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Frequency and Predictors of Potential Drug Interactions among Psychiatry Outpatients on Treatment with Antidepressant Medications

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Antidepressant medications are prescribed to treat depression and related psychiatric illnesses. In patients with depression, many categories of drugs are prescribed to treat clinical conditions and comorbidities. Hence, it is essential to screen such patients for potential drug interactions. The study aimed to assess the frequency of potential drug interactions (pDDIs) associated with antidepressant medications administered to the outpatients of the psychiatry department. This cross-sectional investigation was conducted in a psychiatry outpatient setting. Patients satisfying inclusion criteria were screened for pDDIs by reviewing the patients' electronic case records. All the identified pDDIs were further evaluated using Micromedex database 2.0. A total of 131 eligible patients' case records were reviewed. The frequency of pDDIs between antidepressants and other psychotropic medications, non-psychotropic medications, tobacco, and ethanol was 48.1%, 9.2%, 7.6%, and 3.8%, respectively. Use of more than three medications [RR: 1.5; CI: 1.1-2.1], presence of total [RR: 7.9; CI: 1.1-52.5] as well as psychiatric polypharmacy [RR: 4.8; CI: 1.3-17.9] were identified as predisposing factors of pDDIs. The results of the multiple regression indicated that the model was a significant predictor of pDDIs ($F[3, 127]= 6.368$, $p<0.01$, $R^2 = 0.13$). In comparison, psychiatric polypharmacy was the only variable contributing significantly to the model ($B = -0.423$, $p<.05$). Nearly fifty percent of patients taking antidepressant medications were found to have the potential for developing drug interactions. Review of treatment charts for psychotropic, non-psychotropic, and non-prescription medications, along with different medical conditions that patients suffer from and the social habits of patients, is essential to identify and resolve potential drug interactions in at-risk patients.

Keywords: Antidepressive Agents; Drug interactions; Major depressive disorder, Psychotropic drugs, Hospital Psychiatric Department.

Antidepressants are commonly used drugs in the management of depression and various anxiety disorders [1]. Placebo-controlled trial reveals that different categories of antidepressants demonstrate equal efficacy when administered in comparable doses [2]. The treatment duration of antidepressants may vary from months to years, during which a patient may be prescribed different categories of drugs to treat other clinical conditions or comorbidities. Hence, it is clinically significant

to evaluate the occurrence of potential drug interactions in such patients. Many clinical studies provide instances of potential drug interactions between antidepressants and co-prescribed medications. An interaction between citalopram and diclofenac was reported in a prospective, observational study [3]. The incidence rate ratio (IRR) for selective serotonin reuptake inhibitors (SSRIs) was 1.2, which increased to 12.4 when SSRIs and non-steroidal anti-inflammatory drugs (NSAIDs) were co-administered. On the other hand, when Tricyclic antidepressants (TCAs) and NSAIDs were co-administered, the IRR increased by 2.5[4]. In another study, co-medication of SSRIs with anticoagulation during acenocoumarol maintenance treatment was found to increase the anticoagulation risk when combined with fluvoxamine (Hazard Ratio 2.63) and venlafaxine (Hazard Ratio 2.19)[5].

DDIs are a common cause of concern in psychiatry since most psychiatric illnesses need multiple medications to manage them[6]. The presence of additional non-psychiatric comorbidities, the pharmacokinetics nature of the prescription medicines, and the length of treatment render this group even more sensitive to DDIs [6,7].

Apart from medications, alcohol is known to interact with many drugs as both are metabolized by the same liver enzymes resulting in pharmacokinetic interactions [8]. A study documented an increase in the risk of falling in community-dwelling older adults, possibly due to alcohol and tricyclic and tetracyclic antidepressants combination [9]. The research concluded that the combination of alcohol with tricyclic and tetracyclic antidepressants increased the risk of falling in community-dwelling older persons [10]. Smoking can also interact with antidepressant treatment. Systematic review research found evidence of a drop in the concentration of blood levels of fluvoxamine, duloxetine, mirtazapine, and trazodone among smokers compared to nonsmokers [11]. Some antidepressants' blood levels are known to be lowered in smokers due to the induction of metabolism mediated by CYP1A2 and CYP2B6 enzymes [12].

A review of our literature on antidepressant-related DDIs suggests that pDDIs are frequent in outpatient and inpatient settings. However, the majority of these DDIs were mild to moderate in severity. However, there is a scarcity of data in our research setting on the prevalence and character of antidepressant-related DDIs. Furthermore, not many studies evaluated the type and nature of potential drug-drug interactions (pDDIs) related to antidepressants in psychiatry outpatients in the UAE. In our study, we attempt to identify and document any significant drug interactions associated with antidepressant medications administered to the outpatients of the psychiatry department. The study also attempts to identify variables predicting potential drug interactions. Our study data is anticipated to strengthen the interventional strategies and promote rational therapy with antidepressants.

MATERIALS AND METHODS

This was cross-sectional research undertaken at the Psychiatry outpatient department (OPD) of Ibrahim Bin Hamad Obaidallah Hospital (IBHOH), Ras Al-Khaimah, UAE. Patients of all age groups and both the gender, who fulfilled the mental and behavioral diagnostic criteria of the International classification of disease (ICD-10) and were prescribed with at least one antidepressant medication irrespective of the clinical indication and registered in the psychiatry OPD of IBHOH, were included in the study.

Ethics approval

The study was approved by the institutional Research and Ethics committee and the Ras Al Khaimah Research and Ethics committee (RAK REC) [Reg No. 44/2016-PG-P]. All methods in studies involving human subjects were carried out in compliance with the institutional research committee's ethical standards, the 1964 Helsinki statement, and its subsequent revisions or similar ethical standards.

Assessment of Drug Interactions

The patient's prescriptions were reviewed and analyzed with referral to Micromedex database 2.0 for the presence of potential drug interactions. This database has been widely adopted to identify & analyze potential drug interactions. The drug interactions identified were assessed based on the severity and documentation criteria of the Micromedex database 2.0.

According to Micromedex Database 2.0, drug interaction severity grade "contraindicated"

refers to drugs that are contraindicated for concurrent usage. The interaction is classified as "major" if it is life-threatening and/or requires medical intervention to avoid severe ADRs. It is categorized as " moderate " if an interaction worsens a patient's clinical state or necessitates a treatment change; it is categorized as "moderate." Further, If the interaction has minimal clinical consequences and does not need significant treatment changes, it is categorized as "mild" [13].

The documentation grade "excellent" refers to controlled studies that have shown the presence of interaction. While the term "good" refers to evidence indicating the interaction occurs, well-controlled research is inadequate. While documentation grade "fair" refers to lacking relevant evidence, pharmacologic factors lead physicians to believe the interaction occurs[13].

Data analysis

The obtained data were incorporated into a Microsoft Excel spreadsheet and analyzed using SPSS version 24.0, statistical software for the social sciences. The continuous data were presented as mean SD, while the categorical data were presented as percentages. The Chi-square test was used to examine the relationship between the dependent and independent categorical variables. By calculating relative risk (RR), the predisposing factors for potential drug-drug reactions were identified. In the presence of all of the variables studied, RR greater than one suggests an increased risk of potential drug-drug reactions in the exposed group. The variables tested are gender, nationality, age, general medical conditions, number of drugs prescribed, presence of total polypharmacy, and psychiatric polypharmacy. Polypharmacy categorization stated by Veehoff LJG et al[14]. was used to categorize polypharmacy. Psychiatry polypharmacy refers to the continued use of two or more psychotropic drugs. At the same time, total polypharmacy refers to the continued combined use of two or more psychotropic (antidepressants) and non-psychotropic drugs.

The predictors of pDDIs were detected using multiple regression analysis. A probability value of less than 0.05 was deemed statistically significant, and any value less than 0.01 was deemed highly significant.

RESULTS

Patient demography

The research included 131 patients who met the inclusion criteria. The majority of the study population were females (62%). The mean age of the study population was 44.8 ± 16.6 years). A sizable proportion of the study population were UAE nationals (67%) compared to expatriates (33%). Based on the patients' medical history, 51.1% of patients had other comorbidities/ medical illnesses besides psychiatric conditions. Psychotropic drugs were prescribed in 42% of the patients.

Positive family history of psychiatric illnesses was observed in 32.1% of patients, and 55% of the patients were not known/aware if they had a family history of psychiatric illnesses. Around 8.4% of study patients had a history of suicidal attempts recently or in previous years. Only a tiny proportion of patients had a habit of alcohol consumption (5%), drug abuse (8%), and tobacco smoking (13%).

Three hundred forty-three drugs were prescribed to the study patients (average drugs prescribed per patient 2.62 ± 1.01). The majority of study patients (69.4%) received monotherapy, 29% received two antidepressants, and 1.6% received three antidepressants. The majority of the study patients (36.6%) received SSRIs, followed by serotonin-norepinephrine reuptake inhibitors [SNRIs] (13.7%), Serotonin, and á2-adrenergic antagonist (8.4%), and tricyclic antidepressants [TCAs] (6.9%) as monotherapy.

Frequency of pDDIs between antidepressants and other psychotropic medications

A total of 88 potential drug-drug interactions (pDDIs) involving forty-one drug pairs were identified in 63 patients taking antidepressant medications. The frequency of pDDIs among the psychiatric outpatients receiving antidepressant medications was 48.1%. The mean age of these patients was 44.9 ± 13.7 years. The majority of these patients received three (41.3%), followed by two (28.6%), four (25.4), five (3.1%), and six (1.5%) medications. The psychiatric diagnosis associated with the identified pDDIs in these patients is shown in Table 1. The majority of the detected potential drug interactions were

significant in severity (83%), followed by moderate severity (16%), and 1% was contraindicated. Escitalopram with mirtazapine (7%) was the most commonly documented pDDI. The most frequently interacting drug pairs, their level of severity, and pharmacological consequences are listed in Table 2.

Frequency of pDDIs between antidepressants and non-psychotropic medications

Twenty-one pDDIs involving sixteen drug pairs were identified among twelve patients who received antidepressant medications along with non-psychotropic medications. The frequency of

Table 1. Psychiatric Disorders Associated with The Identified pDDIs in Patients Taking Antidepressants and Other Psychotropic Medications

Diagnosis	ICD-10-CM-Codes	No. of the patients with pDDI, (%)
Major Depressive Disorder	F32.9	14 (22.2)
Generalized Anxiety Disorder	F41.1	9 (14.3)
Obsessive-Compulsive Disorder	F42.9	7 (11)
Bipolar Disorder, Depressed Episode	F31.30	7 (11)
Major Depressive Disorder with Psychotic Features	F33.3	6 (9.5)
Adjustment Disorder with Mixed Anxiety and Depressed Mood	F43.23	2 (3.2)
Anxious Depression	F41.8	2 (3.2)
Panic Disorder	F41.0	2 (3.2)
Schizophrenia	F20.0	2 (3.2)
Substance Abuse	F19.10	2 (3.2)
Post-Traumatic Stress Disorder	F43.10	1 (1.6)
Social Phobia	F40.10	1 (1.6)
Premenstrual Tension Syndromes	N94.3	1 (1.6)
Adjustment Disorder with Depressed Mood	F43.21	1 (1.6)
Borderline Personality Disorder	F60.3	1 (1.6)
Adjustment Disorder with Anxiety	F43.22	1 (1.6)
Schizoaffective Disorder	F25.9	1 (1.6)
Psychosis, Paranoid	F22.0	1 (16)
Somatization Disorder	F45.0	1 (1.6)
Intellectual Disability	F79.0	1 (1.6)
Total Number of Patients		63

Table 2. Most Frequently Interacting Antidepressants and Other Psychotropic Drug Pairs

Type of pDDIs	n (%) of pDDIs	Severity	Documentation	Pharmacological Consequences: May result in Increased Risk of
Escitalopram + Mirtazapine	6 (7)	Major	Fair	Serotonin syndrome
Fluoxetine + Propranolol	6 (7)	Major	Good	Propranolol toxicity
Fluoxetine + Olanzapine	5 (5.9)	Major	Fair	QT-interval prolongation
Mirtazapine +Bromazepam	4 (4.6)	Major	Fair	CNS depression
Venlafaxine +Quetiapine	4 (4.6)	Major	Fair	QT-interval prolongation
Mirtazapine +Duloxetine	4 (4.6)	Major	Fair	Serotonin syndrome
Mirtazapine + Carbamazepine	3 (3.5)	Major	Fair	Serotonin syndrome
Mirtazapine +Venlafaxine	3 (3.5)	Major	Fair	Serotonin syndrome
Clomipramine + Olanzapine	3 (3.5)	Major	Good	Increased risk of seizures
Escitalopram +Olanzapine	3 (3.5)	Major	Fair	QT-interval prolongation
Fluoxetine + Carbamazepine	2 (2.2)	Major	Good	Carbamazepine toxicity

Note: The identified pDDIs were graded based on the severity and documentation as specified by Micromedex database 2.0.

pDDIs in these patients was 9.2%. The mean age of these patients was 59.1 ± 12.2 years. Table 3 represents the psychiatric diagnosis associated with the identified pDDIs in these patients. Among twenty-one identified pDDIs, 71.4% were of major severity, and the remaining were moderate (28.6%) in severity. Escitalopram with levothyroxine (14%) and escitalopram with aspirin (14%) were the most commonly documented pDDIs. Table 4 provides the details of the most frequently interacting drug-pairs, their level of severity, and pharmacological consequences.

Table 3. Psychiatric Disorders Associated with The Identified pDDIs in Patients Taking Antidepressants and non-psychotropic Medications

Diagnosis	ICD-10-CM-Codes	No. of the patients with pDDI (%)
Major Depressive Disorder	F32.9	5 (42)
Generalized Anxiety Disorder	F41.1	2 (17)
Obsessive-Compulsive Disorder	F42.9	2 (17)
Anxious Depression	F41.8	1 (8)
Premenstrual Tension Syndromes	N94.3	1 (8)
Bipolar Disorder, Depressed Episode	F31.30	1 (8)

Table 4. Most Frequently Interacting Antidepressants and non-psychotropic drug pairs

Type of pDDIs	n (%)	Severity	Documentation	Pharmacological Consequences: May result in Increased Risk of
Escitalopram +Aspirin	3 (14)	Major	Excellent	Risk of bleeding
Escitalopram + Levothyroxine	3 (14)	Moderate	Fair	Levothyroxine requirements
Mirtazapine +Levothyroxine	2 (10)	Major	Fair	Therapeutic and toxic effects of both drugs
Fluoxetine +Aspirin	1 (5)	Major	Excellent	Risk of bleeding
Fluoxetine +Diclofenac	1 (5)	Major	Excellent	Risk of bleeding
Clomipramine + Diclofenac	1 (5)	Major	Excellent	Risk of bleeding
Duloxetine +Diclofenac	1 (5)	Major	Excellent	Risk of bleeding
Mirtazapine +Warfarin	1 (5)	Major	Excellent	Raised International Normalised Ratio
Venlafaxine +Clopidogrel	1 (5)	Major	Good	Risk of bleeding
Venlafaxine +Aspirin	1 (5)	Major	Good	Risk of bleeding

Note: The identified pDDIs were graded based on the severity and documentation as specified by Micromedex database 2.0

Table 5. Types of pDTIs and pDEIs associated with antidepressants

Type of pDTIs & pDEIs	n (%)	Severity	Documentation	Pharmacological Consequences: May result in
Mirtazapine + Tobacco	5 (38.5)	Major	Fair	Decreased exposure of CYP1A2 substrates
Agomelatine +Tobacco	4 (30.8)	Major	Fair	Decreased exposure of CYP1A2 substrates
Duloxetine +Tobacco	3 (23)	Major	Fair	Decreased exposure of CYP1A2 substrates
Fluvoxamine +Tobacco	1 (7.7)	Major	Fair	Decreased exposure of CYP1A2 substrates
Mirtazapine + Ethanol	3(60)	Moderate	Good	Psychomotor impairment
Escitalopram + Ethanol	1(20)	Moderate	Fair	Potentiation of cognitive and motor effects of alcohol
Venlafaxine + Ethanol	1(20)	Minor	Fair	Increased Risk of CNS effects

Frequency of potential drug-tobacco interactions (pDTIs)

In our study, seventeen patients smoked tobacco cigarettes, among which pDTIs were identified in ten patients. The average age of these individuals was 31.08 ± 11.08 years. The psychiatric diagnosis among these patients was generalized anxiety disorder (30%), major depressive disorder (20%), substance abuse (20%), borderline personality disorder (10%), adjustment disorder with mixed anxiety and depressed mood (10%) and anxious depression (10%). In addition, we observed distinct types of pDTIs, the severities of which are described in Table 5.

Frequency of potential drug-ethanol interactions (pDEIs)

Among the six patients who consumed alcohol in our study, the pDEIs were identified in five patients as they continued to consume alcohol during the treatment with antidepressants. The mean age of these patients was 44.6 ± 9.54 years. Major depressive disorder (40%), borderline personality disorder (20%), generalized anxiety disorder (20%), and substance abuse (20%) were

Table 6. Association between demographic, disease, and treatment-related variables and presence of pDDIs

Variable		Total number of patients (n=131)		Chi-square	
		Interaction present (n=67)	Interaction absent (n=64)	X^2	p-value
Gender	Male	27 (40.3)	23 (35.9)	0.264	0.719
	Female	40 (59.7)	41 (64.1)		
Nationality	Emirati	43 (64.2)	45 (70.3)	0.558	0.464
	Expatriate	24 (35.8)	19 (29.7)		
Age	< 65 years	61 (91)	55 (85.9)	0.842	0.418
	≥ 65 years	06 (09)	09 (14.1)		
Presence of General Medical conditions	Yes	35 (52.2)	32 (47.8)	2.131	0.564
	No	32 (51.6)	30 (48.4)		
	Unknown	00 (0.0)	02 (100)		
Number of Drugs Prescribed	≤3 drugs	29 (40.8)	42 (59.2)	6.582	0.014*
	> 3 drugs	38 (63.3)	22 (36.7)		
Presence of Total Polypharmacy	Yes	66 (98.5)	51 (79.7)	12.146	0.000**
	No	01 (1.5)	13 (20.3)		
Presence of Psychiatric Polypharmacy	Yes	65 (97)	49 (76.6)	16.983	0.000**
	No	02 (1.8)	15 (23.4)		

*p<0.05 is statistically significant; **p<0.01 is statistically highly significant

Table 7. Predictors of Potential Drug-Drug Interaction

Variable	Total number of patients (n=131)		Relative Risk	
	Interaction present (n=67)	Interaction absent (n=64)	RR (95% CI)	p-value
Number of Drugs Prescribed				
≤ 3 drugs	29 (40.8)	42 (59.2)	1.5 [1.1-2.1]	0.01*
> 3 drugs	38 (63.3)	22 (36.7)		
Presence of Total Polypharmacy				
No	01 (1.5)	13 (20.3)	7.9 [1.1-52.5]	0.02*
Yes	66 (98.5)	51 (79.7)		
Presence of Psychiatric Polypharmacy				
No	02 (1.8)	15 (23.4)	4.8 [1.3-17.9]	0.01*
Yes	65 (97)	49 (76.6)		

*p<0.05 is statistically significant.

the psychiatric diagnoses in these patients. Three types of pDEIs were detected; their severity is compiled in Table 5.

Predictors of pDDIs

Among the various parameters analyzed in the study, a significant association was observed between potential drug interactions and the number of drugs prescribed ($X^2 = 6.582$; $p=0.014$), while an even more significant association was observed for the presence of total polypharmacy ($X^2 = 12.146$; $p<0.01$) and presence of psychiatric polypharmacy ($X^2 = 16.983$; $p<0.01$). The analysis is highlighted in Table 6. Further, the estimation of relative risk revealed that patients using more than three medications are at one and half times more risk of pDDIs; similarly, patients with total polypharmacy and psychiatric polypharmacy are almost eight times and five times more risk of pDDIs respectively ($p<0.01$). The details are presented in Table 7.

Multiple regression was carried out to investigate whether the presence of psychiatric polypharmacy, total polypharmacy, and a total number of drugs could significantly predict pDDIs. The results of the regression indicated that the model explained 13.1% of the variance and that the model was a significant predictor of pDDIs ($F[3, 127]= 6.368$, $p< 0.01$, $R^2 = 0.13$). Only the presence of psychiatric polypharmacy contributed significantly to the model ($B = -0.423$, $p<0.05$). While presence of total polypharmacy ($B = 0.122$, $p=0.52$) and total number of drugs did not ($B= -0.147$, $p=0.08$).

DISCUSSION

Eighty-eight potential interactions were observed in 48.1% of study patients. As a result, the total frequency of pDDIs in the antidepressant-treated study population was 67.2%, of which 83% of patients had pDDIs of major severity. Our study findings were in accordance with a previous study which reported a pDDI prevalence of 57.5%. However, most patients (42.5%) in that study experienced pDDIs of moderate severity [3]. The most common pDDIs documented were with escitalopram and mirtazapine and fluoxetine with propranolol combinations. The commonly prescribed interacting pair were citalopram and diclofenac (11.6%), followed by imipramine and labetalol (10.5%) and fluoxetine and propranolol (9.39%)[3]. Imipramine and methylphenidate were the most commonly interacting pair in a study to determine and evaluate the prevalence and significance of pDDIs in children and adolescents aged d" 18 years receiving antidepressants [13].

Most of the pDDIs documented in our study were significant. However, the prescribed medications' benefits seemed to be greater than the possible risks caused by the pDDIs. Most of the pDDIs were associated with psychotropic medications rather than other medications, but they did not cause any severe clinical outcome. All the documented interactions were in accordance with the recent clinical trials except for one pDDI, which was contraindicated. The contraindications documented in our study are lower than reported earlier [3].

Interactions between Antidepressants and non-psychiatric prescription

Twenty-one pDDIs were identified in 9.1% of the study patients who were prescribed psychiatric and non-psychiatric medications, with an overall frequency of pDDIs in 16% of psychiatric outpatients receiving antidepressants. The most commonly documented pDDIs were escitalopram, levothyroxine (14.3%), escitalopram, and aspirin (14.3%) combinations. The interaction between escitalopram and levothyroxine is moderate but may increase the requirement of levothyroxine. The interaction between escitalopram and aspirin is major and can cause an increased risk of bleeding. The pDDI was commonly observed in patients with major depressive disorder.

Increased risk of bleeding

In our study, interactions were observed with concomitant use of antidepressants and anticoagulants or antiplatelets, resulting in an increased risk of bleeding. Since depressive syndrome is common after stroke, due consideration should be given for potential interactions between antidepressants and anticoagulants or antiplatelets medications. Hence, before selecting an antidepressant in patients on other medications, it is beneficial to refer to an updated drug information database [14].

Concomitant use of some antidepressants and NSAIDs may also increase the risk of bleeding. The bleeding risk is attributed to an SSRI-induced increase in gastric secretion or depletion in platelet

serotonin. The use of a proton pump inhibitor can reduce the risk of gastrointestinal bleeding [15]. Concurrent use of SSRIs and NSAIDs increases the risk of gastrointestinal side effects tenfold over SSRIs alone and fourfold over NSAIDs alone. However, concomitant administration of TCAs with NSAIDs does not have this effect [4].

Drug- tobacco interactions

Among the study population, 12.9% were regular tobacco cigarette smokers. A previous study reported a 20.3% prevalence of smoking among schizophrenic patients in psychiatry outpatient clinics [16]. Drug-tobacco interactions (DTIs) between antidepressant prescription and tobacco smoking were observed in 7.6% of patients. In our study, generalized anxiety disorder was the most common psychiatric disorder associated with DTIs. A higher likelihood of agoraphobia, generalized anger, and panic disorders are caused by increased cigarette smoking in adolescents [17]. Decrease in the plasma concentration of mirtazapine and agomelatine most commonly observed in interaction with tobacco smoking. Smokers using imipramine might require higher doses, while no dose adjustments are required for other tricyclic antidepressants such as amitriptyline or clomipramine [18]. Smokers may require doses higher than the recommended dose in clinical trial data. Dose adjustments may be required in patients who decide to quit or reduce smoking [19]. In patients who decide to quit, US Food and Drug Administration approved bupropion is an excellent choice for patients who want to stop smoking as it can reduce the desire for nicotine and doubles rates of smoking cessation [14].

Drug-ethanol interactions

Six individuals in the research group had a pre-existing habit of taking alcohol, and of them, five (3.8%) were exposed to the medication-alcohol interaction. Major depressive disorder was the most common psychiatric condition associated with drug-ethanol interaction (DEIs). Alcohol consumption is associated with slightly higher rates of major depression [20]. In our study, three types of DEIs were detected. The most common was ethanol interactions with mirtazapine resulting in psychomotor impairment. They were followed by ethanol and escitalopram to potentiate ethanol's cognitive and motor effects. Both interactions were moderate in severity. Another interaction was ethanol with venlafaxine, which may result in an increased risk of CNS effects. This interaction was of minor severity. Acute or chronic ethanol drinking combined with psychiatric medicines may result in several clinically important toxicological interactions.

Ethanol use, both acute and chronic, may alter the pharmacodynamics and pharmacokinetics of such medicines. Pharmacodynamics interaction, such as altering drug action, is more significant than kinetic interaction like enhancing drug metabolism [8]. Ethanol pharmacodynamic interactions involve enhancing the drug's effects, particularly in the CNS (e.g., sedation). Pharmacokinetics interactions result in faster metabolism of the drugs. Chronic ingestion of ethanol may increase microsomal protein and P450, reducing the plasma half-life of many psychiatric medications [8]. It can interfere with the first-pass metabolism of amitriptyline, leading to increased amitriptyline levels in the blood. On the other hand, no severe interactions appear to occur between SSRIs and Ethanol [21].

Predictors of pDDIs

We observed that the study population using more than three medications, total polypharmacy, and psychiatric polypharmacy, had an increased risk of pDDIs. In comparison, research conducted in the same study setting reported the number of drugs and polypharmacy as the predictors of pDDIs among psychiatric inpatients receiving antipsychotic medications [22]. Polypharmacy is a crucial contributing factor associated with increased risk of pDDIs [23]. Research revealed that forecasting polypharmacy and DDI at the time of admission in psychiatric hospitals is critical for effective management, such as pharmaceutical supervision [24].

Limitations of the study

As the prescription analysis was carried out only three days of the week, the study sample was small and may not represent all the psychiatric cases treated in the same setting. Furthermore, in some cases, the patient's electronic medical records did not include information on social and medical histories and the counter drugs prescribed. Additionally, as this study was conducted in a government hospital, the choice of antidepressants was limited.

CONCLUSION

Almost fifty percent of the patients receiving antidepressants were at risk of potential drug interactions. Escitalopram and mirtazapine, followed by mirtazapine and duloxetine, were the most frequent interacting drug pairs. More than three medications, total polypharmacy, and psychiatric polypharmacy increase the risk of pDDIs in patients prescribed with antidepressants. This study contributes to updating the knowledge of the severity of different pDDIs, which benefits clinicians in maintaining patient safety and aids in selecting appropriate antidepressants for relevant groups of patients.

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Conflict of Interest

The authors declare no conflict of interest

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