

Original Research

Evaluation of prescriptions and potential drug-drug interactions of psychotropic drugs in the outpatient department of psychiatry, in a tertiary care teaching hospital of South Odisha: A cross-sectional study

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Abstract:

Background: - Over the past three decades, the number of patients diagnosed with psychiatric disorders has shown a rising trend. In two decades, the global number of Disability Adjusted Life Years (DALYs) due to psychiatric conditions showed a sharp rise from 80.8 million to 125.3 million. The rapidly expanding field of psychopharmacology is challenging the traditional concepts of treatment and constantly seeking new drugs to treat psychiatric disorders. Patients receiving the drugs undergo complex regimens, which leads to drug-drug interaction [DDI]. Evidence in support of polypharmacy being beneficial is slim; rather, there is glowering and growing evidence with increased adverse effects.

Objective:

- To categorise potential DDI using Lexicomp®
- To determine the association of potential drug-drug interaction of psychotropic drugs with psychotropic polypharmacy
- To evaluate types of psychotropic polypharmacy

Material and Method: A cross-sectional study was conducted in the Department of Pharmacology in collaboration with the Department of Psychiatry, MKCG Medical College and Hospital, Odisha. Six hundred and six prescriptions were analysed. Data collected from prescriptions was compiled using standard spreadsheet software MS Excel and analysed using SPSS version 22.0. Lexicomp® was used as a vital study tool for the categorisation of potential DDI. A p-value of <0.05 was considered statistically significant.

Result: Schizophrenia (n=163) was found to be the most common diagnosis. Benzodiazepine (n=520) was commonly prescribed with atypical antipsychotics (n=463). Potential DDI was observed between clozapine with clonazepam and valproate with lorazepam with a severity rating of major. Frequent prescription of trihexyphenidyl (THP) leads to adjunctive polypharmacy. There was a significant association found between potential DDI and psychotropic polypharmacy (p=0.007).

Conclusion: The prescribing of psychotropic medications and psychotropic polypharmacy has risen. Potential DDI identification, mitigation, and reduction of toxicity in patients have become a challenge. It reinforces the need for all stakeholders to participate in continuing education, utilizing tools and formularies for evidence-based and judicious prescribing. Adjuvant Polypharmacy with drugs like THP along with antipsychotics warrants further studies and, if possible, reduction and alteration. If polypharmacy cannot be averted, then switching over to rational polypharmacy is the call of the times.

Key words: pDDI, Psychotropic Polypharmacy, Psychotropic drugs.

INTRODUCTION

Over the past three decades, the number of patients diagnosed with psychiatric disorders has shown a rising trend. Studies and surveys conducted by NIMHANS over the past decade have shown that mental disorders and psychiatric conditions have contributed significantly to morbidity and disability and increasing mortality. In a span of two decades between 1990-2019 the global number of DALYs due to psychiatric conditions showed a sharp rise from 80.8 million to 125.3 million. Likewise, the proportion of global DALYs attributed to mental disorders increased significantly from 3.1% to 4.9% [1]. It is estimated that 301 million people are affected by Anxiety, 280 million by Depression, 40 million by bipolar disorder & 24 million are affected by Schizophrenia

[2]. It has a major impact on overall health with socioeconomic consequences at all levels of healthcare and needs to be approached and addressed in an integrated but definitive process. From a cultural view, mental illness is associated with a significant amount of stigma in Indian society. Persons with mental disorders account for nearly a fourth of the total caseload in primary care settings, highlighting the burden at the peripheral level [3]. As of now, both qualitative and quantitative premises need to be studied and explored. Rapid expansion in the field of Psychopharmacology, wherein traditional concepts and paradigms of pharmacologic treatment, new drugs, as well as new drug discovery and development, has led to many new drug classes entering both on and off-label prescription psychotropic drugs. Consequently, there is an increase in psychotropic medications. Patients receiving the drugs undergo complex regimens, and often, it leads to drug-drug interaction [DDI] between various drug classes. The most prescribed drug classes include antipsychotics, both atypical and typical, mood stabilisers, SSRI, NDRI and TCA, among others. Nowadays, often, 2 or more psychotropic drugs are being used to treat psychiatric conditions, which may lead to psychotropic polypharmacy and this trend has been increasing over the years. Psychotropic polypharmacy can be defined as the use of two or more psychotropic medicines. However, a more deep-end perspective and quantifier approach is required to ascertain the various interrelated domains within the broad premise of psychotropic polypharmacy. The prevalence of polypharmacy varies from 13% to 90%.[4] Evidence in support of polypharmacy being beneficial is slim; rather, there is glowering and growing evidence with increased adverse effects. The simultaneous use of medicines of the same class, for instance, two or more psychotropic drugs, is known as Same Class polypharmacy. Multi-class polypharmacy is the use of psychotropic drugs of different classes. Augmentation polypharmacy, another subtype, is the use of a sub-therapeutic dose of one drug in combination with a drug in a therapeutic dose for the same indication. Adjuvant polypharmacy is the use of a non-psychotropic drug to counter the side effects of a psychotropic drug. [4][5] Polypharmacy is, however, established as a health risk and is associated with increased mortality that might be due to DDI. DDIs may not be “seen” by the physician, especially in outpatients where the combined effects of the drugs can present with almost any clinical symptomatology and outcome. Repeated review auditing of prescriptions of psychotropic drugs is not possible without commitment from researchers, clinicians, and patients, as well as other stakeholders. Psychotropic Polypharmacy is a mortality risk – it has been proven to cause more potentially inappropriate prescribing such as contra-indicated medicines, under or overdosing of medicines, and combining medicines with opposing pharmacodynamics. [6][7] Often, combination medications are used, and this involves a risk of underestimating the extent of polypharmacy to which patients are exposed. Since current studies are becoming more inclined towards psychopharmacology trends and overall mental health, researchers have been deep-diving into all aspects of pharmacologic interventions and their pharmacoepidemiology. The shift in tertiary care hospitals towards prescribing generic names of drugs is being reflected in generic psychotropic drugs, too. Patients have become significantly more open to combat their mental health issues, and caregivers have become more open to consulting psychiatric health care providers. In such a scenario, the value and importance of identifying potential drug-drug interactions is no longer a myth but a hard-fisted reality. Stakeholders at all levels need to avail themselves of the best possible evidence, and one vital dimension is that of potential drug-drug interactions [PDDI]. Psychotropic drugs are unique in the sense that their biological response is dependent on the modification, blockade, or enhancement of various neurotransmitters in the CNS [8]. Any DDI and subsequent adverse effects are bound to obstruct the achievement of therapeutic objectives, and it also affects the quality of life of the patients and their caregivers. More than ever, these warrant research in assessing potential DDI and drugs used in psychiatric patients to categorise and evaluate the trend of prescribing psychotropic drugs.

Aim: - To evaluate the potential drug-drug interactions of psychotropic drugs prescribed to psychiatric outpatients

Objective:

- To categorise potential DDI using Lexicomp®
- To determine the association of potential drug-drug interaction of psychotropic drugs with psychotropic polypharmacy
- To evaluate the types of psychotropic polypharmacy

Material and Methods: The study was conducted between January 2023 to July 2023 in the Department of Pharmacology, MKCG Medical College and Hospital, Berhampur, in collaboration with the Department of Psychiatry, MKCG Medical College and Hospital, Berhampur. It is a cross-sectional study. Permission was obtained from the Institutional Ethics Committee of MKCG Medical College and Hospital, Berhampur.

Sample Size: The sample size estimation was done using the standard formula for the unknown populace, taking the Confidence interval as 99%

$$n = (Z^2 * p * q) / E^2$$

Where:

- n is the required sample size
- Z is the Z-score corresponding to the desired level of confidence

- p is the estimated proportion of the population that possesses the characteristic of interest
- q is 1 - p (the estimated proportion of the population that does not possess the characteristic of interest) E is the desired margin of error (expressed as a proportion)

The sample size, along with 10 % attrition, was calculated to be 606. It is also in tandem with the WHO recommendation of collecting data from a minimum of 600 prescribing encounters for evaluation of prescribing indicators. As per the sample size, Prescriptions from OPD of Psychiatry were collected and analysed. Convenience sampling was done.

Inclusion Criteria: -

The inclusion criteria of the study comprised.

- [a] Study subjects from both genders were included.
- [b] Study subjects enrolled were in 18-year-old age groups.
- [c] Subjects with and without co-morbid conditions as outpatients of the psychiatric department were enrolled.
- [d] Informed consent was obtained from patients or caregivers of the subjects prior to data collection.
- [e] Patients with other comorbidities were included.
- [a] Pregnant and lactating women who were psychiatric outpatients.

Exclusion Criteria: -

The exclusion criteria for the study comprised.

- [b] Uncooperative, agitated patients who were not able to give informed consent were not enrolled in the study.
- [c] Patients from the IPD were not enrolled.
- [d] Patients with renal or hepatic failure were excluded.

Study Procedure:- Socio-demographic parameters were collected from the patient/caregivers and recorded in a predesigned case record form. The prescription data of patients of either sex and above 18 years of age, suffering from a psychiatric illness, and in whom at least one psychotropic drug, irrespective of diagnoses, were obtained. Data collected from prescriptions was compiled using standard spreadsheet software MS Excel. In our study, Lexicomp® was used as a vital study tool for the categorisation of potential DDI as per Risk Rating, Severity Rating, and Reliability Rating.

Study Tool: -

Lexicomp®: - an Internet-based information platform provides clinical information solutions to prescribers in an easy-to-access format along with machine learning.

Case Definitions of Lexicomp®:[9]

Risk Rating: -There are five categories of risk namely **A-** no interaction/**B-**no action needed/**C-**monitor Therapy/**D-** Modify Regimen/**X-**Avoid Combination

Severity Rating: - The severity of the effects of DDIs are categorised under [a]Major [b]Moderate [c]Minor. These indicate the magnitude of the effects and outcome of the DDIs concerned.

Reliability Rating: This rating is an in-built Lexicomp® algorithm that rates the preferred evidence-based drug referential solution to clinicians and researchers, enabling clinical decision-making. Thus, it is a quantitative documentation of the interaction. The rating is spread across four categories: [a] Excellent, [b] Good , [c] Fair and [d] Poor.

Statistical Analysis: Data were compiled using MS Excel and subsequently analysed using SPSS version 22.0. Descriptive data like socio-demographic parameters, diagnosis, and prescribed drugs were expressed in frequency and percentage. The Chi-square test was used to determine the association between potential drug-drug interactions with Psychotropic Polypharmacy. A p-value of <0.05 was considered statistically significant.

RESULT:

Table1: Sociodemographic parameters (n=606)

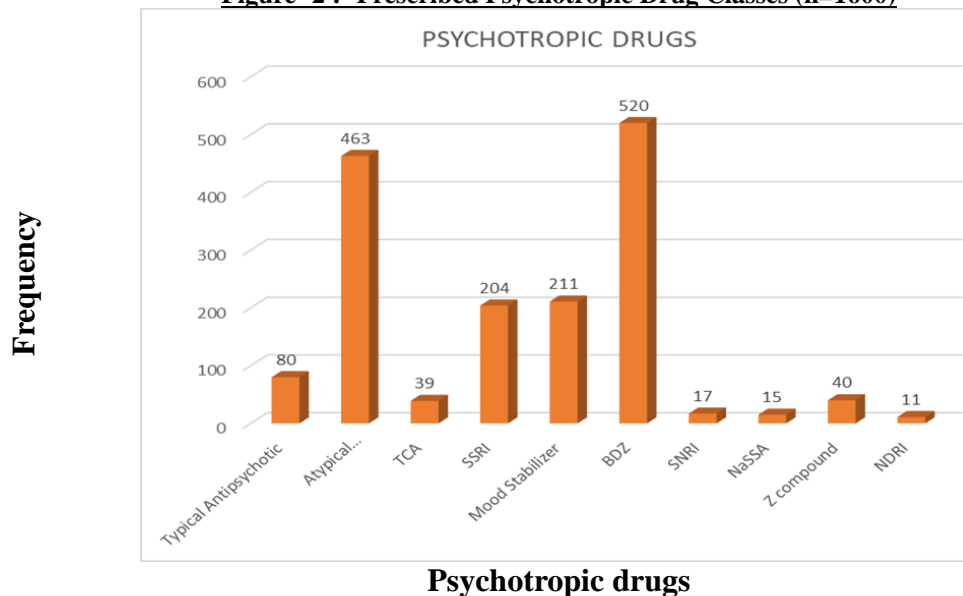
		Frequency	Percentage
Age group	19-29	77	12.7
	30-39	194	32
	40-49	79	13.03
	50-59	148	24.4
	60-69	93	15.3
	70-79	15	2.47
Gender	Male	268	44.3

Employment Status	Female	338	55.7
	Employed	167	27.5
	Unemployed	439	72.5
Marital Status	Married	357	58.9
	Unmarried	199	32.8
	Widow	29	4.7
	Divorced	21	3.4
Family Size	Joint	441	72.7
	Nuclear	165	27.3

Socio-demographic parameters like age groups, gender, employment status, marital status, and family size were expressed as frequency and percentage.

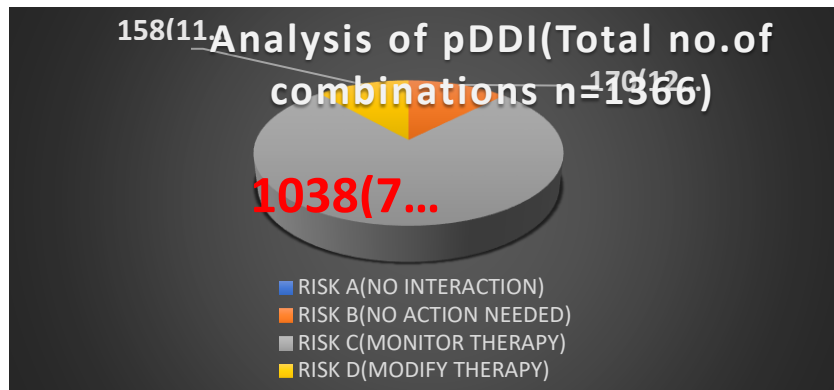
A total 606 numbers of subjects were included in the study. Table no.#1 shows that most of the subjects belonged to the age group of 30-39 years (32%) followed by 50-59 years (24.4%). Subjects belonging to the elderly age group 60-69 were 15.3%. A greater number of subjects were females that are 55.7%. In the study, the frequency of unemployed subjects was more (72.44%). It was seen that the maximum number of subjects were married 357[58.9%]. Only 29 [4.78%] patients were widowed, and 21 [3.46%] were divorced; 72.7% [441] of patients lived in joint families, while 27.3 % [165] lived in nuclear families.

Figure -2 :- Prescribed Psychotropic Drug Classes (n=1600)



Data were expressed in frequency. Out of the total number of psychotropic drugs prescribed in our study population benzodiazepines were the most prescribed [n=520] followed by atypical antipsychotic [n=463], mood stabilisers [n=211], SSRI [n=204], typical antipsychotics [n=80], Z compound [n=40], TCA [n=39], SNRI [n=17], NaSSA [n=15], NDRI [n= 11]. Amongst Benzodiazepines, clonazepam [n=464] and Chlordiazepoxide [n=22] were most prescribed. Divalproex Sodium and Valproic acid was the most prescribed Mood Stabilizers. Among SSRIs, escitalopram followed by Fluoxetine was seen in 102 and 53 prescriptions. Haloperidol [n=63] was the typical Antipsychotic prescribed the most, while risperidone [n=122] and Olanzapine[n=120] were the most prescribed Atypical Antipsychotics. Amitriptyline [n=22] and Dosulepin [n=17] were prescribed most among Tricyclic antidepressants. Zolpidem was the only Z compound class of drug prescribed. In adjunctive therapy, Other significant drugs found while analysing the prescriptions were Amisulpride(n=114), Quetiapine(n=112), Aripiprazole(n=48),and Pimozide(n=34).

Figure:3(Analysis of pDDI)



The above figure depicts that we got 76% pDDI combinations (Risk Rating C), 11.6% pDDI combinations (Risk Rating D), and 12.4% pDDI combinations (Risk Rating B) by analyzing the DDI through the Lexicomp drug interaction tool.

Table -2- DDI with Risk Rating B and Severity Rating Minor

DRUG	COMBINATION WITH	RELIABILITY RATING			
		EXCELLEN T	FAIR	GOOD	POOR
Escitalopram(n=87)	Clonazepam (82%),		Clonazepam, Zolpidem		
	Zolpidem (18%)				
Sertaline (n=64)	Valproate (50%),		Valproate, Clonazepam		
	Clonazepam (50%)				
Fluoxetine (n=19)	Clonazepam (100%)		Clonazepam		

Table 2 depicts a combination of drugs that have Risk rating B and severity rating minor, indicating that no action was needed with the following combinations – Escitalopram+ Clonazepam/Zolpidem, Sertraline+ Valproate/ Clonazepam, and Fluoxetine+ Clonazepam.

Table 3 (RISK RATING C with severity rating moderate)

SEVERIT Y RATING	DRUG	COMBINATION WITH	RELIABILITY RATING			
			EXCELLENT	GOOD	FAIR	POOR
Moderate	Risperidone (n=253)	Clona(28%),THP(45%), Val(20%), Nitra(7%)		Clona THP Nitra	Val	
	Olanzapine (n=176)	Clona(31%),Flu(19%), THP(13%),Lora(10%),Val (10%) ,Ari(9%),Esc(8%)		Clona, THP,Ari, Lora,Val	Flu,Es c	
	Haloperidol (n=133)	THP(34%),Cloza(32%), Clona(29%),Val(5%)		THP,Clon a,Val	Cloza	
	Amisulpride (n=114)	Clona(35%), Serta(30%),Li(20%), Dulo(15%)		Clona	Serta Li Dulo	
	Quetiapine (n=112)	Clona(46%),Esc(33%),TH P(21%)		THP	Esc Clona	
	Aripiprazole (n=48)	Val(34%), Clona(33%), Ola(33%)		Val, Clona, Ola		
	Valproate (n=95)	THP(54%), Clona(46%)		Clona		THP
	Amitryptiline(n =73)	Clona(46%), Chlordiazepoxide(30%), Val(24%)		Chlordiaz epoxide, Clona, Val		

	Pimozide (n=34)	Clona(50%), THP (50%)		Clona, THP		
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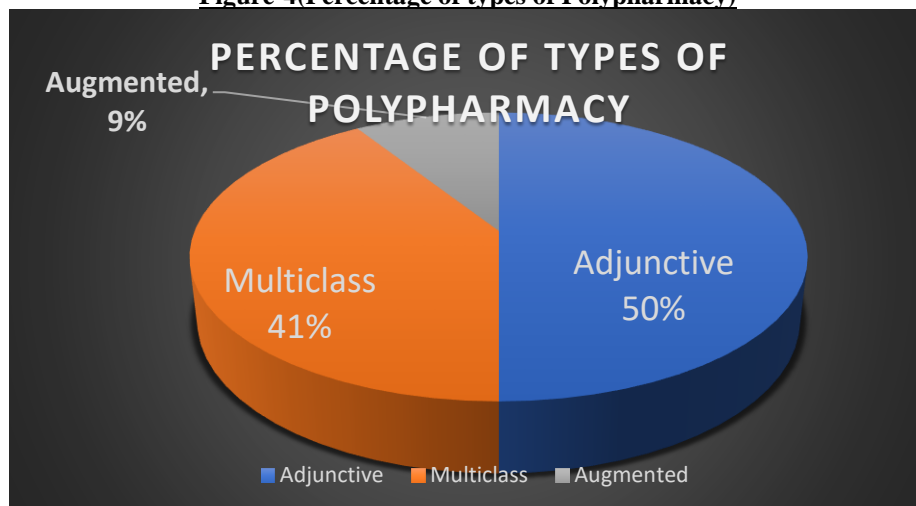
Abbreviations: - Clonazepam=Clona, Valproate=Val, Fluoxetine=Flu, Lorazepam=Lora, Nitrazepam=Nitra, Aripiprazole=Ari, Escitalopram=Esc, Sertaline=Serta, Lithium=Li, Duloxetine=Dulo, Olanzapine=Ola, Clozapine=Cloza In Table -3, the DDI of drugs Risperidone, Olanzapine, Haloperidol, Amisulpride, Quetiapine, Aripiprazole, Valproate, Amitriptyline and Pimozide with various other combinations are depicted and as per the Severity Rating which is C for the above drugs/drug combinations indicated that Monitoring of therapy was warranted for the above drugs, due to chances of patients' conditions deteriorating due to drug drug-interactions. The Reliability rating was found to be good as per Lexicomp®. As depicted in Table no-2, the drug-drug interactions of Risperidone were seen with Clonazepam (28%), THP (45%), and Nitrazepam (7%). Similarly, Olanzapine showed DDIs with Clonazepam, THP, Aripiprazole, Lorazepam and Valproate, while Haloperidol had DDIs with THP, Clonazepam and Valproate. The drugs Amisulpride and Quetiapine showed interaction with Clonazepam and THP, respectively. Clonazepam has DDI with Risperidone, Olanzapine, Haloperidol, Amisulpride, Aripiprazole, Valproate, Amitriptyline and Pimozide. The following combinations showed a Fair rating -Risperidone +Valproate, Olanzapine +Fluoxetine+Escitalopram, Haloperidol +Clozapine, Amisulpride + Sertraline+Li+Duoxetine, Quetiapine + Escitalopram +Clonazepam- despite of DDI as there are no Randomized Controlled Trials.

Table 4- DDI with Risk Rating D and Severity Rating Major

DRUG	COMBINATION WITH	RELIABILITY RATING			
		EXCELLEN T	GOOD	FAIR	POOR
Clozapine(n=141)	Clonazepam (40%), Quetiapine(26%), Haloperidol(17%), THP(17%)			Clonazepam, Quetiapine, Haloperidol, THP	
Valproate(n=17)	Lorazepam(100%)	Lorazepam			

Table -4 depicts DDI with a Risk rating of D and a Severity rating of Major, which warrants Modifying the drug and therapy. The following combinations were found in our study – Clozapine+ Clonazepam/ Quetiapine/ Haloperidol/ THP, Valproate+ Lorazepam.

Figure-4(Percentage of types of Polypharmacy)



Three classes of psychotropic polypharmacy were seen in our study population -Multiclass Polypharmacy was present in 41%. In contrast, 50% of the prescriptions showed Adjunctive Polypharmacy and Augmented Polypharmacy were seen in 9% of the prescriptions.

Figure-5(Frequency of Adjunctive THP prescribed)

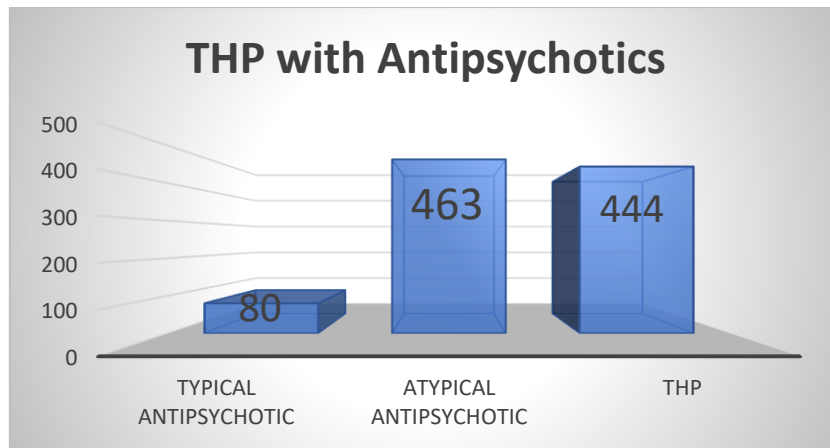


Figure 4 depicts the use of THP as an adjuvant with typical [n=80] as well as atypical antipsychotics [n=463].

Table -5 – Potential Drug-Drug Interaction with Psychotropic Polypharmacy

Prescriptions with pDDI	Prescriptions with Psychotropic Polypharmacy		P value
	PRESENT	ABSENT	
YES	576	17	0.007
NO	10	3	

The association between psychotropic polypharmacy and pDDI was analysed by using the Chi-square test * p value < 0.05 considered as significant.

DISCUSSION:

This cross-sectional study aimed to evaluate the prevalence and types of drug-drug interactions (DDIs) among patients with psychiatric disorders in our outpatient department (OPD) of psychiatry. The results of this study indicate that psychiatric disorders are more prevalent among certain demographic groups, such as middle-aged, female, unemployed, married, and joint family members. These findings are consistent with previous studies that have reported similar associations between common mental disorders and socio-demographic and clinical factors conducted by Sharkar et al. [10] Some possible explanations for these findings are: Middle-aged people may face more stress and challenges in their personal and professional lives, such as financial difficulties, marital problems, career transitions, or health issues, which could increase their risk of developing psychiatric disorders. A maximum number of patients were from the age group 30-39 [32%], while between the age group of 19-29 and 70-79, 12.7% and 2.47% were found in our study. The findings could be due to social stigma, lack of caregiver support due to dysfunctional family lives and lack of awareness in both age groups. Female. Unemployed persons may experience more psychological distress and lower self-esteem due to the loss of income, social status, and identity, as well as the uncertainty and stigma of being jobless. Married persons may have higher levels of psychiatric disorders due to the demands and conflicts of marital relationships, such as communication problems, domestic violence, and infidelity. Joint family members may have more exposure to family stressors and interpersonal conflicts, such as lack of privacy, autonomy, and support, which could affect their mental health. The most common diagnoses encountered in the study were schizophrenia and bipolar disorders, followed by depressive disorders. In this study, The finding that schizophrenia and bipolar affective disorders are the most common psychiatric disorders diagnosed in our outpatient department of psychiatry is consistent with the epidemiological data on the prevalence of these disorders in the general population. According to the National Institute of Mental Health, schizophrenia affects around 1.25%, and bipolar disorder with psychosis affects around 0.31% of the U.S. population [11]. Similarly, a population-based survey in Hong Kong reported that schizophrenia affects 1.25% and bipolar disorder with psychosis affects 0.31% of the Chinese adult population [12]. These rates are higher than those of other psychotic disorders, such as delusional disorder (0.15%) and psychotic disorder not otherwise specified (0.38%). We used the Lexicomp DDI tool to analyse the prescriptions of 606 patients over six months. We found that 76% of the drug combinations were classified as Risk C (monitor therapy with a severity rating of moderate) and 12% as Risk D (consider therapy modification with a severity rating of major) according to the Lexicomp severity rating scale. The most frequently involved drugs in Risk C were benzodiazepines (clonazepam) and tetrahydropalmatine (THP), which were often combined with atypical antipsychotics (risperidone, olanzapine) and mood stabilisers (valproate). In Risk D, we also encountered lorazepam plus valproate and clonazepam plus clozapine combinations. We also found that adjunctive polypharmacy (50%) was more prevalent than multi-class polypharmacy (41%). Moreover, we observed a significant association between DDIs and psychotropic polypharmacy (p = 0.007).

Our findings are consistent with previous studies that reported a high rate of DDIs among psychiatric patients, especially those with complex and chronic conditions [13]. Benzodiazepines are widely used in psychiatry for their anxiolytic, sedative, hypnotic, anticonvulsant, and muscle relaxant effects. However, they also have several drawbacks, such as dependence, tolerance, withdrawal, cognitive impairment, and increased risk of falls and fractures. Moreover, benzodiazepines can interact with other psychotropic drugs, either pharmacokinetically or pharmacodynamically, resulting in reduced or enhanced effects of one or both drugs. For example, benzodiazepines can inhibit the metabolism of clozapine, leading to increased plasma levels and risk of adverse effects such as sedation, hypotension, and agranulocytosis. Benzodiazepines can also potentiate the CNS depression and respiratory depression caused by other sedative drugs, such as typical and atypical antipsychotics [14]. Therefore, the use of benzodiazepines should be limited to short-term and lowest effective dose therapy, and patients should be monitored for signs of toxicity and dependence. Atypical antipsychotics and mood stabilisers are the mainstays of treatment for schizophrenia and bipolar disorder. Still, they can also affect the pharmacokinetics and pharmacodynamics of other drugs by modulating the activity of cytochrome P450 enzymes and transporters [15]. In our study, THP is also responsible for pDDI in both Risk C and D. It is also the major reason for adjunctive polypharmacy. THP is an anticholinergic drug used to treat extra pyramidal symptoms induced by antipsychotics, such as dystonia, akathisia, and parkinsonism. However, THP can also interact with antipsychotics and other drugs by reducing their bioavailability and efficacy. For instance, THP can decrease the absorption of risperidone and olanzapine from the gastrointestinal tract, resulting in lower plasma concentrations and reduced therapeutic effects. THP can also antagonise the cholinergic effects of valproate, which may contribute to its mood-stabilizing action. Moreover, THP can cause anticholinergic side effects, such as dry mouth, blurred vision, constipation, urinary retention, and cognitive impairment. The majority of Tunisian psychiatrists think that trihexyphenidyl on chronic use is associated with a high risk of addiction. Many of them consider that banning THP and substituting it with other anticholinergics may be the solution.[16]. The association between DDIs and psychotropic polypharmacy is not surprising, as the number of potential interactions increases exponentially with the number of drugs prescribed. Psychotropic polypharmacy is common in psychiatric practice, especially for patients with severe and refractory disorders, such as schizophrenia and bipolar disorders. However, polypharmacy also carries the risks of increased adverse effects, reduced adherence, and higher costs. Therefore, the rationale and evidence for each drug combination should be reviewed periodically, and the lowest effective doses and the shortest duration of treatment should be used. Furthermore, the use of decision support tools, such as the Lexicomp DDI tool, can help clinicians identify and avoid potentially harmful DDIs and optimise pharmacotherapy.

CONCLUSION:

There has been rise in patients in psychiatric OPDs in the past decade and more so in the aftermath of COVID-19 across all ages. Consequently, the prescribing of psychotropic medications and psychotropic polypharmacy has also risen. This study showed that DDIs are prevalent and potentially may cause serious outcomes in psychiatric patients with psychotropic polypharmacy. The use of multiple psychotropic drugs may be necessary to achieve optimal therapeutic outcomes for some patients. Still, it also increases the risk of DDIs and ADRs. pDDI identification, mitigation, and reduction of toxicity in patients has become a challenge knocking at our doors. It reinforces the need for all stakeholders to participate in continuing education, utilising tools and formularies for evidence-based and judicious prescribing and modification of agents and regimens wherever required. The use of benzodiazepines and trihexyphenidyl should be prescribed judiciously, limited to the lowest effective dose and the shortest duration possible, and alternative agents with less DDI potential should be considered whenever feasible, which warrants further studies. If this cannot be averted, then switching over to rational polypharmacy is the call of the times.

Strengths of the study: -

The strengths of this study are

- The use of Lexicomp® to categorise psychotropic drugs with the best available evidence.
- Good sample size which spreads across ages and sociodemographic parameters
- Assessing the rising trend of adjuvants like THP prescribing parallel to an antipsychotic class of drugs

Limitations of study: -

Cross-sectional study with convenience sampling.

Funding:

The study received no funding from any authority.

Conflict of Interest:

There was no conflict of interest reported by the authors.

References:

1. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019; *Lancet Psychiatry* 2022;9: 137–50. Published Online January 10, 2022[https://doi.org/10.1016/S2215-0366\(21\)00395-3](https://doi.org/10.1016/S2215-0366(21)00395-3)
2. <https://www.who.int/news-room/fact-sheets/detail/mental-disorders>
3. <http://www.indianmhs.nimhans.ac.in/Docs/Summary.pdf>
4. Kukreja S, Kalra G, Shah N, Shrivastava A. Polypharmacy In Psychiatry: A Review. *Mens Sana Monogr* 2013; 11:82-99.
5. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr.* 2017;17(1):230. Published 2017 Oct 10. doi:10.1186/s12877-017-0621-2
6. Govaerts J, Boeyckens J, Lammens A, et al. Defining polypharmacy: in search of a more comprehensive determination method applied in a tertiary psychiatric hospital. *Ther Adv Psychopharmacol.* 2021;11:20451253211000610. Published 2021 Mar 19. doi:10.1177/20451253211000610
7. Huang YT, Steptoe A, Wei L, Zaninotto P. The impact of high-risk medications on mortality risk among older adults with polypharmacy: evidence from the English Longitudinal Study of Ageing. *BMC Med.* 2021;19(1):321. Published 2021 Dec 16. doi:10.1186/s12916-021-02192-1
8. Greenshaw AJ. Neurotransmitter interactions in psychotropic drug action: beyond dopamine and serotonin. *J Psychiatry Neurosci.* 2003;28(4):247-250.
9. Abbas A, Al-Shaibi S, Sankaralingam S, Awaisu A, Kattezhatu VS, Wongwiwatthananukit S, Owusu YB. Determination of potential drug–drug interactions in prescription orders dispensed in a community pharmacy setting using Micromedex® and Lexicomp®: a retrospective observational study. *International Journal of Clinical Pharmacy.* 2022 Apr 1:1-9.
10. Sharkar, S., Balbuena, L., Marcoux, G. et al. Modeling socio-demographic and clinical factors influencing psychiatric inpatient service use: a comparison of models for zero-inflated and overdispersed count data. *BMC Med Res Methodol* 20, 232 (2020). <https://doi.org/10.1186/s12874-020-01112-w>
11. National Institute of Mental Health. Schizophrenia [Internet]. Available from: 1 [Accessed 2023 Dec 10].
12. Volume 43, Issue 6, November 2017, Pages 1280–1290, <https://doi.org/10.1093/schbul/sbx056> Wing Chung Chang, Corine Sau Man Wong, Eric Yu Hai Chen, Linda Chiu Wa Lam, Wai Chi Chan, Roger Man Kin Ng, Se Fong Hung, Eric Fuk Chi Cheung, Pak Chung Sham, Helen Fung Kum Chiu, Ming Lam, Edwin Ho Ming Lee, Tin Po Chiang, Lap Kei Chan, Gary Kar Wai Lau, Allen Ting Chun Lee, Grace Tak Yu Leung, Joey Shuk Yan Leung, Joseph Tak Fai Lau, Jim van Os, Glyn Lewis, Paul Bebbington, Lifetime Prevalence and Correlates of Schizophrenia-Spectrum, Affective, and Other Non-affective Psychotic Disorders in the Chinese Adult Population, *Schizophrenia Bulletin*,
13. Han K, Cao P, Wang Y, Xie F, Ma J, Yu M, Wang J, Xu Y, Zhang Y, Wan J. A review of approaches for predicting drug–drug interactions based on machine learning. *Frontiers in pharmacology.* 2022 Jan 28;12:814858
14. Demler TL. The role of the pharmacist in mental health care. *Psychiatr Times.* 2020;37(8):22-25.
15. Han K, Cao P, Wang Y, Xie F, Ma J, Yu M, Wang J, Xu Y, Zhang Y, Wan J. A review of approaches for predicting drug–drug interactions based on machine learning. *Frontiers in pharmacology.* 2022 Jan 28;12:814858.
16. Hamzaoui S, Moula O, Mustapha MB, Dridi A, Maamri A, Zalila H. Misuse and addiction to Trihexyphenidyl: perception and attitude of Tunisian psychiatrists. *European Psychiatry.* 2015 Mar 28;30:1097