Original Article

Prevalence and Pattern of Extrapyramidal Side Effects in Patients Receiving Second-Generation Antipsychotics: A Cross-Sectional Study from a Tertiary Care Hospital

Anjana S.Krishnan[1], Hema N.G[2], Kishore M.S[3], Narendra Kumar M S[4]

[1]Postgraduate, Department of Pharmacology, Mysore Medical College, Mysore, Karnataka, India, [2]Professor, Department of Pharmacology, Mysore Medical College, Mysore, Karnataka, India, [3]Associate Professor Department of Pharmacology, Mysore Medical College, Mysore, Karnataka, India, [4]Assistant Professor, Department of Psychiatry, Mysore Medical College, Mysore, Karnataka, India

Abstract

Background: Second-generation antipsychotics (SGAs) are widely used in schizophrenia and other psychotic disorders for their perceived lower risk of extrapyramidal side effects (EPSEs) compared to first-generation agents. However, emerging evidence suggests SGAs are not entirely free from EPSEs. This study aimed to determine the prevalence and pattern of EPSEs in patients on SGAs. **Materials and Methods:** A cross-sectional observational study was conducted from October to December 2024 at the Psychiatry OPD of K.R. Hospital, Mysore. Sixty patients aged ≥18 years with schizophrenia, bipolar disorder, or major depressive disorder with psychotic features, on SGAs for ≥2 weeks, were included. Patients with neurological disorders, concurrent drugs causing movement disorders, substance use, or pregnancy/lactation were excluded. EPSEs were assessed using the Simpson–Angus Scale (SAS) through interviews, clinical examination, and record review. Data were analysed for demographic, clinical, and drug-related associations. **Results:** The mean age was 20–40 years in 60% of participants; 53.3% were male; 45% had schizophrenia. Risperidone was most prescribed (55%), followed by olanzapine (43%). EPSE prevalence was higher with risperidone (21.2%) than with olanzapine (11.5%). Tremors were the most common EPSE (90.9%), followed by akathisia (9%). Duration of treatment was significantly associated with EPSE occurrence ($p = 0.000$), with the highest incidence in the first four weeks. All EPSEs were mild (SAS score 1). **Conclusion:** EPSEs remain clinically relevant with SGAs, especially risperidone. Early treatment duration is a high-risk period, warranting vigilant monitoring and individualized therapy to improve adherence and quality of life.

Keywords: Second-generation antipsychotics, Extrapyramidal side effects, Risperidone, Olanzapine, Simpson–Angus Scale, Schizophrenia.

Received: 28 May 2025 **Revised: 19 July 2025** **Accepted: 14 August 2025** **Published: 28 August 2025**

Introduction

Schizophrenia is a chronic psychiatric disorder with disturbances in perception, thought, social interaction, and emotional expression. The global lifetime prevalence is ~1.1%, ranking among the top 15 causes of disability, with a substantial healthcare and societal burden. In the U.S., economic costs rose from $62.7 billion (2002) to $155.7 billion (2013).[1] In India, the lifetime prevalence of schizophrenia spectrum disorders is 1.41%, with a current prevalence of 0.42%.[2] Antipsychotics are central to treating schizophrenia, bipolar mood disorders (BPD), and other psychoses, classified as first-generation (FGAs) and second-generation antipsychotics (SGAs).[3,4] FGAs are effective for positive symptoms but often cause extrapyramidal side effects (EPSEs) such as dystonia, Parkinsonism, akathisia, and tardive dyskinesia.[5,6] SGAs, modelled after clozapine, were developed to reduce EPSE risk.[5]

Widely prescribed SGAs include risperidone, olanzapine, quetiapine, aripiprazole, and ziprasidone.[4,5] While generally better tolerated, SGAs may still cause EPSEs depending on D_2 receptor affinity—low-affinity agents (clozapine, quetiapine) have lower risk, whereas high-affinity drugs (risperidone, ziprasidone) are associated with a high risk.[3,7] EPSE prevalence varies by drug type, dose, duration, and patient factors such as age, gender, and comorbidities. Cross-sectional studies show a significant occurrence, particularly with FGAs,[8] though SGAs are not exempt. Risk factors include demographics, dose, treatment duration, polypharmacy, and neurobiological vulnerability.[3,9] In BPD, FGAs like haloperidol may cause higher EPSE risk than in schizophrenia, though results vary by agent (e.g., olanzapine shows no such difference).[10]

EPSEs affect compliance, quality of life, and functional outcomes, and can mimic negative symptoms, leading to dose escalation.[11-14] Despite SGA use, large trials and meta-analyses show little difference in tolerability or efficacy compared to FGAs.[5,11,15]

Address for correspondence: Dr. Narendra Kumar M S, Assistant Professor, Department of Psychiatry, Mysore Medical College, Mysore, Karnataka, India.
E-mail: drheggere@gmail.com

DOI:
10.21276/amit.2025.v12.i2.10

How to cite this article: Krishnan AS, Hema N.G, Kishore M.S, Kumar MSN. Prevalence and Pattern of Extrapyramidal Side Effects in Patients Receiving Second-Generation Antipsychotics: A Cross-Sectional Study from a Tertiary Care Hospital. Acta Med Int. 2025;12:44-48.

Given the continued use of both FGAs and SGAs, determining EPSE prevalence and risk factors is essential, especially in diverse populations where genetic, cultural, and healthcare factors influence drug effects.[9] This cross-sectional study investigates EPSE prevalence and determinants in patients on SGAs to guide safer, more effective antipsychotic use.

Objective

The primary objective was to determine the prevalence of extrapyramidal side effects in psychotic patients treated with second-generation antipsychotics.

The secondary objective was to identify the specific types of movement disorders experienced by these patients.

Materials and Methods

Study Design and Setting: This was a cross-sectional observational study conducted over a three month period (October–December 2024) in the Department of Psychiatry, K.R. Hospital, a tertiary care teaching hospital affiliated with Mysore Medical College and Research Institute, Mysore, Karnataka, India. The study was carried out in collaboration with the Department of Pharmacology.

Study Population: The study population comprised adult patients (≥18 years) attending the Psychiatry Outpatient Department (OPD) with a diagnosis of schizophrenia, bipolar affective disorder, or major depressive disorder with psychotic features, who were receiving second-generation antipsychotic (SGA) therapy.

Inclusion Criteria

Age ≥18 years

Clinical diagnosis of schizophrenia, bipolar affective disorder, or psychotic depression.

Receiving SGA therapy for a minimum duration of 2 weeks.

Willingness to provide written informed consent.

Exclusion Criteria

Pre-existing neurological disorders (e.g., Parkinson's disease, Huntington's disease).

Use of medications known to induce movement disorders (e.g., metoclopramide).

History of alcohol or substance use disorders.

Pregnancy or lactation.

Sample Size and Sampling Technique

"A total of 60 eligible patients were recruited through consecutive sampling during routine outpatient department (OPD) hours, from 11:00 a.m. to 1:00 p.m."

Data Collection: After screening for eligibility, participants underwent detailed interviews, clinical examination, and review of medical records. Extrapyramidal side effects (EPSEs) were assessed using the Simpson–Angus Scale (SAS), a validated tool for detecting drug-induced Parkinsonism and related movement disorders. Information on demographic variables, psychiatric diagnosis, antipsychotic type, dosage, and treatment duration was recorded in a structured proforma.

Outcome Measures

Primary outcome: Prevalence of EPSEs among patients receiving SGAs

Secondary outcome: Type and frequency of individual movement disorders

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS trial version 29. Descriptive statistics were expressed as mean ± standard deviation for continuous variables and as frequencies and percentages for categorical variables. Associations between categorical variables were assessed using the Chi-square test, while continuous variables were compared using the Student's t-test. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Mysore Medical College and Research Institute, Mysore, before initiation. All participants received a clear explanation of the study objectives and procedures in their local language, and written informed consent was obtained from each participant. Confidentiality and anonymity of all collected data were strictly maintained throughout the study.

Results

A total of 60 patients attending the Psychiatry OPD at K.R. Hospital were assessed for Extrapyramidal Side Effects (EPSEs) associated with second-generation antipsychotic (SGA) use. The study population included individuals diagnosed with schizophrenia, bipolar disorder, or major depressive disorder with psychotic features. EPSEs were evaluated using the Simpson-Angus Scale, and the findings are summarized below.

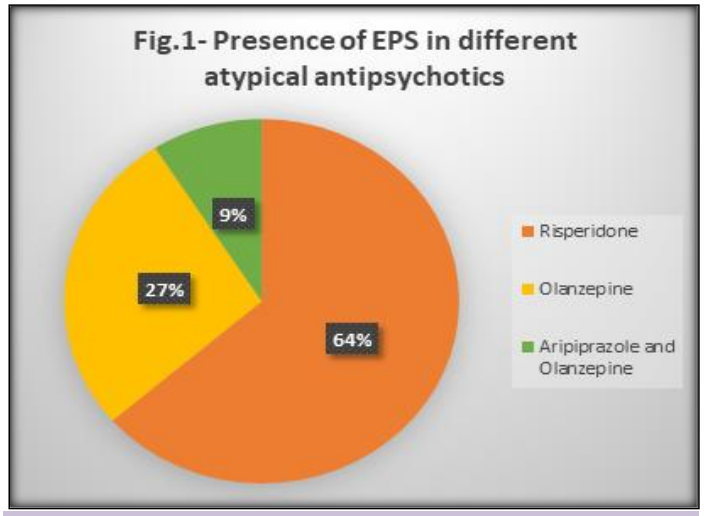

Figure 1: Presence of EPS with respect to atypical antipsychotics used.

The pie chart in [Figure 1] illustrates the distribution of extrapyramidal symptoms (EPS) across different atypical antipsychotics. Risperidone accounted for the majority of EPS cases, contributing to 64% of all observed EPS. Olanzapine was associated with 27% of EPS cases. A smaller proportion (9%) of EPS was reported in patients who received a combination of Aripiprazole and Olanzapine. This figure clearly demonstrates that risperidone has the highest association with EPS among the atypical antipsychotics evaluated in this study.

Table 1: Characteristics of study participants

Sl. No.	Characteristics	N (%)
1	Age	
	20-40 years	36 (60)
	41-60 years	18 (30)
	>60 years	6 (10)
2	Gender	
	Male	32 (53.3)
	Female	28 (46.7)
3	Education	
	Primary education	20 (33.3)
	Secondary education	35 (58.3)
	Higher secondary education	3 (5)
	Graduate	2 (3.3)
4	Religion	
	Hindu	53 (88.3)
	Muslim	4 (6.7)
	Christian	3 (5)
5	Diagnosis	
	Bipolar affective disorder	17 (28.3)
	Psychosis NOS	15 (25)
	Schizophrenia	27 (45)
	Schizophrenia with obsessive compulsive disorder	1 (1.7)
6	Family history of psychiatric illness	
	Yes	7 (11.6)
	No	53 (88.3)
7	History of smoking	
	Yes	9 (15)
	No	51 (85)

In this study of 60 patients, the majority were between 20–40 years of age (60%) and predominantly male (53.3%). Most participants had only primary or secondary education (over 90%), and a significant proportion (45%) were diagnosed with schizophrenia. The majority of the study population were Hindus (88.3%), and only a small percentage reported a family history of psychiatric illness (11.6%) or smoking (15%). These findings reflect a young, low-educated population with schizophrenia being the most common diagnosis.

Table 2: Prescribed daily dose of antipsychotic drug, its dose and time of exposure

Sl. No.	Atypical antipsychotics	Dose Mean (range)	Time of exposure Mean (range)	Total patients N (%)	EPS N (%)
1	Risperidone	2.97 (6)	1.18 (2)	33 (55)	7 (21.2)
2	Olanzepine	7.5 (10)	1.12 (2)	26 (43)	3 (11.5)

Among the 60 patients studied, risperidone was the most commonly prescribed atypical antipsychotic, used by 55% of patients, with a mean dose of 2.97 mg and average treatment duration of 1.18 years. Extrapyramidal side effects (EPS) were observed in 21.2% of patients on risperidone. In contrast, olanzapine was used by 43% of patients at a mean dose of 7.5 mg and average exposure time of 1.12 years, with a lower incidence of EPS (11.5%). These results suggest that risperidone is associated with a higher rate of EPS compared to olanzapine.

Table 3: Presence of EPS with respect to the dosage of atypical antipsychotics

Atypical antipsychotics	Dosage	EPS observed (%)
Risperidone	4mg	3 (27.4)
	6mg	1 (9)
	8mg	3 (27.4)
Olanzepine	5mg	1 (9)
	10mg	2 (18.2)
Aripiprazole +olanzepine	20mg each	1 (9)

Among patients treated with risperidone, extrapyramidal symptoms (EPS) were most commonly observed at doses of 4 mg and 8 mg, with each contributing to 27.4% of EPS cases, while 6 mg was associated with 9% of cases. For olanzapine, 5 mg led to 9% EPS incidence, whereas 10 mg was associated with a higher rate of 18.2%. A combination therapy of aripiprazole and olanzapine at 20 mg each resulted in EPS in 9% of patients.

These findings suggest a dose-related trend in EPS occurrence, particularly with risperidone, and reinforce the need for careful dose selection to minimize adverse effects.

Table 4: Types and severity of EPS

Antipsychotics used	Type of EPS	Frequency (%)	scale and severity
Olanzapine	Akathisia	1 (9)	SAS,1, Normal
Risperidone	Tremors	7 (63.8)	SAS,1, Normal
Olanzapine	Tremors	2 (18.2)	SAS,1, Normal
Aripiprazole and Olanzapine	Tremors	1 (9)	SAS,1, Normal
Total		11 (100)	

Among the 11 cases of EPS observed, tremors were the most frequent, accounting for 90.9% of all cases. Risperidone was associated with the highest number of tremor cases (7 cases, 63.8%), followed by olanzapine (2 cases, 18.2%) and the combination of aripiprazole and olanzapine (1 case, 9%). Akathisia was reported in only one case (9%) and was associated with olanzapine.

All EPS cases were rated as mild (SAS score 1 – Normal), indicating minimal clinical severity despite their presence. This highlights that while EPS can occur even with second-generation antipsychotics, they were generally mild and manageable in this cohort.

Table 5: Association between the appearance of EPS and atypical antipsychotic usage

Factors	Appearance of EPS (%)	Chi-square	p-value
Type of atypical antipsychotics used Risperidone Olanzapine Aripiprazole+olanzapine	 7 (63.6) 3 (27.3) 1 (9.1)	4.32	0.127
Duration of treatment in weeks 2-4 weeks >4 weeks-8 weeks >8 weeks	 5 (45.5) 4 (36.4) 2 (18.1)	18.16	0.000*

The type of atypical antipsychotic used showed a trend toward differing EPS frequencies, with risperidone accounting for the highest proportion (63.6%) of EPS cases, followed by olanzapine (27.3%) and aripiprazole + olanzapine (9.1%). However, this association was not statistically significant (p = 0.127).

In contrast, the duration of treatment had a significant association with EPS occurrence (p = 0.000). EPS appeared more frequently during the first 4 weeks of treatment (45.5%), gradually decreasing with prolonged use. This suggests that early treatment duration is a critical period for the development of EPS, highlighting the importance of close monitoring during initial weeks of atypical antipsychotic therap.

Discussion

This cross-sectional study was conducted to evaluate the prevalence and types of extrapyramidal side effects (EPS) among patients with psychotic disorders who were treated with second-generation antipsychotics (SGAs). Our primary objective was to examine how factors such as age, gender, psychiatric diagnosis, and patterns of antipsychotic use influence the occurrence of antipsychotic-induced movement disorders.

In our study population, most of the patients belong to the 20–40-year age group, with a notable male predominance and lower educational status. Schizophrenia was the most common psychiatric diagnosis among the participants, followed by bipolar disorder and major depressive disorder. These demographic and diagnostic distributions are consistent with findings from previous studies, such as the one conducted by Anjana et al., which also reported a male preponderance among patients on antipsychotic treatment.[3] However, Anjana et al. observed no significant association between psychiatric diagnosis and the type of EPS encountered. In contrast, our study found that patients with schizophrenia experienced a higher prevalence of EPS compared to those with bipolar disorder and major depressive disorder.

Regarding the antipsychotic agents used, risperidone, olanzapine, and aripiprazole (often in combination with olanzapine) were the most frequently prescribed SGAs. Among these, risperidone was associated with the highest rate of EPS. Tremors emerged as the most common extrapyramidal symptom in our cohort. This observation aligns partly with the findings of Scandashree K. et al., who reported tremors in 14% of their study population, though their study also emphasised that risperidone was more often associated with agitation.[12]

Interestingly, in contrast to our findings, the study conducted by Kumar and Sachdev et al. (2009) identified akathisia as the most prevalent EPS among patients receiving SGAs.[7] Furthermore, Gao et al. reported that patients with bipolar disorder, particularly during depressive episodes, were more susceptible to developing acute antipsychotic-induced movement disorders than patients with schizophrenia.[10] However, our study revealed a different trend, with schizophrenia patients exhibiting a higher rate of EPS than those diagnosed with bipolar or depressive disorders.

These discrepancies between our findings and those of previous studies may be attributed to differences in patient demographics, clinical profiles, drug dosages, treatment durations, and methodologies. For instance, risperidone's high affinity for dopamine D2 receptors has been implicated in its relatively higher risk of inducing EPS, particularly at higher doses or in sensitive individuals. Additionally, patient-specific factors such as age, sex, and underlying neurological vulnerability may play a critical role in determining susceptibility to drug-induced movement

disorders.

Overall, our study emphasizes the importance of vigilant monitoring for EPS, even with second-generation antipsychotics, which are often considered to have a lower risk of such adverse effects compared to first-generation agents. Tailoring antipsychotic therapy based on individual risk profiles and early identification of EPS can improve treatment adherence and overall patient outcomes. Further longitudinal studies with larger sample sizes and standardized EPS assessment tools are needed to better understand the risk factors and preventive strategies for EPS in patients receiving SGAs.

Conclusion

This cross-sectional study demonstrates that extrapyramidal side effects (EPSEs) remain a clinically relevant concern in patients receiving second-generation antipsychotics (SGAs), despite their reputation for a more favourable safety profile than first-generation agents. Risperidone showed a higher association with EPSEs, predominantly tremors, with schizophrenia patients exhibiting greater susceptibility than those with bipolar disorder or depression. Younger males and early treatment periods emerged as higher-risk groups, underscoring the need for vigilant monitoring. These findings challenge the assumption of universal safety with SGAs and highlight the importance of individualised drug selection, dose optimisation, and early intervention strategies to enhance treatment adherence, minimise adverse effects, and improve overall patient quality of life.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Aditi K, Brady BL, Dembek C, Williams GR, Kent JM. The incidence and economic burden of extrapyramidal symptoms in patients with schizophrenia treated with second-generation antipsychotics in a Medicaid population. J Med Econ. 2022;25(1):87-98.
2. Hegde PR, Nirisha LP, Basavarajappa C, Suhas S, Kumar CN, Benegal V, et al; NMHS National Collaborators Group. Schizophrenia spectrum disorders in India: A population-based study. Indian J Psychiatry. 2023;65(12):1223-9.
3. Anjana. A, Gayatri. M, Devi D, Poornachandrika P. Comparison between characteristics of patients experiencing Extrapyramidal side effects, between first and second generation antipsychotic use- A retrospective cross-sectional study. Indian J Psychiatry. 2022;64(Suppl 3): S548.
4. Sharumathi SM, Bhavatharini S, Rinu MX, Arun P, Deepalakshmi M. Extrapyramidal effects of first and second generation antipsychotics: a review. Int J Drug Deliv Technol. 2023;13:1623-30.
5. Divac N, Prostran M, Jakovcevski I, Cerovac N. Second-generation antipsychotics and extrapyramidal adverse effects. Biomed Res Int. 2014;2014:656370.
6. Ali T, Sisay M, Tariku M, Mekuria AN, Desalew A. Antipsychotic-induced extrapyramidal side effects: a systematic review and meta-analysis of observational studies. PLoS One. 2021;16(9):e0257129.
7. Kumar R, Sachdev PS. Akathisia and second-generation antipsychotic drugs. Curr Opin Psychiatry. 2009;22(3):293-9.
8. Desai N, Patel PB, Shah S, Patel TK, Shah SN, Vatsala E. Prevalence and pattern of antipsychotic induced movement disorders in a tertiary care teaching hospital in India – a cross-sectional study. Int J Psychiatry Clin Pract. 2017;21(4):330-6.
9. Weng J, Zhang Y, Li H, et al. Study on risk factors of extrapyramidal symptoms induced by antipsychotics and their correlation with symptoms of schizophrenia. General Psychiatry 2019;32:e100026.
10. Gao K, Kemp DE, Ganocy SJ, Gajwani P, Xia G, Calabrese JR. Antipsychotic-induced extrapyramidal side effects in bipolar disorder and schizophrenia: a systematic review. J Clin Psychopharmacol. 2008;28(2):203-9.
11. Peluso MJ, Lewis SW, Barnes TR, Jones PB. Extrapyramidal motor side-effects of first- and second-generation antipsychotic drugs. Br J Psychiatry. 2012;200(5):387-92.
12. Scandashree K, Praveenkumar B, Udaykumar P. A cross-sectional study to assess the adverse effect profile of second-generation antipsychotics: risperidone, olanzapine and quetiapine. Int J Basic Clin Pharmacol. 2016;5(5):1981-7. doi:10.18203/2319-2003.ijbcp20163102.
13. Rummel-Kluge C, Komossa K, Schwarz S, Hunger H, Schmid F, Kissling W, Davis JM, Leucht S. Second-generation antipsychotic drugs and extrapyramidal side effects: a systematic review and meta-analysis of head-to-head comparisons. Schizophr Bull. 2012;38(1):167-77.
14. De Araújo AN, de Sena EP, de Oliveira IR, Juruena MF. Antipsychotic agents: efficacy and safety in schizophrenia. Drug Healthc Patient Saf. 2012;4:173-80.
15. Zhang JP, Gallego JA, Robinson DG, Malhotra AK, Kane JM, Correll CU. Efficacy and safety of individual second-generation vs. first-generation antipsychotics in first-episode psychosis: a systematic review and meta-analysis. Int J Neuropsychopharmacol. 2013;16(6):1205-18.