

# Analysis of Psychotropic Drug Use Pattern and Related Issues in a Tertiary Care Research Centre Apart from Psychiatric Settings

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## ABSTRACT

Objective of the study was to determine the pattern of utilization of psychotropic drugs and the associated problem. A 6-month prospective cross-sectional study was conducted on 110 patients admitted in surgical and general wards in S.S. Institute of Medical Sciences and Research Centre, Davanagere. Data were collected through structured proforma which includes demographic data, prescription pattern of psychotropic drugs, comorbidities and possible DDIs. Data were analyzed using chi square test.

Out of 110 patients, males (66.4%) constituted a majority of subjects. Most of the subjects were in the age group of 31-56 years (51.9%) and they were all residents of rural area and smoking was the most prevalent social habit (24.5%). Majority of the patients were housewives or unemployed (60.9%). Hypertension was the commonest comorbid illness (48.2%). The prevalence of psychotropic drug use was higher in surgical ward patients (75.5%). Alprazolam (44.5%) was the most commonly prescribed drug followed by nortriptyline (19.6%) and pregabalin (22.3%). Monotherapy was preferred by majority of physicians (62.3%).

There was a total of 126 possible DDIs among which 76.1% were considered as

major interaction due to the interaction of alprazolam. Tramadol (95.5%) was the most commonly co-administered drug and anesthetics were most common drugs involved in the interaction. Six ADRs were identified with Alprazolam, nortriptyline and pregabalin.

Rational use of drugs, awareness of DDI, and active participation of clinical pharmacist led to better safety and effective use of psychotropic drugs.

**Keywords:** Alprazolam, psychotropic drugs, prescription pattern, drug-drug interactions

## INTRODUCTION

Antidepressant (ADs) prevalence is estimated to be around 6–10% in the past year and this class is now among the most frequently used drugs by the public at large [1]. This usage has shown an upward trend over the last two decades; in India, For example, ADs is now the third most prescribed class of therapeutic agents [13]. Among psychotropic drugs Antipsychotics, Antidepressants, Anxiolytics is the most commonly prescribed classes of drugs. These drugs are now being increasingly used outside of specialized psychiatric services in many non-psychiatric medical problems including chronic pain syndromes, gastrointestinal disorders, cardiovascular disorders and sleep disturbances. It raises

concerns regarding appropriacy, off-label use and the development of drug-related problems (DRPs). This systematic review of prescribing trends and DRP profile in use would provide a valuable insight into safe and rational use of these drugs in patient management.

The number of non-psychiatric specialties contributing to increased prescription of psychotropic medications are extensive and somewhat surprisingly people are now being prescribed antidepressants without a recognized diagnosis of a mental health problem [11]. There is some evidence although, that at least one third of patients prescribed psychotropic medication do not have a mental health diagnosis at the time of prescribing [12]. In practice standards are rarely adhered to and it has been shown that there is often a discrepancy between the standard which recommends sensible antipsychotic prescription and what actually happens [2]. For patients with existing physical health problems anxiety and depression is a common co morbid illness. Polypharmacy in antipsychotic treatment was evident in that a third of patients on antipsychotic medication were prescribed at least two different agents, studies looking at the nature and correlates of prescription of psychotropic agents within the medical and surgical departments of general hospitals [12]. The use of psychotropic medications off label, that is outside the authorized indications is also common [3]. Moreover,

an estimated 30–50% of individuals treated with antipsychotics exhibit suboptimal response and may experience persistent, serious, adverse effects[2].

### **Drug-Related Problems**

The DRP's can be categorized into the following systems; ABC; pharmaceutical care network Europe (PCNE) classification; Cipolle/Strand/Morley model; Granada consensus; Hanlon model; Hepler-Strand model; Krska system; Mackie; National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP); PI-Doc and the Westerlund model. One of the commonly used systems of classification of DRP's is the Hepler-Strand model. Any event or circumstances which involves medication therapy in which the ideal outcome of drug therapy was actually, or potentially prevented is a DRP. In this model, causes and problems were not separate and the categories involved are:

- a) Untreated indication.
- b) Improper drug selection.
- c) Sub-therapeutic dosage.
- d) Overdosage.
- e) Adverse drug reaction.
- f) Failure to receive medication.
- g) Drug interactions.
- h) Drug use without valid indication.

[6]

Drug use without valid indication.

<b>Subclass</b>	<b>Specific Agents</b>
<b>Monoamine agonists (formerly “antidepressants” and “stimulants”)</b>	
MAOIs	phenelzine, tranylcypromine, isocarboxazid, selegiline
SRI	citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine*, trazodone, venlafaxine, vilazodone
NRI	atomoxetine, desipramine
SNRI	amitriptyline, clomipramine, nortriptyline, desvenlafaxine, duloxetine, imipramine, milnacipran, l-milnacipran, sibutramine, venlafaxine*
SDRI	sertraline
Serotonin/norepinephrine potentiator	mirtazapine
Serotonin partial agonist	buspirone
Dopamine agonists	d-amphetamine, mixed amphetamines, Lisdexamfetamine, d-methylphenidate, R,S-methylphenidate, modafinil, bupropion

<b>GABAergic agonists and other classes (formerly “anxiolytic” or “sedating” agents)</b>	
GABAergic agonists	benzodiazepines (diazepam, lorazepam, alprazolam, clonazepam, among others), gabapentin, zolpidem, zaleplon, zopiclone, eszopiclone
Other	Antihistamines: diphenhydramine, hydroxyzine, doxepin**; Adrenergic antagonists: propranolol, clonidine; Melatonin agonists: ramelteon
<b>Dopamine blockers (formerly “antipsychotics”)</b>	
Dopamine antagonists*	chlorpromazine, haloperidol, perphenazine, thiothixene, thioridazine, trifluoperazine
Dopamine/serotonin antagonists	asenapine, cariprazine, clozapine, iloperidone, lurasidone, olanzapine, lurasidone, paliperidone, quetiapine, risperidone
Dopamine partial agonists	aripiprazole, ziprasidone
<b>Second messenger modifiers(formerly “mood stabilizers”)</b>	
Direct second messenger modifiers	Lithium, Valproate, Carbamazepine
Other (Second messenger modifiers)	Lamotrigine

### **Issues Associated with Psychotropic Use**

Antidepressants are commonly prescribed for non-psychiatric problems in primary care such as, for IBS, neuropathic pain and other chronic pain [14]. The psychiatrist side effects are perhaps poorly described in clinical trials since they are not a common feature of their occurrence in general practice [16]. A major cause of non-adherence to antidepressant therapy is the occurrence of adverse drug reactions; but they are difficult to differentiate from untreated symptoms of depression, and there are few established self-report scales [5]. Concerns have been raised about some of the newer drugs due to increased risk of suicidal ideation [16]. Alprazolam is better than placebo and broadly similar to imipramine for symptomatic treatment according to a comprehensive review; but is common to cause sedation and drowsiness, and its effects on cognition and psychomotor performance has been assessed in a few studies [8]

Previously the benzodiazepines were used to treat anxiety, insomnia and moderate depression, even though there was the risk of discontinuation syndrome; it was with the advent of selective serotonin reuptake inhibitors (SSRIs) that a shift occurred, where the uses of these drugs were expanded [15] in the treatment of obsessional-compulsive disorder, panic

disorder, generalized anxiety, eating disorders, somatoform disorder, premenstrual symptoms and subthreshold depression states, to name a few conditions. Haloperidol, a dopamine D<sub>2</sub> antagonist, is still prescribed for the treatment of schizophrenia, delirium, behavioral disturbance of dementia and less commonly for nausea and vomiting. It is recommended to monitor the ECG, particularly when it is administered intravenously as it has been known to cause QT prolongation, sudden death and torsades de pointes [10].

Association between smoking at follow-up, then prescription for antipsychotics, mood stabilizers, antidepressants and anxiolytics, have been investigated using a longitudinal cohort design, separating ex-smokers from current smokers who were either lightly or heavily dependent on nicotine, and adjusted for many potential confounders including cannabis use, conduct disorder, smoking parents, demographics, psychological distress, and adjusted baseline model for psychotropic medication use in the year preceding the assessment of smoking, in an effort to avoid reverse causality [4].

### **Off-Label Use: Scope and Context**

Off-labeled prescription uses are not uncommon in several subdisciplines including pediatric, neonatal, geriatric, psychiatric, and oncology specialties. Most off-label uses are based on insufficient data,

and about 30% of the usages had reasonable evidence on efficacy or safety from clinical trials [7,18,19]. Given its often sound clinical practice, off-label prescription, defined as a prescription that falls outside indications, doses, regimens, and/or forms approved for the drug, is considered acceptable if there's adequate medical or scientific evidence to justify its use [9,17]. The proportion of residents of a North American community taking psychotropic medications increased from 6.1% in 1988-1994 to 11.1% in 1999-2002. Other studies on prevalence rates of psychotropic medication have been carried out in Europe with nearly three quarters (almost 75%) of residents in aged care facilities taking one or more such medications. A study of a sample population in South America found a prevalence rate of approximately 9.9%, where the most common predictors of psychotropic medication taking were gender (women used more than men), age (older subjects used more than younger subjects), hypertension, and high health care use. In South Asian out-patient settings, more than 40% of adults admitted having used non-prescription psychotropic medication for sleep or relaxation [12].

## **MATERIALS & METHODS**

### Study design and ethical consideration

This prospective, cross-sectional, descriptive study was conducted over a period of six months, from January to June 2024, in the general medicine and surgery Departments of a tertiary care research centre in South India.

### Ethical approval and consent

The proposal was reviewed by the Institutional Ethical Review Board (IERB No. 243-2025). Privacy and confidentiality of patient was maintained throughout the trial.

### Study Population and Sample Size

Sampling Method and sample size Based on reports of 6-10% hospital antidepressant consumption prevalence for a year found in previous studies, the sample size was

calculated. The minimal sample size was determined by using the following formula with a standard normal variate (Z) at 95% confidence interval of 1.96, a predicted prevalence (P) of 10% and a standard error (d) of 5%:

$$\text{Sample Size} = Z\alpha^2 \times P(1-P) / d^2$$

Minimum sample size of eighty occurrences was achieved. 110 more subjects were included to provide reliability to our study. We adopted the method of convenience sampling.

**Inclusion criteria:** Adult subjects aged greater or equal to 18 years admitted on surgery and medicine wards prescribed psychotropic drugs on medical prescription for reasons non psychiatric (e.g. Pain, nausea, vomiting) and who had given written informed consent.

**Exclusion criteria:** non-consenting subjects, subjects below 18 years of age, psychiatric subjects diagnosed with psychiatric disorder upon discharge, uncooperative and hostile subjects.

**Data collection:** The already designed and validated data collection form was filled up from in-patient case files. Information such as social behavior, medical history, diagnosis, prescribed drugs, comorbidities, and demographic profile was recorded. DRPs (drug related disorders) were identified using Hepler-Strand categorization. Suspected ADRs (adverse drug reaction) were recorded using a standard ADR reporting form.

### Interpretation of statistics

Data was entered in Microsoft Excel and was analyzed using IBM SPSS Statistics Version 28. Continuous data was presented as mean standard deviation (SD) while categorical data were presented as frequencies and percentage. Variable associations were assessed using Chi-square test or if necessary, Fisher's exact test and comparisons of quantitative data were made using independent t- test. Statistical significance was set at  $P < 0.05$ .

## **RESULT**

A 100% participation rate from 110 adult inpatients receiving psychotropic drugs in non-psychiatric wards was obtained. There were 37 females (33.6%) and 73 males (66.4%) as shown in Fig 1

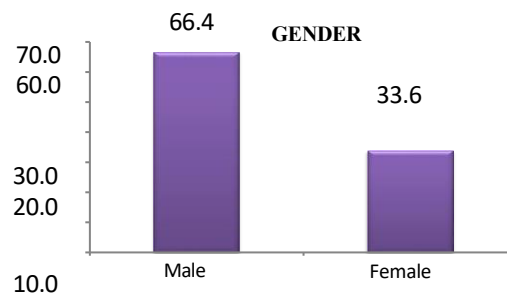
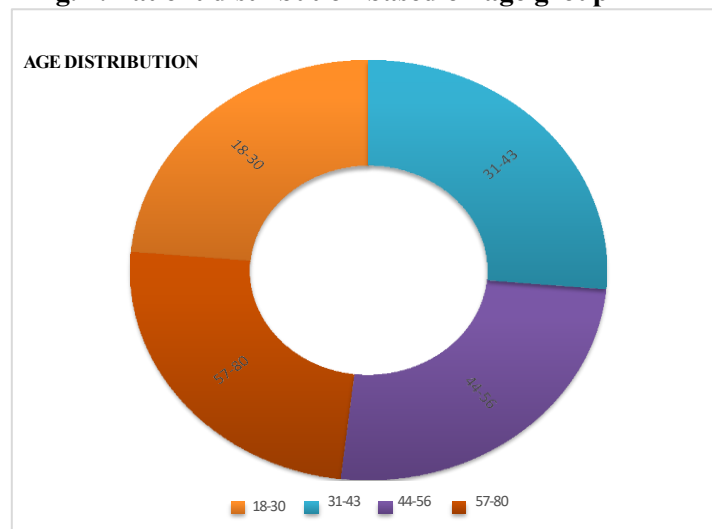


Fig. 1. Patient distribution based on gender

Remarkable data is the grouping of age from all the cases collected as:18-30 group: 26 (23.6%),31-43 group: 29 (26.4%),44-56 group: 28 (25.5%),57-80 group: 27 (24.5%). Most are in the age group 31-43 and 44-56. Fig 2

Fig. 2. Patient distribution based on age group



Of the psychotropics prescribed the most were Alprazolam (44.5%), and the least were Haloperidol (0.6%) and Etizolam (0.6%). Tab 4

PSYCHOTROPIC DRUGS		NO.OF CASES	PERCENTAGE (%)
Benzodiazepines	ALPRAZOLAM	68	44.5
	LORAZEPAM	6	3.9
Anticonvulsants	CLONAZEPAM	5	3.3
	PREGABALIN	34	22.3
	GABAPENTIN	2	1.3
Antidepressants (TCA)	NORTRIPTYLINE	30	19.6
	AMITRIPTYLINE	4	2.6
	SODIUM VALPROATE	2	1.3
Antipsychotics	HALOPERIDOL	1	0.6
Sedatives & Hypnotics	ETIZOLAM	1	0.6
TOTAL		153	100

Tabel 4: Patient distribution based on patient prescribed with different type of Psychotropic drugs

As for psychotropic drugs prescribed as mono and combination therapy it was the most frequent in (62.3%) combination (32.7%). Fig 5

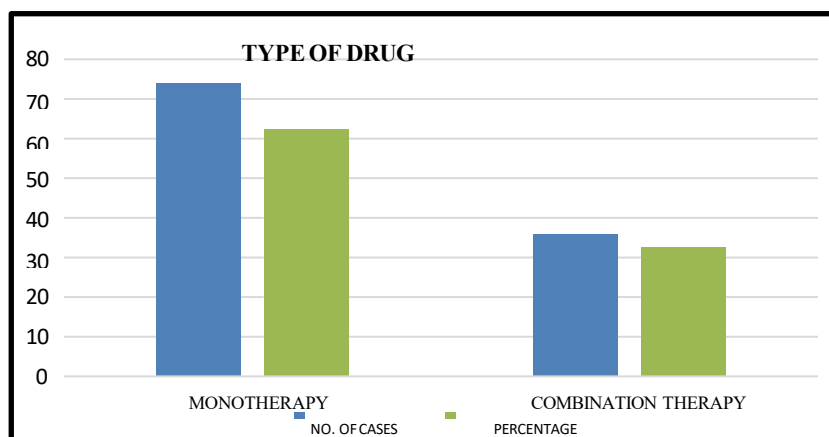


Fig 5: Patient distribution based on monotherapy and combination therapy

As psychotropic drugs were concerned, the greatest number of drug-drug interactions were with Alprazolam (45 interactions) and the smallest number of drug-drug interactions with Lorazepam and Sodium Valproate (1 interaction for each drug). Tab 6

PSYCHOTROPIC DRUGS		NO. OF CASES	POSSIBLE DRUG INTERACTION	
			PRESENT	ABSENT
Benzodiazepines	ALPRAZOLAM	68	45	23
	LORAZEPAM	6	4	2
Anticonvulsants	CLONAZEPAM	5	5	0
	PREGABALIN	34	33	1
	GABAPENTIN	2	2	0
Antidepressants (TCA)	NORTRIPTYLINE	30	29	1
	AMITRIPTYLINE	4	4	0
	SODIUM VALPROATE	2	1	1
Antipsychotics	HALOPERIDOL	1	1	0
Sedatives & Hypnotics	ETIZOLAM	1	1	0
TOTAL		153	125	28

Table 6: patient distribution based on Psychotropic drugs with Possible Drug-Drug Interactions Among the drugs prescribed along with psychotropics, Analgesics were the most frequently involved in interactions, with tramadol being the leading drug

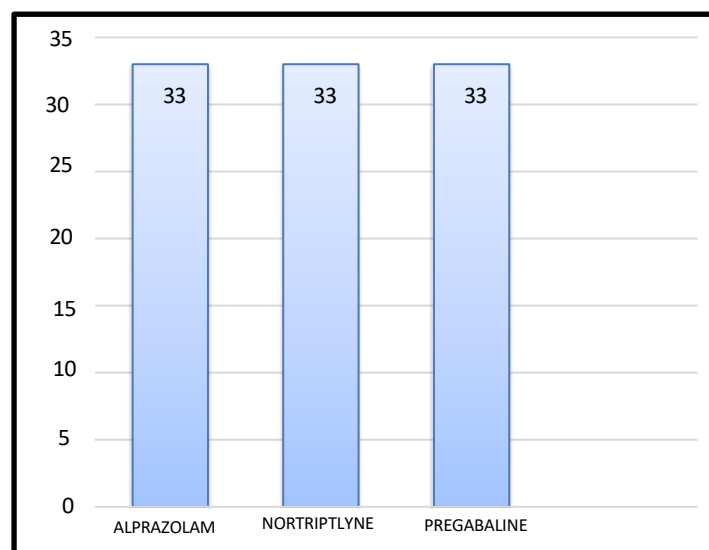
From among psychotropic drugs highest number of major severity drug-drug interaction were recorded for Alprazolam (33 cases) and least for Sodium Valproate, Haloperidol and Etizolam (1 each) Tab.7

PSYCHOTROPIC DRUGS		NO. OF CASES	SEVERITY OF POSSIBLE DRUG INTERACTION		
			MILD	MODERATE	MAJOR
BENZODIAZEPINES	ALPRAZOLAM	45	1	11	33
	LORAZEPAM	5	0	1	4
	CLONAZEPAM	5	0	2	3
	PREGABALIN	33	0	8	25

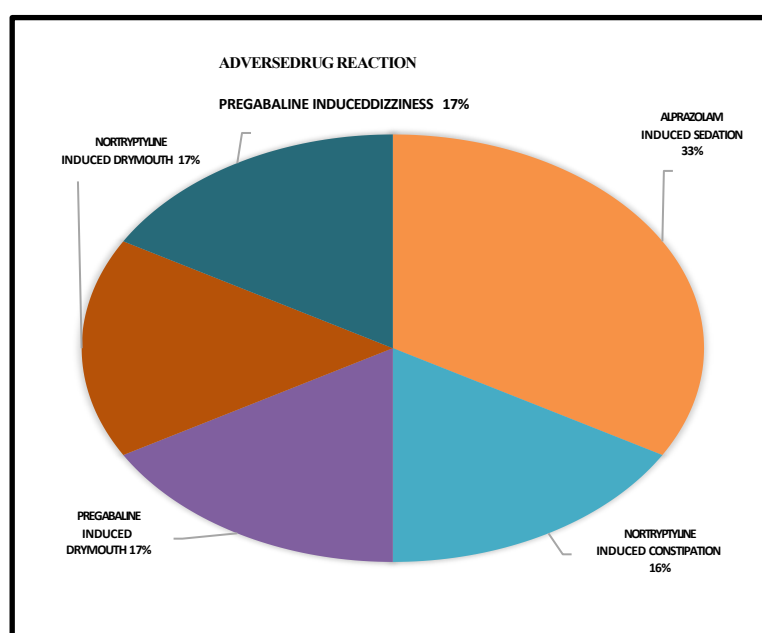
ANTICONVULSANTS	GABAPENTIN	2	0	0	2
ANTIDEPRESSANTS	NORTRIPTYLINE	29	0	6	23
	AMITRIPTYLINE	4	0	1	3
	SODIUM VALPROATE	1	0	0	1
ANTIPSYCHOTICS	HALOPERIDOL	1	0	0	1
SEDATIVES & HYPNOTICS	ETIZOLAM	1	0	0	1
TOTAL		126	1	29	96
PERCENTAGE (%)		100.0	0.8	23.1	76.1

**Table 7: Patient Distribution of drug drug interaction based on severity**

A total of 6 adverse drug reactions (ADRs) was found during the study. The main contributing drugs were Alprazolam (n=2, 33%), Pregabalin (n=2, 33%) and Nortriptyline (n=2, 33%) respectively. Fig.8



**Fig.8 Patient distribution based on drugs which causes adverse drug reaction**



**Fig 8.1 Psychotropic drug induced side effects**

Out of the 6 cases, 3 (50.0%) had probable diagnosis and 3 (50.0%) had possible diagnosis. There was neither a definite nor a doubtful case. FIG 9

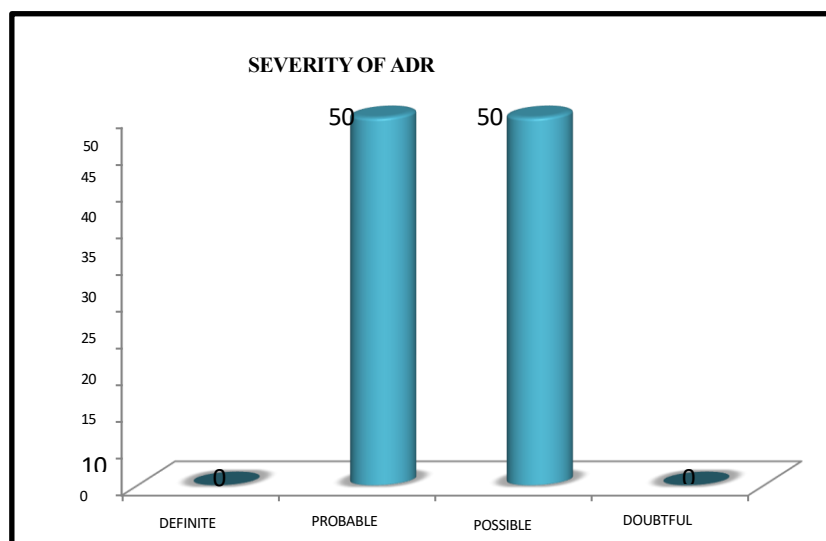


Fig 9. Patient distribution of based on severity of ADR

## DISCUSSION

The current study on 110 patients to whom psychotropics was prescribed on non-psychiatric grounds revealed that, out of the 110 patients 26 (23.6%) were in 18-30 years age group, 29 (26.4%) were in 31-43 years age group, 28 (25.5%) were in 44-56 years age group and 27 (24.5%) were in 57-80 years age group. Hence more of the patients fall in 31-43- and 44-56-years age groups, which is similar to study conducted by Sebastian et al.1

Among the 110 study subjects who received psychotropic drug, males were found to be 73(66.4%) and females were 37(33.6%), hence the prescription pattern shows that, psychotropic drug was more commonly used in male patients. This finding was similar to study reported in Managed Care Journal of America.3

In our study, among the psychotropic drug which was prescribed benzodiazepine was most commonly prescribed class. Alprazolam 44.5% was prescribed than Lorazepam 3.9% and Clonazepam 3.3% whereas out of anti-convulsant pregabalin 22.3% was prescribed than gabapentin 1.3%. Out of anti-depressants nortriptyline

19.6% was prescribed than amitriptyline 2.6% of subjects. Such drugs are usually prescribed to the non-psychiatric patients for sleep induction, anti-anxiety, G.I. Disorder, chronic pain etc. Reported by Hua Chen et al.5

Study also assess the Drug Related Problem (DRP) and Drug Drug Interaction (DDI) found that the DRPs are found higher in the patients in whom psychotropics plus analgesic were given compared to in patients where only psychotropics were given. 76.1% of drug-drug interactions found were of severity type severe, 23.1% were of moderate type and 0.8% was of mild type. Highest drug interactions found for alprazolam, 2nd was for pregabalin, 3rd for nortriptyline. Totally 6 A D R were observed mostly for Alprazolam, pregabalin and nortriptyline. Hence prescribing rational, observing DDI regularly, pharmacist intervention is important for non-psychiatric use of psychotropics.

## CONCLUSION

A prospective study was designed to investigate the utilization of psychotropic drugs and subsequent drug-related problems

in surgical and medical inpatients of a tertiary care teaching hospital. This involved 110 patients. Out of 110 patients, 66.4% were men and were mainly in the age group 31-56 years. Most prescribed psychotropic drug was alprazolam (44.5%) followed by pregabalin (22.3%) and nortriptyline (19.6%). Drugs were mostly prescribed in monotherapy (62.3%). Analgesics were the most concomitantly prescribed drugs. A lot of drug-drug interactions were observed and the most interaction was between tramadol and all the drugs and alprazolam had most interactions. There were 6 adverse drug reactions. We need for rational prescribing, regular follow-up and role of clinical pharmacist.

#### **Declaration by Authors**

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**Conflict of Interest:** No conflicts of interest declared.

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