International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 529-537 www.ijprajournal.com ISSN: 2456-4494

Assessing Adverse Drug Reactions and Medication Compliance for Tricyclic Antidepressants among Depressive Patients in Selected Tertiary Care Hospitals of Kerala, India.

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Date of Submission: 01-05-2024 Date of Acceptance: 10-05-2024

ABSTRACT

Aim & Objectives: This study intends to monitor medication compliance and adverse drug reactions (ADR) to tricyclic antidepressants (TCA) in depressed patients. We also aim to determine which TCA drugs are most frequently used and assess the age and gender distribution of patient population.

Methods: The study was carried out at Psychiatric department of tertiary care hospitals in Kerala, India, with the approval of 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 measured by the Medication Adherence Rating Scale (MARS). The data were analysed using IBM SPSS version 26

Results: Seventy patients who used TCA reported adverse drug reactions. The most often prescribed antidepressant in this study was imipramine. The ADR was blurred vision, insomnia, and hesitancy when urinating. Using a pre-made WHO form, 70 patients in this study were examined for ADRs. Of the ADRs, probable causality accounted for 43%. Of all the ADRs, 54% could have been avoided. Sixty-four percent of the ADRs had mild severity. Socioeconomic barriers were the only ones where a significant effect was seen; non-adherence was not as significant.

Conclusion: A representative profile of the ADRs that are typical in the psychiatric department is provided by this study. In the psychiatry department, clinical pharmacists continue to play a crucial role in improving patient medication adherence by raising patient awareness of illnesses and treatments and offering patient counselling services.

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

I. INTRODUCTION

Globally, depression affects over 264 million people and is a prevalent mental illness. It is a primary cause of disability globally and a significant contributor to the total global disease burden ([1]. The following symptoms of a depressive episode include a low or melancholic mood, pessimistic worry, decreased interest in routine activities, mental slowness and poor concentration, insomnia or increased sleep, significant weight loss or gain as a result of changed eating habits, psychomotor agitation or retardation, feelings of worthlessness or guilt, and decreased energy or libido that last for most days for a period of two weeks [(2)]. Remission of depressive episodes, achieving baseline psychosocial functioning, and preventing relapse and recurrence of depression are the objectives of treatment for psychotic depression [(3)]. Obesity is also associated with depressive disorder, with the risk differing according to gender, ethnicity, the severity of the illness, and the use of antidepressants

Choosing the agent that best fits the patient's needs and preferences is more beneficial for both the clinician and the patient than going with the option that may be considered the clinically best option

The mechanism of action of antidepressants determines their classification. There are four primary classes: tricyclic, selective serotonin reuptake inhibitors (SSRIs), monoamine

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oxidase inhibitors (MAOI), and serotonin-norepinephrine reuptake inhibitors (SNRI). The term "atypical" is typically used to describe other antidepressants; however, this article uses the term "other" in accordance with the British National Formulary (BNF). Every drug causes intricate interactions with the molecules that make up living systems. These processes, whether chemical or physical, primarily function on four levels: Molecular: Enzyme, carrier molecules, receptors, and ion channels. Enzymes, ion channels, and G proteins are examples of cellular transduction. The TCAs prevent serotonin and norepinephrine (NE) from being reabsorbed (5HT). This phenomenon, which is the main way that antidepressants work, alters how neuro-receptors behave physiologically. Additionally, it has been reported that TCAs block histaminic, muscarinic, and alpha1 adrenergic receptors

The medications used have the potential to cause a variety of adverse drug reactions (ADRs), some of which have the potential to be lethal. While there have been significant advancements in our understanding of Depressive Disorder over the last ten years, there are still some unanswered questions about how to diagnose the illness and provide appropriate clinical care. Therefore, better patient adherence, comfort, and symptom remission would all benefit from the management of adverse effects. Sexual dysfunction, gastrointestinal issues, weight gain, apathy, somnolence, exhaustion, and sleep disturbances are typical side effects. Changes in the central nervous system may lead to psychiatric complications. When using antidepressants, peripheral side effects and other serious side effects should be taken into account

Despite the significant effectiveness of pharmaceutical treatment for depressive disorders, patients frequently fail to take their prescription as directed. Examining adherence and persistence is important when discussing how patients take their medications

Patients who take their medications according to prescription in terms of timing, dosage, and frequency are said to be adherent. The last definition of persistence is the degree to which patients take a prescription drug as directed in order to experience therapeutic benefits. Accordingly, persistence refers to the length of time a drug therapy is administered overall, whereas adherence or compliance refers to the level of drug use during therapy. Older adults may be more vulnerable to medication non-adherence, which could have a negative impact on their health in comparison to younger cohorts. Medication adherence in this group is hindered by drug-related factors like dosing schedule, side effects, and polypharmacy, as well as patient-related factors like cognitive function, health literacy, and multimorbidity.

Therefore, the objective of this study was to examine the Adverse Drug Reactions (ADR) and medication adherence among patients using tricyclic antidepressants (TCA) for depression at selected tertiary care hospitals in Kerala, India.

The study also examined the distribution of patients by age and gender, as well as which TCAwere pres cribed most frequently.

II. METHODOLOGY

A prospective observational study was conducted at the psychiatric department in Al Azhar Medical College Hospital, Thodupuzha and Mount Zion Medical College Hospital, Adoor, both in Kerala, India. This research had obtained both administrative and institutional ethics committee approval (AAMC/IEC/2023-2024/12, 14/2023).

A total of 70 patients were enrolled in this study based on the inclusion and exclusion criteria. All participants are provided with a brief introduction to the study and data confidentiality. The patient or caregiver provided a written informed consent printed in language that was easily understood. Relevant information was collected according to the approved predesigned data collection form. Adverse drug events assessed by predetermined WHO form. The Medication Adherence Rating Scale was used to evaluate medication adherence (MARS). Then the data were statistically analysed by IBM SPSS version 26.

Patients of any age or gender who presented to the Psychiatry department with a diagnosis of depressive disorder were included in the study. This included pregnant women with diagnosed depressive disorders. Participation in the study required an understanding of its purpose, a willingness to share health information, and the execution of a document indicating informed consent.

Patients with malignancies and those who were terminally ill were excluded from the study. In addition, individuals with a clinically significant risk of suicide were deemed too severe for inclusion. Those with a history of severe allergic or adverse reactions to the study medications, as well as those with a history of substance abuse, were also excluded. Patients with malignancies and those who were terminally ill were excluded from the

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III. DATA ANALYSIS

The collected data were entered in Microsoft Excel, and the result were analysed using IBM SPSS version 26.

IV. RESULTS AND DISCUSSION

Seventy prescriptions containing tricyclic antidepressants were analysed. Female patients accounted for 61.43%, while male patients represented 38.57%. Females were more susceptible than males. Depression can profoundly affect every facet of a woman's life, encompassing physical health, social interactions, relationships, career, and self-esteem. This complexity can be attributed to factors like reproductive hormones, societal pressures, and the distinct way women respond to stress. Nevertheless, it's crucial to remember that you are not isolated in this. Women are approximately twice as likely to experience depression compared to men. However, depression is manageable, and there are numerous steps one can take to enhance their well-being.

Age group of the patients varies from below 25 to 60. Table 1 displays the distribution of patients according to age groups. Depression can manifest at any point in a person's life, but their stage of life influences their risk. Multiple factors, including family history, physical health, and current life circumstances, play a role in its onset. Individuals must recognize these differences in order to better identify and manage potential depression symptoms.

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 most prevalent psychiatric diagnosis among patients was major depression. Depressive disorder, schizophrenia, bipolar affective disorder, obsessive-compulsive disorder, and anxiety were the most prevalent disorders. Depression is the result of complex interactions between social, psychological, and biological factors. Childhood adversity, personal losses, and unemployment can all play a role in the onset of depression. Both psychological and medical treatments are available for managing depression.

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 presented in Figure 1. The most commonly prescribed TCA medications are Imipramine, Amitriptyline, Nortriptyline, Clomipramine, and Dothiepin. Tricyclic antidepressants (TCAs) are typically prescribed only when other antidepressants have failed to alleviate depression. TCAs increase the availability of serotonin and norepinephrine, which are naturally occurring chemicals in the body that regulate mood. This increased availability contributes to a mood enhancement.

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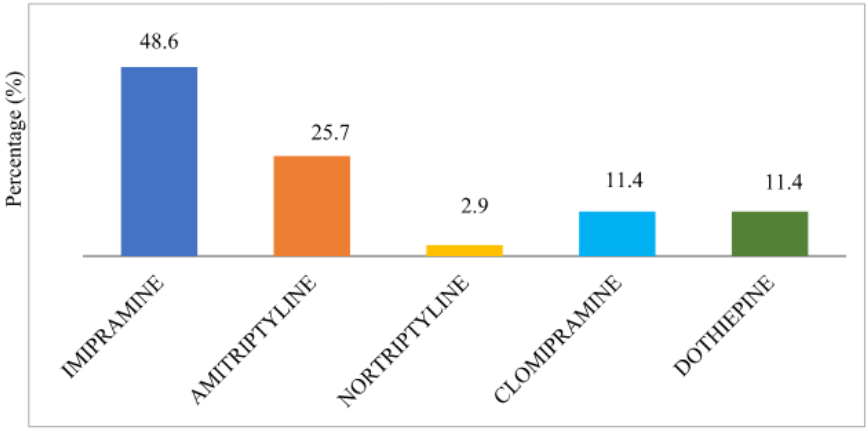

Figure 1: Distribution of TCA Prescribed

Figure 2 illustrates the distribution of adverse drug reactions (ADR) caused by TCA in 26 percent of the 70 patients studied. Common ADRs from TCA include insomnia, dry mouth, blurred vision, and urinary hesitancy. Increased liver enzymes and urinary retention are among the known dangers of TCAs. These drugs can cause blurred vision, constipation, dry mouth (xerostomia), confusion, urinary retention, and a rapid heartbeat by blocking cholinergic receptors (tachycardia). Additionally, blocking alpha-1 adrenergic receptors can lead to a drop in blood pressure upon standing (orthostatic hypotension) and dizziness. The TCA-induced histamine blockade (H1) can also result in drowsiness (sedation), increased appetite, weight gain and confusion.

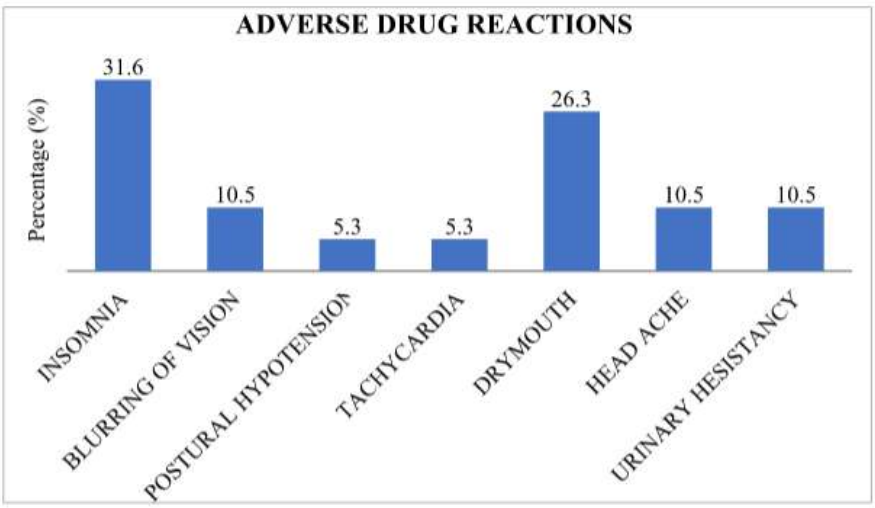

Figure 2: Distribution of patients based on Adverse Drug Reactions

According to the WHO's ADR causality scale, the assessment thoroughly examines both the clinical-pharmacological aspects of a patient's history and the quality of the recorded observation. Pharmacovigilance mainly aims to identify unfamiliar or unforeseen adverse reactions, with less emphasis on other factors like previous knowledge or statistical probability. The precise definitions used in this scale are critical, leading to potential variations in individual interpretations. As illustrated in Figure 3A of this study, the WHO causality scale categorized 44% of ADRs with TCA as "possible" and 22% as "probable." The distinction is that "possible" reactions might have alternative explanations, or there may be a lack of clarity about the effects after stopping the treatment.

International Journal of Pharmaceutical Research and Applications
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The Naranjo Algorithm, also known as the Adverse Drug Reaction Probability Scale, is a tool used to determine the likelihood that a drug caused a specific adverse event. It uses a straightforward questionnaire to assign probability scores. In this study, as detailed in Figure 3B, the Naranjo probability scale categorized 52% of cases as "probable," 31% as "possible," and 15% as "highly probable." This scale helps in evaluating the causal relationship between an observed adverse clinical event and the administration of a drug.

Hartwig's severity scale was used to evaluate the severity of adverse drug reactions (ADRs), as shown in Figure 3C. The results of this investigation revealed that 36% of the reactions were mild and 57% had moderate severity. Based on its effects, the Hartwig Instrument is used to assess the severity of ADR. Healthcare providers can more accurately predict future ADR occurrences, particularly those with moderate to severe intensity, by assessing the severity of ADR in their patients.

ADR assessment using the Modified Shumock and Thornton Preventability Scale is shown in Figure 3D. ADRs can be classified as "definitely preventable," "probably preventable," or "not preventable" using this scale. 36.8% of the reactions were "definitely preventable," 57.9% of the reactions were "probably preventable," and only 5.3% of the reactions were "not preventable," according to the study's findings. Most ADRs could be classified as "probably preventable." Medication errors-related adverse drug reactions are referred to as preventable adverse drug reactions, or PADRs. Among other things, these mistakes can include acts of commission or omission, incorrect medication, dosage, or timing, administering medication to a patient who has a known allergy, and inadequate monitoring.

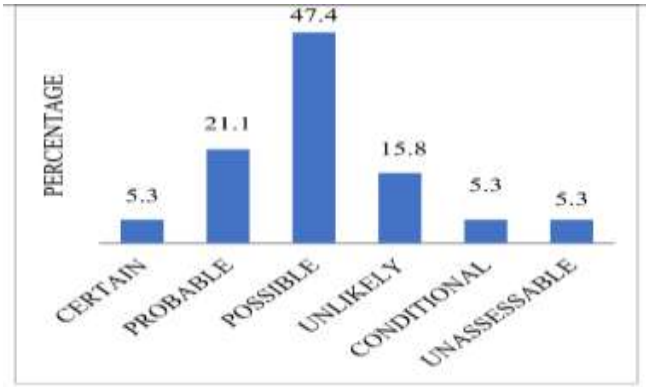

Figure 3 A: Assessment of WHO Causality Scale of ADR

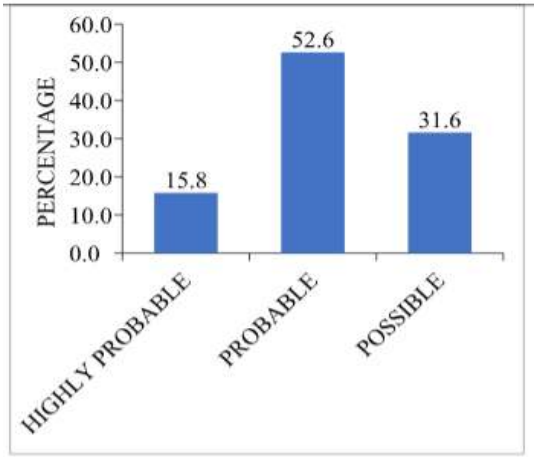

Figure 3 B: Assessment of ADR by Naranjo Probability Scale

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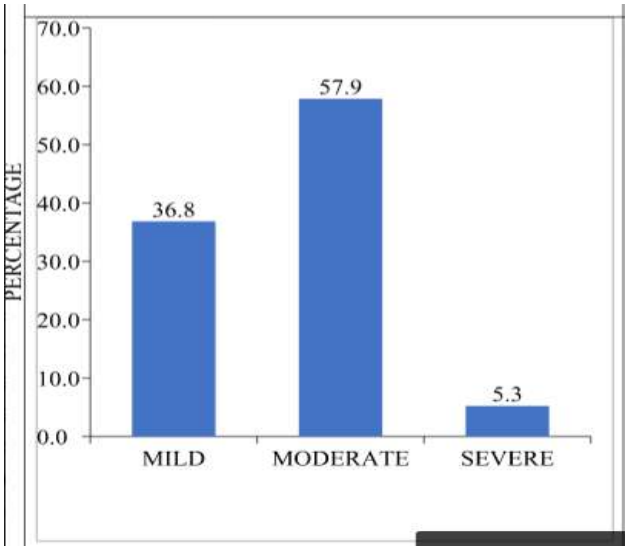

Figure 3 C: Assessment of ADR by Hartwig's Severity Assessment Scale

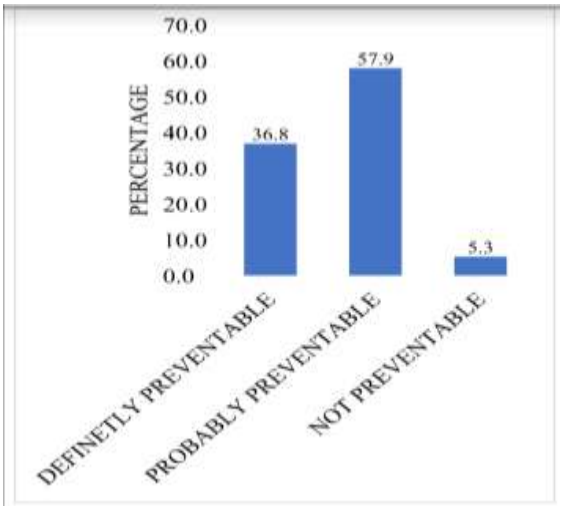

Figure 3 D: Assessment of ADR by Modified shummock thronton preventability scale

Medication non-adherence includes not initiating treatment, not adhering precisely to the recommended regimen, or terminating treatment early. Patients who do not take their antidepressants as prescribed run the risk of relapsing, visiting the ER more frequently, and being admitted to the hospital. Non-adherence can also worsen symptoms, lessen the efficacy of treatment, and decrease the likelihood of remission. As a result, the cost of healthcare as a whole rise. Data regarding patient non-adherence to TCA are shown in Figure 4.

When patients take their medications as prescribed, taking into account the appropriate timing, dosage, and frequency, this is known as adherence. Contrarily, persistence refers to how long a patient keeps taking their medication as directed in order to experience the intended therapeutic benefits. Essentially, persistence examines the entire duration of medication use, whereas adherence concentrates on how consistently a medication is taken during treatment. Figure 4 sheds light on how patients behave when it comes to taking their TCA medications.

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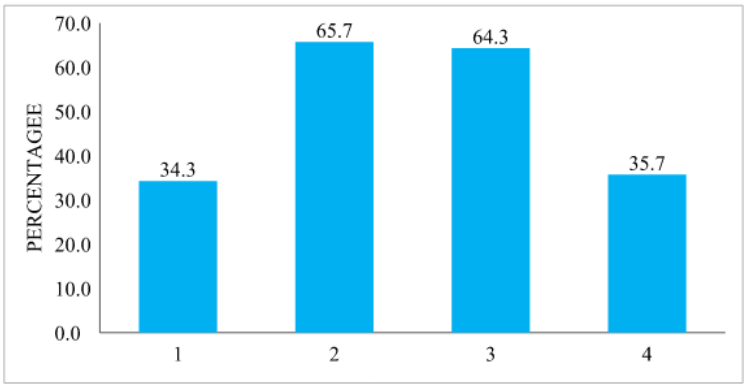

Figure 4. Determination of patients based on before and after medication adherence

The different factors that affect patients' non-adherence. Many factors are associated with adherence or non-adherence and fall into various categories. The WHO divides these components into five primary groups: factors related to the patient, conditions, therapy, socioeconomic status, and the health system. The objectives of this review are to: (a) summarize research on the variables associated with ADM adherence or non-adherence; and (b) evaluate the efficacy of adherence-improving initiatives.

Previous research has demonstrated that age has a major impact on the prevalence of depression. Gender also has a major impact on the prevalence of depression, with women showing two to three times the prevalence rates over a 12-month period compared to men

Depression has been found to be the leading cause of disability in women worldwide. Women are more likely to experience anxiety and depression due to hormonal changes related to menstruation, premenopausal, pregnancy, and the postpartum period, but these are not the only causes. There are probably a number of reasons why there are differences in mental health between the sexes, including biology, genetics, demography, psychological traits, and social influences. The characteristics of mental health disorders are influenced by gender, which also affects a person's willingness to seek help as well as factors like symptom onset, prevalence, treatment approaches, medication choices (such as which drugs to avoid while pregnant), response to treatment, and medication choices. While anxiety and depression are common in women, men typically exhibit symptoms of severe disorders like bipolar disorder and schizophrenia earlier in life. Remarkably, bipolar disorder typically appears later in life in women. Furthermore, the prevalence of substance abuse disorders is higher in men

Attention needs to be paid to the adverse drug reaction (ADR) profile of antidepressants in the context of Indian psychiatric patients. Antidepressant medications can be made safer and more effective by managing adverse drug reactions (ADRs) early on. ADRs are frequent because mental illnesses are often chronic in nature and require lengthy treatment regimens. It is essential to identify risk factors such as age, gender, income, and education level in order to minimize potential harm and determine the proper starting dosage of antidepressants

Medication errors, drug interactions, non-compliance, and adverse drug reactions can all result from taking multiple medications at once. Since no prescription included more than five medications, it can be concluded that the likelihood of these problems was reduced

The type and duration of therapy, the severity of the health issues, medication side effects, drug interactions, related health conditions, treatment costs, the calibre of healthcare facilities, the patient-doctor relationship, and the patient's socioeconomic status are some of the factors that affect adherence to treatment. Spending the time to give support and education and providing a collaborative setting will improve adherence and outcome. Non-adherence to depression treatments is a major problem on a global scale [(15)].

V. CONCLUSION

Studies on drug use look at the social, medical, and financial aspects of drug use. In particular, this study explores medication adherence and tricyclic antidepressant (TCA) adverse reactions in depression patients. Amitriptyline and imipramine have become the most widely used TCAs in tertiary care hospitals. TCAs are frequently associated with side effects such as dry mouth, insomnia, and urinary

hesitancy. It's important to remember that older adults' medication non-adherence may be strongly linked to higher hospitalization and death rates. Since hospital stays in this age group account for a large portion of medical costs, it is imperative to monitor and address medication adherence. This can lower healthcare costs, improve clinical outcomes, and lower the number of hospitalizations. In psychiatry departments, clinical pharmacists continue to play a critical role in improving patient medication adherence by increasing patient awareness of diseases and treatments and providing patient counselling services.

Acknowledgement
The authors thank SciWrite Global (www.sciwriteglobal.com), a medical communication company, for the editorial support.
Funding
None
Conflict of interest
The authors declare that there is no conflict of interest.

REFERENCE

[1]. Virendra Kushwaha1, Pooja Agrawal, Sarita Singh et al 2022 Assessment Of Adverse Drug Reactions Of Antidepressant Drugs Used In Psychiatry Department Of A Tertiary Care Hospital Asian J Pharm Clin Res 15(4) 49-54
[2]. 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
[3]. 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 Second-Generation Antipsychotic Therapy Versus Antidepressant Monotherapy J Manag Care Spec Pharm. 22(5) 588-96
[4]. 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
[5]. 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
[6]. 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
[7]. 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
[8]. Beatriz González, Tasmania del Pino, Pedro SerranoPérez et al Effectiveness of interventions to improve medication adherence in adults with depressive disorders: a meta-analysis BMC Psychiatry 22(487) 1-21
[9]. G van Servellen, BA Heise and R Ellis 2011 Factors associated with antidepressant medication adherence and adherence enhancement programmes: a systematic literature review Mental Health in Family Medicine 8(1) 255–71
[10]. 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.
[11]. Vasundhara Yerkade and Riyaz Ahmed Siddiqui 2017 A drug utilization study of antidepressant drugs in a tertiary care hospital Int J Basic Clin Pharmacol. 6(6) 1405-1409
[12]. Kholoud Bastaki, Mohammed El Anbari and Suhaila Ghuloum 2021 Prescription Pattern of Antidepressants and the Potential for Personalized Medicine in the Qatari Population J. Pers. Med 11(406) 1-11
[13]. Gerdien Franx, Jochanan Huyser and Jan Koetsen ruijter 2014 Implementing guidelines for depression on antidepressant prescribing in general practice: a quasi-experimental evaluation . BMC Family Practice 15(35) 1-7
[14]. Raushan Kumar Ranjan, Manish Kumar, Rajesh Kumar et al 2020 Drug utilization study and adverse drug monitoring of

antidepressant drugs in a tertiary care hospital of Bihar Panacea Journal of Medical Sciences 10(3) 315–319

[15]. Shrestha Manandhar J, Shrestha R, Basnet N et al 2011 Study of Adherence Pattern of Antidepressants in Patients with Depression KATHMANDU UNIVERSITY MEDICAL JOURNAL 15(1) 1-16

[16]. ACKNOWLEDGEMENT

[17]. The authors thank SciWrite Global(www.sciwriteglobal.com), a medical communications company, for the editorial support.

FUNDING
None

CONFLICT OF INTEREST
The authors declare that there is no conflict of interest.