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Nasir Mehmood
Department of Psychology, University of Karachi

Qudsia Tariq
Department of Psychology, University of Karachi

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A RETROSPECTIVE ANALYSIS OF RELAPSE RATES AND MEDICATION COMPLIANCE IN BIPOLAR I AND BIPOLAR II DISORDERS: A COMPARATIVE STUDY

Nasir Mehmood[1], Qudsia Tariq[2]
[1.] *Department of Psychology, University of Karachi*
Karwan-e-Hayat Institute for Mental Health Care, Karachi
[2.] *Department of Psychology, University of Karachi*

Corresponding author: ***Nasir Mehmood*** *Department of Psychology, University of Karachi, Karwan-e-Hayat Institute for Mental Health Care, Karachi* ***Email:*** *nasir.mehmood@keh.org.pk*

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ABSTRACT

Background and objective:
Bipolar disorder is a chronic, serious mental health condition characterized by mood episodes, and medication non-compliance is a significant predictor of relapse. The objective of this study was to investigate the relapse rates and medication compliance in patients with bipolar I and II disorders.

Methods:
This retrospective observational study was conducted at Karwan-e-Hayat Institute for Mental Health Care, Karachi, Pakistan. Medical records of 377 patients diagnosed with bipolar I or bipolar II disorder between July 2019 and June 2022 were retrieved from the Hospital Management System (HMS). Diagnosis was confirmed using DSM-IV criteria. Medication compliance was assessed through prescription refill records, follow-up visits, and clinical documentation. Relapse was defined as any mood episode requiring hospitalization. Descriptive statistics were used to summarize data, and the Chi-square (x^2) test was applied to compare groups. A p-value ≤ 0.05 was considered statistically significant.

Results:
Relapse rates and medication compliance were compared between the two groups using statistical analysis. Results showed that patients with bipolar I disorder had a significantly higher relapse rate (63%) compared to those with bipolar II disorder (15.2%). Additionally, medication non-compliance was more common in the bipolar I group (27.5%) than in the bipolar II group (8.2%).

Conclusion:
These findings highlight the importance of medication adherence and regular follow-up in preventing relapse, particularly in patients with Bipolar I disorder.

Key words: Bipolar I & II, Relapse rate, Medicine compliance

INTRODUCTION

Bipolar disorder (BD) is a chronic and recurrent mood disorder characterized by fluctuations in mood, energy, activity levels, and functional capacity. It encompasses episodes of mania or hypomania and depression, often resulting in significant psychosocial impairment and reduced quality of life.[1] Bipolar disorder is broadly categorized into bipolar I disorder (BD-I) and bipolar II disorder (BD-II). BD-I is defined by the occurrence of at least one full manic episode, with or without major depressive episodes, whereas BD-II requires the presence of at least one hypomanic episode and one major depressive episode, without a history of full mania.[2] Differentiating between these subtypes is clinically important due to differences in symptom severity, illness trajectory, functional outcomes, and treatment response.[3]

Relapse remains one of the most critical challenges in the long-term management of bipolar disorder. Longitudinal studies indicate that individuals with BD spend a substantial proportion of time experiencing syndromal or subsyndromal symptoms, even during maintenance treatment.[3,4] Recurrent episodes

associated with cognitive decline, occupational dysfunction, increased hospitalization rates, and elevated suicide risk.[5,6] The burden of relapse extends beyond clinical deterioration, contributing significantly to healthcare utilization and economic costs.[7]

The course and prognosis of BD-I and BD-II differ in meaningful ways. BD-I is frequently associated with severe manic episodes requiring hospitalization and acute stabilization, often accompanied by psychotic features.[1] In contrast, BD-II is typically characterized by less severe hypomanic episodes but more persistent and recurrent depressive episodes, which may result in prolonged functional impairment.[8,9] Evidence suggests that while BD-I patients may experience more manic relapses, BD-II patients often endure more frequent depressive recurrences, contributing to chronic disability.[9,10] These subtype-specific patterns highlight the necessity of tailored relapse prevention strategies.

Medication adherence is widely recognized as a cornerstone in preventing relapse in bipolar disorder. Mood stabilizers, atypical antipsychotics, and adjunctive psychotherapies have demonstrated effectiveness in reducing recurrence and improving long-term outcomes.[11,12] Despite established efficacy, treatment non-adherence remains a pervasive issue, with reported rates ranging from 20% to 60% across studies.[12,13] Factors contributing to non-adherence include medication side effects, lack of insight, cognitive impairment, substance use, complex treatment regimens, and stigma.[14,15]

Importantly, the determinants of non-adherence may differ between BD-I and BD-II. Patients with BD-I may discontinue medication during manic episodes due to impaired judgment, grandiosity, or perceived recovery.[6,16] Conversely, individuals with BD-II may struggle with adherence due to persistent depressive symptoms, hopelessness, or fatigue.[17,18] Poor adherence has consistently been associated with increased relapse risk, rehospitalization, and worse functional outcomes.[19,20]

The primary objective of this retrospective analysis was to compare the relapse rates and medication compliance between individuals diagnosed with Bipolar I Disorder (BD-I) and Bipolar II Disorder (BD-II). Specifically, this study aimed to:

- Assess the frequency of the patients with BD-I and BD-II.
- Evaluate whether there is a significant difference in the overall relapse rates between BD-I and BD-II.
- Analyze the rates of medication compliance among patients with BD-I and BD-II.

METHODS

This retrospective study analyzed data from the Hospital Management System (HMS) of Karwan-e-Hayat Institute for Mental Health Care, Karachi, Pakistan, spanning the period from July 2019 to June 2022. A total of 377 participants were included, each meeting the inclusion criteria of having received medication for at least six months during the study period.

Psychiatric diagnoses were established using the DSM-IV criteria, confirmed through a detailed review of patients' clinical histories and diagnoses recorded in the HMS. Medication adherence was assessed by analyzing prescription refill records, frequency of follow-up visits, and clinical notes documented in the HMS.

Relapse rates were determined by identifying patients who experienced a mood episode requiring hospitalization, as documented in the HMS. These episodes were defined based on clinical records that described significant changes in mood, behavior, or functionality, necessitating inpatient care.
The Inclusion criteria were;

- The Participants must have a confirmed diagnosis of bipolar I Disorder (BD-I) or bipolar II Disorder (BD-II) according to DSM-IV criteria.
- Participants must have been on medication for at least 6 months during the study period from July 2019 to June 2022.
- Participants must be aged 18 years or older at the start of the study period.
- Participants must have complete hospitalization data available in the Hospital Management System (HMS) for the entire study period.

The exclusion criteria were;

- Participants with incomplete or missing data in the HMS records for the study period.
- Participants with primary psychiatric diagnoses other than BD-I or BD-II.
- Participants with severe co-morbid medical

conditions that could independently influence relapse rates or medication compliance (e.g., severe neurological disorders).

The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Karwan-e-Hayat Institute for Mental Health Care, ensuring adherence to ethical standards for research involving human participants.

The data were entered and analyzed using SPSS 27. Descriptive statistics were computed to summarize demographic and clinical characteristics of the sample. Frequencies and percentages were calculated for categorical variables including age groups, gender, medication compliance levels, and relapse rates.

Inferential statistics were applied to examine differences between Bipolar I and Bipolar II groups. The Chi-square (x^2) test of independence was used to determine the association between bipolar disorder type and categorical variables such as medication compliance and relapse rate. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 377 patients were part of this study; 193 of them with BD-1 and 184 with BD-2. The age distribution showed that the majority of Bipolar-I patients were in the 31-45 age group (40.9%), followed by the 45-60 age group (31.6%).For bipolar-II, the largest group was also 31-45 years (42.4%), but there was a higher percentage of younger patients (18-30 years) at 38%, compared to bipolar-I. Bipolar-II had a noticeable proportion of patients aged 61 and older (12%), which was higher than that of BD-I (2.6%).Gender distribution revealed a clear male predominance in both diagnostic groups. Table 1 demonstrates the demographic characteristics of the study population.

Table 1: Mean of demographic characteristics of patients (n =377)

Characteristics	Frequency	Percentage
Age group Bipolar I		
18-30	48	24.9
31-45	79	40.9
45-60	61	31.6
61-more	5	2.6
Age group Bipolar II		
18-30	70	38
31-45	78	42.4
45-60	14	7.6
61-more	22	12
Gender Bipolar I		
Female	47	24.4
Male	146	75.6
Gender Bipolar I		
Female	52	28.3
Male	132	71.7

Table 2 shows the compliance to treatment of patients with BD-1 and BD-2 in the study polulation.

Table 2: Frequency and percentage of Medicine Compliance Scale			
	Frequency	**Percentage**	**P- Value**
Medicine Compliance Scale Bipolar I			
1-2 Good	140	72.5	
3-4 Poor	53	27.5	0.000
Medicine Compliance Scale Bipolar II			
1-2 Good	169	91.8	
3-4 Poor	15	8.2	

Relapse rates are illustrated in Table 3.

Table 3: Frequency and percentage of Relapse rate			
Characteristics	**Frequency**	**Percentage**	**P- Value**
Relapse rate Bipolar I			
One time	65	33.7	
Two times	56	29	0.000
Three times	31	16.1	
Four & more than four times	41	21.2	
Relapse rate Bipolar II			
One time	156	84.8	
Two times	14	7.6	
Three times	6	3.3	
Four & more than four times	8	4.3	

DISCUSSION

The relationship between medication non-compliance and relapse is bidirectional and cyclical. Non-adherence increases vulnerability to recurrence, while repeated relapses may further undermine motivation and engagement in treatment.[21] Over time, this cycle contributes to illness progression and reduced responsiveness to treatment.[22] Given these complexities, understanding subtype-specific differences in relapse rates and medication compliance is essential for improving individualized treatment planning and long-term management.

The results indicate that the majority of individuals with BD-I fall within the 31–45 age range, accounting for 40.9%, with the next largest group being those aged 45–60 (31.6%). In contrast, BD-II shows a greater proportion of younger patients aged 18–30 (38%) and a notably higher proportion of patients aged 61 years and older (12%), compared to only 2.6% in the BD-I group. This trend aligns with research suggesting that BD-II often begins with depressive episodes at an earlier age compared to BD-I.[23] BD-II typically manifests during late adolescence or early adulthood, whereas BD-I is more commonly identified later, often

between the mid-20s and early 30s.[24,25] The broader age distribution of BD-II may reflect its less severe but more persistent course, which can delay diagnosis.

Data on medication adherence revealed that individuals with BD-II followed their prescribed medication regimen significantly more (91.8%) than those with BD-I (72.5%). Non-adherence was more prevalent among BD-I patients (27.5%) compared to BD-II patients (8.2%). Previous studies indicate that individuals with BD-I frequently experience difficulties with medication adherence due to the disruptive nature of manic episodes, which impair judgment and insight.[25,26] Additionally, the side effects of mood stabilizers and antipsychotics may further reduce adherence. Conversely, BD-II patients, who primarily experience depressive and hypomanic episodes, may have better illness insight and greater motivation to adhere to treatment, resulting in higher compliance.[25] Data on relapse rates indicate that individuals with BD-II are significantly more likely to experience only a single relapse compared to those with BD-I (84.8% vs. 33.7%). In contrast, BD-I patients tend to experience more frequent relapses, with higher proportions reporting multiple episodes. This finding is supported by previous research demonstrating that BD-I is associated with more frequent and severe relapses due to the episodic nature of mania.[26,27] The recurrent nature of manic episodes necessitates more intensive and continuous treatment in BD-I. In comparison, BD-II patients may experience a relatively more stable course with fewer relapses, likely due to better treatment adherence and the less severe nature of hypomanic episodes.[27]

This study has a few limitations that must be considered while interpretating the findings.

1. The study employed a retrospective design, which inherently relies on preexisting data rather than prospectively collected information.
2. The sample size of 377 participants, while sufficient for preliminary insights, limits the statistical power to detect smaller effects or trends. A larger sample size might have provided a more robust representation of relapse patterns and medication adherence rates, allowing for more nuanced subgroup analyses.
3. The data was exclusively collected from patients receiving treatment at the Karwan e Hayat Institute for Mental Health Care which limits the generalizability of the findings to other populations, regions, or healthcare settings. The unique socioeconomic, cultural, and healthcare dynamics of the patients at Karwan e Hayat may not reflect those of broader or more diverse populations, making it challenging to apply the findings universally.

CONCLUSION

Our findings highlight the distinct demographic and clinical profiles of BD-I and BD-II, which are crucial for tailored management. BD-I patients are mainly middle-aged, whereas BD-II patients are younger or older, consistent with earlier onset and broader age range due to BD-II's milder nature). BD-II patients show significantly better medication compliance (91.8% vs. 72.5%) and fewer relapses, attributed to better insight and less severe episodes. These differences underscore the need for individualized treatment strategies for effective management.

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Nasir Mehmood: Concept, Design, Data collection, Data analysis, manuscript writing
Qudsia Tariq; Data interpretation, manuscript revision

All the authors have approved the final version to be published and agree to be accountable for all aspects of the work.