

Antipsychotics and Change of Weight, Menstrual Cycle, and Metabolic Syndrome Components Among Schizophrenic Women: A 12-Week Longitudinal Prospective Study in Tien Giang, Vietnam

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Background: Antipsychotics are associated with side effects like weight gain, obesity, and menstrual disorders in Women, which can reduce treatment compliance and increase cardiovascular, metabolic risks, dementia, and other chronic diseases, as well as increase mortality, and reduce the quality of life in patients. Data on these effects in Vietnam are limited. This study evaluated changes in body weight, BMI, menstrual cycle, and metabolic syndrome components among female schizophrenic inpatients treated with antipsychotics.

Methods: A total of 60 female patients were treated with antipsychotics for at least 3 months before admission. The indicators to be examined, such as weight, BMI, waist circumference, menstrual cycle, blood pressure, and some laboratory tests, including fasting blood sugar, triglycerides, HDL cholesterol, were measured at two points: at baseline and after a 12-week follow-up period.

Results: Following 12 weeks of observation, the study participants exhibited significant increases in body weight and BMI as well as prevalence of amenorrhea compared to baseline ($p < 0.05$). Additionally, the proportion of patients with a waist circumference ≥ 80 cm rose significantly from baseline. Conversely, the number of patients with HDL-C levels < 50 mg/dL decreased significantly compared to baseline.

Conclusion: This study showed an association between increased weight, BMI, and amenorrhea with the use of antipsychotic medications. After 12 weeks of follow-up, the rate of components of metabolic and cardiovascular diseases also increased significantly compared to the baseline. This result is consistent with previous studies. Therefore, in psychiatric clinical practice, physicians should pay attention to these undesirable effects to have appropriate management strategies for patients.

Keywords: weight change, obesity, amenorrhea, follow-up, antipsychotics, Vietnam

Introduction

Antipsychotics are the most commonly prescribed psychotropic medications in the treatment of mental disorders, especially schizophrenia. In addition to their therapeutic effects, antipsychotics also have side effects. Overweight and obesity are among these side effects, especially with atypical antipsychotics.¹ Hakami et al studied 395 patients divided into 2 groups, group 1 used antipsychotics without metformin, group 2 included 86 patients using antipsychotics with metformin, the authors found that in group 1, the rate of weight gain was 64.4% and in group 2 was 38.37%.² Torres et al studied 244 patients with a first psychotic episode treated with antipsychotics. They found that after 3 years of follow-up,

the rate of metabolic syndrome in the patient group increased from 6.6% at baseline to 18.3%, while the rate in the control group was 5.4% and 8.1%, respectively.³ The rate of metabolic syndrome in Corell's study was 37.3% among 367 patients treated with second-generation antipsychotics.⁴ Overweight and obesity in patients elevate the risk of cardiovascular diseases, metabolic syndrome, type 2 diabetes, dementia, and other chronic diseases, as well as increase mortality, reduce the quality of life in patients. In women, the risk of overweight and obesity could be heightened due to physiological and endocrine factors, including hormonal changes during the menstrual cycle, pregnancy, and menopause. In addition, women tend to accumulate more central fat than men, increasing the risk of abdominal obesity. In addition to weight gain and obesity, menstrual disorders, including amenorrhea due to antipsychotics, were also common among women. Savarimuthu et al confirmed the role of antipsychotics in causing amenorrhea in female psychotic patients, and the authors identified factors associated with amenorrhea as antipsychotic use for more than 2 years and treatment by risperidone.⁵ Literature and many studies have shown that antipsychotics that antagonize dopamine receptors in the tuberoinfundibular and limbic systems increase blood prolactin levels, which is the main mechanism for causing menstrual disorders in female patients.^{6,7} The combination of antipsychotic use and these gender factors poses a major challenge in the management of mental health and overweight in female patients.

The relationship between schizophrenia and metabolic disorders is complex, as psychiatric symptoms may exacerbate these side effects. Negative symptoms, such as reduced motivation and social withdrawal, and cognitive impairments common in schizophrenia can lead to sedentary lifestyles, poor dietary habits, and irregular daily routines, all of which contribute to weight gain and metabolic syndrome. Conversely, metabolic abnormalities such as weight gain, dyslipidemia and diabetes mellitus, may influence cognitive and social functioning, potentially exacerbating psychiatric symptoms. For instance, Sayed et al (2023) found that total cholesterol and triglyceride levels were negatively correlated with social cognition in psychotic patients, suggesting that metabolic changes may be influenced by the severity of psychiatric symptoms.⁸ These factors, combined with the pharmacological effects of antipsychotics, may amplify the risk of obesity and related complications, necessitating a comprehensive approach to patient care that addresses both mental and physical health.

In Vietnam, data on overweight, obesity, and menstrual disorders among female patients using antipsychotics are limited. Currently, in the databases available on the internet, we have not found any studies reporting the effects of antipsychotic medications on patients' weight, BMI, or menstrual cycles. Assessment of the impact of antipsychotics on the change of weight, obesity, and amenorrhea in these participants plays an important role in developing timely prevention and intervention strategies. Based on the above situation, this study was conducted to evaluate the change of weight, BMI, and amenorrhea as well as several laboratory tests among female inpatients using antipsychotics, thereby proposing effective management and health care measures for this group of participants.

Subjects and Methods

Subjects

The study population consisted of female schizophrenic inpatients over 18 years old at Tien Giang Psychiatric Hospital, Vietnam, from May 2023 to May 2024 who had been prescribed antipsychotics for at least three months before admission. To provide further detail on pretrial antipsychotic use, medical records were reviewed to confirm the types and duration of antipsychotics used prior to enrolment; however, specific details such as exact dosages were not uniformly available due to variability in pretrial records. These patients or guardians agreed to participate in the study after being fully explained about the research procedure and signing a consent form. Participants were selected using a non-probability, consecutive, convenience sampling approach. Exclusion criteria encompassed pregnant or lactating individuals, primary amenorrhea, those with severe liver or kidney dysfunction, patients with cancer or significant cognitive impairment precluding interview participation, and those concurrently using other psychotropic medications, such as mood stabilizers or antidepressants, during the treatment period. Based on these criteria, a total of 60 inpatients were enrolled during the study period.

Methods

This was a 12-week longitudinal prospective study. We assessed the weight, BMI, and amenorrhea of the patients at two time points: at baseline (T0) and 12 weeks later during follow-up (T1). To classify overweight and obesity, we use the IDI and WPRO standards based on BMI for Asians as follows: underweight BMI $<18.5 \text{ kg/m}^2$, normal: BMI = $18.5 - 22.9 \text{ kg/m}^2$, overweight: BMI = $23 - 24.9 \text{ kg/m}^2$ and obese: BMI from 25 kg/m^2 or higher. Amenorrhea is defined as the absence of menstruation for at least 90 days. In addition, some biochemical tests and clinical indicators were also measured, such as blood pressure, waist circumference, fasting blood glucose (FBG), triglycerides, and HDL-C at baseline and after 12 weeks of follow-up. The results of biochemical tests were statistically analyzed in two ways: method 1 compared the results of biochemical tests according to the classification of the components of metabolic syndrome, and method 2 compared the mean of test results at 2 time points: baseline and 12 weeks of follow-up. We used patients' medical records and a structured questionnaire to survey patient demographic characteristics and previous medical history. Patients with abnormalities in blood pressure, diabetes, and obesity at the baseline would be consulted with internal medicine doctors and treated with medications, exercise, and nutrition regimens as prescribed by these doctors.

Statistical Analysis

All statistical analyses were performed using SPSS version 20.0. For descriptive data, frequencies and percentages were used. In statistical analysis, we used the McNemar test and the paired *t*-test to compare the proportions and mean values of variables at baseline and after 12 weeks of follow-up, respectively. A *p*-value <0.05 was considered statistically significant.

Results

Participant Characteristics at the Baseline

The mean age of the participants was 36.83 (min 17, max 53), the mean BMI at the baseline was 22.50 ± 2.29 , of the 60 patients, 7 patients (11.7%) were classified as obese, 24 patients (40.0%) were overweight, and 1 patient (1.7%) had amenorrhea at baseline. Some clinical characteristics and biochemical test indices at baseline in the study subjects were as follows: waist circumference $\geq 80 \text{ cm}$ (81.7%), blood pressure $\geq 130/85 \text{ mmHg}$ (38.3%), triglyceride $\geq 150 \text{ mg/dL}$ (45%), HDL $< 50 \text{ mg/dL}$ (25%), fast blood glucose $\geq 100 \text{ mg/dL}$ (6.7%) (Table 1).

Table 1 Participant Characteristics

Characteristics	n	Percentage
The mean age	36.83 ± 8.72	Min: 17, max: 53
The weight	55.9 ± 6.45	
BMI		
The mean BMI	22.50 ± 2.29	
$<18.5 \text{ kg/m}^2$	4	6.7
$18.5 - 22.9 \text{ kg/m}^2$	25	41.7
$23 - 24.9 \text{ kg/m}^2$	24	40.0
$\geq 25 \text{ kg/m}^2$	7	11.7
Amenorrhea	1	1.7

(Continued)

Table 1 (Continued).

Characteristics	n	Percentage
Waist circumference $\geq$ 80 cm	49	81.7
Blood pressure $\geq$ 130/85 mmHg	23	38.3
Triglyceride $\geq$ 150 mg/dL	27	45.0
HDL $<$ 50 mg/dL	15	25.0
Fast blood glucose $\geq$ 100 mg/dL	4	6.7

63.3% of patients had used antipsychotics for more than 24 months, 25% of patients used 2 types of antipsychotics, and olanzapine and risperidone were the two most commonly used antipsychotics, with rates of 48.3% and 65%, respectively (Table 2).

Compared to the baseline, the weight, the mean BMI, rates of obesity, amenorrhea, and waist circumference of 80 cm or more among study subjects all increased significantly, while the proportion of patients with HDL-C below 50 mg/dL decreased significantly after 12 weeks of follow-up. Other parameters, such as blood pressure, fasting blood sugar, and triglycerides, showed no significant change compared to the baseline (Table 3).

The mean values of waist circumference, total cholesterol, HDL-C, LDL-C, and Triglyceride all increased significantly, while the mean values of diastolic blood pressure and systolic blood pressure all decreased significantly; only the average value of blood sugar did not change significantly at 12 weeks of follow-up compared to baseline (Table 4).

To explore factors associated with metabolic syndrome components, we conducted a multivariate regression analysis examining age, duration of antipsychotic use, and number of antipsychotics used, but no statistically significant associations were found.

Table 2 Characteristics of Using Antipsychotics Among Participants

Characteristics	n	Percentage
Duration of being treated by antipsychotics		
$\leq$ 24 months	22	36.7
$>$ 24 months	38	63.3
Number of antipsychotics being treated		
1	45	75.0
2	15	25.0
Olanzapine	14	23.3
Risperidone	27	45.0
Quetiapine	3	5.0
Clozapine	1	1.7
Olanzapine + Risperidone	12	20.0
Levomepromazine + Olanzapine	3	5.0

Table 3 Changes in Weight, BMI, Amenorhea, Some Clinical Characteristics, and Biochemical Tests (Being Classified According to the Components of Metabolic Syndrome) at 12-Week Follow-Up Compared with Baseline

Characteristics		Baseline	At 12 Week Follow Up	p value
The Weight		55.9 ± 6.45	60.08 ± 7.38	<0.001
The mean BMI		22.50 ± 2.29	24.19 ± 2.70	<0.001
BMI category				
<18.5kg/m ²		4 (6.7)	1 (1.7)	<0.001
18.5–22.9kg/m ²		25 (41.7)	18 (30.0)	
23 – 24.9kg/m ²		24 (40.0)	12 (20.0)	
≥25kg/m ²		7 (11.7)	29 (48.3)	
Amenorhea	No	59 (98.3)	45 (75)	<0.05
	Yes	1 (1.7)	15 (25%)	
Waist circumference ≥ 80 cm	No	11 (18.3%)	2 (3.3%)	<0.05
	Yes	49 (81.7%)	58 (96.7%)	
Blood pressure ≥ 130/85 mmHg	No	37 (61.7%)	46 (76.7%)	>0.05
	Yes	23 (38.3%)	14 (23.3%)	
Triglyceride ≥ 150 mg/dL	No	33 (55.0%)	30 (50%)	>0.05
	Yes	27 (45.0%)	30 (50.0%)	
HDL-C < 50 mg/dL	No	45 (75.0%)	56 (93.3%)	<0.01
	Yes	15 (25.0%)	4 (6.7%)	
Fast blood glucose ≥ 100 mg/dL	No	56 (93.3%)	56 (93.3%)	>0.05
	Yes	4 (6.7%)	4 (6.7%)	

Table 4 Mean Changes in Waist Circumference, Biochemical Tests, and Blood Pressure at Baseline and After 12 Weeks of Follow-Up

Indicators	At Baseline (T0)	At 12 Week Follow Up	P value
Waist circumference	82,78 ± 4,14	89,20 ± 6,27	< 0.001
Systolic blood pressure	122,17 ± 8,85	119,33 ± 10,87	0,031
Diastolic blood pressure	81,0 ± 8,38	76,83 ± 9,65	0,002
Triglyceride	127,67 ± 45,77	182,15 ± 140,96	0,001
Total Cholesterol	170,21 ± 27,76	194,81 ± 42,68	< 0.001
HDL - C	52,93 ± 10,09	56,04 ± 3,88	0,015
LDL - C	101,59 ± 27,22	116,71 ± 33,10	< 0.001
Fast Blood Glucose	91,49 ± 11,97	91,29 ± 36,25	0,952

Discussion

The results in our Table 1 showed that at the baseline time, 49 patients (81.7%) had a waist circumference of 80 cm or more, 24 patients (40%) were overweight, and 7 patients (11.7%) were obese. In our selection criteria, patients had to have used antipsychotics 3 months before admission, so these effects could also be caused by previous use of antipsychotics. Furthermore, patients with schizophrenia may have negative symptoms, so a lack of exercise, an unbalanced diet, and irregularity can also lead to these manifestations. For these patients, right from the time of admission, we consulted with endocrinology, metabolism, and nutrition experts to advise on treatment drugs, exercise, and nutrition regimens for the patients.

The effects of antipsychotics, especially second-generation medications, on weight gain, obesity, and metabolic syndrome have been demonstrated by many researchers.^{9–11} Ye et al in a systematic review found that antipsychotics cause overweight, metabolic syndrome, and obesity through various mechanisms such as genetics, effects on the central nervous system, neuroendocrine system, and even the gut microbiota.¹² Mortimer Katherine et al, in a mini-review article, reported a 3-fold increased risk of metabolic syndrome in people using antipsychotics.¹³ In a systematic review and meta analysis, Pillinger et al found that with weight change, including 83 studies with 18,750 patients, weight gain was demonstrated in patients using brexpiprazole, risperidone and paliperidone, quetiapine, iloperidone, sertindole, olanzapine, zotepine, and clozapine, of which clozapine caused the most weight gain. Also in this study, when comparing with placebo on BMI change, the authors found that drugs that significantly increased BMI compared with placebo included lurasidone, risperidone and paliperidone, quetiapine, sertindole, clozapine, and olanzapine. Of these, olanzapine was the drug that increased BMI the most.¹⁴ Our study results in Table 3 on weight change and BMI were also consistent with the study results of other authors. Prevalence of patients with BMI ≥ 25 kg/m² increased from 7 patients (11.7%) at baseline to 29 patients (48.3%) at 12 weeks of follow-up. In our study, 39 patients were treated with risperidone and 29 patients were treated with olanzapine (either monotherapy or in combination). The literature has shown that second-generation antipsychotics are associated with a risk of weight gain.¹⁵ However, in our study, only one patient used clozapine, limiting our ability to assess its specific impact on weight gain and metabolic changes. While we reported an increased prevalence of metabolic syndrome components as a risk factor for cardiovascular diseases, the short-term changes observed over 12 weeks may not directly lead to cardiovascular events but contribute to long-term cardiovascular risk.¹⁵ Furthermore, non-pharmacological factors, such as improvements in psychiatric symptoms and the structured environment of inpatient care (eg, regular meals and reduced agitation), may also contribute to metabolic changes, such as increased appetite or weight gain, independent of antipsychotic effects. Due to the absence of longitudinal data on psychiatric symptom severity in our study, we could not directly analyse the relationship between symptom improvement and metabolic outcomes. The side effect of weight gain of antipsychotic drugs occurs not only in adults but also in adolescents. Taylor et al studied 119 children aged 8–19 years with a diagnosis of schizophrenia and schizoaffective disorder treated with molindone, risperidone and olanzapine and found that after 8 weeks, the mean weight gain was 0.74 ± 3.51 kg, 4.13 ± 3.79 kg, 7.29 ± 3.44 kg compared to baseline for molindone, risperidone and olanzapine, respectively.¹⁶ In our study, all patients were taking second-generation antipsychotics, with 3 patients (5%) taking a second-generation antipsychotic in combination with a first-generation antipsychotic (levomepromazine combined with olanzapine) (Table 2). Kalebie et al analyzed 25 studies with 4064 patients treated with antipsychotics in Africa and found that the prevalence of metabolic syndrome was 22% and that risk factors were female sex, older age, and increased BMI.¹⁷ Other meta-analyses have confirmed these results. A multi-treatment meta-analysis by Leucht et al found that all antipsychotics except haloperidol, lurasidone, and ziprasidone were associated with weight gain.¹⁸ Olanzapine and zotepine were significantly more associated with weight gain than the other drugs.¹⁸ In addition, changes in weight, BMI, and some components included in the diagnostic criteria for metabolic disorders, including a waist circumference of 80 cm or more and HDL-C < 50 mg/dL, also changed significantly at 12 weeks of follow-up compared to baseline (Table 3). Similarly, Pillinger et al also found that antipsychotic drugs had significant effects on changes in the concentrations of total cholesterol, triglycerides, HDL-C, LDL-C and glucose concentration; olanzapine and clozapine were shown to be most commonly responsible for these effects.¹⁴ Our study results in Table 4 showed that the average of waist circumference, triglycerides, total cholesterol, LDL-C, and HDL-C all increased significantly at 12 weeks of follow-up compared to baseline. Meanwhile, the average values of systolic blood pressure and diastolic blood pressure decreased significantly,

and fast blood glucose remained unchanged at 12 weeks compared to baseline. The reason for this result is that blood pressure is monitored daily, so when we detect any patient with signs of hypertension, we consult with an internal medicine doctor and use medication to treat hypertension for the patient. The medication used in these patients was calcium channel blockers such as amlodipine. The mechanism of weight gain, obesity, and changes in metabolic syndrome components has been established through many studies. Weight gain with antipsychotics is thought to be due to their effects on serotonin 5-HT_{2A} and 5-HT_{2C}, dopamine D₂ and D₃, histamine H₁, and muscarinic M₃ receptors. The degree of weight gain varies among antipsychotics depending on their affinity for these receptors. Antipsychotics also affect neuropeptides involved in appetite control and energy metabolism. Leptin and adiponectin, adipokines produced in white adipose tissue, have been linked to antipsychotic-induced weight gain. Increased leptin and decreased adiponectin have been found in patients treated with short-term and long-term olanzapine.⁹ As mentioned above, patients with obesity, hyperglycemia, and overweight were consulted with endocrinologists and nutritionists to receive appropriate medication and lifestyle, and diet treatment. However, the proportion of patients with a waist circumference of 80 cm or more continued to increase, and other lipid indices also changed in a negative direction at the 12-week follow-up period (Table 4). This may be due to several reasons. First, reducing waist circumference requires regular and persistent exercise, which is difficult to do with schizophrenic patients in the acute phase, regardless of whether they have negative or positive symptoms. The second reason may be that the continued effects of antipsychotics cause weight and metabolic problems in patients who have not shown these signs at the beginning. These reasons are clearly demonstrated by the results of Table 3. Weight changes, obesity, and components of the metabolic syndrome during treatment with antipsychotic drugs increase the risk of cardiovascular and metabolic diseases in patients, increasing mortality. Cardiometabolic diseases are often associated with a high risk of cognitive and social function impairment in psychotic patients. Sayed S.E in a case-control study of 150 psychotic patients and 120 healthy controls found that total cholesterol and triglyceride levels were negatively correlated with the interpersonal domain of social cognition and total cholesterol levels were positively correlated with the total score of social function.⁸ In addition, for women, appearance is important, so being overweight or obese affects the self-esteem and confidence of schizophrenic patients who already have many complexes and stigmas due to the mental illness itself, which can lead to depression, reduced quality of life, non-compliance with treatment, and even suicide. Therefore, in clinical practice, psychiatrists also need to detect these problems early and work in a multidisciplinary team to support and resolve these problems for patients early, improving the above consequences.

In addition to changes in weight, BMI, and some components of metabolic syndrome, our study results in Table 3 also showed a statistically significant increase in amenorrhea in the study subjects at 12 weeks of follow-up compared to baseline, with rates of 25% and 1.7%, respectively. Many previous studies have also shown a relationship between menstrual disorders, including amenorrhea, and the use of antipsychotics. Bo et al studied 161 female schizophrenic patients who were evaluated at baseline after 6–8 weeks of treatment with risperidone and followed up for 52 weeks. They found that at baseline, the rate of menstrual disorders included 14.3% irregular menstruation, 6.8% oligomenorrhea, and 5% amenorrhea. At 52 weeks of follow-up, the rate of menstrual disorders was 37.9%.¹⁹ Madhusoodanan et al reported that the rate of amenorrhea among female patients treated by risperidone ranges from 1–10%.²⁰ Murke et al, reported that among 113 women receiving antipsychotics with menstrual dysfunction, 15 (30%) had amenorrhea and the rest 70% were oligomenorrhea.²¹ The mechanism of menstrual disorders, including amenorrhea, in patients using antipsychotics is thought to be due to the effect of antipsychotics on dopamine receptors in the pituitary infundibulum, causing hyperprolactinemia.²² Shettima F.B studied 209 schizophrenic patients using antipsychotics and found that the rate of increased prolactin levels was 45.9%. The rate of increased prolactin in the group using typical and atypical antipsychotics was 51.5% and 25.0%, respectively.²³ Several authors have found that risperidone is one of the antipsychotics most commonly associated with amenorrhea.²⁴ Takechi et al found that among patients treated with antipsychotics, those with menstrual disorders had serum prolactin levels 2-fold higher than those without menstrual disorders, and 70% of menstrual disorders were treated with risperidone.²⁵ In our study, the rate of risperidone use was highest, with 27 patients (45%) using it alone and 12 patients (20%) using it in combination with olanzapine (Table 2). Increased prolactin secretion due to antipsychotic use, in addition to causing menstrual disorders including amenorrhea, also leads to galactorrhea in women even when not breastfeeding, reduces sexual function, thereby reducing the quality

of life of patients.²⁶ However, there have been studies that do not support a role for increased prolactin in causing amenorrhea in women taking antipsychotics.²⁷ Chen et al studied 62 women with a first psychotic episode who had not previously used antipsychotics and were followed up after 12 weeks of risperidone treatment and found that serum prolactin levels increased fourfold in women of childbearing age. But there was no difference between the amenorrhea group and the age-matched non-amenorrhea group. In contrast, low estradiol levels before treatment were a risk factor for the development of amenorrhea after 12 weeks of risperidone treatment.²⁷

Side effects on weight, metabolism, and menstrual disorders are all major causes of non-compliance with treatment in patients, increasing the rate of relapse, re-hospitalization, and difficulty in controlling psychiatric symptoms in patients. For these reasons, this study is necessary to detect unwanted effects early, have appropriate management and treatment strategies for patients using antipsychotic drugs, especially for female patients.

Strengths and Limitations

Our study is one of the first to add data on the effects of antipsychotics on weight, metabolism, and menstrual disorders, which seem to be lacking in the Vietnamese community. In addition, we want to prioritize improving the health of women, a group that is still disadvantaged in East Asian culture. Despite these strengths, our study has several limitations. First, the small sample size (n=60) may have limited the statistical power to detect significant associations in our multivariate regression analysis, which was conducted to explore factors associated with metabolic syndrome (eg, age, duration of antipsychotic use, and type of antipsychotic) but yielded no statistically significant results, leading to its exclusion from the manuscript. Second, detailed pretrial antipsychotic use history, such as exact dosages, was not uniformly available due to variability in medical records, restricting our ability to fully assess its impact. Third, the absence of longitudinal psychiatric symptom data prevented analysis of the relationship between symptom improvement and metabolic outcomes. Finally, the 12-week follow-up period was relatively short, and the use of multiple antipsychotics without uniform treatment protocols may have introduced variability. To address these limitations, we recommend future studies with larger sample sizes, longer follow-up periods, standardized antipsychotic regimens, comprehensive pretrial medication histories, and longitudinal assessments of psychiatric symptoms.

Conclusion

This study showed an association between increased weight, BMI, and amenorrhea with the use of antipsychotic medications. After 12 weeks of follow-up, the rate of components of metabolic and cardiovascular diseases also increased significantly compared to the baseline. Non-pharmacological factors, such as improved psychiatric symptoms and the structured inpatient environment (eg, regular meals), may also influence these metabolic outcomes, though our study could not assess the relationship with psychiatric symptom improvement due to the absence of longitudinal symptom data. Only one patient used clozapine, limiting our ability to evaluate its specific effects. These findings highlight the need for early detection and multidisciplinary management strategies, including endocrinology and nutrition consultations, to mitigate weight gain, metabolic disorders, and menstrual irregularities in female schizophrenic patients. Future research should incorporate larger sample sizes, longer follow-up periods, standardized antipsychotic regimens, and longitudinal assessments of psychiatric symptoms to better understand their interplay with metabolic changes and inform comprehensive treatment approaches.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

Ethics Approval

This study involved human participants and was approved by the biomedical ethics committee of Hue University of Medicine and Pharmacy (No H2023/408, issued 02/6/2024). All participants provided informed consent before participating in the study. Participation was voluntary, and patients/ relatives were fully informed about the purpose of the study. This study was carried out in compliance with the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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The authors have no conflicts of interest to declare in this work.

References

1. Neumeier MS, Vetter S, Homan S, et al. Examining side effect variability of antipsychotic treatment in schizophrenia spectrum disorders: a meta-analysis of variance. *Schizophr Bull.* 2021;47(6):1601–1610. PMID: 34374418; PMCID: PMC8530397. doi:10.1093/schbul/sbab078
2. Hakami AY, Felemban R, Ahmad RG, et al. The association between antipsychotics and weight gain and the potential role of metformin concomitant use: a retrospective cohort study. *Front Psychiatry.* 2022;13:914165. PMID: 35686187; PMCID: PMC9170991. doi:10.3389/fpsyt.2022.914165
3. Garrido-Torres N, Ruiz-Veguilla M, Olivé Mas J, et al. Metabolic syndrome and related factors in a large sample of antipsychotic naïve patients with first-episode psychosis: 3 years follow-up results from the PAFIP cohort. *Spanish J Psychiatry Mental Health.* 2023;16(3):175–183. doi:10.1016/j.rpsm.2022.05.003
4. Correll CU, Frederickson AM, Kane JM, Manu P. Metabolic syndrome and the risk of coronary heart disease in 367 patients treated with second-generation antipsychotic drugs. *J Clin Psychiatry.* 2006;67(4):575–583. PMID: 16669722. doi:10.4088/jcp.v67n0408
5. Savarimuthu MK, Bhaskar S, Alexander AM, Kurian S. A cross sectional study on antipsychotic induced amenorrhoea in women attending a tertiary care centre in South India. *Int J Res Med Sci.* 2019;7(6):2067–2071. doi:10.18203/2320-6012.ijrms20192123
6. Bargiota SI, Bonotis KS, Messinis IE, Angelopoulos NV. The effects of antipsychotics on prolactin levels and women's menstruation. *Schizophrenia Treat.* 2013;2013:1–10. doi:10.1155/2013/502697
7. Jiang Q, T L, Zhao L, et al. Treatment of antipsychotic-induced hyperprolactinemia: an umbrella review of systematic reviews and meta-analyses". *Front Psychiatry.* 2024;15:1337274. doi:10.3389/fpsyt.2024.1337274
8. Sayed SE, Gomaa S, Alhazmi A, ElKalla I, Khalil D. Metabolic profile in first episode drug naïve patients with psychosis and its relation to cognitive functions and social cognition: a case control study. *Sci Rep.* 2023;13(1):5435. PMID: 37012300; PMCID: PMC10070352. doi:10.1038/s41598-023-31829-9
9. Dayabandara M, Hanwell 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. PMID: 28883731; PMCID: PMC5574691. doi:10.2147/NDT.S113099
10. Bak M, Fransen A, Janssen J, van Os J, Drukker M. Almost all antipsychotics result in weight gain: a meta-analysis. *PLoS One.* 2014;9(4):e94112. PMID: 24763306; PMCID: PMC3998960. doi:10.1371/journal.pone.0094112
11. Bozyski KM, Whitten JA, Blair ME, Overley AM, Ott CA. Monitoring and treating metabolic abnormalities in patients with early psychosis initiated on antipsychotic medications. *Community Ment Health J.* 2018;54(6):717–724. PMID: 29127566. doi:10.1007/s10597-017-0203-y
12. Ye W, Xing J, Yu Z, Hu X, Zhao Y. Mechanism and treatments of antipsychotic-induced weight gain. *Int J Obes.* 2023;47(6):423–433. PMID: 36959286. doi:10.1038/s41366-023-01291-8
13. Mortimer Katherine RH, Haq KMZU, Lisa C. Second-generation antipsychotics and metabolic syndrome: a role for mitochondria. *Front Psychiatry.* 2023;14. doi:10.3389/fpsyt.2023.1257460.
14. 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):64–77. doi:10.1016/S2215-0366(19)30416-X
15. Chang SC, Goh KK, Lu ML. Metabolic disturbances associated with antipsychotic drug treatment in patients with schizophrenia: state-of-the-art and future perspectives. *World J Psychiatry.* 2021;11(10):696–710. PMID: 34733637; PMCID: PMC8546772. doi:10.5498/wjp.v11.i10.696
16. Taylor JH, Jakubowski E, Gabriel D, Bloch MH. Predictors and moderators of antipsychotic-related weight gain in the treatment of early-onset schizophrenia spectrum disorders study. *J Child Adolesc Psychopharmacol.* 2018;28(7):474–484. PMID: 29920116; PMCID: PMC6154761. doi:10.1089/cap.2017.0147
17. Kelebie M, Kibralew G, Tadesse G, et al. Prevalence and predictors of metabolic syndrome among psychiatric patients receiving antipsychotic treatment in Africa: a systematic review and meta-analysis. *BMC Psychiatry.* 2025;25. doi:10.1186/s12888-025-06894-1.
18. Leucht S, Cipriani A, Spineli L, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet.* 2013;382(9896):951–962. doi:10.1016/S0140-6736(13)60733-3
19. Bo Q, Xing X, Li T, Mao Z, Zhou F, Wang C. Menstrual dysfunction in women with schizophrenia during risperidone maintenance treatment. *J Clin Psychopharmacol.* 2021;41(2):135–139. PMID: 33538534. doi:10.1097/JCP.0000000000001344

20. Madhusoodanan S, Parida S, Jimenez C. Hyperprolactinemia associated with psychotropics – a review. *Hum Psychopharmacol.* **2010**;25:281–297. doi:10.1002/hup.1116
21. Murke MP, Gajbhiye SM, Amritwar AU, Gautam SR. Study of menstrual irregularities in patients receiving antipsychotic medications. *Indian J Psychiatry.* **2011**;53(1):79–80. doi:10.4103/00195545.75550.
22. Canuso CM, Goldstein JM, Wojcik J, et al. Antipsychotic medication, prolactin elevation, and ovarian function in women with schizophrenia and schizoaffective disorder. *Psychiatry Res.* **2002**;111(1):11–20. ISSN 0165-1781. doi:10.1016/S0165-1781(02)00123-3
23. Shettima FB, Wakil MA, Sheikh TL, Abdulaziz M, Wakawa IA, Beida O. Antipsychotics-related hyperprolactinaemia among patients with schizophrenia in Maiduguri. *S Afr J Psychiatr.* **2024**;30:2133. PMID: 38444408; PMCID: PMC10912972. doi:10.4102/sajpspsychiatry.v30i0.2133
24. Tsai L-H. Letters to the editor • arc. *Clin Psychiatr.* **2017**;44(4). doi:10.1590/0101-60830000000132
25. Takechi K, Yoshioka Y, Kawazoe H, et al. Psychiatric patients with antipsychotic drug-induced hyperprolactinemia and menstruation disorders. *Biol Pharm Bull.* **2017**;40(10):1775–1778. PMID: 28966250. doi:10.1248/bpb.b17-00053
26. Odongo E, Byamugisha J, Ajeani J, et al. Prevalence and effects of menstrual disorders on quality of life of female undergraduate students in Makerere University College of health sciences, a cross sectional survey”. *BMC Womens Health.* **2023**;23(1):152. doi:10.1186/s12905-023-02290-7
27. Chen H, Qian M, Shen X, et al. Risk factors for medication-induced amenorrhea in first-episode female Chinese patients with schizophrenia treated with risperidone. *Shanghai Arch Psychiatry.* **2013**;25(1):40–47. PMID: 24991131; PMCID: PMC4054524. doi:10.3969/j.issn.1002-0829.2013.01.008

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