



# Adverse drug reactions monitoring of psychotropic drugs: a tertiary care centre study

## Abstract

**Background:** Many new psychotropic drugs/agents have been developed and found to be effective in the treatment of psychiatric disorders. However, these drugs also exhibit adverse drug reactions (ADRs) which may affect compliance in psychiatric patients. Hence the present study was aimed at monitoring and assessing ADRs caused by psychotropic drugs. **Methods:** A hospital based prospective observational study was carried out in the psychiatry outpatient department of a tertiary care teaching hospital for the duration of six months. Two hundred and two patients were included in the study and ADRs were documented using a predesigned data collection form. The causality assessment was carried out as per the criteria of both the World Health Organization- Uppsala Monitoring Centre (WHO-UMC) and Naranjo scale. Severity and predictability assessment of ADRs were also performed. **Results:** A total of 106 ADRs were observed during the study period with majority of them occurring in 25-35 years of age group (40.56%). Weight gain (18.86%) followed by sedation (16.03%) and insomnia (11.32%) were found to be the commonest ADRs. Risperidone (19.8%) and escitalopram (12.3%) were the drugs responsible for majority of the ADRs. Causality assessment showed that most of ADRs were possible and probable. 94.33% of ADRs were found to be mild and 89% of them were predictable. **Conclusion:** A wide range of ADRs affecting central nervous and metabolic systems were reported with psychotropic drugs. The study findings necessitate the need for an active pharmacovigilance programme for the safe and effective use of psychotropics.

**Keywords:** Psychiatric Disorders. Compliance. Causality. Risperidone. Pharmacovigilance.

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## Introduction

An adverse drug reaction (ADR) is defined by the World Health Organization (WHO) as "any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function".[1] ADRs are the most common drug related adverse event that occur across the world.[2] Patients with psychiatric illness needs lifelong therapy with psychotropic drugs which predisposes them to an array of ADRs.[3] The common adverse effects associated with psychotropic drugs are weight gain, somnolence, tremors, and tardive dyskinesia. These adverse effects tend to deteriorate the mental and physical well-being of the patient and thus lead to patient non-adherence to therapy.[4]

Studies show that the psychotropic drugs most commonly associated with ADRs are antipsychotics and mood stabilisers. Among antipsychotics, conventional antipsychotics (haloperidol) have a higher incidence of ADRs compared to atypical or second generation antipsychotics (olanzapine and risperidone).[5] On the other hand, cardio-metabolic side

effects with atypical antipsychotics pertain to be a matter of conflict even though they have a lower risk for developing extrapyramidal side effects (EPS).[6] The epidemiological statistics of ADR is justified by its high prevalence rate, which varies from three to six per cent of hospital admissions in adults and 24% in the elderly population. They rank fifth among the causes for mortality and attributes for five to ten per cent of hospital costs.[7]

The role of pharmacovigilance in recognising, reporting, and preventing ADRs in a psychiatry unit holds paramount importance as it can protect the patients from preventable harm and apprise the physicians regarding the feasibility of those events in the near future.[8] The pharmacovigilance activities in India requires to be strengthened due to the scarcity of data available related to ADRs especially with psychotropic drugs.[9] Pharmacovigilance in psychiatry can promote detection of ADRs and alert physicians regarding the probability of such events to promote patient safety.[10] The clinical pharmacist plays a vital role in identification, monitoring management and causality assessment of ADRs in patients with psychiatric illness.[11] In India,

pharmacovigilance has a great potential towards safeguarding the patients. There is an immense need to strengthen these activities and develop ADRs profile of psychotropic drugs.[12] However, in India only few studies have looked into ADRs among psychiatric patients.[6,13-17] In this regard this particular study was carried out for a period of six months, at the psychiatric outpatient department (OPD) of a tertiary care teaching hospital to identify and analyse the extent of occurrence of ADRs, its causality, severity, and predictability.

### Aims and objectives

To study ADRs associated with psychotropic drugs.

### Materials and methods

A hospital based prospective observational study was carried out in the psychiatry OPD of MS Ramaiah Medical Teaching Hospital (MSRMTH), Bangalore from January to June 2015. The complete project was done in accordance with the permission granted by MS Ramaiah Ethical Committee.

### Inclusion criteria

- Patients of either gender attending psychiatric OPD.
- Patients treated with one or more psychopharmacological agents in psychiatric OPD.

### Exclusion criteria

- Patients treated on inpatient basis.
- Patients treated with no psychopharmacological agent.
- Patients unable to understand tools and refuse to participate in the study.

### Procedure

Patients diagnosed with psychiatric disorder of either of sex, regardless of co-morbidities were enrolled as per inclusion and exclusion criteria mentioned above. Patients' case notes, medication charts, laboratory reports, outpatient records, and other relevant documents of patients visiting psychiatric OPD were reviewed for ADRs and information was recorded in a suitably designed data collection form. Informed written consent was obtained from the patients. The case sheets were screened for ADRs, and those observed by the consultant and reported by the patients were also noted.

### Tools for assessment

Semi-structured proforma was used to record information including patient demographics, vitals, systemic examination details, chief complaints and history of presenting illness, past medical and medication history, diagnosis, baseline laboratory investigations, and details of current medications including the brand name, generic name, category, dose, frequency, route of administration, and duration of treatment along with a brief description of ADR and its management.

The data regarding suspected ADR was recorded as per the Central Drugs Standard Control Organization (CDSCO) format which consisted of all the available details of suspected

medication(s), concomitant drugs, seriousness and outcome of the reaction.[18] The causality relationship between suspected drug and reaction was established using the Naranjo's Causality Assessment Scale,[19] and classified into definite, probable, and possible. The extent of relationship between the suspected ADR and the drug therapy were assessed using the WHO Probability Assessment Scale,[20] and further classified into certain, probable, and possible. Severity of ADRs was assessed by the Hartwig's Severity Assessment Scale.[21] The severity was broadly categorised into mild, moderate, and severe for each ADR. ADR was categorised as predictable and not predictable based on patient tolerability and incidence rate. Obtained ADRs were classified according to the WHO-System Organ Class (WHO-SOC).[22]

### Statistical analysis

Microsoft word and excel was used to generate pie charts, bar diagrams and for data analysis.

### Results

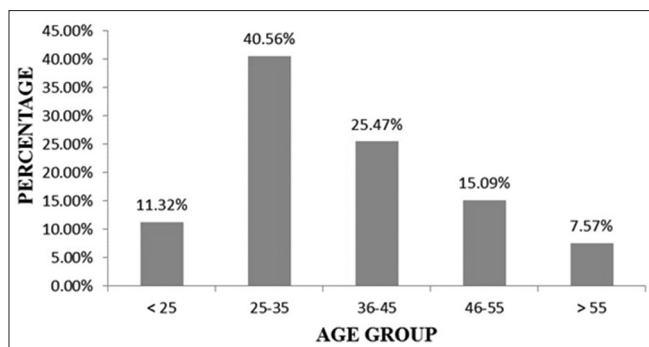
A total of 106 patients were suspected of having at least one ADR out of the 202 participants. Of 106 patients 47 (44.33%) were males and 59 (55.66%) were females. Majority of ADRs were observed in 25-35 years of age group (40.56%) (Figure 1) with most commonly reported ADR of weight gain (18.86%) followed by sedation (16.03%) and insomnia (11.32%) (Table 1).

Antipsychotics (43.39%), antidepressants (24%) followed by benzodiazepines (10%) were the commonest class of drugs responsible for ADRs (Figure 2). Risperidone (19.8%) and olanzapine (9.4%) were the major antipsychotics causing ADRs. Among antidepressants, escitalopram (12.3%) was the major drug responsible for ADRs as it was the commonest antidepressant that was being prescribed.

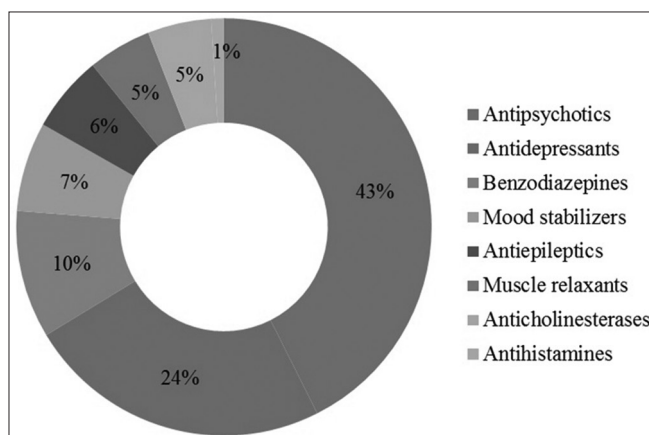
Classification of ADRs based on WHO-SOC criteria revealed the higher incidence of ADRs affecting nervous system which accounted for 49.05% of total ADRs (Figure 3). In our study probable ADRs were more and most of the ADRs

**Table 1:** The different types of adverse drug reactions (ADRs) that occurred during the study period

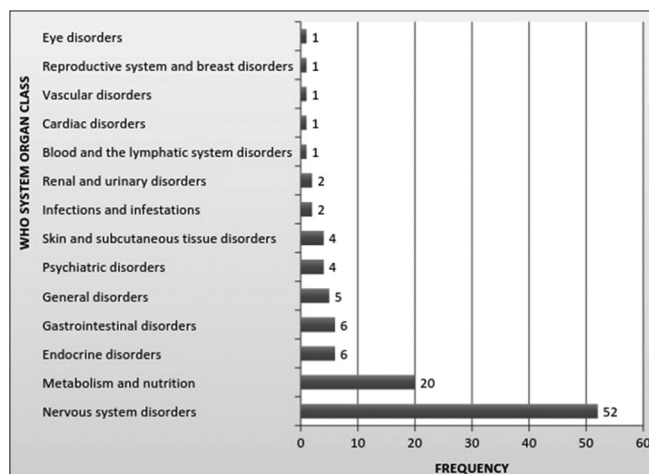
Type of ADR	N (%)
Weight gain	20 (18.86)
Sedation	17 (16.03)
Insomnia	12 (11.32)
Akathisia	6 (5.66)
Tremor	5 (4.71)
Fatiguability	4 (3.77)
Anorexia	3 (2.83)
Hyperprolactinaemia	2 (1.88)
Nausea	2 (1.88)
Rash	2 (1.88)
Others	33 (31.13)
Total	106 (100)



**Figure 1:** The age group distribution of patients with adverse drug reactions (ADRs).



**Figure 2:** The drug classes causing adverse drug reactions (ADRs) with their corresponding percentages.



**Figure 3:** The World Health Organization-System Organ Class (WHO-SOC) of adverse drug reactions (ADRs) with their frequencies.

were mild to moderate in severity. Predictability assessment revealed that 89% of the ADRs were predictable.

## Discussion

ADRs remain a major cause of morbidity, hospital admission, and even death; so, it is essential to recognise

ADRs and to establish a causal relationship between the drug and the adverse event. Monitoring and evaluation of ADRs associated with psychotropic drugs is essential as these medications differ from others as they often affect emotion and cognition.[23] A wide array of psychotropic drugs are available for the treatment of various psychiatric disorders.[24] And the concurrent use of these multiple psychoactive medications in a single patient has now emerged into a common practice in clinical psychiatry which further potentiates the chances of developing ADRs.[25]

In our study females were found to be more affected by ADRs and this is in contrast to the male preponderance observed among patients visiting psychiatry OPD. Similarly, a higher incidence of 54.85% ADRs was identified among female psychiatric patients in a study conducted on identification and management of antipsychotics' ADR by Lucca *et al.*[26] These findings are supported by a study conducted by Lahon *et al.*,[13] even though many of the studies on ADR monitoring in psychiatry are contradictory to this observation. Apart from the common ADRs, EPS like akathisia and tardive dyskinesia were observed more in females which might be related to the hormonal influence in females (higher levels of oestrogen).

Even though majority of ADRs were observed in 25-35 years of age group, our study findings showed that all the elderly patients (>55 years) included in our study experienced at least one ADR. The increased prevalence of ADRs among elderly patients could be substantiated by the predominance of somatic diseases and polypharmacy in elderly compared to younger patients.[27] Particularly, elderly people are more sensitive to the effects of psychiatric medications and are susceptible to ADRs including cardiac toxicity, confusion, and unwanted sedation.[28]

Consistent with previous Indian studies, among all the ADRs reported, maximum number of ADRs was seen in patients who were on antipsychotic drugs.[3,12,15,16] Increased incidence of ADRs such as weight gain, sedation, and insomnia in our study can be substantiated by the increased prescribing of antipsychotics and antidepressants. As reported in previous studies, in our study also olanzapine and risperidone were the common antipsychotics involved in antipsychotics associated ADRs.[6,15,16] Weight gain is more obvious with long term therapy especially with antipsychotics. A variety of complex mechanisms accounts for the weight gain associated with antipsychotics, which includes the interaction between various neurotransmitters like serotonin and dopamine, genetic mechanisms, and activation and interaction between orexigenic and anorexigenic peptides. Most of the psychotropic drugs cause somnolence by either enhancing the effect of gamma-Aminobutyric acid (GABA) at GABA<sub>A</sub> receptor (e.g. benzodiazepines) or by increasing the level of serotonin in the synaptic cleft (e.g. antidepressants).

The highest numbers of ADRs were observed in patients diagnosed with schizophrenia and other psychotic disorders (25.47%) which are consistent with the study conducted by Prajapati *et al.*,[14] carried out in psychiatric OPD of a tertiary care hospital to monitor ADRs. It appears that psychotic



patients are at higher risk for developing ADRs. It might be due to their sedentary life style and involvement of other organ systems during the process of disease progression. However, there is need for prospective studies to test this hypothesis.

Similar to previous observation, among antidepressants, escitalopram (12.3%) was the major drug responsible for ADRs as it was the commonest antidepressant that was being prescribed.[15] Almost half of the observed ADRs were found to affect nervous system according to WHO-SOC, as all the psychotropic drugs are meant to act on the same. This pertains to be a pitfall associated with psychoactive medications as it further causes trouble in psychiatric patients which leads to noncompliance. The data on frequency, severity, probability, and preventability of ADRs emerged out of our study can be used in a healthcare system to identify medications that should be targeted for quality improvement projects and patient education. As most of the ADRs in our study were predictable and thus preventable, it can be concluded that target in high-risk medications that are identified through detailed analysis will have a significant impact on reducing preventable ADRs.

## Conclusions

Our study builds up the ADR figures of psychotropic drugs likely to be encountered in outpatients of a tertiary care teaching hospital in South India. The study results strongly suggests the need for healthcare team to focus on assessing and reporting suspected ADRs for enhancing the quality of monitoring and managing ADRs. The strengthening of existing Governmental Pharmacovigilance Programme of India (PvPI) is essential in order to augment the patient care by collecting and disseminating information to healthcare professionals regarding the occurrence of adverse reactions, to take precautions to prevent as well as to treat them. Perpetual vigil in detecting ADRs along with subsequent dose adjustments should be performed for the safe and effective use of psychotropic drugs which in turn can improve the patients' compliance.

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