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Original Article

Psychiatry/Mental Health Section

Antipsychotic-induced Side-effects among Indian Patients: A Prospective Observational Study

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ABSTRACT

Introduction: Antipsychotic drugs are an effective treatment for most psychotic disorders. Nevertheless, patients' quality of life, adherence, and clinical results may be negatively impacted by these medications' incapacitating side-effects.

Aim: To assess the prevalence, severity, and progression of antipsychotic side-effects in treatment-naive Indian patients using standard scales.

Materials and Methods: The present prospective observational study was conducted in the Psychiatry Department of Dhiraj hospital, Vadodara, Gujarat, India, from October 2023 to March 2025 included 332 treatment-naive patients Glasgow Antipsychotic Side-effect Scale (GASS), Modified Simpson Angus Scale (MSAS), Abnormal Involuntary Movement Scale (AIMS), and Psychotropic-Related Sexual Dysfunction Questionnaire (PRSexDQ-SALSEX) were applied to measure side-effects at baseline, one month, and three months. Serial measurements were also made of weight, Body Mass Index (BMI), glucose, and lipid profile. Statistical tests such as Analysis of Variance (ANOVA) and Kruskal-Wallis with Dunn post hoc analysis were used, and $p<0.05$ was considered statistically significant.

Results: Among the 332 treatment-naive patients {197 (59.3%) females; 135 (40.7%) males} with a mean age of 34.7±10.2 years, 194 (58.5%), 101 (30.4 %), and 37 (11.2%) were treated with monotherapy, two and three-drug combinations, respectively. A total of 199 (60%) patients had weight gain, 166 (50%) sedation, and 149 (45%) Extrapyramidal Symptoms (EPS). At three months, GASS score significantly increased from 0.0 to 13.0 ($p<0.0001$). Cholesterol levels rose from 150.2 mg/dL to 173.5 mg/dL ($p<0.0001$). The clozapine-amisulpride combination demonstrated the most profound movement abnormalities and metabolic issues. Older age ($r=0.34$, $p=0.001$) and long duration of illness ($r=0.28$, $p=0.003$) showed a weak positive correlation with GASS scores.

Conclusion: Antipsychotic medications appear to have very significant side-effects, which underline the importance of frequent individualised monitoring and routine tailored strategies to decrease risks while maintaining efficacy. The most frequently observed side-effects were sexual dysfunction, weight gain, sedation, and EPSs. These findings highlight the need for early, structured monitoring of side-effects and cautious use of antipsychotic polypharmacy in routine clinical practice.

Keywords: Adverse reactions,Drug-related side-effects, Psychotic disorders, Treatment outcome

INTRODUCTION

Psychiatric disorders are one of the most important health issues of our time, with an estimated 1.1 billion affected (1 in 7 people globally), resulting in considerable socioeconomic and healthcare costs [1]. In India, the burden is particularly acute, with prevalence estimates between 9.5 and 370 per 1,000 population, and nearly 20% of adults afflicted with one or more psychiatric disorders [2]. Despite these disturbing figures, there are significant gaps in the provisions for mental healthcare in India, including an acute shortage of essential psychotropic drugs, especially antipsychotic medications, which are critical to treating conditions like schizophrenia and bipolar disorder [3]. This is worsened by systematic gaps like insufficient post-marketing surveillance, as well as a lack of local studies on the performance, safety, and adherence of drugs, resulting in a large number of patients being left untreated or improperly treated [4].

Usage of antipsychotic medication is very important while dealing with psychiatric symptoms however it poses serious issues as well. First generation antipsychotic drugs, such as haloperidol and chlorpromazine positively assist in alleviating positive symptoms like hallucinations and delusions, but these often result in EPS such as Parkinson's disease and tardive dyskinesia [5]. Second generation antipsychotics (olanzapine, risperidone, aripiprazole) were intended to overcome these motor side-effects but come with additional issues of obesity, diabetes, and dyslipidaemia, which increase one's risk of cardiovascular issues [6]. These adverse symptoms have a considerable impact on compliance with treatment. In the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, it was found that 74% of the patients on antipsychotics stopped using them within 18 months, and the main reason for this discontinuation was severe side-effects [7]. Poor compliance leads to greater disease chronicity, elevated relapse rates, and higher costs in health care, burdening the patients and families and the healthcare system [8].

Although there is worldwide acknowledgement of the necessity of proactive monitoring of side-effects, practice in clinical settings in India is quite different. While assessment tools are available on an international level, their use within Indian populations is sparse, hindering the creation of appropriate intervention frameworks [9,10]. So, the present study aimed to assess the prevalence, severity, and temporal progression of antipsychotic-induced side-effects in treatment-naive Indian patients using standardised scales.

The objectives were to: 1) Evaluate the pattern of extrapyramidal, metabolic, and sexual side-effects over three months; 2) compare side-effect burden across commonly used antipsychotic regimens; and 3) identify demographic and clinical predictors of side-effect severity.

MATERIALS AND METHODS

The present prospective observational study was carried out in the Psychiatry Department of Dhiraj Hospital, Vadodara, Gujarat, India, from October 2023 to March 2025. Prior ethical clearance was obtained from the Institutional Ethics Committee (SVIEC/ON/Medi/

BNPG22/Sep/20/54). All participants were included only after they gave written informed consent.

Inclusion criteria: Treatment-naive adults aged 18 to 70 years with newly diagnosed Schizophrenia spectrum and other primary psychotic disorders, who, in accordance with the International Classification of Diseases -11 (ICD-11) criteria [11], required antipsychotic medication were enrolled over a six-month recruitment window within the overall study period.

Exclusion criteria: Exclusion criteria included a history of use of antipsychotics, on or required other psychotropic medications, failure to consent, aged under 18 or over 70 years (to minimise developmental and geriatric factors), and current substance use disorders except nicotine, as it is mostly prevalent in these patients.

Sample size calculation: The sample size was calculated using the formula: $N=4pq/L^2$. For this study, the sample size was calculated assuming a 41.9% prevalence (p) of antipsychotic-induced side-effects, derived from pooled estimates of adverse-effect frequencies reported, and q is its complement (58.1%) [12]. The permissible error L was set at 10%. Hence, this resulted in a required sample size of 277 participants. Accounting for an expected 20% attrition (approximately 55 participants), 332 participants were required and were finally included in the analysis.

Study Procedure

All included patients underwent comprehensive baseline evaluations i.e., demographic data collection (including age, gender etc.,), medical history, psychiatric diagnosis, as well as laboratory tests for metabolic parameters such as weight, BMI, glucose, and lipids. Antipsychotic medications were prescribed according to the clinical diagnosis. The four assessment scales were administered at baseline, one month, and three months to measure the temporal changes in side-effects. These metabolic parameters were also assessed at the mentioned time points.

Assessment instruments and scoring criteria: The physical and psychological side-effects of antipsychotics were assessed using four established instruments in the study, and appropriate language support was provided as and when required.

The GASS is a self-report scale which consists of 22 items assessing sedation and neurologically mediated side-effects, such as extrapyramidal side-effects, in addition to weight gain and cardiovascular/metabolic changes. All the items are rated on a Likert scale, and total scores indicate the overall side-effect burden, where higher scores indicate greater severity. Scores are classified as low, moderate, or high side-effect burden on established cut-offs. This scale has been found reliable (Cronbach's α=0.81) and valid (Comparative Fit Index (CFI) =0.81-0.90, Root Mean Square Error of Approximation (RMSEA)=0.059-0.080) [13].

The PRSexDQ-SALSEX assesses sexual dysfunction due to psychotropics in the areas of libido, erectile or arousal quality, orgasmic function and general sexual satisfaction. The points add up to a score, and higher scores reflect greater severity of that sexual dysfunction (mild, moderate or severe). The reliability of the scale is reasonable (Cronbach's α=0.85) [14].

The MSAS is a clinician-rated scale rating Parkinsonian EPSs (rigidity, tremor, gait disturbance and sialorrhea), scored from normal to severe. The total score represents the severity of EPSs, with higher scores indicating greater motor impairment. The MSAS has strong inter-rater reliability (ICC=0.78-0.85) and validity, as indicated by the high Spearman correlations with clinician-rated EPSs (r=0.72-0.89) [15].

The AIMS is 12 items scale examining involuntary movements in facial, oral, extremity and trunk regions as well as global severity ratings. Items are scored from 0-4 for severity, and higher total scores reflect more severe involuntary movement. The AIMS is used to detect and monitor tardive dyskinesia, as well as other motor abnormalities. Reliability (0.9) and validity (80%) of the scale are high [16].

For all instruments, higher scores always indicate more severe antipsychotic-related adverse effects. In addition to being tested baseline, one month and three months, these scales were measured to explore the temporal progression of side-effect burden.

STATISTICAL ANALYSIS

The statistic data analysis was performed by means of IBM Statistical Package for Social Sciences (SPSS) (v. 25; IBM Corp., Armonk, NY). Demographic and clinical features were summarised by descriptive statistics. Repeated measurements ANOVA were utilised to evaluate changes in scores of the side-effect scales and metabolic parameters over time (baseline, one month, three months). Between-group comparisons of side-effect burden across different antipsychotic regimens and across demographic and treatment-related subgroups were performed using the Kruskal-Wallis test. Correlations between demographic variables, side-effect severity, and metabolic changes were assessed using Pearson's correlation coefficient. To determine independent predictors of the overall side-effect burden at three months, multivariate linear regression analysis was used with the GASS as the dependent variable. Although some variables showed skewed distributions, repeated measures ANOVA were applied due to the large sample size and its robustness to moderate deviations from normality. Median and interquartile range values were additionally reported to better represent skewed data. Statistical significance was set at a p-value <0.05.

RESULTS

The study comprised 332 treatment-naïve patients who started antipsychotic medications. The average age of participants was 34.7±10.2 years, with the majority aged 31-40. Most patients had schizophrenia, followed by brief psychotic disorder and delusional disorder. The average duration of illness was 4.1±2.6 years, with 139 (41.9%) of patients experiencing symptoms for more than two years. More than half of the patients received antipsychotic monotherapy, and the remainder received combination therapy [Table/Fig-1].

Characteristics	Category	n (%)
Age (years)	Mean±SD	34.7±10.2
	18-30 years	83 (25.0%)
	31-40 years	99 (29.8%)
	41-50 years	66 (19.9%)
	51-60 years	51 (15.4%)
	≥61 years	33 (9.9%)
Gender	Male	135 (40.7%)
	Female	197 (59.3%)
Primary diagnosis	Schizophrenia	113 (34.0%)
	Brief psychotic disorder	76 (22.9%)
	Delusional disorder	76 (22.9%)
	Other psychotic disorders	67 (20.2%)
Duration of illness (years)	Mean±SD	4.1±2.6
	≤2 years	193 (58.1%)
	>2 years	139 (41.9%)
Employment status	Skilled	133 (40.0%)
	Semi-skilled	99 (29.8%)
	Unemployed	100 (30.1%)
Antipsychotic regimen	Monotherapy	194 (58.5%)
	Two-drug combination	101 (30.4%)
	≥Three-drug combination	37 (11.2%)

[Table/Fig-1]: Baseline characteristics of the study population (N=332).

The most common side-effects were sexual dysfunction, followed by weight gain, sedation, and EPSs. At three months, 33 (9.9%) of subjects had involuntary movements detected on AIMS [Table/Fig-2].

Side-effects	n (%)
Sedation	166 (50.0%)
Extrapyramidal Symptoms (EPS)	149 (44.9%)
Weight gain	199 (60.0%)
Sexual dysfunction	219 (66.0%)
Involuntary movements (AIMS-based)	33 (9.9%)

[Table/Fig-2]: Overall prevalence of antipsychotic-induced side-effects at 3 months.

Side-effect burden, measured by GASS score, increased from 0.05±0.26 to 13.00±4.30 at three months (F=1306.2, p<0.001). Similar progressive worsening was observed for movement-related side-effects, with significant increases in AIMS and MSAS scores, as well as for sexual dysfunction measured using the PRSexDQ. Metabolic parameters also deteriorated over time. During the three-month follow-up, participants gained an average of 5.68 kg, and BMI increased from 24.0 to 25.8 kg/m^2. Approximately, 26.8% of patients experienced weight gain greater than 5 kg, with a maximum increase of 18 kg, indicating substantial inter-individual variability. Total cholesterol, triglycerides, and fasting glucose increased significantly at all test points [Table/Fig-3].

Clozapine and amisulpride had the highest mean scores on all scales, indicating a higher burden of neurological and metabolic side-effects. They also had the highest frequency of sedation, EPSs, weight gain and sexual dysfunction, and the shortest median time to onset of side-effects. Olanzapine had more metabolic side-effects than risperidone, but risperidone had more EPSs. There were significant differences between treatment groups with a p-value <0.001. Several variables, particularly baseline side-effect scores, demonstrated skewed distributions with a floor effect; therefore, median and interquartile range values were additionally reported [Table/Fig-4].

Median time to major side-effects (shown with Inter-quartile Range (IQR) in parentheses) refers to time to development of clinically significant adverse effects (GASS ≥13).

Weight gain and mean GASS and AIMS scores increased with age. Patients receiving polytherapy had significantly higher scores for side-effects and metabolic burden than patients receiving monotherapy [Table/Fig-5]. In a multivariate regression analysis, clozapine + amisulpride was the best independent predictor of a 3-month higher GASS score, followed by a higher duration of disease, age and baseline BMI. The intensity of side-effects was not predicted based on gender [Table/Fig-6].

Side-effect burden and movement-related adverse effects, weight gain and serum cholesterol rises, and clinical and metabolic side-effects showed weak to moderate positive correlation [Table/Fig-7].

DISCUSSION

The present research sheds much attention on the effects of antipsychotic medications in treatment-naive Indian patients, emphasising the antipsychotics' "prevalent, progressive, and severe" side- effects. Sedation (50%), EPSs (45%), along with weight gain (60%) are some of the most common side-effects of antipsychotic medications, which aligns with findings from the CATIE trial by Lieberman JA et al., where approximately 74% of patients discontinued treatment within 18 months, primarily due to inefficacy or intolerable side-effects [7]. The considerable increase in scores on all assessment scales over the three-month period illustrates the need for routine systematic monitoring of side-effects in clinical practice.

From baseline to three months, the GASS, AIMS, MSAS, and PRSexDQ scores gradually increased, indicating that side-effects typically appear early and worsen quickly. Early side-effects predict poor adherence, relapse, and long-term morbidity, making this temporal pattern clinically significant [7,17]. These results confirm

Parameters	Baseline Mean±SD, median, IQR	1 month Mean±SD, median, IQR	3 months Mean±SD, median IQR	F-statistic	p-value
GASS score	0.05±0.26 {0 (0-0)	8.00±3.74 {8.07 (5.36-10.55)}	13.00±4.30 {13.00 (10.17-15.68)}	1306.2	<0.001
AIMS score	0.03±0.17 {0 (0-0)	1.34±1.14 {1.25 (0.27-2.13)}	2.80±1.54 {2.72 (1.65-3.87)}	516.2	<0.001
MSAS score	0.11±0.13 {0.05 (0-0.18)	2.50±0.71 {2.48 (1.99-2.99)}	4.30±1.26 {4.24 (3.39-5.06)}	2075.4	<0.001
PRSexDQ score	0.05±0.21 {0 (0-0)}	3.20±2.09 {3.14 (1.57-4.71)}	4.81±2.37 {4.51 (3.00-6.65)}	584.6	<0.001
Weight (kg)	60.50±11.09 {59.26 (52.88-67.85)}	63.40±11.29 {63.16 (55.82-70.70)}	66.18±11.95 {65.72 (56.79-74.42)}	20.4	<0.001
BMI (kg/m^2)	24.00±3.96 {24.02 (21.50-26.38)}	24.96±4.08 {24.95 (22.63-27.72)}	25.80±4.18 {25.73 (23.37-28.44)}	16.2	<0.001
Total cholesterol (mg/dL)	150.20±30.70 {149.76 (128.20-169.62)}	163.01±31.83 {162.81 (142.79-183.97)}	173.51±34.93 {172.72 (147.45-193.96)}	42.7	<0.001
Triglycerides (mg/dL)	128.70±35.41 {126.88 (106.50-153.08)}	143.58±37.30 {144.13 (118.86-168.90)}	158.81±39.32 {157.88 (132.94-186.88)}	53.9	<0.001
Fasting glucose (mg/dL)	88.50±13.08 {89.00 (79.97-97.64)}	92.81±13.46 {93.08 (83.68-101.08)}	97.66±14.77 {97.64 (87.88-107.24)}	36.7	<0.001

[Table/Fig-3]: Temporal progression of side-effect scores and metabolic parameters.
Values are expressed as mean±standard deviation and median {Interquartile Range (IQR)}, ANOVA test, p-value <0.05: statistically significant; GASS: Glasgow antipsychotic side-effect scale; AIMS: Abnormal involuntary movement scale; MSAS: Modified simpson–angus scale; PRSexDQ: Psychotropic-related sexual dysfunction questionnaire; BMI: Body mass index

Drug regimen	GASS	AIMS	MSAS	PRSexDQ	Sedation n (%)	EPS n (%)	Weight gain n (%)	Sexual dysfunction n (%)	median time to SE (IQR) (weeks)
Olanzapine (n=99)	15.2±6.4	1.8±2.1	3.2±3.5	4.1±3.2	56 (57%)	33 (33%)	72 (73%)	43 (43%)	10 (8-12)
Risperidone (n=73)	12.8±5.9	2.1±2.8	5.6±4.2	6.2±4.1	37 (50%)	43 (59%)	43 (59%)	47 (64%)	8 (6-10)
Olanzapine + trifluoperazine (n=60)	14.6±7.1	3.4±3.6	4.8±3.9	5.1±3.8	40 (67%)	37 (61%)	50 (83%)	34 (56%)	8 (6-10)
Clozapine + amisulpride (n=37)	20.2±8.3	7.9±5.2	6.4±4.7	7.3±4.9	30 (82%)	30 (82%)	34 (91%)	30 (82%)	4 (2-6)
Other combinations (n=63)	11.9±5.7	2.3±2.9	3.7±3.2	4.6±3.5	26 (42%)	23 (37%)	37 (58%)	26 (42%)	10 (8-12)
F-statistic (ANOVA) # or χ^2 values*	18.3	16.5	11.9	10.6	18.59	35.47	22.25	22.83	-
p-value	<0.001	<0.001	<0.01	<0.01	<0.01*	<0.001*	<0.001*	<0.001*	-

[Table/Fig-4]: Drug-specific burden of adverse effects after 3 months of treatment.
One-way ANOVA for continuous variables; Categorical outcomes (Sedation %, EPS %, Weight gain %, Sexual dysfunction %) calculated using Chi-square test; p-value <0.05 -significant

Subgroups		GASS (Mean±SD)	F (df) p	AIMS (Mean±SD)	F (df) p	Weight gain (kg) at 3 months (Mean±SD)	F (df) p	Sedation n (%)	χ^2 (p)	EPS n (%)	χ^2 (p)	Sexual dys. n (%)	χ^2 (p)
Age group (in years)	18-30	10.2±4.1	25 (3) p=<0.001	1.1±1.6	9.2 (3) p= <0.001	3.14±3.1	4.22 (3) p=0.006	35 (42%)	6.64 (p=0.084)	30 (36%)	4.79 (p=0.188)	45 (54%)	8.89 (p=0.031)
	31-40	13.4±4.8		2.1±2.3		4.27±2.66		52 (53%)		46 (46%)		68 (69%)	
	41-50	14.1±5.2		2.4±2.6		4.10±3.62		36 (55%)		32 (48%)		46 (70%)	
	≥51	15.6±5.9		2.9±3.1		2.25±2.15		52 (62%)		44 (52%)		63 (75%)	
Gender	Male	12.1±4.9	2.1 (1) p=0.149	1.8±2.1	1.40 (1) p=0.232	3.47±3.01	0.56 (1) p=0.456	62 (46%)	1.69 (p=0.194)	56 (41%)	1.02 (p=0.313)	82 (61%)	2.70 (p=0.100)
	Female	13.8±5.2		2.2±2.4		3.74±3.31		106 (54%)		94 (48%)		138 (70%)	
Treatment type	Monotherapy	11.2±4.3	84.3 (1) p= <0.001	1.5±1.9	34.6 (1) (p= <0.001)	3.44±2.94	0.45 (1) p=0.505	85 (44%)	7.96 (p=0.005)	76 (39%)	6.89 (p=0.009)	110 (57%)	19.36 (p=<0.001)
	Polypharmacy	15.6±5.8		2.8±3.0		3.70±3.29		83 (60%)		75 (54%)		111 (80%)	

[Table/Fig-5]: Subgroup differences and predictors of side-effect burden at 3 months.
Univariate analysis; p-value <0.05- statistically significant

Predictors	B (SE)	95% CI	p-value
Clozapine+amisulpride	+5.6 (1.1)	3.4-7.8	<0.001
Age (per year)	+0.04 (0.02)	0.01-0.07	0.02
Duration of illness (years)	+0.3 (0.1)	0.1-0.5	0.01
Baseline BMI	+0.2 (0.1)	0.0-0.4	0.05
Female gender	+1.0 (0.7)	-0.4-2.4	0.15

[Table/Fig-6]: Multivariate regression predicting GASS score at 3 months.
Multivariate linear regression analysis was performed; B= Unstandardised regression coefficient; SE: Standard error; CI: Confidence interval; A p value <0.05- statistically significant

Variables	GASS	AIMS	MSAS	PRSexDQ	ΔWeight	ΔCholesterol
GASS	1	0.52***	0.45***	0.38***	0.39***	0.35***
AIMS	0.52***	1	0.49***	0.28**	0.32**	0.30**
MSAS	0.45***	0.49***	1	0.22*	0.27**	0.25*
PRSexDQ	0.38***	0.28**	0.22*	1	0.21*	0.18
ΔWeight	0.39***	0.32**	0.27**	0.21*	1	0.67***
ΔCholesterol	0.35***	0.30**	0.25*	0.18	0.67***	1

[Table/Fig-7]: Correlation between side-effect scales and metabolic changes over 3 months.
Values represent Pearson's correlation coefficients (r); A p-value <0.05 was considered statistically significant. * p<0.05; ** p <0.01; *** p <0.001

that early detection and intervention are more important than postponed corrective measures.

The burden of side-effects for the combination of clozapine and amisulpride was most negative in all study domains (neurological, metabolic and sexual) compared to all other investigated treatments. Patients who received the combination of medications had significantly higher sum scores in all side-effect scales, more often experienced side-effects and shorter median time to first appearance of major side-effects. Although antipsychotic polypharmacy may be justified in certain cases with treatment resistance, these results are consistent with current data that advise against routine add-on and combination of antipsychotics for additive or synergistic side-effects [18-20]. These findings highlight the need for rational pleiotropic justification, careful dosage, and increased timely monitoring when combination therapy is used.

The metabolic profile in the current study is worrisome, especially because of the relatively young mean age of the study population. Also, the overall mean weight gain observed in the cohort (5.68 kg) exceeded the mean increase reported in any subgroup, where the maximum was 4.3 kg. Notably, approximately 26.8% of patients experienced weight gain greater than 5 kg, with the highest individual increase reaching 18 kg. These findings highlight substantial inter-individual variability, underscoring the importance of considering both group-level trends and individual patient responses when interpreting treatment-related weight changes.

Also increases in BMI, cholesterol, triglycerides and fasting glucose levels within three months illustrate the rapid emergence of cardiometabolic risk with antipsychotic therapy. A quick increase in mean BMI from normal to the overweight category by age indicates timely lifestyle intervention and metabolic profiling. These results are in line with previous evidence on the metabolic risk of second-generation antipsychotics, particularly olanzapine. Meta-analytic evidence by Rognoni C et al., demonstrated significant increases in weight, lipid levels, and glucose parameters associated with second-generation antipsychotics [21]. Similarly, De Hert M et al., reported early onset of metabolic abnormalities, including dyslipidaemia and insulin resistance, often emerging within the first few months of treatment. These findings strongly support existing guidelines recommending regular monitoring of metabolic indices from the initiation of therapy [22].

Drug-specific side-effects identified in this study are consistent with known pharmacological profiles of these medications. Olanzapine induced more metabolic side-effects, while risperidone was more frequently associated with EPSs in accordance with its D2 receptor affinity [23]. The relatively unfavourable risk profile of clozapine-amisulpride combination therapy requires increased caution where a combination continues to be used and reiteration of advice for monotherapy whenever practicable [19].

Subgroup analyses demonstrated that older age and longer duration of illness predicted greater side-effect burden. The older population had higher GASS and AIMS scores and more weight gain, a reflection of increased age-related pharmacokinetic and pharmacodynamic sensitivity [24]. In addition, patients with longer illness duration might comprise a subpopulation in which the biological susceptibility of previous treatments to side-effects had accumulated. Polypharmacy was a concentration-related factor with substantial contribution to increased side-effects severity, indicating the need for avoiding unnecessary drug combinations [20].

Correlation analyses in the present study demonstrated weak-to-moderate positive associations between overall side-effect burden, movement-related adverse effects, and metabolic changes, indicating that these adverse effects tend to co-occur rather than occur in isolation. This finding is consistent with previous literature suggesting that antipsychotic-induced adverse effects often cluster due to shared underlying mechanisms, including dopaminergic blockade, neuroendocrine alterations, and metabolic dysregulation [17,21,22]. Such co-occurrence highlights that neurological and metabolic sequelae are interrelated components of a broader adverse-effect profile rather than distinct entities. These observations underscore the importance of adopting holistic and multidimensional assessment strategies, incorporating both clinical and metabolic monitoring tools, to ensure comprehensive evaluation and early identification of cumulative side-effect burden in patients receiving antipsychotic therapy.

Limitation(s)

In a single-centre study design, there may be limitations to the generalisability, and a follow-up period of three months was perhaps sufficient to detect early side-effects, but not necessarily late side-

effects such as true tardive dyskinesia, as the involuntary movements observed likely represent early or acute phenomena. Further, long-term side-effect curves need to be better defined, and preventive strategies tested in future multicentre studies with longer follow-up. The sample size was calculated using an expected prevalence of antipsychotic-induced side-effects, derived from pooled estimates reported in previous Indian studies. We acknowledge that side-effect prevalence varies across drug classes and study designs, but this pooled estimate was chosen to provide a conservative basis for sample size determination.

CONCLUSION(S)

The present study shows that the burden of side-effects is high and accumulates rapidly among Indian patients receiving antipsychotics in the context of early phase treatment. Regular assessment using validated tools can lead to early identification and intervention, enhancing tolerability, compliance with treatment, and overall clinical outcomes.

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