

Frequency Of Relapse in Bipolar Affective Disorder MTI Ayub Teaching Hospital Abbottabad Khyber Pakhtunkhwa Pakistan.

¹Abid Nisar Khan, Kashif Ahmad², Habib Ullah³, Syed Touseef Shah^{4*}, Arooma Sagheer⁵, Zeest Shah⁶

¹Specialist Registrar Department of Psychiatry and Behavioral Sciences MTI Ayub teaching hospital Abbottabad Email: abidburki007@gmail.com

²Trainee Registrar, Department of Psychiatry and Behavioral Sciences, MTI Ayub Teaching Hospital, Abbottabad

Email: ahmadkashif195@gmail.com

³Resident psychiatrist Department of Psychiatry and Behavioral Sciences, MTI Ayub Teaching Hospital, Abbottabad. Email: hu79669@gmail.com

⁴Resident Psychiatrist, Department of Psychiatry and Behavioral Sciences, MTI Ayub Teaching Hospital, Abbottabad

Email: syedtouseefshah123@gmail.com *Correspondence*

⁵ Resident psychiatrist, Department of Psychiatry and Behavioral Sciences, MTI Ayub teaching hospital Abbottabad Email: saghiraroma@gmail.com

⁶Resident psychiatrist Department of Psychiatry and Behavioral Sciences, MTI Ayub Teaching Hospital, Abbottabad. Email: drzeestshah@gmail.com

ABSTRACT

Bipolar Affective Disorder BPAD is a severe mental illness marked by recurrent episodes of mania/hypomania, depression, or mixed states. It affects 2-4% of the global population, making it the sixth leading cause of disability worldwide. The Global Burden of Disease Study 2013 estimated that 48.8 million people suffered from BPAD, with a higher prevalence in women and individuals aged 25–29 years. BPAD is associated with elevated suicide risk, psychiatric comorbidities, and substantial social and economic burdens. The treatment of BPAD is essential to prevent severe complications, including relapse.

Objective: To determine the frequency of relapse in patients diagnosed with bipolar affective disorder at Ayub Teaching Hospital, Abbottabad.

Study Design: A cross-sectional descriptive study was conducted to assess the frequency of relapse in patients with bipolar affective disorder. The study was carried out at the Department of Psychiatry, Ayub Teaching Hospital, Abbottabad, Pakistan, from July 1st to December 31st, 2022. The study included 80 patients aged between 18–60 years diagnosed with bipolar affective disorder, both male and female, under outpatient follow-up treatment for at least one month. Patients with schizophrenia and those unable to communicate were excluded.

Methods: Data collection involved structured proformas that recorded demographic details, bipolar disorder subtype, and relapse status. The relapse was defined as the return of full syndrome criteria for mania, mixed episodes, or depression following any duration of remission. The collected data were analyzed using SPSS version 10.0, with descriptive statistics, including frequencies, percentages, and mean \pm standard deviation for quantitative variables.

Results: Demographics: The mean age of patients was 33.96 ± 13.97 years, with a mean weight of 55.50 ± 7.88 kg. 55% of the patients were male, and 45% were female. Bipolar Affective Disorder Subtypes: 45% of patients had depression, 22.5% had mania, 27.5% had mixed episodes, and 5% had hypomania. Relapse Frequency: 68.8% of the patients experienced relapse, while 31.3% did not. Age Distribution: 56.3% of patients were under 30 years, and 43.8% were aged 30 years or older. Gender and Bipolar Subtypes: Males showed higher rates of mania and mixed episodes, while females were more likely to have depression. Relapse by Gender: Males had a relapse rate of 70.5%, while females had a relapse rate of 66.7%. Relapse by Age Group: 73.3% of patients below 30 years relapsed, compared to 62.9% in those aged 30 and above.

Conclusions: The study found a high relapse rate of 68.8% among bipolar disorder patients. Treatment adherence and effective management of psychopathology are crucial for preventing relapse. The study highlights the importance of focusing on medication adherence and psychoeducation. Further research is needed to explore mental health care and relapse prevention in low-income countries to improve outcomes for bipolar disorder patients.

Keywords: Relapse, Bipolar Affective Disorder, Depression, Mania/Hypomania, Mixed Affective Episode, Treatment Adherence, Psychopathology, Mental Health Care.

INTRODUCTION

Bipolar Affective Disorder BPAD is a severe mental illness marked by recurrent episodes of mania/hypomania, depression, or mixed states, with a lifetime prevalence of 2–4% globally, making it the sixth leading cause of disability worldwide. According to the Global Burden of Disease Study 2013, 48.8 million people worldwide suffer from

BPAD with higher prevalence in women and individuals aged 25–29 years (1). BPAD carries a significantly elevated risk of suicide and psychiatric comorbidities, contributing to its substantial disease burden. The disorder is chronic and recurrent, creating a significant burden on patients, families, and society, necessitating treatment to avoid complications. Additional burdens include increased

mortality from medical causes, substance abuse (especially alcoholism), and comorbid psychiatric disorders like anxiety and eating disorders (2). The economic impact of BPAD is enormous, with direct costs estimated at \$31 billion and indirect costs reaching \$120 billion in the USA alone (3). BPAD causes are complex, involving both genetic and environmental factors (5). There are two main subtypes of BPAD, type I and type II, with type II being distinguished by the absence of full-blown manic episodes. Despite shared clinical features, BPAD patients are often misdiagnosed, leading to a delay of 5–10 years in diagnosis (6). Relapse is a major challenge in treating bipolar disorder, contributing to high economic and social burdens. Relapse is defined as the return of full syndrome criteria for mania, mixed episodes, or depression after a period of remission, and it often leads to hospitalization, increased suicide risk, and impaired psychosocial recovery. While the risk of relapse in both depression and mania is high, it is difficult to predict and prevent for most patients. Psychosocial stressors, such as Stressful Life Events, also play a significant role in triggering relapses (9). A study by Wesseloo et al. found that postpartum relapse rates were significantly higher (66%) in women with BPAD who were medication-free during pregnancy (10). In a study by Belete et al., the prevalence of relapse was 71% among patients with BPAD in Ethiopia (7). This study aims to determine the frequency of relapse in patients with bipolar affective disorder at Ayub Teaching Hospital, Abbottabad, as there is limited local data compared to Western countries. By assessing the magnitude of relapse in our setting, the study aims to provide local evidence for better management and to reduce the global burden of BPAD. The objective is to determine the frequency of relapse in bipolar affective disorder at Ayub Teaching Hospital, Abbottabad. Operational definitions used in this study include: Depression, Mania/Hypomania, and Mixed Affective Episode, all diagnosed based on ICD-10 criteria. Relapse is defined as the return of full syndrome criteria for mania, mixed episodes, or depression following any duration of remission. This study aims to provide insights into BPAD relapse, promoting early intervention and reducing future recurrences both locally and globally.

METHODS

The study, conducted at the Psychiatry Department of Ayub Teaching Hospital, Abbottabad, aimed to assess the frequency of relapse in patients with bipolar affective disorder. The hospital, a tertiary care center situated on the Silk Road, serves a

diverse population and provides undergraduate and postgraduate teaching. This cross-sectional descriptive study was carried out from July 1st to December 31st, 2022, with a sample size of 80 patients, determined using WHO sample size calculation software. The expected relapse frequency was 71%, with a 95% confidence level and 10% absolute precision. Non-probability convenience sampling was employed, and patients included in the study were those aged 18–60 years, both male and female, diagnosed with bipolar affective disorder and receiving outpatient follow-up treatment for at least one month. Exclusion criteria included patients with schizophrenia and those unable to communicate. Data collection began after obtaining ethical approval, and informed consent was taken from all participants. Detailed histories, clinical examinations, and relevant investigations were conducted, and all information was recorded in a proforma. The study's data were analyzed using SPSS version 10.0, with quantitative variables like age described as mean \pm standard deviation, and categorical variable

RESULTS

The study conducted at Ayub Teaching Hospital Abbottabad aimed to assess the frequency of relapse in bipolar affective disorder. Descriptive statistics showed that the mean age of the 80 patients was 33.96 ± 13.97 years, with weights ranging from 40 to 72 kg. Of the 80 patients, 55.0% were male and 45.0% were female. In terms of bipolar affective disorder types, 45.0% were diagnosed with depression, 22.5% with mania, 27.5% with mixed, and 5.0% with hypomania. Regarding relapse, 68.8% experienced relapse, while 31.3% did not. The age distribution revealed that 56.3% of patients were below 30 years, while 43.8% were aged 30 or above. The gender distribution across bipolar disorder subtypes showed a higher proportion of depression in both males (43.2%) and females (47.2%). The relapse rate was higher in males (70.5%) compared to females (66.7%), though both findings were statistically insignificant ($p=0.584$ and $p=0.716$, respectively). Regarding age and bipolar disorder, depression was most common in the younger age group (48.9%), while the older group had a slightly higher frequency of mixed disorders (34.3%). Regarding relapse, 73.3% of those below 30 years relapsed, while 62.9% of those 30 and above relapsed, with both findings being statistically insignificant ($p=0.654$ and $p=0.316$, respectively). These findings are summarized in the tables presented in the study.

Table 1: Descriptive Statistics

Variable	N	Minimum	Maximum	Mean	Std. Deviation
----------	---	---------	---------	------	----------------

Age (years)	80	18	60	33.96	13.97
Weight (kg)	80	40	72	55.50	7.88

Table 2: Frequency of Gender

Gender	Frequency	Percent
Male	44	55.0%
Female	36	45.0%
Total	80	100.0%

Table 3: Frequency of Bipolar Affective Disorder

Bipolar Affective Disorder	Frequency	Percent
Depression	36	45.0%
Mania	18	22.5%
Mixed	22	27.5%
Hypomania	4	5.0%
Total	80	100.0%

Table 4: Frequency of Relapse

Relapse	Frequency	Percent
Yes	55	68.8%
No	25	31.3%
Total	80	100.0%

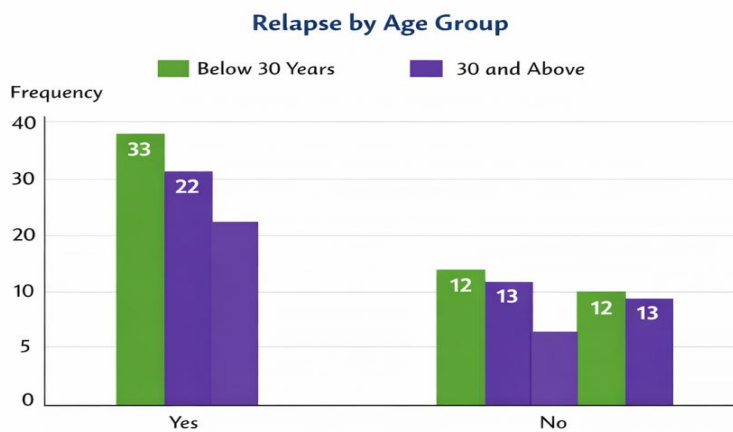
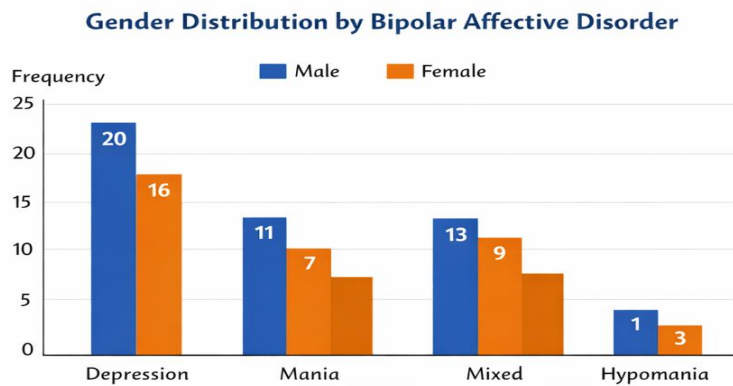


Figure A: Gender Distribution by Bipolar Affective Disorder Figure B: Relapse by Age Group

Figure A Show distribution of gender across four types of bipolar affective disorder. It shows that 45% of the sample is male, with 36% females. The highest frequency is observed for Depression

among both genders. The male gender has higher frequencies in Mania and Mixed disorders, while Hypomania is more common among females. Table Reference **Figure B:** This graph depicts relapse rates across two age groups: Below 30 years and 30 and above. The younger group shows a significantly higher relapse frequency (33 Yes, 12 No), while the older group experiences fewer relapses (22 Yes, 13 No).

DISCUSSION

Prevention of relapse for mental disorders in low- and middle-income countries has been recommended through a stepped care model, integrating both drug and psychological treatments, as reported in study 10. The prevalence of relapse in the current study was found to be higher than previously reported, with 65.9% relapse in Ethiopia, similar to findings in studies 11 and 12, who reported a 71% relapse rate in pregnant mothers with bipolar disorder. Although there are methodological and setting differences, the current study clearly highlights the high magnitude of relapse in low-income settings. These findings align with a community-based study which suggests that bipolar disorder may present a more severe clinical course in developing countries compared to developed nations, as reported in study 11. Additionally, a study emphasizing treatment adherence showed that improving adherence can reduce relapse rates by 61%, with psychoeducation playing a key role in enhancing treatment compliance, as reported in study 13. In this study, the mean age of patients was 33.96 ± 13.968 years, ranging from 18 to 60 years, and the mean weight was 55.50 ± 7.880 , ranging from 40 to 72 kg. The frequency of gender was found to be 44 males (55.0%) and 36 females (45.0%). Regarding the frequency of bipolar affective disorder, 36 (45.0%) patients had depression, 18 (22.5%) had mania, 22 (27.5%) had mixed episodes, and 4 (5.0%) had hypomania. The frequency of relapse in this study was 55 (68.8%) patients, with the remaining 25 (31.3%) having other disorders. These results align closely with findings in study 14. The age distribution showed 45 patients (56.3%) were below 30 years, and 35 (43.8%) were 30 years and above. In the distribution of gender with respect to bipolar disorder, depression was found in 19 (43.2%) male patients, while 17 (47.2%) female patients had depression; similar patterns were observed for mania, mixed episodes, and hypomania, with no statistically significant differences ($p = 0.584$). The frequency distribution of relapse by gender showed 31 (70.5%) male patients and 24 (66.7%) female patients relapsed, with no statistically significant difference ($p = 0.716$). Regarding age group distribution with

respect to bipolar disorder, 22 (48.9%) patients below 30 years had depression, while 14 (40.0%) of those aged 30 and above had depression, with no significant difference ($p = 0.654$). The frequency distribution of relapse by age group showed 33 (73.3%) patients below 30 years relapsed, compared to 22 (62.9%) in the 30 years and above group, again with no significant difference ($p = 0.316$). These findings are consistent with study 14. Treatment adherence plays a crucial role in preventing relapse, and clinicians should focus on improving adherence through interventions like psychoeducation. The current study confirms that medication adherence is key in reducing the relapse rate, and efforts to enhance adherence should be integral to managing bipolar disorder. The high prevalence of relapse in this study underscores the importance of focusing on treatment adherence as a protective factor. Ultimately, this study aims to inspire future research in low-income countries to address mental health care and the prevention of relapse.

Conclusion

This study at Ayub Teaching Hospital, Abbottabad assessed relapse in 80 patients diagnosed with Bipolar Affective Disorder. The findings showed a high relapse frequency: 55 patients (68.8%) experienced relapse, while 25 patients (31.3%) did not. This indicates that relapse is very common among bipolar patients in this setting. Relapse was more frequent in patients younger than 30 years (73.3%) compared to those aged 30 years and above (62.9%), but this difference was not statistically significant. Similarly, relapse was slightly higher in males (70.5%) than females (66.7%), and this difference was also not statistically significant.

Overall, the study concludes that Bipolar Affective Disorder has a substantially high relapse rate in the local population. Therefore, preventing relapse should be a major treatment goal. Medication adherence, regular follow-up, early recognition of symptoms, and psychoeducation for patients and families are essential steps to reduce relapse and improve outcomes. Further research is needed in low-income settings to better understand relapse-related factors and strengthen relapse-prevention strategies.

Recommendations

Patients should adhere strictly to prescribed medications and avoid discontinuation without medical advice. Regular follow-up visits are essential, even during periods of symptomatic improvement. Early warning signs of relapse, including sleep disturbance, increased energy,

pressured speech, low mood, or hopelessness, should be recognized and promptly reported. Maintaining a structured daily routine, adequate sleep, and minimizing stress are important preventive measures. Substance use should be avoided due to its association with relapse. Family support enhances treatment adherence, while timely intervention is crucial in the presence of suicidal ideation. Psychoeducation and counseling play a key role in improving illness insight and preventing relapse.

Author Contributions:

Dr. Abid Nisar Khan: was primarily responsible for the study conception, design, data analysis, and writing of the manuscript. **Dr. Kashif Ahmad:** contributed to data collection, data analysis, and manuscript review. **Dr. Habib Ullah:** in data collection and contributed to manuscript review. **Dr. Syed Touseef Shah:** manuscript writing. **Dr. Arooma Sagheer:** Resident manuscript review. **Dr. Zeest Shah:** manuscript preparation.

Funding and Conflict of Interest:

This study did not receive any funding. The authors declare that there is no conflict of interest regarding the publication of this study.

REFERENCES

- Ashok, A. H., T. R. Marques, S. Jauhar, M. M. Nour, G. M. Goodwin, and A. H. Young. "The Dopamine Hypothesis of Bipolar Affective Disorder: The State of the Art and Implications for Treatment." *Molecular Psychiatry* 22 (2017): 666-79.
- Andrade-González, N., L. Álvarez-Cadenas, J. Saiz-Ruiz, and G. Lahera. "Initial and Relapse Prodromes in Adult Patients with Episodes of Bipolar Disorder: A Systematic Review." *European Psychiatry* 63 (2020): e12.
- Syan, S. K., M. Smith, B. N. Frey, R. Remtulla, F. Kapczinski, G. B. C. Hall, and L. Minuzzi. "Resting-State Functional Connectivity in Individuals with Bipolar Disorder during Clinical Remission: A Systematic Review." *Journal of Psychiatry and Neuroscience* 43 (2018): 298-316.
- López-Muñoz, F., W. W. Shen, P. D'Ocon, A. Romero, and C. Álamo. "A History of the Pharmacological Treatment of Bipolar Disorder." *International Journal of Molecular Sciences* 19 (2018): 2143.
- Amare, A. T., K. O. Schubert, L. Hou, S. R. Clark, S. Papiol, U. Heilbronner, et al. "Association of Polygenic Score for Schizophrenia and HLA Antigen and Inflammation Genes with Response to Lithium in Bipolar Affective Disorder: A Genome-Wide Association Study." *JAMA Psychiatry* 75 (2018): 65-74.
- Sparding, T., E. Pålsson, E. Joas, S. Hansen, and M. Landén. "Personality Traits in Bipolar Disorder and Influence on Outcome." *BMC Psychiatry* 17 (2017): 159.
- Belete, H., T. Ali, and G. Legas. "Relapse and Clinical Characteristics of Patients with Bipolar Disorders in Central Ethiopia: A Cross-Sectional Study." *Psychiatry Journal* 2020 (2020): 8986014.
- Kessing, L. V., K. Munkholm, M. Faurholt-Jepsen, K. W. Miskowiak, L. B. Nielsen, R. Frikke-Schmidt, et al. "The Bipolar Illness Onset Study: Research Protocol for the BIO Cohort Study." *BMJ Open* 7 (2017): e015462.
- Sam, S. P., A. Nisha, and P. J. Varghese. "Stressful Life Events and Relapse in Bipolar Affective Disorder: A Cross-Sectional Study from a Tertiary Care Center of Southern India." *Indian Journal of Psychological Medicine* 41 (2019): 61-67.
- Wesseloo, R., A. M. Kamperman, T. Munk-Olsen, V. J. Pop, S. A. Kushner, and V. Bergink. "Risk of Postpartum Relapse in Bipolar Disorder and Postpartum Psychosis: A Systematic Review and Meta-Analysis." *American Journal of Psychiatry* 173 (2016): 117-27.
- Zhang, D., L. Cheng, Y. Qian, N. Alliey-Rodriguez, J. R. Kelsoe, T. Greenwood, et al. "Singleton Deletions throughout the Genome Increase Risk of Bipolar Disorder." *Molecular Psychiatry* 14 (2009): 376-80.
- Price, A. L., and G. R. Marzani-Nissen. "Bipolar Disorders: A Review." *American Family Physician* 85 (2012): 483-93.
- Ketter, T. A. "Diagnostic Features, Prevalence, and Impact of Bipolar Disorder." *Journal of Clinical Psychiatry* 71 (2010): e14.
- Edvardsen, J., S. Torgersen, E. Røysamb, S. Lygren, I. Skre, S. Onstad, et al. "Heritability of Bipolar Spectrum Disorders: Unity or Heterogeneity?" *Journal of Affective Disorders* 106 (2008): 229-40.
- Berrettini, W. H., T. N. Ferraro, L. R. Goldin, D. R. Weeks, S. E. Detera-Wadleigh, J. I. Nurnberger Jr, et al. "Chromosome 18 DNA Markers and Manic-Depressive Illness: Evidence for a Susceptibility Gene." *Proceedings of the National Academy of Sciences of the United States of America* 91 (1994): 5918-21.
- Reich, T., P. J. Clayton, and G. Winokur. "Family History Studies: V. The Genetics of Mania." *American Journal of Psychiatry* 125 (1969): 1358-69.

17. Lin, P. I., M. G. McInnis, J. B. Potash, V. L. Willour, D. F. Mackinnon, K. Miao, et al. "Assessment of the Effect of Age at Onset on Linkage to Bipolar Disorder: Evidence on Chromosomes 18p and 21q." *American Journal of Human Genetics* 77 (2005): 545-55.
18. McQuillin, A., N. J. Bass, G. Kalsi, J. Lawrence, V. Puri, K. Choudhury, et al. "Fine Mapping of a Susceptibility Locus for Bipolar and Genetically Related Unipolar Affective Disorders, to a Region Containing the C21ORF29 and TRPM2 Genes on Chromosome 21q22.3." *Molecular Psychiatry* 11 (2006): 134-42.
19. Ekholm, J. M., T. Kiesepä, T. Hiekkalinna, T. Partonen, T. Paunio, M. Perola, et al. "Evidence of Susceptibility Loci on 4q32 and 16p12 for bipolar disorder." *Human Molecular Genetics* 12 (2003): 1907-15.
20. Abou Jamra, R., R. Fuerst, R. Kaneva, G. Orozco Diaz, F. Rivas, F. Mayoral, et al. "The First Genomewide Interaction and Locus-Heterogeneity Linkage Scan in Bipolar Affective Disorder: Strong Evidence of Epistatic Effects Between Loci on Chromosomes 2q and 6q." *American Journal of Human Genetics* 81 (2007): 974-86.
21. Kelsoe, J. R., M. A. Spence, E. Loetscher, M. Foguet, A. D. Sadovnick, R. A. Remick, et al. "A Genome Survey Indicates a Possible Susceptibility Locus for Bipolar Disorder on Chromosome 22." *Proceedings of the National Academy of Sciences of the United States of America* 98 (2001): 585-90.
22. Kakiuchi, C., K. Iwamoto, M. Ishiwata, M. Bundo, T. Kasahara, I. Kusumi, et al. "Impaired Feedback Regulation of XBP1 as a Genetic Risk Factor for Bipolar Disorder." *Nature Genetics* 35 (2003): 171-75