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Review Article

Assesment of Antipsychotic Polypharmacy in Patients with Bipolar Affective Disorder in a Tertiary Care Hospital

Dr. Manohar Naik K[1], Dr. Roshan P [2], Dr. Fathimath Hasna[2], Dr. Zainabath T A[2], Dr. Priyanka K[2]

[1]Associate Professor, Department of Pharmacology, Shree Devi College of Pharmacy, Mangalore, Karnataka – 574142

[2] Pharm D Intern, Indiana Hospital And Heart Institute, Pumpwell, Mangalore, Karnataka, 575002

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Corresponding author: Dr. Roshan P

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Abstract:

Bipolar affective disorder is a mental illness characterized by extreme mood swings accompanied by episodes of arousal or depressive emotions. **Aim/Background:** The main aim is to assess the antipsychotic polypharmacy in patients with bipolar disorder.

Result: Out of 68 patients studied, only 7 antipsychotics were prescribed, in which olanzapine was the most common (48.53%), among them (36.8%) antipsychotics polypharmacy. Among 25 patients, (27.9%) were given SGA +SGA combination. A total of 17 Adverse Drug Reactions were observed in which the most common was sleep disturbance (27.9%). Causality assessments showed that majority of Adverse Drug Reactions were categorized as probable (47.5%) and possible (46.25%) in nature by Naranjo's Causality Assessment Scale. A total of 191 potential Drug-Drug Interactions were observed, the most prevalent type of interaction observed was moderate (86.9%), which was Lorazepam+Olanzapine (7.9%).

Conclusion: From the present study, it was concluded that among antipsychotics, 'olanzapine' (SGA) was the drug of choice for bipolar disorder. Considering older patients with bipolar disorder they have increased risk of drug induced adverse events, therefore the use of antipsychotics in this population needs careful consideration. In such cases antipsychotic polypharmacy may lead to better symptom relief and functional outcome with minimization of side effects associated with higher doses of single drug.

Key words: Polypharmacy, Prescribing pattern, Adverse drug reactions, Drug interaction, Bipolar disorder.

INTRODUCTION

Bipolar disorder is a mental disorder characterized by a period of depression and abnormal mood elevations that lasts from days to weeks. It is also known as manic-depressive illness. People usually experience both manic and depressive episodes and some may experience only manic episode without depression[1]. They also have disturbances in their daily psychomotor activities, circadian rhythm and cognition. BPAD is classified into three types – Bipolar Type 1, Bipolar Type 2 and Cylcothymia. Bipolar is diagnosed using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and the World Health Organization's (WHO) International Statistical Classification of Diseases and Related Health Problems, 10th Edition (ICD-10) [2].

Management: The goal of treatment is symptomatic relief from mania-depressive episodes and prevent relapse. The first line therapy for bipolar disorder is mood stabilizer (Lithium carbonate, Lithium citrate) or Divalproex followed by anticonvulsants, antidepressants, antipsychotics.

Treatment specific for mania:

- **First line:** Lithium or Divalproex (or add 2nd generation antipsychotics)
- **Second line**- Lithium + Divalproex (or Carbamazepine or Haloperidol)

Treatment specific for depression:

- **First line:** Lithium or Divalproex or Lamotrigine or Quetiapine or Olanzepine +SSRI or Lithium or Divalproex + Antidepressants or Lithium + Divalproex
- **Second line**- Lithium or Divalproex + Lamotrigine

Maintenance of Bipolar:

- **First line:** Lithium + Divalproex + 2nd generation antipsychotics or Lamotrigine or Risperidone
- **Second line:** Lithium + Divalproex or Carbamazepine
- **Third line:** Phenytoin, Calcitonine, Levetricetam, Gabapentin, Topiramide, Clozapine [3].

Polypharmacy is defined as the use of multiple medications in a patient, or it can also be defined as patients being on 5 or more medicines. The psychiatric polypharmacy problem refers to prescribing two or more psychiatric drugs to a patient at the same time. It can be divided into same class, multi class, adjunctive, augmentation, and total polypharmacy. Antipsychotic polypharmacy refers to the co-prescription of more than one antipsychotic drug. Polypharmacy of antipsychotics are shown to be more effective in treating psychiatric symptoms compared to monotherapy [4].

Materials and Methods

Study Design: This study was a hospital based prospective study.

Duration of Study: The study was carried out for a period of 6 months.

Study Centre: Yenepoya Medical College and Hospital, Mangalore. A 700 bedded multispecialty tertiary care teaching hospital.

Study Population: The study was done in the Department of Psychiatry of a tertiary care teaching hospital. The data was collected from the patients admitted to psychiatry ward over these six months. The hospital caters to both urban and rural population. Most of the patients belong to middle and lower strata of the society.

Sampling Method: All the patients the age of 18 years who are willing to give consent were enrolled in the study. The psychiatry

ward was visited on all six days of the week and information regarding the patient demographics and drug use were recorded in a semi-structured pro forma.

Study Criteria: The study will be carried out by considering the following criteria:

Inclusion Criteria:

- All cases of bipolar affective disorder.
- All the patients above 18years.
- Patients who are willing to participate in the study.

Exclusion Criteria:

- Patients who are not willing to participate.
- Pediatric population and infants.
- Bedridden, severe heart condition patient.
- All pregnant and lactating women

Data Collection Sources:

- Patient consent form
- Patient data collection form
- Patient medical record
- Naranjo's causality assessment scale
- Other data source : articles , journals

Sample Size: By convenient sampling, sampling size was found to be 68.

Methodology: A prospective study will be conducted in the department of psychiatry, Yenepoya Medical College Mangalore for a period of six months. Considering the inclusion and exclusion criteria patient will be enrolled after taking written consent from each patient and/or care givers. A suitably designed data collection form will be used to collect all necessary information about the patient from the patient file and the data collection includes age and sex of patients, name and class of drugs prescribed, past and present medical/medication history, current status and clinical progress of the patient, laboratory investigation, mental status, family history, social history, personal history, dose, frequency and route of administration. ADRs were found by patient interview and spontaneous reporting system by health care professionals. The degree of association of an adverse effect of the drug was done with the help of Naranjo's scale where it involves certain/definite; probable; possible; unlikely/doubtful and drug interactions were identified and checked which were divided into major, moderate and minor using www.drugs.com, www.medscape.com, and Clinirex. The obtained data will be subjected to suitable statistics.

Ethical Approval: The study was approved by the Institutional Ethics Committee of Yenepoya Medical College and Hospital, Mangalore

Data Analysis: The data was recorded and analyzed using Microsoft Excel Worksheet Version 2013.

Result:

A total of 68 patients with BPAD were enrolled in the study out of which 63 patients were prescribed with antipsychotics.

1.Gender Distribution of Patients:

Out of 68 patients studied, 41(60.29%) were males and 27(39.71%) was females.

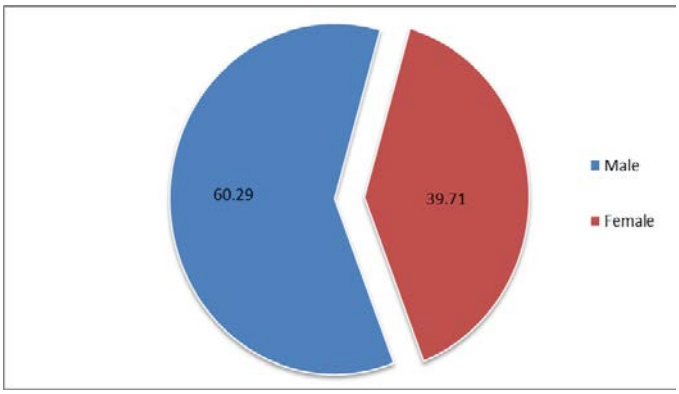

Figure 1.1: Gender Distribution Of Patients

2.Distribution of Patients:

The mean age of the patients was with a minimum age of 18 years and maximum above 45 years.

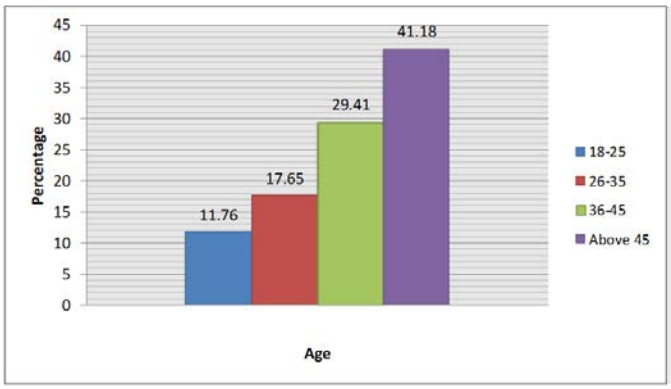

Figure 2.1: Distribution Of Patients

3.Social Habits:

Out of 68 patients, 10(14.7%) were alcoholics and 20(29.4%) were smokers.

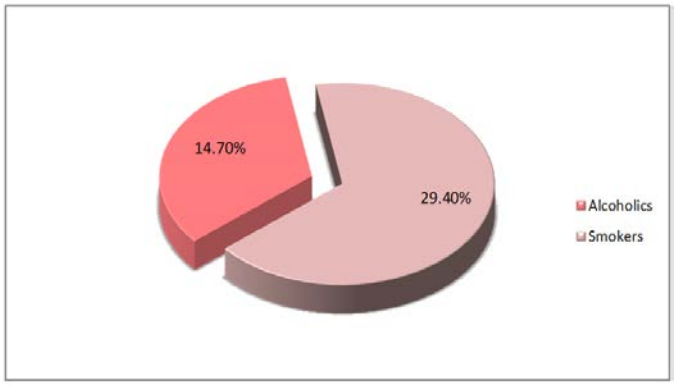

Figure 3.1: Social Habits

4.Family History:

Out of 68 patients, 51(75%) shows no significance of family history and 17(25%) had significant family history.

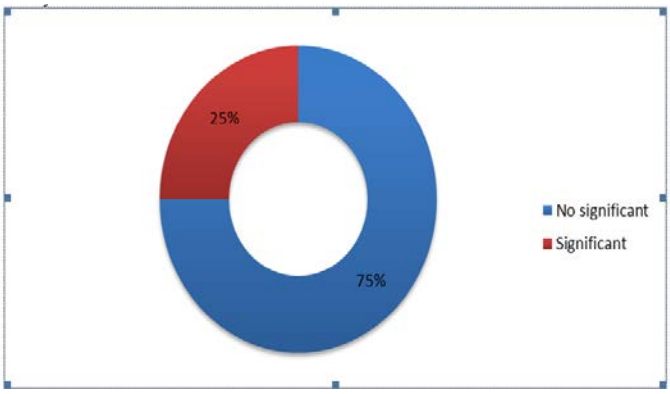

Figure 4.1: Family History

5.Co-morbities:

Out of 68 Bipolar affective disorder patients, 5 patients had hypertension (7.35%) and 5 patient had type 2 diabetes mellitus (7.35%).

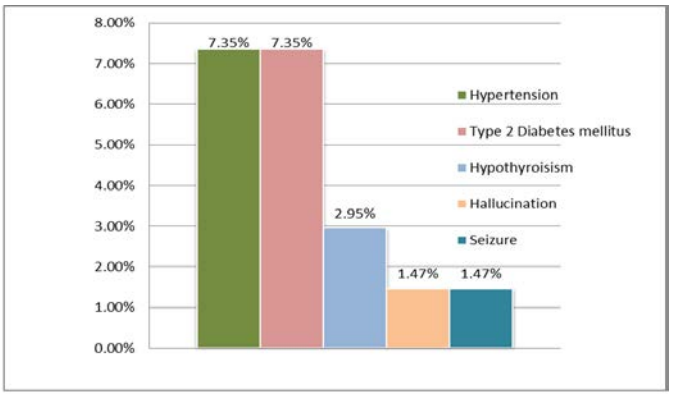

Figure 5.1: Comorbities

6.Prescribing Pattern:

In 68 patients, 94 antipsychotics were prescribed in which olanzapine was given to 33(48.53%) patients followed by haloperidol 21(30.88%).

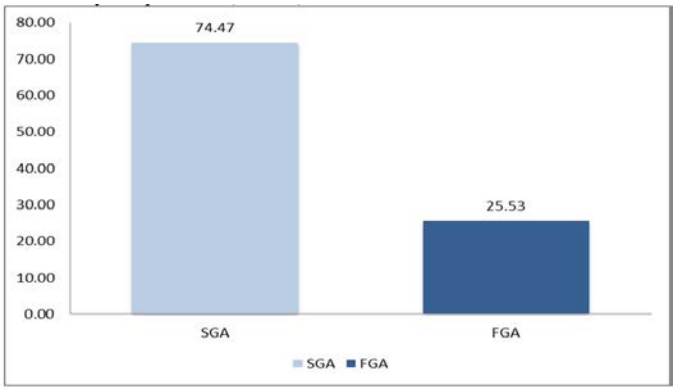

Figure 6.1: Representation of Drugs Prescribed

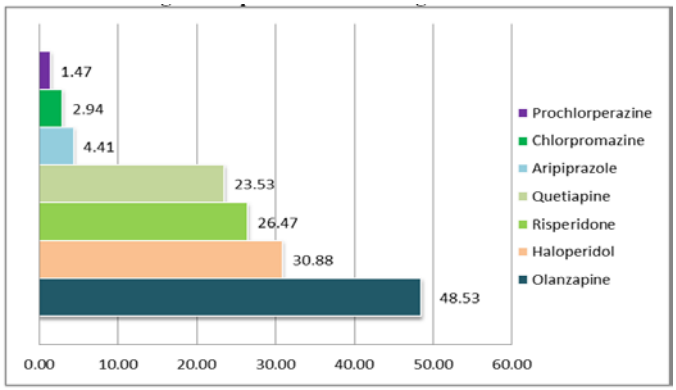

Figure 6.2: Distribution of Antipsychotics In Bipolar Patients

7. Polypharmacy:

Out of 68 patients, 63(92.7%) patients were prescribed with antipsychotics in which 25 (36.8%) had antipsychotic polypharmacy and 38(55.9%) with antipsychotic monotherapy.

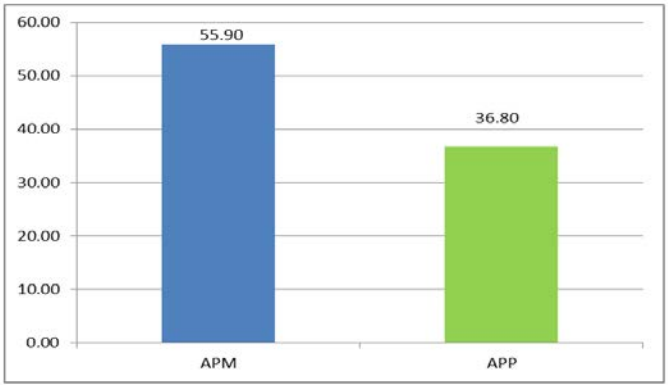

Figure 7.1: Comparison of Apm and app Among Bpad Patients

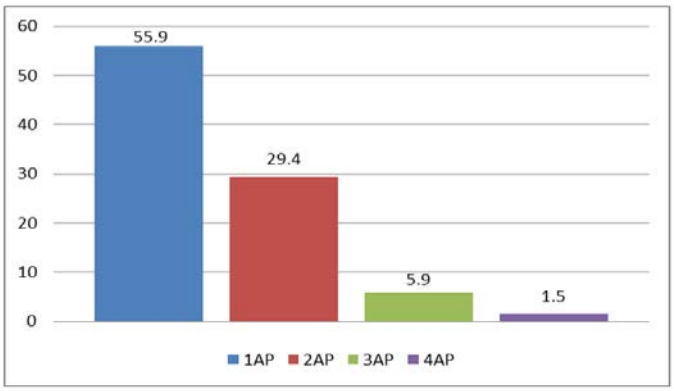

Figure 7.2: Number of Antipsychotic Prescribed Per Prescription

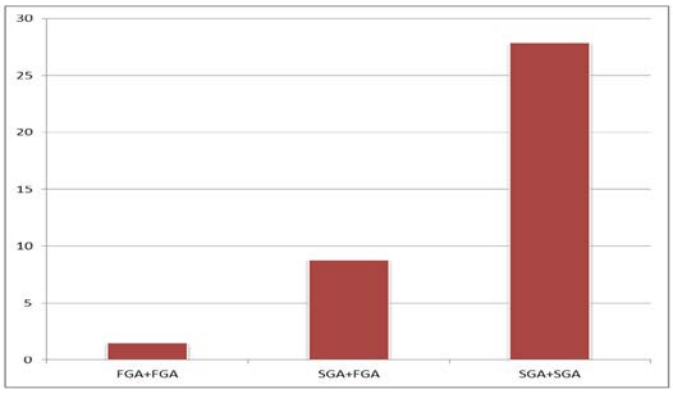

Figure 7.3: Antipsychotic Polypharmacy in Bipolar Patients

8. Adverse Drug Reaction:

- A total of 17 ADRs were observed in 68 patients during the study period. The most common ADR observed was sleep disturbance (27.9%) followed by gastrointestinal disturbance (13.2%).
- ADRs were found by patient interview and spontaneous reporting system by health care professionals. The degree of association of adverse effect of the drug was done with the help of Naranjo's scale.
- The Causality assessments showed that majority of ADRs were categorized as probable in nature.

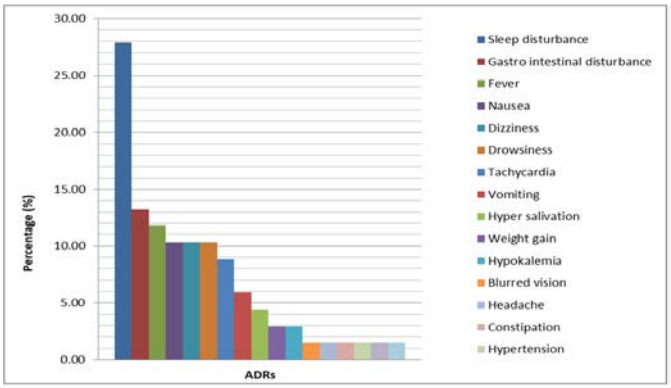

Figure 8.1: Representation of Adr

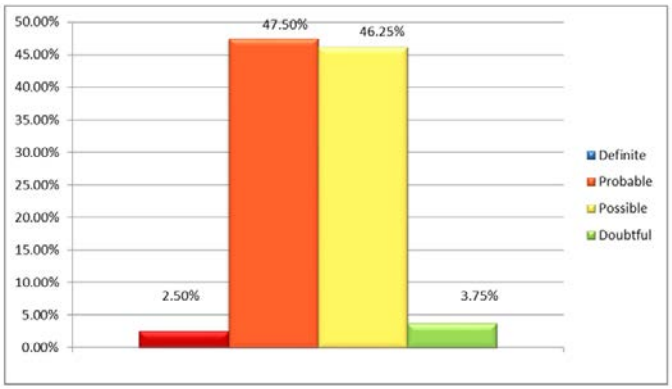

Figure 8.2: Percentage of Naranjo's Score

9.Drug Interaction:

A total of 191 potential drug-drug interactions were observed in 68 patients during the study time.

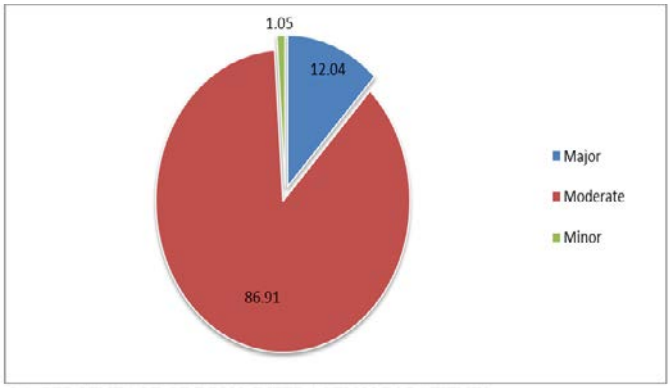

Figure 9.1: Percentage of Drug Interaction in Patients

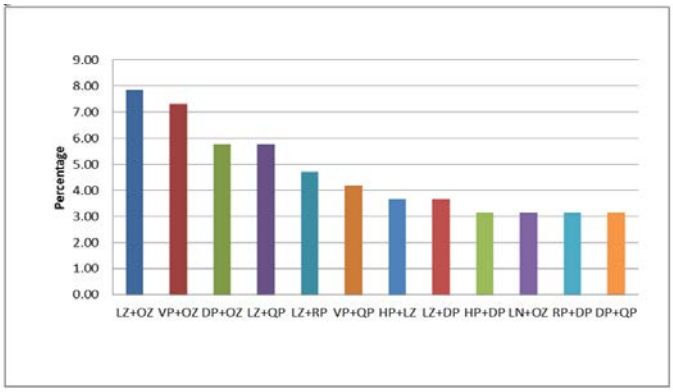

Figure 9.2: Drug Interactions

Discussion:

According to our study, 41(60.29%) patients with bipolar affective disorder were males and 27(39.71%) patients were females (Fig.5.1). The main reason for this high incidence in male population is due to male gender predominance due to various risk factors and comorbidities compared to the female population [5]. The number of male patients suffering from bipolar affective disorder was higher compared to female patients according to our study. Among 68 patients, patients were separated into four different age groups accordingly 18-25 years, 26-35 years, 36-45 years and above 45 years and the number of patients falling into each group was observed as 8(11.76%), 112(17.65%), 20(29.41%), and 28(41.18%) respectively (Fig.6.1). Majority of the patients belongs to the age group of above 45 years [6]. Nearly 10(14.7%) patients out of 68 were alcoholics and 20(29.4%) were smokers (Fig.3.1). Nearly 51 (75%) shows no significance of family history and 17 (25%) had significant family history (Fig.4.1). In the present study, most patients (79.40%) had no comorbidities. Hypertension (7.35%) and Type 2 diabetes mellitus (7.35%) was the most common comorbid condition, followed by hypothyroidism (2.95%), hallucination (1.47%), seizure (1.47%) (Fig.5.1).The possibilities include a genetic relationship, a causal relationship (in which diabetic vascular lesions contribute to mania) or the

effect of psychotropic medication and associated weight gain. Most prescribed antipsychotic in our study population was SGA (74.4%) (Fig.6.1), in which most commonly prescribed were Olanzapine (48.53%), followed by Risperidone (26.47%), Quetiapine (25%) and Aripiprazole (5.91%) respectively and in case of FGA (25.3%); most commonly prescribed drug was found to be Haloperidol (32.35%) (Fig.6.2). Atypical antipsychotics seem to be preferable than typical antipsychotics in treating BPAD, because they have substantially lower risk of extra pyramidal neurological effects. This study is supported by Grover S et al, were olanzapine was the most commonly prescribed antipsychotic drug for Bipolar disorder [7]. Among 68 patients of bipolar affective disorder, 63(92.7%) were prescribed with antipsychotics (Fig.7.1), in which 25(36.8%) had antipsychotic polypharmacy and 38(58.9%) had antipsychotic monotherapy (Fig.7.2). Among 25 patients, 19(27.9%) were given SGA+SGA combination followed by FGA+SGA (8.8%) and FGA+FGA (1.5%) (Fig.7.3). A total of 17 ADRs were observed in 68 patients during the study period. The most common ADR observed was sleep disturbance (27.9%) followed by gastro intestinal disturbance (13.2%) (Fig.8.1). Causality assessments showed that majority of ADRs were categorized as probable (47.5%) and possible (46.25%) in nature by Naranjo's Causality Assessment Scale (Fig.8.2)[8]. A total of 191 potential drug-drug interactions were observed. We analyzed the DDIs into major, moderate and minor. The most prevalent type of interaction observed in our study was moderate (86.9%) followed by major (12.04%) and minor (1.05%) (Fig.9.1).The most common drug-drug interaction was Lorazepam + Olanzapine (7.9%) followed by Sodium valproate + Olanzapine (7.3%) (Fig.9.2)[9].

It is a single centred study; validity of findings would increase if it was multi-centred. Only a small population was included for small study duration. More valid result could have been obtained if the study were conducted for at least a period of one year with more patients. The study didn't include cost analysis to find the economic burden caused by polypharmacy.

Conclusion:

From the study it was concluded that, the use of antipsychotic polypharmacy in patients with BPAD needs careful consideration. Considering older patients with bipolar disorder they have increased risk of drug induced adverse events, therefore the use of antipsychotics in this population needs careful consideration. In such cases antipsychotic polypharmacy may lead to better symptom relief and functional outcome with minimization of side effects associated with higher doses of single drug.

Abbrevation:

BPAD: Bipolar affective disorder; **FGA**: First generation antipsychotics; **SGA**: Second generation antipsychotics; **SSRI**: Selective serotonin reuptake inhibitors; **ADR**: Adverse drug reactions; **DDIs**: Drug-drug interactions; **APM**: Antipsychotic monotherapy; **APP**: Antipsychotic polypharmacy.

Author's Acknowledgment

The authors of the study are heartily thankful for the guidance and support received from all the members who contributed to this project, it was vital for the success of the project.

Author's Contribution

Author's role - study concept and design, acquisition of subjects and/or data, analysis and interpretation of the data, presentation of manuscript.

Available Data and Material

All the information related to the study is embedded within the manuscript.

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