 2007; 41(5): 411-8.
33. Kirby D, Harrigan S, Ames D. Hyponatraemia in elderly psychiatric patients treated with Selective Serotonin Reuptake Inhibitors and venlafaxine: a retrospectiave controlled study in an inpatient unit. Int J Geriatr Psychiatry. 2002 Mar; 17(3): 231-7.
34. Egger C, Muehlbacher M, Nickel M, Geretsegger C, Stuppaeck C. A review on hyponatremia associated with SSRIs, reboxetine and venlafaxine. Int J Psychiatry Clin Pract. 2006; 10(1): 17-26.
35. Wilkinson TJ, Begg EJ, Winter AC, Sainsbury R. Incidence and risk factors for hyponatremia following treatment with fluoxetine or paroxetine in elderly people. Br J Clin Pharmacol. 1999; 47: 211–217.
36. Fisher A, Davis M, Croft-Baker J, Purcell P, McLean A. Citalopram-induced severe hyponatremia with coma and seizure. Case report with literature and spontaneous reports review. Adverse Drug React Toxicol Rev. 2002; 21: 179–187.