Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/wymf7n66

ASSESSMENT OF PATTERN, CAUSALITY, SEVERITY AND PREVENTABILITY OF ADVERSE DRUG REACTIONS OF ANTIDEPRESSANT DRUGS USED IN PSYCHIATRY DEPARTMENT OF A TERTIARY CARE HOSPITAL

Dr Sarita Singh[1], Dr. Mangesh Kumar Tripathi[2*], Dr Himanshu Sharma[3]

[1]Assistant Professor, **Department of Pharmacology, Kalyan Singh Government Medical College Bulandshahr, Uttar Pradesh, India**
[2*]Assistant Professor, **Department of Pharmacology**, G.S.V.M. Medical college, Kanpur, Uttar Pradesh, India
[3]Associate Professor, **Department of Pharmacology**, G.S.V.M. Medical college, Kanpur, Uttar Pradesh, India

***Corresponding Author:** Dr. Mangesh Kumar Tripathi
*Assistant Professor, Pharmacology Department, G.S.V.M. Medical college, Kanpur, Uttar Pradesh , India

Abstract

Background: Antidepressant medications are a cornerstone in the management of depressive and various anxiety disorders, significantly improving the quality of life for millions worldwide. Antidepressants are commonly prescribed for a variety of psychiatric disorders. However, their use is associated with a spectrum of adverse drug reactions (ADRs), which may impact patient compliance and therapeutic outcomes.

Objectives: To evaluate the pattern, severity, and preventability of ADRs associated with antidepressant drugs in the psychiatry department of a tertiary care hospital.

Methods: A prospective observational study was conducted over a 12-month period among patients receiving antidepressant therapy. ADRs were identified, documented, and analyzed using standard pharmacovigilance tools such as Causality Assessment Scale Naranjo's Scale, Modified Hartwig and Siegel Severity Scale, and the Schumock and Thornton Preventability Scale.

Results: A total of 329 ADRs were reported in 122 patients. The most common antidepressants associated with ADRs were selective serotonin reuptake inhibitors (SSRIs), particularly Escitalopram and Venlafaxine. The most frequent ADRs were central nervous system effects (51.67%), followed by gastrointestinal disturbances (40.72%) and sexual dysfunction (4.25%). Causality assessment classified 97.95% of ADRs as 'possible', and 2.05% as 'probable'. In terms of severity, 92% were 'mild' and 8% 'moderate'. Preventability assessment indicated that 7% of ADRs were ' preventable' and 93% 'not preventable'. **Conclusion:** The study highlights the importance of continuous ADR monitoring, especially for antidepressant medications. Most ADRs were mild and not preventable, emphasizing the need for careful selection, monitoring, and patient education to improve drug safety.

Introduction

Depressive disorders and anxiety disorders represent a significant global health burden, impacting mental well-being, functional capacity and societal productivity. Adverse reactions to the drugs are one of the main unavoidable risk factors in the use of drug therapy. It has been described by the world

health organization (WHO) as a "noxious, unintended and undesired effect of a drug, which occur at doses normally used in humans for prophylaxis, diagnosis or cure of a disease".[1]India is said to be the second highest market for the sale of prescription drugs in the world, yet only about 2% of the adverse drug reactions are reported.. The main cause for this low figure is the underreporting of the ADRs.[2] In recent years, there has been a shift in the worldwide prescription trends for antidepressants, moving away from traditional medications such as tricyclics and MAO inhibitors towards selective serotonin reuptake inhibitors (SSRIs) and new types of antidepressants .[3] Antidepressants are extensively used for treating major depressive disorder, anxiety disorders, and other psychiatric conditions. Identification and reporting of these ADRs is extremely crucial as it may possibly help the treating physicians on being vigilant while prescribing those drugs and achieving a substantial reduction in healthcare cost.[4] Pharmacotherapy for psychiatric disorders is frequently associated with adverse drug reactions (ADRs). Different drugs may need to be tried in a patient to control the symptoms, which increases the risk of ADR. Almost all the psychiatric diseases have temporary cure and the treatment is lifelong.[5] Compared to western countries where ADR reporting is practiced on a regular basis, in India under-reporting of ADRs is a major problem; reasons include lack of time, knowledge regarding filling up of the ADR reporting forms and underestimating its importance.[6]

Reporting of ADRs is must and each treating physicians should consider it as their professional duty so as to safeguard patient's wellbeing and to reduce the cost involved in their treatment. Continuous monitoring and assessment of ADRs is crucial for optimizing the safe use of these drugs. Hence, this study was undertaken to assess the causality, severity and preventability of ADRs reported of different antidepressant drugs including newer antidepressant in a tertiary care hospital, Kanpur.

Aims and Objectives

This study aims to:

- Assess the pattern of ADRs due to antidepressants.
- Evaluate the causality, severity, and preventability of these ADRs.
- Contribute data to improve pharmacovigilance practices in psychiatric care.

Methodology

A prospective observational study was conducted in the department of Pharmacology in collaboration with Psychiatry Department over a period of 12 months of a tertiary care hospital in Kanpur .Patients diagnosed with depression and are on antidepressants attending out- patient department of psychiatry were enrolled in the study.

Inclusion Criteria:

- Patients of either gender, aged ≥18 years.
- Diagnosed with psychiatric illnesses and prescribed at least one antidepressant.
- Willing to provide informed consent.

Exclusion Criteria:

- Patients with co-morbidities where ADR source could not be clearly attributed to antidepressants.
-Patients unable to respond to verbal questions.
-Pregnant and Lactating females

Data Collection:

Detailed patient history, including demographic details, diagnosis, drug therapy, and suspected ADRs, was collected. Patient with depression were acknowledged with the help of DASS-21 Scale. Any adverse effects which were observed were recorded in the "Adverse Drug Event Reporting Form" which was prepared by the CDSCO, Government of India. Each ADR was evaluated for:

- Causality: Naranjo's Scale

- Severity: Modified Hartwig and Siegel scale
- Preventability: Schumock and Thornton scale

Statistical Analysis:
Data were analyzed using descriptive statistics. Frequencies and percentages were used for categorical variables.

4. Results

Demographics:
The present study was conducted in Department of Pharmacology in collaboration with Department of Psychiatry, G.S.V.M Medical College,Kanpur. A total number of 122 patients encountered with various types of ADRs during our study period, that is ,January 2020–July 2021. A total number of ADRs recorded were 329. Hence, the burden of ADR due to antidepressant drug was 2.6 ADR per patient.

Table 1-Demographic Profile of Patients

S.NO	Characteristics	n=122	%(Percentage)
1	**Gender**		
	Male	72	59%
	Female	50	41%
2	**Age(years)**		
	<20	6	4.9%
	21-40	62	50.8%
	41-60	46	37.7%
	>60	8	6.6%
3	**Literacy**		
	Literate	78	63.9%
	Illiterate	44	36.1%
4	**Employment**		
	Employed	70	57.4%
	Unemployed	52	42.6%

From table, it can be concluded that incidence of ADRs was more in male patients as compared to female counterpart. ADRs were more common in 21–40 year age group, Illiterate patients were found to be the risk factor for developing ADRs. In our study,employed population encountered ADRs more frequently than the unemployed ones.

ADR Pattern:

Table-4 Organ System wise ADR burden

S. No	Organ System	No. of ADRs	ADR %
1	Central nervous system	170	53.24%
2	Gastrointestinal	134	41.63%
3	Reproductive system	14	2.04%
4	Miscellaneous	8	2.04%
5	Cardiovascular system	3	1.05%
	Total	**329**	**100**

Maximum burden of ADRs was due to involvement of the central nervous system (CNS) anxiety, followed by gastrointestinal(Constipation), reproductive system(decreased libido), miscellaneous (Weight gain) and cardiovascular system (postural hypotension).

Drug-wise - Distribution of ADRs:

Table-5 percentage of patients distribution according to the drugs.

S.NO	Drugs	No. of Patients	%
1	Escitalopram	30	27.27%
2	Venlafaxine	24	21.81%
3	Paroxetine	10	9.09%
4	Desvenlafaxine	10	9.09%
5	Fluoxetine	6	5.45%
6	Sertraline	2	1.81%
7	Mirtazapine	8	7.27%
8	Levomilnacipran	5	4.54%
9	Nortriptyline	1	0.98%
10	Amitriptyline	3	2.72%
11	Duloxetine	5	4.54%
12	Sertraline	2	1.81%
13	Clomipramine	2	1.81%
14	Trazodone	2	1.81%
	Total	**110**	**100%**

Distribution of ADRs according to the ADR types

All reported ADRs were categorized into six types according to the expanded Rawlins and Thompson classification. All the ADRs were of Type A. There were no ADR of Type – B, C, D, E, and F in our study.

Causality Assessment: All the ADRs were analyzed for the causality according to the Naranjo's probability scale. Out of total 329 ADRs, majority were in possible category (97.95%) followed by probable category (2.05%). There was no ADR which was classified as doubtful or definite category.

Severity Assessment:

- Mild: 92%
- Moderate: 8%

Preventability Assessment:

- Not preventable: 93%
-Preventable: 7%

5. Discussion

Depressive disorders and anxiety disorders represent a significant global health burden, impacting mental well-being, functional capacity, and societal productivity. Antidepressant drugs, including Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), Tricyclic Antidepressants (TCAs), and Monoamine Oxidase Inhibitors (MAOIs), have revolutionized psychiatric care. While highly effective, their use is frequently complicated by the occurrence of adverse drug reactions (ADRs). These reactions can lead to patient discomfort, reduced adherence to treatment, increased healthcare costs, and, in severe cases, significant morbidity and mortality.The incidence and pattern of ADRs in this study are consistent with existing literature, with SSRIs being most commonly implicated. CNS effects and Gastro-intestinal symptoms were the most frequent. A significant number of ADRs were mild and preventable, pointing to the need for improved monitoring and awareness among clinicians. Our study evaluated ADRs due to antidepressants among depressive patients in the Department of pharmacology in collaboration with Department of Psychiatry in GSVM Medical College, Kanpur. Some people resist taking antidepressants because

they do not like to admit that something is wrong with them. Others dislike the idea of being dependent on a chemical substance to keep their mood level or lacking a sense of control over life .[7]

In our study, burden of ADR was 2.6/patient which was greater than the study done by Lucca *et al*.[8] (1.2ADR/patient) and less than the study conducted by Sankhi *et al*.[9](4.5ADR/patient).This difference in per patient burden of ADRs can be due to difference in drug treatment. Our study's discovery aligns with Tripathi A et al., who also found that escitalopram was the most frequently prescribed antidepressant, with sertraline following closely behind .[10] The drug responsible in our study Escitalopram (SSRIs) and in study done by Sridhar *et al*.[11]was Fluoxetine. (23.12%) was the most common drug prescribed as monotherapy similar to our study followed by fluoxetine (20.62%), sertraline (11.87%) [12]. As per literature, SSRI causes more ADR than other antidepressants as SSRI are more commonly used.

In our study, maximum burden of ADR was found in males than female. Males (58.18%) affected more with ADR than female (41.82%)with male: female ratio 1.44. This is in line with the previous study Barvaliya *et al*.[13]male(57.3%)was affected more with ADRs than female (42.7%) with male: female ratio 1.34. In other studies conducted by Mansuri et al[14],Lucca *et al*.[8]Sridhar *et al*.[11]and Sengupta *et al*.[15],observed male predominance with male: female ratio1.05,1.02,and2.19,respectively and differ with Sankhi *et al*.[9],the male-to-female ratio was 1:1.35, also females experienced a higher incidence of ADRs (5.56%) than males (3.63%).The gender difference in ADR frequency can be due to literacy rate more in males, they have more knowledge related to disease, treatment and complications as compared to females. Females have less knowledge regarding the same due to daily household work and more of due to their ignorant behaviour.

In our study, maximum patients who encountered ADRs were in age group 21–40 years. Mean age group of patients in our study was 32.5 years which is inconsistent with study conducted by Mansuri et al[14],Barvaliya *et al*.[13],Sengupt a *et al*.[15],Lucca *et al*.[8],Sridhar *et al*.[11],and Patel *et al*.[16],mean age of patients in these studies was 37.88 years, 34.4 years, 35.6 years, 39.31 years, and 36.15 years, respectively. This finding may be because of high prevalence of psychiatric illness in this age group (20–40), it can be due to the fact that this age group falls in reproductive age and hormonal changes are maximum. Differ with study conducted by Rajesh *et al*. [17] in which most common age group involved was 41–60 years. In our study, patients who were employed present with more ADRs than the unemployed ones. One plausible reason behind this finding can be that employed patients were economically sound and had better access to the treatment.

In our study, frequency of ADRs, there was no significant difference in two population subgroups with respect to gender, employment, and literacy, which differ from other study conducted by Sridhar *et al*.[11], Sengupta *et al*. [15] in which statistically significant finding was found between gender, employment, and age group.

In our study, literate patients were found to have more burden of ADR than the illiterate patients. This finding is similar with the previous study Sankhi *et al*.[9];while differ with studies conducted by Bhavani *et al*. [18] and Modayll *et al*. [19] The most common drug responsible for ADR was Escitalopram of class SSRI in our study. This finding is inconsistent with most of the previous studies Mansuri et et al[14],Sankhi *et al*. [9], Lucca *et al*. [8], Sridhar *et al*. [11], and Sengupta *et al*. [15] and differs from studies conducted by Barvaliya *et al*[13].and Sankhi *et al*.[9] in which tricyclic antidepressants were most commonly implicated for the development of maximum burden of ADRs.

The most common organ system involved due to ADRs was CNS in our study. This finding is in line with some previous studies Sridhar *et al*.[11],Sengupta *et al*.[15],and Barvaliya *et al*.[13]and differs from other studies conducted by Sankhi *et al*. [9], Aburamadan *et al*. [21],and Driessen *et al*. [22]in which gastrointestinal system was most commonly involved.

In this study Causality assessment by Naranjo's scale largely favored "possible " associations(97.95%).This finding is in line with most of the previous studies Atul *et al*.[20], Patel *et al*.[16], Bhavani *et al*.[18], Nagpal *et al*.[23],and Barvaliya *et al*.[13]and differs from some studies Sankhi *et al*.[9],

Aburamadan *et al*.[21],and Gummadi *et al*.[24] in which most of ADRs were of probable type Majority of the suspected ADRs were mild in nature. This finding was in accordance with two other studies in which most of the ADRs were mild to moderate in severity i.e Barvaliya et al .[13] Aburamadan *et al*.[21].In contrast, a study conducted by Grohmann et al. reported a rate of 1.6% of severe ADRs.[21.]Majority of the suspected ADRs were of not preventable type which is similar to the study conducted by Kurmi et al[25] and shah et al [26]reported the majority of ADRs as not preventable type followed by probably preventable.[8], in contast to study conducted by Aburamadan *et al* [21] ADRs were probably preventable type. Highlighting the challenge in establishing definite causation in polypharmacy settings. Severe ADRs, though infrequent, warrant special attention, particularly in vulnerable populations.

Conclusion

This research highlights the equal distribution of depressive disorder between genders, with the highest occurrence seen in individuals aged 18-30 years. Escitalopram was found to be the primary SSRI. Antidepressants, while essential in psychiatric treatment, are associated with a significant risk of ADRs. Structured pharmacovigilance systems, timely reporting, and clinician-patient communication can reduce the burden of ADRs and enhance therapeutic outcomes.

Recommendations

- Integrate ADR monitoring into routine psychiatric care.
- Train healthcare providers in pharmacovigilance and risk minimization.
- Counsel patients on potential ADRs and early reporting.
- Promote use of standardized assessment tools.

Limitations

- Single-center study; limited generalizability.
- Underreporting of mild ADRs possible due to subjective variability.
- No long-term follow-up for delayed ADRs.

References

1. Ahmad A, Patel I, Balkrishnan R, Mohanta GP, Manna PK.An evaluation of knowledge, attitude and practice of Indian pharmacists towards adverse drug reaction reporting: a pilot study. Persp Clin Res. 2013;4(4):204.
2.Amita Jindal A,Kumar1 R,Kumar2 S,Kaur A,Kiranjit,Raj R.Pattern of adverse drug reactions reported at the adverse drug reaction monitoring centre at tertiary care teaching hospital in North India:Int J Basic Clin Pharmacol. 2023 May;12(3):375-378.
3.Ghosh P, Barman S, Roy D and Roy S: Pattern of antidepressant prescription in patients suf fering from depressive disorder in a tertiary care hospital. Int J Pharm Sci & Res 2022;13(2): 942-47
4.Doshi MS, Patel PP, Shah SP, Dikshit RK. Intensive monitoring of adverse drug reactions in hospitalized patients of two medical units at a tertiary care teaching hospital. J Pharmacol Pharmacother. 2012;3(4):308-13.
5.Rajkumar RP, Melvin G. Pharmacovigilance for psychiatrists: An introduction. Indian J Psychiatry 2014;56:176-81.
6.Kharkar M, Bowalekar S. Extent of under reporting of Adverse Drug Reactions (ADRs) in India: evaluation using Logistic Regression Analysis (LRA) model. J Clin Trials. 2014;4:155.
7.Martínez A. A Way of Bridging the Gap between Psychological Treatments and Antidepressant Medication. Int J Depress Anxiety 2019;2:010. doi: 10.18203/2319-2003.ijbcp20150366.
8.Lucca JM, Madhan R, Gurumurthy P, Dushad R. A prospective observational study to evaluate safety reporting of antidepressants at a tertiary care hospital in India. Indian J Pharmacol 2014;46:543-6. doi: 10.4103/0253-7613.150344, PMID 25821314.

9.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. doi: 10.4103/0253-7613.140591, PMID 25298586.
10.Tripathi A, Avasthi A, Desousa A, Bhagabati D, Shah N and Kallivayalil RA: Prescription pattern of antidepressants in five tertiary care psychiatric centres of India. Indian J Med Res 2016; 143 (4): 507-12
11.Sridhar SB, Al-Thamer SS, Jabbar R. Monitoring of adverse drug reactions in psychiatry outpatient department of a Secondary Care Hospital of Ras Al Khaimah, UAE. J Basic Clin Pharm 2016;7:80-6.
12.Mishra S, Swain T, Mohanty M. Patterns of prescription & efficacy evaluation of antide pressants in a tertiary care teaching hospital inEastern India. Asian J Pharm Clin Res 2012; 5(3):193-6
13.Barvaliya S, Panchal JR, Desai MK, Parikh M. Pattern of adverse drug reactions into psychiatric patients. Int J Basic Clin Pharmacol 2019;8:1059. doi: 10.4103/2229-3485.86883, PMID 22145123
14. Mansuri. Z, Bhavasar. R, Parmar.P, Damor.R,Joshi.H.To Evaluate the Efficacy and Safety Profile of Antidepressant Drugs used in Cases of Depression: A Prospective Cohort Study.International Journal of Pharmaceutical and Clinical Researche-ISSN: 0975-1556, p-ISSN: 2820-264.
15.Sengupta G, Bhowmick S, Hazra A, Datta A, Rahaman M. Adverse drug reaction monitoring in psychiatry out-patient department of an Indian teaching hospital. Indian J Pharmacol 2011;43:36-9. doi: 10.7860/JCDR/2017/24009.9873, PMID 28658799.
16.Patel TK, Bhabhor PH, Desai N, Shah S, Patel PB, Vatsala E, *et al*. Adverse drug reactions in a psychiatric department of tertiary care teaching hospital in India: Analysis of spontaneously reported cases. Asian J Psychiatr 2015;17:42-9. doi: 10.4103/0976-0105.183263.
17.Rajesh R, Vidyasagar S, Nandakumar K. RETRACTED by plagiarism: Highly active antiretroviral therapy induced adverse drug reactions in Indian human immunodeficiency virus positive patients. Pharm Pract (Granada) 2011;9:48-55. doi: 10.1016/j.ajp.2015.07.003, PMID 26216702
18.Bhavani KB, Hema NG, Sangeetha. A prospective observational study of adverse drug reactions to antidepressants: Type and risk factors in a tertiary care teaching hospital. Int J Basic Clin Pharmacol 2014;3:380- 4.
19.Modayil RR, Harugeri A, Parthasarathi G, Ramesh M, Prasad R, Naik V, *et al*. Adverse drug reactions to antidepressants. An experience of spontaneous reporting and intensive monitoring from centers in India. Pharmacoepidemiol Drug Saf 2010;19:247-55.
20.Atul J, Arpita S, Ajay V, Maneesh S. Assessment of awareness towards pharmacovigilance program of India and reporting of adverse drug reactions among nurses in a tertiary care hospital. Int J Basic Clin Pharmacol 2018;7:1357-64.
21.Aburamadan, Sridhar S, Tadross T. Adverse drug reactions to antipsychotic medications, intensive monitoring of adverse drug reactions to antipsychotic medications in the inpatient psychiatry department of a secondary care hospital of UAE. Int J Pharm Investig 2018;8:151-6. doi: 10.1002/pds.1907, PMID 20066675
22.Driessen M, Schulz P, Jander S, Ribbert H, Gerhards S, Neuner F, et al. Effectiveness of inpatient versus outpatient complex treatment programs in depressive disorders: A quasi-experimental study under naturalistic conditions. BMC Psychiatry 2019;19:380. doi: 10.1176/ ajp.149.10.1335, PMID 1530069
23.Nagpal M, Tayal V, Kumar S, Gupta U. Adverse drug reactions in patients diagnosed with depression and were on antidepressants. Adv Pharm Technol Res 2012;3:62-7. doi: 10.7860/JCDR/2013/4985.3041, PMID 23905119
24.Gummadi T, Harave VS, Aiyar LN, RajaLekshmi SG, Kunnavil R. Adverse drug reaction monitoring in a tertiary care psychiatry setting: A comparative study between inpatients and outpatients. Indian J Psychol Med 2017;39:306-11. doi: 10.4103/0253-7176.207328, PMID 28615765.

25.Kurmi P, Paul PK, Dutta SK, Das S. To study the pattern of adverse drug reaction of antipsychotic drugs in a tertiary care hospital of Assam. Int J Pharm Tech Res 2015;8:101-5.
26.Aashal Shah et al., A Prospective Study of Adverse Drug Reactions in Patients with Bipolar Disorder in Psychiatry OPD.Journal of Clinical and Diagnostic Research. 2017 May, Vol-11(5): FC24-FC28