Pharmacology and Clinical Pharmacy Research
Volume 10 No. 1 April 2025
ISSN:2527-7322 | e-ISSN: 2614-0020
doi: 10.15416/pcpr.v10i1.60838

Incidence of Metabolic Syndrome from Atypical Antipsychotic Therapy in Schizophrenia Patients

Indah K. Utami*, Yasinta Rakanita, Dea A. Tompa, Niluh P. Dewi

College of Pharmaceutical Sciences Pelita Mas, Palu, Indonesia

Abstract

The long-term effects of atypicals may include weight gain, insulin resistance, and hyperglycemia. The objective of this study is to determine the incidence of metabolic syndrome associated with the use of atypical antipsychotics, whether used alone or in combination therapy. This study was conducted in Palu, Madani Hospital, and Anutapura Hospital. This study used a prospective cross-sectional design with a sample of 40 outpatient participants who received atypical antipsychotics clozapine, olanzapine, and risperidone either singly or in combination therapy at least 3 months. Data analysis used IBM SPSS version 29 with chi-square significance p <0.05. Blood samples and blood pressure measurements were taken from the patient to determine the presence of metabolic syndrome. Determination of metabolic syndrome if there are at least 3 out of 5 criteria: body mass index (BMI) ≥25 kg/m², blood pressure ≥130/85 mmHg, triglycerides ≥150 mg/dL, HDL ≤40 mg/dL, and fasting blood glucose ≥110 mg/dL. Demographic variables based on gender were dominated by males at (58%), based on age, dominated by the adult group (77.5%), based on education at the high school level (40%), private sector employment (48%), and unmarried status (78%). Based on data analysis, the administration of single drugs risperidone, clozapine, and olanzapine showed no significant difference with a p-value of 0.062 > 0.05 regarding the incidence of metabolic syndrome. The combination group also produced similar data with a p-value of 0.071 > 0.05. The use of other medications was found to be most prevalent with antimuscarinic trihexyphenidyl (THP) (29.6%) and the benzodiazepine diazepam (22.2%). The use of atypical antipsychotics does not have a significant impact on the side effects of metabolic syndrome with a p-value of 0.062 > 0.05 in the single group, and p= 0.071 > 0.05 in the combination group. Recommendation for future research, for the medication usage criteria, to use only the atypical antipsychotics olanzapine or clozapine.

Keywords: Atypical, Metabolic Syndrome, Schizophrenia

Corresponding author: Indah K. Utami. College of Pharmaceutical Sciences Pelita Mas, Palu, Indonesia.
Email: indahkurniautamiii@gmail.com
Received: 14 January 2025 **Revised**: 17 February 2025 **Published:** 14 April 2025.

Introduction

Schizophrenia is a mental disorder that results in physiological dysfunction in individuals, both in personal and social contexts[1]. The Indonesian Health Profile presented by the Indonesian Health Survey (SKI) in 2023 showed that the incidence of schizophrenia in Indonesia reached 315,621. This incidence spread across all provinces in Indonesia, with the highest rate in the province of DI Yogyakarta at 9.3%, followed by the province of Central Java at 6.5% and West Sulawesi at 5.9%[2].

The management of schizophrenia therapy uses both typical and atypical antipsychotics. Typical antipsychotics are the first generation, while atypical antipsychotics are the second generation. The difference between these two classes of antipsychotic drugs lies in their side effects[3,4]. Atypical antipsychotics are more frequently used because they can significantly reduce both positive and negative symptoms and have a lower risk of extrapyramidal syndrome (EPS)[5].

However, the long-term effects of using this medication include metabolic changes such as weight gain, insulin resistance, and hyperglycemia[6]. Research conducted by Morrel et al concluded that atypical antipsychotics are associated with adverse metabolic side effects[7]. Atypical antipsychotics, particularly olanzapine, have higher efficacy compared to other atypical drugs. However, it is necessary to consider the side effects produced, such as weight gain and metabolic issues[8].

Research on the incidence of metabolic syndrome in the combination therapy of risperidone and clozapine has been conducted by al Farizi. The results of the study showed a significant relationship with BMI values[9]. However, in that study, the measurement of metabolic syndrome only used 3 criteria, namely body mass index (BMI) and blood pressure (systolic and diastolic). In this study, the researcher focuses on the side effects of metabolic syndrome by measuring 5 criteria of metabolic syndrome according to WHO criteria cited from the Ministry of Health in relation to the use of atypical antipsychotics, whether alone or in combination, so that medical practitioners can be more aware and cautious in administering atypical antipsychotics[10].

Based on the above description, the researcher was interested in conducting a study on adverse events/side effects of metabolic syndrome from atypical antipsychotic therapy, particularly on the use of clozapine, olanzapine, and risperidone, whether alone or in combination therapy, in schizophrenia patients at outpatient clinics in hospitals in the city of Palu.

Method

This study was conducted at two hospitals in Palu, Central Sulawesi Province: Madani Hospital and Anutapura Hospital, over two months from June to July 2024. This research is presented with 3 variables, namely demographic variables, metabolic syndrome characteristic variables, and atypical antipsychotic usage variables concerning the incidence of metabolic syndrome. The demographic variables include: age, gender, education, occupation, and marital status. The metabolic syndrome characteristic variables include blood tests to see triglyceride, high density lipoprotein (HDL), and fasting glucose levels, as well as BMI and blood pressure measurements.

The variable of atypical antipsychotic usage concerning the incidence of metabolic syndrome presents a statistical analysis of atypical antipsychotic usage concerning

the incidence of metabolic syndrome. This research method was conducted prospectively and cross-sectionally, with sample selection meeting the inclusion criteria, including: adult patients aged >18 years diagnosed with schizophrenia, family members of patients who are willing and sign the informed consent, outpatients receiving atypical antipsychotics clozapine, olanzapine, and risperidone in single and combination therapy for <3 months[11] and a maximum of 1 year. The exclusion criteria include: patients who have changed medication within <3 months, patients who experience relapse and are uncooperative during blood sampling, and patients who have consumed antihypertensive, diabetes mellitus (DM), and cholesterol medications before using atypical antipsychotics.

Sample calculation

Every day, the average number of schizophrenia patient visits was 40–50 patients at Madani Hospital and 10–20 patients at Anutapura Hospital, Palu. However, the majority were just family members who came to pick up the medication, unless there were other complaints that made the patient come and consult directly with the doctor. This was what made it difficult for researchers to obtain more significant number of patients.

The determination of the sample size in this study used the Taro Yamane formula as follows[12]:

$$n = \frac{N}{N^d+1}$$

Description:
n = Number of sample
N = Total known population
d = Precision set

In this study, the error tolerance was 10%. So, the calculation based on the formula above was:

$$n = \frac{66}{66\times0.1^2+1}$$

$$n = \frac{66}{(66\times0.01+1)}$$

$$n = \frac{66}{0.66+1}$$

$$n = \frac{66}{1.66}$$

n = 39,75 rounded up to 40 samples

Determination of Metabolic Syndrome

If there are at least 3 out of 5 criteria, pre-metabolic syndrome has at least 2 out of 5 criteria, and the nonmetabolic syndrome group, there is an increase of 1 or no increase in all metabolic syndrome criteria as follows[13,14]

- BMI ≥30kg/ m2,
- Blood pressure ≥130/85 mmHg,
- Triglycerides ≥150 mg/dL,
- HDL ≤40 mg/dL, and
- Fasting blood glucose ≥110 mg/dL.

Blood samples were taken during the examination of triglycerides, HDL, and fasting blood glucose. Meanwhile, the measurement of BMI value was done by measuring the patient's weight (in kilograms) divided by the square of the patient's height (in meters)[15]. A BMI value <18.5 was defined as underweight, 18.5–22.9 as normal weight, 25–29.9 as overweight, and above 30 as obesity. Blood pressure measurement was conducted using a sphygmomanometer. High blood pressure or hypertension is defined as a systolic blood pressure ≥140 mmHg and a diastolic blood pressure ≥90 mmHg[16–18].

Data analysis

Patient examination data were analyzed by using IBM SPSS version 29. Univariate analysis was used to assess and describe the data on weight, height, BMI, triglycerides, and fasting glucose in relation to the use of atypical antipsychotics. Bivariate analysis was used to examine the relationship between metabolic syndrome categories and the use of atypical drugs using chi-square. A significant

relationship is indicated if the chi-square analysis result was p <0.05.

Ethical Aspects

This study was conducted after obtaining approval from the Ethics Committee of the Faculty of Medicine at Tadulako University, with approval number 5295/UN28.1.30/KL/2024.

Result and Discussion

Based on the research results, demographic variables were obtained based on gender, age, education, occupation, and marital status. The variable characteristics of metabolic syndrome included blood tests to measure triglyceride, HDL, and fasting glucose levels, as well as BMI and blood pressure measurements. The variable of atypical antipsychotic use on the incidence of metabolic syndrome involved statistical analysis of the use of atypical antipsychotics on the incidence of metabolic syndrome. Here were the demographic variables of the patients.

Table 1 shows the distribution of schizophrenia patients by gender, predominantly male (58%), by age, predominantly in the adult group at (77.5%) or equivalent to 31 out of a total of 40 patients. Furthermore, by education, it was predominantly high school graduates (40%), with the highest occupation being in the private sector (48%), and by marital status, the majority were in the unmarried group (78%).

The results of the measurement of metabolic syndrome characteristics in Table 2 showed an increase in triglyceride levels in 26 patients, an increase in fasting glucose levels in 25 patients, and an increase in blood pressure in 15 patients.

Table 3 showed the use of single atypical antipsychotic drugs was dominated by risperidone (48%), with a metabolic syndrome incidence of 16%. The second highest use of antipsychotics was in the combination group, with a metabolic syndrome incidence of 20%. The third highest use was of single clozapine, but it had the highest metabolic syndrome incidence among all groups, at 57%.

Table 4 shows the use of other medications was found to be highest for the antimuscarinic trihexyphenidyl (THP) (29.6%), the benzodiazepine diazepam (22.2%), and the typical antipsychotic haloperidol as well as the benzodiazepine clobazam (4.9%).

The research results on schizophrenia patients, based on patient characteristics, revealed a higher prevalence in males (58%) compared with females (42%). This aligns with the study conducted by Li, Zhou, and Yi, which also found that schizophrenia was more common in males, with a nearly 1.4:1 ratio. The onset of schizophrenia occurs 3.2–4.1 years earlier in males compared with females, allowing women to acquire knowledge for a longer period and manage social functions better than men[19]. Hormonal differences also influence these findings, with estrogen predominating in women. This hormone, particularly estradiol-17β, has mechanisms that protect against and mitigate the worsening of schizophrenia symptoms, including oxidative stress, apoptosis, inflammation, and excitotoxicity[20].

Based on age classification, it was divided into 3 groups according to the Ministry of Health, namely adolescents (10–18 years), adults (19–59 years), and the elderly (>60 years). However, in this study, the adolescent group from the age of 18 was used, as this age group predominantly shows clear schizophrenia diagnoses, and also refers to the inclusion criteria where patients have been using atypical medication for more than 3 months. The results of this study found that

ISSN:2527-7322 | e-ISSN: 2614-0020

the incidence of schizophrenia was higher in the adult age group (77.5%). In line with this, research conducted by Ambar Wulandari also showed that the adult group dominated all age groups, with a percentage of 77.3%. Someone is required to work and earn an income for themselves, their family, and their environment. This causes the adult age group to experience excessive mental or emotional pressure[21].

In this study, based on education level, respondents were divided into 5 groups, namely elementary school, junior high school, senior high school, bachelor's degree, and no formal education. The results of this study showed that most of the participants' highest level of education was up to high school. This is similar to the research conducted by Agustaria Ginting, where the highest level of education among the patients was mostly in the high school group (42%)[22]. This is influenced by the onset of schizophrenia, where the initial symptoms of schizophrenia show a sharp increase in the age range of 15–25 years for men and 15–30 years for women. As a result, most education attained only reaches the high school level, where the symptoms of the disease begin to appear[23].

Based on the level of employment, this study is divided into 5 groups, namely students, private sector employees, retirees, military personnel, and unemployed. The results of this study showed that the most common employment level was in the private sector (48%). Where the patients were not bound by government agencies. This is in line with the research conducted by Chafi et al., where the dominant employment percentage of schizophrenia patients is in the private sector or trading (42.5%)[24]. Career disruption has a significant impact on people with schizophrenia, even for those who manage to find employment. The duration of employment tends to be relatively short, less than 1 year[25].

The results of measuring the criteria for metabolic syndrome through blood tests (HDL, triglycerides, and fasting glucose) and measuring blood pressure and BMI, showed significant results for the fasting glucose criterion $p= 0.020 < 0.05$, triglycerides $p= 0.020 < 0.05$, and HDL $p= 0.010 < 0.05$. The triglyceride group had the highest side effect incidence with 26 occurrences compared to the other groups. Based on previous research, the concentration of triglycerides and fasting glucose increased after using quetiapine, olanzapine, zotepine, and clozapine. The increase in fasting triglyceride and glucose changes based on the degree of change with the highest value is 0.970[26].

Another criterion was that the increase in BMI and blood pressure, both systolic and diastolic, did not yield significant results, where the p-value > 0.05. This was in line with the research conducted by Farizi, where risperidone and clozapine showed no clinically significant relationship with the increase in systolic and diastolic blood pressure [9]. Another meta-analysis conducted by Dayabandara concluded that patients treated with clozapine and olanzapine showed the maximum weight gain compared to treatment with risperidone, where patients only experienced moderate weight gain[27].

Some other studies used the characteristics of metabolic syndrome with waist circumference measurements. However, in this study, the researchers used BMI values to avoid prolonged physical contact during blood sampling and other data collection, as some patients seemed uncomfortable. The relationship between the administration of atypical antipsychotics and the incidence of metabolic syndrome can be seen in Table 3. In this study, the grouping of drugs was divided into 5 groups, namely 3

ISSN:2527-7322 | e-ISSN: 2614-0020

groups of single atypical antipsychotics and 2 groups of combined atypical antipsychotics. The single atypical antipsychotic group consists of risperidone, clozapine, and olanzapine. The use of risperidone as a single atypical antipsychotic is more dominant (48%) compared to other groups. This is in line with the research conducted by Paula et al., where the use of the atypical antipsychotic risperidone is more dominant (21.6%) than other antipsychotics[28]. Meanwhile, the single antipsychotic clozapine was 18%. Looking at the results of the metabolic syndrome measurement, the group taking the single antipsychotic clozapine was more dominant in causing metabolic syndrome (57%) compared to risperidone (16%). However, the chi-square test showed p= 0.062 > 0.05, which means there is no significant relationship between single atypical antipsychotics and the occurrence of metabolic syndrome.

Risperidone affects the D2, D3, 5-HT2a, and 5-HT2c receptors. This causes dopamine and serotonin levels to stabilize. Additionally, risperidone does not have a significant impact (level I) on the incidence of metabolic syndrome, as it is the least atypical group within the atypical spectrum[29]. The mechanism of action of risperidone shows its therapeutic effects through some D2 blockade for positive symptoms, but is more dominant on serotonin like 5HT2A for negative symptoms. Atypical antipsychotics have a loose binding to the D2 receptor, allowing them to quickly dissociate from the receptor, which results in a lower incidence of extrapyramidal symptoms (EPS)[30]. Therefore, the consideration of choosing Risperidone is deemed safer to avoid causing metabolic syndrome events.

On the contrary, clozapine and olanzapine, within the concept of atypical spectrum, fall into the most atypical (level III) category, which impacts the side effects of metabolic syndrome, as these drugs affect H1, α2, BDNF, M1 receptors, and GlyT activity. The induction of olanzapine and clozapine affects the most important organ in the central nervous system (CNS), namely the hypothalamus, while in the peripheral nervous system (PNS) it affects the liver, pancreatic β-cells, adipose tissue, and skeletal muscle, which directly cause metabolic syndrome[31,32]. Therefore, in line with the results of this study, clozapine causes metabolic syndrome (57%). In this study, the number of subjects used was relatively small (40 patients), as only a few patients could be directly contacted and involved in this research. Thus, this can also affect the results of the statistical analysis. Clozapine has a mechanism of action by antagonizing dopamine and serotonin receptors, which is effective against both positive and negative symptoms. This drug binds to dopamine receptors D1–5, with a higher affinity for the D4 receptor than the D2 receptor. Both the antagonistic properties of D4 and 5-HT2A contribute to the reduction of negative symptoms and result in fewer extrapyramidal side effects[33].

Olanzapine has antimuscarinic effects, including dry mouth, constipation, and urinary retention. Some of the side effects include extrapyramidal symptoms and lower epileptogenic effects compared to other antipsychotics. However, this drug causes metabolic side effects, including diabetes, hyperlipidemia, and weight gain[34].

The atypical combination of risperidone and clozapine is the highest antipsychotic combination (25%) compared to other groups. This is in line with the research conducted by Dania et al. where the highest number of subjects (17) used the atypical antipsychotic combination of risperidone and clozapine[35]. The combination of the atypical antipsychotics risperidone and clozapine causes metabolic

syndrome events in 2 out of 10 groups using this combination. Until now, risperidone is the most widely used augmentation agent for clozapine. In line with that statement, a study conducted by Henderson DC et al. involved 12 patients with psychotic symptoms who were previously refractory to clozapine monotherapy, and were then given clozapine combined with risperidone for 4 weeks. At the end of the clinical trial, 10 patients showed a reduction in total brief psychiatric rating scale (BPRS) scores of 20% or more[36,37].

In Table 4, the most commonly used adjunctive medications are the antimuscarinic group, trihexyphenidyl (THP) (29.6%) and the benzodiazepine group, diazepam (22.2%). This is in line with the research conducted by Rahajeng[38], where the combination of risperidone and THP is the most frequently used combination, totaling 279 (22.16%)[30]. This is also related to the risk of side effects caused by risperidone, namely anxiety, headaches, and extrapyramidal symptoms. Therefore, the administration of THP is intended as prophylaxis before the onset of extrapyramidal syndrome side effects. THP has a stronger central effect than a peripheral one[39].

In addition to THP, the administration of diazepam is intended to reduce agitation caused by the use of risperidone. Research conducted by Karsa and Lisal revealed that patients receiving a combination of risperidone and diazepam therapy during the treatment period experienced a significant decrease in Positive and Negative Syndrome Scale - Excited Component (PANSS-EC) scores[40].

The limitations of this study is the researcher did not record the duration of the patient's treatment. The research team only observed the duration of treatment for subjects who met the inclusion criteria on the hospital device used by staff, and they had to take turns with the staff who were currently calling the names of patients for examination. Therefore, the timing was not conducive for using the device used by hospital staff. Another limitation of this study is that the researchers used a 10% error range because the number of participants involved was small, causing the estimates to change during the research. Therefore, this significantly affects the conclusion regarding the sampling effect of atypical antipsychotic use on the incidence of metabolic syndrome. Additionally, it would be better to use a narrower group of atypical antipsychotics, specifically level 3 on the atypia spectrum.

Conclusion

Based on statistical analysis in this study, it can be concluded that the use of atypical antipsychotics, both single and combined, does not have a significant impact on the side effects of metabolic syndrome. However, there was an increase in the value of one or two of the five criteria for metabolic syndrome in schizophrenia patients.

Acknowledgements

The authors express their gratitude to STIFA Pelita Mas Palu for fully funding this research, and to Madani General Hospital of Central Sulawesi Province and Anutapura General Hospital of Palu City for facilitating this study.

Funding

This research was funded by the Sekolah Tinggi Ilmu Farmasi Pelita Mas Palu, under contract number 558/STIFA-PL/I/2024.

Conflict of Interest

The authors declare no conflict of interest related to this study.

References

1. Putri IA. Schizophrenia: A Literature Study. *Journal of Public Health and Medical Studies*. 2022;1(1):1-12. doi:10.56282/JPHMS.V1I1.257
2. Ministry of Health. Health Development Policy Agency. Indonesian Health Survey. Published online 2023:1-965. [Accessed November 26, 2024]. *https://www.badankebijakan.kemkes.go.id/hasil-ski-2023/*
3. Permata A, Ardianto N. The Appropriateness of Antipsychotic Use in Schizophrenia Patients at Dr. Radjiman Wediodiningrat Mental Hospital. *Indonesian Journal of Pharmaceutical (e-Journal)*. 2023;3(3):2775-3670. doi:10.37311/ijpe.v3i3.23235
4. Candra Eka Puspitasari, Ni Made Amelia Ratnata Dewi, Siti Rahmatul Aini, Raisya Hasina, Iman Surya Pratama. Prescription Patterns of Antipsychotics for Schizophrenia Patients at RSJ Mutiara Sukma, NTB Province, in 2020. *Journal of Science and Health.* 2022;4(3):308-312. doi:10.25026/jsk.v4i3.1151
5. Weng J, Zhang Y, Li H, Shen Y, Yu W. Study on risk factors of extrapyramidal symptoms induced by antipsychotics and its correlation with symptoms of schizophrenia. *Gen Psychiatr.* 2019;32(1):100026. doi:10.1136/gpsych-2018-100026
6. Ardiansyah H, Azis U, Susanto HF, Limoa E. The Influence of Atypical Antipsychotic Medication on Weight Gain and Fasting Blood Glucose Levels in Schizophrenia Patients at Dadi Regional Special Hospital, South Sulawesi Province. T*ambusai Education Journal*. 2024;8:10915-10920.
7. Morell R, Curtis J, Watkins A, et al. Cardio-metabolic risk in individuals prescribed long-acting injectable antipsychotic medication. *Psychiatry Res*. 2019;281:112606. doi:10.1016/j.psychres.2019.112606
8. Komossa K, Rummel-kluge C, Hunger H, Schmid F. Olanzapine versus other atypical antipsychotics for schizophrenia. *Europe PMC Funders Group*. 2014;(3). doi:10.1002/14651858.CD006654.pub2. Olanzapine
9. Al Farizi GR, Perwitasari DA, Dania H, Barliana MI, Yuliani S. Adverse Events of Risperidone and Clozapine Combination Therapy on Schizophrenic Patients at Magelang Mental Hospital. *Indonesian Journal of Clinical Pharmacy*. 2021;10(3):159-171. doi:10.15416/ijcp.2021.10.3.159
10. Wira Gotera, Ida Bagus Aditya Nugraha. Focus on Metabolic Syndrome. Directorate General of Health Services. Published online April 18, 2022. [Accessed April 18, 2023]. *https://yankes.kemkes.go.id/view_artikel/2372/fokus-pada-sindrom-metabolik*
11. Riordan HJ, Antonini P, Murphy MF. Atypical Antipsychotics and Metabolic Syndrome in Patients with Schizophrenia: Risk Factors, Monitoring, and Healthcare Implications. American Health and Drugs Benefits. 2011;4:292-302. *www.idf.org/webdata/docs/IDF_Meta_def_final.pdf.*
12. Professor P. Onumanyi, Professor J. S. Sadiku, Professor S. O. Ale, Professor A. R. T. Solarin. ABACUS. Mathematical Association Of Nigeria. (Professor Usman KO, ed.).; 2021. *https://www.researchgate.net/publication/373515793*
13. Li Q, Wang P, Ma R, Guo X, Sun Y, Zhang X. A novel criterion of metabolically healthy obesity could effectively identify individuals with low cardiovascular risk among Chinese cohort. *Front Endocrinol (Lausanne).* 2023;14. doi:10.3389/fendo.2023.1140472
14. Dziky Muhammad, Fillah Fithra Dienny. he Relationship Between Vitamin A, C, and E Intake and the Incidence of Metabolic

Syndrome in Obese Adolescents. *Journal Of Nutrition College*. 2016;5:289-297. doi:https://doi.org/10.14710/jnc.v5i4.16423
15. Shalitin S, Phillip M, Yackobovitch-Gavan M. Do changes in BMI during the COVID-19 pandemic persist in the post-pandemic period in a pediatric population attending health care clinics? A longitudinal study. *Horm Res Paediatr*. Published online October 28, 2024:1-22. doi:10.1159/000542293
16. Andri J, Permata F, Padila P, Sartika A, Andrianto MB. Reduction of Blood Pressure in Hypertensive Patients Using Slow Deep Breathing Exercise Intervention. *Silampari Nursing Journal*. 2021;5(1):255-262. doi:10.31539/jks.v5i1.2917
17. Ambarwati H, Rosyid FN. Self Management is Related to Blood Pressure Values in Hypertensive Patients. *Journal of Telenursing (JOTING)*. 2024;6(1):728-735. doi:10.31539/joting.v6i1.9335
18. Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. *Nat Rev Cardiol*. 2021;18(11):785-802. doi:10.1038/s41569-021-00559-8
19. Li X, Zhou W, Yi Z. A glimpse of gender differences in schizophrenia. *Gen Psychiatr*. 2022;35(4):100823. doi:10.1136/gpsych-2022-100823
20. Gogos A, Sbisa AM, Sun J, Gibbons A, Udawela M, Dean B. A Role for Estrogen in Schizophrenia: Clinical and Preclinical Findings. *Int J Endocrinol*. 2015;2015. doi:10.1155/2015/615356
21. ambar wulandari AIF. The Incidence of Schizophrenia in Inpatients at RSUD Dr. H. Soewondo Kendal. *Higeia Journal Of Public Health Research And Development*. 2023;7(4):562-573.
22. Agustaria Ginting, Friska Sri Handayani br. Ginting, Dina Sinar Agustina Siregar. Characteristics of Schizophrenia Patients at PROF. DR. M. ILDREM Psychiatric Hospital from 2018-2021. JJRIKUF: *Journal of General Health Science Research*. 2024;2.
23. Häfner H. From Onset and Prodromal Stage to a Life-Long Course of Schizophrenia and Its Symptom Dimensions: How Sex, Age, and Other Risk Factors Influence Incidence and Course of Illness. *Psychiatry J*. 2019;2019:1-15. doi:10.1155/2019/9804836
24. Chafi YK, Amare T, Haile K, Damene W, Tesfaye G, Minichil W. Prevalence and correlates of job loss among schizophrenia outpatients at St. Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia; cross sectional study. *PLoS One*. 2020;15(12):e0242352. doi:10.1371/JOURNAL.PONE.0242352
25. Waghorn G, Chant D, White P, Whiteford H. Delineating disability, labour force participation and employment restrictions among persons with psychosis. *Acta Psychiatr Scand*. 2004;109(4):279-288. doi:10.1046/J.1600-0447.2003.00269.X
26. Pillinger T, McCutcheon RA, Vano L, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: a systematic review and network meta-analysis. *Lancet Psychiatry.* 2020;7(1):64. doi:10.1016/S2215-0366(19)30416-X
27. Dayabandara M, Hanwella R, Ratnatunga S, Seneviratne S, Suraweera C, de Silva VA. Antipsychotic-associated weight gain: Management strategies and impact on treatment adherence. *Neuropsychiatr Dis Treat.* 2017;13:2231-2241. doi:10.2147/NDT.S113099
28. Rumagit P, Tampa'i R, Pareta D, Tombuku J. Potential Drug Interaction of

Antipsychotics in Paranoid Schizophrenia Patients at Prof. Dr. V.L Ratumbuysang Psychiatric Hospital. *The Tropical Journal of Biopharmaceutical)*. 2021;4(1):88-96. www.Medscepe.com

29. Carli M, Kolachalam S, Longoni B, et al. Atypical Antipsychotics and Metabolic Syndrome: From Molecular Mechanisms to Clinical Differences. *Pharmaceuticals*. 2021;14(3):238. doi:10.3390/PH14030238
30. Bazzoni M, Adragna C, Carucci S. Risperidone. *Medico e Bambino*. 2023;42(2):111-115. doi:10.53126/MEB42111
31. Carli M, Kolachalam S, Longoni B, et al. Atypical Antipsychotics and Metabolic Syndrome: From Molecular Mechanisms to Clinical Differences. *Pharmaceuticals*. 2021;14(3):238. doi:10.3390/PH14030238
32. Stephen M. Stahl. *Stahl's Essential Psychopharmacology Neuroscientific Basis and Practical Application Fourth Edition*. Cambridge University Press; 2013.
33. Stępnicki P, Kondej M, Kaczor AA. Current concepts and treatments of schizophrenia. *Molecules*. 2018;23(8). doi:10.3390/molecules23082087
34. Sachdeva V, Ashraf S, Inam S, et al. Olanzapine-Induced Bradycardia. *Primary Care Companion for CNS Disorders*. 2023;25(4):48464. doi:10.4088/PCC.22cr03453
35. Dania H, Faridah IN, Rahmah KF, Abdulah R, Barliana MI, Perwitasari DA. The Relationship Between Antipsychotic Therapy Administration and the Incidence of Extrapyramidal Syndrome Side Effects in Outpatient Patients at a Hospital in Bantul, Yogyakarta. *Indonesian Journal of Clinical Pharmacy*. 2019;8(1). doi:10.15416/ijcp.2019.8.1.19
36. Henderson DC, Golf DC, Connolly CE, Borba CP, Hayden D. Risperidone added to clozapine: Impact on serum prolactin levels. *Journal of Clinical Psychiatry*. 2001;62(8):605-608. doi:10.4088/JCP.V62N0805
37. Josiassen RC, Joseph A, Kohegyi E, et al. Clozapine augmented with risperidone in the treatment of schizophrenia: A randomized, double-blind, placebo-controlled trial. *American Journal of Psychiatry.* 2005;162(1):130-136. doi:10.1176/APPI.AJP.162.1.130/ASSET/IMAGES/N620F4.JPEG
38. Rahajeng B, Akbar SK. Study on the Use and Side Effects of Risperidone at Grhasia Mental Hospital Yogyakarta. CERATA *Journal of Pharmaceutical Sciences*. 2024;14(2):123-131. doi:10.61902/cerata.v14i2.597
39. Wati H, Hidayati R, Rizky M. The Influence of Antipsychotic Combination on Side Effects Extrapyramidal Syndrome in Schizophrenia Patients Inpatient Care at Sambang Lihum Psychiatric Hospital Banjarbaru. *Borneo Journal of Pharmascientech*. 2024;08(01):78-86.
40. Karsa NS, T.Lisal S. The Effectiveness of Risperidone and Diazepam in Schizophrenic Patients with Agitation. *Wal'afiat Hospital Journal*. 2023;04(02):117-127.

Table 1. Distribution of schizophrenia patients.

Parameters	n	Percentage (%)
Gender		
Male	23	58%
Female	17	42%
Age (years)		
Adolescents (18)	1	2,5 %
Adults (19-59)	31	77,5 %
Elderly (> 60)	8	20 %
Education		
Not Attending School	4	10 %
Elementary School	5	13 %
Junior High School	7	18 %
Senior High School	16	40 %
Bachelor's degree	8	20 %
Occupation		
Not working	16	40 %
Student	1	3 %
Private sector	19	48 %
Retired	3	8 %
National Millitary	1	3 %
Marital		
Not married	31	78 %
Married	9	23 %

Table 2. Characteristics of Metabolic Syndrome

Characteristic	n	Mean	P value
Fasting glucose ≥110 mg/dl	25	114.625	0.02 < 0.05
BMI >30 kg/ m^2	5	24	0.697 > 0.05
Blood pressure Systolic ≥130 mg/dl Diastolic ≥75 mg/dl	15	 128.43 77.95	0.80 > 0.05
Triglycerides ≥150 mg/dl	26	187.15	0.02 < 0.05
HDL ≤40 mg/dl	6	59.55	0.01 < 0.05

Table 3. The use of antipsychotics in relation to metabolic syndrome.

Medicine	Type	n	Metabolic Syndrome (n)	Pra metabolic syndrome (n)	Non metabolic syndrome (n)	p
Risperiodne	Single	19 (48%)	3 (16%)	9 (47%)	7 (37%)	0,062
Olanzapine	Single	3 (8%)	-	2 (67%)	1 (33%)	
Clozapine	Single	7 (18%)	4 (57%)	2 (29%)	1 (14%)	
Risperidone + olanzapine + clozapine	Combination	1 (3%)	1 (100%)	-	-	0,071
Rirperidone + clozapine	Combination	10 (25%)	2 (20%)	3 (30%)	5 (50%)	
Total		**40**				

Table 4. Use of Supportive Medications.

Drug Class	Medication	n	Percentage (%)
Antimuscarinic	THP	24	29.6 %
Typical Antipsychotic	Chlorpromazine	3	3.7 %
	Haloperidol	4	4.9 %
	Trifluoperazine	2	2.5 %
Proton Pump Inhibitor	Omeprazole	3	3.7 %
	Lansoprazole	1	1.2 %
Beta Blocker	Propranolol	1	1.2 %
Benzodiazepine	Diazepam	18	22.2 %
	Lorazepam	3	3.7 %
	Clobazam	4	4.9 %
	Alprazolam	2	2.5 %
Mucolytic	Acetylcysteine	1	1.2 %
Vitamin	Vitamin B6	3	3.7 %
	Curcuma	1	1.2 %
Analgesic	Sodium Diclofenac	1	1.2 %
Antidepressant	Maprotiline	3	3.7 %
	Fluoxetine	2	2.5 %
	Sertraline	1	1.2 %
Anticonvulsant	Valproic acid	4	4.9 %
TOTAL		**81**	**100 %**

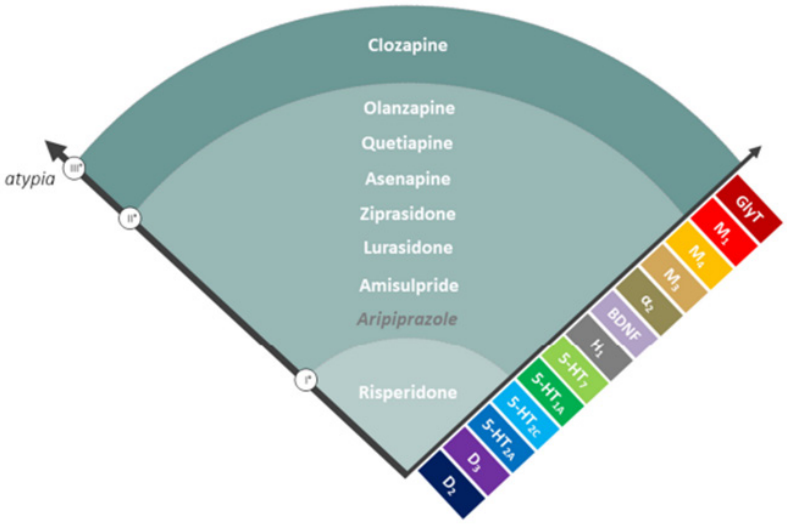

Figure 1. Atypical Spectrum[29].