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Research Article

Comparison and Assessment of Prescribing Pattern of Psychotropic Agents in Bipolar Affective Disorder with Mania and Depression

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Abstract

INTRODUCTION: Bipolar disorder is a recurring chronic disorder characterized by mood, state, and energy fluctuations. Individuals differ in symptoms, course, severity, and response to treatment. It is critical to know the current knowledge of the evolving pharmacological and psychological strategies in bipolar disorder.

Primary Objective: To compare and assess the prescribing pattern of psychotropic agents in bipolar affective disorder with mania and depression in a tertiary care teaching hospital.

Secondary Objectives:

- Determination of risk and cofactors associated with Bipolar Disorder
- Assessment of treatment modalities

DESIGN: Prospective observational study

RESULTS: The most commonly prescribed drug combination was Mood stabilizer + Antipsychotics + Benzodiazepine combination, 5(33.3%) in bipolar depression and9(60.0%) in bipolar mania. A very small percentage of patients (6.7%) received ECT. The most commonly prescribed drug was valproic acid (Mood stabilizer), 7(46.7%) in bipolar depression and 14(93.3%) in bipolar mania.

CONCLUSION: According to the data, Mood stabilizers were found to be the most commonly prescribed drug. Combination treatments are prevalent, reflecting the complexity of managing bipolar disorder. Although various genetic and environmental risk factors are identified, the attributable risk of individual elements is often less.

KEYWORDS: Bipolar disorder, Mania, Depression, Valproic acid

INTRODUCTION

Bipolar disorder is a chronic condition characterized by variations in mood, energy, and behavior. It is one of the leading causes of disability among adolescents, causing cognitive and functional impairments as well as an increased risk of suicide.[1] According to studies, patients with bipolar disorder spend more time in depressive episodes and recover more slowly than in a manic phase.[2] Suicide is more likely to occur during mixed or depressed mood states.[3]

STAGES OF BIPOLAR DISORDER

Bipolar 1	At least one mixed or maniac episode + At least one major depressive episode
Bipolar 2	The syndrome of major depressive episodes and hypomanic episodes has been called bipolar II disorder.[4,5]
Cyclothymia	Periods of hypomanic symptoms alternate with periods of depressive symptoms. Full criteria for a manic or major depressive episode are not met.[5,6,7]
Rapid cycling	It is a malignant form described by four or more mood episodes, i.e., depressive, manic, hypomanic, and mixed episodes within a 12-month period.[6]

Epidemiology – The lifetime prevalence of bipolar disorder is 1.3 to 1.6%. The disease has a two to three times higher mortality rate than the general population.[8]There is no direct connection between race/ethnicity, socioeconomic status, and location (e.g., rural vs. urban).[9]

Etiology- The cause of the bipolar disorder is unknown. Early life trauma, life events, alcohol consumption, and other

substance use can influence the disease's onset and progression.[10]

The course of the illness-

Bipolar disorder is commonly misdiagnosed because of its variable course and mood episodes.[10,11] .Females are more likely to have mixed states, depressive episodes, and rapid cycling compared to men. Males are more likely to develop manic episodes.[12]

Clinical presentation –

There are four types of mood episodes in bipolar disorder: mania, hypomania, depression, and mixed episodes.[13]

Depressive episodes- Severe lack of interest in activities, weight loss or gain, trouble sleep problems, feeling hopeless.[14] The risk of suicide is significantly increased.[15]

Manic episodes -The mood is characterized as feeling high or optimistic, extremely irritable, and the resulting overactivity is typically unproductive.[16]

Hypomania – It is a milder type of mania. Symptoms are similar to mood disturbances caused by cocaine or antidepressants. No significant reduction in social or occupational activity. Delusions and hallucinations are absent.[10]

Mixed episodes- They are described as having both depressive and hypomanic or manic symptoms or a rapid alternation of the three symptomatic forms.[5]

TREATMENT OF BIPOLAR DISORDER

The assessment may cover the history of the number of previous episodes, type of the first episode, the polarity of illness, duration and severity of episodes, presence or absence of suicidal behavior, seasonal variation in the onset of symptoms, presence of rapid cycling and features of ultra-rapid cycling.[17]

Psychosocial treatment for bipolar disorder:

Bipolar disorder is characterized by a significant psychosocial impairment, low rates of medication adherence, interpersonal dysfunction, and cognitive impairment. Each of these domains is adequately addressed by psychotherapeutic interventions, particularly when delivered in combination with pharmacotherapy.[18]

Electroconvulsive Therapy [ECT] is a medical procedure for the treatment of severe psychiatric disorders. Its primary purpose is to rapidly relieve psychiatric symptoms. It is available for patients who are pregnant, unresponsive to more standard treatments, or unable to tolerate first-line treatments. For patients who are manic or depressed during the first trimester of pregnancy, ECT is usually the safest and most effective treatment.[19]

METHODOLOGY

A prospective observational study was carried out on the inpatients of the concerned department for a period of six months at Yenepoya Medical College and Hospital, Mangalore. A patient information sheet was given to the patients, and informed consent was obtained from the patient and/ or the caregivers. About 30 patients were selected for the study based on inclusion and exclusion criteria. Patient data were collected using a patient data collection form which included the demographic details, mental status examination, diagnosis, and medications. Assessment of prescription patterns was done by analyzing the prescription of 30 patients.

STUDY DESIGN

This study was a hospital-based prospective and observational study.

STUDY CENTRE

The study was conducted in the department of Psychiatry ward, Yenepoya Medical College, Derlakatte, Mangalore.

STUDY DURATION

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

SAMPLE SIZE

By convenient sampling, the sample size was found to be 30.

STUDY CRITERIA

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

Inclusion criteria:

- Subjects diagnosed with Bipolar Affective Disorder (BPAD ICD-10 F 31) with Mania and Bipolar Affective Disorder with Depression at the Psychiatry department who are willing to give written informed consent for the participation.
- Availability of caregivers.
- Patients who are 18 years old and above of either sex.

Exclusion criteria:

- Patients/Caregivers are unwilling to give the consent form.
- Pediatric patients
- All pregnant and lactating women.

DATA COLLECTION TOOLS:

Patient consent form: Consent was collected either from the patient or bystander using a self-designed consent form. The consent form was made in two languages: English and Kannada.

Patient data collection form:

Data was collected using a self-designed data collection form, which consists of details like patient demographics, mental status examination, diagnosis, drug therapy, and other relevant information.

ETHICAL APPROVAL: The study was approved by the Institutional Ethics Committee of Yenepoya Medical College and Hospital, Mangalore.

STATISTICAL ANALYSIS:

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) Version 22 and Microsoft Excel version 13. Statistical hypothesis testing uses paired t-test to assess the existence of a statistically significant association between the variables tested. We considered the 5% level of significance as statistically significant. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation, frequency, and charts.

RESULTS

Age-Wise Distribution

Table 1.1: Frequency and percentage distribution of samples according to age.

Age in years	Frequency	Percentage
18-35	8	26.7
36-50	14	46.7
Above 50	8	26.7

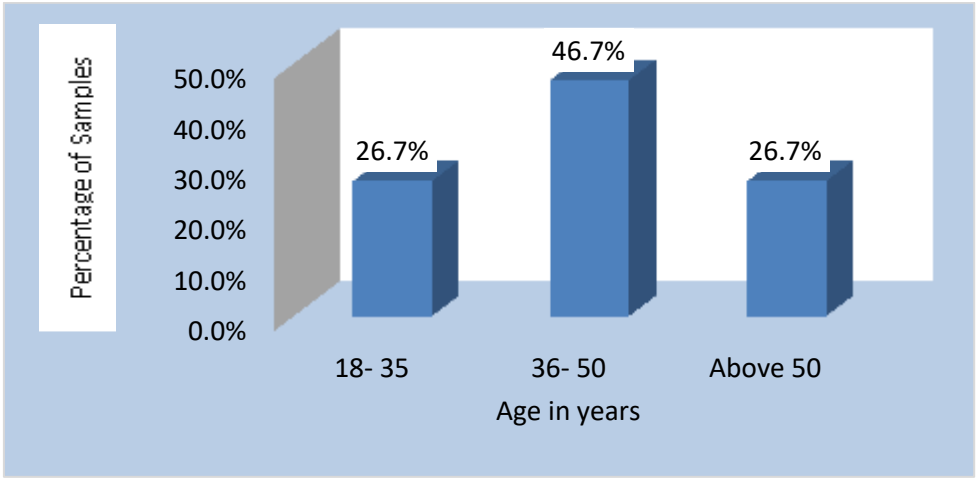

Figure 1.1: Bar diagram representing percentage distribution of samples according to age.

Gender-Wise Distribution of Patients

Table 1.2: Frequency and percentage distribution of samples according to sex N=30

Sex	Bipolar depression (N=15)		Bipolar mania (N=15)	
	Frequency	Percentage	Frequency	Percentage
Male	7	46.7	12	80.0
Female	8	53.3	3	20.0

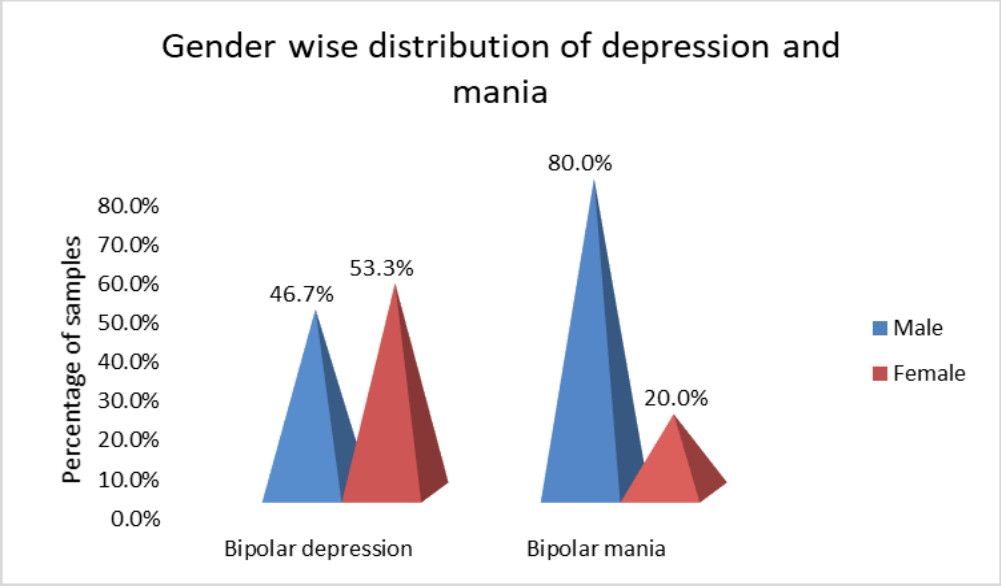

Figure 1.2: Percentage distribution of samples with bipolar depression and mania according to gender.

Family History Wise Distribution

Table 1.3: Frequency and percentage distribution of samples according to family history N=30

Family history	Frequency	Percentage
Significant	19	63.3
Not significant	11	36.7

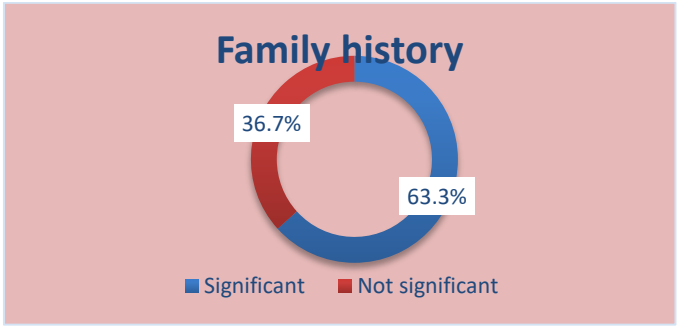

Figure 1.3: Doughnut representing percentage distribution of samples according to family history

According to Suicidal Thoughts

Table 1.4: Frequency and percentage distribution of samples according to suicidal thought N=30

Suicidal thought	Bipolar depression (N=15)		Bipolar mania (N=15)	
	Frequency	Percentage	Frequency	Percentage
Nil	5	33.3	15	100.0
Death wishes	8	53.3	-	-
Suicidal attempts	1	6.7	-	-
Death wishes and Suicidal attempts	1	6.7	-	-

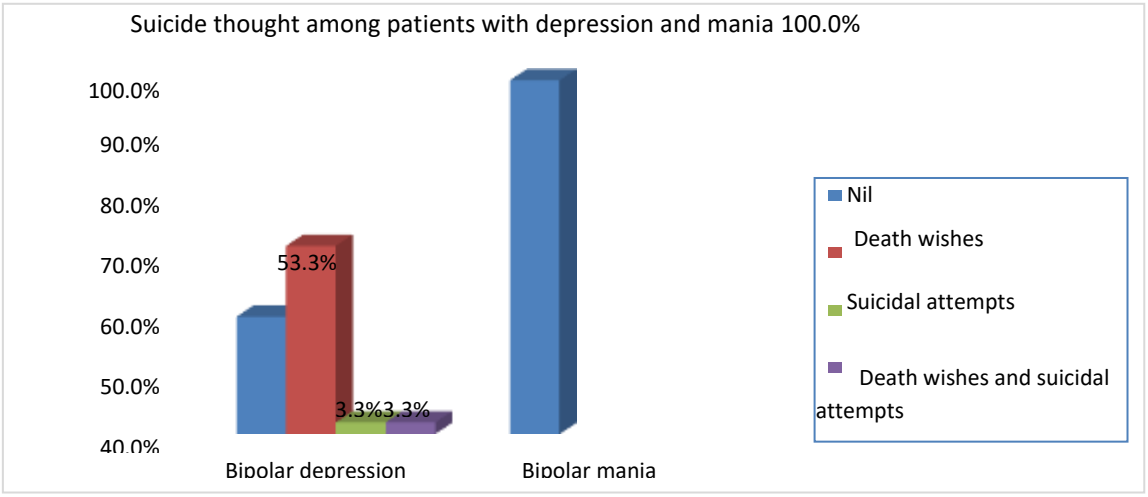

Figure 1.4: Percentage distribution of samples with bipolar depression and mania according to suicidal thoughts

According to the Distribution of Drugs Prescribed

Table 1.5.a: Frequency and percentage distribution of drugs prescribed for patients with bipolar mania and depression. N=30

Drug class	Drugs	Bipolar depression (N=15)		Bipolar mania (N=15)	
		Frequency	Percentage	Frequency	Percentage
Mood stabilizers	Lithium	6	40.0	1	6.7
	Valproic acid	7	46.7	14	93.3
	Oxcarbazepine	3	20.0	0	0.0
	Clonazepam	6	40.0	2	13.3
Benzodiazepines	Lorazepam	5	33.3	9	60.0
	Diazepam	2	13.3	1	6.7
	Olanzapine	6	40.0	8	53.3
Antipsychotics	Quetiapine	6	40.0	8	53.3
	Lurasidone	2	13.3	0	0.0
	Haloperidol	1	6.7	10	66.7
	Escitalopram	3	20.0	0	0.0
Antidepressant	Fluoxetine	1	6.7	0	0.0

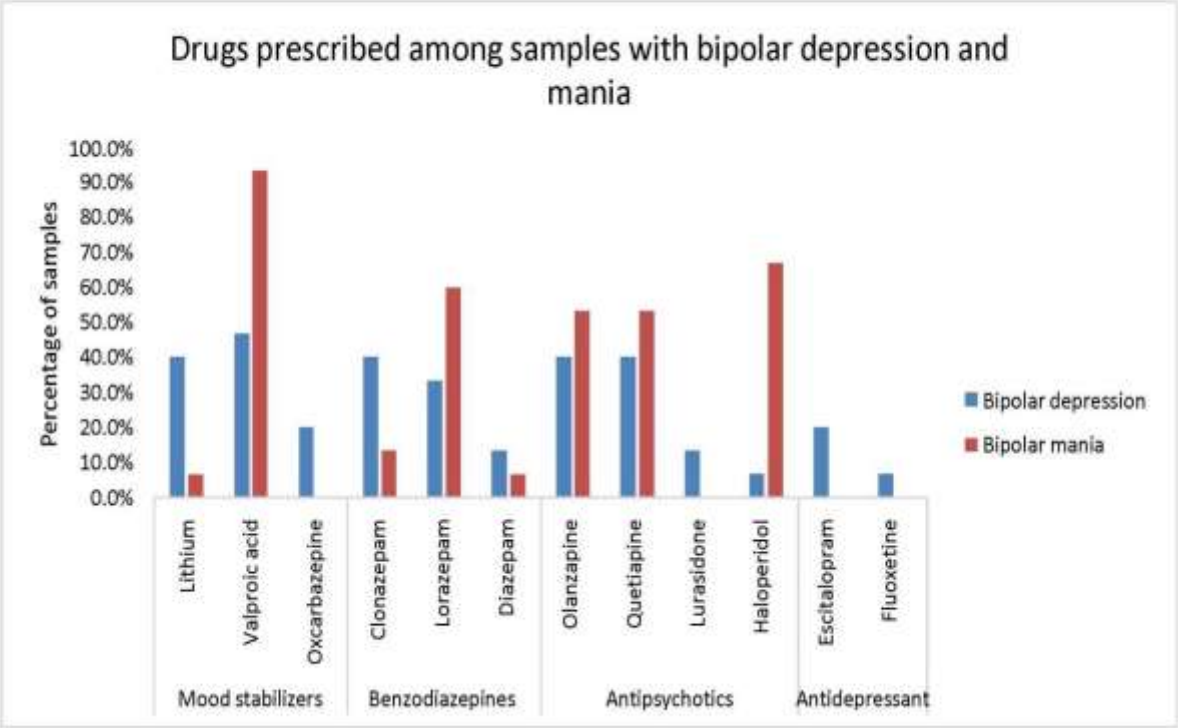

Figure 1.5.a: Percentage distribution of drugs prescribed for patients with bipolar mania and depression.

According to the Type of Therapy

Table 1.5.b: Frequency and percentage distribution of samples according to the type of therapy N= 30

Drug combination	Bipolar depression (N=15)		Bipolar mania (N=15)	
	Frequency	Percentage	Frequency	Percentage
Monotherapy	0	0	0	0
Dual therapy	7	46.7	6	40.0
Poly therapy	8	53.3	9	60.0

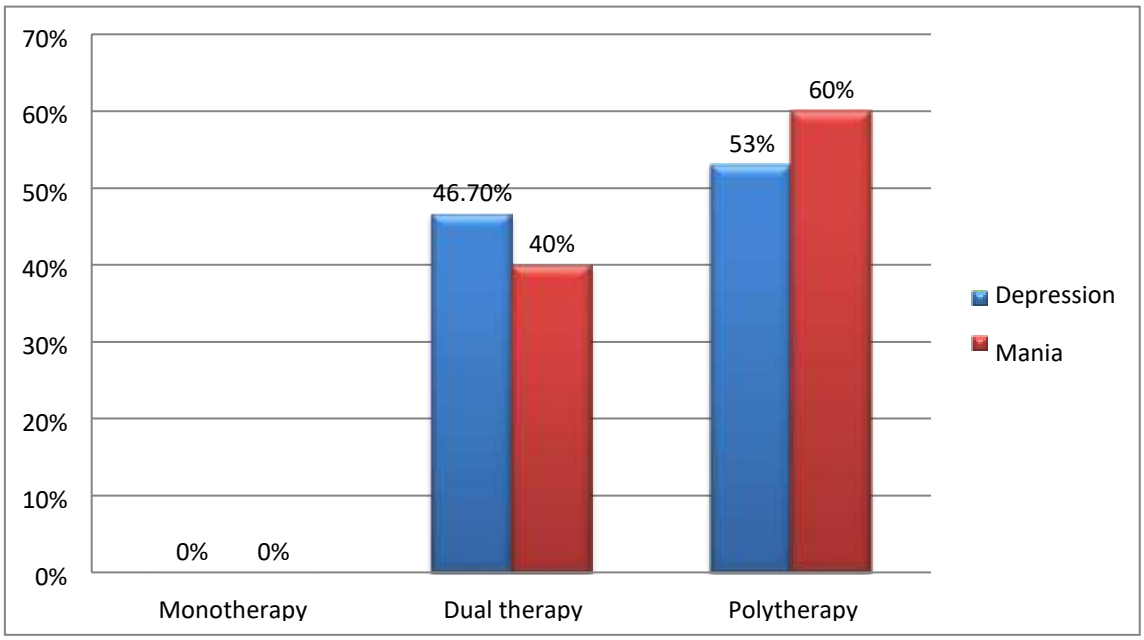

Figure 1.5.b: Bar diagram representing frequency and percentage distribution of samples according to the type of therapy

According to Drug Combination

Table 1.5.c: Frequency and percentage distribution of samples according to the drug combination N= 30

Drug combination	Bipolar depression (N=15)		Bipolar mania (N=15)	
	F	%	F	%
Dual therapy				
Mood Stabilizers + Antipsychotics	3	20.0	5	33.3
Mood Stabilizers + Benzodiazepenes	1	6.7	-	-
Antipsychotics + Benzodiazepenes	2	13.3	1	6.7
Antidepressants + Benzodiazepenes	1	6.7	-	-
Poly therapy				
Mood Stabilizers + Benzodiazepines + Antipsychotics	5	33.3	9	60.0
Mood Stabilizers + Benzodiazepines + Antidepressants	2	13.3	-	-
Mood Stabilizers + Antipsychotics + Benzodiazepines + Antidepressants	1	6.7	-	-

Bipolar Depression Drug Combination:

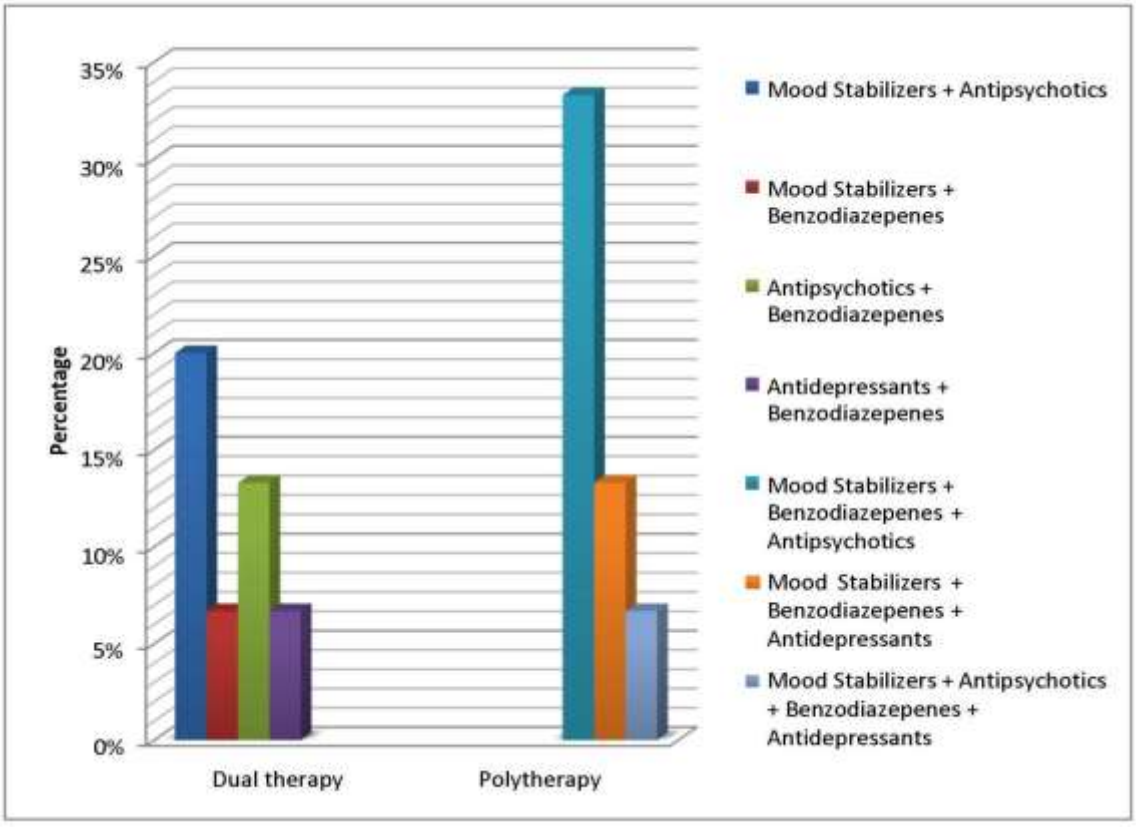

Fig 1.5.c.i: Bar diagram representing frequency and percentage distribution of samples according to drug combination (bipolar depression)

Bipolar Mania Drug Combination:

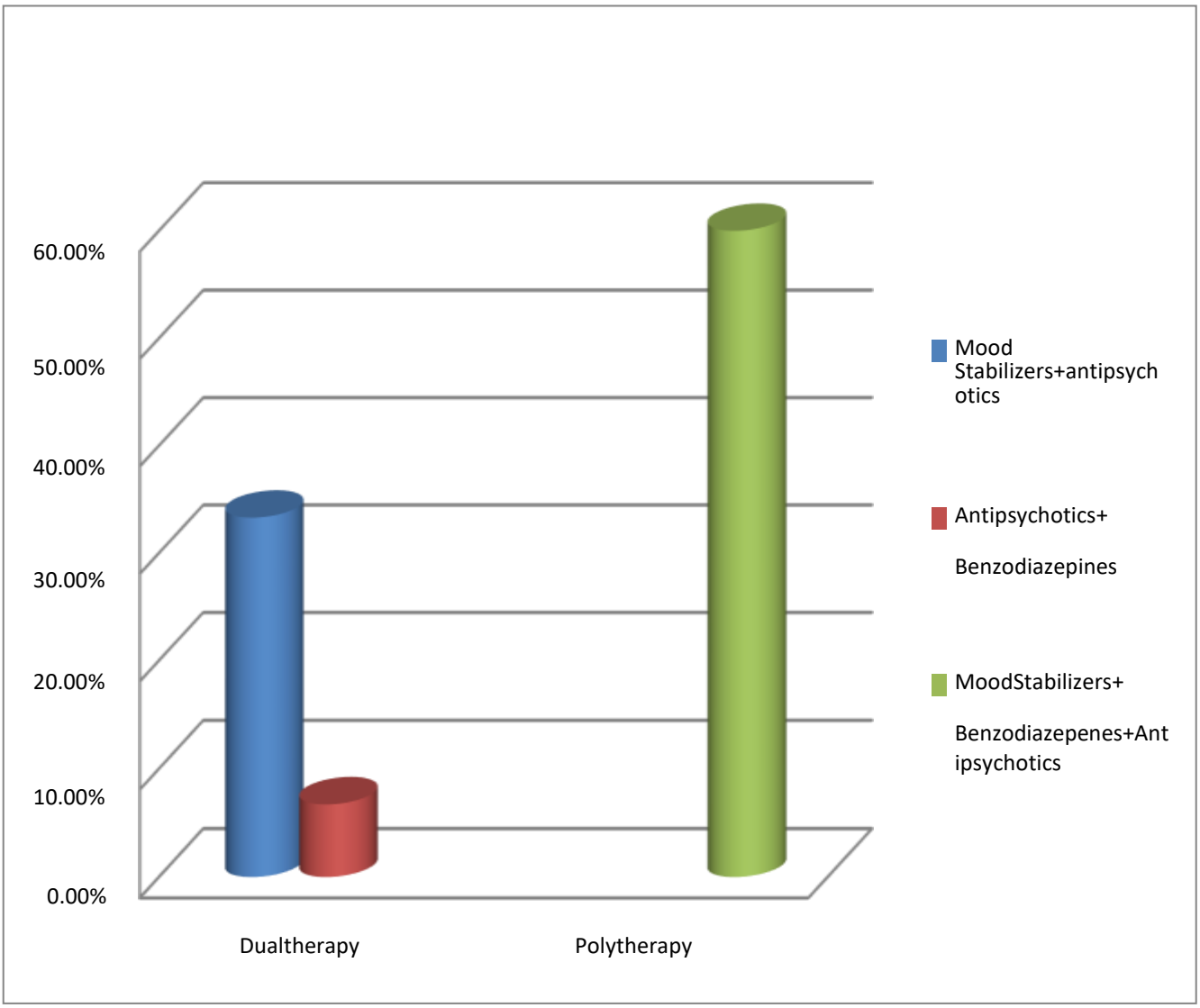

Fig.1.5.c.ii: Bar diagram representing frequency and percentage distribution of samples according to drug combination(bipolar mania)

According to Treatment Modality

Table 1.6: Frequency and percentage distribution of samples according to treatment modality N=30

Treatment modality	Bipolar mania (N=15)	
	Frequency	Percentage
Psychotropic drug therapy	30	100.0
Psychosocial therapy	24	80.0
ECT	2	6.7

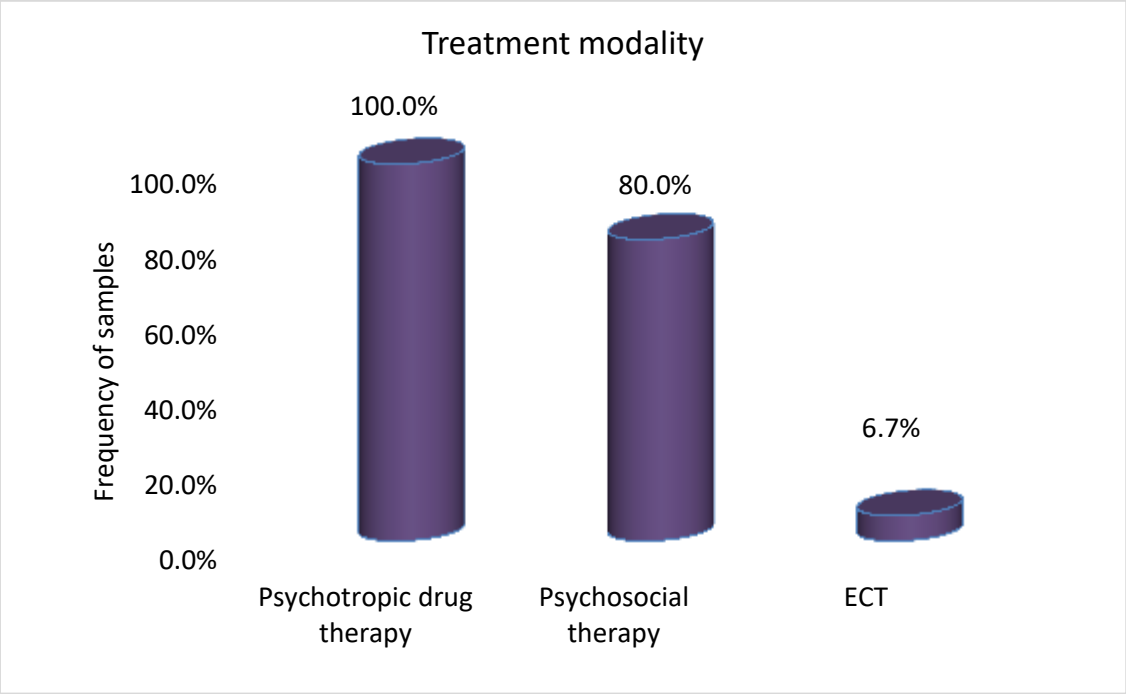

Figure 1.6: Cylindrical diagram representing percentage distribution of samples according to treatment modality

DISCUSSION

This study was carried out with the aim of comparing and assess the prescribing pattern of psychotropic agents in bipolar mania and bipolar depression in a tertiary care teaching hospital. In a sample group of 30, patients were classified into different age groups that are 18-35, 36-50, and above 50, and the number of patients in each group was observed as 8(26.7%), 14(46.7%) and 8(26.7%) respectively. The majority of patients were present in the 36-50 age group, which was supported by **Levine J et al.**[20] In bipolar depression, female subjects 8(53.3%) predominated over male subjects 7(46.7%). In bipolar mania, male subjects 12(80%) predominated over female subjects 3(20%). This indicates that males are usually more present with manic episodes than females, and females are more present with depressive episodes than males. The study was supported by **Vega p et al.**[21]

Nearly 19(63.3%) patients had a significant family history, and 11(36.7%) patients had a non-significant family history of bipolar disorder. Patients with a significant family history are at great risk, and this is common in bipolar disorder, supported by **Benazzi F et al.**[22] In patients diagnosed with bipolar depression, 8(53.35%)patients had death wishes,1(6.7%)patient attempted suicide, and 1(6.7%) patient had both attempted suicide and death wishes. None of the patients diagnosed with bipolar mania had death wishes or suicide attempts. The polarity of the current mood episode is one of the most significant determinants of suicidal activity in bipolar disorder: depressive episodes carry the greatest risk, whereas suicidal behavior is uncommon in (euphoric) mania. The study was supported by **Dome P et al.**[23] In the study, 8(26.7%) patients had stressful life events which can trigger bipolar disorder, and 22(73.3%) didn't have any stressful life events. The study was supported by **Johnson SL et al.**[24] In bipolar depression, 7(46.7%) patients were treated with dual therapy, and 8(53.3%) people were treated with polytherapy. In bipolar mania, 6(40%) patients were treated with dual therapy, and 9(60%) of patients were treated with polytherapy. None of the patients were treated with monotherapy. Combination therapy was preferred over monotherapy in order to effectively control mood symptoms and reduce relapse. The study was supported by **Lin D et al.**[25] The most commonly prescribed drug combination was Mood stabilizer + Antipsychotic + Benzodiazepine combination, 5(33.3%) in bipolar depression and 9(60.0%) in bipolar mania, which is supported by **Trivedi Jk et al.**[26] The most commonly prescribed mood stabilizer was valproic acid 7(46.7%) in bipolar depression and 14(93.3%) in bipolar mania, followed by Lithium 6(40%) and 1(6.7%), oxcarbazepine to 3(20%) patients. A potential objective reason for the decrease in the use of lithium might be a more delayed antimanic effect, which is supported by **Walpoth-Niederwanger M et al.**[27] The most commonly prescribed Benzodiazepine in bipolar depression was Clonazepam 6(40%), followed by lorazepam 5(33.3%) and diazepam 2(13.3%). In bipolar mania, lorazepam 9(60%) was prescribed the most, followed by Clonazepam 2(13.3%) and diazepam 1(6.7%). Among antipsychotics, Second generation antipsychotics such as olanzapine and quetiapine were both prescribed to 6(40%) in bipolar depression, and 8(53.3%) in bipolar mania commonly prescribed, followed by lurasidone 2(13.3%). The First generation of Antipsychotic haloperidol was prescribed to 1(6.7%) bipolar depressive patients and 10(66.7%) bipolar manic patients. Among antidepressants, escitalopram was prescribed to 3(20%) patients, followed by fluoxetine which was given to 1(6.7%) patient. Antidepressants are prescribed with mood stabilizer because they can induce mania, and it is not given in the manic phase, which was supported by **Lim Pz et al.**[28] The results indicate that patients spent ever-increasing amounts on psychotropic medication, in particular second-generation antipsychotics and valproic acid, supported by **Hayesh J et al.**[29] There are three treatment modalities for bipolar disorder, i.e., psychotropic drug therapy, psychosocial therapy, and ECT. Psychotropic drugs were given to all patients, psychosocial therapy was given to 24 (80%) patients, and ECT was given to 2(6.7%)patients. ECT should be considered if the risk to self or others is high, psychotic features are present, or there has been a previous response to ECT or in severe cases. A very small percentage of patients received electroconvulsive therapy (ECT), despite its well-documented efficacy in the

treatment of both phases of the disorder. The study was supported by **Lim pz et al**.[28]

CONCLUSION

From the present study, it may be concluded that valproic acid is the most prescribed drug in both bipolar depression and bipolar mania. Combination therapy was used in the treatment to effectively control mood episodes, and the most commonly prescribed combination therapy was mood stabilizer with Benzodiazepine and antipsychotic. When compared to the use of first generation antipsychotics,the use of second generation antipsychotic increased. The clinicians do not fully comply with all recommendations as it is meant to advise rather than mandate a particular type of treatment and the treatment is individualized.

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Author Contributions:

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

Study concept: Dr.Ajmal Shajahan, Dr.Angel Princy K R, Dr.K Muhammed Safwan, Dr.Mahima M.S, Dr.Fathima Jaleela.M.A

Acquisition of subjects and/or data: Dr.Ajmal Shajahan, Dr.Angel Princy K R, Dr.K Muhammed Safwan, Dr.Mahima M.S, Dr.Fathima Jaleela.M.A

Interpretation of data: Dr.Ajmal Shajahan, Dr.Angel Princy K R,Dr. K Muhammed Safwan, Dr.Mahima M.S, Dr.Fathima Jaleela.M.A

Preparation of Manuscript: Dr.Ajmal Shajahan, Dr.Angel Princy K R,Dr. K Muhammed Safwan, Dr.Mahima M.S, Dr.Fathima Jaleela.M.A

Declaration of Conflicting Interests

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Available data and material:

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

Conflict of Interest:

The authors declare no conflict of interest.

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