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ORIGINAL RESEARCH

Prevalence of Metabolic Syndrome in Patients on Long-term Antipsychotic Medication

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ABSTRACT

Introduction: Background: Metabolic syndrome is a major issue in patients treated with long-term antipsychotic medication and associated with increased cardiovascular morbidity as well as mortality. In the current study, we assessed its presence and risk factors in our population. **Methods:**A cross-sectional analysis of 370 subjects aged between 18 and 65 years who were treated with antipsychotics for at least year was performed. The obtained data included demographic data, psychiatric history and metabolic parameters. Metabolic syndrome was diagnosed according to the NCEP ATP III criteria. Risk factors were identified by bivariate and multivariable logistic regression analyses. **Results:** The occurrence rate of metabolic syndrome was 37.8%. The most prevalent component was raised waist circumference, affecting 51.9% of the population, followed by low HDL cholesterol at 48.1% and elevated triglycerides at 44.1%. Olanzapine exhibited the highest occurrence rate of metabolic syndrome (47.8%), whilst aripiprazole demonstrated the lowest frequency (27.0%). The age (adjusted odds ratio [AOR] 1.03, 95% confidence interval [CI] 1.01-1.05) and length of antipsychotic usage (AOR 1.07, 95% CI 1.03-1.11) were found to be significant predictors. Olanzapine was found to have a considerably increased likelihood of causing metabolic syndrome compared to aripiprazole, with an adjusted odds ratio (AOR) of 2.41 and a 95% confidence interval (CI) of 1.22-4.76. **Conclusion:**This study demonstrated the significant frequency of metabolic syndrome among patients taking long-term antipsychotic medications and identified age, duration of treatment, and antipsychotic type as key risk factors. These findings highlight the importance of regular metabolic monitoring, personalised therapy selection, and integrated therapies for managing metabolic risks in this sensitive population.

Keywords: Metabolic Syndrome, Antipsychotic Medications, Cardiovascular Risk, Psychiatric Disorders, Metabolic Monitoring

INTRODUCTION

Metabolic syndrome (MS) is an array of interrelated physiological, biochemical, clinical and metabolic factors that directly contribute to the risk of cardiovascular disease (CVD), type 2 diabetes mellitus and all-causes of mortality (Saklayen et al. 2013)A conventional characteristic of this syndrome has been that it is defined by the presence combination several clinical risk factors which include central obesity, insulin resistance dyslipidemia and hypertension. The increasing awareness of the high levels of metabolic syndrome in individuals with severe mental illness, especially those treated for long periods with antipsychotic medication has come to light over recent years.

Although antipsychotic drugs are essential for the treatment of mental disorders such as schizophrenia, bipolar disorder and major depression, they have been associated with the development of various metabolic abnormalities. The second-generation (atypical) antipsychotics, introduced in the 1990s were a significant advance because they effectively treated psychotic symptoms and lowered the risk of extrapyramidal side effects. However these Western drugs have the potential to rise weight gain, glucose dysregulation and lipid abnormalities-associated features of metabolic syndrome (De Hert et al., 2011). Overall, the relationship between antipsychotic treatment and metabolic syndrome is complex. Although some antipsychotics have a higher metabolic burden than others, the problem is class wide. For example, clozapine and olanzapine stand out as agents associated with ongoing high risk-weight gain and metabolic syndrome; whereas aripiprazole or ziprasidone have generally been

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considered built on a lower-risk scheme (Pillinger et al., 2020).

The exact pathophysiology of Metabolic Syndrome in patients on Antipsychotics is still controversial. However it has been hypothesized that antipsychotic medications may have Direct effects on hypertensive appetite regulation: Antipsychotics can interfere with neurotransmitter systems known to be involved in the central control of food intake, which might increase responsiveness to energy dense foods and hence result weight gain as a side effect (Reynolds & Kirk, 2010). Changes in glucose metabolism; Certain antipsychotics may act on insulin sensitivity and peripheral tissue glucose uptake (Burghardt et al., 2018). Antipsychotics may change lipid metabolism directly resulting indyslipidemia through the alteration of synthesis and breakdown of lipids (Khasawneh& Shankar, 2014). Sedentary behavior: Sedation and locomotor inhibition; Some antipsychotics have sedative properties which may reduce energy expenditure, thus increasing the risk for weight gain (Bak et al., 2014).

The rate of metabolic syndrome is highly variable depending on the study, but it appears to occur in 11–69% of patients treated with antipsychotic monotherapy for at least one year. There are many differences in the prevalence of metabolic syndrome and much variability could be due to patient population characteristics, definition of metabolic syndrome criteria used as well which type antipsychotic medication is being prescribed (Mitchell et al., 2013). The wide variety of data highlights the need for additional, systematic and standardised research in this area. Hefty Impact of Metabolic Syndrome on Severe Mental Illness Psychiatric disorders reduce life expectancy in comparison to the general population, due mainly to cardiovascular and other metabolic disturbances (Walker et al. 2015). This health disparity is even worse by metabolic syndrome. In addition, the presence of metabolic abnormalities in persons with psychiatric disorders may also have a negative effect on drug adherence, quality of life and clinical response to therapy as well.

The prevalence of metabolic syndrome is highly variable from one study to another in patients on long-term antipsychotic treatment and ranges anywhere between 11% and 69%. The variation in results is influenced by multiple factors, such as differences among the population being studied, difference criteria used to define metabolic syndrome and different type of antipsychotic medication (Mitchell et al., 2013). The heterogeneity of the data is noteworthy and underscores need for further well-designed overall studies in this area. Metabolic syndrome poses a significant effect on patients suffering from severe mental disorders. This my be in part because individuals with psychiatric problems have a lower life expectancy compared to the general population, mainly due to cardiovascular disease and other metabolic consequences (Walker et al. 2015). Indeed, metabolic syndrome exacerbates this health disparity. In addition, the presence of metabolic abnormality may seriously affect medication compliance, quality life and overall therapy results of psychiatric patients.

Notwithstanding these challenges, a number of encouraging approaches have arisen to tackle metabolic syndrome in this demographic. These measures involve the use of standardised metabolic monitoring techniques in psychiatric care settings and the integration of lifestyle treatments into mental health treatment plans. When it is medically suitable, exploring a transition to antipsychotic medications that have a lower risk of metabolic side effects can be advantageous. Additionally, the utilisation of supplementary drugs to address particular metabolic irregularities has demonstrated potential. Ultimately, implementing collaborative care strategies that incorporate mental health experts, primary care practitioners, and specialists in endocrinology and cardiology can result in a more thorough and efficient treatment of both psychiatric symptoms and metabolic well-being. Research in this field is constantly developing, with current studies investigating new methods to reduce the metabolic hazards linked to the use of antipsychotic medications. These investigations encompass the exploration of possible advantages of metformin and other drugs that enhance insulin sensitivity, the examination of the impact of nutritional supplements, and the creation of antipsychotic medications with enhanced metabolic profiles. The objective of this study was to determine the prevalence of metabolic syndrome in patients who had been using antipsychotic medication for a prolonged duration and to identify the risk factors associated with this specific group.

METHODOLOGY

Study Design: We conducted a cross-sectional observational study to ascertain the prevalence of metabolic syndrome in patients on long term antipsychotic medications. This design was chosen to reflect a snapshot of the metabolic profile in their current chronic state and also for detecting potential relationships related with antipsychotic medication utilisation, which is subdivided by gender specific drug use.

Study Site: This study was conducted in the Department of Psychiatric Government Medical College, Jalaun Orai a tertiary care Hospital. The site was chosen for its wide-ranging patient population and available full medical records and laboratory facilities.

Study Duration: The study was conducted over 12 months from May2022 to June 2023. This period was considered long enough to recruit a representative sample and collect detailed data with seasonal changes in the metabolic parameters being limited.

Sampling and Sample Size: This study used a consecutive sampling method to select subjects who fulfilled the inclusion criteria. This is estimated as 769

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through the formula for estimating a population proportion with specified absolute precision. Based on earlier studies (Mitchell et al., 2013) in Inuits for the prevalence of metabolic syndrome of 32.5% at confidence level of 95%, with absolute precision group difference acceptable up to maxmum ±5%; a final sample size head count was determined, would be need total at least n =334 participants. A total number of 370 participants were recruited to adjust for attrition or missing data and dropouts.

Inclusion and Exclusion Criteria: Patients aged 18-65 years who had been on continuous antipsychotic medication for at least 6 months were eligible for inclusion in the study. Exclusion criteria included pregnancy, a history of bariatric surgery, current use of medications known to significantly affect metabolism (e.g., systemic corticosteroids), and the presence of severe medical conditions that could independently influence metabolic parameters (e.g., uncontrolled thyroid disorders, active malignancy). Patients with a diagnosis of substance use disorder (except for nicotine dependence) were also excluded to minimize confounding factors.

Statistical Analysis

Statistical analysis was done with SPSS 26.0 (IBM Corp., Armonk, NY, USA). Data was summarised on the research population demographics and clinical characteristics. Continuous variables were reported as means, standard deviations, medians, or interquartile ranges depending on distribution. For categorical variables, we used frequencies and percentages. The proportion of participants meeting NCEP ATP III criteria determined metabolic syndrome prevalence with 95% confidence. Bivariate studies used chi-square tests for categorical variables and independent t-tests or Mann-Whitney U tests for continuous data to investigate metabolic syndrome and risk factors. After adjusting for confounding factors, multivariable logistic regression identified metabolic syndrome predictors. A stepwise backward technique was utilised to choose variables with p-value < 0.2 in bivariate analysis for the first model. The final model contained covariates with p-value < 0.05 and generated odds ratios with 95% confidence intervals.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee prior to commencement. Written informed consent was obtained from all participants after providing a detailed explanation of the study objectives and procedures. For patients with impaired decision-making capacity, consent was obtained from their legal guardians. All data were de-identified to ensure confidentiality, and participants were assigned unique study identification numbers. Participants were informed of their right to withdraw from the study at any time without affecting their ongoing medical care. Those identified as having metabolic syndrome or other significant health concerns during the study were provided with appropriate medical advice and referrals for further management.

RESULTS

The study population of 370 participants had a mean age of 42.5 years, with a slight male predominance (54.3%). Schizophrenia was the most prevalent diagnosis (50%), followed by bipolar disorder (30%). The average duration of antipsychotic use was 7.3 years, indicating long-term treatment. Olanzapine was the most commonly prescribed antipsychotic (24.9%), closely followed by risperidone (23%). The high percentage of current smokers (35.9%) highlights a significant cardiovascular risk factor in this population in Table 1.

Metabolic syndrome was present in 37.8% of participants, a notably high prevalence. Among the individual components, elevated waist circumference was most common (51.9%), suggesting a high rate of central obesity showed in Table 2. Low HDL cholesterol (48.1%) and elevated triglycerides (44.1%) were also prevalent, indicating significant lipid abnormalities. Elevated blood pressure (41.9%) and fasting glucose (35.9%) were less common but still affected a substantial portion of the population. These findings underscore the multifaceted nature of metabolic disturbances in patients on long-term antipsychotic treatment.

The prevalence of metabolic syndrome varied considerably among different antipsychotic medications. Olanzapine was associated with the highest prevalence (47.8%), followed by quetiapine (39.2%) and risperidone (38.8%). In contrast, aripiprazole had the lowest association (27%). This significant variation highlights the differential metabolic risks associated with various antipsychotics. The data supports current clinical guidelines recommending careful consideration of metabolic risk when selecting antipsychotic agents, particularly for long-term use. It also suggests the potential benefits of switching to more metabolically neutral options when clinically appropriate in Table 3.

Bivariate analysis revealed significant associations between metabolic syndrome and several factors. Age was significantly higher in those with metabolic syndrome (46.3 vs 40.2 years, $p<0.001$), as was the duration of antipsychotic use (8.9 vs 6.3 years, $p<0.001$). There was a trend towards higher prevalence in males and current smokers, though these did not reach statistical significance. The diagnosis of schizophrenia showed a non-significant trend towards higher metabolic syndrome prevalence in Table 4. These findings suggest that older age and longer antipsychotic treatment duration may increase the risk of metabolic syndrome.

Multivariable logistic regression analysis confirmed age and duration of antipsychotic use as independent risk factors for metabolic syndrome. Each year of age increased the odds by 3% (AOR 1.03, 95% CI 1.01-

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1.05), while each year of antipsychotic use increased the odds by 7% (AOR 1.07, 95% CI 1.03-1.11). Compared to aripiprazole, olanzapine use was associated with significantly higher odds of metabolic syndrome (AOR 2.41, 95% CI 1.22-4.76). Current smoking showed a trend towards increased risk but didn't reach statistical significance showed in Table 5. These results emphasize the importance of regular metabolic monitoring, especially in older patients and those on long-term treatment.

Table 1: Demographic and Clinical Characteristics of Study Participants (N=370)

Characteristic	n (%) or Mean ± SD
Age (years)	42.5 ± 11.8
Gender	
- Male	201 (54.3%)
- Female	169 (45.7%)
Diagnosis	
- Schizophrenia	185 (50.0%)
- Bipolar disorder	111 (30.0%)
- Major depressive disorder	59 (15.9%)
- Other	15 (4.1%)
Duration of antipsychotic use (years)	7.3 ± 5.2
Antipsychotic medication	
- Olanzapine	92 (24.9%)
- Risperidone	85 (23.0%)
- Quetiapine	74 (20.0%)
- Aripiprazole	63 (17.0%)
- Others	56 (15.1%)
Smoking status	
- Current smoker	133 (35.9%)
- Non-smoker	237 (64.1%)

Table 2: Prevalence of Metabolic Syndrome and Its Components (N=370)

Metabolic Syndrome Component	n (%)
Metabolic syndrome (≥3 components)	140 (37.8%)
Elevated waist circumference	192 (51.9%)
Elevated triglycerides	163 (44.1%)
Low HDL cholesterol	178 (48.1%)
Elevated blood pressure	155 (41.9%)
Elevated fasting glucose	133 (35.9%)

Table 3: Prevalence of Metabolic Syndrome by Antipsychotic Medication (N=370)

Antipsychotic Medication	Total n	Metabolic Syndrome n (%)
Olanzapine	92	44 (47.8%)
Risperidone	85	33 (38.8%)
Quetiapine	74	29 (39.2%)
Aripiprazole	63	17 (27.0%)
Others	56	17 (30.4%)

Table 4: Risk Factors Associated with Metabolic Syndrome (Bivariate Analysis)

Risk Factor	Metabolic Syndrome Present (n=140)	Metabolic Syndrome Absent (n=230)	p-value
Age (years, mean ± SD)	46.3 ± 10.5	40.2 ± 12.1	<0.001
Gender (male), n (%)	83 (59.3%)	118 (51.3%)	0.137
Duration of antipsychotic use (years, mean ± SD)	8.9 ± 5.8	6.3 ± 4.6	<0.001
Smoking (current), n (%)	59 (42.1%)	74 (32.2%)	0.052
Diagnosis (Schizophrenia), n (%)	77 (55.0%)	108 (47.0%)	0.132

Table 5: Multivariable Logistic Regression Analysis of Factors Associated with Metabolic Syndrome

Variable	Adjusted Odds Ratio	95% CI	p-value
Age (per year increase)	1.03	1.01-1.05	0.002
Duration of antipsychotic use (per year)	1.07	1.03-1.11	<0.001

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Antipsychotic medication (ref: Aripiprazole)			
- Olanzapine	2.41	1.22-4.76	0.011
- Risperidone	1.68	0.84-3.37	0.142
- Quetiapine	1.72	0.85-3.49	0.133
- Others	1.16	0.53-2.54	0.71
Smoking (current vs. non-smoker)	1.49	0.96-2.31	0.078

DISCUSSION

The present study aimed to determine the prevalence of metabolic syndrome among patients on long-term antipsychotic medication and to identify associated risk factors. Our findings reveal a high prevalence of metabolic syndrome in this population and highlight several important risk factors that warrant attention in clinical practice and future research.

Our study found that 37.8% of patients on long-term antipsychotic medication met the criteria for metabolic syndrome. This prevalence is consistent with previous meta-analyses and large-scale studies in similar populations. An example is a comprehensive evaluation and statistical analysis conducted by Mitchell et al. (2013), which found that 32.5% (95% CI: 30.1%–35.0%) of individuals diagnosed with schizophrenia and related illnesses had this condition. The somewhat higher incidence in our study can be attributed to the inclusion of patients with different psychiatric disorders and the prolonged use of antipsychotics in our sample. The prevalence we discovered is significantly more than the reported prevalence in the general population, which usually falls between 20% and 25% (Saklayen, 2018). This difference underlines the substantial metabolic strain linked to extended antipsychotic usage and emphasises the necessity for focused interventions in this susceptible group.

Examining the specific elements of metabolic syndrome, shown in Table 2, the most common abnormality was having an enlarged waist circumference. This was something experienced by 51.9% of patients. Next comes low levels of HDL cholesterol, something that affects 48.1% of people After that is high triglyceride levels, something that affects 44.1% of those subjects. The findings of this study were in line with other research which suggests that the use of antipsychotic medication is associated with significant metabolic disturbances, including weight gain and lipid abnormality (De Hert et al., 2011). The significant concentration of central obesity, demonstrated by increased waist circumference, was particularly worrying about its strong correlation with insulin resistance and cardiovascular risk. What they found provides evidence in support of the theory that antipsychotics can directly regulate hunger and fat distribution (Reynolds & Kirk., 2010). These lipid abnormalities add serious cardiovascular risk in particular population groups. Such as low levels of high-density lipoprotein (HDL) and high levels of triglycerides.

According to our analysis of syndrome prevalence in relation to different antipsychotic medication (Table 3), the data show remarkable differences between agents. Olanzapine had the highest prevalence of metabolic syndrome (47.8%), followed by quetiapine (39.2%) and risperidone (38.8%). In contrast, aripiprazole was the least likely to be associated with metabolic syndrome (27.0%). These results were largely consistent with those of previous studies or meta-analyses of the metabolic risk profiles for these drugs. As was pointed out repeatedly throughout the book, even research laboring under this type of misunderstanding still has value and is worth preserving though it may have little immediate impact on clinical practice. Pillinger et al. (2020) found from a comprehensive network meta-analysis that olanzapine was associated with the most severe metabolic derangements of any antipsychotic drug, while aripiprazole was among those with most favorable metabolic profile. Upon reflection our results underscore the importance of considering metabolic risk when choosing antipsychotic medication for long-term use. The lower prevalence of metabolic syndrome associated with aripiprazole in our study (27.0% vs. 37.8% overall) is consistent with its reputation as a less metabolically aggressive form. This characteristic can be attributed to its unique pharmacological profile, including partial agonism at dopamine D2 and serotonin 5-HT1A receptors (Stip&Tourjman, 2010).

Several important risk factors for metabolic syndrome in this population was turned up: age and duration of exposure to antipsychotic drugs were independent predictors with each year increasing chances of developing a metabolic syndrome by three percent (AOR 1.03, 95% CI 1.01-1.05) to seven % respectively (AOR 1.07, 95% CI 1.03-1.11). The link between age and metabolic syndrome that is so clearly demonstrated in the general population appears to be intensified in patients with quisqualic acid poisoning in line with the longest time of using prescription antipsychotics. This finding highlights that there need to be age-appropriate metabolic monitoring and interventions in this population. The high association between duration of antipsychotic treatment and metabolic syndrome risk is indeed noteworthy. This connection has been seen in longitudinal studies before, such as the study conducted by Srisurapanont et al. (2015), which recorded that in a cohort of patients with schizophrenia the prevalence rate rose from 20% at the start to 35% after one year on antipsychotic drugs. Our results suggest that this risk is accumulating over a long period, the need for continuous metabolic monitoring and management strategies throughout antipsychotic therapy.

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The medication type also emerged as a significant factor in our multivariable analysis of patients with schizophrenia. Compared to aripiprazole, olanzapine was associated with significantly higher odds of metabolic syndrome (AOR 2.41, 95% CI 1.22-4.76).It is still well known from previous studies that these medications exert metabolic risk and indicates the importance of considering metabolic risk profile when selecting antipsychotic agents (American Diabetes Association et al., 2004). Smoking owns an increasing trend at our multiple variable models which, while not achieving statistical significance (AOR 1.49, 95% CI 0.96-2.31, p=0.078).The high prevalence of smoking in our sample (35.9%) is consistent with previous reports of disproportionately elevated smoking rates for individuals with severe mental illness (e.g., de Leon & Diaz, 2005). In light of the known cardiovascular risks associated with smoking, this finding underscores the urgent need for integrated treatment programs that address smoking cessation alongside psychiatric care.

An important finding of this study is the high prevalence of metabolic syndrome and its components. It is one of the first pathological studies to show a clear relationship between antidepressant medication and metabolic syndrome. In light of our results, we recommend that regular monitoring for metabolic disorders among patients receiving long-term antipsychotic treatment should be carried out as a matter of urgency. Based on our findings, the current guideline of baseline and follow-up assessments in weight, waist circumference, blood pressure, fasting glucose, and lipid profiles for all patients receiving antipsychotic treatment (American Diabetes Association, et al., 2004) is supported. The differential metabolic risk among various antipsychotic medications demonstrated by our study underscores the need for individualized treatment selection While remission of symptoms still taking precedence over metabolic risk in deciding which antipsychotic is prescribed, attention attention should nevertheless be paid to this aspect of treatment especially for patients with active metabolic defects or risk factors cardiovascular disease. When clinically suitable patients experiencing major metabolic disturbances may usefully switch to antipsychotics of good metabolic profile (e.g., aripiprazole).

Our results also highlight the need for a multifaceted approach to metabolic risk management in this population. Given the strong association between duration of antipsychotic use and metabolic syndrome risk, early intervention is crucial. Lifestyle interventions; Structured programs addressing diet, physical activity, and smoking cessation should be integrated into psychiatric care plans. The STRIDE study by Green et al. (2015) demonstrated the feasibility and effectiveness of lifestyle interventions in reducing cardiovascular risk factors among individuals with serious mental illnesses.Pharmacological interventions; For patients with specific metabolic abnormalities, appropriate medications (e.g., metformin for glucose dysregulation, statins for dyslipidemia) should be considered in collaboration with primary care providers or specialists.Antipsychotic switching or dose optimization; When metabolic abnormalities persist despite other interventions, switching to an antipsychotic with a more favorable metabolic profile or optimizing the dose of the current medication may be considered, always balancing metabolic and psychiatric outcomes.Collaborative care models; Given the complex interplay between psychiatric and metabolic health, integrated care approaches involving mental health professionals, primary care providers, and specialists in endocrinology and cardiology are essential for comprehensive management.

Study Limitations

Limitations Although our study contributes to the knowledge ofthe prevalence and risk factors of metabolic syndrome in long-term antipsychotic-treated patients, some limitations should be noted. The design of the study was cross-sectional and hence causality between antipsychotic use and metabolic outcomes cannot be established. For that purpose larger longitudinal studies are needed to properly explore the temporal pattern of metabolic syndrome onset in this sample.

Future directions

More research is needed to determine how best to reduce metabolic risks among people taking antipsychotic medications. This might include long-term prospective studies that follow metabolic profiles of people newly placed on antipsychotics, research in the genetic and environmental contributions to an individual susceptibility to these side effects,as well as practical tests which could prevent or treat such patients before they become a clinical problem. It can also mean testing new drugs with better profiles of activity. The research direction is led by a desire to improve overall patient outcomes and the metabolic side effects of antipsychotic medication.

CONCLUSION

Our research shows that people who are on antipsychotic medication for a long time have large numbers of metabolic syndrome. Moreover we disproportionately find a bunch of profound risk factors as well such as age, duration of their antipsychotic use and specific type of anti-psychotic drug they may be on. These findings highlight the urgent need for early metabolic-monitoring and intervention strategies in psychiatric care settings. Therefore, identification of these metabolic concerns and an integrated approach to treat them might help us contribute toward enhancing general health status and quality of life in those who receive long-term antipsychotic treatment.

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Conflicts of Interest
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