Original Research Article

A Study of Adverse Drug Effects/Adverse Drug Reactions in Patients with Obsessive Compulsive Disorder

.

ABSTRACT

Aims: To identify and record adverse effects/adverse drug reactions in patients receiving pharmacotherapy for obsessive compulsive disorder visiting Psychiatry OPD of King George's Medical University, Lucknow and to assess the causality of adverse drug reactions reported by these patients.

Study design: A prospective observational study

Place and Duration of Study: This study was conducted in the Department of Pharmacology, in collaboration with Department of Psychiatry, King George's Medical University, Lucknow between February 2023 to January 2024.

Method: Patients receiving pharmacotherapy for ObsessiveCompulsive disorder were recruited into the study after satisfying inclusion and exclusion criteria and observed for Adverse drug reaction.Causality of the observed ADRs assessed.

Results: A total of 72 patientswere included in the study out of which 37(51.3%) developed ADR during the study period. Most of the ADR occurred in 18-30 years group(62.1%) with majority in male group(54%). Psychic type ADRs were commonly observed (54%)with majority reported with fluoxetine (72.9%) and dyspepsia (24.3%) was the most commonly observed ADR. On causality assessment, most of the ADRs belonged to possible type(75.7%). 75.7% ADR required symptomatic treatment and remaining 24.3% resolved spontaneously.

Conclusion: This study provides a representative profile of the ADRs which can be expected in OCD patients receiving pharmacotherapy. During the study period 51.3% experienced adverse drug reactions and psychic ADRs were more common with fluoxetine being the most common suspected drug. The causality majorly belonged possible category. Regular monitoring of ADRs in psychiatry OPD and educating the patients about ADR can reduce the risk and it may improve the quality of care, reduction in cost of treatment, adherence to drugs and improved outcome.

Keywords: Adverse drug reactions, Fluoxetine,Obsessive Compulsive disorder, Selective serotonin reuptake inhibitors, Tricyclic anti-depressants, UKU, Y-BOCS

1.INTRODUCTION

Obsessive–compulsive disorder (OCD) is a chronic, disabling disorder that is characterized by recurrent thoughts(obsessions) and rituals (compulsions) over and over, which are considered excessive or unreasonable by the patient(1). A highly prevalent and chronic condition that is associated with substantial globaldisability (2). OCD is the fourthmost common psychiatric illness after depression, alcohol/substance abuse,and social phobia, with a lifetime incidence of 1.6% in community surveys (3) and is considered to be the world's tenth biggest cause of disability. The World Health Organisation (WHO) estimates that roughly 1% of the worldwide population suffers from OCD (4). OCD is represented by a diverse group of symptoms that includesintrusive thoughts, rituals,preoccupations,and compulsions. An obsession is a recurrent and intrusive thought, feeling, idea or sensation and in contrast to thiscompulsion is a conscious, standardized, recurrent behaviour such as counting, checking or avoiding (5). Obsessions and compulsions are time consuming, distressing and are often resisted unsuccessfully. Individuals with OCD perceives their symptoms as normal,that they were similar to other people, and that their behaviours and thoughts were part of their personality. It was only when symptoms began to markedly disrupt daily life and functioning, inaddition to causing major distress, that they realize that these were pathological orindicative of having a psychiatric problem, warranting a visit to the clinic (6). If untreated, OCD is a chronic illness with a waxing and waning ofsymptoms. Although OCD can develop at any age, the majority of cases appear in adolescence and early adulthood,with the average onset age ranging from 22 to 36 years (7). According to the International OCD Foundation, theaverage age of onset for OCD is 19 years. However, OCD can occur in youngsters as early as 2 or 3 years old. OCD affects males and women equally. However, other research 1 imply that men acquire OCD at a younger age than women. Furthermore, some data suggests that women may have more severe OCD symptoms than males (8).

Treatment of OCDinvolves various strategies including pharmacotherapy, psychotherapy , psychosurgery and neuro-modulation interventions. Selective serotonin reuptake inhibitors (SSRIs) are the preferreddrugs.Thesemedications increase and regulate the concentration of serotonin in the brain(9). Alternatives to SSRIs include clomipramine (TCA) and serotonin and norepinephrine reuptake inhibitors. Treatment of resistant cases includes augmentation

with atypical antipsychotics, pindolol, buspirone, and glutamate-blocking agents(10). SSRIs are generally better toleratedthan other agents, but common side effects like nausea, vomiting, insomnia, drowsiness, headache, decreased sexdrive, and agitation occurs. Some of the less common adverse effects of SSRIs reported are extrapyramidal symptoms (EPS), serotonin syndrome, QT prolongation, rash, birth defects, hyponatremia, andcataracts (11). The most common side effects of clomipramine are dry mouth, sedation, dizziness, and weight gain.All of the SRIs can cause sexual problems. Clomipramine can also cause problems with blood pressure and irregular heartbeats, so that children and adolescents and patients with preexisting heart disease who are treated withclomipramine must haveelectrocardiograms (EKGs) before beginning treatment and at regularintervals during treatment. Higher doses than listed in the package insert and a longer trial are often needed for SSRIs thancompared to other psychiatric disorders(10). These higher doses are associated with more severe side effects. An adverse drug reaction (ADR, or adverse drugeffect) can be defined as 'an appreciably harmful or unpleasant reaction resulting from an intervention related to theuse of a medicinal product; adverse effects usually predict hazard from future administration and warrant preventionor specific treatment, or alteration of the dosage regimen, or withdrawal of the product'(12). OCD necessitates the use of drugs for extended periods, ranging from months to years. Because of the prolonged duration of treatment, it islinked with a wide spectrum of adverse drug reactions . ADRs associated with psychotropic medicines can occur evenat standarddosages used in the treatment of acute and chronic mental problems and can lead to noncompliance andIn certain cases, cessation of therapy(13). In psychiatry units, pharmacovigilance can play a critical role in identifyingADRs and alerting clinicians to the potential andcircumstances of such occurrences thus saving the patients from preventableharm. ADR monitoring aids in the development of appropriate interventional programs to manage,prevent, and minimize the risk of developing ADRs, hence lowering therapeutic costs (14).

2.METHODOLOGY

2.1 Study Design : A prospective observational study.

2.2 Study Setting: Study was conducted in the Department of Pharmacology, in collaboration with Department of Psychiatry,King George's MedicalUniversity, Lucknow.

2.3 Study Period : Total duration of the study was 1 year from February 2023 to January 2024 with subject participation for four weeks.

2.4 Study Sample:

- All New/Old patients attending adult psychiatric OPD in Department of Psychiatry, King George's Medical University Lucknow, on the specified days of the week and diagnosed to be suffering from obsessive compulsive disorder by the consultant in-charge and satisfying the selection criteria for the study were included.
- The research protocol was approved by Institutional Ethics Committee of King George's Medical University (KGMU), Lucknow. (vide letter number : XVI-PGTSC-IIA/P57)
- Written informed consent was obtained from all the study participants.

2.5 Selection criteria for selecting patients

2.5AInclusion Criteria

- Patients with confirmed diagnosis of obsessive compulsive disorder as per ICD -11 diagnostic criteria.
- Patients aged between 18 to 60 years.
- Patients who have not received any psychiatric medications during the last 4 weeks.
- Patients willing to give a written informed consent.

2.5BExclusion Criteria

- Patients having any major medical/surgical illness or on continuous treatment for any medical disorder.
- Patient in whom evaluation is not possible due to any reason.

2.6 Sampling Method

Consecutive sampling was done until adequate sample size was reached.The firstpatient was recruited after obtaining Ethical Committee approval

2.7Assessment tools used in the study

i. Semi-Structured Proforma for recording socio-demographic and clinical details of the patients designed for the study.

ii. Yale-Brown Obsessive Compulsive Scale (Y-BOCS): To rate the severity and type of symptoms in patients with OCD (21).

iii. The UKU Side Effect Rating Scale : Used forassessing the side effects of medications prescribed to OCD patients(22).

3. RESULTS

3.1 Socio-demographic characteristics of study participants

The study encompassed 72 patients, out of which 42(58.3%) participants fell within the 18-30 years range, indicating a substantial representation of younger individuals. Conversely, a smaller proportion, comprising 15.3%, fell within the31-40 years bracket. Notably, the 41-50 years group accounted for 19.4% of the cohort, while the older age range of 51-60 years constituted a minority at 6.9%. The gender distribution within the study cohort comprised 43 male participants, constituting 59.7% of the total, while female participants numbered 29, representing 40.3%. Out of 72, 7(9.7%) patients were from rural locality and remaining 65(90.3%) belonged to urban area. Family type showed that 6(8.3%) belonged to joint family and 66(91.7%) to nuclear type. Marital status showed that 48(66.7%) patients were married and 24(33.3%) unmarried. Education status of the patient showed that 16(22.8%) graduates , 27(37.5%) intermediate education, 20 (27.7%) high school and 9(12.5%) were illiterates. Employment status of the study participants showed that 27(37.5%) were students, 5(6.9%) government employees, 10(13.8%) private job, 22(30.5%) housewives and 8(11.1%) were unemployed. (Table 1)

Table 1: Socio-demographic characteristics of study participants

Socio-demographic	Category	Number (%)
Age(yrs)	18-30 yrs	42(58.3%)
	31-40 yrs	11(15.3%)
	41-50 yrs	14(19.4%)
	51-60 yrs	5(6.9%)
Sex	Males	43(59.7%)
	Females	29(40.3%)
Domicile	Rural	7(9.7%)
	Urban	65(90.3%)
Family type	Joint	6(8.3%)
	Nuclear	66(91.7%)
Marital status	Married	48(66.7%)
	Unmarried	24(33.3%)
Education	Graduate	16(22.8%)
	Intermediate	27(37.5%)
	Highschool	20(27.7%)
	Illiterate	9(12.5%)
Occupation	Student	27(37.5%)
	Government job	5(6.9%)
	Private job	10(13.8%)
	Housewife	22(30.5%)

	Unemployed	8(11.1%)

3.2Adverse effects /ADR observed during the study

A total of 37 out of 72 patients (51.3%) experienced adverse effects or adverse drugreactions (ADR) during thestudyperiod. (Figure 1)

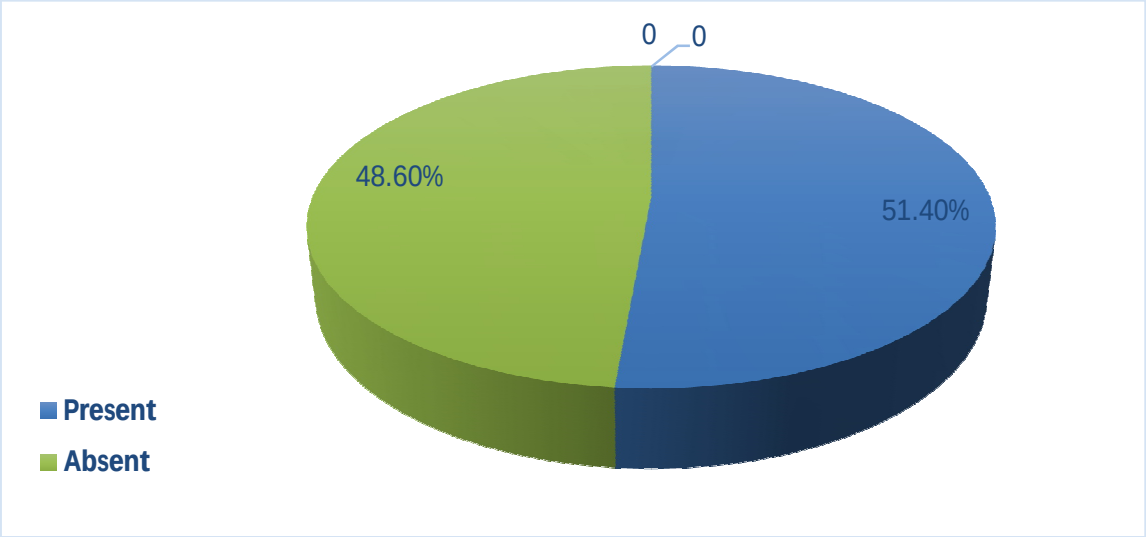

Figure 1: Adverse effects /ADR observed during the study

3.3 Age wise distribution of ADR

Among the 37 ADRs, 23(62.1%) occurred in 18-30 years group, 8 (21.6%) belonged to 31-40 age group and 3(8.1%) each in 41-50 and 51-60 age bracket. Table 3 summarizes the age wise distribution of ADR.(Table 2)

Table 2: Age wise distribution of ADR

Age(years)	Number of ADR	% of ADR
18-30	23	62.16
31-40	8	21.62
41-50	3	8.1
50-60	3	8.1
Total	37	100

3.4 Gender wise distribution of ADR

Among the 37 ADRs observed 20(54%) occurred in male group, and17(46%) in females. (Table 3)

Table 3: Gender wise distribution of ADR

Gender	Number of ADR	% of ADR
Male	20	54
Female	17	46
Total	37	100

3.5 Spectrum of Adverse Drug Reactions According to UKU-SERS

According to the UKU side effect rating scale, out of 37 ADRs 20(54%) were psychic ADRs ,4(10.8%) eachneurologic and autonomic type and others were 9(24.3%).Among the individual ADRs , dyspepsia 9(24.3%) was themost commonly suspected ADR followed by troubled/decreased sleep 7(18.9%), anxiety 6(16.2%), restlessness5(13.5%) , nausea 4(10.8%), tremors 3(8.1%) , drowsiness 2(5.4%) and headache 1(2.7%). (Table 4& Figure 2)

Table 4 -Adverse Drug Reactions According to UKU-SERS

Type of ADR	Number of ADR(%)	ADR(number)
Psychic ADR	20(54%)	Decreased/trouble sleep(7) Sedation(2) Restlessness(5) Anxiety(6)
Neurologic ADR	4(10.8%)	Tremors(3) Headache(1)
Autonomic ADR	4(10.8%)	Nausea(4)
Others	9(24.3%)	Dyspepsia(9)

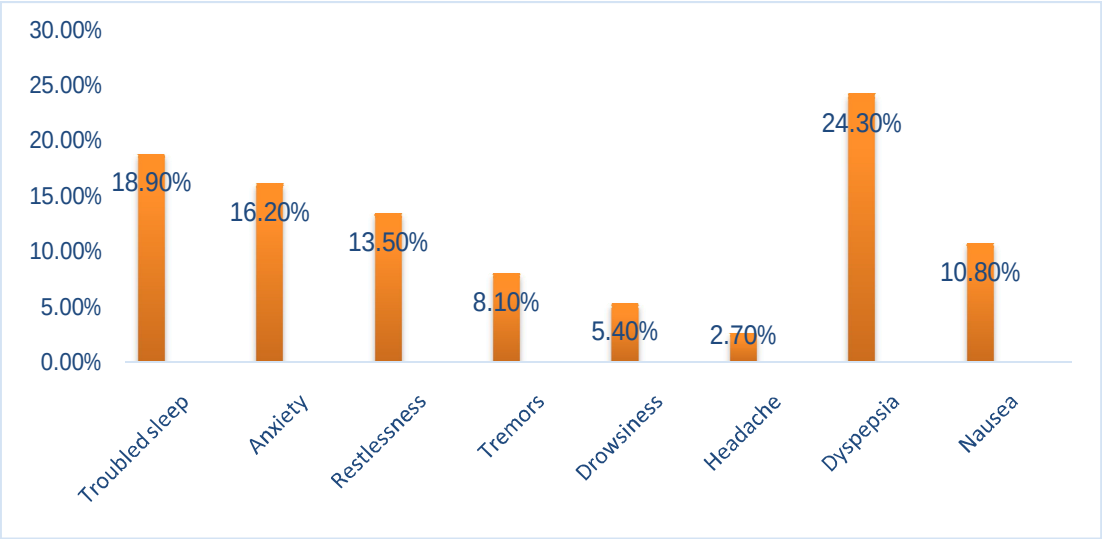

Figure 2: **spectrum of ADRs observed among study participants**

3.6 Drugsresponsiblefor adverse drug reactions among study participants

Out of the drugs suspected for ADR fluoxetine was implicated in 72.9% of cases. Sertraline and clomipraminewere each associated with 10.8% of cases, while paroxetine and etizolam were involved in 5.4% of cases each.Escitalopram was reported in 2.7% of cases.

Table 5 summarizes the different ADRs observed and drugsimplicated.

Table 5 : The suspected drugs causing adverse drug reactions (ADRs)

Suspected drug	Number of ADR(%)	ADR(n)
Fluoxetine	27(72.9)	Decreased/troubled sleep(5) Anxiety(4) Restlessness(5) Drowsiness(1) Headache(1) Nausea(1) Dyspepsia(7)
Paroxetine	2(5.4%)	Decreased sleep(1) Anxiety(1)
Sertraline	1(2.7%)	Decreased sleep
Escitalopram	1(2.7%)	Dyspepsia
Clomipramine	4(10.8%)	Anxiety(1) Tremors(1) Nausea(1) Dyspepsia(1)

Etizolam	2(5.4%)	Tremors(1) Anxiety(1)

3.7Causality assessment of the observed adverse drug reactions

The causality of the observed ADRs was assessed by UKU Side effect rating scale according to this scalemajority, 75.7%, were categorized as "possible" causality. A lesser proportion, 24.3%, was classified as "probable" causality. (Figure 3)

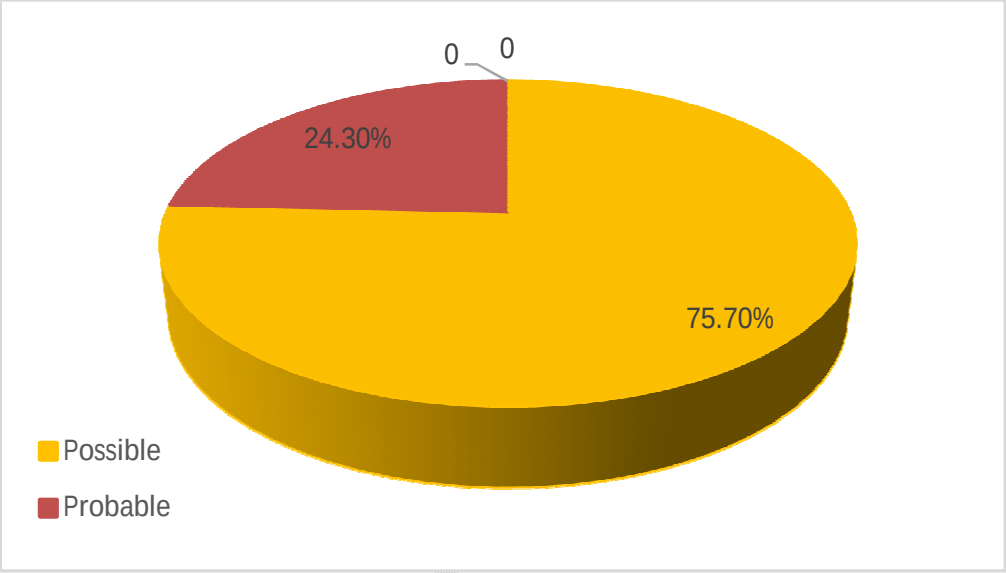

Figure 3 : Causality of observed ADRs by UKU scale

3.8Degree/consequence of ADR according to UKU scale

The consequence of the observed ADR were assessed by UKU side effect rating scale In the present study28(75.7%) belonged to degree 2 as they required symptomatic treatment and remaining 9(24.3%) into degree 1 as they not required reduction in dose or change in drug.(Table 6)

Table 6: Degree/consequence of ADR according to UKU scale

Degree	Number of ADR(N-37)	% of ADR
Degree 0	0	0

Degree 1	9	24.3
Degree 2	28	75.7
Degree 3	0	0

4. DISCUSSION

This prospective observational research included 72 participants (43 males and 29 females) across various age ranges. The majority of participants 42 (58.3%) were between the ages of 18 and 30, showing a significant representation of young people.

During the trial period 51.3% study participants experienced adverse effects or adverse drug reactions (ADR). The evidence from the literature suggests that the incidence of ADRs in psychiatric OPDs in India varies from 6.41% to 41.9% [15-17]. The disparity in the incidence rate reported from different studies might be due to variable study duration and reporting culture. Studies using the spontaneous reporting method generally detect lower incidences of ADRs. The higher percentage of ADR in this study was due to active intervention in reporting and follow up. According to the UKU side effect rating scale , psychic ADRs constituted 54% of the total ADR observed as these drugs act on CNS. Similar to this study, Gawali et al.2017 found the most common organ system affected by ADRs to be CNS [15]. Psychic ADR is followed by, others type(24.3%), neurologic(10.8%) and autonomic(10.8%).Among the psychic ADRs decreased/troubled sleep was most commonly reported followed by restlessness, anxiety and sedation. Ambwani et al.2021 reported sedation as the most common ADR [18].

Among the neurological ADR tremors were reported commonly followed by headache. Mathew et al 2020 also reported tremor as the most common neurological ADR[22]. Nausea was the ADR reported in autonomic category and dyspepsia in others category.

In the present study, fluoxetine(72.9%) was the most common drug causing ADRs, followed by sertraline (10.8%), clomipramine (10.8%), paroxetine (5.4%), etizolam (5.4%), and Escitalopram (2.7%). Sankhi et al. 2020 also showed that SSRIs were the most common drug group causing most of the ADRs [24].

Causality assessment using the UKU side effect rating scale showed that 75.7% of ADRs were of “possible” type and remaining 24.3% probable type. This observation is supported by

previous studies [17, 18, 20]. Sridhar et al, study found more possible (45.5%) causal relationship followed by probable (34.9%) [13]. Above findings suggest possible relationship is most common which could be explained by usage of more than one drug or other alternative cause may be responsible for ADR.

The consequence of the observed ADR by UKU side effect rating scale showed that 75.7% belonged to degree 2 as they required symptomatic treatment to ameliorate symptoms of ADR and remaining 24.3% into degree 1 as they not required reduction in dose or change in drug.

5. CONCLUSION

This study provides a representative profile of the ADRs which can be expected in OCD patients receiving pharmacotherapy. YBOCS score assessment showed significant improvement in OCD symptoms by the drugs prescribed. During the study period 51.3% experienced adverse drug reactions and psychic ADRs were more common followed by others , neuropathic and autonomic ADRs. The drug causing most ADRs was fluoxetine. The causality evaluation of reported ADRs revealed that majority belonged to possible category & a lesser to probable causality. Majority got symptomatic therapy to ameliorate ADR-related symptoms. A lesser number did not require any intervention since the ADRs resolved themselves. Regular monitoring of ADRs in psychiatry OPD and educating the patients about ADR can reduce the risk and it may improve the quality of care, reduction in cost of treatment, adherence to drugs and improved outcome.

CONSENT

Patients were recruited in the study after obtaining written informed consent.

ETHICAL APPROVAL

The study was initiated after obtaining approval from Institutional Ethics Committee(vide letter no.: XVI-PGTSC-IIA/P57) and the Patients were recruited in the study after obtaining written informed consent.

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