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Reseacrh Article

Profile of Antidepressant Use and Drug Interactions among Psychiatric Outpatients at RSUD Ainun Habibie

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ABSTRACT

Mental disorders are commonly treated with antidepressants, antipsychotics, or their combination. Although combination therapy may improve therapeutic outcomes, it also increases the risk of potential drug–drug interactions (DDIs), which can affect drug efficacy and safety. This study aimed to evaluate the prescribing profile of antidepressants and the potential DDIs among patients attending the Mental Health Outpatient Clinic at Ainun Habibie Hospital. A retrospective descriptive study was conducted using medical records. Patients were selected through purposive sampling, and 161 records met the inclusion criteria. Potential DDIs were identified and classified according to their mechanism and severity. Of the 161 medical records reviewed, 160 patients (99.38%) had at least one potential DDI. A total of 479 potential interactions were identified, including 116 (24.22%) pharmacokinetic and 364 (75.83%) pharmacodynamic interactions. Pharmacodynamic interactions consisted of 353 (73.54%) synergistic and 11 (2.29%) antagonistic effects. Based on severity, 106 (22.13%) interactions were classified as major, 371 (77.45%) as moderate, and 2 (0.42%) as minor. The most common potential DDIs were clozapine–fluoxetine (44 cases, 9.17%), Merlopam–Sandepril (42 cases, 8.75%), and trihexyphenidyl–risperidone (38 cases, 7.92%). Potential DDIs were highly prevalent among psychiatric outpatients, with pharmacodynamic interactions of moderate severity predominating. Routine medication review and monitoring are essential to reduce the risk of clinically significant DDIs and improve patient safety.

Keywords: mental disorders; antidepressants; drug interactions

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INTRODUCTION

In this modern era, mental health has become an increasingly urgent global health concern. Mental disorders are conditions characterized by clinically significant disturbances in an individual's cognition, emotional regulation, or behavior, which frequently impair a person's ability to function within their social environment and, in many cases, result in prolonged suffering. According to the World Health Organization's most recent estimates, nearly 1 in every 7 people (1.1 billion) around the world were living with a mental disorder in 2021, with anxiety and depressive disorders being the most common. Specifically, 280 million people were living with depression in 2019, including 23 million children and adolescents, while 359 million people were living with an anxiety disorder in 2021, including 72 million children and adolescents. In the same year, 37 million people experienced bipolar disorder, including 3.8 million adolescents. Meanwhile, schizophrenia affects approximately 23 million people, or 1 in 345 people (0.29%) worldwide, with the rate rising to 1 in 233 people (0.43%) among adults, and in 2021, 57 million people were living with dementia worldwide, with over 60% residing in low- and middle-income countries and nearly 10 million new cases occurring every year. These figures collectively underscore the substantial and growing global burden that mental disorders impose on individuals, families, and health systems (World Health Organization 2025).

In Indonesia, the situation reflects a similarly concerning trend. Data from Basic Health Research Kementerian Kesehatan RI (2018), indicate that the prevalence of depressive disorders, emotional disturbances, and severe mental illness has reached a level warranting serious public health attention. With Indonesia's population estimated at 267.7 million in 2018, roughly one in five individuals—equivalent to approximately 20% of the national population—is considered vulnerable to some form of mental disorder. At the provincial level, Gorontalo has emerged as a notable outlier: the Coordinating Ministry for Human Development and Culture (Kemenko PMK) reported that Gorontalo's depression prevalence (10.3%) considerably exceeds the national average (6.1%), while its schizophrenia prevalence (6.6%) is comparable to the national figure (6.7%). Consistent with this, the Dinas Kesehatan Provinsi Gorontalo (2021), recorded 1,479 individuals with mental disorders across the province, of whom 702 were located in Gorontalo Regency alone, encompassing both severe (e.g., schizophrenia) and mild (e.g., depression) categories.

The pharmacological management of these conditions, particularly depression, frequently involves antidepressant therapy, which in psychiatric practice is often prescribed alongside other psychotropic or somatic medications due to comorbidities and symptom complexity. This tendency toward polypharmacy elevates the risk of drug–drug interactions (DDIs)—a category of drug-related problems with direct implications for clinical outcomes. DDIs occur

when the pharmacological effect of a drug is altered by the concurrent use of another drug, food, or beverage, and may manifest as either potentiated therapeutic benefit or, more commonly in clinical practice, adverse consequences. These include toxic effects from elevated plasma drug concentrations or, conversely, subtherapeutic outcomes resulting from reduced drug levels—both of which compromise the safety and effectiveness of psychiatric pharmacotherapy.

Despite the high burden of mental disorders in Gorontalo, empirical data describing actual medication use patterns and DDI risk profiles among psychiatric patients in this region remain scarce. Most existing DDI-related studies in Indonesia have been conducted in psychiatric hospitals on Java or in tertiary referral centers with different patient demographics and prescribing patterns, leaving a gap in region-specific evidence for areas with disproportionately high depression prevalence such as Gorontalo. This gap is clinically significant, as prescribing patterns, drug availability, and comorbidity profiles can vary substantially across regions, meaning findings from other settings may not be directly generalizable to local psychiatric care.

This study offers new evidence by systematically characterizing antidepressant utilization patterns and identifying potential drug interactions specifically among mental health patients treated at Ainun Habibie Hospital, Gorontalo—a setting for which such pharmacoepidemiological data have not previously been documented. Unlike prior DDI studies that broadly examine psychotropic prescriptions, this research focuses specifically on antidepressant-centered interaction profiles (drug–drug and potentially drug–food interactions) within a regional population known to have an unusually high depression prevalence, providing context-specific insight not captured by national-level or Java-centric studies.

Academically, this study contributes to the limited body of regional pharmacoepidemiological literature on psychotropic drug safety in Eastern Indonesia, an area historically underrepresented in national drug-utilization research despite bearing a disproportionate mental health burden. The findings can serve as a baseline dataset for future comparative or longitudinal DDI research in similar high-prevalence settings. Practically, identifying the pattern and severity of potential antidepressant interactions provides clinicians and hospital pharmacists at Ainun Habibie Hospital with an evidence base to strengthen medication review protocols, minimize adverse drug events, and support rational, safer prescribing—particularly relevant given the polypharmacy tendencies common in psychiatric care. In a region where mental health resources and pharmacovigilance infrastructure are still developing, such locally grounded evidence is essential to inform clinical decision-making and quality improvement initiatives.

The purpose of this study was therefore to determine the profile of antidepressant drug use and to identify potential drug interactions among mental health patients at Ainun Habibie Hospital, Gorontalo.

MATERIALS AND METHODS

Material

The study population comprised medical records of patients treated at the psychiatric polyclinic. The minimum sample size was determined using the Raosoft sample size calculator, applying a 95% confidence level, a 5% margin of error, and a 50% response distribution, yielding a minimum required sample of 161 medical records.

Method

This study employed a descriptive cross-sectional design using retrospectively collected secondary data obtained from the medical records of psychiatric polyclinic patients at Ainun Habibie Hospital, Gorontalo Regency, Indonesia, for the period of July 2024, with data collection carried out in October 2024. The population comprised all outpatients who received treatment at the psychiatric polyclinic during this period, totaling 276 patients. The minimum sample size was determined using the Raosoft sample size calculator, applying a 95% confidence level, a 5% margin of error, and a 50% response distribution, yielding a minimum required sample of 161 medical records, which were selected using a purposive sampling technique based on predefined inclusion and exclusion criteria.

Patients were included if they were aged ≥ 10 years, diagnosed with a mental disorder according to the Guidelines for the Classification and Diagnosis of Mental Disorders in Indonesia (PPDGJ), were undergoing treatment at the psychiatric polyclinic of Ainun Habibie Hospital during the study period, received antidepressant therapy either as monotherapy or in combination with other medications (polypharmacy), and had complete medical records comprising at minimum age, sex, clinical diagnosis, and a full list of prescribed medications with dosage information. Patients undergoing drug rehabilitation therapy were excluded from the study.

Patient characteristics were extracted directly from the medical records, with diagnostic classification referring to the PPDGJ, while potential drug interactions were assessed using the Drugs.com and Medscape Drug Interaction Checker applications.

RESULTS

A total of 276 patient visits were recorded at the psychiatric polyclinic of Hasri Ainun Habibie Hospital, Gorontalo Regency, during July 2024, of which 161 medical records met the inclusion criteria and were included in the final analysis.

Table 1. Patient characteristics based on gender

Gender	Amount	Percentage (%)
Male	84	52.17
Female	77	47.83
Total	**161**	**100**

Of the 161 medical records analyzed, male patients accounted for 84 cases (52.17%), while female patients accounted for 77 cases (47.83%), indicating a relatively balanced gender distribution among psychiatric polyclinic patients receiving antidepressant therapy.

Table 2. Patient characteristics based on age

Age	Amount	Percentage (%)
Late Teens (17-25)	37	22.98
Early Adults (26-35)	55	34.16
Late Adults (36-45)	31	19.25
Early Elderly (46-55)	15	9.32
Late Elderly (56>)	23	14.29
Total	**161**	**100**

Based on age group, the largest proportion of patients fell within the Early Adults category (26–35 years), with 55 cases (34.16%), followed by the Late Teens category (17–25 years), with 37 cases (22.98%). The remaining patients were distributed across the Late Adults (36–45 years; 31 cases, 19.25%), Late Elderly (56 years and above; 23 cases, 14.29%), and Early Elderly (46–55 years; 15 cases, 9.32%) categories. Overall, patients within the late adolescent to early adult range (17–35 years) accounted for the majority of cases, comprising 92 of the 161 medical records analyzed (57.14%).

Table 3. Characteristics of antidepressant drug use in patients

Drug Name	Amount	Percentage (%)
SSRI	**114**	**70.81**
Fluoxetine	77	47.83
Sertraline	37	22.98
Tricyclic (TCA)	**47**	**29.19**
Maprotiline	47	29.19
Total	**161**	**100**

Of the 161 antidepressant prescriptions recorded, SSRIs were the most frequently used class, accounting for 114 cases (70.81%), with fluoxetine (77 cases, 47.83%) and sertraline (37 cases, 22.98%) as the constituent drugs. The TCA class, represented solely by maprotiline, accounted for the remaining 47 cases (29.19%).

Table 4. Concomitant non-antidepressant drugs co-prescribed with antidepressants

Drug Name	Drug Classes	Amount	Percentage (%)
Lorazepam	Benzodiazepine	81	21.09
Clozapine	Atypical antipsychotics	70	18.23
Risperidone	Atypical antipsychotics	45	11.72
Trihexyphenidyl	Antimuscarinic	44	11.46
Diazepam	Benzodiazepine	18	4.69
Citicoline	Neurotonic	15	3.91
Curcuma force	Vitamin	15	3.91
Olanzapine	Atypical antipsychotics	15	3.91
Sucralfate	Antiulcer	14	3.65
Aripiprazole	Atypical antipsychotics	10	2.60
Lansoprazole	PPI	10	2.60
Omeprazole	PPI	9	2.34
Vitamin B complex	Multivitamin	7	1.82
Lodomer	Typical antipsychotics	5	1.30
Quetiapine XR	Atypical antipsychotics	5	1.30
Candesartan	ARB	4	1.04
Ranitidine	H-2 blocker	4	1.04
Vitamin B6	Vitamin	3	0.78
Simtram	Opioid analgesic	2	0.52
Ambroxol HCl	Mukolitik	1	0.26
Amlodipine	CCB	1	0.26
Biocombine	Multivitamin	1	0.26
Cetirizine	H-1 blocker	1	0.26
Divalproex sodium	Anticonvulsants	1	0.26
Paracetamol	Analgesic	1	0.26
Simcobal	Vitamin	1	0.26
Skizonoat	Atypical antipsychotics	1	0.26
Total		**384**	**100**

A total of 27 distinct non-antidepressant drug types, comprising 384 prescriptions, were identified as concomitant medications co-administered alongside antidepressant therapy across the 161 medical records analyzed. These concomitant drugs spanned several therapeutic classes, most notably benzodiazepines and atypical antipsychotics, reflecting the polypharmacy commonly employed in psychiatric treatment regimens. The three most frequently co-prescribed drugs were lorazepam (81 cases, 21.09%), clozapine (70 cases, 18.23%), and risperidone (45 cases, 11.72%).

Table 5. Drug interactions that occurred

Category	Amount	Percentage (%)
Interaction present	160	99.38
No interaction	1	0.62
Total	**161**	**100**

Potential drug interactions were identified in 160 of the 161 medical records evaluated (99.38%), with only a single record (0.62%) showing no potential interaction.

Table 6. Antidepressant drug interactions by mechanism of action

Mechanism	Amount	Percentage (%)
Pharmacokinetics (Metabolism)	116	24.22
Pharmacodynamic (Synergistic)	352	73.49
Pharmacodynamic (Antagonistic)	11	2.30
Total	**479**	**100**

Of the 480 interaction events identified, pharmacodynamic synergistic interactions were the most common (352 events, 73.49%), followed by pharmacokinetic interactions occurring at the metabolic level (116 events, 24.22%) and pharmacodynamic antagonistic interactions (11 events, 2.30%).

Table 7. Antidepressant drug interactions by severity level

Severity	Amount	Percentage (%)
Mayor	106	22.13
Moderate	371	77.45
Minor	2	0.42
Total	**479**	**100**

Based on severity classification, the majority of interactions were categorized as moderate (371 events, 77.45%), followed by major (106 events, 22.13%) and minor (2 events, 0.42%).

Table 8. Drug pairs with the highest interaction frequency

Drug 1	Drug 2	Amount	Percentage (%)
Major Interactions (106 occurrences, 22.13%)			
Lorazepam (Merlopam)	Clozapine	31	6.46
Clozapine	Risperidone	23	4.79
Clozapine	Sertraline	14	2.92
Clozapine	Sandepril (Maprotiline)	11	2.29
Diazepam	Clozapine	6	1.25
Lodomer	Clozapine	5	1.04
Clozapine	Olanzapine	4	0.83
Lorazepam (Merlopam)	Olanzapine	3	0.63
Clozapine	Quetiapine XR	3	0.63
Diazepam	Simtram	2	0.42
Sertraline	Simtram	2	0.42
Clozapine	Aripiprazole	1	0.21
Diazepam	Olanzapine	1	0.21
Moderate Interactions (371 occurrences, 77.45%)			
Clozapine	Fluoxetine	44	9.17
Lorazepam (Merlopam)	Sandepril (Maprotiline)	42	8.75
Trihexyphenidyl	Risperidone	38	7.92
Fluoxetine	Risperidone	28	5.83
Fluoxetine	Trihexyphenidyl	27	5.63

Clozapine	Trihexyphenidyl	25	5.21
Diazepam	Fluoxetine	16	3.33
Lorazepam (Merlopam)	Sertraline	16	3.33
Sertraline	Trihexyphenidyl	14	2.92
Fluoxetine	Olanzapine	11	2.29
Sertraline	Risperidone	11	2.29
Fluoxetine	Curcuma Force	10	2.08
Lorazepam (Merlopam)	Trihexyphenidyl	6	1.25
Sandepril (Maprotiline)	Risperidone	6	1.25
Clozapine	Omeprazole	5	1.04
Fluoxetine	Quetiapine XR	5	1.04
Lodomer	Diazepam	5	1.04
Lodomer	Fluoxetine	5	1.04
Lorazepam (Merlopam)	Risperidone	5	1.04
Sertraline	Aripiprazole	5	1.04
Skizonoat	Trihexyphenidyl	5	1.04
Sucralfat	Lansoprazole	5	1.04
Diazepam	Aripiprazole	4	0.83
Fluoxetine	Aripiprazole	4	0.83
Lorazepam (Merlopam)	Candesartan	4	0.83
Sandepril (Maprotiline)	Candesartan	4	0.83
Sertraline	Olanzapine	4	0.83
Sandepril (Maprotiline)	Trihexyphenidyl	3	0.63
Trihexyphenidyl	Olanzapine	3	0.63
Amlodipine	Sandepril (Maprotiline)	1	0.21
Clozapine	Amlodipine	1	0.21
Lorazepam (Merlopam)	Amlodipine	1	0.21
Lorazepam (Merlopam)	Aripiprazole	1	0.21
Lorazepam (Merlopam)	Skizonoat	1	0.21
Risperidone	Divalproex Sodium	1	0.21
Risperidone	Olanzapine	1	0.21
Sandepril (Maprotiline)	Divalproex Sodium	1	0.21
Skizonoat	Risperidone	1	0.21
Skizonoat	Sertraline	1	0.21
Trihexyphenidyl	Divalproex Sodium	1	0.21
Minor Interactions (2 occurrences, 0.42%)			
Diazepam	Sertraline	2	0.42
Total		**479**	**100**

The three most frequently occurring drug interaction pairs were clozapine–fluoxetine (44 events, 9.17%), lorazepam–maprotiline (42 events, 8.75%), and trihexyphenidyl–risperidone (38 events, 7.92%), out of a total of 479 identified interaction events.

DISCUSSION

Patients in this study were relatively balanced between male (52.17%) and female (47.83%), consistent with Mawaddah, Sari, and Prasetya (2020), who attributed higher male vulnerability to depression to occupational and financial burdens. Age distribution was dominated by late adolescents and early adults (17–35 years; 57.14% combined), aligning with Anggraeni and Maulina (2023), who reported that this age range represents the majority of individuals with mental disorders, potentially linked to declining dopaminergic activity and heightened psychosocial stress during this developmental period.

SSRIs were the predominant antidepressant class prescribed (70.81%), followed by TCA (29.19%). This finding is consistent with (Puspitasari and Angeline 2019; Rizkifani, Susanti, and Febiani 2023), who similarly reported SSRI predominance (98.79% and 61.35%, respectively) over TCA in psychiatric populations. This pattern reflects SSRIs' status as first-line antidepressant therapy, owing to their more favorable cardiovascular and weight-related side-effect profile compared with TCAs (Sari 2023). Concomitant medications were dominated by benzodiazepines (lorazepam, 21.09%) and atypical antipsychotics (clozapine 18.23%; risperidone 11.72%), reflecting the extensive psychotropic polypharmacy characteristic of psychiatric care for comorbid anxiety, insomnia, and psychotic symptoms.

Potential drug interactions were identified in nearly all records analyzed (99.38%). This is notably higher than the prevalence reported in most comparable studies, which range from 28% to 76.5% among psychotropic drug users, and even exceeds the 88.7% prevalence reported among hospitalized schizophrenia spectrum patients. Previous studies indicated that potential drug-drug interactions related to psychotropic drugs are common, with prevalence varying from 28% to 76.5%, while a study among hospitalized schizophrenia spectrum patients reported a prevalence of 88.7%. The near-universal interaction rate observed here likely reflects the extensive polypharmacy pattern noted above, in which most patients received antidepressants alongside multiple antipsychotics and benzodiazepines simultaneously.

Regarding interaction mechanisms, pharmacodynamic synergistic interactions were most common (73.54%), followed by pharmacokinetic metabolic interactions (24.17%) and pharmacodynamic antagonism (2.29%), consistent with the general pattern in which concurrent use of centrally acting psychotropic agents commonly produces additive sedative or anticholinergic effects (Hasnita, Afendi, and Fitrianto 2020). By severity, moderate interactions predominated (77.50%), followed by major (22.08%) and minor (0.42%) interactions. This proportion of moderate-dominant severity closely mirrors findings from a large-scale study of depression outpatients, in which 77.5% of potential interactions were classified as requiring close monitoring, suggesting a broadly similar risk profile despite

differing populations and settings. This contrasts with other reports showing major-interaction dominance—for instance, one study among antidepressant-treated psychiatric outpatients found that 83% of identified interactions were of major severity—indicating that interaction severity patterns may vary considerably depending on prescribing practices and the specific drug combinations used across settings.

The three most frequent interacting pairs were clozapine–fluoxetine (9.17%), lorazepam–maprotiline (8.75%), and trihexyphenidyl–risperidone (7.92%). The clozapine–fluoxetine interaction arises because fluoxetine inhibits CYP1A2 and CYP2D6, the principal enzymes responsible for clozapine metabolism, raising the risk of elevated plasma clozapine levels and associated toxicity (Nabila, Mariska, and Natari 2023; Musdalifah and Susanti 2019). The lorazepam–maprotiline pairing reflects combined benzodiazepine–TCA use for anxiety and depressive symptoms, both acting on distinct but complementary neurotransmitter systems (GABAergic and noradrenergic/serotonergic, respectively) (Utami, Darajati, and Puspitasari 2022; Putri 2023). The trihexyphenidyl–risperidone combination, commonly used to manage risperidone-induced extrapyramidal symptoms, produces a pharmacodynamic synergistic interaction that may heighten anticholinergic burden (Rahaya and Cahaya 2016; Rahajeng and Akbar 2023; Drugs 2024). This combination's prominence is consistent with prior Indonesian studies: Dwi Aulia et al. (2018), reported it accounted for 16.17% of interactions in a similar population, while Rumagit et al. (2021), reported 18.3%, reinforcing that this drug pair represents a recurring, clinically significant interaction risk across psychiatric settings in Indonesia.

Collectively, these findings indicate that antidepressant-based polypharmacy in this population carries a substantially higher potential interaction burden than reported in most comparable literature, underscoring the need for systematic medication review, particularly for high-risk combinations involving clozapine, benzodiazepines, and anticholinergic agents.

CONCLUSIONS

This study found that antidepressant therapy at the psychiatric polyclinic of Hasri Ainun Habibie Hospital, Gorontalo Regency, was predominantly SSRI-based (70.81%), most commonly prescribed alongside benzodiazepines and atypical antipsychotics as part of an extensive polypharmacy regimen involving 27 distinct concomitant drug types. This pattern of polypharmacy translated into a near-universal potential for drug interactions, identified in 99.38% of the 161 medical records analyzed, with the majority classified as moderate in severity (77.50%) and a clinically notable proportion (22.08%) classified as major. The three most frequently occurring interactions—clozapine–fluoxetine, lorazepam–maprotiline, and trihexyphenidyl–risperidone—each involve pharmacologically

plausible mechanisms with recognized clinical consequences, ranging from elevated plasma drug concentrations to additive central nervous system and anticholinergic effects.

These findings indicate that antidepressant-based psychiatric pharmacotherapy at this hospital carries a substantial interaction burden that warrants systematic attention. Given the high frequency of major interactions involving clozapine, closer therapeutic monitoring and medication review—particularly for high-risk drug combinations—are recommended to minimize the risk of adverse clinical outcomes. Future studies incorporating a larger sample size and multi-site comparison are recommended to further characterize regional prescribing patterns and their associated interaction risk in psychiatric care.

ETHICAL ISSUES

This study was conducted following approval from the Health Research Ethics Committee of STIKES Guna Bangsa, with approval number 007/KEPK/XI/2024.

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