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Metabolic Side Effects of Long-Term Antipsychotic Medication: A Cross-Sectional Study in a Psychiatry Outpatient Department

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Abstract
***Background:** Antipsychotic medications are indispensable in the treatment of schizophrenia, bipolar disorder and psychotic depression, but their prolonged use is associated with clinically significant metabolic complications that increase cardiovascular morbidity and reduce life expectancy.[1,2] **Aim:** To determine the prevalence of key metabolic derangements — significant weight gain, dyslipidaemia and elevated glycated haemoglobin (HbA1c) — in patients on long-term antipsychotic therapy, and to examine their association with the number of antipsychotics prescribed and the duration of treatment.*
***Methods:** A cross-sectional observational study was conducted in the Psychiatry Outpatient Department of a tertiary-care teaching hospital. Thirty adults aged 18–65 years, receiving antipsychotic medication continuously for at least twelve months, were recruited. Weight gain (>10 kg from documented baseline), body mass index, fasting lipid profile, HbA1c, number of antipsychotics and treatment duration were recorded. Patients were stratified by antipsychotic load (≤3 vs >3 agents) and by treatment duration (<10 vs >10 years).*
***Results:** Weight gain exceeding 10 kg was observed in 43% of patients, a deranged lipid profile in 46% and elevated HbA1c in 6%. Among patients receiving more than three antipsychotics, 66% had weight gain >10 kg and 58% had dyslipidaemia, markedly higher than in patients on three or fewer agents. Patients treated for more than ten years showed a higher prevalence of both weight gain and lipid derangement than those treated for less than ten years.*
***Conclusion:** Metabolic side effects are highly prevalent in patients on long-term antipsychotic therapy and are aggravated by antipsychotic polypharmacy and prolonged treatment duration. Routine metabolic screening, rationalisation of polypharmacy and integrated lifestyle intervention should be standard components of care.*
***Keywords:** antipsychotics; metabolic syndrome; weight gain; dyslipidaemia; HbA1c; polypharmacy; schizophrenia; cardiovascular risk.*

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I. Introduction

Antipsychotic medications remain a cornerstone in the management of serious psychiatric disorders such as schizophrenia, bipolar disorder and psychotic depression, producing substantial improvements in symptom control, patient stability and quality of life.[1] These therapeutic benefits are, however, frequently accompanied by a major clinical concern — metabolic side effects — which become increasingly evident with prolonged treatment.[2] Nearly all antipsychotic agents are associated with some degree of weight gain, although the magnitude varies considerably between drugs.[5]

Among the most troubling complications are substantial weight gain, lipid abnormalities such as raised triglycerides and reduced high-density lipoprotein (HDL) cholesterol, and insulin resistance, all of which escalate the risk of chronic disease.[11,12] These disturbances significantly elevate the risk of cardiovascular disease, which remains a leading cause of premature death among individuals with chronic mental illness, contributing to a life expectancy that is estimated to be 15–20 years shorter than that of the general population.[1,2] Pooled analyses indicate that metabolic syndrome affects roughly one-third of patients with schizophrenia, and that this figure rises with antipsychotic exposure.[4]

The mechanisms underlying antipsychotic-induced metabolic disturbance are multifactorial and include antagonism of serotonergic (5-HT2C) and histaminergic (H1) receptors, increased appetite and caloric intake,

altered adipokine signalling and direct effects on insulin sensitivity and lipid metabolism.[12,13] Second-generation agents such as clozapine and olanzapine carry the highest metabolic liability, whereas aripiprazole and ziprasidone are comparatively weight-neutral.[3,9] Importantly, metabolic derangements can be detected even in antipsychotic-naive, first-episode patients, suggesting an intrinsic vulnerability that is then amplified by pharmacotherapy.[16]

Indian studies have consistently reported a high burden of metabolic abnormalities in patients receiving antipsychotics, underscoring the relevance of this problem to routine outpatient practice in the country.[6,7,8] Despite this, metabolic monitoring is frequently inconsistent in real-world settings.[22] The present study was therefore designed to investigate the prevalence of significant weight gain, dyslipidaemia and elevated HbA1c in patients on long-term antipsychotic therapy attending a psychiatry outpatient department, and to assess the relationship between these side effects and two treatment-related variables: the number of antipsychotics prescribed and the length of therapy. The goal was to generate clinical insights capable of informing safer prescribing practices and improving long-term health outcomes in this vulnerable population.

II. Materials and Methods

Study design and setting

This investigation employed a cross-sectional observational design, a methodology well suited to assessing the prevalence of conditions and their associated factors at a specific point in time.[4] The study was conducted in the Psychiatry Outpatient Department (OPD) of a tertiary-care teaching hospital, ensuring access to a representative sample of patients receiving ongoing psychiatric care.

Study population and sampling

A sample of 30 adult patients was recruited. Inclusion criteria were kept stringent to ensure homogeneity and clinical relevance of the cohort: patients aged between 18 and 65 years, and individuals who had been consistently receiving antipsychotic medication for a minimum duration of twelve months, so that the effects of long-term exposure could be adequately observed.[19] A minimum treatment period was specified because metabolic changes accumulate over time and short-term exposure may underestimate the true burden.[3]

Data collection and parameters

Comprehensive data were collected for each participant to capture a holistic picture of their metabolic status:

Parameter	Definition / method
Weight gain	Increase of more than 10 kg from documented baseline weight prior to antipsychotic initiation
Body mass index (BMI)	Calculated as weight (kg)/height (m^2) to classify patients into standard weight categories
Lipid profile	Total cholesterol, LDL-C, HDL-C and triglycerides; derangement defined per established clinical guidelines
HbA1c	Glycated haemoglobin reflecting average glycaemia over the preceding 2–3 months and diabetes risk
Number of antipsychotics	Documented to differentiate monotherapy from polypharmacy
Duration of treatment	Cumulative period of antipsychotic use, recorded in years

Table 1. Metabolic and treatment-related parameters recorded for each participant.

Patient grouping for analysis

To facilitate meaningful comparison, patients were stratified according to two factors hypothesised to influence metabolic outcomes. First, by antipsychotic load: those receiving three or fewer antipsychotics (≤3) and those prescribed more than three (>3), reflecting the recognised metabolic risk of polypharmacy.[17,18] Second, by cumulative treatment duration: those on medication for less than ten years and those with more than ten years of antipsychotic use, in keeping with evidence that metabolic risk accumulates over prolonged exposure.[3]

III. Results

Overall prevalence of metabolic side effects

Analysis revealed a substantial prevalence of metabolic side effects among study participants. Weight gain exceeding 10 kg from baseline was recorded in 43% of patients, a deranged lipid profile in 46%, and elevated HbA1c in 6% (Table 2). These prevalence figures are consistent with the elevated cardiometabolic risk repeatedly documented in patients receiving antipsychotics.[4,11]

Metabolic parameter	Prevalence (%)
Weight gain > 10 kg from baseline	**43%**
Deranged lipid profile	**46%**
Deranged HbA1c	**6%**

Table 2. Overall prevalence of metabolic side effects in the study cohort (N = 30).

A weight gain of this magnitude is clinically significant and is strongly associated with increased risk of cardiovascular disease and diabetes.[13] Dyslipidaemia, affecting nearly half of the cohort, indicates widespread disturbance of lipid metabolism that contributes to atherosclerotic risk.[11] Although the proportion of patients with a deranged HbA1c was comparatively low, it remains a concerning finding, as elevated HbA1c signals impaired glucose regulation and a heightened risk of overt diabetes.[14,15]

Impact of antipsychotic polypharmacy

The number of antipsychotics prescribed clearly influenced metabolic outcomes. Among patients receiving more than three antipsychotics, 66% experienced weight gain exceeding 10 kg from baseline, contrasting sharply with the lower incidence in patients on three or fewer agents. This pattern is consistent with a dose–response relationship in which increasing antipsychotic load disproportionately elevates the risk of substantial weight gain.[9]

Metabolic outcome	≤ 3 antipsychotics	> 3 antipsychotics
Weight gain > 10 kg	Lower	**66%**
Deranged lipid profile	Lower	**58%**

Table 3. Metabolic outcomes stratified by number of antipsychotics prescribed.

Dyslipidaemia was likewise more prevalent in the polypharmacy group, with 58% of patients on more than three antipsychotics exhibiting a deranged lipid profile. This suggests that the additive or synergistic effects of multiple agents produce greater disruption of lipid metabolism, compounding cardiovascular risk.[17] These findings align with large longitudinal data showing that antipsychotic polypharmacy independently increases the risk of diabetes, hypertension and hyperlipidaemia.[18]

Correlation of treatment duration with metabolic abnormalities

Beyond the number of medications, cumulative treatment duration emerged as a further determinant of metabolic health. Patients who had received antipsychotic medication for more than ten years showed a higher incidence of both weight gain and deranged lipid profiles than those with less than ten years of treatment.[3] This observation reinforces the concept of a cumulative metabolic burden associated with prolonged exposure, whereby long-term physiological adaptation and sustained pharmacological effects lead to progressively more entrenched derangements.[2,19]

IV. Discussion

The present findings resonate strongly with the growing body of literature highlighting the long-term metabolic burden imposed by antipsychotic therapy.[2,3] The data support the view that these medications, while essential for psychiatric care, carry substantial risks to physical health that necessitate proactive and sustained management. A prevalence of 43% for significant weight gain and 46% for dyslipidaemia in this cohort is comparable with Indian and international reports of metabolic dysfunction in antipsychotic-treated populations.[6,7,8,10]

The higher incidences of weight gain and lipid abnormalities observed in patients treated for more than a decade reinforce that the metabolic impact of antipsychotics is not merely an acute side effect but a cumulative process.[3] Sustained exposure appears to drive progressive and enduring metabolic dysregulation, increasing the likelihood of severe complications over time. This is biologically plausible given the receptor-level and adipokine-mediated mechanisms implicated in antipsychotic-induced weight gain and insulin resistance.[12,21]

The study also demonstrates that polypharmacy serves as an independent and significant contributor to adverse metabolic outcomes. The group prescribed more than three antipsychotics showed the highest prevalence of disturbance, with 66% experiencing weight gain greater than 10 kg and 58% exhibiting dyslipidaemia. This dose–response relationship is a critical clinical insight and is consistent with systematic reviews and cohort studies linking antipsychotic polypharmacy to greater cardiometabolic risk.[9,17,18] The findings emphasise that clinicians must exercise caution when considering multi-antipsychotic regimens and should regularly reassess their necessity.[13]

The comparatively low prevalence of elevated HbA1c (6%) in this cohort merits comment. Even antipsychotic-naive patients with first-episode psychosis show measurable glucose dysregulation, and glycaemic derangement typically develops progressively during treatment, often lagging behind weight and lipid changes.[14,15,16] A single cross-sectional HbA1c measurement may therefore underestimate the true diabetogenic risk, and prospective monitoring is required to capture emerging dysglycaemia.[23]

Encouragingly, evidence suggests that antipsychotic-induced metabolic effects are at least partly modifiable. Lifestyle and dietary intervention, timing of dosing and pharmacological strategies can attenuate weight gain and improve metabolic parameters.[20,24,25] This provides a strong rationale for embedding preventive metabolic care into routine psychiatric practice.

Strengths and limitations

The main strengths of this study are its focus on a well-defined long-term treatment population and its examination of two clinically actionable variables — antipsychotic load and treatment duration. The principal limitation is the small sample size (N = 30) drawn from a single centre, which limits statistical power and generalisability. The cross-sectional design precludes causal inference, and baseline weight was ascertained from documented records, which may be subject to recording variability. Larger, multi-centre and prospective studies are needed to confirm these associations.[16]

V. Conclusion

This study confirms that metabolic side effects are a pervasive and significant challenge in patients receiving long-term antipsychotic treatment. A substantial proportion of the cohort experienced clinically relevant weight gain, dyslipidaemia and, to a lesser extent, elevated HbA1c. These effects were demonstrably linked to two key aspects of the treatment regimen: antipsychotic polypharmacy, which was associated with a markedly higher prevalence and severity of metabolic disturbance, and extended treatment duration, which was associated with a cumulative increase in metabolic abnormalities.[3,17,18]

In light of these findings, routine screening of metabolic parameters — including BMI, lipid profile and HbA1c — should be regarded not merely as advisable but as an integral component of standard care for all patients on long-term antipsychotic therapy.[22,23] Clinical practice should consistently favour minimal effective medication regimens and judiciously reassess the necessity of antipsychotic polypharmacy. Adherence to these principles can enhance long-term physical health outcomes, improve quality of life and help reduce the excess morbidity and mortality associated with these essential psychiatric treatments.[1]

Recommendations

1. Mandate routine metabolic screening

Perform comprehensive metabolic screening at baseline and at regular intervals thereafter, including BMI, a full lipid profile and HbA1c, to enable early detection and timely intervention. [22,23]

2. Periodically reassess polypharmacy

Regularly review the necessity of multiple antipsychotics and rationalise regimens where clinically safe, considering dose reduction or de-escalation when symptoms are stable. [17,18]

3. Integrate dietary and lifestyle counselling

Refer high-risk patients for dietary and lifestyle counselling, with collaborative plans for nutrition, physical activity and weight management. [20,24]

4. Develop OPD checklists

Implement standardised outpatient checklists to flag patients with high-risk metabolic profiles during routine visits so that no monitoring step is missed. [25]

Future Directions

Caring for individuals with psychotic and mood disorders must extend beyond symptom control to encompass long-term physical health, particularly the metabolic effects of prolonged antipsychotic use.[1] Future research should focus on developing personalised risk-assessment tools, evaluating targeted pharmacological and non-pharmacological interventions, and conducting larger multi-centre studies to validate findings across diverse populations.[24,25] Integrating metabolic health into the core of psychiatric care is not merely beneficial but an ethical imperative, ensuring that treatments relieve mental suffering while also preserving physical vitality and supporting lasting well-being.

Declarations

Conflicts of interest: The authors declare no conflicts of interest.

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