ASSESSING ADVERSE REACTIONS AND COMPLIANCE WITH TRICYCLIC ANTIDEPRESSANTS IN DEPRESSIVE PATIENTS IN ANDHRA PRADESH

Srinivas Angapelly[1], Niranjan Babu Mudduluru[*2], Sireesha Policharla[3]

[1]Department of Pharmaceutical Chemistry, Seven Hills College of Pharmacy, Tirupati, A.P., India
[2]Department of Pharmacognosy, Seven Hills College of Pharmacy, Tirupati, A.P., India
[3]Department of Pharmaceutical Chemistry, Seven Hills College of Pharmacy, Tirupati, A.P., India

Corresponding Author
Dr. M. Niranjan Babu

Professor, Department of Pharmacognosy, Seven Hills College of Pharmacy, Tirupati, A.P., India – 517561Contact: 7702484513Email: principal.cq@jntua.ac.in

ABSTRACT

Aim & Objectives: This study aims to monitor medication compliance and adverse drug reactions (ADRs) to tricyclic antidepressants (TCAs) in depressed patients. Additionally, it seeks to identify the most frequently used TCA drugs and assess the age and gender distribution of the patient population. **Methods:** The study was conducted in the psychiatric department of tertiary care hospitals in AP, India, with approval from the administrative and institutional ethics committees. Seventy patients from the psychiatric department participated after understanding the study's purpose and providing informed consent. Information was collected via pre-approved forms, and medication adherence was measured using the Medication Adherence Rating Scale (MARS). Data analysis was performed using IBM SPSS version 26. **Results:** Seventy patients using TCAs reported adverse drug reactions. Imipramine was the most frequently prescribed antidepressant in this study. The reported ADRs included blurred vision, insomnia, and hesitancy when urinating. Using a pre-made WHO form, 70 patients were examined for ADRs. Probable causality accounted for 43% of the ADRs, 54% of which could have been avoided. Sixty-four percent of the ADRs were of mild severity. Socioeconomic barriers were the only significant factor affecting non-adherence, which was not as prominent. **Conclusion:** This study provides a representative profile of the typical ADRs observed in the psychiatric department. Clinical pharmacists play a crucial role in improving patient medication adherence by raising awareness about illnesses and treatments and offering patient counselling services.

Key words: Adverse drug reactions, TCA, medication adherence, depression

INTRODUCTION

Globally, depression affects over 264 million people, making it a prevalent mental illness. It is a primary cause of disability worldwide and a significant contributor to the total global

,

disease burden . Symptoms of a depressive episode include a low or melancholic mood, pessimistic thoughts, decreased interest in routine activities, mental slowness, poor concentration, insomnia or excessive sleep, significant weight loss or gain due to changes in eating habits, psychomotor agitation or retardation, feelings of worthlessness or guilt, and decreased energy or libido, lasting for most days over a two-week period . The goals of treatment for psychotic depression are the remission of depressive episodes, achieving baseline psychosocial functioning, and preventing relapse and recurrence of depression [1].

Depressive disorder is also associated with obesity, with risks varying according to gender, ethnicity, illness severity, and the use of antidepressants. Choosing an antidepressant that best fits the patient's needs and preferences is often more beneficial than selecting the clinically 'best' option. Antidepressants are classified based on their mechanism of action into four primary classes: tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs). Other antidepressants are typically referred to as "atypical"; however, this article follows the British National Formulary (BNF) and uses the term "other"[2].

Every drug interacts intricately with the molecules in living systems, functioning primarily on four levels:
- **Molecular:** Enzymes, carrier molecules, receptors, and ion channels.
- **Cellular:** Enzymes, ion channels, and G proteins involved in cellular transduction.

TCAs work by preventing the reabsorption of serotonin and norepinephrine (NE), altering the behavior of neuro-receptors. Additionally, TCAs have been reported to block histaminic, muscarinic, and alpha1 adrenergic receptors. The medications used for depression can cause a variety of adverse drug reactions (ADRs), some of which can be severe or even lethal. Despite significant advancements in our understanding of Depressive Disorder over the last decade, there remain unanswered questions about diagnosing the illness and providing appropriate clinical care [3]. Managing adverse effects is crucial for improving patient adherence, comfort, and symptom remission. Common side effects include sexual dysfunction, gastrointestinal issues, weight gain, apathy, somnolence, fatigue, and sleep disturbances. Central nervous system changes may lead to psychiatric complications, and peripheral side effects should also be considered when using antidepressants[4].

Even though pharmaceutical treatments for depressive disorders are highly effective, patients often fail to take their medications as prescribed. It is important to examine adherence and persistence to understand how patients manage their medication regimens. Adherence refers to taking medications according to the prescribed timing, dosage, and frequency. Persistence is the extent to which patients continue taking a prescribed drug to achieve therapeutic benefits[5]. Thus, persistence refers to the overall duration of drug therapy, while adherence or compliance refers to the consistency of drug use during therapy.

Older adults may be more susceptible to medication non-adherence, which can negatively impact their health compared to younger cohorts. Medication adherence in this group is hindered by factors such as dosing schedules, side effects, and polypharmacy, as well as patient-related factors like cognitive function, health literacy, and multimorbidity [6].

The objective of this study was to examine adverse drug reactions (ADR) and medication adherence among patients using tricyclic antidepressants (TCA) for depression at selected tertiary care hospitals in AP, India. The study also explored the distribution of patients by age and gender, and identified the most frequently prescribed TCAs[7].

Methodology:

A prospective observational study was conducted at the psychiatric departments of Al Azhar Medical College Hospital, Thodupuzha, and Mount Zion Medical College Hospital, Adoor, both located in AP, India. This research received approval from both administrative and institutional ethics committees (AAMC/IEC/2023-2024/12, 14/2023)[8].

Seventy patients meeting the study's inclusion and exclusion criteria were enrolled. All participants were provided with a concise overview of the study objectives and assured of data confidentiality. Written informed consent, in easily understandable language, was obtained from each patient or their caregiver. Relevant data were collected using a pre-designed data collection form approved for this purpose. Adverse drug events were assessed using a predetermined WHO form, and medication adherence was evaluated using the Medication Adherence Rating Scale (MARS). Statistical analysis was performed using IBM SPSS version 26[9].

Patients of any age or gender diagnosed with depressive disorder and presenting to the Psychiatry department were eligible for inclusion, including pregnant women with diagnosed depressive disorders. Participation required comprehension of the study's purpose, willingness to share health information, and the signing of an informed consent document.

Patients with malignancies, terminal illnesses, or a clinically significant suicide risk were excluded from the study. Additionally, individuals with a history of severe allergic or adverse reactions to the study medications, as well as those with a history of substance abuse, were excluded from participation.

Results and Discussion:

Seventy prescriptions containing tricyclic antidepressants were analyzed in this study. Female patients accounted for 61.43%, while male patients represented 38.57%. Females were found to be more susceptible to depression than males. Depression can profoundly impact various aspects of a woman's life, including physical health, social interactions, relationships, career, and self-esteem. This complexity can be attributed to factors such as reproductive hormones, societal pressures, and the unique ways in which women respond to stress. It's important to note that experiencing depression does not mean one is alone in their struggles. Women are

approximately twice as likely as men to experience depression, highlighting the need for effective management strategies and support systems to enhance well-being.

The age distribution of the patients ranged from below 25 to 60 years. Table 1 presents the distribution of patients across different age groups. Depression can onset at any stage of life, influenced by factors such as family history, physical health conditions, and current life circumstances. Understanding these factors is crucial for identifying and managing potential symptoms of depression effectively.

Table 1: Distribution of Patients Based on Age Group

Age Group	No. of Patients	Percentage of Patients
Below 25	12	17.1
25 - 35	17	24.3
35 - 45	20	28.6
45 and above	21	30.0
Total	70	100.0

According to Table 2, the predominant psychiatric diagnosis among patients was major depression. Other prevalent disorders included depressive disorder, schizophrenia, bipolar affective disorder, obsessive-compulsive disorder, and anxiety. Depression arises from intricate interactions involving social, psychological, and biological factors. Childhood adversity, personal losses, and unemployment can all contribute to its onset. Effective management of depression involves both psychological therapies and medical treatments.

Table 2: Diagnosis Pattern Among Patients

Diagnosis	No. of Patients (N=70)	Percentage of Patients
Bipolar affective disorder	20	28.5%
Schizophrenia	10	14.2%
Obsessive compulsive disorder	05	7.14%
Depressive disorder	32	45.7%
Anxiety	03	4.28%

The distribution of TCA prescriptions is depicted in Figure 1. The most frequently prescribed TCA medications include Imipramine, Amitriptyline, Nortriptyline, Clomipramine, and Dothiepin. Tricyclic antidepressants (TCAs) are usually prescribed when other antidepressants have proven ineffective in treating depression. TCAs work by enhancing the availability of serotonin and norepinephrine, natural chemicals in the body that regulate mood. This increased availability helps improve mood.
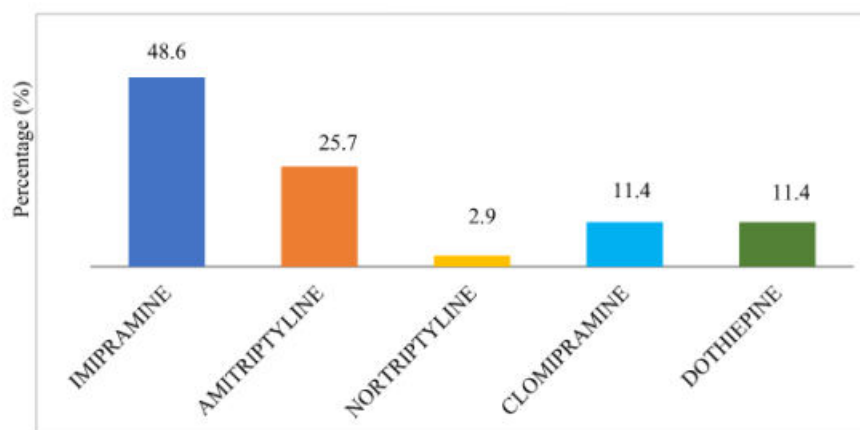
Figure 1: Distribution of TCA Prescribed

Figure 2 illustrates the distribution of adverse drug reactions (ADRs) observed in 26 percent of the 70 patients included in the study. Common ADRs associated with TCAs include insomnia, dry mouth, blurred vision, and urinary hesitancy. TCAs are known to pose risks such as elevated liver enzymes and urinary retention. These medications can also cause blurred vision, constipation, dry mouth (xerostomia), confusion, urinary retention, and rapid heartbeat by blocking cholinergic receptors (leading to tachycardia). Additionally, blocking alpha-1 adrenergic receptors may result in orthostatic hypotension (a drop in blood pressure upon standing) and dizziness. TCA-induced histamine blockade (H1) can also cause sedation, increased appetite, weight gain, and confusion.
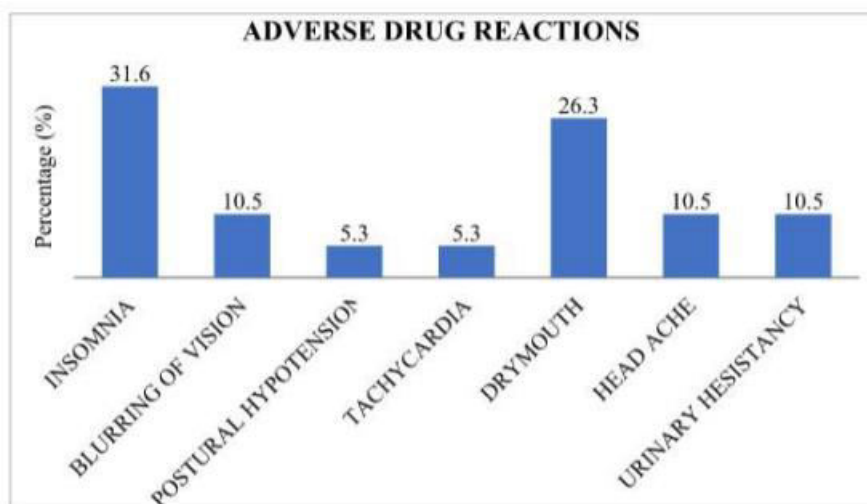

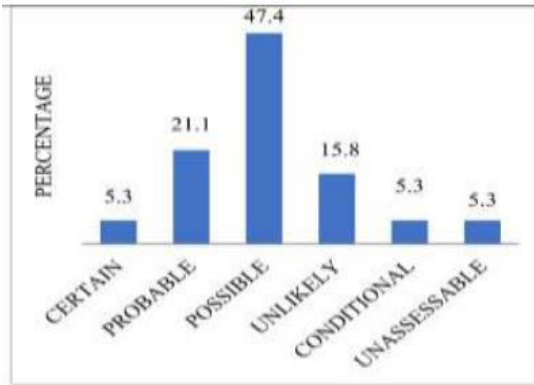**Figure 2: Distribution of patients based on Adverse Drug Reactions**
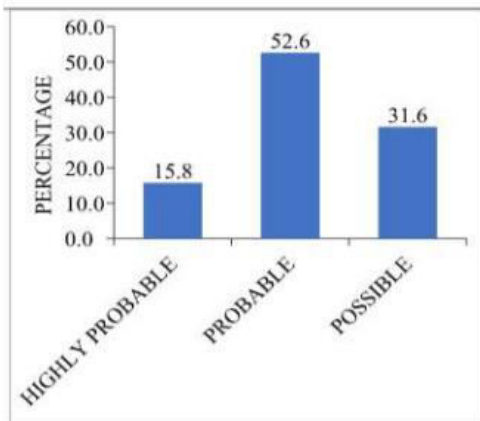
Figure 3 A: Assessment of WHO Causality Scale of ADR

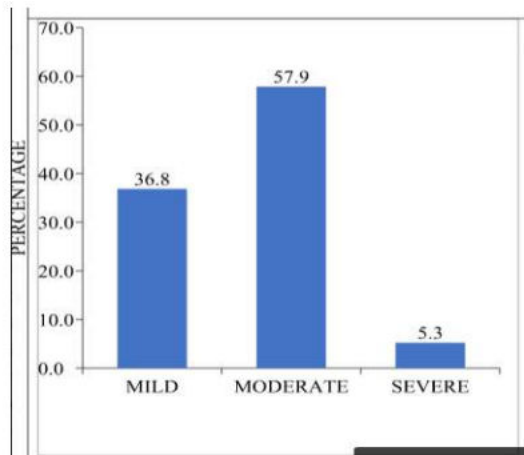**Figure 3 B: Assessment of ADR by Naranjo Probability Scale**

Figure 3 C: Assessment of ADR by Hartwig's Severity Assessment Scale
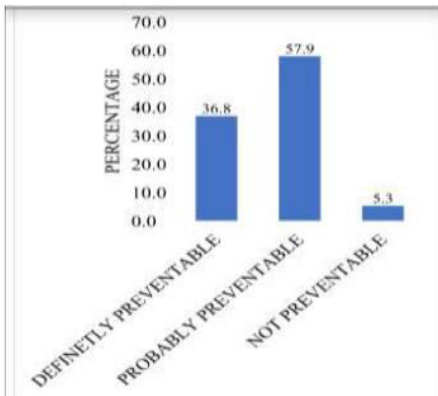
Figure 3 D: Assessment of ADR by Modified shummock thronton preventability scale

CONCLUSION

Research on medication usage examines the social, medical, and economic dimensions of drug administration. This study specifically investigates medication adherence and adverse reactions to tricyclic antidepressants (TCAs) among patients with depression. Amitriptyline and imipramine emerge as the most commonly prescribed TCAs in tertiary care hospitals. TCAs frequently induce side effects such as dry mouth, insomnia, and urinary hesitancy. It is crucial to note that medication non-adherence among older adults may significantly correlate with higher rates of hospitalization and mortality. Given that hospital stays in this demographic contribute substantially to healthcare expenses, monitoring and addressing medication adherence is essential. This approach can potentially reduce healthcare costs, enhance clinical outcomes, and diminish hospital admissions. In psychiatric settings, clinical pharmacists continue to play a pivotal role in enhancing patient medication adherence through disease and treatment education and offering counseling services.

REFERENCES

[1]. Vasundhara Yerkade and Riyaz Ahmed 2017 A drug utilization study of antidepressant drugs in a tertiary care hospital Int J Basic Clin Pharmacol 6(6) 1405-1409

[2]. Dawn N, Kim-Romo, Karen L. Rascati et al 2009 Medication Adherence and Persistence in Patients with Severe Major Depressive Disorder with Psychotic Features: Antidepressant and SecondGeneration Antipsychotic Therapy Versus Antidepressant Monotherapy J Manag Care Spec Pharm. 22(5) 588-96

[3]. Richard Morriss, Freya Tyrer, Francesco Zaccardi et al Safety of antidepressants in a primary care cohort of adults with obesity and depression PLOS ONE | https://doi.org/10.1371/journal.pone.0245722 2021 1/16

[4]. Annie LeBlanc, Jeph Herrin, Mark D. Williams, et al 2015 Shared Decision Making for Antidepressants in Primary Care A Cluster Randomized Trial JAMA Internal Medicine 175(11) 1761-70

[5]. Paul Bogowicz, Helen J Curtis, D Phil et al 2021 Trends and variation in antidepressant prescribing in English primary care: a retrospective longitudinal study BJGP Open DOI: 10.3399/BJGPO.2021.0020 1-12

[6]. Swati Mishra, Trupti Rekha Swain and Manjushree Mohanty 2013 Adverse Drug Reaction Monitoring of Antidepressants in the Psychiatry Outpatients Department of a Tertiary Care Teaching Hospital Journal of Clinical and Diagnostic Research 7(6) 1131-1134

[7]. Beatriz González, Tasmania del Pino, Pedro SerranoPérez et al Effectiveness of interventions to improve medication adherence in adults with depressivedisorders: a meta-analysis BMC Psychiatry 22(487) 1-21

[8]. G van Servellen, BA Heise and R Ellis 2011 Factors associated with antidepressant edication adherence and adherence enhancement programmes: a systematic literature review Mental Health in Family Medicine 8(1) 255–71

[9]. Caroline A. Walsh, Caitriona Cahir, Sarah Tecklenborg et al 2019 The association between medication non-adherence and adverse health outcomes in ageing populations: A systematic review and meta-analysis Br J Clin Pharmacol. 85(1) 2464–2478.