



Drug Prescription Pattern of Psychotropic Drugs Used for the Management of Schizophrenia in a Tertiary Care Speciality Hospital in South Kerala

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Authors' contributions

This work was carried out in collaboration among all authors. Author DD designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SPK and KGR supervised the study. All authors read and approved the final manuscript.

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ABSTRACT

An individual affected by psychotic illness is usually a burden to both the society as well as their family in terms of non-productivity. The WHO recognized the significance of mental health and defined it as "a state of complete physical, mental and social well-being". A psychiatric or psychotropic medication refers to a psychoactive substance administered to exert an effect on the chemical makeup of the brain and nervous system. A hospital based cross sectional observational study was undertaken in the Mental Health Centre, Trivandrum. All psychiatric drugs prescribed was collected with the help of data collection form and analysed with Excel and SPSS. The study data indicated that highest percentage of drugs used was coming under the classification antipsychotic agents (63.25%), followed by antianxiolytic agents (21.25%), antiepileptic agents (9.34%), antimania agents (3.07%) and antidepressants (3.07%). Highly prescribed antipsychotic agent was Risperidone (12.93%) followed by haloperidol (11.40%), Promethazine (10.50%). This study was conducted in a govt hospital, so all medicine was free of cost. Due to the poor financial quality of life of psychiatric patients, prescribers were forced to write the hospital available medicine to the patients. The main limitation of this study was, it is only a single centered study so the result was very limited. So multicentered study is recommended to get a better result to find out the prescribing pattern and pattern of schizophrenia in Kerala.

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1. INTRODUCTION

Psychiatry became a specialty within medicine in the early 1800s. In the first century of its existence, the field concerned itself with severely disordered individuals confined to asylums or hospitals. Around the turn of the 20th century, Sigmund Freud published theories on the potential cause of some of these less severe disorders and termed them psycho-neuroses. These disorders impaired relationships and work, or produced odd symptoms such as paralysis or mutism that could not be explained medically. Freud developed psychoanalysis to treat these "neurotic" patients. However, psychiatry soon became the specialty known for providing this treatment and psychoanalysis became the first treatment for psychiatric outpatients. It also created a split in the field, which continues to this day, between biological psychiatry and psychotherapy [1]. Many psychiatric disorders are inheritable and among them, schizophrenia, bipolar disorder, and attention-deficit hyperactivity disorder are the most heritable. The interaction and combination of different genes contribute to the risk of psychiatric disorders. With the help of modern genomic technologies, genotyping has become relatively easier, cheaper and accurate. This will certainly improve researchers' ability to identify risk-associated genetic variants in a single study containing tens to thousands of patients. Unfolding of such genetic clues over the next few years would help scientists discover newer ways to investigate and treat neurobiological dysfunctions [2].

Schizophrenia is a chronic and severe mental disorder affecting 20 million people worldwide [2] and it is characterized by distortions in thinking, perception, emotions, language, sense of self and behaviour. Common experiences include hallucinations (hearing voices or seeing things that are not there) and delusions (fixed, false beliefs). Worldwide, schizophrenia is associated with considerable disability and may affect educational and occupational performance. People with schizophrenia are 2-3 times more likely to die early than the general population [3]. This is often due to preventable physical diseases, such as cardiovascular disease, metabolic disease and infections. Stigma, discrimination and violation of human rights of people with schizophrenia is common. Schizophrenia is treatable. Treatment with medicines and psychosocial support is effective.

Facilitation of assisted living, supported housing and supported employment are effective management strategies for people with schizophrenia [2].

Antipsychotic medications are primarily indicated for the treatment of schizophrenia and other psychotic disorders. The drugs used for the treatment of schizophrenia was categorized as first-generation antipsychotics (FGAs) or 'typical' or 'conventional' and second-generation antipsychotics (SGAs) or 'atypical' antipsychotics. The chance of adverse effects associated with FGAs, led to the introduction of the SGA medications in the 1990s. Hence, the present study was carried out to observe the prescribing pattern of antipsychotics in tertiary care mental hospital, assess the trends in prescription writing and the prevalence of antipsychotic usage in the community.

2. METHODOLOGY

2.1 Study Area

Mental Health Centre, Trivandrum Kerala; it is a tertiary mental health institute under department of health, Government of Kerala with over 500 inpatient bed ,over 4000 inpatients and 40000 outpatients per year.

2.2 Study Population

About 137 patient were selected based on the inclusion and exclusion criteria

2.3 Study Design

A hospital based prospective, cross-sectional observational study.

2.4 Criteria for Selection Patients

2.4.1 Inclusion criteria

Subject who were seeking treatment at Psychiatry IPD for various psychiatric disorders and willing to participate.

Patient from all age groups and both sexes were included.

Those who understood the purpose of the study and were ready to provide information regarding

their health status and those who signed an informed consent documents.

2.4.2 Exclusion criteria

Not willing to participate.

Having a history of substance abuse, malignancies and terminally ill.

Being judged clinically to be at a suicidal risk (too serious to be excluded in the study).

Those unable to comprehend for other reasons and mentally retard.

2.5 Sampling Technique

Consecutive sampling was used till the adequate sample size is reached. The first patient was recruited after obtaining ethical committee clearance.

2.6 Study Duration

Starting from January 2019 to July 2020.

2.7 Study Procedure

Data of patients during the study period was collected in the data collection form after ethical clearance committee approval. Following data was

collected for analysis. a) Patient demographic details like: Age, Sex, final diagnosis, Employment status, Marital status, educational status, economic status, family history, contributing factors, drugs, route of administration, dosage form, frequency of administration, number of drugs prescribed by generic name, number of prescribed drugs which are available in hospital drug store are collected and recorded.

2.8 Data Analysis

Data analysis was done by EXCEL and SPSS.

3. RESULTS AND DISCUSSIONS

3.1 Age wise Classification of Patients

Out of 442 patients recruited, 137 were diagnosed with schizophrenia based on ICD 10 classification. Among the 137 patients high percentage of patients were belong to 31-40 years of age group (30.7%) followed by 41-50 years (29.2%), 21-30 years (18.2%), 51-60 years (15.3%), 6.6% of <20 years, 61-70 years and >70 years. That means among the overall patients average age was 35.5 years (Fig. 1). But Yıldız M et al [4] study showed that the mean age for the onset of the illness was found to be 23.5 [4].

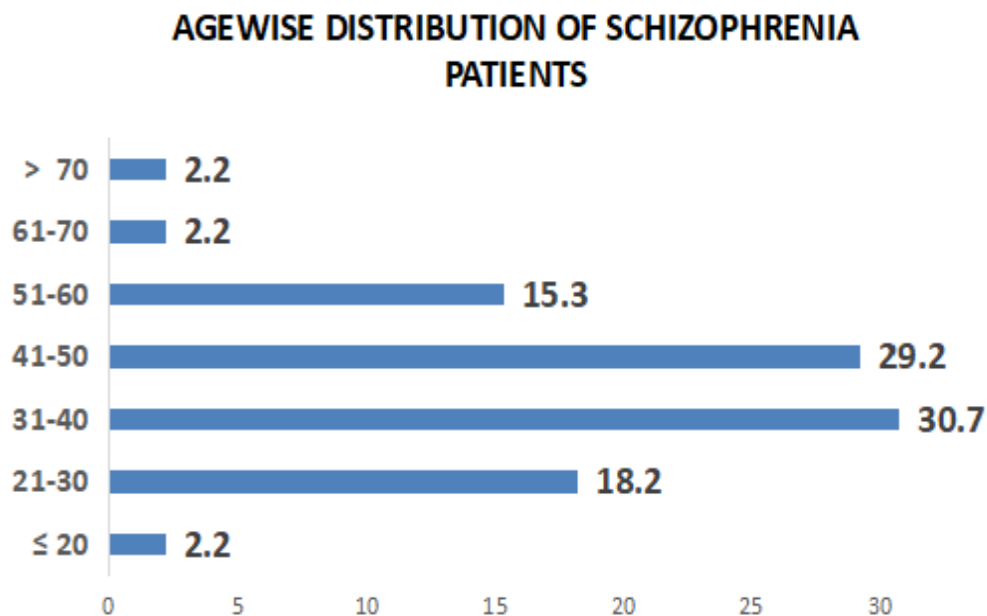


Fig. 1. Agewise distribution of patients

3.2 Genderwise Distribution of Patients

Among overall (137) patients, 52% were male and 48% were female. This result showed the similarity with the study conducted by Koujalgi SR et al [5] the result showed that in the gender category, the number of male respondents in the schizophrenia group were 57 (57%) and 43 (43%) were observed as female respondent [5] (Fig. 2).

3.3 Marital Status of Schizophrenia Patients

Out of 137 schizophrenia patients, 46.7% became married followed by 32.1% unmarried, 15.3% divorced and 5.8% widow. The result was same as the study conducted by sushma et al [4] explained that 76 patients were married, and 24 were unmarried [6]. But the sum of unmarried and divorced was higher than married reveals that the disease affect the patient's quality of life. The study conducted by Koujalgi SR et al [5] and the result of their study showed that 57 (57%) schizophrenics remained unmarried, (29%) of the respondents in the schizophrenia group were observed as married. When comparison was made in the divorce category, 14 (14%) of the schizophrenics were found to be divorced [5] (Fig. 3). The result of this study reveals that the society will not accept a psychiatric patients. That may leads to social withdrawal and being alone, this mentality of public's towards the psychiatric patients may leads to mental trauma. The govt and some NGO started some rehabilitation center and rehabilitation programme for patients those who discharged from the hospitals.

3.4 Religious Status of Schizophrenia patients

In somecases religions play an important factor for treatment. The data suggested that ,among 137 patients, high percentage were came from Hindu religion (60.6%) followed by Muslim (22%) and Christian [6] (17%). The result was same as the study conducted by sushma et al [7] explained that schizophrenia was found to be more common in Hindus (93%) compared with Muslims (7%). The leading occurrence of schizophrenia is seen among Hindus and in married people, similar to finding of Nepal study. Because India is a Hindu dominated country so obviously most of the patients are expected to be from Hindu religion [8] (Fig. 4).

3.5 Economic Status of Schizophrenia Patients

In this study we used Kuppuswamy's socioeconomic status for identifying the patients economic status. It was found that 100% of patients among 137 were living with lower economic status and also they were living in rural area. But the study conducted by sushma et al [7] explained that it was more commonly seen in people from urban area (66%) than rural (44%). Since it was a hospital based study and the hospital was undertaken by govt of kerala. Only poor people or lower economic people prefer govt hospital rather than private hospital due to the high treatment cost. Middle class and upper class patients and their family prefer private hospital and private consultation (Table 1).

3.6 Educational Status of Schizophrenia Patients

Early social and cognitive alterations in schizophrenia, associated with familial liability and environmental exposures, may contribute to lower than expected educational achievement. The study data explained that 53.3% of patients had high school education followed by 26.3% middle school education, 9.5% illiterate, 7.3% graduates, 2.9% professional qualification and 0.7% had primary education. Means that majority of schizophrenia patients completed their high school education.

3.7 Occupational Status of Schizophrenia Patients

The employment rates are high in India, the mental health of persons affect their employment status. As far as occupation is concerned, schizophrenia is commonly seen in unemployed people (89.8%) followed by 5.1% skilled workers, 4.4% professionals and 0.7% semiskilled workers. This is similar to the conclusion of research done by sushma et al. [7] as it revealed that Schizophrenia was more commonly seen in unemployed people (39%) (Fig. 6). The study found that belonging to rural area reduces the possibility of maintaining employment status. Those from rural area were either employed in skilled labor or semiskilled work like weaving, tailoring and coolies. Once they lose a job due to mental disorder they may not find other similar opportunities and therefore, remain unemployed. People with schizophrenia are prone to human rights violations both inside mental health institutions and in communities. Stigma of the

disorder is high. This contributes to general health care, education, housing and discrimination, which can in turn limit access to employment [9].

DERWISE DISTRIBUTION OF CHIZOPHRENIA PATIENTS

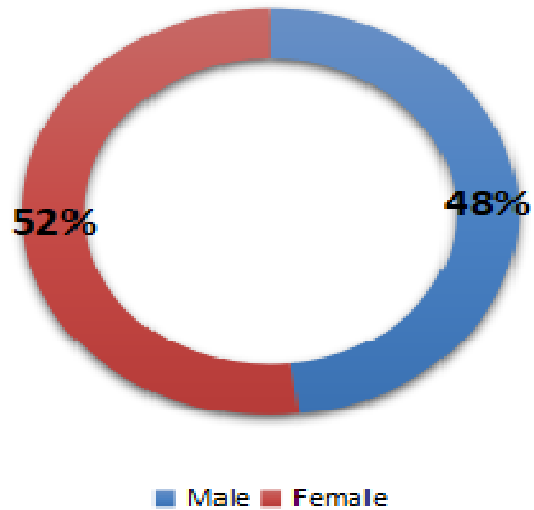


Fig. 2. Genderwise distribution of patients

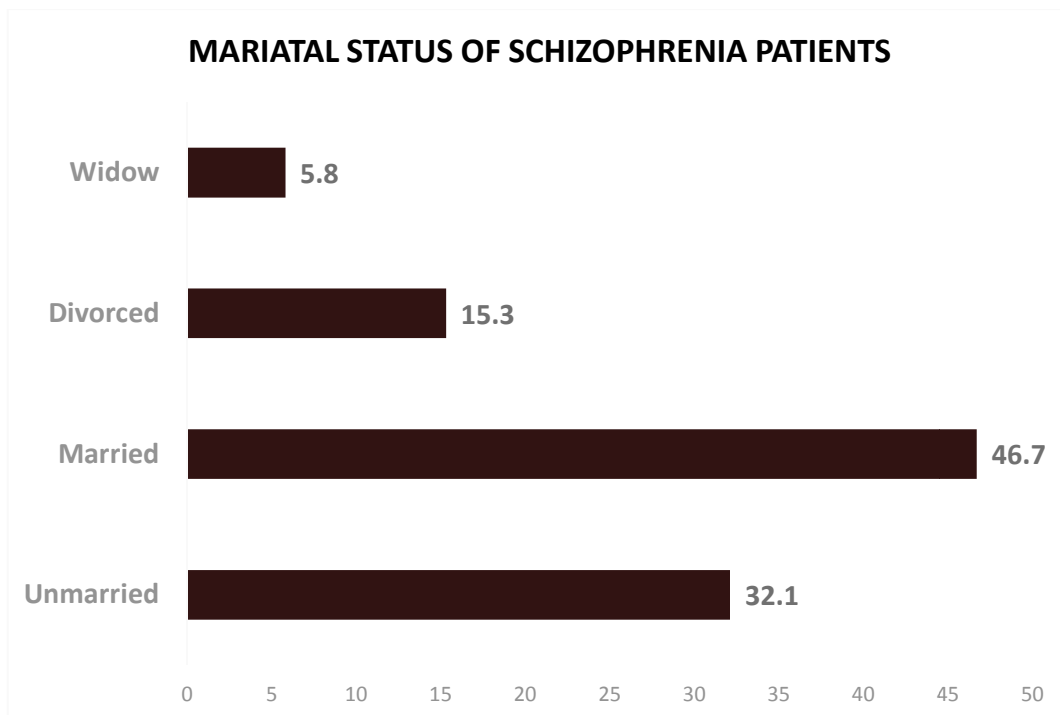


Fig. 3. Mariatal status of schizophrenia patients

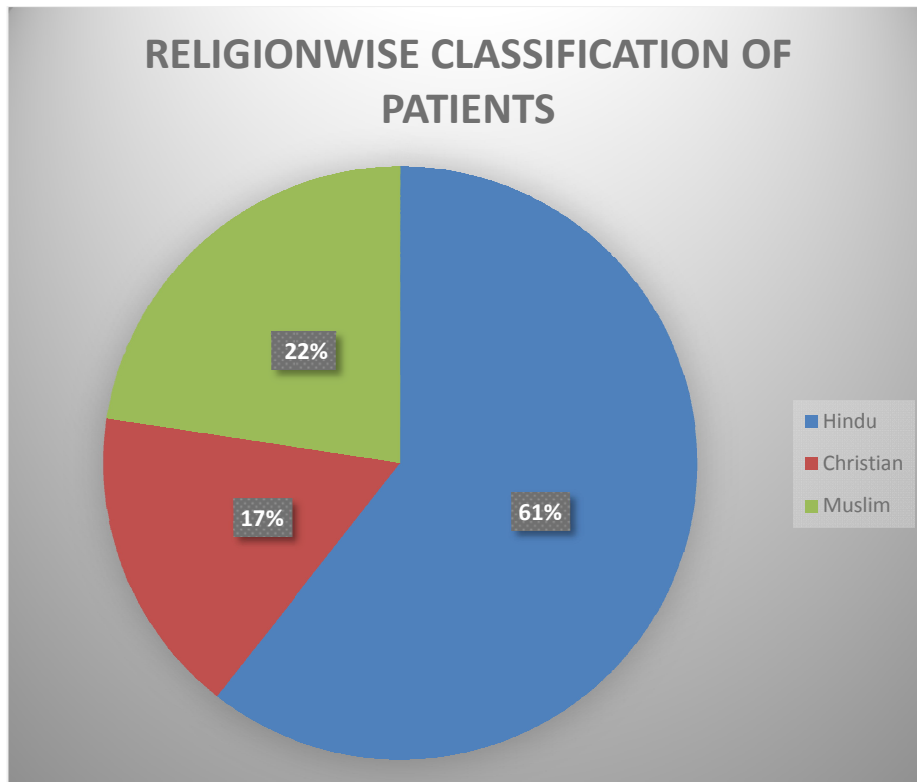


Fig. 4. Religious status of schizophrenia patients

EDUCATIONAL STATUS OF SHIZOPHRENIA PATIENTS

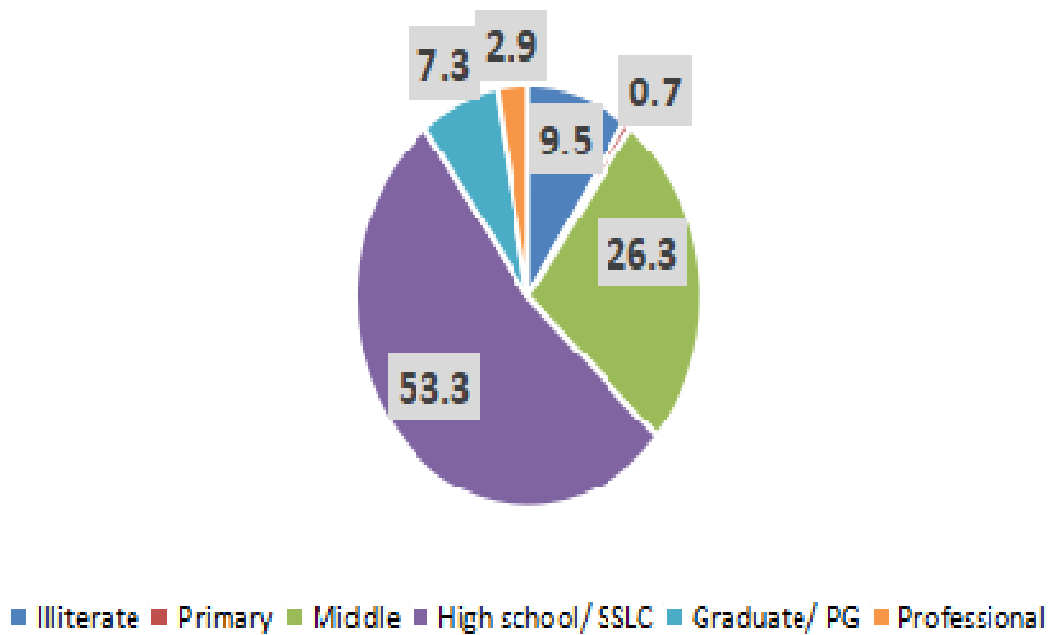


Fig. 5. Educational status of schizophrenia patients

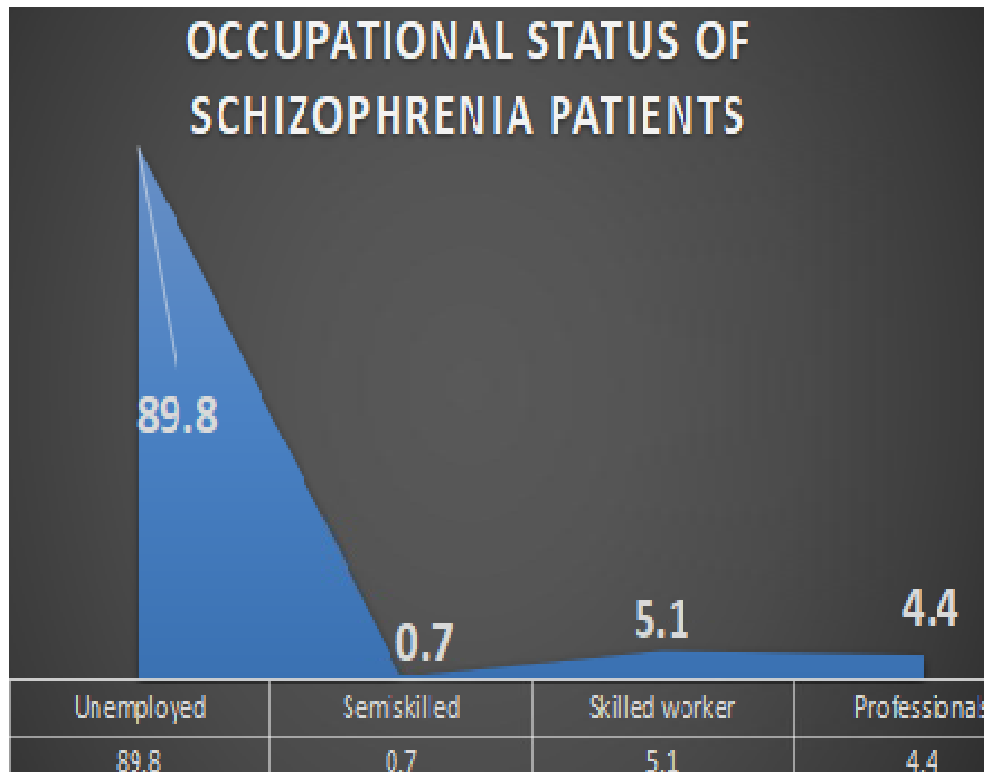


Fig. 6. Occupational status of schizophrenia patients

Table 1. Economic status of schizophrenia patients

Socio economic status	Schizophrenia	
	f	%
Upper	0	0
Lower	137	100
Total	137	100

3.8 Association of Family History in Schizophrenia

Among 137 patients majority of patients does not have any history of schizophrenia in their family members (69.3%). 8.8% was reported with the history with father followed by 6.6% mother, 2.9% siblings, 0.7% both parents, 0.7% father & siblings, 1.5% mother and siblings and 8.8% other relatives (Fig. 7). This result shows a little similarity with the study conducted by Jun Chou et al [10] the prevalence of schizophrenia in individuals with an affected first-degree relative is 6.3-fold higher, and with an affected second-degree relative 2.4-fold higher than in the general population, indicating a dose-response relationship between the risk of schizophrenia and genetic distance [10] (Fig. 7).

3.9 External Contributing Factors in the Development of Schizophrenia

Among 137 patients, 4.4% used frequent alcohol followed by 5.8% smoking, 4.4% cannabis 4.4% nicotine and 0.7% was reported as stress is a contributing factor. This result showed a similarity with the study conducted by Nielsen SM et al [11] showed that diagnosis of substance abuse increased the overall risk of developing schizophrenia [hazard ratio (HR) 6.04, 95% confidence interval (CI) 5.84-6.26]. Cannabis (HR 5.20, 95% CI 4.86-5.57) and alcohol (HR 3.38, 95% CI 3.24-3.53) presented the strongest associations [11] (Fig. 8). Research has not identified one single factor. It is thought that an interaction between genes and a range of environmental factors may cause schizophrenia.

Psychosocial factors may also contribute to schizophrenia [9].

3.10 Drugs Used for the Management of Schizophrenia

Treatment options for management of schizophrenia can be broadly classified as antipsychotic medications, electroconvulsive therapy (ECT), adjunctive medications and psycho-social interventions. The essential choice is between using an antipsychotic belonging to the class of typical antipsychotics (FGA-first-generation antipsychotic) or from the atypical group (SGA-second-generation antipsychotic). The study data indicated that highest percentage of drugs used was coming under the classification antipsychotics agents, including both typical and atypical (63.25%), followed by antianxiotic agents (21.25%), anti-epileptic agents (9.34%), anti-mania agents (3.07%) and antidepressants (3.07%) (Fig. 9).

3.11 Antipsychotic Utilisation Pattern in Schizophrenia

In this study 32.52% prescriptions were atypical antipsychotics, and typical antipsychotics were 29.50% which is comparable to the studies done by Nukala S et al [12]. Risperidone was the most commonly prescribed (12.93%) followed by haloperidol (11.40%), Promethazine (10.50%), olanzapine (6.40%), quetiapine (3.71%), Chlorpromazine (2.70%), Fluphenazine (10.50%), Zuclopenthixol (0.25%), Flupenthixol (0.64%), clozapine (4.45%), amisulpride (1.02%) and third generation antipsychotics Aripiprazole (1.28%). This showed a trend towards the use of newer atypical antipsychotics which are known to

be better tolerated with less extrapyramidal symptoms than the typical antipsychotics. Anticholinergic should be used along with risperidone for the prophylaxis and management of EPS (Table:2, Fig. 10). In a similar Indian study conducted by Iliaz et al. In 2013-2014, most commonly prescribed antipsychotic was Risperidone (40.8%) followed by Quetiapine (8.62%), Olanzapine (4.02%), Amisulpride (4.02%), Aripiprazole(0.57%). But study conducted by Munjely et al [13] showed that atypical antipsychotics were prescribed more than typical ones. In present study haloperidol (22.9%) was the most frequently prescribed antipsychotic followed by Olanzapine (20.9%), Risperidone (18%), Clozapine (12.7%), Fluphenazine (9%), Chlorpromazine (8.2%), Trifluoperazine (7.4%), Quetiapine (2%) and Aripiprazole(1.6%) [13].

3.12 Antidepressants Utilisation Pattern among Schizophrenia Patients

Antidepressants are generally used as concomitant medication with antipsychotics in patients with schizophrenia. Among the 3.07% of prescribed antidepressants 2.60% of selective serotonin re uptake inhibitors, 0.13% of tricyclic antidepressants and 0.40% atypical antidepressants were used. The study showed the details of percentage of prescription of various antidepressants were found are Escitalopram (1.15%), followed by Sertaline (0.64%), fluoxetine (0.51%), fluvoxamine (0.25%), bupropion (0.25%) and mirtazapine (0.13%) (Table 3, Fig. 11). The combination of a second-generation or atypical antipsychotic agent with an SSRI has been reported the most popular choice among psychiatrists worldwide [14].

Table. 2. Antipsychotic utilisation pattern in schizophrenia

Classification	Drug Name	N	Percentage	Percentage	
First Generation(Typical)	Phenothiazines	Chlorpromazine	21	2.70%	29.50%
		Fluphenazine	31	4.00%	
		Promethazine	82	10.50%	
	Butyrophenones	Haloperidol	89	11.40%	
		Thioxanthins	Zuclopenthixol	2	
	Flupenthixol		5	0.64%	
Second Generation (Atypical)	Qutiapine	29	3.71%	32.52%	
	Risperidone	101	12.93%		
	Olanzapine	50	6.40%		
	Clozapine	66	4.45%		
	Amisulpride	8	1.02%		
Third Generation	Aripiprazole	10	1.28%	1.28%	

FAMILY HISTORY OF SCHIZOPHRENIA

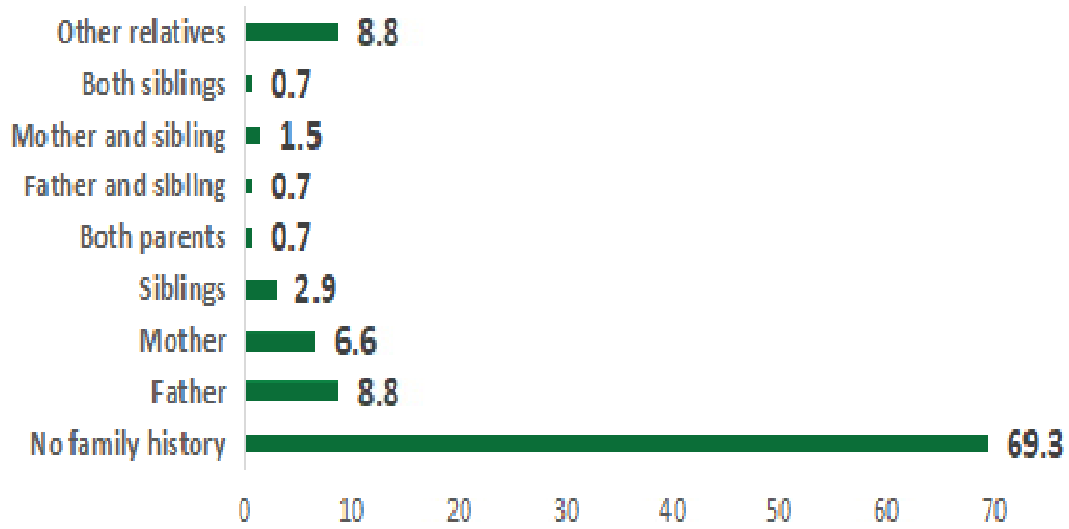


Fig. 7. Association of family history in schizophrenia

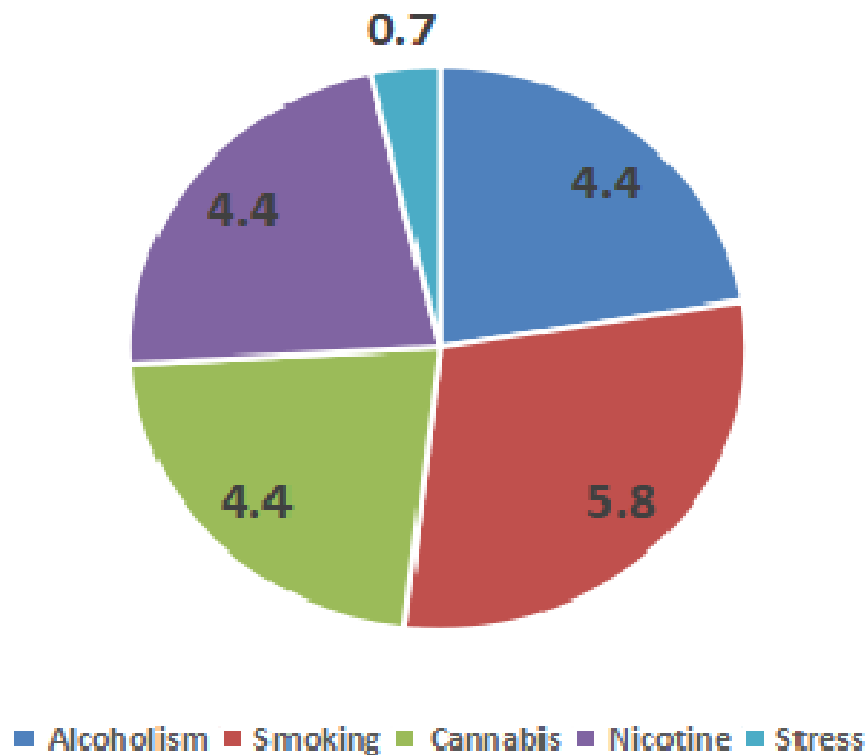


Fig. 8. External contributing factors in the development of schizophrenia

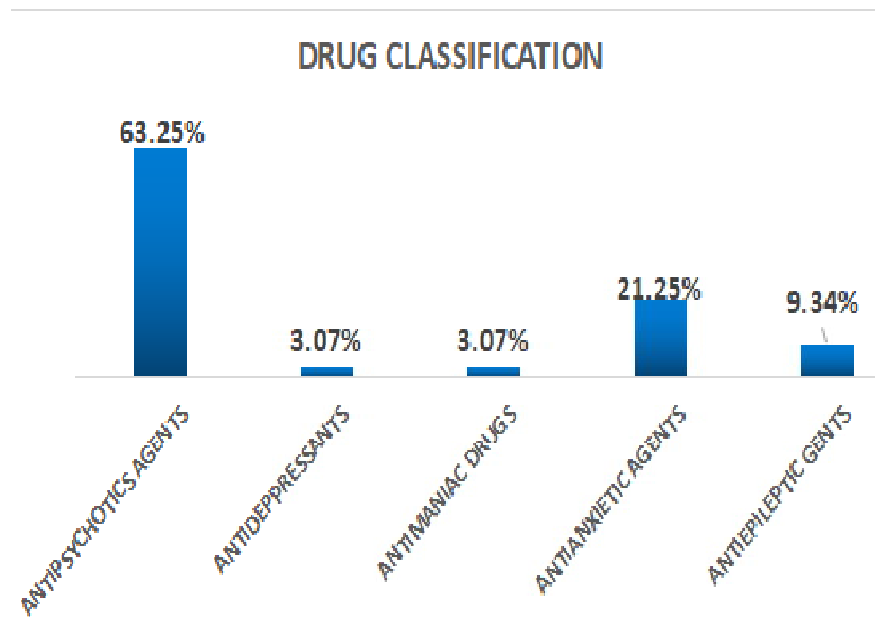


Fig. 9. Drugs used for the management of schizophrenia

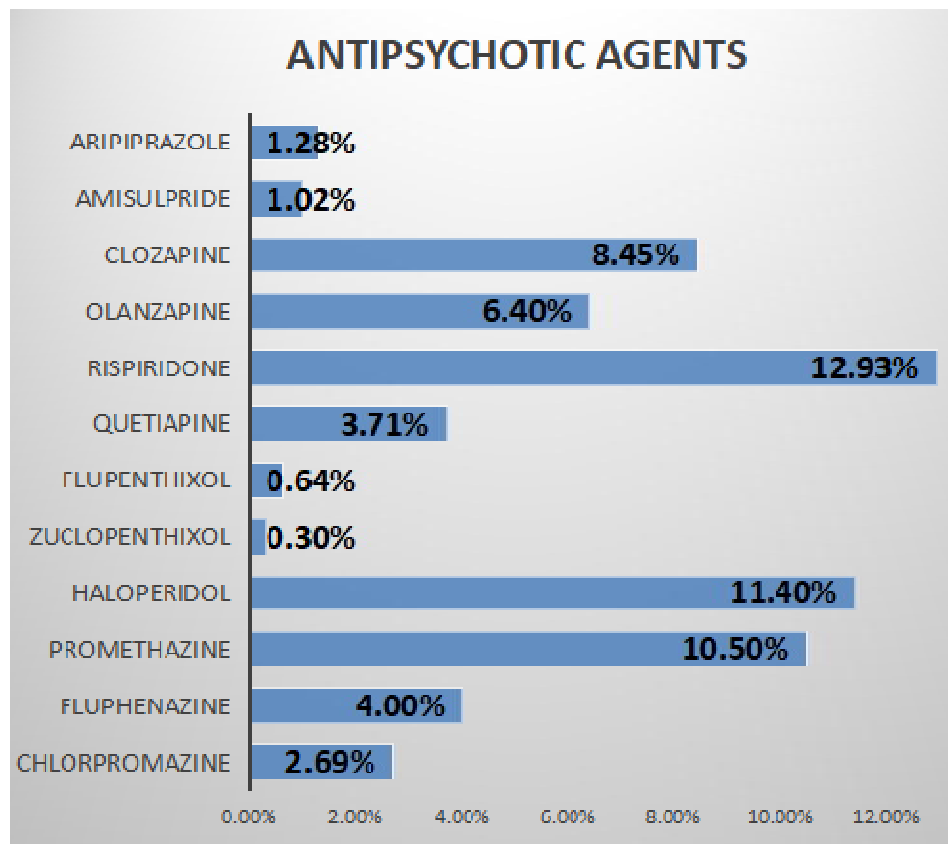


Fig. 10. Antipsychotic utilisation pattern in schizophrenia

Table 3. Antidepressants utilisation pattern among schizophrenia patients

SI No	Drug class	Percentage
	Ssris	2.60%
	Tca	0.13%
	Atypical	0.40%
	Antidepressant	

3.13 Antianxiety Agents Prescription Pattern among Schizophrenia Patients

The presence of the comorbidity of anxiety in schizophrenia results in reduced cognitive functioning, increases the severity of comorbid medical conditions, increases the risk of reoccurrence, adds to internalized stigma, reduces functioning, and has a negative impact on the overall outcome for the patient. Anti-anxiety medications mainly used to reduce the symptoms of anxiety, such as panic attacks or extreme fear and worry. Out of total antianxiotic drugs prescribed (21.25%), majority were benzodiazepines, short acting 11.14% and long acting 9.90%. The details of percentage of drugs prescribed was lorazepam 9.73% followed by diazepam 5.12%, Clonazepam 4.74%, nitrazepam 1.41%, chlordiazepoxide 0.13% and phenobarbital from barbiturate category 0.13%. Alprazolam was not prescribed to any patients because of its dependency. Lorazepam was used both intravenous and oral route and others were used as per oral route of administration.

The study showed similarity with the study conducted by Perumal et al. [15] showed that anti-anxiety drugs prescribed, majority were Benzodiazepines [15]. (Fig. 12). In practice, two strategies are available to satisfactorily manage the severe anxiety associated with acute psychotic episodes: the use of sedative antipsychotic drugs or the use of adjuvant benzodiazepines therapy. These sedative antipsychotics have been shown to have anxiolytic effects at low doses both in nonpsychotic patients and during acute psychotic episodes. In order to prevent the risk of benzodiazepine dependence and rebound anxiety on the cessation of treatment, the use of benzodiazepines should be for as short a period as possible. Benzodiazepines should be prescribed in combination with non-sedative disinhibitory atypical antipsychotics [16].

3.14 Antimania and Antiepileptics Drugs Prescribed in Schizophrenia, Mood Stabilizing Agent

The oldest and most studied of mood stabilizers is lithium. Many drugs that were first developed as anticonvulsants also act as mood stabilizers. Mood stabilizers are not the drugs of choice in the treatment of schizophrenia. Commonly prescribed mood stabilizing agents in schizophrenia include carbamazepine, valproic acid and lamotrigine. Gabapentin and topiramate are also coming under the classification of anticonvulsants that may act as mood stabilizers,

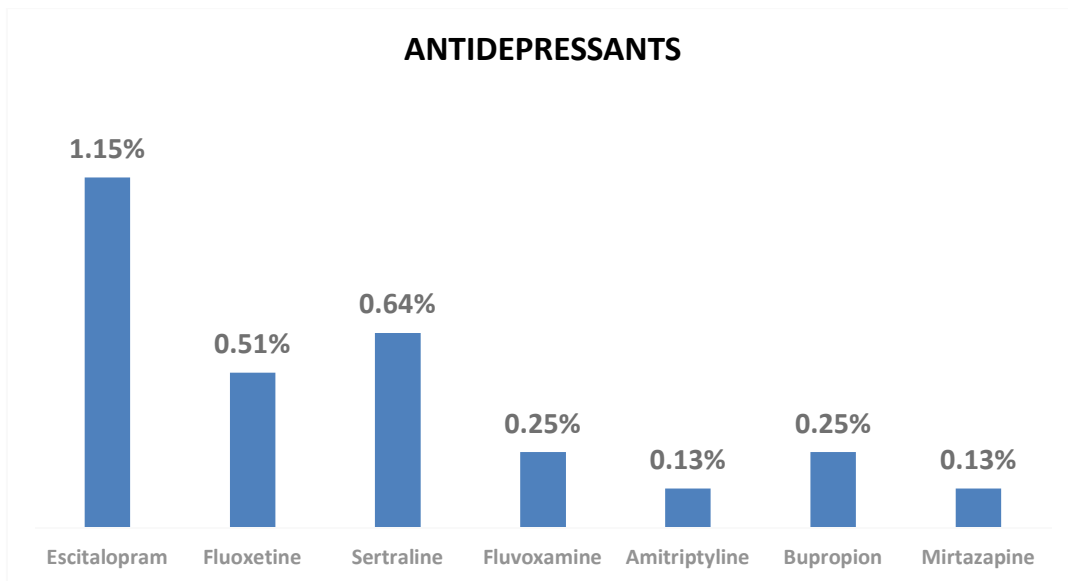


Fig. 11. Antidepressants utilisation pattern among schizophrenia patients

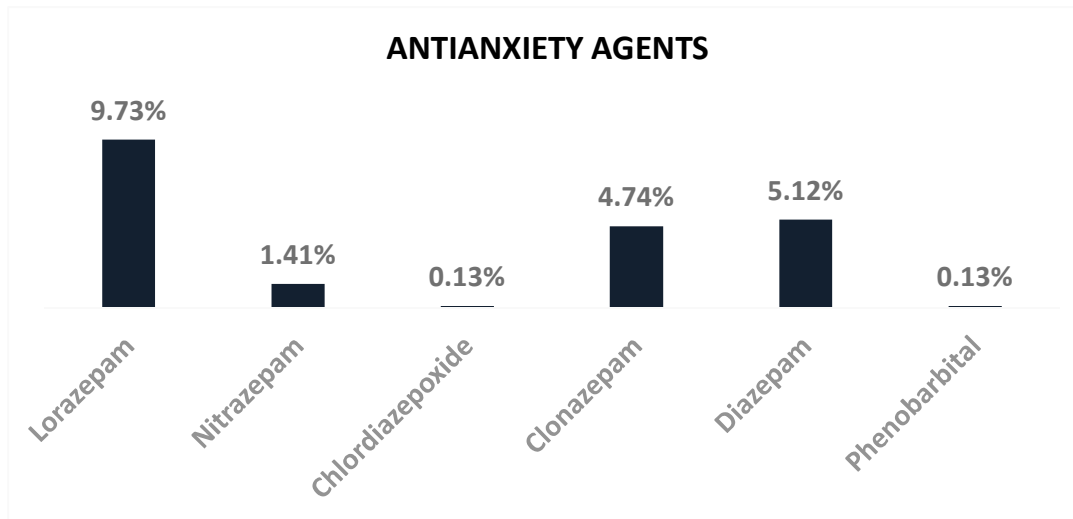


Fig. 12. Antianxiety agents prescription pattern among schizophrenia patients

but they are usually given in addition to other medications. In this study it was found that, in the case of schizophrenia the highly prescribed mood stabilizing agent was Lithium (3.07%) (24 prescription) and Lamotrigine 9.34% (73 patients). Lamotrigine is expected to influence the positive, negative, affective and cognitive symptoms of schizophrenia [15]. but could be considered. Lithium blood levels can increase to dangerous levels when a person becomes severely dehydrated. So every patient who take lithium was advised to drink eight to 12 cups of fluid per day to avoid severe dehydration and routine monitoring of serum lithium level was monitored during the course of therapy. The signs that the amount of lithium in the body is higher than it should be include severe nausea, vomiting and diarrhea, shaking and twitching, loss of balance, slurred speech, double vision and weakness. Lamotrigine may be the most effective and highly prescribed mood stabilizer. The starting dose of lamotrigine should be very low and increased very slowly over four weeks or more. This approach decreases the risk of potential side-effect.

4. CONCLUSIONS

In India, the studies in the field of psychiatry is very less in number as compared with other speciality. This study reveal the prescription pattern of psychotropic drugs in mental health. It provides opportunities for enhancing the quality of mental healthcare in our environment, through awareness creation for rational and cost-effective use of psychotropic medicines. This study

explain the, financial background literacy rate and employment status of patients. That will help to identify the socioeconomic status of schizophrenia patients. And also number of patients in this study was came from lower income background and many of them used alcohol, cannabis and nicotine. It was suggested that Schizophrenia was more common in low-income individuals compared to their non-low-income counterparts. Lower income, unemployment, low literacy rate, unmarried and divorce may influence the disease occurrence and pattern. In recent years, newer atypical anti-psychotic agents such as olanzapine, risperidone, quetiapine and clozapine have provided a better control of symptoms and have fewer adverse effects than typical anti-psychotic agents. The newer atypical antipsychotics have also proved to be better in improving the negative symptoms, cognitive dysfunction and are efficacious in neuroleptic-resistant schizophrenia [17,18]. The study concluded that whatever the guidelines are their, the pattern of prescription was always depends on the availability of drugs in hospital pharmacy or community pharmacy. This study was conducted in a govt hospital, so all medicine was free of cost. Due to the poor financial quality of life of psychiatric patients (89% were unemployed), prescribers were forced to write the hospital available medicine to patients. High cost medication may leads to medication noncompliance. The main limitation of this study was, it was a single centered study so the result was very limited. So multicentered study is recommended to get a better result to find out

the prescribing pattern and pattern of schizophrenia in kerala and also further research is essential to improve prescribing practice in schizophrenia.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Ethically approved from the Institution's Ethical Committee of mental health centre, Trivandrum.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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