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# Antidepressant prescription patterns and polypharmacy in outpatient psychiatry: a cross-sectional study

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*Background and aim:* Prescription patterns of antidepressants have changed over the years with a shift towards newer antidepressants with better tolerability and safety. Polypharmacy is common in psychiatry settings. The study aimed to evaluate the antidepressant drug prescription pattern and polypharmacy in a psychiatry outpatient setting. *Investigations:* This prospective observational study was conducted in a psychiatric outpatient clinic. The medication use data of eligible patients were collected. In addition, the rationale of antidepressant medication prescription, the defined daily dosage (DDD), the prescribed daily dose (PDD), and the PDD to DDD ratio were assessed. The assessment of prescription polypharmacy was conducted utilizing the framework provided by the National Association of State Mental Health Program Directors. *Results:* Data from 131 patients was analyzed. Major depressive disorder (32.8%) was the most common disorder for which antidepressants were prescribed. The majority, 91 (69.4%), received monotherapy. Selective serotonin reuptake inhibitors were the most frequently prescribed drugs in 69 (52.7%). Mirtazapine was the most frequently 32(24.4%) prescribed drug. Escitalopram and mirtazapine were the most commonly prescribed combination therapy (4.6%). Antipsychotic medications (37.4%) were the most widely co-prescribed medications, along with antidepressants. The PDD to DDD ratio was less than 1 for mirtazapine and imipramine; they were ≥1 for others. Psychiatric polypharmacy was documented in 87.1% of prescriptions. The total polypharmacy was not significantly ($p>0.05$) associated with demographic, illness, and treatment-related variables. *Conclusion:* Selective serotonin reuptake inhibitors were the most commonly prescribed antidepressants, monotherapy, and combination therapy. A substantial amount of patients received concomitant administration of antidepressants or psychotropic drugs, warranting careful monitoring.

## 1. Introduction

Depression and anxiety disorders are prevalent psychiatric illnesses that can cause significant morbidity and mortality (Bobo et al. 2022; Jagtap et al. 2020). Antidepressants are the cornerstone of treatment for these disorders (Ballenger et al. 2000). While prescribing antidepressant medication, factors such as efficacy, response rate, tolerability, safety, drug interactions, dose schedule, titration, and cost must all be considered (Albalushi et al. 2021).

Prescription patterns of antidepressants have changed over the years with a shift towards newer antidepressants with better tolerability and safety profiles (Luo et al. 2020; Westenberg et al. 2006). Furthermore, antidepressants have been used to treat anxiety disorders and other mental illnesses in addition to depression (Schneider et al. 2019). However, concerns about the potential risks associated with antidepressants, such as the risk of suicidal ideation and behavior, have led to more cautious prescribing practices, particularly in children and adolescents (Carvalho et al. 2016).

Antidepressant prescription trends vary among countries and situations based on cost, drug availability, healthcare policies, prescriber psychiatric training, and preferred treatment modalities (Luo et al. 2020; Uchida et al. 2007; Grover et al. 2013). A Plethora of studies have documented the prescription pattern of antidepressant medications. The majority of these studies have documented SSRIs as the most preferred antidepressants over other antidepressants (Luo et al. 2020; Dunn et al. 1999; Rode et al. 2014). Some of these studies have reported SSRI usage in more than 75% of their study population (Luo et al. 2020; Ara et al. 2022).

Given the rising prevalence of depression and anxiety disorders, polypharmacy in treating these conditions has increased globally (Kukreja et al. 2013). Besides, antidepressants belong to the drug subclasses most frequently prescribed in combination in psychiatry settings (Díaz-Caneja et al. 2014). Polypharmacy is common and often considered justifiable in the therapeutic management of psychiatric patients presenting with severe and complex symptoms, treatment resistance, relapse, co-morbidities, or multimorbidity (Yatham et al. 2018). Polypharmacy, on the other hand, raises the risk of medication-related issues such as drug-drug interactions, adverse drug responses, and non-adherence, leading to increased hospitalization, poor therapeutic outcomes, and increased healthcare costs (Halli-Tierney et al. 2019). The prevalence of polypharmacy with antidepressants globally varies from 11 to 85% (Hu et al. 2022; Stassen et al. 2022)).

Although polypharmacy is a common practice in managing psychiatric disorders, there is little reasoning regarding its efficacy (Sarkar et al. 2017). There is minimal information currently available regarding the prevalence and pattern of polypharmacy among the UAE's psychiatric patients. Hence, this study would shed light on the prevalence of polypharmacy in patients receiving antidepressants and would be extremely effective in strengthening interventional techniques and promoting rational antidepressant therapy. Understanding the prescription patterns and polypharmacy in patients receiving antidepressants is critical for optimizing treatment, reducing medication-related problems, and improving healthcare delivery for this vulnerable patient population. This study aims to address this gap in knowledge by assessing the prescription patterns and polypharmacy in patients receiving antidepressants in an outpatient psychiatric department in the UAE.

## 2. Investigations and results

### 2.1. Study design, setting, and duration

The current investigation lasted for eight months and was carried out within the psychiatric outpatient department of a secondary-care hospital in the Northern Emirates of the United Arab Emirates.

### 2.2. Ethics committee approval

The research protocol was granted permission by the Ras Al Khaimah MoH regional Research and Ethics Committee. [MOHP/RAK/SUBC/No.44/2016-PG-P].

### 2.3. Study criteria

The research encompassed participants who met the diagnostic criteria for mental and behavioral problems outlined in the International Classification of Disease (ICD-10), regardless of age or gender. The subjects in this study were prescribed a minimum of one antidepressant medication and were enrolled as patients in the outpatient clinic specializing in psychiatry. The study eliminated those who were not administered any antidepressant medicines and instead received only psychotherapy, psycho-education, and cognitive behavioral therapy. In addition, we chose to remove those who were admitted as inpatients and were undergoing treatment with antidepressant medicines.

### 2.4. Study sample size

The sample size was calculated using the Raosoft® sample size calculator. The minimum sample size required to achieve a 5% margin of error with a 90% confidence level, given a 7.2% margin of error, was determined to be 130.

### 2.5. Data collection

The study data were obtained from patients' prescriptions and electronic health records in accordance with the research protocol. The information gathered included the patient's age, gender, nationality, medication history, co-morbidities, concomitant medications, and details of all prescribed medications.

### 2.6. Assessment of prescription pattern

The information gathered was entered into a form specifically created for the research. The study investigators ensured the completeness of the collected data. The prescriptions were assessed for type, dose, administration route, duration of therapy, monotherapy, and combination therapy. Antidepressant prescription patterns were represented as defined daily doses (DDD), prescribed daily doses (PDD), and PDD ratio to DDD. DDD was acquired from the WHO Collaborating Center for Drug Statistics Methodology. PDD was calculated concurrently by averaging the daily doses of antidepressants given to the study population. Subsequently, the estimated PDD was divided by the medication's DDD to establish the PDD to DDD ratio.

### 2.7. Assessment of polypharmacy

Prescription polypharmacy was evaluated using the framework developed by the National Association of State Mental Health Program Directors and categorized as same-class, multi-class, adjunctive, augmentation, and total polypharmacy (National Association of State Mental Health Program Directors 2023).

### 2.8. Data analysis

The data analysis used version 27.0 of the Statistical Package for the Social Sciences (SPSS). The chi-square test assessed the association between the study variables and the polypharmacy outcome variable. The predictors of polypharmacy were evaluated using multivariate binary logistic regression (OR=1, CI=95%). A significance level of less than 0.05 was deemed to be statistically significant.

### 2.9. Demographic characteristics

A total of 131 patients who satisfied the inclusion criteria were included in the analysis. The average age of the patients was 44.8±6.6 years, with the majority (81, 62%) female. The mainstream of the study patients, 88 (67%), were UAE nationals, and 67 (51.1%) had co-morbidities besides psychiatric conditions. The most common co-morbidity was hypertension (33, 25.2%), followed by diabetes (23, 17.6%), dyslipidemia (17, 13%), and asthma (8, 6.1%). Most patients were treated previously with antidepressants 81 (62%). Of all the patients enrolled in the study, 42 (32.1%) patients had a positive family history of psychiatric disorders. Table 1 shows the demographic information for the study participants.

**Table 1: Patient demographics**

| Demographic parameters | No. of patients (%) [n=131, (%)] |
|---|---|
| **Gender** | |
| Male | 50 (38.2) |
| Female | 81 (61.8) |
| **Nationality** | |
| Local | 88 (67.1) |
| Expatriate | 43 (32.8) |
| **Past medical history (General medical conditions)** | |
| Present | 67 (51.1) |
| Absent | 62 (47.3) |
| Unknown | 2 (1.5) |
| **Past medication history (Previous treatment with antipsychotics)** | |
| Yes | 81 (61.8) |
| No | 50 (38.2) |
| **Previous treatment with other psychotropics** | |
| Yes | 55 (42) |
| No | 76 (58) |
| **Family history of psychiatric illness** | |
| Yes | 42 (32) |
| No | 17 (13) |
| Unknown | 72 (55) |
| **Current employment status** | |
| Employed | 31 (23.6) |
| Not employed | 100 (76.3) |
| **Current marital status** | |
| Single | 33 (25.2) |
| Married | 84 (64.1) |
| Divorced | 8 (6.1) |
| Widowed | 6 (4.6) |
| **Alcohol use** | |
| Yes | 6 (4.6) |
| No | 125 (95.4) |
| **Illicit Drug Use** | |
| Yes | 11 (8.4) |
| No | 120 (91.6) |
| **Tobacco use** | |
| Yes | 17 (13) |
| No | 114 (87) |
| **Number of suicidal attempts (current or previous)** | |
| None | 120 (91.6) |
| One or more | 11 (8.4) |

**Table 2: Medical diagnosis of the study patients.**

| Medical Diagnosis | ICD-10-CM-Codes | No. of patients n(%) |
|---|---|---|
| Major depressive disorder | F32.9 | 43 (32.8) |
| Generalized anxiety disorder | F41.1 | 17 (13) |
| Obsessive-compulsive disorder | F42.9 | 9 (6.8) |
| Major depressive disorder with psychotic features | F33.3 | 7 (5.3) |
| Substance abuse | F19.10 | 6 (4.5) |
| Adjustment disorder with mixed anxiety and depressed mood | F43.23 | 4 (3) |
| Bipolar disorder, depressed episode | F31.30 | 3 (2.2) |
| Anxious depression | F41.8 | 3 (2.2) |
| Adjustment disorder with depressed mood | F43.21 | 3 (2.2) |
| Borderline personality disorder | F60.3 | 3 (2.2) |
| Somatization disorder | F45.0 | 3 (2.2) |
| Bipolar disorder manic episode | F30 | 3 (2.2) |
| Dementia | F03 | 3 (2.2) |
| Panic disorder | F41.0 | 2 (1.5) |
| Schizophrenia | F20.0 | 2 (1.5) |
| Adjustment disorder with anxiety | F43.22 | 2 (1.5) |
| Schizoaffective disorder | F25.9 | 2 (1.5) |
| Bipolar disorder I | F31.60 | 2 (1.5) |
| Bipolar disorder II | F31. 81 | 2 (1.5) |
| Conversion disorder | F44.0 | 2 (1.5) |
| Post-traumatic stress disorder | F43.10 | 1 (0.75) |
| Social phobia | F40.10 | 1 (0.75) |
| Premenstrual tension syndromes | N94.3 | 1 (0.75) |
| Psychosis, paranoid | F22.0 | 1 (0.75) |
| Intellectual disability | F79.0 | 1 (0.75) |
| Alcohol use disorder | F10 | 1 (0.75) |
| Chronic nausea anxiety | F41.9 | 1 (0.75) |
| Mood insomnia | F51.05 | 1 (0.75) |
| Autistic disorder | F84.0 | 1 (0.75) |
| Nocturnal enuresis | N39.44 | 1 (0.75) |

**Abbreviations:** ICD: International Classification of Diseases

The majority of the patients had major depressive disorder (43, 32.8%), followed by generalized anxiety disorder (17, 12.9%) and obsessive-compulsive disorder (9, 6.8%). Table 2 displays the medical diagnoses of the study patients.

### *2.10. Prescription pattern of antidepressants*

A total of 343 medications were prescribed to 131 individuals during the study period, resulting in an average of 2.62 + 1.01 drugs per patient. A total of twelve antidepressants were prescribed to study patients, as well as the average amount of antidepressants administered per patient was 1.3±0.49. A majority (69.4 %) of the study patients were prescribed a single antidepressant drug, whereas 29 and 1.5% of the study patients received dual and triple antidepressant therapy. Selective serotonin reuptake inhibitors (SSRIs) constituted the predominant class of antidepressant medications taken as monotherapy, accounting for 35.9 % of prescriptions, followed by serotonin-norepinephrine reuptake inhibitors (SNRIs) in 13.7 % of patients. Serotonin and α-2 adrenergic antagonists and SSRI were the most common (6.9 %) dual antidepressant therapy**,** whereas two patients received triple therapy (SSRI+ SNRI + TCA and SNRI + TCA+ melatonergic antidepressant, each). The details of antidepressant prescribing patterns in the study subjects are presented in Table 3.

Mirtazapine, a serotonin and -2 adrenergic antagonist drug, was the most frequently (in 32 patients) prescribed antidepressant, either as mono or dual therapy, followed by escitalopram, an SSRI (29 patients). Whereas maprotiline and imipramine (TCAs) were the least frequently (in 2 patients each) used antidepressants among the study patients.

### *2.11. PDD, DDD values, and PDD/DDD ratio for the antidepressants*

A majority (7 out of 12) of the antidepressants were prescribed within the adequate PDD to DDD ratio (0.8-1.3), whereas four antidepressants were prescribed with high (1.4-1.8) and one was with low (0.5) PDD to DDD ratio. Table 4 displays the PDD, DDD, and the ratio of PDD to DDD for the antidepressants administered to the patients who were part of the study.

### *2.12. Prescription analysis with selected WHO drug use indicators*

The data was analyzed to establish the number and proportion of prescriptions or drugs and particular drug usage indicators defined by the WHO. The utilization rate of drugs prescribed by their generic name, dispensed from the hospital pharmacy, and listed in the Ministry of Health (MoH) Formulary of the United Arab Emirates (UAE) was 100% for each category.

**Table 3: Prescription patterns of antidepressant medications**

| Type of antidepressant/s | No. of patients (%) [n=131, (100)] |
|---|---|
| **One antidepressant** | **91 (69.4)** |
| **Selective Serotonin Reuptake Inhibitor (SSRI)** | **47 (35.9)** |
| Escitalopram | 19 (14.5) |
| Fluoxetine | 20 (15.2) |
| Fluvoxamine | 3 (2.3) |
| Paroxetine | 5 (3.8) |
| **Serotonin-Norepinephrine Reuptake Inhibitor (SNRI)** | **18 (13.7)** |
| Venlafaxine | 9 (6.9) |
| Duloxetine | 9 (6.9) |
| **Tricyclic Antidepressant (TCA)** | **9 (6.9)** |
| Clomipramine | 2 (1.5) |
| Amitriptyline | 4 (3) |
| Maprotiline | 1 (0.75) |
| Imipramine | 2 (1.5) |
| **Serotonin and α-2 adrenergic antagonist** | **11 (8.4)** |
| Mirtazapine | 11 (8.4) |
| **Melatonergic antidepressant** | **6 (4.6)** |
| Agomelatine | 6 (4.6) |
| **Two antidepressants** | **38 (29)** |
| **One Serotonin and α-2 adrenergic antagonist + one SSRI** | **9 (6.9)** |
| Mirtazapine + Escitalopram | 6 (4.6) |
| Mirtazapine + Fluoxetine | 3 (2.3) |
| **One melatonergic antidepressant + one SSRI** | **7 (5.3)** |
| Agomelatine + Escitalopram | 3 (2.3) |
| Agomelatine + Fluoxetine | 3 (2.3) |
| Agomelatine + Paroxetine | 1 (0.75) |
| **One TCA + One SSRI** | **7 (5.3)** |
| Clomipramine + Escitalopram | 1 (0.75) |
| Clomipramine + Fluoxetine | 1 (0.75) |
| Clomipramine + Fluvoxamine | 2 (1.5) |
| Mirtazapine + Venlafaxine | 3 (2.3) |
| **One Serotonin and α-2 adrenergic antagonist + One SNRI** | **4 (3)** |
| Mirtazapine + Duloxetine | 4 (3) |
| **One melatonergic antidepressant + One SNRI** | **4 (3)** |
| Agomelatine + Duloxetine | 3 (2.3) |
| Agomelatine + Venlafaxine | 1 (0.75) |
| **One SNRI + One TCA** | **2 (1.5)** |
| Venlafaxine + Clomipramine | 1 (0.75) |
| Venlafaxine + Maprotiline | 1 (0.75) |
| **One Serotonin and α-2 adrenergic antagonist + One melatonergic antidepressant** | **4 (3)** |
| Mirtazapine + Agomelatine | 4 (3) |
| **One Serotonin and α-2 adrenergic antagonist + One TCA** | **1 (0.75)** |
| Mirtazapine + Amitriptyline | 1 (0.75) |
| **Three antidepressants** | **2 (1.5)** |
| **One SSRI + one SNRI + one TCA** | **1 (0.75)** |
| Fluoxetine + Duloxetine + Clomipramine | 1 (0.75) |
| **One SNRI + one TCA+ One melatonergic antidepressant** | **1 (0.75)** |
| Duloxetine + Amitriptyline + Agomelatine | 1 (0.75) |

**Table 4: PDD, DDD values, and PDD/DDD ratio for the antidepressants**

| Type of antipsychotic/s | No. of patients (%) | ATC Code | PDD (mg) | DDD (mg) | PDD/DDD |
|---|---|---|---|---|---|
| Mirtazapine | 32 (24.4) | N06AX11 | 24.3 | 30 | 0.8 |
| Escitalopram | 29 (22.1) | N06AB10 | 13.2 | 10 | 1.3 |
| Fluoxetine | 28 (21.3) | N06AB03 | 28.5 | 20 | 1.4 |
| Agomelatine | 22 (16.8) | N06AX22 | 26.1 | 25 | 1.0 |
| Duloxetine | 18 (13.7) | N06AX21 | 71.6 | 60 | 1.1 |
| Venlafaxine | 15 (11.4) | N06AX16 | 178.3 | 100 | 1.7 |
| Clomipramine | 8 (6.1) | N06AA04 | 100 | 100 | 1 |
| Paroxetine | 6 (4.6) | N06AB05 | 33.3 | 20 | 1.6 |
| Amitriptyline | 6 (4.6) | N06AA09 | 75 | 75 | 1 |
| Fluvoxamine | 5 (3.8) | N06AB08 | 180 | 100 | 1.8 |
| Maprotiline | 2 (1.5) | N06AA21 | 112.5 | 100 | 1.1 |
| Imipramine | 2 (1.5) | N06AA02 | 50 | 100 | 0.5 |

**Abbreviations:** ATC: Anatomical Therapeutic Chemical, DDD: Defined Daily Doses, PDD: Prescribed Daily Doses

### *2.13. Co-prescribed medications*

A majority (64.1 %) of the study patients were co-prescribed with other psychotropic drugs along with antidepressants. Most (48.8 %) patients received one co-prescribed medication, followed by two (14.5 %), and one received three co-prescribed drugs. Antipsychotics were the most frequently (49, 37.4%) co-prescribed medications, followed by sedatives and anxiolytics (31, 23.6%) and mood stabilizers (21, 16 %). In addition, 12 patients (9.1 %) were co-prescribed with beta-blockers.

### *2.14. Polypharmacy*

Our study used the National Association of State Mental Health Programme Directors Categorization for Polypharmacy classification.[21] The categories are:

I. Same-Class Polypharmacy
Polypharmacy refers to using more than one medicine from the same medication class. None was detected in this study.

II. Multi-class Polypharmacy
The use of full therapeutic doses of more than one drug from various classes of drugs for the same symptom group is considered multi-class polypharmacy. Multi-class polypharmacy was seen in forty patients, accounting for roughly 30.5% of the study group.

III. Adjunctive Polypharmacy
It is described as using one medicine to treat another treatment's side effects or secondary symptoms from a different drug class. Adjunctive Polypharmacy was evidenced in two (1.5%) of the patients.

IV. Augmentation Polypharmacy
The approach involves the utilization of a reduced dosage of one medicine and administering another medication from a distinct class at its recommended therapeutic dosage to address a shared cluster of symptoms. Augmentation polypharmacy was documented in 50 (37.5%) patients.

V. Total Polypharmacy
The metric referred to in this context is the aggregate number of medications a patient consumes, also known as the total drug load. (including prescription, non-prescription, or OTC medications), defined as total polypharmacy. In our study, 17 (12.9%) patients were on monopharmacy (single drug). Total polypharmacy was documented in 114 (87.1%) patients. Out of these, 46 (35%) patients were prescribed two medications, 43 (33%) were prescribed three medications, 22 (16.8%) had four medications prescribed, two (1.5%) patients had five medications prescribed, and one (0.8%) patient was prescribed six medications. Categorization for Polypharmacy among Study Population is presented in Table 5.

**Table 5: Categorization for polypharmacy among study population**

| Type of polypharmacy | n (%) [n=131] |
|---|---|
| ***Same-class polypharmacy*** | 00 |
| ***Multi-class polypharmacy*** | |
| • SSRI + Alpha-2 Antagonists | 09 (6.9) |
| • SSRI+ Melatonin Agonists | 07 (5.3) |
| • SNRI+ Alpha-2 Antagonists | 07 (5.3) |
| • SSRI +TCA | 04 (3.1) |
| • SNRI+ Melatonin Agonists | 04 (3.1) |
| • Alpha-2 Antagonists + Melatonin Agonists | 04 (3.1) |
| • SNRI +TCA | 02 (1.5) |
| • Alpha-2 Antagonists +TCA | 01 (0.8) |
| • SSRI+SNRI+TCA | 01 (0.8) |
| • SNRI+TCA+ Melatonin Agonists | 01 (0.8) |
| ***Adjunctive polypharmacy*** | |
| • Fluoxetine + Mebeverine | 01 (0.8) |
| • Fluoxetine + Propranolol | 01 (0.8) |
| ***Augmentation polypharmacy*** | |
| • Antidepressant + Benzodiazepine | 31 (23) |
| • Antidepressant + Beta-blocker | 12 (9.2) |
| • Antidepressant + Antipsychotic | 07 (5.3) |
| ***Total polypharmacy*** | |
| • Two medications | 46 (35) |
| • Three medications | 43 (33) |
| • Four medications | 22 (16.8) |
| • Five medications | 02 (1.5) |
| • Six medications | 01 (0.8) |

### *2.15. Association between demographic factors, diagnostic characteristics, treatment-related variables, and the presence of total polypharmacy*

The variables under investigation include gender ($\chi2 = 0.075$, $p = 0.794$), age ($\chi2 = 0.618$, $p=0.422$), and the presence of non-psychiatric co-morbidity ($\chi2 = 0.492$, $p = 0.782$) were not significantly ($p>0.05$) associated with polypharmacy using Chi-square test.

## 3. Discussion

Prescription pattern monitoring studies are tools for evaluating prescribing, dispensing, and distributing medicines. The main object of these studies is to enable the rational use of medicines. Prescription patterns may vary from one country to another because healthcare models determine them, including cost, availability,

psychiatric training, and preferred treatment modalities. For example, a study from Qatar reports that escitalopram is the most widely used antidepressant in their research setting (Bastaki et al. 2021). While another Indian study found a preference for duloxetine over other antidepressants (Trivedi et al. 2010). In a research conducted in Nigeria, amitriptyline was the most commonly given antidepressant since it was four times less expensive than fluoxetine (Ezenduka et al. 2014). The discrepancies mentioned earlier in the prescription practices underscore the impact of several factors, including cultural norms, economic factors, and regulatory laws, on the selection of antidepressant medications. The findings specified above highlight the need to perform research relevant to particular regions to enhance comprehension and resolution of mental health requirements across diverse countries.

The current study seeks to identify a trend in the antidepressant-prescribing pattern in an outpatient secondary care hospital in the Northern Emirates of UAE. The analysis of antidepressant prescription trends in the UAE might yield significant insights into the prevailing mental health scenario and facilitate the identification of potential deficiencies or opportunities for enhancing treatment approaches.

In the present investigation, the primary psychiatric disease for which antidepressant medications were most commonly prescribed was major depressive disorder. Following that were generalized anxiety disorder and obsessive-compulsive disorder. In a previous study, it was discovered that a considerable proportion of patients diagnosed with depressive disorder were prescribed antidepressant drugs, with a subsequent predominance of such prescriptions among patients identified with anxiety disorders (Soh et al. 2015). Major depressive disorders were identified as the predominant diagnosis in various investigations conducted (Gauthier et al. 2017). The data mentioned above indicate that major depressive disorder is consistently acknowledged as a frequent condition that necessitates the administration of antidepressant medication across various research and geographical regions.

The aggregate quantity of medications administered in the present investigation was 2.62±1.01 per patient. The total number of antidepressants prescribed was 1.3±0.49 per patient. Similar results (average number of drugs prescribed/prescription – 2.06 and average number of antidepressants prescribed/prescription – 1.1) were reported by a previous study (Ghos et al. 2014) All the medicines prescribed in the study were generic as our study setting. In an earlier study, 99% of the prescribed drugs were generic (Gho et al. 2014). All antidepressants were administered in oral dosage form, and none of the patients required antidepressants in injectable form. This observation suggests that the patients in the study were able to manage their depression through oral medication alone effectively. The high percentage of prescribed generic names indicates a cost-effective and rational treatment approach.

The majority of patients (70.9 %) in our study were prescribed antidepressant monotherapy, followed by dual and triple therapy in 29% and 1.6% of the study population, respectively. A similar proportion of patients receiving antidepressant monotherapy was observed in a previous study (Bae et al. 2011). Escitalopram and mirtazapine were our study's most commonly prescribed combination therapy (4.6 %), followed by mirtazapine and duloxetine (3 %). A study conducted by Blier P et al. documented that mirtazapine in conjunction with an SSRI provided more improvement than monotherapy and had significantly higher remission rates than an SSRI alone (Blier et al. 2010). In contrast, a randomized controlled trial in treatment-resistant depression found no substantial advantage for mirtazapine in addition to an SSRI or an SNRI over a placebo (Kessler et al. 2018). These findings suggest that antidepressant monotherapy remains the preferred treatment approach for most patients. However, the use of combination therapy, particularly with escitalopram and mirtazapine, is also prevalent and may be considered in certain cases to enhance treatment efficacy.

Treatment initiation with concomitant use of two antidepressants is discouraged (Grover et al. 2013). One approach to optimizing antidepressant drug therapy is to augment the first medication with a second antidepressant with an alternative action mechanism. A combination of antidepressants may help resolve depression symptoms, rapidity of action, control associated (non-depressive) symptoms such as anxiety, improve social function and quality of life, and prevent relapse (Si et al. 2014).

SSRIs were the most frequently prescribed antidepressants (52.7 %), either in single or combination therapy. Similar findings have been observed in some previous reports (Soh et al. 2015; Bae et al. 2011). Several factors are considered when choosing antidepressant medication: efficacy, response rate, tolerability, safety, drug interactions, dosing schedule, titration, and patient preference (Boyce et al. 2021). Because of their lower likelihood of side effects and more acceptable pharmacological profile, SSRIs are the most often prescribed antidepressants. Recent guidelines recommend the use of SSRIs as the first-line agents for depressed patients (American Psychiatric Association, 2000).

Mirtazapine was this study's most commonly prescribed medicine (24.4 %), followed by escitalopram and fluoxetine at 22.1 % each. In contrast, one study indicated that escitalopram (32 %) was the most often used antidepressant and was closely followed by fluvoxamine (20.5 %) (Rode et al. 2014). Apart from escitalopram, some studies have observed paroxetine (Uchida et al. 2007), imipramine (Gauthier et al. 2017), sertraline (Shireman et al. 2002) and as commonly prescribed drugs. This difference in the prescription pattern is due to differences in the study setting, type of patients, local and international guidelines, availability and affordability of medicine, and psychiatrist preference based on experience.

All the study population received optimum antidepressant maintenance dosing. When there was a partial response to antidepressant treatment, the antidepressant medication dose was raised before switching to another antidepressant medication. Because of characteristics such as quick metabolism, some patients may require higher-than-recommended doses of drugs exceeding Food and Drug Administration (FDA) labeling (American Psychiatric Association 2000).

The ratio of PDD to DDD is often used to determine dosage adequacy. In our study, the PDD to DDD ratio of mirtazapine was 0.8, and for duloxetine, it was 1.1. In contrast, Lahon et al. (2011) conducted a study that revealed a ratio of less than 1 for duloxetine and mirtazapine; for other antidepressants, it was ≥1: In comparison, another study documented a PDD/DDD ratio equal to 1 for sertraline and escitalopram and less than 1 for other antidepressants (Hussain et al. 2018). Subsequently, another study reported that for a majority (78 %) of prescribed antidepressants, the ratio was less than 1. Thus, patients with recurring illnesses were more likely to be treated with antidepressants and other psychotropic medications during their initial bout of depression than patients with just one episode of depression (Van Weel-Baumgarten et al. 2000).

The majority of research participants (69.4%) were given only one antidepressant medication. Dual or triple antidepressant medication was necessary for just 29 % and 1.6 % of patients, respectively. The guidelines do not recommend the concomitant use of more than one antidepressant (American Psychiatric Association 2000). Generally, the observed clinical practice guidelines in this study regarding the prescription of antidepressants were in accordance with the American Psychiatric Association and British Association for Psychopharmacology guidelines (American Psychiatric Association 2000; Cleare et al. 2015).

The average total number of medicines prescribed and the average total number of antidepressants administered to study patients were 2.62±1.01 and 1.3±0.49, respectively. The WHO indicators recommend that the average number of drugs prescribed per encounter be less than three. In addition, there were no encounters with injections prescribed. All prescribed drugs were generic, and all medications were from the Ministry of Health (MOH) Formulary of UAE. These findings are in accordance with the WHO prescribing indicators for measuring drug use in health outpatient facilities (Rode et al. 2014; Ezenduka et al. 2014)

### *3.1. Polypharmacy*

Our study attempted to assess the polypharmacy in patients receiving antidepressants. Numerous studies undertaken in various regions across the globe have examined the occurrence and factors

influencing the use of multiple medications (polypharmacy) among individuals receiving psychiatric drugs. Although polypharmacy is a commonly used term in health science-related research, there is no consensus around a single definition of polypharmacy (Monégat et al. 2014). Still, the literature has conflicting definitions regarding the criteria for polypharmacy (Taghy et al. 2020). Daily use of five or more medicines is the most generally documented definition of polypharmacy (Masnoon et al. 2017). Notably, the numerical delineations of polypharmacy encompass a spectrum spanning from a minimum of two to a maximum of ten or more medications.

Polypharmacy is classified into different categories in various literary works, namely mild, moderate, significant, excessive, and severe polypharmacy, which are determined based on the number of medications involved (Masnoon et al. 2017). Most research incorporated in examining psychiatric polypharmacy has employed the criterion of "utilizing two or more medications belonging to the same chemical class or possessing similar pharmacological actions to treat the same medical condition."(Kukreja et al. 2013). These criteria help to identify instances where multiple medications are being used in a potentially redundant or overlapping manner. However, it is crucial to note that the classification of polypharmacy varies according to the specific setting and subject of study.

We adopted the **N**ational Association of State Mental Health Programme Directors' categorization of psychotropic polypharmacy in our study. Compared to our findings, a study reported same-class (5.8 %), multi-class (32.3 %), adjunctive (62.6 %), augmentation (7.9 %), and total (97.5 %) psychotropic polypharmacy in an outpatient setting (Adeponle et al. 2007). In our study, none of the patients had same-class polypharmacy, and our study documented a lower prevalence of total polypharmacy. In contrast, a study conducted in Palestine revealed that 81 % of the prescriptions exhibited multi-class polypharmacy, whereas adjunctive and same-class polypharmacy were observed in 50 % and 32 % of the prescriptions, respectively (Hattab et al. 2023). The different results might be because the Palestinian study included prescriptions for psychotropic and antipsychotic drugs, which could have led to a higher rate of multi-class, adjunctive, and same-class polypharmacy. It is important to note that our study focused on polypharmacy in patients receiving antidepressants, which could explain the variation in results.

In contrast to our findings, a study reported a lower rate of multi-class polypharmacy (20.9 %) in study patients. It was found that augmenting polypharmacy happened when an SSRI and a benzodiazepine were given together in 13.7 % of cases, while only 1.2 % of patients had tricyclic antidepressant and benzodiazepine treatment. Moreover, only 1 % of the patients were treated with lithium and antidepressants (De las Cuevas et al. 2004). These findings suggest that the combination of an SSRI and a benzodiazepine is more commonly prescribed in an outpatient setting compared to a tricyclic antidepressant and a benzodiazepine. This prescribing pattern may indicate a preference for using newer antidepressant medications in combination with benzodiazepines for treating patients in this setting. Discrepancies in these findings could be attributed to differences in psychiatric training and each country's civil culture and healthcare system (Yang et al. 2018).

In contrast, a research investigation conducted inside a residential psychiatric setting in Belgium revealed the prevalence of psychotropic polypharmacy involving same-class medications to be 71.5 %, multi-class medications to be 82.5 %, augmentation strategies to be 20.6 %, and adjuvant approaches to be 35.5 % (Govaerts et al. 2021). These findings indicate that the frequency of polypharmacy varies greatly depending on the context and population investigated. Healthcare providers need to consider these differences when making treatment decisions and managing medication regimens for their patients.

The accessibility and availability of various medications in various countries, as well as cultural attitudes toward mental health and medication use, could also have an impact on these variations in treatment approaches. Furthermore, it is crucial to note that the study may have only examined a subgroup of individuals, and more research is needed to understand the reasons for these inconsistencies properly.

The prevalence of benzodiazepine augmentation polypharmacy in our study was found to be 23 %, whereas beta-blockers were reported at 9.2 % and antipsychotics at 5.35 %. It is believed that the incorporation of atypical antipsychotics into the treatment regimen of antidepressants can enhance both response and remission rates. Aripiprazole has been granted approval by the FDA for its utilization as an augmentation agent in the therapeutic management of major depressive disorder (Nelson et al. 2008). Furthermore, evidence supports the addition of fluoxetine to olanzapine (Bobo et al. 2009). Quetiapine and aripiprazole should be used in conjunction with either an SSRI or an SNRI. When used with other antidepressants, risperidone has been demonstrated to be effective (Nizamie et al. 2015).

Antipsychotics combined with antidepressants are a potential method for treating major depressive disorder. Researchers discovered that individuals who received antipsychotics and antidepressants in combination had a much better rate of response than those who received monotherapy (Zhou et al. 2015).

Additionally, the remission rate was also improved in the combination therapy group. There is substantial empirical support from controlled trials for the use of augmentation strategies, including antidepressants and benzodiazepines, in the management of generalized anxiety disorder and social anxiety disorder. Benzodiazepines have been found to mitigate the intensity of anxiety symptoms effectively and offer prompt relief in conjunction with SSRIs. The concomitant use of antidepressants with beta-blockers is warranted, particularly in cases where there is a notable presence of bodily manifestations of anxiety (Nizamie et al. 2015). Studies have documented psychotropic polypharmacy as a common prescribing practice and often justifiable. The regular assessment of the concurrent administration of many drugs is necessary in order to improve the quality and safety of mental healthcare (Alharbi et al. 2019).

Although our study did not establish a correlation between the overall prevalence of polypharmacy and demographic, diagnostic, or treatment-related factors, prior research has indicated that variables such as gender, age, marital status, history of hospitalization, presence of severe mental illness, multiple psychiatric diagnoses, and inadequate healthcare staffing are all associated with the use of multiple psychotropic medications (Ishtiak-Ahmed et al. 2023; Costa et al. 2017). These findings imply that particular risk factors and contextual variables may lead to the usage of psychotropic polypharmacy in mental health care. Understanding these associations can help inform targeted interventions and policies to improve the appropriateness and safety of medication management in this population (Kukreja et al. 2013).

The investigation undertaken had several limitations. The investigation was first done at a singular center, including a constrained sample size, thus limiting its ability to generalize findings accurately. Furthermore, the study only lasted a few months. Some patients' social and medical backgrounds and information about over-the-counter medications were missing from their electronic medical records. The study hospital's antidepressant options were limited. Because this was a cross-sectional observational study, no causal interpretation of observed findings could be made.

### *3.2. Conclusions*

Our study findings propose that most psychiatric outpatients receive antidepressants as monotherapy, most commonly for major depressive disorder. SSRIs were the most frequently prescribed antidepressants, probably due to their safety profiles compared to other antidepressants. The most frequently prescribed drug was mirtazapine, and antipsychotics were the most frequently co-administered drugs. Rational antidepressant prescribing was effectively implemented in the study setting and was in concordance with the recommendations of the international guidelines. The study did not document any same-class polypharmacy. Psychiatric polypharmacy was evident in our study, highlighting the importance of careful review by healthcare providers considering the potential risks and benefits of combining multiple medications to ensure optimal patient outcomes. None of the demographic, illness, or treatment-related variables were associated with total polypharmacy. Further research is needed to understand the reasons behind this prescribing pattern and its impact on patient outcomes. The study warrants a large multicenter study to generalize the findings of this study.

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**Supplementary table 1: Prescription analysis with selected WHO drug use indicators**

| WHO Indicators | Values |
|---|---|
| Total number of prescriptions | 131 |
| Total number of drugs | 343 |
| Average number of drugs prescribed per prescription | 2.62 ± 1.01 |
| % of the drugs prescribed by generic name | 100% |
| % of the drugs supplied from the hospital pharmacy | 100% |
| % of injectable drugs prescribed per day | 0.0% |
| Total number of antidepressant drugs | 173 |
| The average number of antidepressants prescribed per prescription | 1.3 ± 0.49 |
| % of drugs prescribed from Ministry Of Health (MOH) Formulary of UAE | 100% |
| % of patients treated without drugs | 0% |

**Supplementary Table 2: Correlation of prescribed antidepressants and diagnosis**

| Psychiatric Diagnosis | Antidepressants | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | MI | E | FT | AG | D | V | C | P | AM | FA | MA | I |
| Major Depressive Disorder | 11(34.3) | 14(48.2) | 7(25) | 9(40.9) | 4(22.2) | 5(33.3) | 0 | 3(50.0) | 3(50.0) | 1(20.0) | 0 | 0 |
| Generalized Anxiety Disorder | 6(18.7) | 3(10.3) | 5(17.8) | 3(13.6) | 3(16.6) | 1(6.6) | 0 | 1(16.6) | 0 | 0 | 0 | 0 |
| Obsessive-Compulsive Disorder | 0 | 1(3.4) | 2(7.1) | 2(9.0) | 2(11.1) | 1(6.6) | 6(75) | 1(16.6) | 1(16.6) | 2(40.0) | 0 | 0 |
| Major Depressive Disorder with Psychotic Features | 1(3.1) | 2(6.8) | 2(7.1) | 1(4.5) | 0 | 2(13.3) | 1(12.5) | 0 | 0 | 0 | 29(100) | 0 |
| Substance Abuse | 2(6.2) | 0 | 0 | 1(4.5) | 2(11.1) | 1(6.6) | 0 | 0 | 1(16.6) | 0 | 0 | 0 |
| Adjustment Disorder with Mixed Anxiety and Depressed Mood | 1(3.1) | 1(3.4) | 0 | 2(9.0) | 0 | 0 | 0 | 1(16.6) | 1(16.6) | 0 | 0 | 0 |
| Bipolar Disorder, Depressed Episode | 0 | 1(3.4) | 1(3.5) | 0 | 0 | 1(6.6) | 0 | 0 | 0 | 0 | 0 | 0 |
| Anxious Depression | 1(3.1) | 2(6.8) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1(20.0) | 0 | 0 |
| Adjustment Disorder with Depressed Mood | 2(6.2) | 0 | 1(3.5) | 1(4.5) | 2(11.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Borderline Personality Disorder | 1(3.1) | 1(3.4) | 0 | 0 | 1 | 1(6.6) | 0 | 0 | 0 | 0 | 0 | 0 |
| Somatization Disorder | 1(3.1) | 0 | 0 | 1(4.5) | 2(11.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Bipolar Disorder Manic episode | 0 | 0 | 1(3.5) | 0 | 0 | 2(13.3) | 0 | 0 | 0 | 0 | 0 | 0 |
| Dementia | 3(9.3) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Panic Disorder | 0 | 0 | 1(3.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Schizophrenia | 0 | 0 | 1(3.5) | 0 | 0 | 0 | 1(12.5) | 0 | 0 | 0 | 0 | 0 |
| Adjustment Disorder with Anxiety | 0 | 1(3.4) | 0 | 0 | 0 | 1(6.6) | 0 | 0 | 0 | 0 | 0 | 0 |
| Schizoaffective Disorder | 0 | 0 | 2(7.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Bipolar Disorder I | 0 | 1(3.4) | 1(3.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Bipolar Disorder II | 0 | 0 | 1(3.5) | 0 | 1(5.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Conversion Disorder | 0 | 0 | 1(3.5) | 1(4.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Post-Traumatic Stress Disorder | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1(20.0) | 0 | 0 |
| Social Phobia | 0 | 0 | 1(3.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Premenstrual Tension Syndromes | 1(3.1) | 1(3.4) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Psychosis, Paranoid | 0 | 0 | 1(3.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Intellectual Disability | 0 | 1(3.4) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Alcohol use Disorder | 0 | 0 | 0 | 1(4.5) | 1(5.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Chronic nausea anxiety | 1(3.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Mood Insomnia | 1(3.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Autistic Disorder | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1(50.0) |
| Nocturnal Enuresis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1(50.0) |

MI: Mirtazapine; E: Escitalopram; FT: Fluoxetine; AG: Agomelatine; D: Duloxetine; V: Venlafaxine; C: Clomipramine; P: Paroxetine; AM: Amitriptyline; FA: Fluvoxamine; MA: Maprotiline; I: Imipramine.