

Pharmacist-led Review of Drug Utilization of Antipsychotic Medications in a Tertiary Government Hospital in Cebu City, Philippines

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ABSTRACT

Background. Mental health remains a significant public health concern in the Philippines, with schizophrenia posing major burdens on individuals, families, and society. Antipsychotic drugs are still the most effective treatment. However, the prevalence of irrational drug use in psychiatric patients, including antipsychotic polypharmacy and non-adherence, has been associated with negative outcomes such as increased adverse effects, rehospitalization, higher cost, and impaired quality of life. To address this, drug utilization studies are crucial for developing strategies to optimize healthcare resource use, address drug use issues, promote rational prescribing, and improve patient access.

Objectives. The study evaluated the prescribing patterns of antipsychotic medications among inpatients with schizophrenia in a tertiary government hospital in Cebu City, Philippines, which aimed to identify patterns of drug use, potential drug therapy problems, and examine the appropriateness of use.

Methods. The study utilized a retrospective observational design. A review of medical records was carried out from January 1, 2022, to December 31, 2022. Data collected includes patient demographics, diagnosis, and prescribed antipsychotic medications. Descriptive statistics in Microsoft Excel® were used to report findings, and a Poisson regression model in IBM SPSS Software version 25 was used to analyze the data.

Results. A total of 109 patient medical records were screened, with 33 records selected based on the inclusion criteria. Risperidone (35.4%) was the most prescribed antipsychotic drug. A higher inclination towards the use of second-generation antipsychotics was observed than first-generation antipsychotics. Paliperidone palmitate injection had the highest consumption (4.8056 defined daily doses/100 bed days) among the antipsychotics. It was found that underinvestment in newer medications limits patient access. Significant relationships were found between the number of drugs per medication order and male gender ($p = 0.002$) and substance abuse disorder ($p = 0.07$). The average number of antipsychotic drugs prescribed per medication record was 1.97, while the average number of drugs per patient was 3.82. All the medications were prescribed by their generic names and sourced from the Philippine National Drug Formulary. Injectable drugs accounted for 19.05% of the total medications. Drug therapy problems, such as drug-drug interactions (82%) and therapeutic duplication (58%), were prevalent. There were substance use disorders (9.09%) as a comorbidity among patients studied.



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Conclusion. There is a prescribing trend towards second-generation antipsychotics, with risperidone being the most frequently prescribed antipsychotic medication. Utilization patterns of antipsychotics generally conformed to the WHO standard recommendations. This study highlights the high consumption of paliperidone palmitate injection, which calls for further research on antipsychotic consumption in patients with comorbid substance use disorder. Strengthening pharmacist involvement in patient care alongside policy-driven approaches can improve access, optimize therapy, and ensure quality antipsychotic medication use.

Keywords: *drug utilization, antipsychotics, substance-related disorders, schizophrenia, risperidone*

INTRODUCTION

Schizophrenia is a disabling and chronic psychiatric disorder characterized by hallucinations, delusions, and impairment of cognitive and social functioning. In the Philippines, one million Filipinos suffer from schizophrenia.¹ Several effective treatment approaches are available, including medication, psychoeducation, family interventions, and psychosocial rehabilitation.¹⁻³

Antipsychotic medications remain the most effective treatment. They are classified into first-generation antipsychotics (FGAs) or typical antipsychotics, and second-generation antipsychotics (SGAs) or atypical psychotics. FGAs primarily work by inhibiting dopamine (D_2) receptors, while SGAs have a broader mechanism of action, exerting a dual antagonistic effect on both D_2 and serotonin receptors. This allows SGAs to manage a wider range of symptoms, including positive, negative, and cognitive symptoms of schizophrenia.⁴ Despite the proven efficacy of antipsychotic medications, non-adherence is common among psychiatric patients. The Adherence in Schizophrenia (ADHES) survey in the Philippines, which included 71 psychiatrists, highlighted that while 48% of patients were fully adherent ($\geq 90\%$ of prescribed doses), 23% took only 30% of their medication.⁵ The reported poor adherence contributes to negative outcomes, leading to increased hospitalization rates and higher healthcare costs.^{6,7} Furthermore, the annual cost of treating individuals with schizophrenia in private settings ranged from approximately ₱19,095 to ₱306,942 for inpatient care, and from ₱21,489 to ₱1,464,817 for outpatient services. Only 5.6% of the national budget in 2024 was allocated towards the health sector. This limited allocation of resources imposes significant barriers for Filipinos, including high out-of-pocket expenses and limited access to affordable mental health care.^{8,9}

Addressing these challenges requires responsive approaches such as drug utilization reviews (DUR), which can help develop strategies to optimize healthcare resources, address drug-related issues, promote rational prescribing, and

improve patient access in resource-limited settings. With no standardized treatment guidelines for schizophrenia in the Philippines, periodic assessment of prescribing practices in health care facilities is essential to evaluate the current treatment approaches and provide policymakers with relevant data to refine drug procurement and prescribing policies.¹⁰ Additionally, research suggests that implementing a retrospective DUR program can identify drug use issues, educate practitioners on rational prescribing, reduce physician interventions, and significantly impact compliance with prescribing indications in the future, benefiting both individual patients and the specific target population.¹¹ To date, the clinical prevalence of antipsychotic drug utilization in hospitals in the Philippines remains unknown. This study was the first to evaluate the antipsychotic drug utilization among inpatients diagnosed with schizophrenia at a tertiary government hospital, aimed to examine prescribing patterns based on World Health Organization (WHO) indicators, and quantify drug consumption using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) system. Furthermore, this study identifies potential drug therapy problems and analyzes the relationship between patient sociodemographic factors and antipsychotic use.

METHODS

Study Design and Setting

The study employed a retrospective observational design. Medical records of inpatients with schizophrenia admitted at a general tertiary government-owned hospital (with a 1500-bed capacity) in Cebu City, Philippines, from January 1 to December 31, 2022, were reviewed.

The Center for Behavioral Sciences, situated in a tertiary government hospital, is a nationally recognized mental health facility that delivers comprehensive psychiatric and psychological services to residents of Cebu City and its neighboring provinces.

Inclusion and Exclusion Criteria

A medical record is included if it satisfies the following conditions: (1) diagnosed with schizophrenia; (2) prescribed antipsychotic medications; and (3) adult patients, aged 18 to 65 years, who were admitted or transferred to the psychiatric department during the specified period. We excluded medical records (1) of children, adolescents, and pregnant patients; (2) with incomplete drug information that cannot be assessed for dose, dosage form, frequency, duration (days/months), or dosage instructions; (3) of newly diagnosed patients who have not been prescribed antipsychotic medications; and (4) of patients with other psychiatric disorders other than schizophrenia. Medical records with missing data were excluded from the analysis to maintain data integrity. No data imputation methods were applied.

Research Instrument and Data Collection

An electronic data collection form was created using Epi Info 7.2™, developed by the Centers for Disease Control and Prevention, and Microsoft Excel 365 (Microsoft Corporation, USA). The collected data included patient demographics (age and gender), diagnosis, comorbidities, prescribed medications, dosage, dosage form, route of administration, frequency, duration of the medications (start and end dates), length of hospital stay, and drug therapy problems. To ensure anonymity of the eligible medical records, a unique code consisting of a combination of letters and three numerical figures was used. A pharmacist from the hospital's Department of Pharmacy served as a co-investigator and facilitated access to patient medical records in collaboration with the hospital's medical records office. All data were stored on password-protected, encrypted devices and retained for one year after manuscript submission. Afterwards, data on all devices was securely erased, including permanent deletion from digital trash bins, to ensure complete protection.

All prescribed antipsychotics were analyzed using WHO Prescribing Indicators. The following parameters were assessed: (1) the average number of drugs prescribed per medication record, (2) the average number of antipsychotics per medication order, (3) the percentage of drugs prescribed by generic name, (3) the percentage of encounters involving an injection, and (4) the percentage of medicines prescribed from the National Formulary. Additionally, the WHO anatomical therapeutic chemical (ATC)/defined daily dose (DDD) methodology was applied to determine drug consumption, expressed as defined daily dose per 100 bed-days. Drug consumption was calculated using the formula:

Equation 1:

$$\text{DDD}/100 \text{ bed days} = \frac{\text{Number of units administered in a given period (mg)}}{\text{DDD (mg)} \times \text{number of days in period} \times \text{number of beds} \times \text{occupancy index}} \times 100$$

Equation 2:

$$\text{Occupancy index} = \frac{(\text{Total in patient service days for a period})}{(\text{Total in patient bed counts} \times \text{No. of days in the study period})}$$

where bed-day is defined as a day during which a patient was confined to a hospital bed and stayed overnight, and the occupancy index was obtained from the 2022 Annual Health Facility Statistical Report of the tertiary hospital.

To identify drug therapy problems, prescribed medication from patient records was evaluated using treatment guidelines and online resources from the Drugbank, Elsevier Clinical Pharmacology by Clinicalkey Texas Health and Human Services, MIMS Philippines, Medscape, Medicine Access Program for Mental Health (MAP-MH) Guidelines, the American Psychiatric Association, and the Royal Australian and New Zealand College of Psychiatrists. All drug pairs given at the same time, as recorded in patient medical records,

were checked for significant drug-drug interactions. Only medications administered on the same day were analyzed for drug-drug interactions using an online drug interaction tool, DrugBank. The prescribing order of each medication was also recorded. In this study, Elsevier Clinical Pharmacology was used to detect cases of therapeutic duplication or drugs from the same chemical or pharmacological class that were prescribed and administered together.

After identifying drug therapy problems, the appropriateness of antipsychotic use was evaluated using a modified medication appropriateness index adopted from Hanlon and Schmadier.¹² The tool assessed indication, dosage, drug interactions, contraindications, and therapeutic duplication. Each medication was rated using a 3-point Likert scale, with median scores interpreted as 0 ("Appropriate"), 1 ("Moderately Appropriate"), and 2 ("Inappropriate"). To ensure reliability, a pilot study was conducted on ten medical records. Intra-observer reliability was assessed by comparing evaluations conducted at different times. The principal investigator assessed the records initially, followed by the co-investigator one week later using the same sample. In cases of disagreement, the research consultant reviewed the results for confirmation. Additionally, the tool's reliability was verified by measuring Cronbach's alpha.

Data Processing and Statistical Analysis

The study utilized descriptive statistics, and the data gathered were reported in frequencies, means, and percentages. Poisson regression analysis was used to evaluate the relationship between two independent variables (number of drugs per medication order and number of antipsychotics per medication order) and three categorical dependent variables (age, gender, and comorbidities). Furthermore, Poisson regression was employed because the outcome variables represent count data, which are non-negative and follow a Poisson distribution. This model is suitable for analyzing the effect of categorical predictors on count outcomes, as it accounts for the discrete rather than continuous nature of the data.¹³ Analysis was performed using Social Sciences (SPSS) Version 25® developed by IBM Corporation.

Ethical Considerations

The study protocol was approved by the Vicente Sotto Memorial Medical Center Research Ethics Committee (REC CODE: VSMHC-REC-O-2023-198).

RESULTS

Only 33 medical records were found to meet the inclusion criteria; the remaining medical records (n = 73) were excluded due to the following reasons, (1) incomplete/missing chart, (2) medical records not within the admission and discharge data, (3) patients had been diagnosed with other psychotic disorders and personal risk factors, and (4) age did not fall within the specified age range (Figure 1).

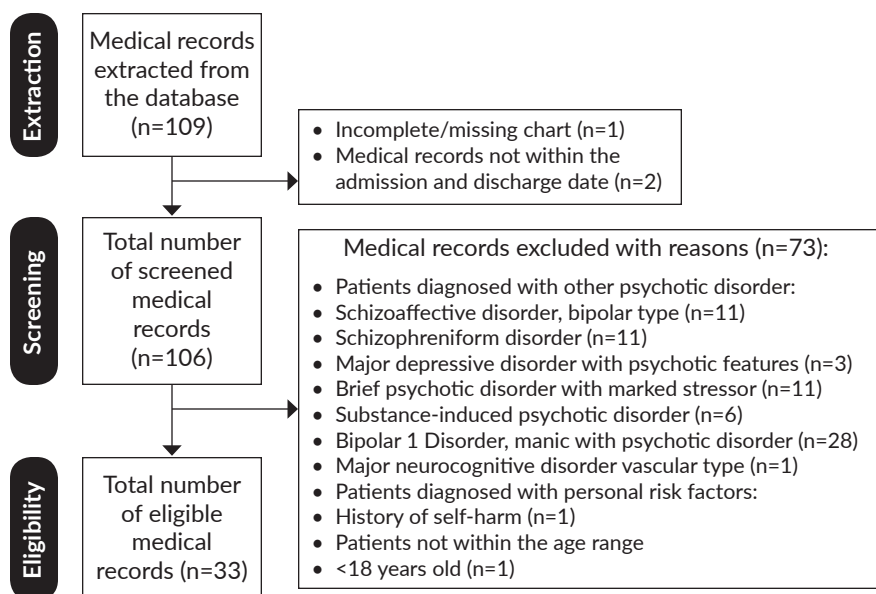


Figure 1. PRISMA study flow diagram.

Table 1. Sociodemographic and Clinical Characteristics of Inpatients with Schizophrenia (N = 33)

Parameters	Total n (%)
Gender	
Male	21 (64)
Female	12 (36.)
Age (years)	
18-22	5 (15)
23-27	6 (18)
28-32	5 (15)
33-37	5 (15)
38-42	6 (18)
43-47	2 (6)
48-52	2 (6)
53-57	2 (6)
Mean (SD)	33.73 (10.50)
Comorbidities	
Substance-abuse	5 (9)
Hypertension	3 (3)
Asthma	1 (2)

From the eligible medical records, the majority of the patients (63%) were male. The study population's age varied between 18 and 57 years, with a mean age of 33.73 years (SD 10.50). Most of the patients ($n = 6$, 18%) belong to the age groups 23 to 37 and 38 to 42 years. The common comorbid condition was substance abuse ($n = 5$), followed by hypertension ($n = 3$) and asthma ($n = 1$). Details about the other sociodemographic profile and clinical characteristics are shown in Table 1.

A total of 126 drugs were prescribed in 33 medical records during the study period, of which 65 (51.6%) were antipsychotics. The data showed an average of 1.97 antipsychotic medications while the overall average of drugs prescribed per patient was 3.82. All oral and injection formulation of antipsychotics (100%) were prescribed using their generic name and sourced from the Philippine National Drug Formulary. Additionally, 24 (19.1%) of these were administered via parenteral route. The results of the WHO Prescribing Indicators are summarized in Table 2.

The most frequently prescribed antipsychotic was risperidone (35%), followed by olanzapine (15%), paliperidone (14%), chlorpromazine (11%), haloperidol decanoate injection (9%), clozapine (6%), fluphenazine decanoate injection (5%), and the same percentage (2%) for oral haloperidol, aripiprazole, and quetiapine. Table 3 shows the distribution of the antipsychotics prescribed. Out of 65 antipsychotics prescribed, 48 (74%) were second-generation antipsychotics and 17 (26%) were first-generation antipsychotics.

Following the assessment of the frequency of the antipsychotics, the relationship between the number of prescribed drugs per medication order and number of antipsychotics prescribed to the demographic characteristics (e.g., age, gender and comorbidities) was assessed. Table 4 displays a

summary of results using Poisson regression model on the number of drugs per medication order.

Based on the results, being male and having substance abuse disorder were considered significant in the model. The rest of the variables, including age, hypertension, and asthma, were not significant enough to establish such relationships.

In terms of the relationship between the number of antipsychotics prescribed per medication order and demographic characteristics, the results show that none of the variables were considered significant at the 95% confidence level (Table 5). The observed variation in statistical significance across factors in Tables 4 and 5 reflects sample size limitations and sensitivity of the model. A single significance level, commonly 95%, is typically used in inferential analysis; however, given the variability of the results, specific confidence levels were reported to reflect the strength of association for each factor rather than omitting potentially relevant variables.

The total antipsychotic consumption was 7.8556 DDD per 100 bed-days. Of the 65 antipsychotics prescribed, paliperidone palmitate (4.86 DDD per 100 bed days) has the highest consumption. Table 6 presents the DDD per 100 bed-days of antipsychotic drugs listed currently in the Anatomical Therapeutic Chemical (ATC) classification system.

Among the 33 medical records evaluated, drug-drug interaction was the common drug therapy problem (DTP) identified, occurring in 27 medical records (81.8%), followed by therapeutic duplication (57.6%) (Table 7).

Furthermore, drugs taken on the same day were screened for drug-drug interactions using an online tool, Drugbank.com. Among 93 drug-drug interactions identified, majority (81%) were classified as moderate interaction, (Figure 2).

From the identified drug therapy problems, appropriateness of use was further assessed. The findings revealed that

Table 2. Prescribing Practices Using WHO Core Prescribing Indicators^{14,15} (N = 126)

WHO Core Prescribing Indicators	WHO Standard	Result
Average number of drugs per encounter	1.6-1.8	3.82
Average number of antipsychotics per encounter	1.6-1.8	1.97
Percentage of drugs prescribed by generic name	100.00%	100.00%
Percentage of injectable drugs prescribed	13.40%-24.10%	19.05%
Percentage of drugs prescribed from the national formulary	100.00%	100.00%

Table 3. Utilization of Antipsychotics in Tertiary Government Hospital of Cebu City (N = 65)

Antipsychotic Medication	No. of Antipsychotics Prescribed	Percentage
Risperidone	23	35
Olanzapine	10	15
Paliperidone palmitate, injection	9	13
Haloperidol decanoate, injection	6	9
Clozapine	4	6
Fluphenazine decanoate, injection	3	5
Haloperidol, oral	1	2
Quetiapine	1	2
Aripiprazole	1	2

Table 4. Relationship between Demographic Characteristics to the Number of Drugs Prescribed

Variables	Beta Estimates	p-value	Interpretation
Age	0.007167	0.41	Not significant
Gender (Female)	0.213001	0.29	Not significant
Gender (Male)	0.952786 ¹	0.002	Significant up to 99% confidence
Substance use	0.411905 ²	0.07	Significant up to 90% confidence
Hypertension	-0.163680	0.69	Not significant
Asthma	-0.044673	0.93	Not significant

¹Significant at the 1% level ($p < 0.01$)²Significant at the 10% level ($p < 0.10$)**Table 5.** Relationship of Demographic Characteristics to the Number of Antipsychotic Drugs Prescribed

Variables	Beta Estimates	p-value	Interpretation
Age	0.004061	0.74	Not significant
Gender (Female)	0.106253	0.71	Not significant
Gender (Male)	0.459140	0.29	Not significant
Substance	0.238880	0.47	Not significant
Hypertension	-0.301136	0.63	Not significant
Asthma	0.382948	0.54	Not significant

Not significant at the 5% level ($p < 0.05$)**Table 6.** ATC/DDD Classification with Calculated Defined Daily Dose (DDD) per 100-bed days of Antipsychotic Medications

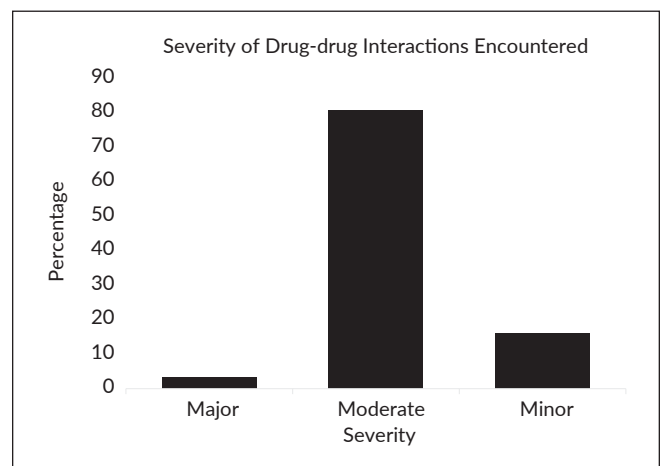
Antipsychotic Medications	ATC code	DDD	DDD per 100 bed days
Chlorpromazine	N05AA01	15	0.1386
Haloperidol, oral	N05AD01	9	0.0809
Haloperidol decanoate, injection	N05AD01	9	0.0840
Fluphenazine decanoate	N05AB02	75	0.6931
Aripiprazole	N05AX12	13	0.1232
Clozapine	N05AH02	23	0.2156
Olanzapine	N05AH03	71	0.6561
Paliperidone palmitate, injection	N05AX13	520	4.8056
Quetiapine	N05AH04	0.13	0.0012
Risperidone	N05AX08	114	1.0572
Total			7.8556

Table 7. Assessment of Drug Therapy Problems Encountered

Drug Therapy Problems	No. of Identified DTP	Percentage
Severe side effects	0	0.00%
Contraindications	0	0.00%
Drug-drug interactions	27	81.82%
Incorrect dosage	0	0.00%
Therapeutic duplication	19	57.58%

Table 8. Medication Appropriateness Index of Antipsychotics

Criteria	Median Score	Interpretation
Indication	0	Appropriate
Dosage	0	Appropriate
Drug-drug interaction	2	Inappropriate
Contraindication	0	Appropriate
Therapeutic duplication	1	Moderately Appropriate
Total MAI score	0	Appropriate

**Figure 2.** Percentage of the severity of drug-drug interactions (N = 93).

antipsychotics were used appropriately. The results indicate that the drug indication, dosage, and contraindication are "appropriate," with a median score of 0. Therapeutic duplication was considered "moderately appropriate," with a median score of 1. However, drug-drug interaction was rated as "inappropriate," with a median score of 2. Table 8 shows the MAI score of antipsychotic use using different criteria.

DISCUSSION

Second-generation antipsychotics (73.85%) were frequently prescribed by physicians, particularly risperidone (35.4%) and olanzapine (15.4%), which is attributed to their broad spectrum in managing major types of psychopathologies, including positive, negative, and mood symptoms, cognitive impairment, as well as reducing the risk of suicide and decreasing aggression.⁴ These are parallel to the findings reported by Kumar et al. and Tripathi et al. in which risperidone is used in the clinical treatment of schizophrenia in adults and adolescents, providing effective symptom reduction in both the long-term and short-term.^{16,17} Olanzapine, on the other hand, has been shown to be clinically effective with improved quality of life. Several studies indicated a lower incidence of extrapyramidal symptoms compared to typical and some atypical antipsychotics, which is a risk factor for non-compliance and discontinuation.^{18,19} These medications are preferred oral antipsychotics because they are well-tolerated and have fewer side effects.²⁰ However, the usage of antipsychotics to treat schizophrenia shows significant variations; the study by Jyothi et al. reported olanzapine (27.98%) as the most used antipsychotic, followed by risperidone (20.98%).²¹ A drug use pattern of antipsychotics at a psychiatry outpatient department in India reported olanzapine (77.06%) as the most frequently used antipsychotic, while another study showed that risperidone (21%) and quetiapine (20%) were the most prescribed.²² In Cebu City, risperidone and olanzapine emerged as frequently prescribed; other reports showed varying prescribing preferences, with first-generation antipsychotics being the most prescribed.²³ Hence, no antipsychotic usage seems to be uniform across different countries.

Among the prescribed antipsychotics, paliperidone palmitate had the highest consumption at 4.8056 defined daily dose per 100 bed-days. This measure allows comparison across settings to assess whether supply is adequate, excessive, or insufficient, providing policymakers and healthcare providers with insights for informed drug management and policy decisions. It also promotes rational drug use of essential medications, particularly in low-income countries. Long-acting formulations like paliperidone palmitate offer distinct advantages due to their extended-release nature, which provides more stable plasma concentrations. Additionally, as the primary active metabolite of risperidone, paliperidone palmitate is believed to exhibit greater efficacy.²⁴ Long-acting formulations effectively improve medication

adherence and reduce relapse and rehospitalization in adults with schizophrenia-spectrum disorders. The long-acting formulation allows maintenance doses to be administered at intervals ranging from one week to several months, enhancing affordability and accessibility.²⁵ This is beneficial in resource-limited settings like the Philippines, where mental health budgets and continuous care access are constrained.²⁶ Furthermore, challenges such as inadequate procurement planning, inefficient distribution system, and weak inventory monitoring, as reported by the Commission on Audit in the Department of Health, further limit the availability of psychotropic medications in public facilities.²⁷ Hence, effective programs are essential to promote the use of long-acting injections as a non-coercive treatment option due to perceived or internalized stigma that is a barrier to help-seeking behavior in Filipinos.²⁸

The high prevalence of men (63.6%) identified in this study was similar to the findings by Banerjee et al., Rode et al., Munjely et al., and Tripathi et al.^{17,29-31} Similarly, a systematic review supports this finding, reporting a median male: female ratio of 1.4:1 in the incidence of schizophrenia.³² Most of the patients were between 23 and 27 (18.18%) and 38 and 42 (18.18%) years of age, with a mean age of 33.73. A statistically significant correlation between the lower age of onset of schizophrenia and resulting in poorer outcomes due to more negative symptoms, relapses, and more hospitalizations was previously reported. Men typically experience an earlier onset of the disease, which is 3.2 to 4.1 years earlier than women. Men also exhibit poorer social functioning, severe negative symptoms, and a higher rate of alcohol and substance use disorders, which was also observed in this study, with substance abuse disorder (9.09%) being a common comorbidity.³³ Furthermore, the findings of the study showed a significant relationship between being male and having a substance abuse disorder (SUD) as a comorbidity to the number of drugs prescribed, with *p*-values of 0.002 and 0.07, respectively. Males were associated with a 2.6 times higher expected number of drugs compared to females, whereas having SUD as a comorbidity is associated with a 1.5 times higher expected number of drugs per medication order. Individuals with schizophrenia are frequently diagnosed with comorbid SUDs, which contribute to premature mortality and dysfunction.³⁴ This implies longer inpatient treatment because substance use significantly exacerbates symptoms, hinders treatment response, and negatively impacts the course of the illness.³⁵ This is further supported by Halsall et al., who found that over 50% of individuals with a psychotic disorder experience alcohol or substance use issues, dramatically worsening their clinical outcomes.³⁶ Moreover, SUDs are highly prevalent among individuals with schizophrenia, linked to an early onset of symptoms, and are more commonly seen among men. Possible consequences of comorbid substance use include lower treatment adherence, worsening of psychotic symptoms, poorer long-term outcomes, higher rates of hospitalization, and increased likelihood of violence,

victimization, suicide, homelessness, infectious disease, and premature mortality. Hence, individuals with comorbid SUDs require more intensive care and targeted socio-behavioral intervention.³⁷

A nationwide retrospective cohort study conducted in Finland and Sweden showed that the use of clozapine antipsychotic polytherapy and long-acting injectables, such as paliperidone palmitate, was associated with lower risks of both SUD-related and psychiatric hospital admission among patients with schizophrenia.³⁸ A meta-analysis reported the superiority of clozapine, olanzapine, and risperidone over other antipsychotics in the treatment of schizophrenia and comorbid SUD.³⁹ One potential mechanism is that comorbid SUDs and schizophrenia may share abnormalities in the mesolimbic dopamine system, affecting drug reward, sensitization, and craving. Substance use could negatively interact with the effects of antipsychotic drugs on the brain receptor level. Given that high D₂ receptor increases substance use risk, the low affinity of clozapine to D₂ receptor reduces reactivity and craving. Reduced craving may result in less frequent and lower amounts of substance use in patients with schizophrenia who are prone to developing SUDs, as well as in patients with schizophrenia and comorbid SUD, thereby diminishing the likelihood of mental and physical symptoms and reducing the risk for hospital readmission and complications related to SUDs.⁴⁰ Additionally, there were reports of reduced adherence to antipsychotics in patients with comorbid SUDs than in those with schizophrenia alone. This illness has a huge economic impact, including mortality and unemployment, and may lead to lifelong disability. Hence, consideration should be given to long-acting injectables, which have been associated with better adherence and lower risk of hospital admission than their oral counterparts.⁴¹

During the evaluation of the prescribed medications using the WHO Prescribing Indicators, the average number of antipsychotics per medication order was 1.97, whereas the overall average number of drugs per medication order was 3.82, indicating significant use of non-psychotropic medications such as antiparkinsonian and antihistamine. It was observed that antipsychotics were prescribed along with the following medications: (1) biperiden 2 mg for extrapyramidal symptoms given every night, (2) diphenhydramine 50mg/mL for sleep, (3) haloperidol 5mg/mL as needed for agitation, and (4) paliperidone palmitate 100mg/mL as needed for agitation or maintenance for schizophrenia. This practice exceeds WHO recommendations, reflecting routine use of drug combinations to address extrapyramidal symptoms, agitation, and insomnia, which may have contributed to the high percentage of drug therapy problems, specifically drug interactions and therapeutic duplication. Although monotherapy is the preferred approach in treatment guidelines, prescribing more than one drug may be necessary to achieve a greater and more rapid therapeutic response in psychiatric disorders that are poorly controlled by monotherapy. A tertiary hospital in Quezon City reported a notable trend in psychotropic prescribing, which highlighted

a preference towards selective serotonin reuptake inhibitors (48.6%), followed by benzodiazepines (24.5%) and atypical antipsychotics (20.6%). The high occurrence of moderate drug interactions suggests a continued reliance on combination pharmacotherapy in psychiatric care.⁴² Global surveys on psychotropic prescribing patterns conducted among adult Asians with schizophrenia have reported antipsychotic polypharmacy rates as high as 50%, particularly in Vietnam (59.2%) and Japan (57.4%).⁴³ In addition, a study conducted by Sunny et al. provides estimates that inpatients diagnosed with psychiatric disorders have a higher incidence of potential drug-drug interactions.⁴⁴ These variations in prescribing patterns may stem from the differences in diagnoses, clinicians' hesitation to prescribe psychotropics, cultural perceptions, stigma, and inadequate education regarding the etiology and management of psychiatric disorders.⁴⁵ Thus, monitoring of therapeutic outcomes, introduction of preventive measures, and timely clinical pharmacist interventions are essential to reduce or control the occurrence of unwanted drug-drug interactions, medication errors, and other drug-related problems.^{26,46}

All the medications were prescribed by their generic names, consistent with the study conducted by Bello et al. in a tertiary government hospital in Nigeria.⁴⁷ A low percentage of generic prescribing may indicate unavailability of generic drugs due to patent restrictions, prescribers' lack of trust in generic drugs, or patients' preference for branded or innovator products. Additionally, a 100% adherence to the national formulary was also observed, which was higher than the adherence rates reported in India (55.02%, 58.36%, and 72.41%).^{16,17,48} The study setting is a government-owned hospital, which likely contributed to the high rates of both generic prescribing and formulary adherence, reflecting compliance with established prescribing regulations.⁴⁹ Lastly, the percentage of encountered injectable drugs (19.05%) was within the WHO standard. These formulations are relatively expensive but necessary when there is non-compliance with oral medications and for controlling aggressive behavior, as observed in this study. It is worth noting that only 0.065% of the national health budget was allocated towards mental health services, which could potentially limit patient access to long-acting formulations.⁵⁰ This study provides valuable insights into antipsychotic consumption. While this study does not provide an exact depiction of actual usage, data from this study expanded on the understanding of drug utilization of antipsychotics in tertiary hospitals.

The appropriateness of antipsychotic use was evaluated using the modified medication appropriateness index (MAI) tool, which assesses various criteria of medication use such as indication, effectiveness, dosage, directions, potential drug-drug interactions, drug-disease interactions, therapeutic duplication, duration of therapy, and cost.¹² In this study, all the drug pairs concurrently administered, as documented in the patient's medical record, were screened for potentially significant interactions. The date of administration and

discontinuation was noted. Only drugs administered on the same day were analyzed for drug-drug interactions. The results showed that drug-drug interaction was deemed inappropriate, with a median score of 2. According to the online drug interaction tool, most of the drug-drug interactions of antipsychotics alter pharmacokinetics or pharmacodynamics, which merits a significant rating or a score of 2.⁵¹ The drug interactions found in this study were of moderate severity, with an average of 3.82 medicines per medication order, including combination antipsychotics, an antiparkinsonian agent, and an antihistamine. This reflects a complex treatment regimen that may increase the risk of adverse effects due to interactions while also potentially reducing therapeutic effectiveness.

Therapeutic duplication is defined as a risky overlap of drugs within the same class. Duplicate therapy was identified when drugs from the same chemical or pharmacological class were prescribed at the same time.⁵² Given that the order of prescribing was known, the recently prescribed drug received a "C" rating or was given a score of 2, while the other drug received a "B" rating (score of 1). The most common antipsychotic duplication observed was between oral antipsychotics and antipsychotic injection. Practice guidelines recommend long-acting injectable (LAI) formulations, typically as monotherapy, for patients with established nonadherence. However, concomitant use of oral antipsychotics and long-acting formulations is prevalent, with studies reporting concurrent prescribing frequencies of 21% to 76%. In this study, the most common antipsychotic combination was risperidone and paliperidone palmitate. A meta-analysis found that both risperidone and paliperidone palmitate were effective in reducing Positive and Negative Syndrome Scale (PANSS) scores, suggesting that a combination of both may provide comprehensive symptom management. People on maintenance with oral risperidone could easily switch to paliperidone palmitate injection.⁵³ In addition, patients who receive at least seven days of oral risperidone following paliperidone palmitate initiation experience a shorter hospitalization period and a lower treatment failure rate. However, studies caution against this combination because oral risperidone metabolizes paliperidone, and this combination has not been well established.^{54,55} The Texas Medication Antipsychotic Algorithm recommended an antipsychotic combination only after failure of the clozapine combination with either a 1st or 2nd generation antipsychotic.⁵⁶ Clozapine was associated with lower hospitalization rates than other monotherapies. Additionally, patients prescribed with more than one antipsychotic had 7%-13% decreased risk of rehospitalization compared to those treated with monotherapy ($p < 0.001$). This is a common approach that appears to be effective in a group of worse individuals who have not been diagnosed with "treatment refractory" schizophrenia. This practice was more common among younger patients, those receiving long-acting injectable antipsychotics and anticholinergic medications, and those in settings with a high patient-to-psychiatrist

ratio.⁵⁷ However, because of the lack of strong and consistent evidence, combining antipsychotics is not recommended.⁵⁸

In the study setting, factors such as non-adherence, poor treatment response with monotherapy, and a psychiatrist-to-patient ratio of 0.41 highlight the gaps in psychiatric care, which resulted in frequent use of combination antipsychotic and therapeutic duplication.⁵⁹ Given these findings, careful monitoring of adverse effects for those prescribed combination antipsychotics and individual patient response is recommended to optimize patient safety and treatment outcomes. Further evaluation of the prescribed medications revealed that no inappropriate ratings were given for indication, dosage, or contraindications, yielding a total MAI median score of 0, indicating that the respondents found the medications appropriate. Prescribing physicians were not consulted to understand the reason why they prescribed those drugs. Only the principal investigator and co-investigator assessed the appropriateness of antipsychotic use. The study also did not examine the clinical significance of the appropriateness ratings; thus, it is unclear whether patients with appropriate ratings had better clinical outcomes than those who received inappropriate ratings (or vice versa). Nonetheless, understanding the reasons for medication inappropriateness in psychiatric care impacts how physicians treat patients with mental disorders. This practice encourages continuous learning among healthcare professionals and rationalization, leading to safer treatment strategies and reduced healthcare costs.

The study recognized several limitations. The limited sample size and single-site setting result in insufficient statistical power and limit the generalizability of the findings among patients with schizophrenia admitted to Philippine government hospitals. Retrospective DUR does not significantly affect prescribing quality. However, pharmacist-led interventions reduce the use of inappropriate medications and overall cost in inpatient settings. The absence of inpatient admission in 2021 and the specific inclusion and exclusion criteria further constrained the study. Additionally, eligible medical records could not be identified before conducting the study due to strict hospital regulations on data access. As a result, only a limited number of eligible medical records were evaluated, resulting in insufficient statistical power and limiting its ability to represent the entire population of schizophrenia patients prescribed antipsychotics. The study also encountered challenges with handwritten electronic medical records, leading to the exclusion of incomplete drug information and illegible handwriting. The tool for identifying therapeutic duplication flagged drugs from the same class as unnecessary duplications, but did not assess whether these duplications were beneficial or harmful. Furthermore, standard practice guidelines in the hospital were not available during the course of the study, and the tools utilized in the study were not validated by subject experts. It should be considered that the therapy of schizophrenia patients is highly variable, and the treatment approach for each patient is tailored to their

specific needs. Overall, this study summarizes the prescribing practices of antipsychotics for inpatients with schizophrenia at a tertiary government hospital. Continuous monitoring of antipsychotic medications can support stakeholders, including policymakers and hospital administrators, in prioritizing funding for mental health services and improving accessibility to treatment options.

CONCLUSION

The study highlights a prescription trend towards second-generation antipsychotics, with risperidone being the most frequently prescribed antipsychotic medication. Utilization patterns of antipsychotics generally conform to the WHO standard recommendations. The high consumption of paliperidone palmitate injection calls for further research on antipsychotic consumption in patients with comorbid substance use disorder. These findings support evidence-based prescribing through continuous drug utilization reviews, formulary management, and prescriber education. Furthermore, strengthening pharmacist involvement and policy-driven approaches can improve access, optimize therapy, and ensure quality medication use.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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