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DRUG UTILIZATION AND PRESCRIPTION PATTERN OF ANTIDEPRESSANTS IN PSYCHIATRIC DEPARTMENT OF A TERTIARY CARE TEACHING HOSPITAL: AN OBSERVATIONAL STUDY

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Abstract:
Objective: The present observational prospective clinical-pharmacological study aimed to assess the drug utilization and prescription pattern of antidepressants in the psychiatric outpatient department at Mahatma Gandhi Medical College & Hospital, Jaipur.
Methods: The study spanned six months, and prescriptions of 100 patients were recorded including patient's demographic details, diagnosis, drug name, dose duration and frequency. Patients' consent was sought before data collection. Rationality of the prescriptions were assessed using WHO core prescribing indicators.
Results: The findings of the study showed that depression was more common among males and in the 21-40 years age bracket. The most frequent diagnosis was endogenous depression with mixed depressive anxiety disorder being the second most frequent. Among the antidepressants, escitalopram, which is usually co-administered with clonazepam was the most common and fluoxetine was the second most common. The use of multiple drugs was common, with three drugs being the most used and most patients were on one-month courses. A meager 9% of the drugs were prescribed by their generic name; 46% of the drugs belonged to the National List of Essential Medicines. The use of FDCs was observed in 8. 2% of the prescriptions.
Conclusion: The present study concluded that further improvements are needed in prescribing practices of antidepressants. Several problems such as low compliance with generic prescribing, insufficient utilization of essential medicines, high levels of polypharmacy and FDCs that lead to higher costs, possible side effects, and interactions stress the significance of increasing the role of rational prescribing to increase the effectiveness of treatment and decrease the costs of healthcare.

Keywords: Drug utilization, antidepressants, prescription patterns, psychiatric care, rational prescribing, fixed-dose combinations, generic drugs.

1. Introduction

Depression is a prevalent mental disorder with a lifetime prevalence of more than 5%, a global burden of more than 300 million people affected, and a high mortality, morbidity, and disability rate. Alone, depression is estimated as largest contributor to non fatal health loss accounting for 7. 5%

YLDs(years lost to disability) and 2% of DALYs (Disability adjusted life years) in 2015 and is projected to rank second globally by 2030 (WHO, 2017; Murray et al., 2012; Mathers & Loncar, 2006; WHO, 2017).

India has a large stake, with 57 million people experiencing depression, or 18% of the global total. This number is expected to rise because of factors such as modernization and urbanization that are occurring at a very fast rate in societies (Ray &Chogtu, 2011). Depression is the state of being low-spirited or unhappy and being unable to perform normal activities for two weeks or more. It is present in both males and females but more so in females (Kessler, 2003; NICE, 2009).

Pharmacological and non-pharmacological therapy is applied in the management of depression. Medications like antidepressants are beneficial in improving mental health and social adjustment; psychotherapy including CBT is also effective (Ferguson, 2001; Kessler et al., 2009; Hamid Reza Motavallyzadeh et al., 2013). Nevertheless, the area of study of psychiatric illness is still a growing concept in health care systems, and more research is required on the rational use of antidepressants and prescription audit (Ghosh &Royachaudhary, 2014; Trivedi et al., 2010; Einarson, 2008).

Drug utilization studies as described by the World Health Organization are the marketing, distribution, prescription, and use of drugs with special regard to the medical, social, and economic consequences of these processes and are useful in the encouragement of rational use of drugs. These studies use indices to assess the prescribing behavior, patients' treatment, and physical facility environment (Laporte et al., 1983; Chiles et al., 1999; Hirschfeld et al., 2000; McManus et al., 2000; Mohanta et al., 2008).

The consumption of antidepressants has evolved and the newer categories like SSRIs and atypical antidepressants have replaced the older ones due to the side effects (Mishra et al., 2012; Barnett, 2002; Laporte et al., 1983). The following are some of the factors that are considered when choosing antidepressants; severity of depression, previous episodes, and other diseases (Bennet, 2010; Ghosh &Royachaudhary, 2014).

The research that was done at Mahatma Gandhi Medical College & Hospital aims at identifying the current trend of using antidepressants, promotingthe appropriate use of antidepressants, and suggesting measures that would improve the management of the patients and reduce cases of prescription deficiencies. The findings of the research are believed to enhance the current practices of using antidepressants and the efficacy of the treatment process (Olfson& Marcus, 2010).

1.1 Aim

To analyze the drug utilization and prescription pattern of antidepressant drugs in psychiatric OPD in a tertiary care hospital.

1.2 Objectives

1. To estimate the prescription pattern of antidepressant drugs in Psychiatric patients.
2. To analyze and estimate the prescription pattern based on WHO core drug use indicators.

2. Material and Methods

Study Design: This prospective observational study was carried out from July 2019 to December 2019 in the Department of Pharmacology , Mahatma Gandhi Medical College & Hospital, a 1000-bed tertiary care teaching hospital in Jaipur. The objective of the study was to assess the trends in the use of antidepressants. The study was approved by the institutional ethics committee before the start of the study.

Duration: July 2019 to December 2019

Setting: Department of Pharmacology, Mahatma Gandhi Medical College, with the Psychiatric Department of Mahatma Gandhi Hospital, Jaipur.

Consent: Participants' written, and informed consent was sought and received from all the participants.

Sample Size: All patients attending the psychiatric OPD of the hospital and those who were on antidepressants were included in the study.

Inclusion Criteria:
- All patients diagnosed with depression in the psychiatric OPD, who were prescribed antidepressants, and are above the age of 18 years.

Exclusion Criteria:
- Depression associated with other comorbid situations
- Pregnant and lactating women.
- Patients who were not willing to give their consent
- Psychiatric department patients admitted to the hospital

Data Collection: Prescription information was collected on a prescription-specific case report forminformation of patient's age, sex, diagnosis, hospital number, and details of the drug prescribed including the name of the drug, dose, duration, frequency of administration, etc. Data were analyzed using WHO core drug use indicatorsand percentage calculations for drugs prescribed by generic name, brand name, and from the essential drug list, and number of preparations in combinations.

Statistical Analysis: Data were recorded on Microsoft Excel 2007 and all results were presented in percentage form. The analysis of results was done and presented in the form of graphs and tables.

3. Observations and Results

The data were collected from the psychiatric department of Mahatma Gandhi Medical College & Hospital, Jaipur, from July 2019 to December 2019 with 100 cases. The prescription patterns were evaluated & analyzed based on WHO indicators.

3.1 Demographic Parameters

Details recorded in prescriptions were the patient's name, gender, age, address, diagnosis, dosage form, dose, and frequency.

Table 1: List of gender, age, and marital status-wise distribution of patients

Variable	Category	Number of Subjects (N=100)	Percentage (%)
Sex	Male	61	61%
	Female	39	39%
Age (in years)	0-20	12	12%
	20-40	46	46%
	40-60	34	34%
	>60	8	8%
Marital Status	Single	13	13%
	Married	62	62%
	Others (Divorced, widow, remarried)	25	25%

The gender and age-wise distribution of total patients observed is shown in Table 1. The predilection of female and male patients was 39% and 61%, respectively.The majority of the subjects included in this study belong to the age group of 21-40 years (49%),followed by the age group of 41-60 years(31%), followed by subjects of more than 60 years(12%).Married people have a higher predilection rate than unmarried people and others.

3.2 Assessment of differences in pattern among various types of depressive illness

Out of 100 prescriptions that have been evaluated, Endogenous depression was the most common type of depression (28%) followed by mixed depressive anxiety disorder (26%), moderate depressive episode without somatic symptoms (19%), moderate depressive disorder with dissociative disorder (15%), bipolar depression (12%), depression associated with post-traumatic stress disorder (1%), postpartum depression (1%).

Table 2: List of distribution of patients according to the diagnosis

Diagnosis of Patients	Number of Patients (%)
Endogenous depression	28%
Mixed depressive anxiety disorder	26%
Moderate depressive episode without somatic symptoms	19%
Moderate depressive disorder with dissociative disorder	15%
Bipolar depression	12%
Depression associated with post-traumatic stress disorder	1%
Postpartum depression	1%

3.3 Assessment of differences in sex patterns among various depressive illnesses

Out of 100 prescriptions that have been evaluated, Endogenous depression was most frequently observed in males (18%) followed by females (10%). Mixed depressive anxiety disorder was observed in 16% of males followed by females (10%). Moderate depressive episode without somatic symptoms was observed in 13% of males followed by females (6%). Bipolar depression was observed in 8% of males followed by 4% of females. Depression associated with PTSD &postpartum depression was observed in 2% of females only.

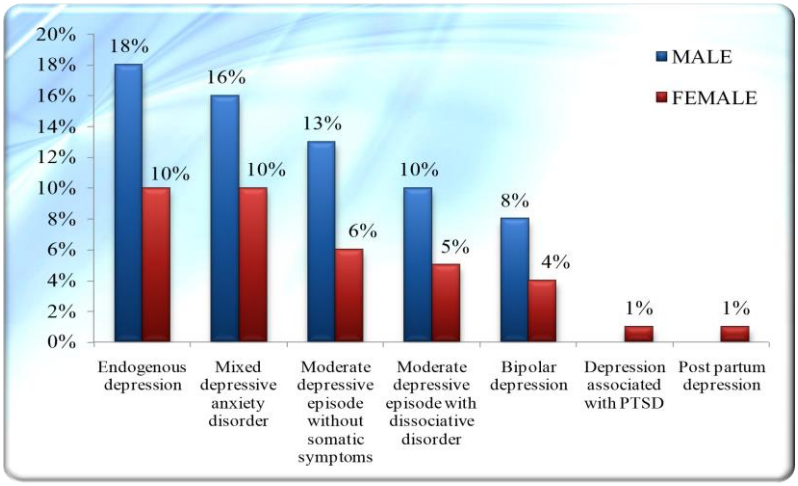

Figure 1: Pattern of sex differences among various depressive illnesses

3.4 Assessment of prescribing frequency of various antidepressants in the study population

Most of the patients were prescribed antidepressants that belong to the SSRIs group followed by SNRIs, TCAs & atypical antidepressants (Table 3). Among SSRIs, the most frequently prescribed drug was escitalopram (60%) followed by fluoxetine (13%). Among SNRIs, Desvenlafaxine was prescribed to 7% of the population followed by Duloxetine (3%). Among TCAs, Amitriptyline was prescribed to 5% of the population followed by clomipramine (2%) and melitracen (1%). Among atypical antidepressants, Bupropion was prescribed to 4% of the population followed by Mirtazapine.

Table 3: List of Antidepressants prescribed most frequently in the study population

Drug Category	Antidepressant Prescribed	Number of Patients (%)
SSRIs	Escitalopram	60%
	Fluoxetine	13%
	Fluvoxamine	7%
	Paroxetine	4%
	Sertraline	2%
SNRIs	Desvenlafaxine	7%
	Duloxetine	3%
TCAs	Amitriptyline	5%
	Clomipramine	2%
	Melitracen	1%
Atypical Antidepressants	Bupropion	2%
	Mirtazapine	4%

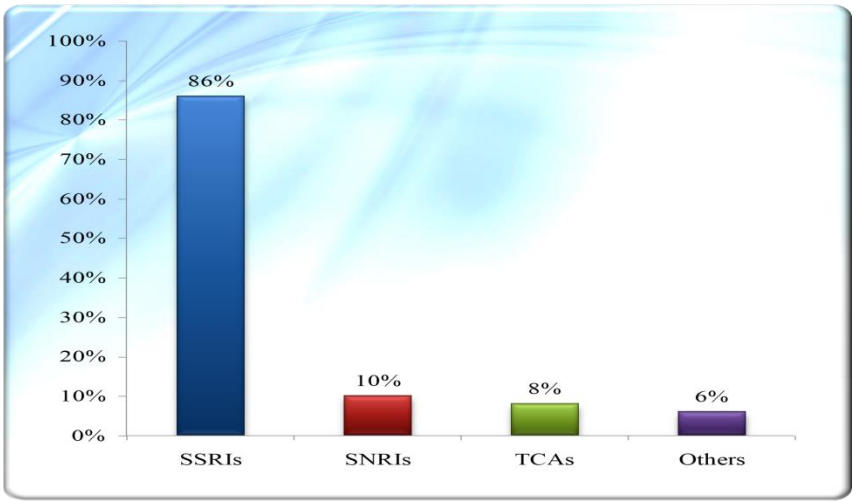

Figure 2. Pattern and prescribing frequency of antidepressants in patients

3.5 Assessment of list of other psychotropic drugs used in combination with antidepressants in depressive illness

Various other psychotropic drugs were also used in combination with antidepressants which include anxiolytics (62%), antipsychotics (5%), and mood stabilizers (2%) (Figure 6). Among anxiolytics,clonazepam was prescribed to (42%) followed by Etizolam (8%) and aripiprazole (6%), lorazepam (4%), alprazolam (2%). 5% of the patients were co-prescribed antipsychotics along with antidepressants for treatment of their psychotic symptoms. Among antipsychotics, Olanzapine was prescribed in 3% of the population followed by flupenthixol (2%). Lithium, as a mood stabilizer, was prescribed to 2% of the population.

Table 4: List of prescribing frequency of other psychotropic drugs used in combination with antidepressants in depressive illness

Category	Medication	Number of Patients (%)
Anxiolytics	Clonazepam	42%
	Etizolam	8%
	Aripiprazole	6%
	Lorazepam	4%
	Alprazolam	2%
Antipsychotics	Olanzapine	3%
	Flupenthixol	2%
Mood Stabilizer	Lithium	2%

3.6 Assessment of pattern and prescribing frequency of other prescribed medications in the study population

Other categories of drugs that were prescribed to the study population includebeta-blockers (24%), folic acid tablets (16%) and multivitamins (14%) have topped the chart. Other drugs that were co-prescribed in the study population were calcium lactate (7%), Naproxen (6%), PCM (2%), chlorpheniramine (4%), Synthetic levothyroxine (4%), sumatriptan (2%), pseudoephedrine (2%), dextromethorphan (2%), sodium valproate (2%) & oxcarbazepine (1%).

Table 5: List of prescribing frequency of other co-prescribed medications in patients

Medication	Number of Patients (%)
Propranolol	24%
Folic acid tablets	16%
Multivitamins	14%
Calcium lactate	7%
Naproxen	6%
Chlorpheniramine	4%
Synthetic levo thyroxine	2%
PCM	2%
Pseudoephedrine	2%
Sumatriptan	2%
Dextromethorphan	2%
Sodium valproate	2%
Oxcarbazepine	1%

3.7 Assessment of the number of drugs prescribed per prescription in the study population

The total number of drugs prescribed in the study population was analyzed. Out of 100 patients that have been included in the study, 32 were prescribed 3 drugs which accounted for a maximum number of people followed by 24 patients who were prescribed 4 drugs, and 20 patients were prescribed 2 drugs.

Table 6: List of the number of drugs prescribed per patient

Number of Drugs	Number of Patients (%)
1	6%
2	20%
3	32%
4	24%
5	8%
6	6%
7	4%

3.8 Assessment of prescribing frequency of polypharmacy:-

Polypharmacy was practiced in 96% of the population while monotherapy was practiced in only 6% of the population.

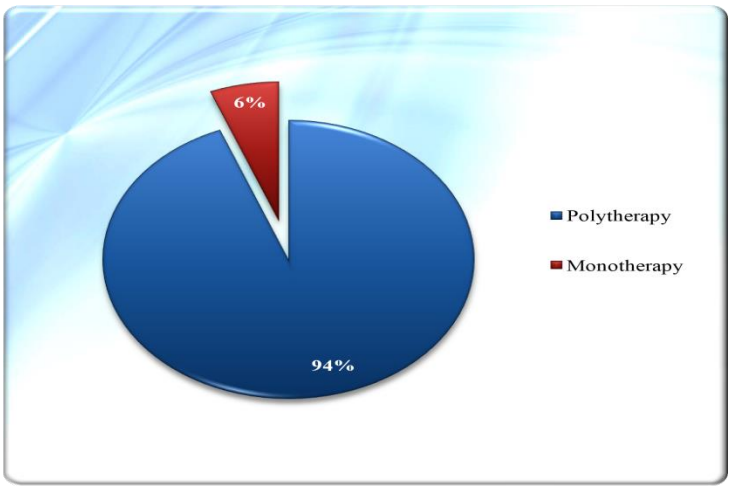

Figure 3. The pattern of prescribing frequency of polypharmacy among medical practitioners

3.9 Assessment of duration of treatment among patients: -

Among 100 patients that were involved in the study, 32 patients were on treatment for 1 month, followed by 26 patients on treatment of 2 weeks, 14 patients on treatment of 1 week, 10 patients on 3-week treatment, and only 8 patients on treatment of more than 1 month. The duration of prescribing was an average of 3 weeks, which may be because of the longtime taken by antidepressants to control symptoms.

Table 7: List of duration of treatment in patients

Duration	Number of Patients (%)
<1 week	6%
1 week	14%
2 weeks	26%
3 weeks	10%
1 month	32%
>1 month	8%

3.10 Assesment of prescribing frequency of drugs prescribed by generic name and brand name:-

A major proportion of drugs were prescribed by brand name (91%) while only a few (9%) were prescribed by generic names, which is not by the guidelines given by WHO. The use of generic medicines in the prescription is one of the most important criteria that promote rational utilization of drugs.

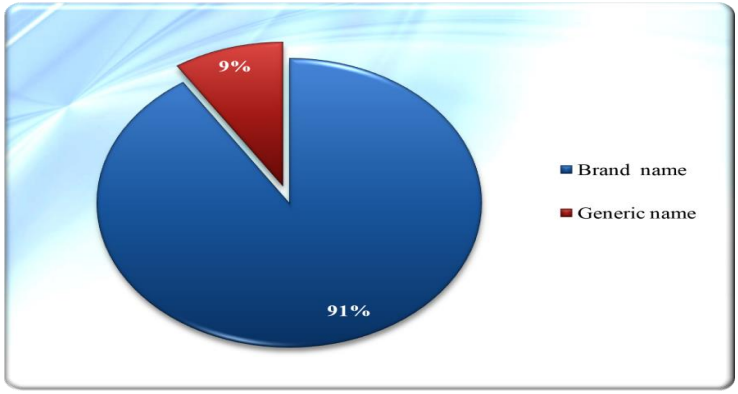

Figure 4.The pattern of prescribing frequency of drugs prescribed by generic name & brand name

3.11 Assessment of prescription patterns based on WHO Drug prescribing & Facility indicators:

The average number of antidepressants per prescription was 1.18%. No injections were prescribed in the study population. Only 9.35% of drugs were prescribed by generic name while the rest of the drugs were prescribed by brand name. The total number of drugs prescribed in 100 prescriptions was 342. The percentage of drugs prescribed from the national list of essential medicines was 46%. Average number of antidepressant drugs per prescription was 1.18%.

Table 8: WHO drug prescribing & facility indicators:

Category	Indicator	Statistics
Prescribing Indicators	Average number of drugs per prescription	3.42%
	Average number of antidepressant drugs per prescription	1.18%
	Percentage of prescriptions containing FDCs	8.2%
	Percentage of drugs prescribed by generic name	9.35%
	Percentage of prescriptions with an injection prescribed	Nil
	Percentage of drugs prescribed from NLEM	46.99%
Facility Indicators	Availability of copy of essential drug list	Yes
	Availability of key drugs	Yes

3.12 Assessment of prescribing frequency of fixed-dose combinations in patients

Out of 100 patients that have been observed in the study population, a total of 82 patients received the combination regimens. A combination of SSRIs with Benzodiazepines (62%) was most frequently used by psychiatrists followed by a combination of BZDs with propranolol (14%).

Table 9: List of prescribing frequency of fixed-dose combinations in patients

Fixed Dose Combinations Prescribed	Number of Patients (%)
Escitalopram + Clonazepam	62%
PCM + Chlorpheniramine + Pseudoephedrine	1%
Clonazepam + Propranolol	14%
Etizolam + Propranolol	10%
Pantoprazole + Domperidone	9%
Naproxen + Domperidone	1%
Paroxetine + Clonazepam	4%
Flupentixol + Melitracin	2%
Sumatriptan + Naproxen	1%
Chlorpheniramine + Dextromethorphan	2%
Nicotinamide + Cyanocobalamine	4%
Methylcobalamine + Niacinamide + Vit. B6	6%

3.13 Assessment of most frequently prescribed antidepressants in the study population

The maximum prescribed drug was Escitalopram (60%), followed by fluoxetine (13%), Desvenlafaxine (7%) &amitriptyline (5%).

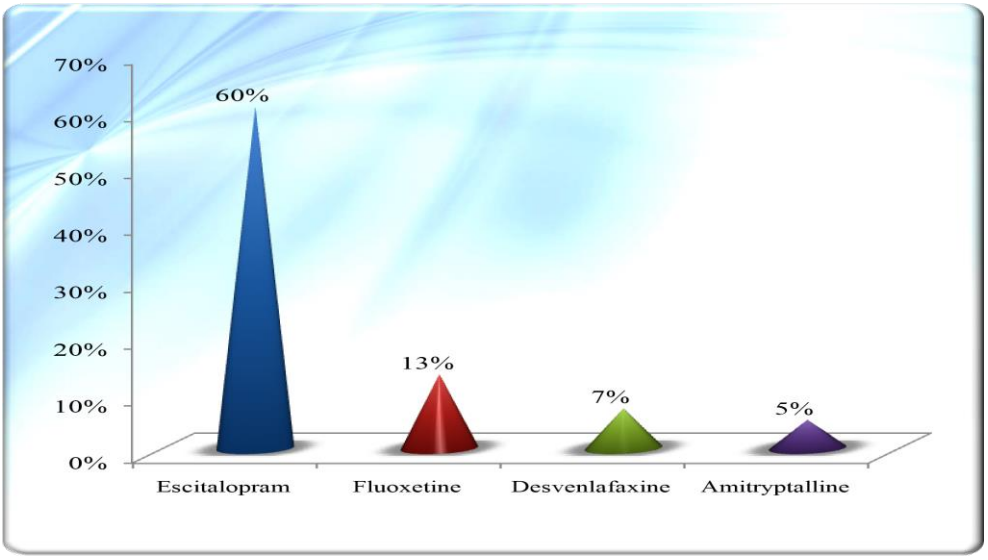

Figure 5. Pattern of most frequently prescribed antidepressants

4. Discussion

This work focused on the analysis of the prescriptions of antidepressants in a tertiary care teaching hospital and the following trends were observed. Depression was more common among males (61%).. This observation is in accord with some of the studies though it is contrary to other studies that have indicated that women have higher rates of depression. Grover et al. also stated that the gender distribution in terms of prescriptions was also balanced.

Regarding the age distribution, the greatest number of prescriptions was issued to patients of 21 to 40 (46%) and 41 to 60 (34%) years. This is due to several reasons such as this group has higher incidences of mood disorders, increased health consciousness, literacy levels, availability of better health facilities, and a variety of drugs to treat mood disorders. This contrasts with a study done in Australia where the highest prescription rate was observed among the 30-39 years age group.

The study of the prescriptions confirmed that endogenous depression &mixed depressive anxiety disorder were the most frequently diagnosis. Escitalopram (with clonazepam) and fluoxetine were the most commonly prescribed antidepressants because of the side effects associated with TCAs and MAO inhibitors classes. Among anxiolytics , Clonazepam were frequently co-prescribed with antidepressants. This observation is in accord with some other studies .Siddiqui et al. (2013) conducted a retrospective study of 400 patients regarding the prescription of antidepressants. Their study showed that Escitalopram and Fluoxetine were preferred, and the choice was given to SSRIs because of the safety aspect. This study also highlighted the fact that SSRIs are the most frequently used class of antidepressants.In contrast to a previous study done by Siddhartha Ghosh et al. (2014) in which prescriptions of 510 patients attending a tertiary care hospital were reviewed. This study discovered that the most prescribed antidepressant was Sertraline, while the second most common was Amitriptyline.

Multiple drug use was common, with most patients on one month course.Only 9% of drugs were prescribed generically .Fixed dose combinations were used in 8.2% of patients.Many patients were on multiple medications; the majority of the patients 94% were on polypharmacy. Polypharmacy is reported to be more costly compared to monotherapy as there are issues of drug interaction and side effects.

The same study also revealed that there is a preference for branded drugs over generic drugs; only 9% of the prescriptions contained generic drugs. This preference results in higher treatment costs and the demonstration effect of the pharmaceutical firms. According to WHO, generics are to be employed to decrease costs and improve patients' adherence, while most physicians still prescribe branded medications.

Some FDCs were seen to have been taken especially of Escitalopram and Clonazepam. Even though FDCs help enhance patient compliance and reduce the level of non-adherence, their use should be justified by co-morbid anxiety disorders to avoid the combination of drugs and side effects.

About the pattern of drug utilization, the patients preferred SSRIs particularly Escitalopram because they have fewer side effects compared to TCAs and MAO inhibitors. MAO inhibitors were never used, and TCAs were used less often because of side effects. Lithium which was used for bipolar depression was not frequently used because of its extremely narrow safety margin, while atypical antipsychotics like Olanzapine were used in refractory cases and for the negative symptoms associated with psychosis.

Hence, the study focuses on the need to assess the relevance of the antidepressant prescription to improve the safety of the patient, their adherence to the prescribed treatment, and the costs of the treatment.

5. Recommendations

The following are important recommendations for the rational use of drugs and enhancement of health care outcomes. It is therefore important to establish national regulatory institutions to oversee the prescription and use of the drugs. These bodies should ensure that the labeling is followed, that the dangerous drugs are restricted, and that the usage of the drugs is properly managed. Furthermore, the formation of the drug and therapeutic committees at the district and hospital level can aid in following the clinical guidelines and usage of the necessary medicines. The integration of PPT as one of the components of an undergraduate program will equip future HC professionals with the knowledge of rational prescribing. Supervision, auditing, and feedback are needed to maintain the standards at the necessary level. It is possible to state that media and medical camps together with public education campaigns can be rather helpful in increasing the level of knowledge of the rational use of drugs. It is suggested that pharmaceutical firms should avoid offering large financial incentives to physicians since these may result in over-prescription. Governments must spend sufficiently on the availability of medicines and healthcare personnel while applying the right regulations and relying on independent information. CME programs should be mandatory for healthcare practitioners so that they can be able to implement the best practices. Prescribers also have a major role in providing generic drugs and ensuring the prescription is up to date. Compliance with other measures that have been set by the medical councils such as prescribing generic drugs also improves the rational use of drugs. It should be based on proper diagnosis, and reduction of multiple medications and should refer to national essential medicine's lists. Therefore, the measures taken and the promotion of general awareness among doctors and the public can go a long way in attaining the objective of rational, safe, and efficient utilization of drugs. managing drug costs, enhancing the healthcare systems, avoiding medication mistakes, assessing the efficiency of drug therapy, and recognizing the sectors that require more education of the practitioners (Barbui et al., 2009). The importance of these studies is to promote the rational and safe use of drugs, establish the benchmarks for the best healthcare practice, and to give feedback to the physicians about their prescribing habits (Furukawa et al., 2003). Twelve interventions as recommended by WHO can be implemented to support the rational use of medicines; these are the formation of national committees for policy, development of clinical norms, and public education (Grover et al., 2013). The average number of drugs per encounter, the percentage of drugs prescribed by generic name, and the use of antibiotics and injections are some of the indicators that are used to monitor drug use, which in turn enhances the standards and the practices of prescribing drugs (Ambwani & Mathur, n.d.).

6. Limitations:

Small sample size. More data need to be collected from other medical centres & hospitals to evaluate & to extend the generalizability of results

7. Conclusion

A cross-sectional study was conducted on 100 psychiatric outpatients' prescriptions using WHO core drug use indicators to identify notable trends in the prescription of antidepressants. Depression was most prevalent among patients aged between 20 and 40 years, with 46% of the participants affected; male patients were more affected with 61%, and married patients affected with 62%. The study also revealed that out of all the types of depression, endogenous depression was the most common, with 28% of the patients, while 26% of the patients had mixed depressive anxiety disorder.

Escitalopram together with clonazepam was the most often prescribed antidepressant, while fluoxetine was also commonly used. Thus, polypharmacy was used in 94% of cases. One of the major concerns identified was that 91% patients were prescribed branded drugs over generic drugs, and only 46% of the drugs prescribed belonged to the National List of Essential Medicines. FDCs were prescribed to 8. 2% of patients, and the most common ones are Escitalopram and clonazepam.

The study shows that the population continues to use drugs irrationally despite the WHO guidelines and efforts from the government. The enhancement of awareness among doctors is essential for the proper use of antidepressants, fewer prescription rates, and fewer drug interactions and side effects. The goals should include the protection of patient's rights and the improvement of treatment outcomes with an emphasis on the decrease of the consumption of expensive and patented drugs and the increase of the consumption of cheap and effective first-line drugs and essential medicines.

The study thus highlights issues with generic prescribing, essential medicine utilization, polypharmacy & FDCs leading to higher costs and potential side effects.So, Rational prescribing practices are necessary to improve the effectiveness of treatment and to reduce healthcare costs,with a focus on generic medicines.

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