RESEARCH ARTICLE

Drug utilization pattern and adverse drug reactions in patients on antidepressants

Tejashwini K[1], Aruna Bhushan[2], Suma S[3], Rajendrakumar Katte[4]

[1]Department of Pharmacology, A. C. S. Medical College and Hospital, Chennai, Tamil Nadu, India, [2]Department of Pharmacology, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India, [3]Department of Physiology, A. C. S. Medical College and Hospital, Chennai, Tamil Nadu, India, [4]Department of Psychiatry, Belagavi Institute of Medical Sciences, Belagavi, Karnataka, India.

Correspondence to: Aruna Bhushan, E-mail: teja16k@gmail.com

ABSTRACT

Background: Depression is the most common mental illness, it is on the rise globally, and when patients do not follow prescribed antidepressant regimen or discontinue the therapy, it results in suboptimal treatment, relapse rate, and poor quality of life. **Aims and Objectives:** The present study is designed to study the drug utilization pattern observed in patients receiving antidepressants in the psychiatry department and to study adverse drug reactions (ADR) observed in patients receiving antidepressants. **Materials and Methods:** The study was conducted in the psychiatry department of BIMS hospital, Belagavi. 598 prescriptions with antidepressants were collected in a specially designed pro forma containing demographic, disease, and drug data. Moreover, during their follow–up, ADRs if any were noted. The data were analyzed statistically and the results were expressed as numbers and percentage. **Results:** A total of 598 patients were analyzed. Among these, 57.86% were male and 42.13% were female. Most commonly affected age group and those who received maximum of the antidepressants were between 41 and 60 years. Fluoxetine (48.32%) was the most prescribed antidepressant. The total number of drugs prescribed was 957, with the average number of drugs per prescription being 1.60. In our study, 75.65% of drugs were prescribed by their generic name and the remaining 24.35% were brand names. **Conclusions:** There is a need for drug utilization studies to encourage rational and appropriate use of drugs. Moreover, there is a growing concern to monitor and analyze the ADRs or any drug interactions to antidepressant drug pattern use. In this study, the use of antidepressants in patients was found to be appropriate.

KEY WORDS: Depression; Drug utilization study; Antidepressants

INTRODUCTION

Depression, nowadays, has become a major health issue, which affects person's quality of life. Many drugs have been discovered for the treatment of depression, but the drugs which are being used may be underdosed or overdosed so which may lead to either suboptimal treatment or adverse effects due to drugs, respectively. Henec, to improve the quality of treatment, drug utilization studies (DUS) can be used. DUS emphasizes on the rationality of drug use as well as provides valuable evidence-based guidance for making policy decisions at various levels of health care.[1] These studies estimate the number of patients exposed to drugs and to what extent the drugs are being used in certain area, describing the pattern of drug use. In individual patients, rational drug use implies the prescription of well-documented drug in an optimal dose for the right indication at an affordable price. Inappropriate use of drugs will increase the risk of

adverse drug reactions (ADR) and also financial burden to the patientsThe problem of inappropriate use of drugs is seen in both developing as well as developed countries, resulting a major risk in medical practice.[2]

Several methods of DUS have been used internationally and regionally such as the methods used for qualitative studies to identify the differences in use in different countries. Studies on prescription pro forma target on analyzing the pattern of drug use among patient categories such as age, gender, and diagnosis.[3] The ultimate goal of DUS is to facilitate rational drug use and to develop strategies to utilize health resources in the most efficient manner. It is particularly needed in a developing country like India where 72% of all health-care burden is borne by the patients.[4] There is also no availability of proper reporting of medication errors in the hospital due to irrational drug use. Drugs play a very important role in maintaining human health quality. Emergence of newer drugs and increase recognition of delayed adverse effects have stimulated interest in the study of prescribing patterns of drugs.

Depression is characterized by sad mood, pessimistic worry, diminished interest in normal activities, mental slowing and poor concentration, insomnia or increased sleep, significant weight loss or gain, psychomotor agitation or retardation, feelings of guilt and worthlessness, decreased energy, and libido and suicidal ideation occurring for a period of at least 2 weeks. It affects an individual's ability to work, study, sleep, eat, and enjoy the once pleasurable activities which produce a large burden for self. Major depressive disorder is associated with a significant impairment of social and interpersonal functioning.[5] Antidepressant prescribing pattern has also changed globally over the last few years.[6] Many patients with major depression have recurring episodes, and it requires long-term treatment of their illness.

DUS are an inexpensive tool for the evaluation of current prescribing patterns; therefore, this kind of studies is useful to suggest modifications to achieve rational and cost-effective therapeutic practices in health care. Therefore, the aim of this study is to assess the pattern of use of different classes of antidepressants and ADR.

MATERIALS AND METHODS

Data were collected from outpatient prescriptions study which was carried out in the Department of Psychiatry, BIMS, Belagavi. It was a prospective observational study done during the period of April 1st 2016 to September 30th 2016. A total of 598 patients on antidepressants were included in our study. Inclusion criteria: (a) All outpatients on antidepressants of either sex, aged between 18 and 60 years attending psychiatry department, and (b) all patients diagnosed with depression and any other related conditions who were prescribed with antidepressants were included in the study. Exclusion criteria: (a) Pregnant and lactating mothers and (b) inpatients of psychiatry department were excluded from the study.

Method of Collection of Data

After obtaining approval and clearance from the Institutional Ethical Committee, the data werecollected prospectively by direct observation in specially designed pro forma containing relevant detail such as patient details including registration number, age, gender, and diagnosis (according to Montogomery–Asberg Depression Rating Scale), disease data, and drug data. Drugs prescribed with generic or brand name, dosage, route, frequency of administration, and ADR were collected as per pro forma. The prescribed drugs were classified according to the anatomical therapeutic chemical (ATC)-defined daily dose (DDD) classification.

In our study, for each prescription, there were multiple doses of antidepressants prescribed, and the average of the daily doses of antidepressant was taken as prescribed daily dose (PDD). And then, PDD-to-DDD ratio was calculated.

Statistical Application

The drugs are classified based on the WHO-ATC classification. The data collected were analyzed statistically using descriptive statistics, namely mean and standard deviation for quantitative variables and nonparametric tests for qualitative variables. The analysis was performed using Chi-square test, and the results were expressed as numbers and percentage. Significant values- p value of <0.05.

RESULTS

A total of 598 cases were selected based on the inclusion criteria in the psychiatry department and were analyzed.

The most common antidepressant drug prescribed among patients was fluoxetine (50.27%), followed by sertraline (40.29%), amitriptyline (25.31%), and escitalopram (3.43%) in depressive disorder.

Age in years

Most commonly affected age group and those who received a maximum of the antidepressants were in the age group of 41–60 years and are shown in Figure 1.

Sex-wise Distribution

Majority of the patients receiving antidepressants in depressive disorder were males as compared to females which reflects the population at risk. The male preponderance is seen in all age groups as shown in Table 1.

Common disorders among the patients receiving antidepressants were depressive disorder (92.47%), schizophrenia with depression (6.18%), and bipolar affective disorder (BPAD) (1.5%). Of these, depressive disorder was

the most common psychiatric diagnosis and is shown in Figure 2.

Marital Status

In our study, majority of the individuals suffering from depressive disorder were married followed by unmarried and divorcees and are shown in Table 2.

Occupational Status

The highest rate of patients suffering from depressive disorder was employees followed by housewives, unemployees, students, laborers, and farmers and is shown in Figure 3.
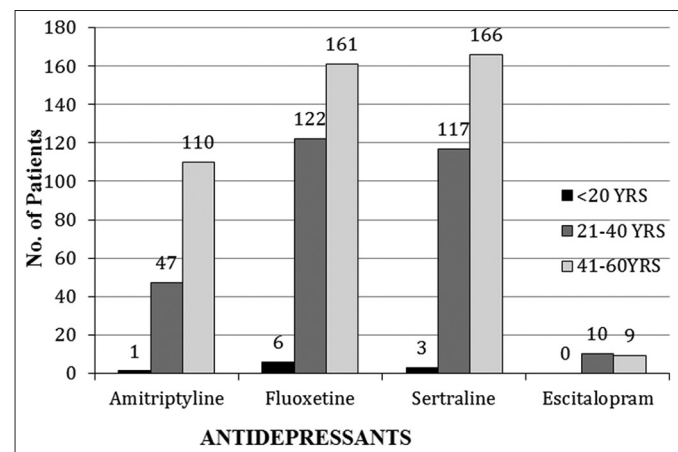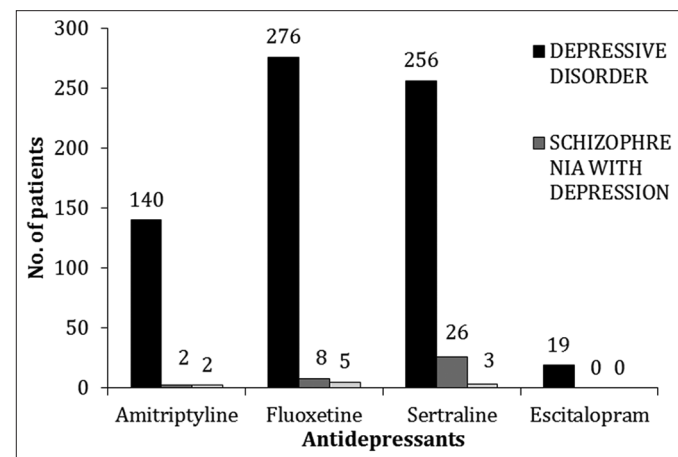

Figure 1: Age-wise distribution

Figure 2: Prevalence of psychiatric disorders and use of antidepressants

Educational Status

In our study, the highest rate of depression was seen in patients with secondary education followed by primary education, patients with no education, and those with tertiary education and is shown in Table 3.

Concomitant Medications

In our study, patients taking concomitant drugs along with antidepressants were anxiolytics (27.91%), antipsychotics (6.51%), antihypertensive drugs (0.66%), antidiabetic drugs (0.99%), and anti-Parkinsonism drugs (0.33%) is shown in Table 4.

In our study, the mean daily dose of antidepressants is shown in Table 5.

Number of Drugs per Prescription

In our study, majority of the patients received antidepressants as monotherapy (49.16%) and is shown in Figure 4.

The WHO Prescribing Indicators

As per the WHO prescribing indicators, the results were obtained and depicted in Table 6.

ATC-DDD Classification

All antidepressant drugs were coded by ATC classification.

In our study, for each prescription, there were multiple doses of the antidepressants prescribed, and the average of the daily doses of antidepressant was taken as PDD. And then, PDD-to-DDD ratio was calculated and is depicted in Table 7.

ADR

Patients visiting the outpatient department of psychiatry were scheduled for follow-up once in 15 days to receive a new prescription, and during their follow-up, they were enquired for ADR. Main adverse reactions were nausea (0.83%), dry mouth (0.83%), and weight gain (0.83%) associated with amitriptyline treatment. With fluoxetine treatment, weight gain (1.67%) and nausea (1.5%) were more common. Nausea (2.17%), weight gain (2.0%), gastritis (1.33%), and insomnia (0.83%) were the more common adverse effects

Table 1: Sex-wise distribution					
Indication	Number of patients (%)		Total number of patients (%)	Chi-square	*P*- value
	Male	**Female**			
Depressive disorder	320 (57.86)	233 (42.13)	553 (92.47)	13.68	*$P<0.01$
Schizophrenia with depression	17 (48.57)	18 (51.42)	35 (1.5)	0.02	$P>0.05$
BPAD	5 (55.55)	4 (44.44)	9 (5.85)	0.12	$P>0.05$

*statistically significant, BPAD: Bipolar affective disorder

seen with sertraline. Insomnia (0.66%) was associated with escitalopram and is shown in Figure 5.

DISCUSSION

Depression is a serious medical disorder which can negatively affect a persons' personal and general health. The cause of depression is mainly due to a combination of genetic, psychological, and environmental factors. Moreover, some of the risk factors are family history of the depression, lifestyle changes, substance abuse, chronic health conditions, and medications and may be partially improved or completely unchanged after the treatment with antidepressant medications.

In our study, based on the inclusion criteria in the psychiatry department, a total of 598 cases were selected and were analyzed. The number of drugs prescribed was 957 in total. Fluoxetine (48.32%) was the most common antidepressant drug prescribed among patients, followed by sertraline (47.82%), amitriptyline (26.42%), and escitalopram (3.17). Patients aged between 41 and 60 years were the ones commonly affected, consuming maximum of the antidepressants, which accounts to 59.30% of the total patients. Majority of the patients receiving antidepressants for depressive disorder in our study were males (57.86%) as compared to females (42.13%), and in our study,
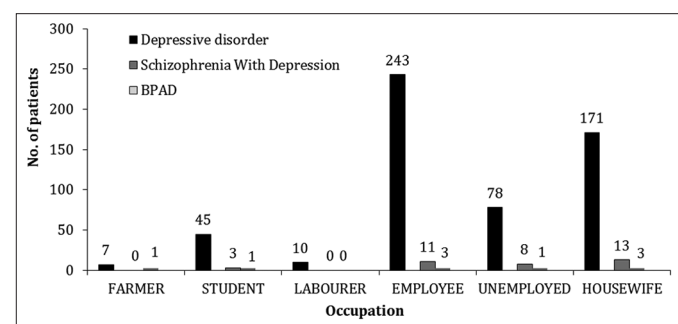
common disorders among the patients receiving antidepressants were depressive disorder (92.47%), schizophrenia with depression (6.18%), and BPAD (1.5%). In our study, majority of patients who received antidepressants were married (81.58%) and housewives (30.86%) followed by unmarried (14.62%) and divorcees (3.05%); the highest rate of patients receiving antidepressants based on the occupational status for depressive disorder was employees (43.86%) least seen in farmers (1.26%) in our study; the highest rate of depression was seen in secondary and post-secondary schooling, whereas lowest in pre-secondary schooling and in no education patients in our study; the most common concomitant medication taken along with antidepressants are the following drugs anxiolytics, antipsychotics, antihypertensive drugs, antidiabetic drugs, and anti-Parkinsonism drugs. Most of the patients, in our study, received antidepressants as monotherapy (49.16%). With fluoxetine treatment, weight gain and nausea were more common. Nausea, weight gain, gastritis, and insomnia were more common adverse effects seen with sertraline. Insomnia was associated with escitalopram treatment. In our study, 75.65% of drugs were prescribed by their generic name and no fixed dose combinations were used.

In our study, based on the inclusion criteria in the psychiatry department, a total of 598 cases were selected and were analyzed. The number of drugs prescribed was 957 in total. Fluoxetine (48.32%) was the most common antidepressant drug prescribed among patients, followed by sertraline (47.82%), amitriptyline (26.42%), and escitalopram (3.17), these results are against with other study where the most common antidepressant prescribed among patients was escitalopram,[7] and in other study, selective serotonin reuptake inhibitor (SSRI) was the frequently used drug among depression.[8] Nowadays, the drugs as the first choice for most of the psychiatrists to treat depression are SSRIs and SNRIs, and these drugs also have indisputable place in the management of depression. Combination of tricyclic antidepressants with SSRIs is of great value in the treatment of resistant depression.[9] Patients aged between 41 and 60 years

Figure 3: Prevalence of psychiatric disorders based on occupational status

Table 2: Prevalence of psychiatric disorders based on marital status					
Diagnosis	**Married (%)**	**Unmarried (%)**	**Divorcee (%)**	**Chi-square**	***P*- value**
Depressive disorder (554)	452 (81.58)	81 (14.62)	20 (3.61)	593.11	*P<0.001
Schizophrenia with depression (35)	28 (80)	4 (11.42)	3 (8.57)	34.33	*P<0.01
BPAD (9)	8 (88.8)	1 (11.11)	0 (0)	5.44	*P<0.05

*statistically significant, BPAD: Bipolar affective disorder

Table 3: Prevalence of psychiatric disorders based on educational status					
Drug name	**Primary (%)**	**Secondary (%)**	**Tertiary (%)**	**No education**	**Chi-square**	***P*- value**
Depressive disorder (554)	248 (44.76)	255 (46.02)	29 (5.23)	21 (3.79)	371.49	P<0.001
Schizophrenia with depression (35)	15 (42.85)	14 (40)	1 (2.85)	5 (14.28)	16.09	P<0.01
BPAD (9)	4 (44.44)	5 (55.55)	0 (0)	0 (0)	0.12	P>0.05

BPAD: Bipolar affective disorder

Table 4: Concomitant drugs along with antidepressants

Concomitant medications

Category of drugs	Number of patients (%)
Anxiolytics	
Clonazepam	164 (27.42)
Alprazolam	2 (0.33)
Diazepam	1 (0.16)
Antipsychotics	
Risperidone	17 (2.84)
Olanzapine	22 (3.67)
Antihypertensive drugs	
Amlodipine	2 (0.33)
Atenolol	2 (0.33)
Antidiabetic drugs	
Metformin	3 (0.50)
Glimipiride	2 (0.33)
Voglibose	1 (0.16)
Anti-Parkinsonism drugs	
Trihexyphenidyl	2 (0.33)

Table 5: Mean daily dose of antidepressants

Antidepressants	Number of prescriptions	Mean dose
Amitriptyline		
25 mg	147	25±0
Fluoxetine		
20 mg 40 mg	290	20.13±1.66
Sertraline		
50 mg 100 mg	299	30.45±10.34
Escitalopram		
10 mg	19	10±0

Table 6: Assessment of prescribing pattern as per selected WHO drug use indicators

The WHO drug use indicators	Percentage (%)
Number of drugs per prescription	
One	49.16
Two	40.80
Three	9.36
Four	0.66
Average number of drugs per encounter	1.60
Percentage of drugs prescribed by generic	75.65
Percentage of drug encounter with antibiotics	NIL
Percentage of drug encounter with injection	NIL
Percentage of drugs prescribed from essential drug list	46.81

Figure 4: Number of drugs per prescription
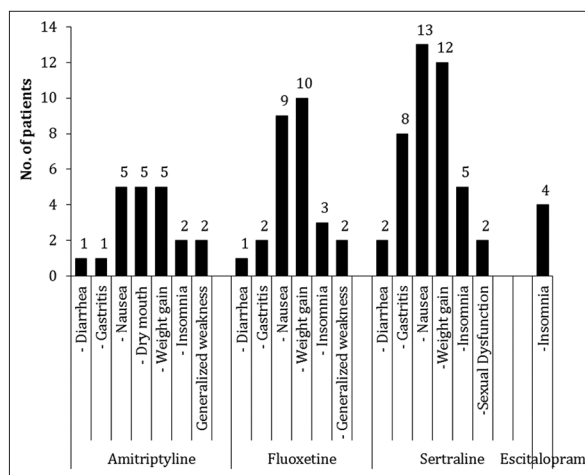
Figure 5: Adverse drug reactions associated with antidepressants

the reasons for the results in our study. However, our findings are in contradict with the study by Ghosh and Chaudhury,[10] showing that 51.96% of patients taking antidepressants belonged to the age group of 18–30 years. The prevalence of depression is high in adolescence compared to children or adults, the probability of depression increases from 5% in early adolescence to as high as 20% by the end of this stage,[11] whereas the increasing prevalence of depression in late life is due to either a prodrome of dementia or psychological or biological response to the events such as physical illness and caregiving, which occurs more commonly in later life.[12] In another study, consumption of antidepressants was found to be higher among patients aged >60 years.[13]

Majority of the patients receiving antidepressants for depressive disorder in our study were males (57.86%) as compared to females (42.13%), as this could be due to more stress at work, where males are more affected than females. Our findings are in contrast with the study, showing that the percentage of female and male patients was 51.50% and 48.50%, respectively.[14] Women appear to be more sensitive to develop depression at even lower levels of stress and also to show exaggerated neuroendocrine responses to

were the ones commonly affected, consuming a maximum of the antidepressants, which accounts to 59.30% of the total patients. Age is one of the determinants of mental health status because as the age advances, person becomes more sensitive for all the circumstances, and this could be one of
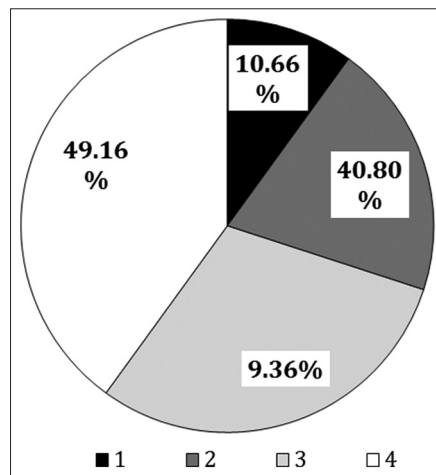
Table 7: Antidepressants coded with ATC with DDD classification

N06A Antidepressants

ATC code	Drug name	Class of drug	DDD	PDD	PDD/DDD
N06AA09	Amitriptyline	TCAs	75	26.53	0.35
N06AB03	Fluoxetine	SSRIs	20	22.06	1.10
N06AB06	Sertraline	SSRIs	50	33.97	0.67
N06AB10	Escitalopram	SSRIs	10	10	1

ATC: Anatomical therapeutic chemical, DDD: Defined daily dose, SSRIs: Selective serotonin reuptake inhibitor, PDD: Prescribed daily dose

stress.[15,16] Moreover, this gender discrepancy could also be due to the prevalence of illness where they tend to report their symptoms of depression compared to male patients.[17] In our study, common disorders among the patients receiving antidepressants were depressive disorder (92.47%), schizophrenia with depression (6.18%), and BPAD (1.5%). Of these, depressive disorder was the most common psychiatric disorder. Depression is being the most common mental illness and is on the rise globally. The findings of our study are in consistent with the other study, which shows that the most common disorders among the patients attending psychiatry OPD were depression 36.33%, followed by anxiety 27.5% and schizophrenia 17%.[18] The various psychosocial factors which have been shown to be associated with depression include loneliness, poor social or family support, isolation, dependency, lack of family care and affection, insufficient time spent with children, stressful life events, perceived poor health, lower level of spirituality, and higher use of emotion-based coping. The lifestyle and dietary factors that have been linked with depression include lack of hobby, irregular dietary habits, substance use or smoking, and lack of exercise.[19] In our study, majority of patients who received antidepressants were married (81.58%) and housewives (30.86%) followed by unmarried (14.62%) and divorcees (3.05%), and the reason for our findings could be due to constant stress in married life which causes a higher incidence of depression. Our findings are in consistent with the study by Dutta *et al*.[20] which showed that majority of patients received antidepressants were married (76%) and housewives (45.14%). Another study which showed patients who were on psychotropic drugs almost had an even distribution between patients who were married (36.4%) and those who were unmarried (38.6%).[21] Patten *et al*.[22] in their study found significant interactions among sex, age, and marital status with single women reporting lower rates of depression with increased age and single men reporting increasing rates of depression. The highest rate of patients receiving antidepressants based on the occupational status for depressive disorder were employees (43.86%) least seen in farmers (1.26%) in our study, this could be due to lack of appreciation, job unsatisfaction, job demands, job security, level of physical activity, income, and time pressure, and all these factors can make an individual

to lose their confidence levels and end up in depression. Our findings are in contrast with another study showing among male-dominated occupational groups, and depression was found high in machine operators, laborers, farmers, and unskilled manual workers.[23] Some of the international studies showed that farmers of French and Canada were found to have less depression than comparison groups, but farmers in the Norway and UK found higher levels of depression than comparison groups.[24] Another study showed that spouses weekly working hours significantly associated with individual's risk of developing depressive symptoms and suicidal ideation which indicates that individual's long working hours not only affect on their own mental health but also on their spouses.[25] The highest rate of depression was seen in secondary and post-secondary schooling whereas lowest in pre-secondary schooling and no education patients. Depression in overeducated individuals occurs when education does not provide satisfactory jobs, challenges with high competitions in their jobs, and non-implementation of their skills on work or could be more workload with less pay. All these factors can lead to depression. The findings in our study are in consistent with the findings of an another study where the respondents whose education level was less than secondary school have the lowest rate of lifetime depression (9.1%) and the highest rate of lifetime depression (13.4%) is seen among those with other post-secondary education.[26] In our study, the most common concomitant medication taken along with antidepressants are the following drugs anxiolytics, antipsychotics, antihypertensive drugs, antidiabetic drugs, and anti-Parkinsonism drugs. Dose equivalence of antidepressants is critically important for clinical practice and research.[27] In our study, mean daily dose of amitriptyline was 25 ± 0, fluoxetine was 20.13 ± 1.66, sertraline was 30.45 ± 10.34, and escitalopram was 10 ± 0. In a study by Mohanta *et al*.,[28] mean daily dose of fluoxetine was 26.50 and sertraline was 52.63. Most of the patients in our study received antidepressants as monotherapy (49.16%). In a study by Rush *et al*.[29] where they compared the monotherapy with the combined therapy to enhance depression outcomes, they did not find any significant differences in the outcomes of patients treated with single medication with those patients treated with a combination of antidepressants. A study by Tianmei *et al*[30] concludes that frequency and severity of side effects has been increased due to use of antidepressant as polypharmacy. All antidepressant drugs were coded by ATC classification in our study. The current classification of drugs was introduced by the World Health Organization in 1976.[31] In ATC classification, A refers to the anatomical site of action, T refers to the therapeutic indication, and C refers to the chemical class of the drug.[32] The DDD is the assumed average maintenance dose per day for a drug which is used for its main indication in adults.[33] DDD is used for pharmacoepidemiology studies in a setting where a consumption of one DDD per day is implied to compare costs,[34] to analyze compliance, and to calculate prevalence of disease.[35] Drug utilization figures expressed in DDDs are

generally reported in units that control for population size differences. This estimate is useful for the drugs prescribed chronically such as antidepressants, antipsychotics, and many others.[36] The PDD is the average daily amount of a drug that is actually prescribed.[33] A ratio which was <1 was seen in case of sertraline and amitriptyline indicating underdosing. A ratio which was >1 was seen for fluoxetine indicating overdosing, and other antidepressant drug such as escitalopram showed a PDD–to-DDD ratio which was equal to 1 indicating adequate dosing. In a study by Lahon *et al.*,[37] adequate dosing was seen for all the antidepressants, except for duloxetine and mirtazapine for which under-dosing was prevalent.

Patients who are on long-term treatment had to visit the outpatient department of psychiatry for follow-up once in every 15 days, and at that time, the ADRs reported were noted. Main ADRs were nausea, dry mouth, and weight gain associated with amitriptyline treatment. With fluoxetine treatment, weight gain and nausea were more common. Nausea, weight gain, gastritis, and insomnia were more common adverse effects seen with sertraline. Insomnia was associated with escitalopram treatment which is in contrast with a study by Mukherjee *et al.*[38] in which the common ADR was dry mouth followed by nausea and tremor, and in another study agitation, anxiety and insomnia were the common ADRs associated with the use of antidepressants.[39] In our study, 75.65% drugs were prescribed by their generic name and no fixed dose combinations were used. A total of 46.81% drugs were prescribed from the WHO model list of essential drug medicines[40] and all the drugs prescribed were dispensed from hospital pharmacy. There was no history of suicidal tendencies among patients, and also switching of antidepressants during treatment was not seen.

The results of our study would have been more precised with larger sample size. Follow-up of these patients for longer duration would have provided more information about the efficacy and safety of the antidepressants prescribed.

CONCLUSION

DUS in recent years has become a popular tool to be used in the evaluation of health systems. Among the major mental illnesses, depression has been one of the toughest to subdue. Antidepressants were used to treat major depressive disorder and other conditions of mental illness. There is a need for DUS to encourage rational and appropriate use of drugs. There should be a concern among the health care personnel to monitor and analyze the ADR or any drug interactions to antidepressant drugs prescribed. In our study, majority of prescriptions were prescribed according to standard guidelines. The use of antidepressants in patients found to be appropriate and most of the drugs were prescribed by generic name. The data of DU studies analyzed will be of great value to the clinicians to validate information on better and safer

use of drugs and also to reduce the ADR. As depression is a chronic disorder, for a disease to subside, one should continue taking medications, but we could not ascertain whether medications that were dispensed were actually taken, for which further studies with proper monitoring and long-term follow-up should be done.

REFERENCES

1. Sharonjeet K, Sujit R, Navjot K, Nusrat S, Ashish B, Promila P, *et al*. Drug utilization study in medical emergency unit of a tertiary care hospital in North India. Emerg Med Int 2014;2014:1-5.
2. Al Balushi KA, Al-Shibli S, Al-Zakwani I. Drug utilization patterns in the emergency department: A retrospective study. J Basic Clin Pharm 2013;5:1-6.
3. John LJ, Devi P, Guido S. Utilization profile of gastrointestinal medications among the critically ill patients of a tertiary care hospital. Jordan J Pharm Sci 2013;6:299-307.
4. Niti M, Mittal R, Singh I, Nusrat S, Malhotra S. Drug utilization study in a tertiary care center: Recommendations for improving hospital drug dispensing policies. Indian J Pharm Sci 2014;76:308-14.
5. Turchi F, Cuomo A, Amodeo G, Favaretto E, Righini S, Mellina E, *et al*. The neural bases of social cognition in major depressive disorder: A review. Riv Psichiatr 2017;52:137-49.
6. Aksha M, Kamlesh P. Drug use pattern of antidepressant agents in psychiatric patients -A prospective study. NHL J Med Sci 2013;2:33-6.
7. Chattar KB, Karve AV, Subramanyam A, Tondare SB. Prescription pattern analysis of antidepressants in psychiatric outpatient department of tertiary care hospital in India. Asian J Pharm Clin Res 2016;9:77-9.
8. Nahas AR, Sulaiman SA. Prescribing patterns of antidepressants among depressive men in Malaysia: A survey. J Young Pharm 2018;10:98-101.
9. Ramachandraih CT, Subramanyam N, Bar KJ, Baker G, Yeragani VK. Antidepressants: From MAOIs to SSRIs and more. Indian J Psychiatry 2011;53:180-2.
10. Ghosh S, Chaudhury SR. Prescribing pattern of antidepressant drugs in a tertiary care hospital of Eastern India. J Chem Pharm Res 2014;6:2593-7.
11. Green H, McGinnity A, Meltzer H, Ford T, Goodman R. Mental Health of Children and Young People in Great Britain. London: Palgrave; 2004.
12. Fiske A, Wetherell JL, Gatz M. Depression in older adults. Annu Rev Clin Psychol 2009;5:363-89.
13. Bose D, Muraraiah S, Chandrashekar H. Evaluation of patterns and predictors of off-label prescribing of antidepressants in psychiatry at a tertiary care hospital - An analytical cross-sectional study. Nat J Physiol Pharm Pharm 2017;7:183-8.
14. Doshi CM, Hedamba R, Darji NH, Patel B, Trivedi HR, Tiwari D. Drug utilization study of psychotropic drugs in outdoor patients in a tertiary care hospital attached with a medical college. Int J Basic Clin Pharm 2015;4:1220-3.
15. Bouma EM, Ormel J, Verhulst FC, Oldehinkel AJ. Stressful life events and depressive problems in early adolescent boys and girls: The influence of parental depression, temperament and family environment. J Affect Disord 2008;105:185-93.

16. Kendler KS, Kuhn J, Prescott CA. The interrelationship of neuroticism, sex, and stressful life events in the prediction of episodes of major depression. Am J Psychiatry 2004;161:631-6.

17. Patton GC, Coffey C, Romaniuk H, Mackinnon A, Carlin JB, Degenhardt L, *et al.* The prognosis of common mental disorders in adolescents: A 14-year prospective cohort study. Lancet 2014;383:1404-11.

18. Chaturvedi R, Sharma P. Drug utilization study of psychotropic drugs prescribed in psychiatry opd of L. N. medical college associated J. K. hospital, Bhopal District, Madhya Pradesh. J Evol Med Dent Sci 2016;5:3242-4.

19. Grover S, Malhotra N. Depression in elderly: A review of Indian research. J Geriatr Ment Health 2015;2:4-15.

20. Dutta S, Kaul V, Beg MA, Singh NK, Dutta S, Bawa S. A comparative drug utilization study of depression patients between tertiary care teaching hospital and private practitioners of Dehradun City, Uttarakhand. J Drug Deliv Ther 2015;5:45-9.

21. Moore S, Jaime LK, Maharajh H, Ramtahal I, Reid S, Ramsewak FS, *et al.* The prescribing of psychotropic drugs in mental health services in Trinidad. Rev Panam Salud Publica 2002;12:207-14.

22. Patten SB, Wang JL, Williams JV, Currie S, Beck CA, Maxwell CJ, *et al.* Descriptive epidemiology of major depression in Canada. Can J Psychiatry 2006;51:84-90.

23. Roche AM, Pidd K, Fischer JA, Lee N, Scarfe A, Kostadinov V. Men, work and mental health: A systematic review of depression in male-dominated industries and occupations. Saf Health Work 2016;7:268-83.

24. Cohidon C, Imbernon E, Gorldberg M. Prevalence of common mental disorders and their work consequences in France, according to occupational category. Am J Ind Med 2009;52:141-52.

25. Yoon JH, Kang MY. The crossover effect of spouses' long working hours on depressive symptoms and suicidal ideation. Ind Health 2016;54:410-20.

26. Akhtar-Danesh N, Landeen J. Relation between depression and sociodemographic factors. Int J Ment Health Syst 2007;1:4.

27. Hayasaka Y, Purgato M, Magni LR, Ogawa Y, Takeshima N, Cipriani A, *et al.* Dose equivalents of antidepressants: Evidence-based recommendations from randomized controlled trials. J Affect Disord 2015;180:179-84.

28. Mohanta G, Manavalan R, Prabha K, Prasanna M. Retrospective utilization patterns of antidepressant medications. Internet J Third World Med 2008;7:1.

29. Rush AJ, Trivedi MH, Stewart JW, Nierenberg AA, Fava M, Kurian BT, *et al.* Combining medications to enhance depression outcomes (CO-MED): Acute and long-term outcomes of a single-blind randomized study. Am J Psychiatry 2011;168:689-701.

30. Si T, Wang P. When is antidepressant polypharmacy appropriate in the treatment of depression? Shanghai Arch Psychiatry 2014;26:357-9.

31. Zohar J, Nutt DJ, Kupfer DJ, Moller HJ, Yamawaki S, Spedding M, *et al.* A proposal for an updated neuropsychopharmacological nomenclature. Eur Neuropsychopharmacol 2014;24:1005-14.

32. Rao TS, Andrade C. Classification of psychotropic drugs: Problems, solutions, and more problems. Indian J Psychiatry 2016;58:111-3.

33. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC Classification and DDD Assignment. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2002.

34. Donohue JM, Fischer MA, Huskamp HA, Weissman JS. Potential savings from an evidence-based consumer-oriented public education campaign on prescription drugs. Health Serv Res 2008;43:1557-75.

35. Doro P, Benko R, Kosik E, Matuz M, Tóth K, Soós G. Utilization of oral antihyperglycemic drugs over a 7-year period (1998–2004) in a Hungarian population and adherence to drug therapy. Eur J Clin Pharmacol 2005; 61:893-7.

36. WHO Collaborating Centre for Drug Statistics Methodology. WHO 3. Defined Daily Dose(DDD). Available from: http://www.Error!Hyperlinkreferencenotvalid.17. [Last accessed on 2001 Jul 19].

37. Lahon K, Shetty HM, Paramel A, Sharma G. A retrospective drug utilization study of antidepressants in the psychiatric unit of a tertiary care hospital. J Clin Diagn Res 2011;5:1069-75.

38. Mukherjee S, Sen S, Chatterjee SS, Era N, Ghosal M, Tripathi SK. Adverse drug reaction monitoring of antidepressants in the psychiatry outpatient department at a tertiary care teaching hospital in India: A cross-sectional observational study. Eur J Psychol Educ Stud 2015;2:14-9.

39. Mishra S, Swain TR, Mohanty M. Adverse drug reaction monitoring of antidepressants in the psychiatry outpatients department of a tertiary care teaching hospital. J Clin Diagn Res 2013;7:1131-4.

40. WHO Model list of Essential Medicines 2017. Available from: http://www.who.int/medicines/publications/essentialmedicines/en/17. [Last accessed on 2000 July 19].