

## Analysis Of Prescribing Pattern And Adverse Drug Reactions of Selective Serotonin Reuptake Inhibitors (SSRIS) In A Psychiatry Out-Patient Department of A Tertiary Care Teaching Hospital

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**Abstract:** **Background:** Selective Serotonin Reuptake Inhibitors (SSRIs) is a group of drugs which are widely used as antidepressants. Their use is not just limited as antidepressant but they are also useful in treatment of anxiety, bulimia nervosa (an eating disorder), obsessive-compulsive disorder, panic disorder, and premenstrual dysphoric disorder (PMDD). The drugs in this group are equally efficacious with minimum side effects, which are tolerable. Their safety profile is better as compared to tricyclic antidepressants. This study was designed with the aims to analyse the prescribing pattern and adverse drug reactions of SSRIs in psychiatry outpatient setup of tertiary care teaching hospital. **Methodology:** An observational cross sectional study conducted at psychiatric outpatient department of tertiary care teaching hospital over a period of three months. All the patients prescribed a selective serotonin reuptake inhibitor were enrolled in the study. Data regarding the demographic details, diagnosis, past and family history, presence of comorbid conditions, prescribed SSRI and other antipsychiatric drugs along with their dosage regimens and adverse drug reactions were entered in predesigned case record form analyzed in number and percentage. **Results:** Majority of the patients (75 patients) were less than 50 years of age. Male to female ratio was 1.17. Most common indication for prescribed SSRI is major depressive disorder (82 patients). 27 participants were having associated comorbid conditions, Out of the six available SSRIs in hospital pharmacy, sertraline, escitalopram and fluoxetine were prescribed. Lorazepam, amitriptylin, clonazepam, diazepam and alprazolam were commonly co-prescribed antipsychiatric medications. Out of 35 patients developed adverse drug reactions, most common ADR was anxiety in 14% of patients followed by headache and alteration of appetite in 10% of patients each. **Conclusion:** Major depressive disorder was the most common indication for prescribing SSRI. Sertraline is the most commonly prescribed SSRI. The dosage range of prescribed SSRIs were according to the standard therapeutic guidelines. Benzodiazepines were the most commonly co-prescribed antipsychiatric drugs. Percentage and type of occurrence of adverse drug reactions to SSRIs were similar to that found in literature. Future study of long duration is required to confirm these findings.. [Neelam S Natl J Integr Res Med, 2019; 10(3):5-10]

**Key Words:** Depression, SSRI, Sertraline, Major Depressive Disorder

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**Introduction:** Since their discovery in 1984, number of SSRIs have been introduced and approved for various psychiatric disorders. They act by increasing the extracellular level of the serotonin by inhibiting its reuptake into the presynaptic cell.<sup>1</sup> Initially, they were approved for the use in the treatment of various types of depression. But later on they are found to be efficacious and approved for the treatment of generalized anxiety, panic, social anxiety as well as obsessive compulsive disorders.<sup>2, 3</sup> Selective serotonin reuptake inhibitors (SSRIs) are well tolerated as compared with the older tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) and are generally recommended as first line pharmacological treatment for depression.<sup>4</sup> Pharmacokinetic properties (half life and method of elimination) as well as side effects profile vary significantly among SSRIs.<sup>5</sup> For example, paroxetine has been associated with more weight gain and a higher incidence of sexual dysfunction, and sertraline

with a higher incidence of diarrhea than other SSRIs.<sup>6</sup> In addition to these, there are significant differences in the drug interactions among SSRIs.<sup>7</sup> These factors may be responsible for the selection of particular agent amidst SSRIs. Currently six SSRIs- fluoxetine, fluoxamine, sertraline, paroxetine, citalopram and escitalopram are available for the use in India. Out of these, Sertraline, escitalopram and fluoxetine are included in essential medicine list and available in this tertiary care hospital. Hence observation and analysis of the prescribing pattern of SSRIs will be helped to identify the factors responsible for the selection of particular SSRI not only amongst other pharmacological agents available for the management of psychiatric disorders but also amidst SSRI. No such kind of study has been conducted in this institute hence present was designed with the aims to analyse prescribing pattern and adverse drug reactions of SSRIs in a tertiary care teaching hospital with following objectives: Analysis of

prescribing pattern of SSRIs in relation to diagnosis  
 Analysis of the dosage regimen of SSRIs  
 Analysis of co-prescribed other antipsychiatric agents  
 Analysis of adverse drug reactions developed with SSRIs

**Methodology:** An observational cross-sectional study was carried out in a psychiatry out patient department (OPD) of a tertiary care teaching hospital after prior approval of institutional human ethics committee. Patients attending psychiatry OPD who were prescribed SSRI were included in the study. While those patients who were not willing to give informed consent and less than 18 years of age were excluded from the study.

All the study patients who followed above mentioned inclusion and exclusion criteria were enrolled in the study during 3 months period. Detailed information of the demographic details of the patient, diagnosis, prescribed SSRI (drug, dose, route, frequency of administration and duration of treatment) as well as coprescribed drugs along with their dosage regimen were filled in the predesigned structured and validated case record form. Following parameters were analysed.

Demographic details of patients  
 Patients having positive family history and past history  
 Presence and pattern of associated systemic illnesses  
 Prescription of different SSRIs according to diagnosis  
 Dosage of SSRIs prescribed  
 Co-prescription of other antipsychiatric agents  
 Occurrence of ADRs and their types  
 Above parameters were analysed in number and percentages

**Results:** A total 100 patients were enrolled into the study according to patient selection criteria. Out of these, 71 patients were prescribed SSRI before the enrolment in the study while 29 patients were prescribed SSRI for the first time. Majority of the patients were less than 50 years of age. (75 patients) Distribution of patients according to the age is depicted in table 1. 54 patients were male while the rest were female. The most common indication for the prescription of SSRIs is major depressive disorder (82 patients). Prescription of SSRIs according to different indications were depicted in table 2.

**Table 1: Distribution of patients according to age**

Age group	Number of patients
18-30	26
31-40	27
41-50	22
51-60	16
61-70	6
71-80	3

**Table 2: Prescription of SSRIs according to indication**

Diagnosis	Number of patients
Major depressive disorder	82
Anxiety	4
Bipolar mood disorder	4
Schizophrenia	1
OCD	1
Psychotic depression	1
Depression due to alcohol withdrawal	1
Anxiety with Major depressive disorder	4
Headache with Major depressive disorder	1
Trigeminal neuralgia	1

Out of 100 study participants, 27 participants were having associated other psychiatric illnesses too. Presence of other co-morbid conditions is mentioned in table 3.

**Table 3: Presence of other systemic illnesses**

Systemic illness	Number of patients
Hypertension	18
Diabetes	6
Hypothyroidism	3
Migraine	1
Hypercholesterolemia	2
Skin disease	1
GIT problem	1
Hypotension	4

Presence of positive past psychiatry history was noted in 12 patients while positive family history was noted in 13 patients. Personal history in terms of addiction, allergy was positive in 21 patients. In personal history, study participants were having addictions like tobacco chewing (5), smoking (5), masala/mava (8), alcohol (1) and chhikani(1).

Out of the six available SSRIs in hospital pharmacy, sertraline (78), escitalopram (17) and

fluoxetine (5) were prescribed. Different strength of SSRIs prescribed are mentioned in table 4.

**Table 4: Different strength of prescribed SSRI**

SSRI	Strength	No. of Patients
Sertraline	25 mg	4
	50 mg	46
	75 mg	5
	100 mg	19
	200 mg	5
Escitalopram	10 mg	14
	20 mg	3
Fluoxetine	20 mg	5

In 76 patients, there were co-prescription of other psychiatric agents. Details are mentioned in table 5.

**Table 5: Co-prescription of other antipsychiatric drugs**

Co-prescription of other antipsychiatric drugs		Number of patients
Lorazepam	1 mg	5
	2 mg	20
	3 mg	2
	4 mg	1
	5 mg	1
Amitryptiline	25 mg	15
	50 mg	9
	100 mg	1
Clonazepam	.25 mg	2
	.5 mg	21
	.75 mg	11
	1 mg	3
Diazepam	2.5 mg	1
	5 mg	7
Alprazolam	.25 mg	2
	.5 mg	2
	2 mg	1
Olanzapine	2.5 mg	1
	5 mg	1
	10 mg	1
Risperidone	2 mg	2
	4 mg	2
Imipramine	25 mg	1
	100 mg	1
Mirtazepine	15 mg	1
Sodium valproate	1200 mg	2
Lithium carbonate	300 mg	1
Clozapine	75 mg	1
Amisulpiride	60 mg	1

In study participants, who had been prescribed SSRI before the enrollment in the study, no changeover were made in 99 participants. Out of 100 study participants, adverse drug reactions were reported in 35 patients. Details of adverse drug reactions to SSRIs are mentioned in table 6.

**Table 6: Adverse drug reactions to SSRIs**

Adverse drug reaction	Number of patients
Dysphoric mood	12
Headache	10
Anxiety	14
Constipation	2
Vomiting	2
Alteration in appetite	10
Giddiness	2
Weakness	1
Body pain	1
Sleep disturbance	3
Vertigo	1
Erectile dysfunction	1

**Discussion:** Prevalence of psychiatric illnesses is increasing now a days. These illnesses not only increase morbidity and mortality of the patient but there is overall decline in socioeconomic status of the society. Out of all psychiatric illnesses, Major depressive disorder (MDD) is the most common psychiatric illness. It is considered to be a serious medical disorder which can negatively affect a persons' personal and general health. Over a period of time, prescribing pattern of anti-depressants has been considerably changed and SSRIs and newer atypical antidepressants are preferred over tricyclic antidepressants and mono-amine oxidase inhibitors because of better tolerability profile<sup>8,9</sup>. According to American Psychiatric Association guidelines, SSRIs are unanimously regarded as treatment of choice for depression.<sup>10,11</sup> In addition to depression, SSRIs have been proved effective for the treatment of anxiety disorders, including obsessive-compulsive disorder (OCD), panic disorder, social phobia, bulimia nervosa and post traumatic stress disorder.<sup>12</sup>

Age is considered to be very important factor for mental status of the individual. As the age advances, occurrence of mental illnesses is usually increasing.<sup>13</sup> But there can be exception to this generalization also. A study conducted by Ghosh and Chaudhary 2014<sup>14</sup> concluded that more than 50% of patients taking antidepressants were belong to age group of 18-30 years. But in

present study, majority of the patients were below the age of 50 years.

Similar results were observed in the study conducted by Kavitha VD et al. 2017 and Karak S et al. 2016, where majority of the patients fell in the age group of 21-40 years.<sup>15,16</sup>

In present study there is slightly more male female ratio<sup>1,17</sup>, which is contrary to other studies in which females are having higher incidence of psychiatric illnesses especially depression and hence prescribing SSRIs<sup>17,18,19</sup>. Women appear to be more sensitive to develop depression at even lower levels of stress and also to show exaggerated neuroendocrine responses to stress.<sup>18,19</sup> Moreover, this gender discrepancy could also be due to the prevalence of illness where they tend to report their symptoms of depression compared to male patients.

In present study, Sertraline is the most commonly prescribed SSRI, followed by escitalopram and fluoxetine. But According to the studies conducted by Pradhan S G et al. 2017<sup>20</sup>, Ray S et al 2011,<sup>21</sup> Kennedy SH et al 2006<sup>11</sup> and Azorin JM et al 2004<sup>22</sup> escitalopram is preferred amongst all SSRIs because of its superiority in terms of efficacy. Selection of particular SSRIs, amidst all SSRIs depends on many factors. Current practice guidelines recommend that selection should be based on past experience of treatment, tolerability, patient preference and cost.<sup>23,24</sup>

In present study, all the drugs were prescribed by their generic name. While in study conducted by Kavitha VD 2017 drugs prescribed by generic names were 80%.<sup>15</sup> According to the WHO and also guidelines by Medical Council of India, Drugs should be prescribed by their generic names. In the present study, author found that 100% of the antidepressants were prescribed according to the standard recommended therapeutic doses of the drugs. Similar results were found in a study by Ghosh S et al where all antidepressants were within the recommended dose ranges<sup>14</sup>. In present study, all the prescribed SSRIs were from hospital formulary, so cost could be a determinant factor for the treatment adherence. Hence patient adherence could have been improved because of it.

In present study, prescription of SSRI is not combined with any other antidepressant agent. This finding is supported by Tejaswini K et al.

2019<sup>13</sup> and Rush et al. 2011<sup>25</sup>, in which monotherapy with antidepressant is preferred. In a study by Rush et al. 2011<sup>25</sup>, it was found that there was no advantage of polytherapy in terms of outcome of depression as compared to monotherapy. Additionally Tianmei et al 2014<sup>26</sup> concluded that frequency and severity of side effects has been increased due to use of multiple antidepressant agents.

In present study, more than two third of the patients were co-prescribed benzodiazepines. Out of these, clonazepam was the most preferred<sup>27</sup> followed by lorazepam<sup>29</sup>. These can be justified by the fact that in majority of patient have anxiety component was present additionally to depression. In addition to this, insomnia was found in nearly all patients. Co-prescription of benzodiazepines can also be explained by agitation and restlessness produced by SSRIs. Present study findings were supported by Pradhan S G et al. 2017, in which nearly one-third of subjects (N=67; 33.5%) were prescribed a benzodiazepine, with clonazepam and lorazepam being the most preferred agents. Similar findings were observed by other investigators such as Grover S et al 2013, Mohanta G et al 2008 and Onishi Y et al 2013.<sup>27,28,29</sup>

In present study, Agitation and anxiety<sup>26</sup>, Headache<sup>10</sup> and alteration in appetite<sup>10</sup> were the commonly reported adverse drug reactions. These findings are supported by studies conducted by Mukherjee s et al.2015 and Mishra S et al. 2013<sup>30,31</sup>

**Conclusion:** Sertraline was the most commonly prescribed SSRI followed by escitalopram and fluoxetine. In addition to other indications, major depressive disorder was ranked the top. Strength of the prescribed all SSRIs were within therapeutic dosage range. Benzodiazepines were the most commonly co-prescribed agents. Eventhough the sizable patients developed ADRs, but their pattern and frequency of occurrence is similar to other published literature. Future, long term study is required to confirm these findings.

**Study Limitations:** The study was based on the first prescription of the patients. A follow up study would be a better determining factor for the analysis of prescriptions, to see if there were any changes in the drugs prescribed over a period of time as well as to evaluate the side effects and compliance of the patients too.

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