

Prevalence and factors associated with polypharmacy among patients treated for psychiatric disorders in Palestine

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Received: (26/11/2021), Accepted: (3/3/2022)

ABSTRACT

Objectives: Polypharmacy has emerged as a standard clinical practice in treating psychiatric disorders. This study investigates the prevalence of polypharmacy among patients treated for common psychiatric disorders and the factors associated with this practice. **Methods:** The current cross-sectional study included all the prescriptions that were issued over the period between October 2018 and January 2019 for patients diagnosed with anxiety, depression, schizophrenia, schizoaffective and bipolar disorders in an outpatient psychiatry clinic in the north of West Bank, Palestine. **Results:** A total of 1045 prescriptions were analyzed. The mean age of the patients for whom the prescriptions were made was 47.3 years (SD= 13.6); half were between 36 and 55 years old, and one-third were females. Half of the cases were diagnosed with schizophrenia, while the rest were diagnosed with bipolar, depression, schizoaffective, or anxiety. Polypharmacy was found in 877 prescriptions (84%). One-third of the patients have been prescribed two drugs, while one-third received three, and the rest received four or more. Patients with schizophrenia, schizoaffective and bipolar disorders have a higher rate of polypharmacy than patients with anxiety and depression ($p=0.000$). Patients aged 36 and 55 were more likely to have polypharmacy than younger or older ones ($p=0.001$). The rate of polypharmacy was not different according to gender. Multi-class, adjunctive, and same-class polypharmacy was found in 81%, 50%, and 32% of the prescriptions. **Conclusions:** Our results suggest that polypharmacy among psychiatric patients is common in Palestine. Age and diagnosis should pay more attention to selected patients to avoid harmful drug-drug interactions.

Keywords: Psychopharmacology, Psychiatric Disorders, Polypharmacy, Prevalence.

INTRODUCTION

Polypharmacy has become a frequent clinical practice in treating various psychiatric disorders. Over the last few decades, the frequency of polypharmacy among psychiatric patients has ranged from 13 to 90 percent, significantly decreasing individuals on monotherapy [1]. Using two or more mental drugs in the same patient or two or more medications of the same chemical class of pharmacologic activities to treat the same problem is known as psychiatric polypharmacy [2].

Polypharmacy is influenced by several elements, including disease biology, the physician, the patient, and sociocultural circumstances. The presence of refractory disease or disease misdiagnoses/missed diagnoses is a

biological variable. Physicians can also play a role in this regard, as many of them believe that treating psychiatric diseases with a single medication is insufficient, especially when there is a need to treat a specific symptom or co-morbidities found in psychiatric patients or the need to treat the primary drugs' side effects pharmacologically. Patient factors that cause polypharmacy include the consumer-choice paradigm and patient noncompliance. Finally, the social aspect comprises a market-based system that relies on consumer choice, a fragmented health-care system, and pressures on treating physicians, who may begin the patient on numerous therapies to achieve speedy improvement. [3].

Due to the increasing prevalence of psychiatric polypharmacy, the "National Association of State Mental Health Program Directors (NASMHPD)" classified this practice into different types [4]. The first type is termed "same-class polypharmacy," which refers to "the use of more than one medication from the same class," while the second type, "multi-class polypharmacy," stands for "the use of more than one medication from different classes for the same symptom cluster." This is the most prevalent type of polypharmacy, with the most common example being the use of benzodiazepines and selective serotonin reuptake inhibitors (SSRIs), followed by the use of tricyclic antidepressants (TCA) and benzodiazepines [4]. The third type of polypharmacy is termed "adjunctive polypharmacy," which means "the use of a medication to treat the side effects of another medication from a different pharmacological class," such as the use of anticholinergic drugs in schizophrenia patients to manage the extrapyramidal symptoms that come with antipsychotic therapy. [5]. "Augmentation polypharmacy" refers to "the use of one medication at a lower-than-normal dose and another medication from a different class in a full therapeutic dose for the same symptom cluster." "Total polypharmacy" is "the total count of medications used in a patient, or total drug load" [1].

To our knowledge, polypharmacy in psychiatry practice was not addressed previously in Palestine. This study aimed to assess the prevalence of polypharmacy among psychiatric patients in an outpatient setting and investigate factors associated with it in an occupied country, Palestine.

METHODS

Study design and setting

This retrospective cross-sectional study focused on registered patient prescriptions, which included information on age, sex, patients' diagnoses, and the prescribed psychiatric medicines, all of which were collected using a data collection form. Atypical antipsychotics, typical antipsychotics, TCAs, SSRIs, benzodiazepines, anticonvulsants, lithium, and anticholinergics were the eight classes of medications.

There is just one major psychiatric referral hospital in Bethlehem in the West Bank, which provides secondary treatments to the entire West Bank population. Outpatient clinics, distributed throughout the West Bank cities, provide primary psychiatric health treatments.

The study was conducted in a mental outpatient clinic in the northern West Bank.

The outpatient prescriptions are stored in a database on Avicenna software, used by the Palestinian Ministry of Health's medical centers. The identity numbers (ID) of the patients who were followed up at the clinic were first collected from the clinic's registry. The ID number was then used to search for each patient's prescription. All prescriptions written from October 2018 to January 2019 were gathered. Assuming that each patient visits the clinic once a month, the written prescriptions should indicate the total number of prescriptions written. However, the study was conducted over four months to detect any missing prescriptions owing for any reason. Only those prescriptions issued for individuals diagnosed with depression, anxiety disorders, schizophrenia, bipolar affective disorder, and schizoaffective disorders were included in this study. We included the patient's most recent prescription, which contained the prescribed drugs.

Statistical analysis

Collected data were analyzed using SPSS® software, Version 21 (IBM Corp, USA). For each form of polypharmacy, the frequencies and rates were calculated and compared to gender, age, and diagnosis. Each type of polypharmacy was subjected to the same analysis. The Chi-square test was used to analyze characteristics linked to total polypharmacy and other forms of polypharmacy, with p-values less than 0.05 considered significant.

RESULTS

Sample size and general characteristics of the patients

For this study, a total of 1045 prescriptions were used. The characteristics of the patients for whom the prescriptions were written are shown in Table 1. Around two-

thirds of the patients (65%) were males, with an average age of 47.3 ± 13.6 years (mean \pm SD), and around half of them (52.8%) were between the ages of 36 and 55. Almost half of the patients were diagnosed with

schizophrenia, with the remainder having bipolar disorder (15.8%), depression (15.2%), schizoaffective disorder (11.1%), and anxiety (5.1%), respectively.

Table (1): Characteristics of patients in an outpatient psychiatric clinic in Palestine.

	Characteristics (n=1045)	Frequency (n)	Percentage (%)
Gender	Male	674	64.5
	Female	371	35.5
Age class (years)	2-17	8	0.8
	18-35	227	21.7
	36-55	539	51.6
	≥ 56	271	25.9
Diagnosis	Schizophrenia	552	52.8
	Bipolar disorder	165	15.8
	Depression	159	15.2
	Schizoaffective disorder	116	11.1
	Anxiety disorder	53	5.1

Prevalence and factors associated with polypharmacy

In 877 prescriptions, polypharmacy was discovered (84 percent). Approximately a third of the patients (n=274, 31%) were prescribed two medications, 245 (28%) were prescribed three drugs, and 141 (16.1%) were prescribed four drugs. The most recommended combinations were fluphenazine/trihexyphenidyl, haloperidol/trihexyphenidyl, and chlorpromazine/trihexyphenidyl.

The rate of polypharmacy was not different according to gender. However, age, class, and diagnosis affected the rate of polypharmacy. As shown in (Table 2), patients aged between 36 and 55 years were more likely to have prescriptions with polypharmacy than younger or older ones (p-value = 0.001). Patients diagnosed with depression or anxiety were less likely to have polypharmacy than those diagnosed with schizophrenia, bipolar, or schizoaffective disorders (p-value < 0.001).

Table (2): Distribution of polypharmacy according to gender, age, class, and diagnosis.

	Characteristics (n=1045)	Polypharmacy, n (%)	P-value
Gender	Male (674)	560 (83.1)	0.321
	Female (371)	317 (85.4)	
Age class (years)	2-17 (8)	4 (50)	0.001
	18-35 (227)	183 (80.6)	
	36-55 (539)	472 (87.6)	
	≥ 56 (271)	218 (80.4)	
Diagnosis	Schizophrenia (552)	494 (89.5)	<0.001
	Depression (159)	103 (64.8)	
	Anxiety disorder (53)	27 (50.9)	
	Bipolar disorder (165)	148 (89.7)	
	Schizoaffective disorder (116)	105 (90.5)	

Prevalence and factors associated with different types of polypharmacy

Same class polypharmacy" was found in 332 (32%) prescriptions. The most common prescribed combinations were fluphenazine/chlorpromazine, fluphenazine/haloperidol, haloperidol/ chlorpromazine, clozapine/ risperidone, and amitriptyline/ clomipramine, respectively. Multi-class polypharmacy was found in 842 (81%) of the prescriptions. The most common prescribed combinations were fluphenazine/trihexyphenidyl, haloperidol/ trihexyphenidyl, and chlorpromazine/ trihexyphenidyl, respectively. "Adjunctive polypharmacy was found in 519 (50%) prescriptions. The most common prescribed combinations were the same as those for multi-class polypharmacy.

As shown in (table 3), the rate of the different types of polypharmacy was not different according to gender. However, same-class polypharmacy was more common among patients aged 36 to 55 than in other age classes. Moreover, same-class polypharmacy was more common among patients diagnosed with schizophrenia than other psychiatric disorders. Multi-class polypharmacy was higher in patients diagnosed with schizophrenia, schizoaffective and bipolar disorders than in those diagnosed with depression and anxiety. Adjunctive polypharmacy was more common among patients aged 36 to 55 than in other age classes. Also, Adjunctive polypharmacy was more common among patients diagnosed with schizophrenia and schizoaffective disorders than other psychiatric disorders.

DISCUSSION

This study explored the prevalence and factors associated with polypharmacy in patients treated for common psychiatric disorders in an outpatient psychiatry clinic in Palestine. The prevalence of polypharmacy was very high (84%) and correlated with the diagnosis and patient's age, while no correlation was found with gender.

Concerning the prevalence of polypharmacy in this study, it was high compared to other studies, where the prevalence of polypharmacy was lower. For

example, the rate of polypharmacy in the "Canary Islands health service clinical records database" was 41.9%, and the overall prevalence of polypharmacy among patients followed at psychiatric outpatient clinics in two tertiary hospitals in Saudi Arabia was 46.9% [6–9]. This could be explained by the fact that half of our sample population was patients diagnosed with schizophrenia, a factor that was significantly associated with polypharmacy. Consequently, this high rate of polypharmacy was associated with a high rate of Drug-Drug interactions; half of these were severe and necessitated drug discontinuation as they could harm patients' health [10]. Another consequence of polypharmacy is the financial burden, as irrational drug prescriptions could unjustifiably increase the cost of treatment and waste money, a problem that cannot be neglected, especially in a country with a fragile economy like Palestine.

Concerning the factors associated with polypharmacy, diagnosis and age were significantly associated. It was observed that patients with schizophrenia, schizoaffective and bipolar disorders have a higher polypharmacy rate than patients with anxiety and depression. This finding is similar to another previous study made in East Asia, which found that schizophrenia is a factor that increases the rate of polypharmacy [11]. It was also observed that patients whose age was between 36 and 55 years were more likely to have prescriptions with polypharmacy compared to younger or older ones, and this is in line with a previous study conducted in Saudi Arabia, which found that patients with psychosis and bipolar disorders, especially those aged 25–45 years are exposed to high psychotropic polypharmacy [9]. The rates of polypharmacy were not different according to gender. This observation was similar to other studies that did not report any difference in polypharmacy rates. However, few studies reported a correlation with gender, like a study in Sweden that reported that females with depression were more prone to polypharmacy than males [12].

Regarding the prevalence of the different types of polypharmacy, same-class polypharmacy was the most common type.

The four most commonly prescribed combinations consisted of two typical antipsychotics for treating schizophrenia and schizoaffective disorders. This practice could be justified as one of the options used in refractory schizophrenia who did not adequately respond to at least two trials of antipsychotic medication of adequate dose and duration [13]. For treating such patients, two other strategies are often employed: increasing the dose of the currently administered antipsychotic or switching to another atypical antipsychotic [14]. The fifth most common combination used in same-class polypharmacy was amitriptyline/clomipramine. This may also be due to refractory depression, which typically refers to inadequate response to at least one antidepressant trial of adequate doses and duration [15] and can be treated by pharmacological augmentation strategies that include treatment with a combination of antidepressants [16].

In Multi-class polypharmacy, the most commonly prescribed combinations consisted of trihexyphenidyl added to typical antipsychotics. These combinations were the same as those for adjunctive polypharmacy, where the use of anticholinergic drugs and typical antipsychotics was observed among most of the patients with schizophrenia. This combination is commonly employed to control the extrapyramidal symptoms associated with typical antipsychotic drugs [6,17].

The study setting is restricted to mental health services; thus, non-psychotropic drugs' use was not documented. If considered, the rate of polypharmacy might increase. Besides, the short duration of the study might affect the results since possible seasonal variations in the course of the disease might impact the prescribing patterns over time.

CONCLUSION

Our results suggest that polypharmacy among psychiatric patients is common in Palestine. Age and diagnosis should pay more attention to selected patients to avoid harmful drug-drug interactions. The results demonstrated the need to review the risks and causes that lead to polypharmacy to help minimize the associated risks and to improve the overall mental health care in Palestine.

Ethics approval and consent to participate

Ethics approval was obtained from the Institutional Review Board of An-Najah National University.

Consent for publication

We declare that all of the authors have read and approved the paper. The paper has not been published previously, nor is it considered by any other journal.

Availability of data and materials

Not applicable

Author's contribution

Suhail Hattab: conceptualization, writing first draft, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, and writing review and editing. **Naim Kittana:** writing first draft, formal analysis, inquiry, methodology, resources, software, validation, visualization, and writing review and editing. **Layth Qasarweh:** writing first draft, data curation, formal analysis, inquiry, resources, software, validation, visualization, and writing review and editing. **Malek Ahmaro:** writing first draft, data curation, formal analysis, research, resources, software, validation, visualization, and writing review and editing. **Yazid Atatre:** writing first draft, data curation, formal analysis, research, resources, software, validation, visualization, and writing review and editing. **Yasin Tayem:** ideation, methodology, resources, software, validation, visualization, writing review, and editing.

Competing interest

The authors declare that there are no conflicts of interest.

FUNDING

None

ACKNOWLEDGMENTS

The authors would like to thank An-Najah National University and the Palestinian Ministry of Health for making this research possible.

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