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*Original Research Article*

# ADR Monitoring in Psychiatric Out Patient Department of a Tertiary Care Hospital

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## ABSTRACT

**Aim:** To study the incidence of ADRs' in psychiatry OPD.
**Material and Methods:** During the study period of 12 months, 167 patients with ADRs to psychopharmacological agents (PPAs) were detected by spontaneous and intensive reporting system from the health care professionals which was accomplished either by filling the notification slip and communicating personally.
**Observations:** Patients experienced maximum ADRs in Age group of (21 to 35 years) that is 62 (37.12%) followed by 40 (23.95%) in age group of 36 to 50 years. Majority of patients who developed ADRs were male 107 (64.07%). central nervous system is most commonly affected system was involved in 93 (47.20%) patients followed by gastrointestinal system in 27 (13.70%) patients. By Naranjo's scale, Majority of the ADRs 171 (86.80%) were scored probable, 26 (13.19), were scored possible 26 (13.19%).
**Conclusion:** Maximum number of ADRs observed with Olanzapine 28(14.21%) followed by Risperidone 23(11.67%), Trifluoperazine 20(10.15%), Haloperidol 18(9.13%), Clozapine 17(8.62%).

***Keywords:*** ADR monitoring, Psychiatry, OPD.

## INTRODUCTION

Mental and behavioural disorders account for 12% of the global burden of disease. It is estimated that nearly 450 million people from a mental or behavioural disorder in the World. Nearly 10% of total population suffers from these disorders. In 1990, it was estimated that 10% of Disability Adjusted Life Years (DALYs) across all age group were due to depressive disorder, suicide and alcohol related problems. A selective examination in 15-44 years and gender specific terms indicate that depressive disorders, alcohol abuse suicide ,Schizophrenia, bipolar disorders and panic disorders rank high among causes .Depression ranks third among men and second among women. It is estimated that India alone has about 100 million people in need of mental health services. [1]

Patients with psychiatric disorders are often managed with pharmacotherapy. Because of the chronic and relapsing nature of some of these disorders, most practice guidelines recommend that medications should be continued for several months or years. [2-4] As a result, patients are at risk of experiencing a variety of adverse drug reactions (ADRs).

At times, these ADRs can be life-threatening (such as neuroleptic malignant syndrome) [5] or disabling (such as drug-induced Tardive dyskinesia). [6] It is important for psychiatrists to be aware of the processes involved in identifying and reporting ADRs, especially those that are

new or unrecognized. These processes form the basis for the medical discipline of pharmacovigilance. Pharmacovigilance has been defined by the World Health Organization (WHO) as the science and activities related to the detection, assessment, understanding, and prevention of adverse drug effects. [7] As such, pharmacovigilance is not a "specialist" activity: It is one that must be carried out by all those involved in caring for patients on medication, including doctors, nurses, and pharmacists. [8,9]

The birth of pharmacovigilance has a close relationship to psychiatry. [10] This relationship has continued to the present day. In a recent review of nine major ADRs reported in Europe from 1995 to 2008, two of them involved psychotropic - seizures with bupropion, and suicidality in children taking SSRI antidepressants [11] while the latter was identified by a re-analysis of data from the pharmaceutical industry, the former was identified through physician reports. In an analysis of ADRs reported to the FDA between 1998 and 2005, many of the frequently implicated drugs were psychotropics**.** [12] - antipsychotics (clozapine, olanzapine, risperidone), antidepressants (duloxetine, sertraline, paroxetine, bupropion), mood stabilizers (carbamazepine, valproate, lamotrigine), and even anti-ADHD medication (atomoxetine). Now, as then, clinicians have a key role in identifying and reporting new or serious adverse drug effects.

Most of the psychiatric illnesses need long term or even life- long therapy, making the patients more prone for the development of significant ADRs and decrease patient compliance. Off-label use, combination therapies and newer indications for older drugs have lead to change in the ADR profiles of many well known psychotropic drugs. [13,14]

Growing public concern over drug safety has stressed the importance of pharmacovigilance, especially in India where ADRs contribute to significant economic burden. Although spontaneous reporting system is the core of data generation in pharmacovigilance, active drug surveillance increases the detection of ADRs and adds to its benefits. Active monitoring done by the physician following prescription of drugs is also an important way to improve rational drug prescribing. [15] Hence this study has been taken up to supplement the institutional pharmacovigilance programme and improve our knowledge on the pattern of ADRs in psychiatric patients in our hospital.

**Aim of study**: To study the incidence of adverse drug reactions (ADRs) in outpatient Department of Psychiatry.

## MATERIALS AND METHODS

A study for detection, classification, assessment and causality analysis of adverse drug reaction (ADRs) to psychopharmacological agents was conducted in Out Patient Department (OPD) of Psychiatry, tertiary medical hospital over a period of twelve months from 01.01.2014 to 31.12.2014. The study was approved by the institutional ethics committee. Patients meeting the inclusion criteria were included in the study.

**Inclusion Criteria**

1. Patient attending Psychiatric outpatient department & receiving psychotropic agents.
2. Patients who consent for participation from legally acceptable representative (LAR) and assent where person is incapable to give consent.
3. Patients >12 Years Old

**Exclusion Criteria**

1. Patients below 12 years of age.
2. Patients not receiving any psychopharmacological agents
3. Patients where process of consent was not possible (Brought from jail or court)

**Study details**

National Pharmacovigilance Programme (NPVP) has been constantly performing activities related to detection, assessment, understanding and preventions of adverse effects or any other medicine related problems.

A study for detection, classification, assessment and causality analysis of ADRs to any psychopharmacological agent was conducted in the Out Patient Department of psychiatry. The study was based on intensive monitoring and spontaneous or voluntary reporting system, which is the predominant method of NPVP. The reporter included the treating psychiatrist.

The spontaneous reporting system in Pharmacovigilance is a process of collecting, assessing, presenting and interpreting suspected ADRs. Case reports acquired from spontaneous reports are assessed by first evaluating cases individually and secondly interpreting the aggregated data.

In the intensive event recording certain hospital based ADR reporting schemes designate a group of individuals to screen a defined population specifically to detect ADRs and relate them to specific drugs.

A longitudinal observational study conducted in OPD of tertiary care hospital. Patient data about ADRs were collected and recorded in the CDSCO Adverse Drug Reaction reporting form (as in Proforma No I). Every attempt was made to personally interview and examines the patients presenting with ADRs. Patients satisfying the inclusion criteria were individually recognized and information about their details, adverse reaction, suspected drug and the concomitantly administered drugs were recorded in the ADR form (as in Proforma No I) . Of the total 197 ADRs reported during the period of 12 months, all patients were personally examined and interviewed.

The above information about ADRs to Psychopharmacological agents thus obtained were then compiled and analyzed to establish a causal link between the suspected drug and the adverse event. The causality assessment was done with the opinion of the reporting psychiatrist, Post graduate guide and with the help of standard textbooks and journals. WHO assessment scale was used for the causality analysis and subsequently, the ADRs were classified as certain, probable, possible, unlikely and unclassified.

## OBSERVATION AND RESULTS

**Table 1: Different organ system affected by ADRs**

| System affected | Number of ADRs (n=197) | Percentage of ADRs |
|---|---|---|
| Central nervous | 93 | 47.20% |
| Gastrointestinal | 27 | 13.70% |
| Others | 20 | 10.15% |
| Musculoskeletal | 16 | 8.12% |
| Anticholinergic | 15 | 7.61 % |
| Metabolic changes | 13 | 6.59 % |
| Cardiovascular | 10 | 5.07% |
| Dermatology | 03 | 1.52% |

It shows different organ system affected by ADRs, central nervous system is most commonly affected system was involved in 93(47.20%) patients followed by Gastrointestinal system in 27(13.70%)

**Table 2: Reported adverse drug reactions**

| Sr. no | Adverse drug Reactions | Number of ADRs(n=197) | Percentage of ADRs |
|---|---|---|---|
| 1 | Tremors | 31 | 15.73% |
| 2 | Sedation | 19 | 9.64% |
| 3 | Weight gain | 13 | 6.59% |
| 4 | Fatigue | 10 | 5.07% |
| 5 | Tachycardia | 10 | 5.07% |
| 6 | Extrapyramidal reactions | 9 | 4.56% |
| 7 | Sweating | 7 | 3.55% |
| 8 | Constipation | 7 | 3.55% |
| 9 | Muscle pain | 6 | 3.04% |
| 10 | Anxiety | 6 | 3.04% |
| 11 | Vomiting | 6 | 3.04% |
| 12 | Dizziness | 5 | 2.53% |
| 13 | Abdominal pain | 5 | 2.53% |
| 14 | Dry mouth | 5 | 2.53% |
| 15 | Gl ulcer | 5 | 2.53% |
| 16 | Insomnia | 4 | 2.03% |
| 17 | Sexual dysfunction | 4 | 2.03% |
| 18 | Agitation | 4 | 2.03% |
| 19 | Decreased co-ordination | 4 | 2.03% |
| 20 | Weakness | 4 | 2.03% |
| 21 | Diarrhea | 4 | 2.03% |
| 22 | Slurred speech | 4 | 2.03% |
| 23 | Mental confusion | 4 | 2.03% |
| 24 | Loss of appetite | 3 | 1.52% |
| 25 | Ataxia | 3 | 1.52% |
| 26 | Urinary retention | 3 | 1.52% |
| 27 | Skin rash | 3 | 1.52% |
| 28 | Apnea | 3 | 1.52% |
| 29 | Blurring of vision | 2 | 1.01% |
| 30 | Hiccups | 2 | 1.01% |
| 31 | Crawling sensationon scalp | 1 | 0.50% |
| 32 | Flatulence | 1 | 0.50% |

There were maximum number of ADRs reported of tremors 31(15.73%), sedation 19 (9.64%), Weight gain 13(6.59%) and Extra pyramidal reactions 9(4.56%)

**Table 3: ADR Distribution according to the Naranjo's Algorithm Probability scale**

| Naranjo's scale | Number of ADRs (n=197) | Percentage |
|---|---|---|
| Probable | 171 | 86.80 % |
| Possible | 26 | 13.19 % |
| Unlikely | 00 | 00 % |
| Definite | 00 | 00 % |

When analysed ADRs by Naranjo's scale, Majority of the ADRs 171(86.80%) were scored probable and 26(13.19), were scored possible 26(13.19%). There were no definite cases because rechallenge was not performed.

**Table 4: Severity of ADRs According to Modified Hartwig and Siegel Scale**

| Severity of ADRs | Number of ADRs(n=197) | Percentage ofADRs |
|---|---|---|
| Mild | 148 | 75.12% |
| Moderate | 48 | 24.36 % |
| Severe | 1 | 0.50 % |

Severity of ADRS were analyzed with modified Hartwig scale, 148(75.12%) were mild, 48(24.36%) were moderate, 1(0.50%) was severe. Moderate reaction was commonly observed with female, mild & severe ADRs were more common in male.

**Table 5: List of suspected drugs causing ADRs**

| Suspected drugs | Number of ADRs(197) | Percentage of ADRs (%) |
|---|---|---|
| Trifluoperazine | 20 | 10.15% |
| Trifluoperazine+trihexyphenydyl | 07 | 3.55% |
| Olanzapine | 28 | 14.21% |
| Risperidone | 23 | 11.67% |
| Lithium | 10 | 5.07% |
| Clozapine | 17 | 8.62% |
| Amitriptyline | 09 | 4.56% |
| Haloperidol | 18 | 9.13% |
| Carbamazepine | 08 | 4.06% |
| Imipramine | 10 | 5.07% |
| Lorazepam | 11 | 5.58% |
| Fluoxetine | 13 | 6.59% |
| Sertraline | 05 | 2.53% |
| Amisulpride | 06 | 3.04% |
| Trihexyphenidyl | 12 | 6.09% |

Maximum number of ADRs observed with Olanzapine 28(14.21%) followed by Risperidone 23(11.67%), Trifluoperazine 20(10.15%), Haloperidol 18(9.13%) and Clozapine 17(8.62%).

## DISCUSSION

Present study was planned for assessment, classification and causality analysis *of* Adverse Drug Reactions (ADRs) to Psychopharmacological agents (PPAs) in patients of psychiatry OPD in the tertiary medical hospital. Total 197 ADRs to PPAs were voluntarily and intensively reported by treating psychiatrist and resident doctor of pharmacology department in tertiary medical hospital during the study period of twelve months. The information thus gathered about ADRs to PPAs were compiled and analyzed to study their age and sex wise distribution, onset, causality analysis, nature, type and severity.

In this study, antipsychotic and antidepressant were the most commonly prescribed psychotropics drugs in our hospital .Antipsychotics were responsible for most ADRs followed by antidepressant, in the present study. This was similar to the study conducted by Sengupta et al**.** [16] and Lohan k et al. [17] Olanzapine was responsible for maximum number of side effect followed by risperidone, Trifluoperazine, Haloperidol. Olanzapine responsible for weight gain and metabolic side effect. Trifluoperazine was responsible for tremors and extrapyramidal side effect. Maximum number of adverse effect observed was tremors. .

The causality analysis of ADRs with the suspected drug in this study showed 86.80% probable followed by 13.19% of ADRs as possible. The scale used for the causality analysis of ADRs was the WHO assessment scale and opinion of psychiatrist. Here, most of the ADRs unlikely to be attributed to concurrent or other drugs or chemicals, and which follow a clinically reasonable response on withdrawal. Sevene

EC et al. (2008) [18] conducted study of ADRs in rural districts of Mozambique and assessed ADRs according to WHO scale showed 14.86% of ADRs were certain followed by 60.81% as probable. Also study in India by Jose J et al. (2006) [19] showed that upon causality assessment, majority of the reports were rated as probable (53.7%). In our study had no certain cases since the suspected ADRS were mostly mild to moderate severity. In this cases where dechallenge was done , Rechallenge was not attempted with the offending drug .This is in contrast ,Brazilian study [20] where 24 cases were found to be Definite after rechallenge was attempted.

In the present study, most common system affected due ADRs was CNS in 47.20% followed by GIT in 13.70% patients, Musculoskeletal in 8.12% patients. Anticholinergic ADRs were observed in 7.61% patients and metabolic system was affected in 6.59 % patients. Grohmann R et al. (1984) [21] in 1984 showed that the most frequent ADRs collected by intensive monitoring were sedation, extrapyramidal signs, disturbances of the autonomic nervous system and increase in transaminases, while those collected by spontaneous reporting system were Parkinsonism, akathisia, sedation, toxic delirium and increased transaminases. The difference in the systems affected due to ADRs might be because of difference in prescribing preferences at the different hospitals and there may be difference in the demographic characteristics of patients as well. Clayton AH et al. (2002) [22] states that selective serotonin reuptake inhibitors (SSRIs) and venlafaxine extended release (XR) are associated with higher rates of sexual dysfunction than bupropion or nefazodone. In our study, 4 cases of sexual dysfunction were observed only due to SSRIs.

In the present study, the occurrence of severity of ADRs was found to mild in 75.12%, moderate in 24.36% and severe in 0.50 % of patients. Study in India by Jose J et al. (2006) [23] showed mild and moderate reactions accounted for 50.5 and 43.9% respectively. Grohmann R et al. (2004) [24] conducted study in Germany in 2004 and showed that severe ADRs due to psychopharmacological agents occurred in 1.4 % of exposed patients. The difference in the severity of ADRs might be due to difference in prescribing preferences at the different hospitals and there may be difference in the demographic characteristics of patients.

Present study revealed the nature and presentation of different ADR to PPAs with a positive attempt to estimate incidence and establish a causal link between the suspected drug and ADR. However, the inherent limitation of this study was under reporting. The likely causes of under reporting during this study were elements of subjectivity regarding the disease and the ADR, fear of legal action and queries from the patients about the harm caused to them. Another problem was that sometimes patients were found disinterested in telling about the self-medications or over the counter drugs or medicines they were taking since long period.

**Summary**

Patients experienced maximum ADRs in Age group of (21 to 35 years) that is 62 (37.12%) followed by 40 (23.95%) in age group of 36 to 50 years Majority of patients who developed ADRs were male 107(64.07%),central nervous system is most commonly affected system was involved in 93(47.20%) patients followed by gastrointestinal system in 27(13.70%) patients. by Naranjo's scale, Majority of the ADRs 171(86.80%) were scored probable, 26(13.19), were scored possible 26(13.19%).

Severity of ADRS were analyzed with modified Hartwig scale 148(75.12%) were mild , Moderate 48(24.36%), 1(0.50%) was severe moderate reaction were commonly observed with female, mild & severe ADRs were more common in male On comparing the clinical diagnosis it was seen that , There were maximum number of

cases of schizophrenia 40% followed by bipolar disorder 25%.

## CONCLUSION

Maximum number of ADRs observed with Olanzapine 28(14.21%) followed by Risperidone 23(11.67%), Trifluoperazine 20(10.15%), Haloperidol 18(9.13%), Clozapine 17(8.62%).

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