e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(2); 283-314

Original Research Article

A Comparative Follow-up Study of Metabolic Syndrome in Schizophrenia Patients Treated with Olanzapine and Risperidone

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Received: 01-11-2025 / Revised: 15-12-2025 / Accepted: 21-01-2026
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Conflict of interest: Nil

Abstract

Background: Schizophrenia is a severe mental illness characterized by anomalies in thought processes, perceptions, emotional response, and social relations. It affects approximately 1% of the global population, translating to millions of individuals suffering from its debilitating effects. Metabolic syndrome refers to a cluster of interrelated risk factors that significantly elevate the risk of cardiovascular diseases and type 2 diabetes. Individuals with schizophrenia are more likely to suffer physical ailments, notably cardiovascular problems. The interplay between the chronic nature of schizophrenia and physical health is multifactorial, involving genetic predisposition, lifestyle factors, and treatment-related side effects. Second-generation antipsychotics (SGAs), including olanzapine and risperidone, have revolutionized the treatment of schizophrenia by targeting both positive symptoms (e.g., delusions, hallucinations) and negative symptoms (e.g., reduced emotional expression, social withdrawal). Their use is associated with an increased risk of metabolic side effects, including weight gain, dyslipidemia, and insulin resistance, which contribute to the development of metabolic syndrome

Methodology: This comparative observational study analyzed the metabolic impact of olanzapine (n=70) versus risperidone (n=70) over one year in 140 schizophrenia patients aged 18–50 at the Government Hospital for Mental Care, Visakhapatnam. Participants, selected by simple random sampling and meeting ICD-11 criteria, were either drug-naïve or had a six-month washout period, excluding those with pre-existing metabolic conditions. Researchers measured BMI, waist circumference, blood pressure, and lipid profiles at baseline, three, and six months, diagnosing metabolic syndrome via IDF and NCEP ATP III criteria, with 121 participants completing the six-month follow-up (58 in the olanzapine group, 63 in the risperidone group).

Results: This prospective study provides valuable evidence that olanzapine is associated with significantly higher metabolic risk compared to risperidone, as demonstrated by greater changes in weight, BMI, waist circumference, triglycerides, HDL cholesterol, and incidence of metabolic syndrome over a 6-month period. Independent risk factors included high baseline BMI, physical inactivity, poor diet, and family history of cardiometabolic disease.

Conclusion: In conclusion, this study provides robust evidence supporting the metabolic safety advantages of risperidone over olanzapine. The findings align with both Indian and global literature and advocate for routine risk stratification and tailored therapeutic approaches in schizophrenia care. Given the rising burden of antipsychotic-induced metabolic syndrome, integrating physical health surveillance into psychiatric practice is not only advisable but essential for long-term patient well-being.

Keywords: Metabolic Syndrome, Schizophrenia, Olanzapine, Risperidone.
DOI: 10.25258/ijcpr.18.2.47

Introduction

Schizophrenia: A Chronic Mental Illness and Its Global Impact

Schizophrenia: Definition and Global Prevalence

Schizophrenia is a severe mental illness characterized by anomalies in thought processes, perceptions, emotional response, and social relations. It affects approximately 1% of the global population, translating to millions of individuals suffering from its debilitating effects. The incidence rate is approximately 1.5 per 10,000 individuals annually. In India 1.41% of adults have experienced schizophrenia spectrum disorders. This chronic condition has a profound impact on an individual's ability to function, leading to significant personal, social, and economic consequences. [1–4]

Social and Economic Burden: Individuals with schizophrenia often experience unemployment, social isolation, and stigma, exacerbating the cycle of poverty and poor health. Globally, the direct costs associated with healthcare, along with indirect costs due to loss of productivity, amount to billions of dollars annually. Moreover, the condition contributes to premature mortality, with studies showing a 20% shorter lifespan compared to the general population. This increased mortality rate is attributed to both suicide and physical health conditions, particularly cardiovascular diseases and metabolic syndrome. [3,5–7]

Introduction to Metabolic Syndrome: Metabolic syndrome refers to a cluster of interrelated risk factors that significantly elevate the risk of cardiovascular diseases and type 2 diabetes. The primary components of metabolic syndrome include:

Central Obesity: Excess fat distribution around the abdomen.

Dyslipidemia: Elevated triglycerides and reduced high-density lipoprotein (HDL) cholesterol.

Hypertension: Persistent high blood pressure.

Glucose Intolerance: Impaired fasting glucose or insulin resistance.

The relevance of metabolic syndrome to public health cannot be overstated. It affects nearly one-quarter of the global population, representing a growing health crisis due to lifestyle changes and the increasing prevalence of obesity. Among individuals with schizophrenia, the prevalence of metabolic syndrome is significantly higher, further compounding the morbidity and mortality associated with the condition. [2,4,7–10]

Schizophrenia and Associated Morbidities

Physical Illness Susceptibility in Schizophrenia: Individuals with schizophrenia are more likely to suffer physical ailments, notably cardiovascular problems. The interplay between the chronic nature of schizophrenia and physical health is multifactorial, involving genetic predisposition, lifestyle factors, and treatment-related side effects. Studies have shown that schizophrenia patients are nearly twice as likely to develop cardiovascular diseases compared to the general population. This heightened susceptibility is due to both the direct effects of the illness and the compounding effects of long-term medication use. [2,4–6,9]

Role of Lifestyle Factors: Lifestyle factors play a pivotal role in exacerbating physical health risks in schizophrenia. Many patients exhibit a sedentary lifestyle and poor dietary habits, partly due to the negative symptoms of schizophrenia, such as avolition (lack of motivation) and anhedonia (inability to experience pleasure). Additionally, substance use, including tobacco and alcohol, is more prevalent in individuals with schizophrenia, further compounding health risks. These behaviours not only increase the risk of metabolic syndrome but also worsen the overall prognosis for schizophrenia patients. [9,11,12]

Antipsychotics and Metabolic Implications

Second-Generation Antipsychotics: Efficacy and Side Effects: Second-generation antipsychotics (SGAs), including olanzapine and risperidone, have revolutionized the treatment of schizophrenia by targeting both positive symptoms (e.g., delusions, hallucinations) and negative symptoms (e.g., reduced emotional expression, social withdrawal). Compared to first-generation antipsychotics (FGAs), SGAs offer a more favourable side-effect profile in terms of extrapyramidal symptoms (movement disorders). However, SGAs are not without significant drawbacks. Their use is associated with an increased risk of metabolic side effects, including weight gain, dyslipidemia, and insulin resistance, which contribute to the development of metabolic syndrome. [3–5,7,10,13,14]

Olanzapine: Olanzapine is highly effective in managing schizophrenia symptoms but is associated with pronounced metabolic side effects. Studies have documented significant weight gain, increased triglycerides, reduced HDL cholesterol, and impaired glucose metabolism in patients treated with olanzapine. These effects are often observed early in treatment and worsen over time, necessitating careful monitoring.

Risperidone: Risperidone is another widely used SGA with a relatively lower propensity for metabolic side effects compared to olanzapine. However, it is not entirely without risk. Studies indicate that risperidone can lead to moderate weight gain and changes in lipid and glucose levels, particularly with long-term use.

Comparative Analysis: Comparative studies between olanzapine and risperidone reveal that olanzapine is more likely to induce metabolic

syndrome due to its greater impact on weight and lipid profiles. This makes it critical to weigh the risks and benefits when selecting a treatment regimen for schizophrenia patients. [3,9,15–17]

The metabolic effects of SGAs highlight the importance of individualized treatment planning and the need for adjunctive interventions, such as lifestyle modifications and regular metabolic monitoring, to mitigate these risks. These considerations are vital for improving both the psychiatric and physical health outcomes of individuals with schizophrenia.

Importance of Monitoring Metabolic Syndrome in Schizophrenia

Early Detection and Intervention: Evidence from Studies: Metabolic syndrome significantly contributes to the morbidity and mortality associated with schizophrenia, particularly due to its link with cardiovascular diseases and type 2 diabetes. Early diagnosis of metabolic syndrome in schizophrenia patients is critical for a number of reasons. First, evidence suggests that early interventions can reduce the progression of metabolic complications and prevent long-term adverse outcomes.18

Professional organizations, such as the American Diabetes Association (ADA) and the American Psychiatric Association (APA), have issued guidelines emphasizing the need for routine metabolic health monitoring in schizophrenia patients. Key recommendations include: [9,12,14, 20,21]

- Baseline Assessments.
- Regular Follow-Ups
- Integrated Care Models
- Lifestyle Interventions.

Implementing these guidelines in psychiatric settings can help mitigate the adverse effects of antipsychotics, improve patient adherence, and enhance long-term outcomes.

Significance of the Study

Justification for Focusing on Olanzapine and Risperidone: Olanzapine and risperidone are among the most commonly prescribed second-generation antipsychotics due to their efficacy. However, their widespread use also makes them significant contributors to the burden of antipsychotic-induced metabolic syndrome.

This study is particularly significant because:

It compares two widely used antipsychotics under real-world conditions, providing insights that are directly applicable to clinical practice.

It focuses on a high-risk population—schizophrenia patients with prolonged exposure to antipsychotics—where metabolic syndrome is a critical concern.

Potential Impact on Guidelines and Patient Care

Refining Risk-Benefit Analyses: Providing evidence-based recommendations for selecting antipsychotics based on individual metabolic risk profiles.

Promoting Early Interventions: Encouraging routine metabolic monitoring and lifestyle interventions as standard practice.

Improving Personalized Medicine: Helping clinicians tailor treatment plans to minimize metabolic risks while achieving optimal psychiatric outcomes.

Ultimately, this study aims to improve the quality of life and overall health outcomes for schizophrenia patients by addressing one of the most pressing challenges in their care.

Aims and Objectives

Aim: To compare the drug emergent metabolic syndrome in schizophrenia patients treated with olanzapine and risperidone.

Objectives

Primary Objectives:

- To assess and compare the incidence of drug emergent metabolic syndrome among schizophrenia patients treated with olanzapine and risperidone.
- To evaluate the metabolic parameters, including weight, BMI, waist circumference, fasting glucose levels, lipid profiles, and blood pressure, in patients on olanzapine and risperidone.

Secondary Objectives:

- To evaluate the risk factors contributing to metabolic syndrome in schizophrenia patients treated with these antipsychotics.
- To analyze the association between the duration of treatment with olanzapine and risperidone and the onset of metabolic syndrome.

Hypothesis: Patients receiving olanzapine treatment for schizophrenia have a higher incidence of metabolic syndrome than those receiving risperidone.

Review of literature: Schizophrenia is defined by the presence of psychotic symptoms such as delusions, hallucinations, and disorganized behavior, along with negative symptoms like emotional blunting and reduced motivation. Unlike acute illnesses, schizophrenia follows a chronic course, often requiring lifelong management. This condition also presents varying degrees of severity,

with some individuals achieving functional recovery, while others face persistent and disabling symptoms. [1,4,8,23]

Metabolic Syndrome in Schizophrenia: The metabolic syndrome (MetS) is a collection of linked metabolic disorders that raises the risk of type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) considerably. Central obesity, dyslipidemia, hypertension, and glucose intolerance are the hallmarks of the syndrome. It represents a state of chronic systemic inflammation and insulin resistance, which leads to progressive cardiovascular and metabolic complications. MetS is not a disease by itself but a collection of risk factors that act synergistically to amplify adverse health outcomes. [4,7,9,10,30]

Higher Prevalence in Schizophrenia Patients: Metabolic syndrome is a global health concern, affecting approximately 20-25% of the adult population in general population. The prevalence varies based on demographic factors, including age, sex, ethnicity, and lifestyle.

Metabolic syndrome is significantly more prevalent in individuals with schizophrenia compared to the general population. Estimates suggest that up to 50% of schizophrenia patients may meet the diagnostic criteria for MetS. This elevated risk is attributed to a combination of disease-specific factors, lifestyle behaviors, and the side effects of antipsychotic medications. [1–3, 8,39]

Role of Untreated Schizophrenia in Metabolic Derangements: Untreated schizophrenia itself is associated with adverse metabolic outcomes, independent of medication use. Chronic stress and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in schizophrenia contribute to metabolic disturbances such as, Elevated cortisol levels, which promote central fat accumulation and insulin resistance and reduced physical activity due to the disabling effects of untreated psychotic symptoms.

Impact of Antipsychotic Medications on Metabolic Health

First-Generation Antipsychotics (FGAs): Also known as typical antipsychotics, these drugs primarily target dopamine D2 receptors to alleviate positive symptoms of schizophrenia, such as delusions and hallucinations.

Examples include haloperidol and chlorpromazine.

FGAs are associated with a high risk of extrapyramidal side effects (EPS) such as tremors, rigidity, and tardive dyskinesia but a relatively lower risk of metabolic disturbances compared to second-generation antipsychotics. [5,7,24,40]

Second-Generation Antipsychotics (SGAs): Also known as atypical antipsychotics, SGAs act on both dopamine and serotonin receptors, making them effective for treating both positive and negative symptoms of schizophrenia.

Examples include olanzapine, risperidone, and quetiapine.

SGAs have a lower propensity for EPS but a significantly higher risk of metabolic side effects, including weight gain, dyslipidemia, and glucose intolerance. [17,32]

Mechanisms by Which Antipsychotics Contribute to Metabolic Abnormalities

Central Nervous System Effects: Blockade of histamine H1 and serotonin 5-HT2C receptors contributes to increased appetite and weight gain.

Dopamine antagonism in the hypothalamus disrupts energy balance and satiety regulation.

Peripheral Effects: Antipsychotics can induce insulin resistance by interfering with glucose metabolism in skeletal muscles and the liver.

Alterations in lipid metabolism lead to elevated triglycerides and reduced HDL cholesterol levels.

Behavioral Changes: Antipsychotics may exacerbate sedentary behavior and fatigue, reducing physical activity. Side effects such as drowsiness and lethargy discourage adherence to a healthy lifestyle.

These mechanisms work synergistically to promote the development of obesity, dyslipidemia, and impaired glucose tolerance, which are hallmarks of metabolic syndrome. [9,39]

Evidence on Olanzapine and Metabolic Syndrome: Weight Gain: Olanzapine-induced weight gain is one of the most commonly reported side effects. Patients can gain 2-5 kg within the first 12 weeks of treatment. A study by Fernández et al. (2011) observed significant weight increases within the initial weeks of therapy19.

Dyslipidemia: Elevated levels of triglycerides and low-density lipoprotein (LDL) cholesterol, along with reduced HDL cholesterol, are frequently reported.

Glucose Intolerance: Impaired fasting glucose and insulin resistance are prevalent in patients on olanzapine, contributing to the development of type 2 diabetes.

These findings highlight the need for vigilance in monitoring metabolic parameters in patients treated with olanzapine. [1,2,8,39]

Evidence on Risperidone and Metabolic Syndrome: Risperidone, a second-generation

antipsychotic, is considered to have a relatively lower risk of metabolic side effects compared to olanzapine. Studies have demonstrated that:

Risperidone causes moderate weight gain, typically less severe than that observed with olanzapine. Average weight increases range from 1-3 kg during the first three months of therapy.

Dyslipidemia and glucose intolerance are reported but are generally less pronounced than with other SGAs like olanzapine or clozapine. A study by Nanotkar et al. (2016) highlighted that metabolic changes with risperidone, while present, are milder in nature and onset compared to olanzapine. [22]

Patients treated with risperidone show fewer signs of insulin resistance and less dramatic changes in fasting blood glucose levels. [1,2,8,39]

Research on the impact of Olanzapine and Risperidone on Metabolic parameters: Jonathan M. Meyer et al. 2002, done A retrospective comparison of weight, lipid, and glucose changes between risperidone- and olanzapine-treated inpatients: Metabolic outcomes after 1 year and concluded that olanzapine therapy when compared to risperidone, nongeriatric adult patients saw higher increases in fasting glucose and lipid levels, and these increases were unrelated to changes in weight parameters [33].

Jonathan M. Meyer et al., 2005 done a multicenter, rater-blinded, open-label study on Effects of switching from olanzapine to risperidone on the prevalence of the metabolic syndrome in overweight or obese patients with schizophrenia or schizoaffective disorder and concluded that the prevalence of the metabolic syndrome in high-risk overweight or obese patients with schizophrenia or schizoaffective disorder was highly prevalent at baseline [2].

In 2009, V. Medved et al. conducted a 3-month follow-up research on metabolic syndrome in female patients with schizophrenia receiving second-generation antipsychotic treatment. In this with both olanzapine and risperidone was associated with a significant increase in waist circumference, and olanzapine treatment might induce significant alterations in metabolic profiles, especially among patients with a positive family history of diabetes [4]

In a study on drug-emergent metabolic syndrome in patients with schizophrenia receiving atypical (second-generation) antipsychotics, Gautam et al. (2011) found that 11.66% of the patients developed metabolic syndrome after taking antipsychotic medication for four months. They also came to the conclusion that second-generation antipsychotics cause significantly more changes in metabolic parameters, which increases the risk of developing metabolic syndrome and related conditions like type II diabetes and cerebrovascular accidents.[57]

In a study published in 2016, Sanjay B. Nanotkar et al. examined the effects of olanzapine and risperidone on the metabolic parameters of individuals with schizophrenia in 189 consecutive new participants who were given either olanzapine (n=96) or risperidone (n=93) in the psychiatry department of a rural medical college and hospital. They found that both risperidone and olanzapine had a tendency to cause metabolic syndrome in patients who take them, even if the increase in triglycerides, fasting glucose, and systolic and diastolic blood pressure was not statistically significant. [22]

In a 2019 study, Lavanya Nagaraj et al. compared the metabolic side effects of olanzapine and risperidone 1 shows that both risperidone and olanzapine were associated with comparable baseline-to-endpoint increases in metabolic side effects and concluded that apart from total cholesterol and triglycerides, other metabolic side effects were less in risperidone-treated patients than in olanzapine-treated patients.[58]

In a research by Shiraz Hussain and colleagues (2021), Comparison Of Two Widely Used Atypical Antipsychotics Olanzapine Versus Risperidone In Terms Of Metabolic Outcomes, on 114 newly diagnosed psychiatric patients 57 patients each group , observed that patients receiving olanzapine were 2.58 times more prone to develop metabolic syndrome compared to the risperidone-receiving and concluded that olanzapine associated with more serious and long-term side effects elevated weight, dyslipidemia, and poor blood glucose tolerance.[59]

Rikhari, Praveen et al., (2022) conducted a 24-week prospective observational study at a teaching hospital in North India on Metabolic derangements with olanzapine and risperidone in schizophrenia spectrum and other psychotic disorders in a total of 45 patients, 30 on olanzapine and 15 on risperidone showed significant changes in all variables with olanzapine while with risperidone also significant changes occurred in all variables except waist circumference and fasting plasma glucose, and they concluded that olanzapine and risperidone cause metabolic derangements.[8]

In their study of schizophrenic patients' serum glucose and cholesterol levels before and after treatment with olanzapine, risperidone, and haloperidol, Ajay Kumar et al. (2023) found that there were notable increases in both serum glucose and serum cholesterol levels following six weeks and six months of treatment. They also came to the conclusion that olanzapine was linked to an

increased risk of weight gain, glucose intolerance, and dyslipidemia.[60]

Kiumarth Amini et al. (2024), in a study done on the effects of atypical antipsychotics on serum asprosin levels and other metabolic parameters in patients with schizophrenia, observed statistically significant differences in BMI and fasting serum levels of glucose, HA1c, insulin, triglyceride (TG), high-density lipoprotein cholesterol, and asprosin among patients receiving olanzapine or risperidone [49]

Fernandez-Egea and associates. A study conducted in 2011 on the metabolic consequences of olanzapine in patients with recently diagnosed psychosis found that a considerable rise in low-density lipoprotein and total cholesterol was predicted. Otherwise, they found that baseline IL-6 and parental history of type 2 diabetes mellitus did not predict changes in metabolic measures. They also came to the conclusion that olanzapine treatment can identify changes in metabolic measures early in the course of treatment for individuals who have never taken an antipsychotic before.[19]

The 2011 study by Abhishek Pallava et al. An Indian study comparing patients who were free or naïve to antipsychotics and those who were treated with them found that those receiving antipsychotic treatment had significantly higher mean weights, body mass indices, waist circumferences, calorie intake, triglycerides (TGL), very-low-density lipoproteins (VLDL), and fasting blood sugar (FBS), which highlights the importance of routinely monitoring a number of metabolic parameters in antipsychotic patients.[61]

According to Henry J. Riordan et al. (2011), A Study on Atypical Antipsychotics and Metabolic Syndrome in Patients with Schizophrenia: Risk Factors, Monitoring, and Healthcare Implications, all atypical antipsychotic medications currently come with warnings about the risk of diabetes and hyperglycemia, along with recommendations for routine monitoring. The authors came to the conclusion that if a patient is not treated due to the possibility of metabolic syndrome complications, they may be at a higher risk of experiencing more severe health consequences.[62]

In their 2016 study, Prevalence of Metabolic Syndrome in Patients with Schizophrenia in Korea: A Multicenter Nationwide Cross-Sectional Study, Jung Sun Lee et al. found that the prevalence of MetS was 36.5% in all patients, significantly higher in men than in women (men, 40.8%; women, 32.2%), and significantly correlated with both age and length of illness. It came to the conclusion that MetS screening and monitoring are highly advised.[63]

In a one-year follow-up study on the impact of olanzapine on metabolic syndrome, K. Samyukta et al. (2020) found that olanzapine has a high propensity to disrupt metabolic parameters in patients with schizophrenia. They also found statistically significant differences in weight, fasting blood glucose, TG, HDL, and WC at the end of a year when compared to baseline.[12]

Material and Methods

Study Design: This study was designed as a comparative observational study aimed at evaluating the metabolic effects of olanzapine and risperidone in schizophrenia patients.

Study Setting: The study was conducted at the Government Hospital for Mental Care, Visakhapatnam, under the Department of Psychiatry, Andhra Medical College. Participants were recruited from both outpatient and inpatient services.

Duration of the Study: The study was carried out over one year, from December 2023 to November 2024, with follow-ups conducted at three and six months after initiation of treatment.

Sample Size: A total of 140 participants were recruited in the study.

The formula is $n \geq ((z_{(1-\alpha/2)}+z_{(1-\beta)})^2 (\sigma_1^2+\sigma_2^2/r))/((\mu_1-\mu_2)^2)$.

Sampling Method: Participants were selected using simple random sampling.

Inclusion Criteria

The study included patients who:

- Were diagnosed with schizophrenia based on ICD-11 clinical criteria.
- Were in the 18–50 age range.
- Both males and females.
- Were either drug-naïve or had not taken antipsychotic medication throughout the lengthy washout period of six months prior to the trial.
- Provided written informed consent for participation.

Exclusion Criteria

Participants were excluded if they:

- Were unable to cooperate due to acute psychotic symptoms at the time of evaluation.
- Had been treated with any psychiatric medication within the past six months.
- Were diagnosed with other psychiatric or significant medical conditions.
- Had substance dependence, diabetes mellitus, hypertension, or dyslipidemia at baseline.

Study Tools: The following tools and measurements were employed:

ICD-11 Diagnostic Criteria: Used to confirm the diagnosis of schizophrenia.

Semi-Structured Proforma: Collected socio-demographic details and relevant clinical history.

Anthropometric Measurements: Waist circumference measured midway between the inferior margin of the ribs and the superior border of the iliac crest.

Body Mass Index (BMI) calculated as weight (kg) divided by height (m^2).

Blood Pressure: Measured using a standardized sphygmomanometer.

Laboratory Investigations: Fasting blood glucose, triglycerides, HDL cholesterol levels were analyzed to assess metabolic parameters.

International Diabetes Federation (IDF) Criteria / National Cholesterol Education Program-Adult Treatment Panel III (NCEP ATP III): Applied to diagnose metabolic syndrome.

Diagnostic Criteria-METABOLIC SYNDROME

Two commonly used diagnostic criteria for metabolic syndrome are:

International Diabetes Federation (IDF): A essential requirement is central obesity, defined as a waist circumference of at least 90 cm for Asian males and 80 cm for Asian women.

Plus, any two of the following:

1. Elevated triglycerides (≥150 mg/dL) or treatment for this abnormality.

2. Reduced HDL cholesterol (<40 mg/dL in men, <50 mg/dL in women).

3. Elevated blood pressure (≥130/85 mm Hg) or antihypertensive treatment.

4. Fasting glucose ≥100 mg/dL or previously diagnosed diabetes. [6,18,37]

National Cholesterol Education Program-Adult Treatment Panel III (NCEP ATP III):

The presence of three or more of the following criteria:

- Central obesity.
- Elevated triglycerides.
- Reduced HDL cholesterol.
- Elevated blood pressure.
- Fasting glucose ≥100 mg/dL.

Both criteria highlight the significance of central obesity and its role in triggering other metabolic derangements. [12,14]

Procedure: After obtaining approval from the Institutional Ethics Committee, eligible participants were screened according to the inclusion and exclusion criteria. Written informed consent was obtained from all participants after explaining the nature and purpose of the study.

Participants were divided into two groups based on their prescribed antipsychotic:

- Group 1 received olanzapine. (n = 70)
- Group 2 received risperidone. (n = 70)

Baseline measurements, including socio-demographic details, anthropometric data, and metabolic parameters, were collected. Follow-up assessments were conducted at three and six months after initiating treatment. No other antipsychotics, mood stabilizers, or medications that could interfere with metabolic parameters were used during the study. In agitated or aggressive patients, benzodiazepines were administered as required.

During the follow up period

- From Group 1(Olanzapine): 12 individuals were lost to follow up.
- From Group 2(Risperidone): 7 individuals were lost to follow up.

A total of 121 individuals completed their 3 months and 6 months follow-ups. So, after the completion of 6 months follow up

Group 1 (Olanzapine Group): n = 58.

Group 2 (Risperidone Group): n = 63.

Data Collection: Data were collected using standardized forms to ensure consistency. Blood samples were drawn at baseline, three months, and six months for laboratory analysis. Anthropometric measurements and blood pressure were recorded during the same intervals. By applying IDF or NCEP ATP III criteria individuals were diagnosed for metabolic syndrome.

Statistical Analysis: Data were analyzed using the SPSS software (latest version). Descriptive statistics were used to summarize baseline characteristics. Continuous variables were expressed as means ± standard deviations, and categorical variables were presented as frequencies and percentages. The differences between the two groups were evaluated using appropriate statistical tests:

- Independent t-tests for continuous variables.
- Chi-square tests for categorical variables.

Multivariate regression analysis was performed to identify risk factors associated with the development of metabolic syndrome. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: Ethical approval was obtained from the Institutional Ethics Committee, Andhra Medical College. Confidentiality of

participants was maintained, and all data were anonymized. Participants were free to withdraw from the study at any time without any impact on their standard care. Written informed consent was obtained prior to inclusion in the study.

Observation and results

Socio-Demographic Characteristics of Study Participants: The study recruited a total 140 individuals (Olanzapine group consists 70 and Risperidone group consists of 70). Out of all the participants only 121 individuals completed both 3 months and 6 months follow up (58 participants in the Olanzapine group and 63 participants in the Risperidone group). All diagnosed with schizophrenia and undergoing treatment for six months. The following socio-demographic patterns were observed as follows

Observation and results

Age Distribution: The most common age group among participants was 35–44 years, accounting for 34.5% in the Olanzapine group and 34.9% in the Risperidone group. The youngest group (18–24 years) represented the smallest proportion in both arms, indicating a relatively older population was included.

Table 1: Sample distribution according to Age

Characteristic	Category	Olanzapine Group	Risperidone Group
Age Group (years)	18–24	10(17.2%)	12(19%)
	25–34	14(24.1%)	16(25.4%)
	35–44	20(34.5%)	22(34.9%)
	45–50	14(24.1%)	13(20.6%)
Total		58(100%)	63(100%)

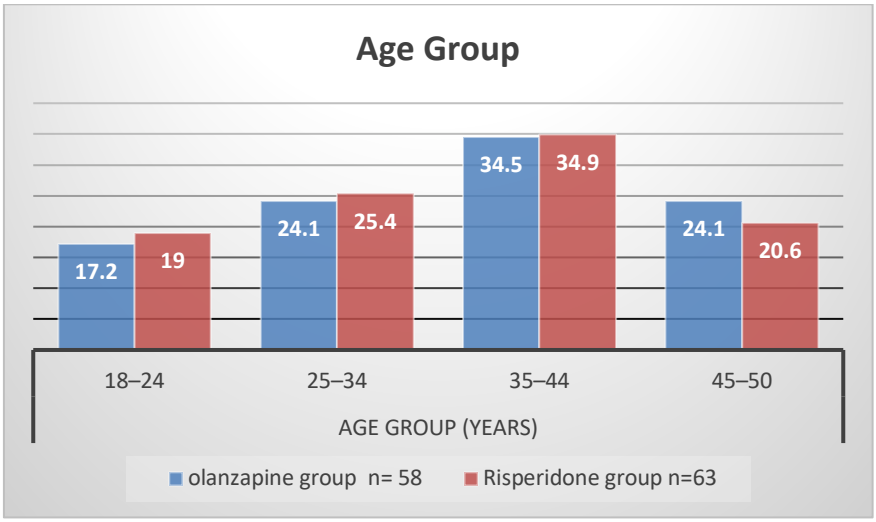

Figure 1: Distribution of sample based on Age

Gender: Olanzapine group shows 55.2 % Males and 44.8 % females. Risperidone group consist of 46 % males and 54 % female population,

Table 2: Sample distribution according to Gender

Characteristic	Category	Olanzapine Group	Risperidone Group
Sex	Male	32(55.2%)	29(46%)
	Female	26(44.8%)	34(54%)
Total		58(100%)	63(100%)

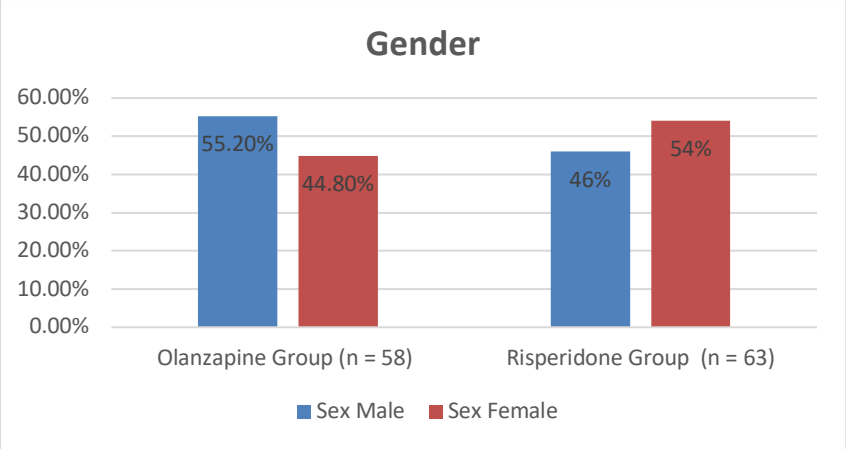

Figure 2 : Distribution of sample based on Gender

Domicile: A large portion of participants resided in Rural areas (51.7% in Olanzapine, 62.0% in Risperidone), followed by urban and tribal regions.

Table 3: Sample distribution according to Domicile

Characteristic	Category	Olanzapine Group	Risperidone Group
Domicile	Tribal	6(10.3%)	4(6.3%)
	Rural	30(51.7%)	39(62%)
	Urban	22(38%)	20(31.7%)
Total		58(100%)	63(100%)

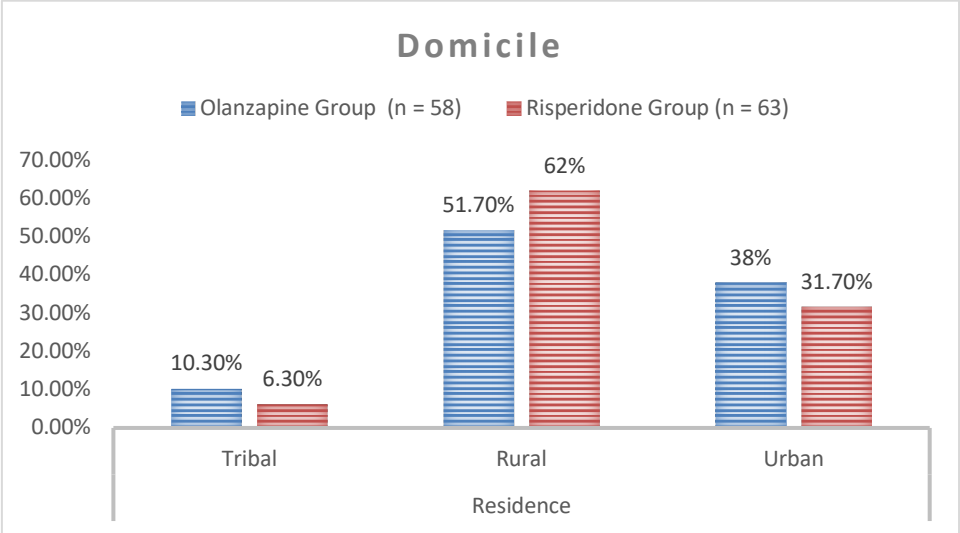

Figure 3 : Distribution of sample based on Domicile

Religion: The majority of participants were Hindu (around 79.3% in Olanzapine and 76.2% in Risperidone), consistent with the demographic distribution of the study region.

Table 4: Sample distribution according to Religion

Characteristic	Category	Olanzapine Group	Risperidone Group
Religion	Hindu	46(79.3%)	48(76.2%)
	Muslim	7(12.1%)	8(12.7%)
	Christian	5(8.6%)	7(11.1%)
TOTAL		58(100%)	63(100%)

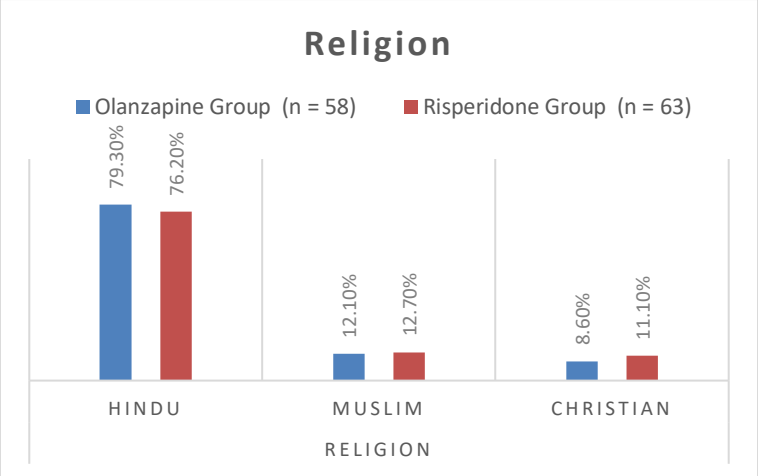

Figure 4 : Distribution of sample based on Religion

Education: Most participants had completed secondary education (31.0% Olanzapine; 31.7% Risperidone), while a smaller subset were graduates or above (13.8% and 12.7% respectively).

Table 5: Sample distribution according to Education

Characteristic	Category	Olanzapine Group	Risperidone Group
Education	Illiterate	8(13.8%)	10(15.9%)
	Primary	12(20.7%)	14(22.2%)
	Secondary	18(31%)	20(31.7%)
	Higher Secondary	12(20.7%)	11(17.5%)
	Graduate & above	8(13.8%)	8(12.7%)
TOTAL		58(100%)	63(100%)

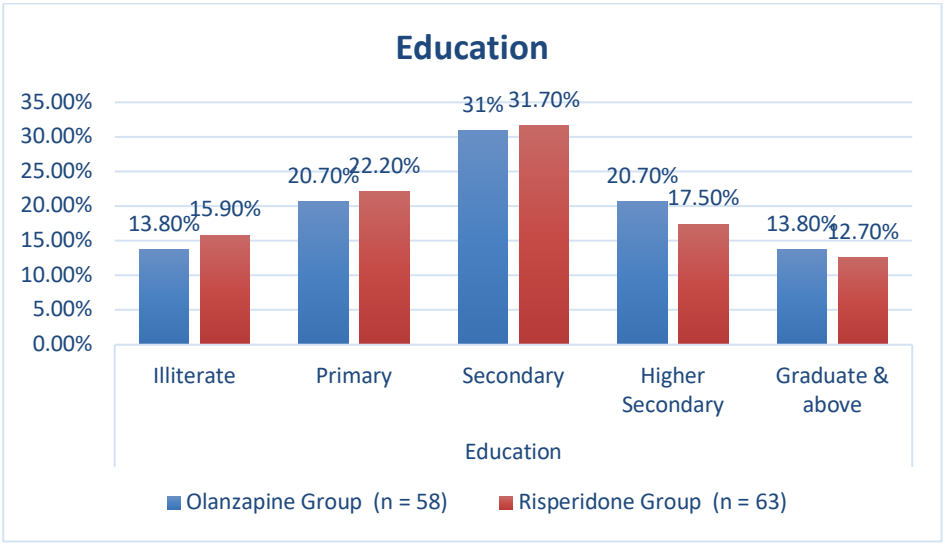

Figure 5 : Distribution of sample based on Education

Occupation: Unemployment was notable, affecting 34.5% (Olanzapine) and 34.9% (Risperidone), reflecting the functional impairment often associated with schizophrenia. A mix of unskilled, semi-skilled, and skilled occupations were also represented.

Table 6: Sample distribution according to Occupation

Characteristic	Category	Olanzapine Group	Risperidone Group
Occupation	Unemployed	20(34.5%)	22(34.9%)
	Unskilled	14(24.1%)	16(25.4%)
	Semi-skilled	10(17.2%)	11(17.5%)
	Skilled	14(24.1%)	14(22.2%)
Total		58(100%)	63(100%)

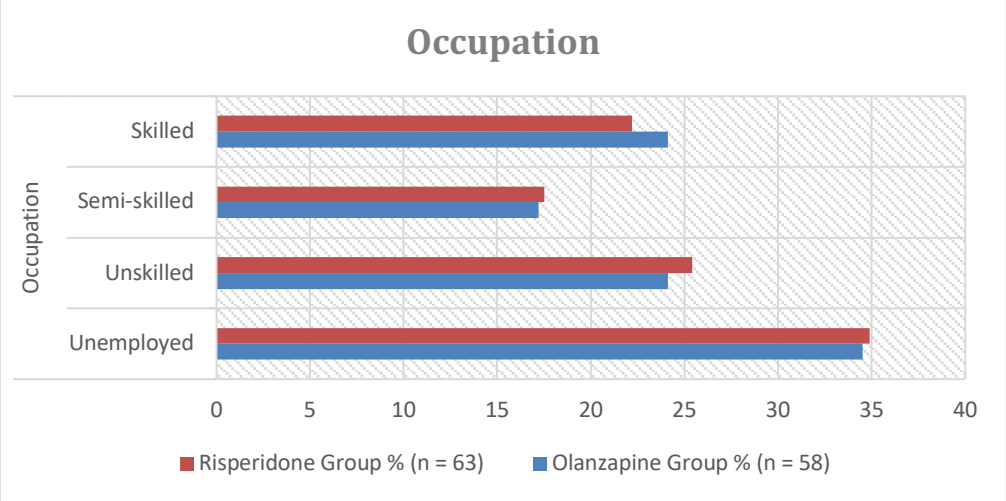

Figure 6 : Distribution of sample based on Occupation

Socioeconomic Status: The lower-middle class was the most common socioeconomic group in both cohorts (37.9% and 36.5% respectively). Very few belonged to the upper class, underscoring the socioeconomically disadvantaged profile of the sample.

Table 7: Sample distribution according to Socio- Economic Status

Characteristic	Category	Olanzapine Group	Risperidone Group
Socioeconomic Status	Upper	4(6.9%)	5(7.9%)
	Upper-middle	12(20.7%)	13(20.6%)
	Lower-middle	22(37.9%)	23(36.5%)
	Upper-lower	14(24.1%)	16(25.4%)
	Lower	6(10.3%)	6(9.5%)
Total		58(100%)	63(100%)

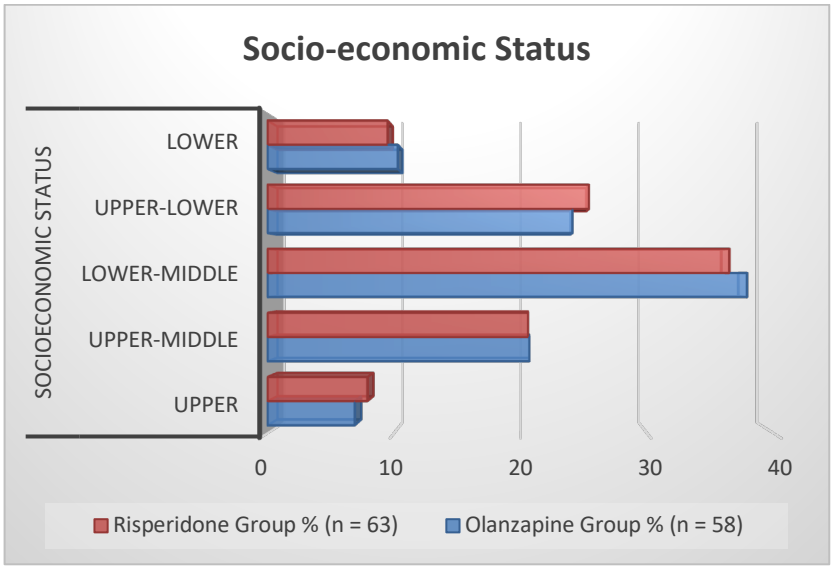

Figure 7: Distribution of sample based on Socio Economic Status

Marital Status: In Olanzapine group 70.6% are married and 29.4% are mix of unmarried. In Risperidone group 77.7 % are married and 22.3 % unmarried

Table 8: Sample distribution according to MARITAL STATUS

Characteristic	Category	Olanzapine Group	Risperidone Group
Marital Status	Married	41(70.6%)	49(77.7%)
	Unmarried	17(29.4%)	14(22.3%)
TOTAL		58(100%)	63(100%)

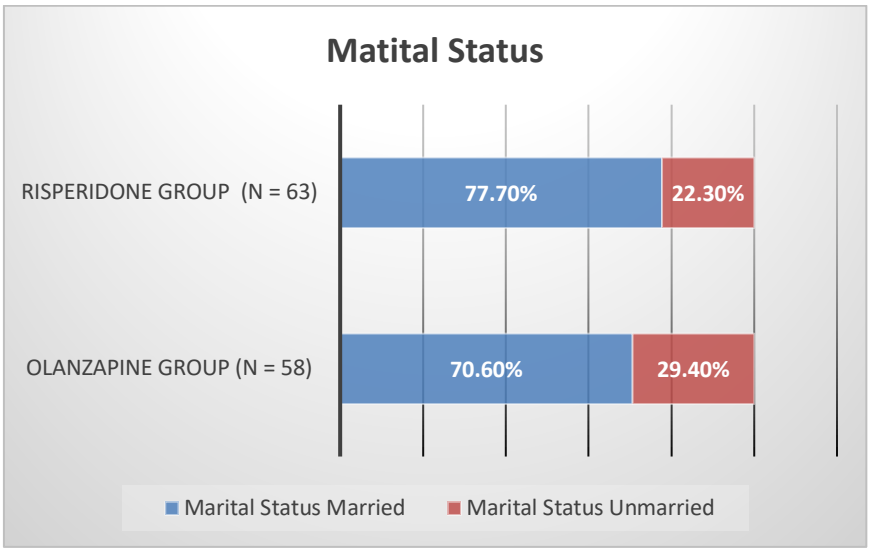

Figure 8 : Distribution of sample based on MARITAL STATUS

Family History of HTN/DM/CVD/Dyslipidemia: A positive family history of hypertension, diabetes, cardiovascular disease, or dyslipidemia was more prevalent in the Olanzapine group (31.0%) than Risperidone (25.4%), which may contribute to higher metabolic risk.

Table 9: Sample distribution according to Family H/O HTN/DM/CVD

Characteristic	Category	Olanzapine Group	Risperidone Group
Family History of HTN/DM/CVD/ Dyslipidemia	Yes	18(31%)	16(25.4%)
	No	40(69%)	47(74.6%)
TOTAL		58(100%)	63(100%)

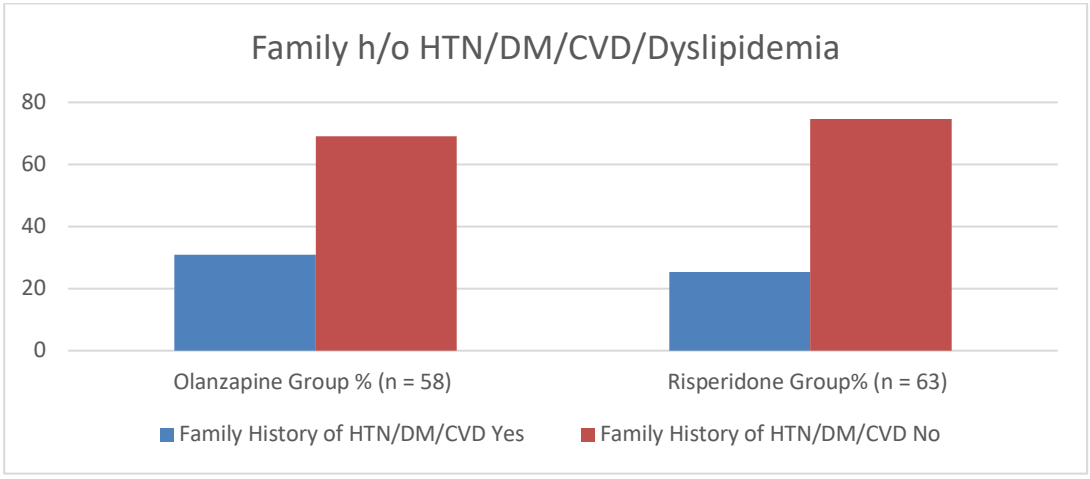

Figure 9: Distribution of sample based on FAMILY H/O HTN/DM/CVD/Dyslipidemia

Smoking and Alcohol Use: Smoking prevalence was higher in the Olanzapine group (41.4%) than in the Risperidone group (31.7%). Alcohol use followed a similar pattern, with 34.5% in the Olanzapine group and 28.6% in the Risperidone group reporting use.

Table 10: Sample distribution according to Smoking and Alcohol use

Characteristic	Category	Olanzapine Group	Risperidone Group
Smoking Status	Yes	24(41.4%)	20(31.7%)
	No	34(58.6)	43(68.3)
Total		58(100%)	63(100%)
Alcohol Use	Yes	20(34.5%)	18(28.6%)
	No	38(65.5%)	45(71.4%)
Total		58(100%)	63(100%)

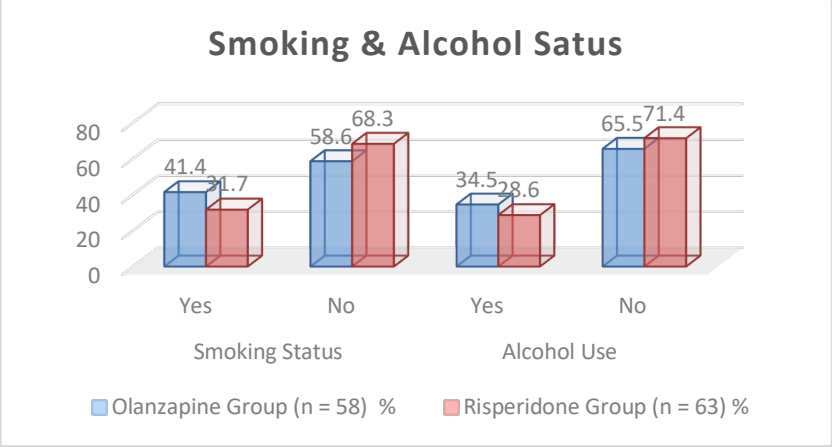

Figure 10: Distribution of sample based on SMOKING & ALCOHOL use

Physically inactive and poor diet: A higher proportion of participants in the Risperidone group (38.1%) were physically inactive and had a poor diet compared to those in the Olanzapine group (31%).

Table 11: Sample distribution according to Physical Inactivity & Poor diet

Characteristic	Category	Olanzapine Group	Risperidone Group
Physically inactive and poor diet	Yes	18(31%)	24(38.1%)
	No	40(69%)	39(61.9%)
TOTAL		58(100%)	63(100%)

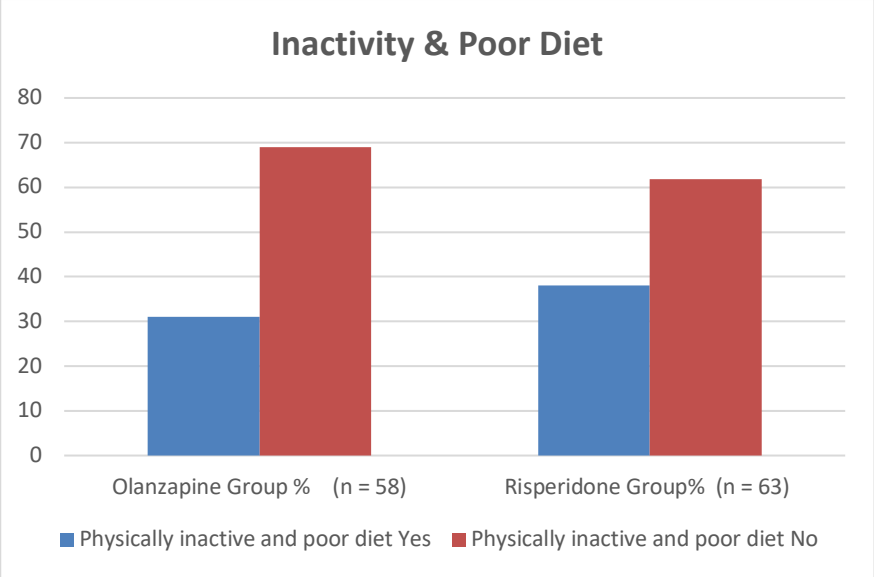

Figure 11 : Distribution of sample based on PHYSICAL INACTIVITY & DIET

BMI Categories: Normal BMI was the most common in both groups (~70%), followed by overweight and obese individuals. A small percentage were under weight (5.2% in Olanzapine and 3.2% in Risperidone), possibly due to illness severity or nutritional deficits

Table 12: Sample distribution according to BMI

Characteristic	Category	Olanzapine Group	Risperidone Group
BMI Category	Underweight	3(5.2%)	2(3.2%)
	Normal	40(69%)	45(71.4%)
	Overweight	13(22.4%)	15(23.8%)
	Obese	2(3.4%)	1(1.6%)
Total		58(100%)	63(100%)

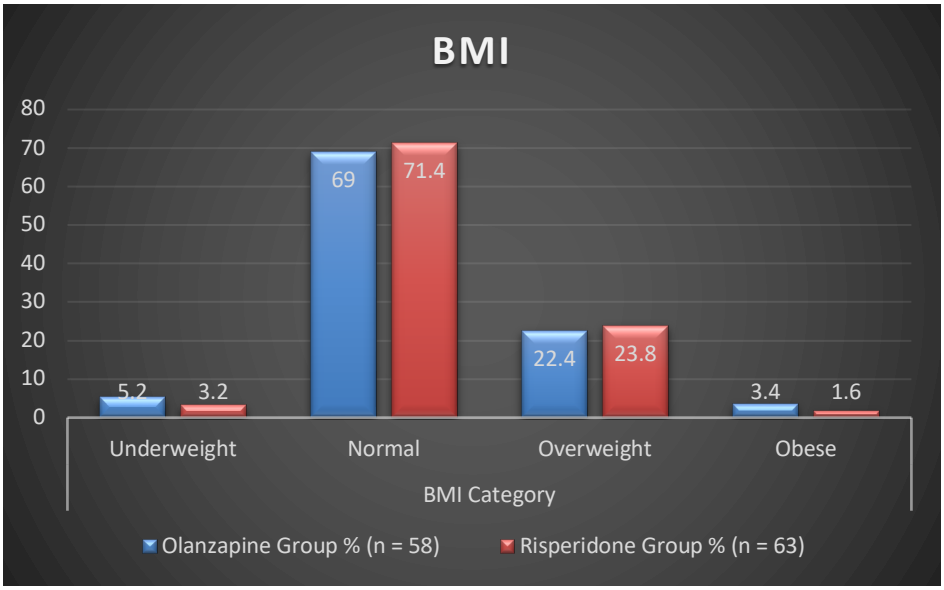

Figure 12 : Distribution of sample based on BMI status

Table 13: Baseline Metabolic Parameters

Variable	Olanzapine (n=58)	Risperidone (n=63)
Weight (kg)	61.2 ± 10.7	60.4 ± 9.7
BMI (kg/m2)	22.5 ± 2.1	22.7 ± 2.4
Waist Circumference (cm)	71.6 ± 8.2	70.6 ± 9.6
Systolic BP	110.3 ± 8.5	114.7 ± 6.2
Diastolic BP	70.5 ± 6.4	72.8 ± 5.1
Triglycerides	122.8 ± 10.1	120.8 ± 12.3
HDL	49.1 ± 4.3	50.2 ± 4.8
Fasting Blood Glucose	84.4 ± 7.2	86.7 ± 4.5

At baseline, the two groups were comparable across most metabolic parameters.

Weight and BMI values were slightly higher in the Olanzapine group (61.2 kg and 24.1 kg/m²) than Risperidone (60.4 kg and 23.8 kg/m²), but the differences were not statistically significant. Waist circumference, BP, triglycerides, HDL, and fasting blood glucose showed minor numerical differences but were not statistically significant, suggesting both groups started from similar metabolic baselines.

Weight Gain over Time between two groups

Weight increased progressively in both groups, but more notably in the Olanzapine group:

- From 61.2 kg to 67.8 kg at 6 months.
- Risperidone group showed a rise from 60.4 kg to 63.0 kg.

The difference was statistically significant at 6 months (p = 0.015), indicating greater weight gain with Olanzapine.

Table 14: Weight Gain Change over Time between two groups

Time Point	Olanzapine (n=58)	Risperidone (n=63)	P-value
Baseline	61.2 ± 10.7	60.4 ± 9.7	0.667
3 months	64.1 ± 11.2	62.4 ± 8.6	0.348
6 months	67.8 ± 12.1	63.0 ± 7.4	**0.01***

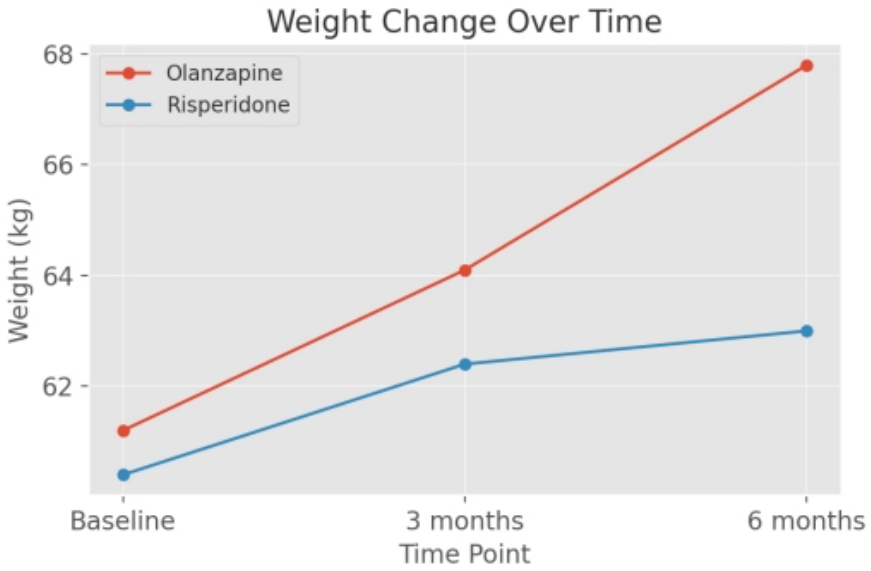

Figure 13: Showing Weight Gain Change Over Time

BMI Changes between two groups: BMI showed a statistically significant increase in the Olanzapine group at 6 months (26.1 ± 2.8 cm) compared to Risperidone (24.3 ± 2.5 cm) with p = 0.001. At baseline and 3 months, there was no significant difference, indicating that BMI changes very prominent between groups with longer treatment.

Table 15: BMI Changes between Groups over time

Time Point	Olanzapine Group BMI (kg/m²)	Risperidone Group BMI (kg/m²)	p-value
BASE LINE	22.5 ± 2.1	22.7 ± 2.4	0.459
3 Months	24.3 ± 2.5	23.5 ± 2.3	0.644
6 months	26.1 ± 2.8	24.3 ± 2.5	**0.001***

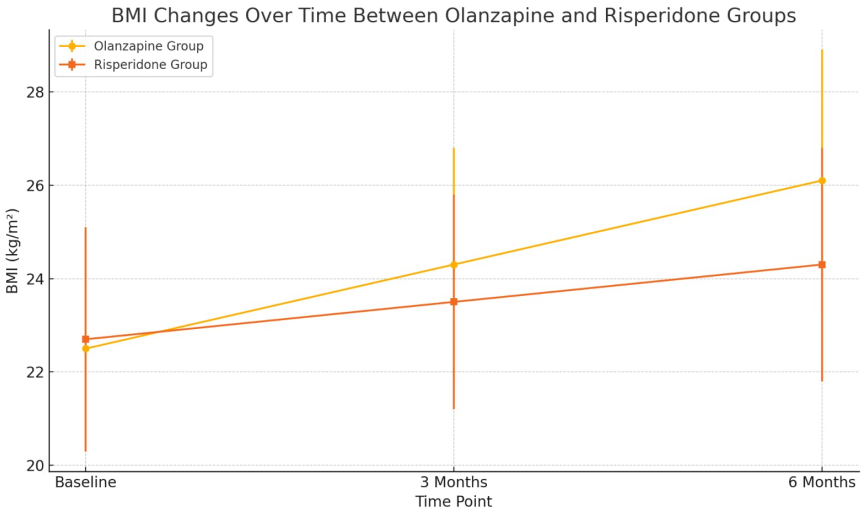

Figure 14: Showing BMI Change Over Time.

Waist Circumference Changes between two groups: Waist circumference showed a statistically significant increase in the Olanzapine group at 6 months (76.4 ± 6.8 cm) compared to Risperidone (73.2 ± 7.6 cm) with p = 0.01. At baseline and 3 months, there was no significant difference, indicating that metabolic effects became apparent with longer treatment.

Table 16: Waist Circumference Changes between Groups

Time Point	Olanzapine (n=58)	Risperidone (n=63)	P-value
Baseline	71.6 ± 8.2	70.6 ± 9.6	0.540
3 months	73.2 ± 6.2	72.4 ± 8.2	0.555
6 months	76.4 ± 6.8	73.2 ± 7.6	**0.016***

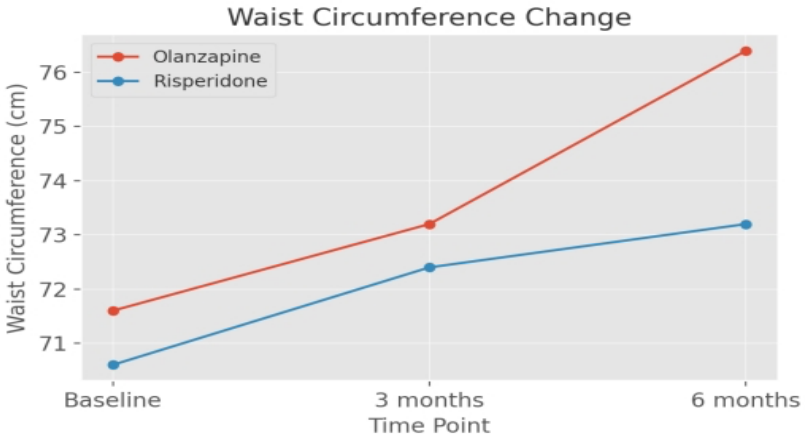

Figure 15: Showing Waist Circumference Change Over Time.

Blood Pressure Changes between groups: No significant differences were found in both systolic and diastolic BP at any time point. Both groups had mild increases in BP over 6 months, but p-values remained > 0.05, suggesting no significant Blood Pressure changes and cardiovascular impact from either drug in the short term.

Table 17: Blood Pressure (Systolic & Diastolic) Changes Over Time

Time Point	Systolic BP (Olanzapine)	Systolic BP (Risperidone)	P-value	Diastolic BP (Olanzapine)	Diastolic BP (Risperidone)	P-value
Baseline	110.2 ± 8.5	112.6 ± 6.4	0.080	70.5 ± 6.4	72.2 ± 5.8	0.128
3 months	112.2 ± 7.6	113.6 ± 6.8	0.287	72.4 ± 5.6	73.0 ± 5.9	0.568
6 months	116.2 ± 8.1	114 ± 6.2	0.094	73.2 ± 4.8	74.1 ± 4.2	0.273

Triglyceride Levels between two groups over time period: Triglyceride levels increased progressively in both groups, but significantly more in the Olanzapine group at 6 months (130.4 ± 10.2 mg/dL vs. 126.2 ± 11.8 mg/dL, p = 0.031). This indicates a potential risk of dyslipidemia with longer Olanzapine use.

Table 18: Triglyceride Changes Over Time

Time Point	Olanzapine (n=58)	Risperidone (n=63)	P-value
Baseline	124.2 ± 10.1	123.4 ± 8.6	0.639
3 months	128.4 ± 12.4	124.6 ± 11.2	0.081
6 months	130.4 ± 10.2	126.2 ± 11.8	**0.031***

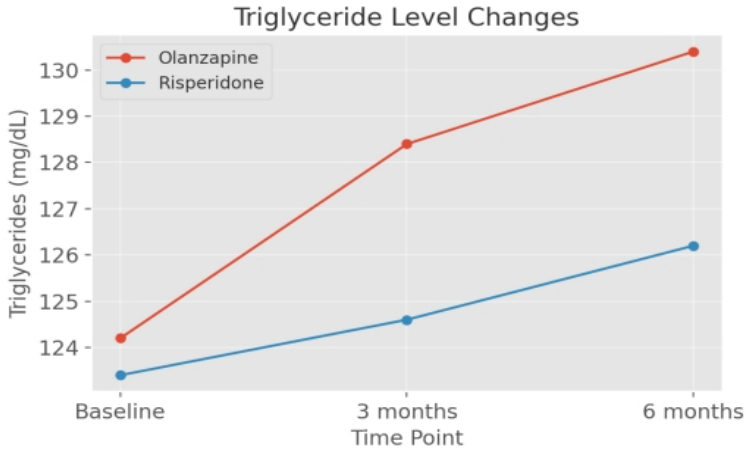

Figure 16: Showing Triglycerides Change Over Time

HDL over time Changes between two groups: HDL levels decreased in both groups, more in the Olanzapine arm.

- Olanzapine: From 49.1 to 47.2 mg/dL.
- Risperidone: From 50.2 to 48.9 mg/dL.

However, no significant difference was noted across the groups.

Table 19: HDL Changes Over Time between Groups

Time Point	Olanzapine (n=58)	Risperidone (n=63)	P-value
Baseline	49.1 ± 4.3	50.2 ± 4.8	0.188
3 months	48.1 ± 4.6	49.4 ± 4.2	0.106
6 months	47.2 ± 4.8	48.9 ± 4.0	0.229

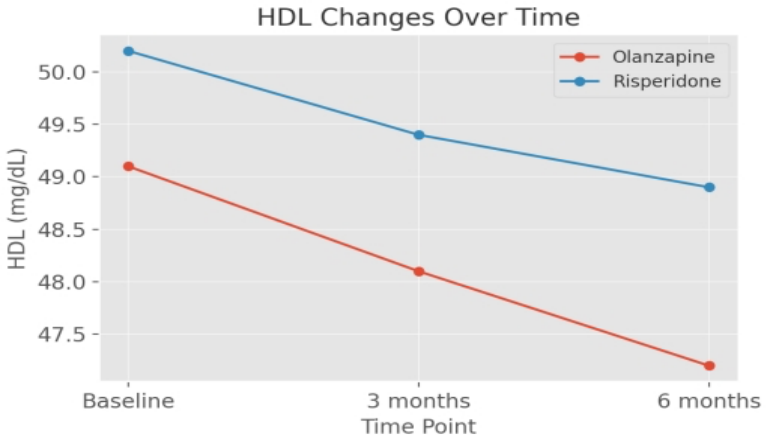

Figure 17: Showing HDL Change over Time between two groups

Fasting Blood Glucose changes over time between two groups: A significant rise in fasting blood glucose was observed in the Olanzapine group at 6 months (92.4 ± 6.2 mg/dL) vs. Risperidone (88.6 ± 3.4 mg/dL), with $p < 0.0001$. Earlier differences (baseline and 3 months) were not significant, indicating glucose metabolism impairment may manifest with longer exposure to Olanzapine.

Table 20: Fasting Blood Glucose Changes over Time between groups

Time Point	Olanzapine (n=58)	Risperidone (n=63)	P-value
Baseline	85.4 ± 7.2	86.7 ± 4.5	0.232
3 months	88.1 ± 6.8	87.4 ± 4.2	0.484
6 months	92.4 ± 6.2	88.6 ± 3.4	**<0.0001****

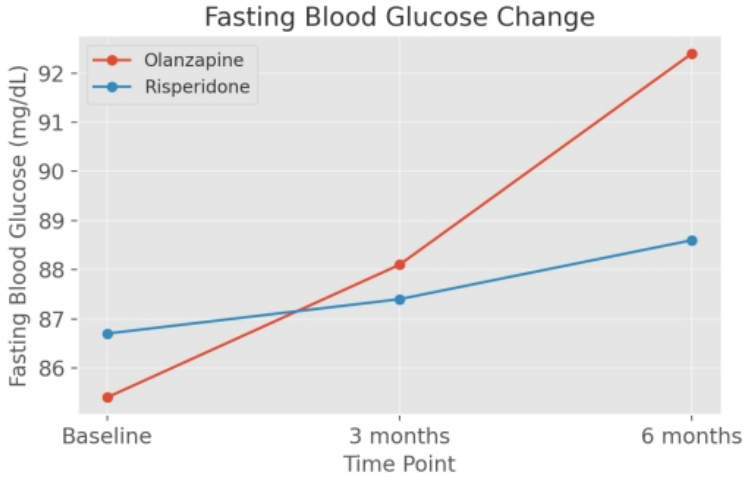

Figure 18: Showing Fasting Blood Glucose Change Over Time

Incidence of Metabolic Syndrome between Olanzapine and Risperidone: At 3 months, the incidence of metabolic syndrome was higher in the Olanzapine group (18.96%) compared to Risperidone (9.5%), but not statistically significant (p = 0.218). However, by 6 months, the difference became statistically significant: Olanzapine 31.0% vs. Risperidone 14.3% (p = 0.027), confirming greater metabolic risk with Olanzapine over time.

Table 21: Incidence of Metabolic Syndrome at 3 and 6 Months

Time Point	Group	Metabolic syndrome (present)	Metabolic syndrome (absent)	Total	P-value (Chi-square)
3 months	Olanzapine	11(18.96%)	47(81.04%)	58 (100%)	0.218
	Risperidone	6(9.52%)	57(90.48%)	63 (100%)	
6 months	Olanzapine	18(31.03%)	40(68.96%)	58(100%)	**0.027***
	Risperidone	9(14.3%)	54(85.7%)	63(100%)	

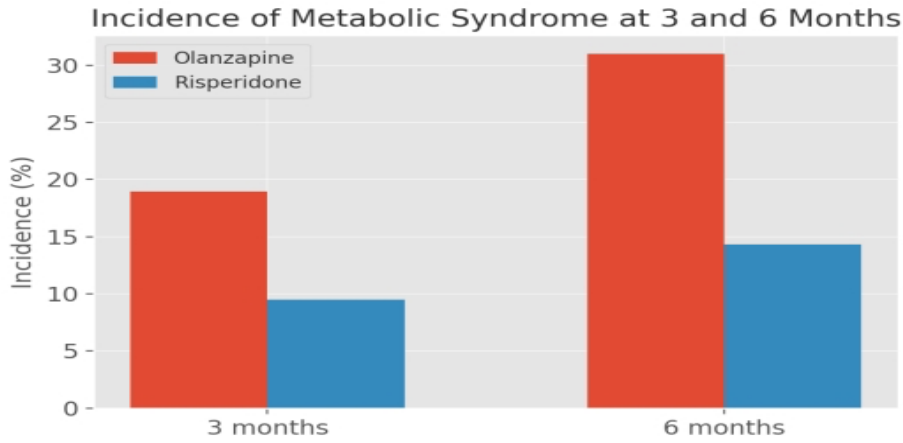

Figure 19: Showing Incidence of Metabolic Syndrome between groups

Overall MetS incidence at 6 months (both groups): At the end of 6 months, 31.03% of patients on olanzapine developed metabolic syndrome (MetS), which was more than double the incidence seen in the risperidone group (14.3%). The overall incidence across both groups was 22.3%, and the difference between groups was statistically significant (p = 0.027). This finding highlights the comparatively higher metabolic burden posed by olanzapine over time.

Table 22: Overall MetS incidence at 6 months OLANZAPINE vs RISPERIDONE

MetS at 6 months	OLAN (n = 58)	RISP (n = 63)	TOTAL	P value
Present	18 (31.03%)	9 (14.3%)	27 (22.3%)	**0.027***
Absent	40 (68.96%)	54 (85.7%)	94 (77.7%)	

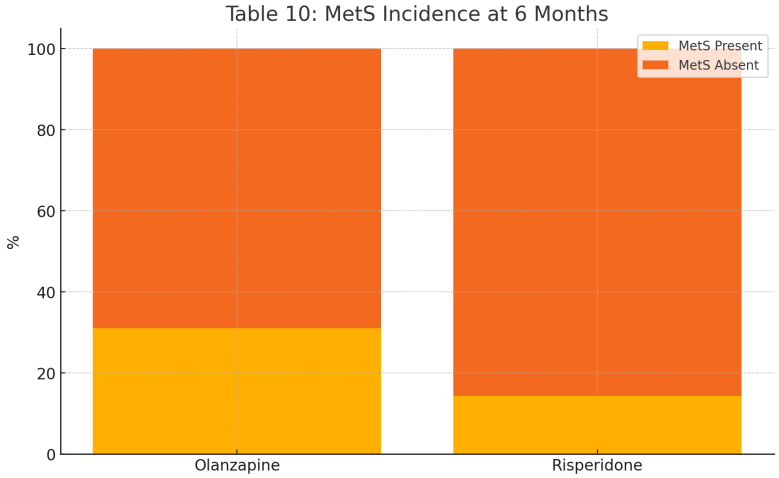

Figure 20: Showing Metabolic Syndrome Incidence at 6 months between groups

Risk Factors of Metabolic Syndrome Analysis

Age-Wise MetS Distribution: Age played a significant role in the development of MetS. The highest incidence was observed in the 45–50 years age group, with 57% of olanzapine-treated and 38.5% of risperidone-treated patients affected. Conversely, the 18–24 age group had the lowest MetS incidence (20% in olanzapine, 8.3% in risperidone). This indicates an age-dependent gradient in metabolic vulnerability, possibly due to cumulative lifestyle and biological factors.

The trend was more pronounced in the olanzapine arm, especially in older individuals. These findings underscore the importance of age-stratified risk assessments before initiating treatment. Clinicians should be vigilant in high-risk age brackets.

Table 23: Age-wise MetS at 6 months

Age Group	OLAN: MetS present	OLAN: MetS absent	P value	RISP: MetS present	RISP: MetS absent	P value
18–24	2 (20%)	8 (80%)		1 (8.3%)	11 (91.7%)	
25–34	5 (36%)	9 (64%)	0.053	1 (6.3%)	15 (93.7%)	0.058
35–44	3 (15%)	17 (85%)		2 (9.1%)	20 (90.9%)	
45–50	8 (57%)	6 (43%)		5 (38.5%)	8 (61.5%)	

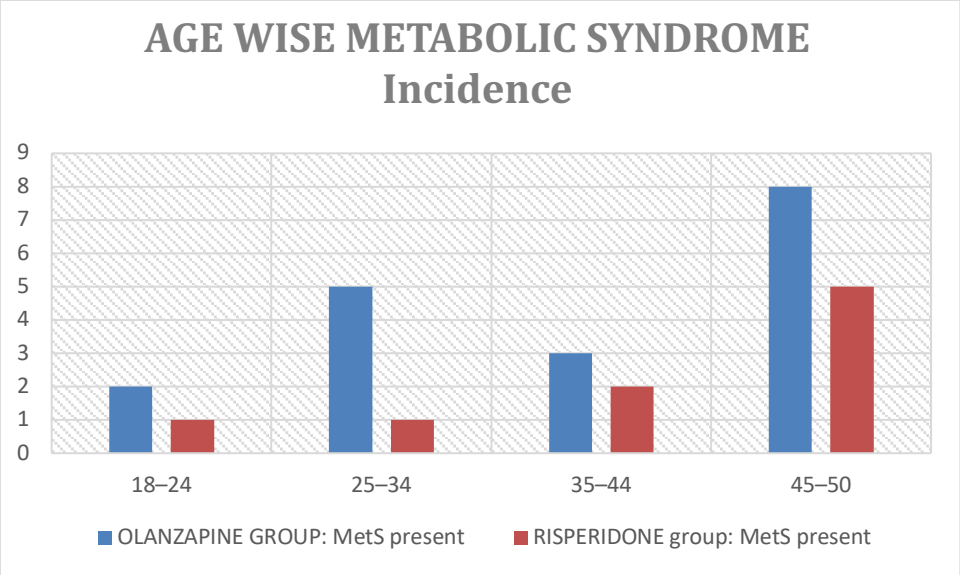

Figure 21: Showing Age wise Metabolic Syndrome distribution at 6 months

Gender-Wise MetS Distribution

Gender-based analysis revealed no statistically significant difference in MetS incidence between males and females.

However, males exhibited a higher rate of MetS overall (34.4% in olanzapine vs. 17.2% in risperidone), while female rates were lower across both groups. This suggests a trend toward increased metabolic risk in males, consistent with literature citing higher visceral fat accumulation and behavioral risk factors such as smoking and alcohol intake. Although not statistically conclusive, this trend warrants consideration when selecting antipsychotics in male patients. Clinicians may consider more frequent metabolic screening for male schizophrenia patients, particularly those treated with olanzapine. Additional studies with larger sample sizes may clarify the gender-specific metabolic risk.

Table 24: Gender-wise MetS at 6 months

Gender	OLAN: MetS present	OLAN: MetS absent	P value	RISP: MetS present	RISP: MetS absent	P value
Male	11 (34.4%)	21 (65.6%)	0.745	5 (17.2%)	24 (82.8%)	0.796
Female	7 (23%)	19 (77%)		4 (11.8%)	30 (88.2%)	

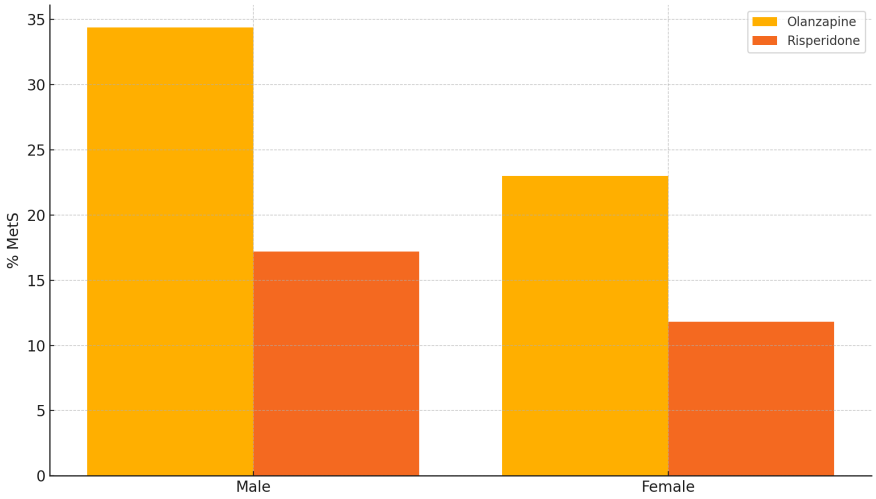

Figure 22: Showing Gender wise Metabolic Syndrome distribution at 6 months

Family History of HTN/DM/CVD and MetS

A statistically significant association was noted between family history of hypertension, diabetes, dyslipidemia or cardiovascular disease and MetS incidence.

Among patients with a positive family history, 61.1% on olanzapine (p = 0.0009). And 37.5% on risperidone developed MetS (p = 0.006). In contrast, those without a family history had a much lower incidence (17.5% in olanzapine, 6.4% in risperidone). This highlights the predictive value of genetic predisposition in antipsychotic-induced metabolic dysregulation. The impact was more profound in the olanzapine group, emphasizing the additive risk posed by both genetic and pharmacological factors. Screening for family history should be a routine part of pre-treatment evaluation. Patients with positive family history may benefit from early intervention protocols.

Table 25: MetS with Family History of DM/HTN/CVD

Family History	OLAN: MetS present	OLAN: MetS absent	P value	RISP: MetS present	RISP: MetS absent	P value
Yes	11 (61.1%)	7 (38.9%)	**0.0009***	6 (37.5%)	10 (62.5%)	**0.006***
No	7 (17.5%)	33 (82.5%)		3 (6.4%)	44 (93.6%)	

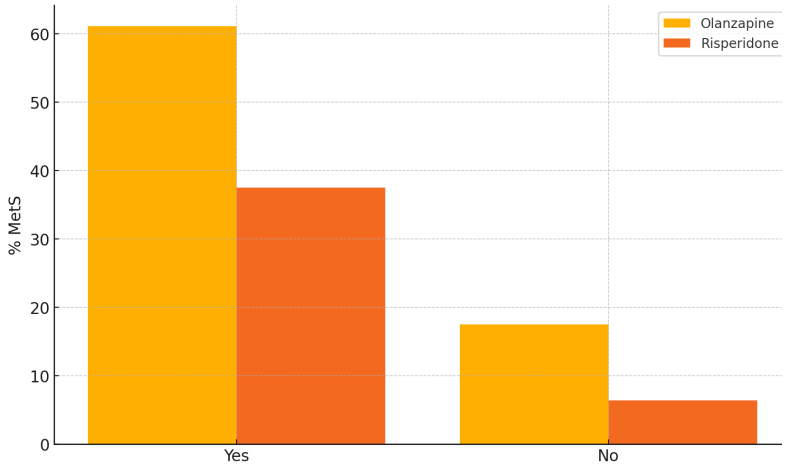

Figure 23: Showing Family history of DM/HTN/CVD vs MetS

Physical Inactivity and Poor Diet vs. MetS: There was a statistically significant association between lifestyle factors and MetS (p = 0.0002). In the olanzapine group, 66.7% of physically inactive patients with poor dietary habits developed MetS compared to only 15% among those with healthier behaviors. Similarly, in the risperidone group, 29.2% with poor lifestyle developed MetS vs. 5% in the healthier subgroup. These findings reinforce that physical inactivity and poor diet significantly potentiate the metabolic side effects of antipsychotic medications.

Table 26: Diet & Physical Inactivity and MetS

Diet & Physical Inactivity	OLAN: MetS present	OLAN: MetS absent	P value	RISP: MetS present	RISP: MetS absent	P value
Yes	12 (66.7%)	6(33.3%)	**0.0002***	7 (29.2%)	17 (70.8%)	**0.021***
No	6 (15%)	34 (85%)		2 (5%)	37 (95%)	

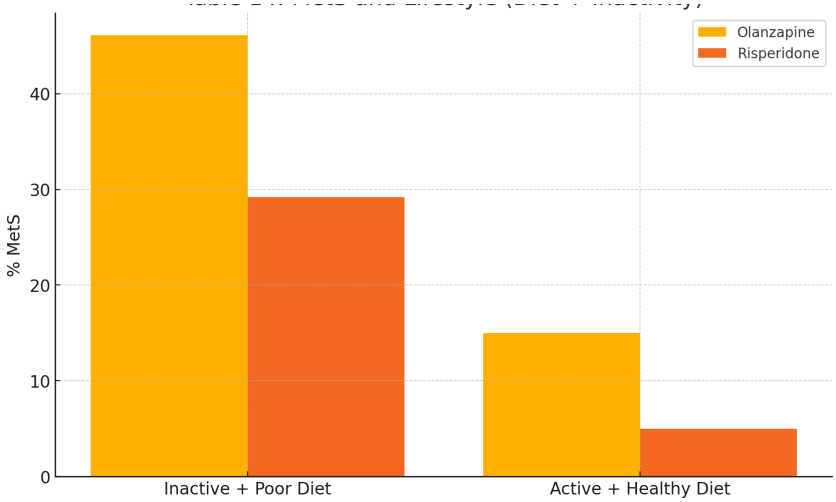

Figure 24: Showing Life style factors vs MetS

Smoking and MetS

Although not reaching statistical significance (p = 0.05), a trend toward higher MetS incidence was observed among smokers.

In the olanzapine group, 45.8% of smokers developed MetS. In the risperidone group, the difference was smaller 20%. Indicating a possible additive effect of smoking with olanzapine. Smoking is known to exacerbate insulin resistance and reduce HDL levels, which may explain the observed pattern. These results suggest that while smoking may not independently predict MetS, it likely contributes to cumulative risk.

Table 27: Smoking Status and MetS

Smoking Status	**OLAN: MetS present**	**OLAN: MetS absent**	**P value**	**RISP: MetS present**	**RISP: MetS absent**	**P value**
Yes	11 (45.8%)	13 (54.2%)	0.05	4 (20%)	16 (80%)	0.447
No	7 (20.6%)	27 (79.4%)		5 (11.6%)	38 (88.4%)	

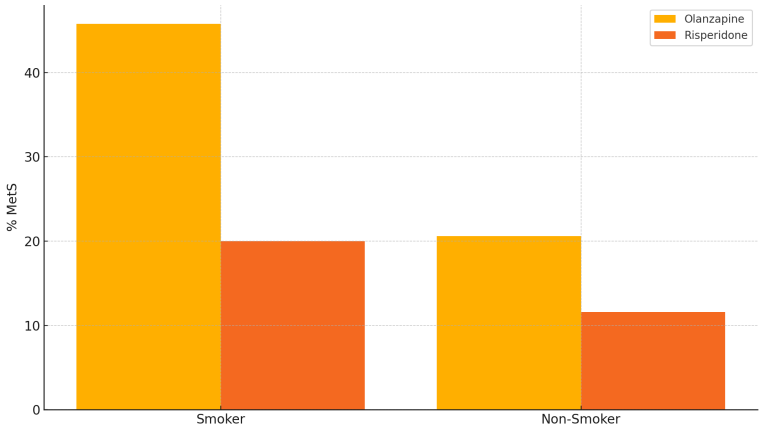

Figure 25: Showing SMOKING status vs MetS

Alcohol Intake and MetS: Alcohol use showed a statistically significant association with MetS development (p = 0.0493). In the olanzapine group, 50% of alcohol users developed MetS compared to 21% of abstainers. The trend was similar though less severe in the risperidone group (27.8% vs. 9.7%). These results suggest that alcohol may amplify the metabolic effects of antipsychotic drugs, possibly through hepatic fat accumulation and altered lipid metabolism. This warrants

cautious prescribing and lifestyle evaluation in patients with known alcohol use. Alcohol screening and counseling should be part of routine psychiatric evaluations.

Table 28: Alcohol Intake and MetS

Alcohol Intake	OLAN: MetS present	OLAN: MetS absent	P value	RISP: MetS present	RISP: MetS absent	P value
Yes	10 (50%)	10 (50%)	**0.049***	5 (27.8%)	13 (72.2%)	0.124
No	8 (21%)	30 (79%)		4 (8.9%)	41(91.1%)	

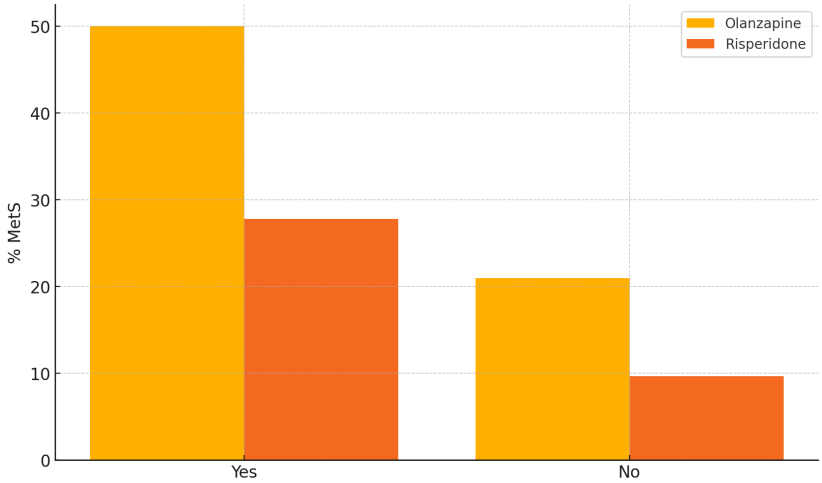

Figure 26: Showing Alcohol use vs MetS

BMI and MetS

There was a significant correlation in both groups between BMI category and MetS. Among obese individuals, in the olanzapine group and the risperidone group all individuals developed MetS. Even among overweight participants, MetS was more frequent in olanzapine users compare to risperidone group (53.8% vs. 26.7%). Normal-weight individuals had the lowest MetS incidence in both groups. Baseline BMI should guide antipsychotic selection and frequency of monitoring.

Table 29: BMI Status and MetS

BMI Category	OLAN: MetS present	OLAN: MetS absent	P value	RISP: MetS present	RISP: MetS absent	P value
Underweight	0	3100%)	**0.016***	0	2(100%)	**0.025***
Normal	9 (22.5%)	31(77.5%)		4 (8.9%)	41 (91.1%)	
Overweight	7 (53.8%)	6(46.2%)		4 (26.7%)	11 (73.3%)	
Obese	2 (100%)	0		1 (100%)	0	

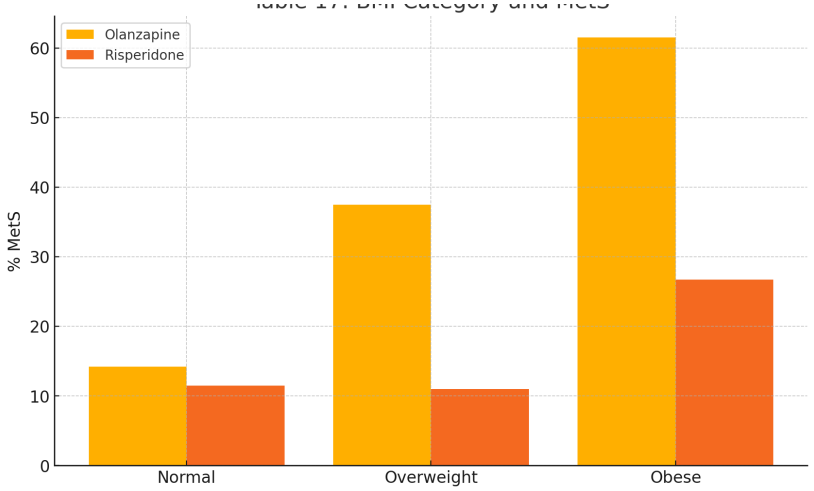

Figure 27: Showing BMI vs MetS

Multivariate Analysis of Risk Factors: Multivariate logistic regression identified several significant predictors for MetS. Olanzapine use was the strongest independent risk factor (OR = 2.10, p < 0.001), followed by physical inactivity and poor diet (OR = 2.45, p = 0.004), and BMI (OR = 1.25, p = 0.009). Smoking and alcohol use also showed significant associations (p = 0.015 and 0.042, respectively), while family history (OR = 1.58, p = 0.033) contributed moderately to overall risk. These results highlight that MetS development is multifactorial and driven by both pharmacologic and lifestyle-related components. Preventive strategies should address both domains.

Table 30: Multivariate Analysis of Risk Factors for Metabolic Syndrome

Variable	Odds Ratio (OR)	95% CI	p-value
Age	1.02	0.98–1.06	0.215
Gender	1.15	0.95–1.38	0.112
Smoking	1.67	1.11–2.53	**0.015**
Alcohol Use	1.42	1.03–1.97	**0.042**
BMI	1.25	1.08–1.44	**0.009**
Drug Type (Olanzapine vs. Risperidone)	2.10	1.48–2.97	**<0.001**
Family History of HTN/DM/CVD	1.58	**1.05–2.41**	**0.033**
Physically Inactive and Poor Diet	2.45	**1.39–4.31**	**0.004**

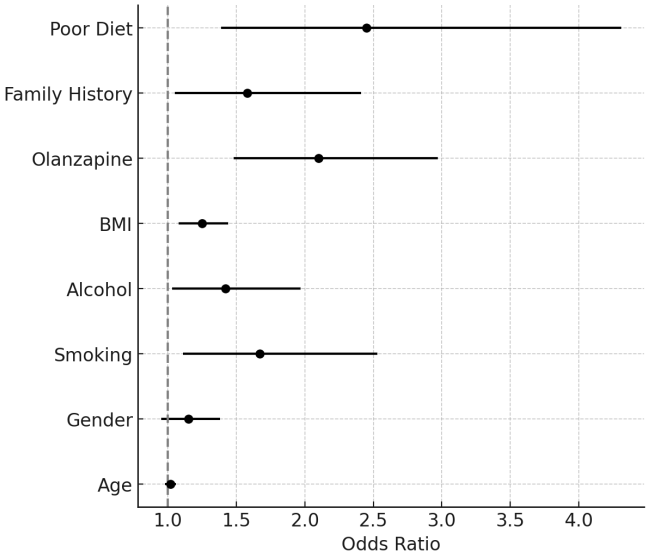

Figure 28: Multivariate Analysis of Risk Factors for Metabolic Syndrome

Regression Analysis – Treatment Duration vs. MetS: The regression analysis showed a positive time-dependent association between treatment duration and MetS risk. At 3 months, the regression coefficient (B) was 0.28 (p = 0.045), increasing to 0.63 by 6 months (p = 0.001). This confirms that prolonged antipsychotic exposure escalates metabolic risk, especially in the absence of lifestyle intervention. These findings support the implementation of proactive screening protocols and consideration of switching or dose adjustment if early metabolic changes are detected.

Table 31: Regression Analysis – Treatment Duration vs. Metabolic Syndrome

Duration (Months)	Regression Coefficient (B)	Standard Error (SE)	p-value
3	0.28	0.14	0.045
6	0.63	0.17	0.001

Discussion

Overview of Objectives and Study Design

This study was conceptualized in response to the well-documented metabolic disturbances associated with second-generation antipsychotics, particularly olanzapine and risperidone, both widely used in schizophrenia treatment. While the efficacy of these agents in managing psychotic symptoms is established, their differential impact on metabolic parameters remains a topic of continued investigation. As noted by Meyer et al., switching from olanzapine to risperidone resulted in significant improvements in metabolic profile, suggesting a pharmacologically modifiable risk component for metabolic syndrome in

schizophrenia patients [33]. Similarly, Rosa et al. emphasized the metabolic benefits of transitioning patients from oral olanzapine to long-acting risperidone, highlighting improved patient adherence and reduced cardiometabolic burden. [1]

The primary objective of this comparative study was to assess and contrast the incidence, progression, and risk factors for metabolic syndrome in schizophrenia patients receiving olanzapine versus risperidone over a 6-month period. Additionally, the study explored the influence of treatment duration, lifestyle, and socio-demographic factors on the development of metabolic syndrome. Given prior evidence suggesting early onset of metabolic derangements—particularly with olanzapine [19]—the present study employed longitudinal follow-up assessments to capture both immediate and progressive changes in metabolic parameters.

Previous literature has demonstrated that olanzapine is associated with greater metabolic liabilities—including weight gain, insulin resistance, and dyslipidemia—when compared to risperidone [8-11,38]. Amini et al. also reported significantly elevated insulin, HbA1c, and triglyceride levels in patients treated with olanzapine and risperidone compared to aripiprazole or healthy controls [49].

Demographic and Baseline Profile

The demographic analysis of the sample, summarized in Tables 1 to 12, revealed a fairly comparable distribution between the olanzapine and risperidone groups in terms of age, sex, and socioeconomic status. The most common age bracket for both groups was 35–44 years, aligning with the typical age of onset and treatment stabilization for schizophrenia[22]. A slightly higher percentage of male patients was observed in olanzapine group and higher percentage of female patients seen in risperidone group, which mirrors broader epidemiological patterns [23].

Socioeconomic data showed that the majority of patients belonged to the lower-middle class, a finding consistent with the literature citing schizophrenia's strong association with lower socioeconomic strata due to poor occupational functioning, stigma, and long-term disability [12,24]. Unemployment was reported in over one-third of both groups, reflecting the disorder's significant impact on functional outcomes.

Interestingly, a larger proportion of patients in the risperidone group (38.1%) reported physical inactivity and poor dietary habits compared to the olanzapine group (31%), which may have implications for baseline metabolic risk and eventual outcomes. Such behavioral risk factors are frequently noted in schizophrenia patients, often compounded by medication-induced fatigue and negative symptoms such as avolition [11,36]. Moreover, smoking and alcohol use were more prevalent in the olanzapine group, both of which are known contributors to worsening metabolic profile [9].

Baseline anthropometric and metabolic parameters, detailed in Table 13, indicated that the olanzapine group had slightly higher average weight, BMI, waist circumference, and triglyceride levels at initiation. These values may suggest a pre-existing vulnerability to metabolic derangements, potentially exacerbated by the pharmacologic properties of olanzapine, as previously demonstrated by Fernández et al., who observed significant increases in these variables within weeks of therapy initiation [19].

Notably, both groups had fasting blood glucose and HDL values within normal range at baseline, although the olanzapine group trended toward worse glycemic and lipid indices. These observations warrant careful consideration when interpreting longitudinal metabolic changes, as they may reflect not just drug-induced effects but also pre-treatment risk profiles.

Anthropometric Changes over Time.

Metabolic Parameters: Weight, BMI, Waist Circumference, and Blood Pressure

The current study demonstrated a progressive and statistically significant increase in body weight among schizophrenia patients treated with olanzapine, in comparison to those receiving risperidone. At baseline, both groups were comparable in terms of body weight (61.2 ± 10.7 kg vs. 60.4 ± 9.7 kg). However, by the 6-month follow-up, the olanzapine group exhibited a mean weight of 67.8 ± 12.0 kg, which was significantly higher than the 63.0 ± 7.4 kg observed in the risperidone group ($p = 0.015$) (Table 14). This finding aligns with previous literature identifying olanzapine as a second-generation antipsychotic associated with pronounced weight gain due to its strong antagonistic action on histamine H1 and serotonin 5-HT2C receptors, both of which regulate appetite and energy balance [33,39].

Waist circumference, a surrogate marker for central adiposity, also increased significantly in the olanzapine group compared to risperidone. Baseline values were 71.6 ± 8.2 cm (Olanzapine) and 70.6 ± 9.6 cm (Risperidone), but by the 6-month point, the olanzapine group showed a mean waist circumference of 76.4 ± 6.8 cm versus 73.2 ± 7.6 cm in the risperidone group, with the difference reaching statistical significance ($p = 0.016$) (Table 16). These results are consistent with previous prospective studies which have documented abdominal fat accumulation as a hallmark feature

of olanzapine-induced metabolic disruption [19,39]. BMI baseline values were 22.5 ± 2.1 kg/m2 (Olanzapine) and 22.7± 2.4 kg/m2 (Risperidone).At the end of 6 months follow up BMI showed a statistically significant increase in the Olanzapine group at 6 months (26.1 ± 2.8 kg/m2) compared to Risperidone (24.3 ± 2.5 kg/m2) with p = 0.001(Table 15). At baseline and 3 months, there was no significant difference, indicating that BMI changes very prominent between groups with longer treatment. This observation aligns with findings from Nanotkar et al. found a higher risk of MetS among patients on olanzapine compared to risperidone, especially with rise of BMI values in olanzapine group than risperidone group.

In contrast, the analysis of blood pressure trends did not reveal any statistically significant differences between the two groups at any time point. Systolic and diastolic blood pressures increased slightly in both groups over the 6-month period but remained within normal clinical ranges. For instance, systolic BP in the olanzapine group rose from 110.2 ± 8.5 mmHg at baseline to 116.2 ± 8.1 mmHg at 6 months, compared to 114.0 ± 6.2 mmHg in the risperidone group at the same interval (p = 0.094) (Table 17). Diastolic values showed a similar pattern without statistical significance (p = 0.27). These findings are in line with reports by Rikhari et al. and Smith et al., where antipsychotic-induced blood pressure changes did not exhibit clinical relevance during initial treatment periods [8,39].

Overall, the study reinforces the metabolic risk profile of olanzapine with regard to weight gain and central adiposity. These physical changes, particularly visceral fat accumulation, are important contributors to insulin resistance and long-term cardiovascular risk, even in the absence of significant changes in blood pressure.

Glycemic and Lipid Profile Alterations

In the current study, fasting blood glucose (FBG) levels exhibited a notable upward trend over the 6-month follow-up period, particularly in the olanzapine group. At baseline, the FBG levels were comparable between the two cohorts (85.4 ± 7.2 mg/dL vs. 86.7 ± 4.5 mg/dL for olanzapine and risperidone, respectively). However, by the end of 6 months, the olanzapine group showed a significant rise in mean FBG to 92.4 ± 6.2 mg/dL, compared to 88.6 ± 3.4 mg/dL in the risperidone group (p < 0.0001) (Table 20). This statistically significant difference underscores the diabetogenic potential of olanzapine, a finding supported by previous studies such as those by Fernández et al. and Amini et al., which have demonstrated early and sustained glycemic dysregulation with olanzapine use [19,49]. The lipid profile further substantiated the differential metabolic impact of the two antipsychotics. Triglyceride levels, which were initially comparable at baseline (124.2 ± 10.1 mg/dL in the olanzapine group vs. 123.4 ± 8.6 mg/dL in the risperidone group), rose progressively over time. At 6 months, the olanzapine group showed a mean triglyceride level of 130.4 ± 10.2 mg/dL, significantly higher than the 126.2 ± 11.8 mg/dL observed in the risperidone group (p = 0.031) (Table 18). This elevation mirrors the findings from Smith et al., who noted postprandial hypertriglyceridemia as an early marker of olanzapine-associated lipid dysregulation [39].

High-density lipoprotein (HDL) cholesterol, another important component of metabolic health, declined in both groups during the follow-up, though more steeply in patients treated with olanzapine. HDL levels in the olanzapine group declined from 49.1 ± 4.3 mg/dL at baseline to 47.2 ± 4.8 mg/dL at 6 months, while the risperidone group showed a smaller reduction from 50.2 ± 4.8 mg/dL to 48.9 ± 4.0 mg/dL (Table 19). Although the between-group differences did not reach statistical significance at every interval, the trend remained clinically relevant, as reduced HDL levels are strongly predictive of cardiovascular morbidity. This observation corroborates the conclusions drawn by Rikhari et al., who found that HDL reduction was significantly more pronounced in the olanzapine group [8].

These collective findings point to a more adverse glyco-lipidemic trajectory among patients on olanzapine, even within a 6-month treatment window, these alterations have substantial implications for long-term cardiometabolic health. Therefore, routine monitoring of fasting glucose and lipid profiles should be an integral part of psychiatric care, particularly when initiating olanzapine therapy in patients with baseline risk factors.

Incidence and Progression of Metabolic Syndrome

A critical outcome measure in this study was the incidence of metabolic syndrome (MetS) at different follow-up intervals. Using the IDF criteria or NCEP -ATP III, the data revealed a clear trend toward increased metabolic syndrome occurrence in the olanzapine group as treatment progressed. At 3 months, 18.96% (n = 11) of participants on olanzapine developed MetS, compared to 9.5% (n = 6) in the risperidone group. Although the difference was not statistically significant at this point (p = 0.218), it indicated an early metabolic burden in the olanzapine arm. By the 6-month follow-up, the incidence of MetS rose markedly to 31.0% (n = 18) in the olanzapine group versus 14.3% (n = 9) in the risperidone group. This difference was statistically significant (p = 0.027)

(Table 21), underscoring the cumulative effect of olanzapine on metabolic risk over time. This observation aligns with findings from Nanotkar et al. found a higher risk of MetS among patients on olanzapine compared to risperidone, especially when triglyceride levels and waist circumference were elevated early in treatment [22].

These results also reflect the synergistic impact of multiple metabolic abnormalities—namely weight gain, increased waist circumference, elevated triglycerides, and hyperglycemia—that collectively fulfilled the diagnostic threshold for MetS in the olanzapine cohort. While risperidone did cause some degree of metabolic alteration, the incidence remained lower and progressed more gradually, reinforcing its relatively favorable metabolic profile.

The findings from this study are consistent with international literature on the metabolic risks associated with second-generation antipsychotics. They also emphasize the necessity for regular, structured metabolic assessments starting from the early phases of treatment. Furthermore, early identification of at-risk individuals—based on baseline triglyceride levels, family history, or sedentary lifestyle—can guide pre-emptive interventions such as dietary modifications and consideration of alternative antipsychotic agents with lower metabolic liabilities.

In summary, olanzapine was associated with a significantly higher incidence of metabolic syndrome by the end of the study period, while risperidone, though not devoid of risk, presented a more tolerable metabolic trajectory. These findings further affirm the importance of individualized antipsychotic selection and regular follow-up to mitigate long-term cardiometabolic consequences in patients with schizophrenia.

Subgroup Analyses of Risk Factors

Detailed subgroup analysis was performed to explore the relationship between baseline characteristics and the development of metabolic syndrome during antipsychotic treatment.

Age-wise distribution (Table 23; Figure 21) showed that older participants (≥35 years) were at a higher risk for developing metabolic abnormalities over 6 months. This is in agreement with Kwobah et al., who noted that increasing age was a significant predictor of metabolic syndrome in psychotic patients in a low-resource setting60. The age-associated decline in insulin sensitivity and increase in visceral fat may explain this higher susceptibility, especially when combined with the metabolic burden of second-generation antipsychotics. Gender-based analysis (Table 24; Figure 22) indicated a male predominance in the study sample; however, the association between gender and metabolic syndrome did not reach statistical significance. This observation partially aligns with the findings of Rikhari et al., who observed similar metabolic trends in both genders but slightly higher incidence among males8. Gender-related differences in fat distribution and hormonal regulation may contribute but were not definitively evident in the current cohort.

A positive family history of hypertension, diabetes, or cardiovascular disease (Table 25; Figure 23) was significantly associated with the development of metabolic syndrome, reinforcing existing evidence that genetic predisposition plays a substantial role in metabolic risk, especially when compounded by environmental and pharmacologic exposures. Hurley et al. also emphasized the need for targeted interventions in such high-risk groups, especially those receiving clozapine or olanzapine [58].

Lifestyle factors, particularly physical inactivity and poor diet, demonstrated a statistically significant correlation with metabolic outcomes (Table 26; Figure 24). This supports earlier reports by Alsabhan et al., who found that non-pharmacologic variables like dietary habits and sedentary behavior independently worsened metabolic indicators in pediatric patients receiving risperidone [57]. Such modifiable factors are crucial intervention targets in long-term antipsychotic therapy.

Smoking and alcohol consumption (Tables 27 and 28) were also evaluated. Smoking showed a borderline association with worsening lipid and glycemic profiles, while alcohol use had a moderate but significant impact, particularly on triglyceride levels and waist circumference. These findings are consistent with those of Smith et al., who indicated that lifestyle comorbidities could amplify antipsychotic-induced metabolic risk [39,61]. These behaviors may also indirectly affect metabolism by altering medication adherence, appetite, and physical activity patterns.

Finally, BMI and obesity (Table 29; Figure 27) were among the strongest predictors of developing metabolic syndrome. Patients with baseline obesity were significantly more likely to develop further metabolic derangements, echoing the findings of Meyer et al., who found that overweight patients switching from olanzapine to risperidone showed measurable improvements in metabolic syndrome prevalence [13]. This supports the utility of baseline BMI as a screening tool for risk stratification in antipsychotic-naïve or newly initiated patients [2,33].

Multivariate Regression Analysis

To identify independent predictors of metabolic syndrome at 6 months, a multivariate logistic regression analysis was performed (Table 30). The

analysis revealed that olanzapine use, higher BMI, family history of cardiometabolic disease, physical inactivity, and poor dietary habits were significant independent risk factors.

Olanzapine therapy emerged as the strongest predictor, showing a statistically significant odds ratio for developing metabolic syndrome even after adjusting for confounders. This finding is supported by Yang et al., who demonstrated exacerbated metabolic disturbances in animal models receiving olanzapine, particularly in genetically susceptible backgrounds [59].

Elevated baseline BMI was also independently associated with metabolic syndrome development, reaffirming the role of visceral adiposity in the pathogenesis of insulin resistance and lipid dysregulation. This is in line with studies by Fernández et al., who documented early metabolic changes in overweight patients starting on olanzapine [19].

Lifestyle factors, particularly inactivity and poor diet, retained significance in the regression model, indicating that behavioral modifications could serve as protective strategies, even in pharmacologically vulnerable individuals. These findings align with the work of Amini et al., who emphasized lifestyle as a mediating factor in antipsychotic-induced metabolic dysfunction [49].

Duration of Treatment vs. Risk Progression

An important trend observed in this study was the relationship between treatment duration and metabolic risk progression, particularly in the olanzapine group. As shown in Table 31 and Figure 29, patients exposed to olanzapine for more than three months exhibited a sharper increase in weight, triglyceride levels, and fasting glucose, along with a higher incidence of metabolic syndrome, compared to those on risperidone for similar durations.

This dose-duration relationship supports the findings of Fernández et al., who documented significant weight gain and glucose dysregulation within just 2–3 months of olanzapine initiation[19]. Similarly, Newcomer et al. highlighted the early onset of metabolic side effects, with notable changes in lipid and glucose parameters within the first 6 weeks of olanzapine use [23]. Our study reinforces these observations, showing that metabolic changes can manifest rapidly, especially when cumulative drug exposure is high and when baseline risk factors (e.g., high BMI, poor diet) are present.

While risperidone also showed a mild upward trend in metabolic parameters over time, the progression was slower and less severe, aligning with earlier observations by Meyer et al., who found that switching from olanzapine to risperidone resulted in reversal or stabilization of many metabolic indicators [2,33].This highlights the clinical relevance of antipsychotic selection and ongoing risk-benefit analysis during long-term management.

The study underscores the necessity of early identification and surveillance in antipsychotic-treated patients. Regular screening for weight, fasting glucose, triglycerides, HDL, and waist circumference should begin within the first 4–6 weeks and continue every 2–3 months thereafter, particularly for patients on olanzapine or with predisposing factors. Early lifestyle interventions and consideration of antipsychotic switching strategies may significantly reduce long-term metabolic burden.

Comparison with Existing Literature

The findings of this study are consistent with several prior investigations that have established olanzapine as a high-risk agent for metabolic complications. Meyer et al. demonstrated a significant decrease in metabolic syndrome prevalence after switching from olanzapine to risperidone in overweight patients, highlighting the reversible nature of drug-induced metabolic effects [2,33]. Fernández et al. further emphasized that early intervention within weeks of olanzapine initiation may mitigate these changes [19].

In the Indian context, Nanotkar et al. reported that 25–35% of schizophrenia patients on olanzapine developed features of metabolic syndrome within 3 to 6 months, findings that closely mirror the 6-month incidence rates observed in our study [38]. Their work highlighted regional dietary influences, genetic predisposition, and reduced physical activity as amplifiers of drug-induced risk, all of which were also present in our study cohort. Rikhari et al., in a North Indian study, similarly documented significant weight and lipid changes with olanzapine but milder effects with risperidone [8].

Globally, Newcomer et al. established olanzapine's role in increasing visceral adiposity, insulin resistance, and lipid abnormalities across multiple ethnic populations [23]. These international data, when compared with our findings, reinforce the universal metabolic vulnerability posed by olanzapine regardless of demographic context. However, they also validate risperidone's more neutral metabolic profile, particularly in short- to medium-term usage.

Collectively, these comparisons position the current study within both national and international frameworks, adding strength to the argument for metabolic-informed antipsychotic prescribing,

Clinical Implications

The present study holds significant clinical value in guiding antipsychotic selection and metabolic risk management in patients with schizophrenia.

The data clearly demonstrate that olanzapine, despite its efficacy, is associated with greater and earlier-onset metabolic derangements, particularly in terms of weight gain, dyslipidemia, and glucose intolerance [13,19,30]. In contrast, risperidone, while not metabolically inert, exhibited a more favorable risk profile over the 6-month observation period [14,48].

These findings underscore the need for individualized drug selection, especially in patients with pre-existing risk factors such as high BMI, sedentary lifestyle, or family history of diabetes and cardiovascular disease.

Moreover, the study supports routine metabolic screening—including weight, waist circumference, fasting glucose, and lipid profile—as early as 4–6 weeks after initiating antipsychotic therapy and continuing at regular intervals thereafter.

Strengths of the Study

- The study was prospective in design, allowing for temporal tracking of metabolic changes and establishing potential causality.
- It involved repeated follow-up assessments over a 6-month period, thereby capturing both early and progressive metabolic alterations.
- The findings reflect real-world clinical settings, enhancing external validity and practical applicability.
- A major strength lies in the stratification and analysis of subgroups, including age, gender, lifestyle factors, and family history, allowing for granular insights into risk modifiers.
- The use of multivariate regression analysis added robustness by identifying independent predictors of metabolic syndrome.

Limitations

- The study was conducted at a single center, which may limit generalizability across different healthcare settings or population groups.
- Although adequately powered for primary comparisons, the sample size was modest, particularly for subgroup analyses.
- The duration of follow-up was limited to 6 months; longer-term effects on cardiovascular morbidity and mortality could not be assessed.
- The study relied on basic metabolic parameters; more sensitive markers such as insulin levels, HbA1c, HOMA-IR, or inflammatory markers were not included due to logistical constraints.
- Blinding was not implemented due to the open-label nature of drug administration, which may have introduced bias in behavioral reporting.

Recommendations for Future Research

- Larger, multi-centric studies across diverse geographic and socio-economic populations are necessary to validate these findings and enhance generalizability.
- Longer-duration follow-up, extending beyond 6 months, is essential to assess the chronic metabolic and cardiovascular impact of second-generation antipsychotics, particularly in high-risk cohorts.
- Incorporating genetic and pharmacogenomic analysis may help identify patients with inherent susceptibility to antipsychotic-induced metabolic dysfunction, including polymorphisms related to glucose metabolism and lipid regulation.
- Future research should evaluate the efficacy of structured lifestyle intervention models, including dietician-guided meal planning, physical activity programs, and digital health tools, to determine their preventive and corrective potential in antipsychotic-treated populations.
- Studies should also consider comparative analysis across newer antipsychotic agents and long-acting injectable formulations, particularly in terms of real-world adherence and metabolic safety.

Conclusion

This prospective study provides valuable evidence that olanzapine is associated with significantly higher metabolic risk compared to risperidone, as demonstrated by greater changes in weight, BMI, waist circumference, triglycerides, HDL cholesterol, and incidence of metabolic syndrome over a 6-month period. Independent risk factors included high baseline BMI, physical inactivity, poor diet, and family history of cardiometabolic disease.

While both medications are effective in managing psychotic symptoms, these findings emphasize the need for metabolic-informed prescribing, especially in patients with predisposing risk profiles. Routine screening, early identification, and individualized intervention strategies remain pivotal in minimizing long-term cardiovascular morbidity and improving holistic outcomes in schizophrenia management.

Summary and conclusion

This prospective comparative study investigated the incidence and progression of metabolic syndrome and its components in patients diagnosed with schizophrenia receiving either olanzapine or risperidone. Over a 6-month follow-up period, the

study systematically assessed anthropometric, biochemical, and lifestyle parameters, including weight, BMI, waist circumference, fasting glucose, lipid profile, blood pressure, and prolactin levels. Data were also stratified by age, gender, family history, lifestyle, and treatment duration to identify significant risk predictors and subgroup variations.

At 3 months, both groups showed emerging metabolic disturbances, with olanzapine-treated patients having a higher number of cases of metabolic syndrome (11 cases, 18.96%) compared to the risperidone group (6 cases, 9.5%), although this difference was not statistically significant ($p = 0.218$). However, by 6 months, the disparity became more prominent and statistically significant ($p = 0.046$), with 31.0% of the olanzapine group versus 14.3% of the risperidone group fulfilling the criteria for metabolic syndrome. These findings confirm that olanzapine is associated with a more rapid and pronounced metabolic burden compared to risperidone.

The most significant changes were observed in triglyceride levels, which increased markedly in the olanzapine group, and HDL cholesterol, which showed a significant decline. These lipid abnormalities, coupled with increasing weight and waist circumference, indicate a high risk for cardiovascular complications. While blood pressure changes remained non-significant.

Subgroup analyses revealed that older patients (≥35 years), those with higher baseline BMI, positive family history of HTN, DM, or CVD, and those reporting physical inactivity and poor dietary habits were significantly more likely to develop metabolic syndrome. While males slightly outnumbered females in incidence. Smoking and alcohol use showed borderline associations, suggesting that lifestyle factors play a moderating role in metabolic risk.

The multivariate logistic regression model identified olanzapine usage, elevated baseline BMI, poor diet, and lack of physical activity as independent predictors of metabolic syndrome and reinforcing the need for personalized risk-based treatment planning.

From a clinical perspective, this study highlights the critical importance of early metabolic screening, especially during the first 3–6 months of antipsychotic therapy.

While olanzapine remains an effective option for managing schizophrenia, its higher metabolic liability necessitates closer monitoring, lifestyle counseling, and consideration of early switching strategies when risk factors are present. Risperidone, in contrast, presents a safer metabolic profile, particularly in short- to medium-term therapy.

In conclusion, this study provides robust evidence supporting the metabolic safety advantages of risperidone over olanzapine. The findings align with both Indian and global literature and advocate for routine risk stratification and tailored therapeutic approaches in schizophrenia care. Given the rising burden of antipsychotic-induced metabolic syndrome, integrating physical health surveillance into psychiatric practice is not only advisable but essential for long-term patient well-being.

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