Section: Psychiatry

Original Research Article

TEMPERAMENT AS ENDOPHENOTYPE OF BIPOLAR AFFECTIVE DISORDER: A CROSS-SECTIONAL STUDY

Narendra Pratap Singh Rajput[1], Jagdish Singh Meena[2], Aditi Patel[2]

[1]DNB Psychiatry, Assistant Professor, Department of Psychiatry, Mahaveer Institute of Medical Sciences and Research, Bhopal, Madhya Pradesh, India
[2]MD Psychiatry, Assistant Professor, Department of Psychiatry, Mahaveer Institute of Medical Sciences and Research, Bhopal, Madhya Pradesh, India

Received : 07/09/2025
Received in revised form : 22/10/2025
Accepted : 10/11/2025

Keywords:
Bipolar affective disorder, affective temperament, TEMPS-A, endophenotype, cyclothymic temperament, hyperthymic temperament.

Corresponding Author:
Dr. Aditi Patel,
Email: munnu1012.np@gmail.com

DOI: 10.47009/jamp.2025.7.6.74

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (6); 385-391

ABSTRACT

Background: Affective temperament is a heritable personality component influencing emotional reactivity and mood regulation. Certain temperamental profiles may serve as endophenotypic markers of bipolar affective disorder (BPAD), linking genetic vulnerability to its clinical manifestation. The aim and objective is to compare the distribution of affective temperaments among patients with BPAD in remission, their first-degree relatives (FDRs), and normal healthy controls (NHCs), and to identify temperaments that may act as potential endophenotypes. **Materials and Methods:** This cross-sectional study was conducted at Mahaveer Institute of Medical Sciences and Research, Bhopal, in 2024 and included 90 participants (30 BPAD, 30 FDR, 30 NHC). Diagnosis and remission were confirmed using M.I.N.I., HAM-D, and YMRS scales. Affective temperaments were assessed with the 50-item TEMPS-A questionnaire, and data were analyzed using SPSS v20 with Chi-square tests ($p < 0.05$). **Result:** Hyperthymic (76.7%) and cyclothymic (56.7%) temperaments were predominant among BPAD patients. Compared to NHCs, BPAD patients showed significantly higher frequencies of cyclothymic (56.7% vs 10%, $p < 0.001$), hyperthymic (76.7% vs 40%, $p = 0.004$), and irritable (16.7% vs 0%, $p = 0.02$) temperaments. FDRs also differed significantly from controls in cyclothymic traits (40% vs 10%, $p = 0.007$). **Conclusion:** Cyclothymic and hyperthymic temperaments are closely associated with BPAD, while the presence of cyclothymic traits among unaffected relatives supports their role as stable, heritable, state-independent endophenotypes. Recognition of these temperaments may help in early identification and preventive interventions for individuals at risk of bipolar disorder.

INTRODUCTION

The concept of endophenotype in psychiatry was introduced by Gottesman and Shields about 45 years ago, though significant interest in its application has grown only recently.[1] The term, originally coined by John and Lewis in insect biology, described internal, microscopic traits ("endophenotypes") influencing visible characteristics ("exophenotypes").[2] Endophenotypes are considered more suitable for genetic analysis since their variability depends on fewer genes, offering simpler clues to disease mechanisms and making psychiatric disorders more tractable for genetic study.[3]

The modern view of bipolar disorder dates to the mid-19th century. Falret described alternating mania and depression with symptom-free intervals as "circular insanity," while Baillarger proposed "dual-form insanity," without such intervals.[4] Kahlbaum supported Falret's perspective, aligning with Griesinger's idea that transitions from melancholia to mania were natural.[5] Kraepelin later emphasized periodicity, favorable prognosis, and strong familial aggregation as distinguishing features from dementia praecox and introduced the concept of mixed states.[6] His work laid the foundation for the bipolar spectrum concept, later termed manic-depressive illness (MDI).[7]

The DSM-III (1980) divided MDI into bipolar disorder and major depressive disorder,[8] echoing Leonhard's earlier distinction between bipolar and unipolar psychoses.[9] Akiskal and Mallya (1987) expanded this further through the "soft bipolar spectrum," encompassing hypomanic depressions (bipolar II), cyclothymic and hyperthymic traits, and medication-induced hypomania (bipolar III).[10] Akiskal and Pinto later described a continuum of forms such as Bipolar 1/2, II½, and III.[11,12] Ghaemi et al. proposed grouping all atypical presentations under "bipolar spectrum disorder (BSD)".[13]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Temperament, the heritable biological core of personality influencing mood and energy, has long been linked to psychiatric illness.[14] Kraepelin identified four temperaments—cyclothymic, manic, depressive, and irritable—commonly observed in patients and their relatives.[14] Akiskal later defined five affective temperaments: depressive, hyperthymic, cyclothymic, irritable, and anxious, viewing bipolar disorder as a continuum from temperament to illness.[15] Cloninger described related biological dimensions—novelty seeking, harm avoidance, reward dependence, and persistence—linked to specific neurotransmitters.[16,17]

Affective temperaments influence onset, course, and treatment outcomes in mood disorders.[18,19] Depressive temperament predominates in major depression, while cyclothymic and hyperthymic types are characteristic of bipolar illness.[20] Cyclothymic individuals, often female, tend to have more episodes, borderline traits, and family histories of mood or anxiety disorders, whereas hyperthymic patients show more manic episodes and hospitalizations.[21] Hyperthymic and cyclothymic temperaments are frequently associated with bipolar family history, while depressive temperament is linked with mood disorders in general.[22–26] Genetic studies reaffirm these associations, suggesting temperaments may confer evolutionary advantages as reservoirs for affective disorder genes.[27]

Despite several international studies, there is limited Indian research examining temperament profiles in bipolar patients and their relatives. Understanding these affective temperaments as possible endophenotypes could provide valuable insight into the heritability and genetic basis of bipolar disorder. Therefore, the present study aimed to compare the prevalence of affective temperaments among patients with bipolar affective disorder, their healthy first-degree relatives, and healthy controls.

MATERIALS AND METHODS

Study Site: The present study was conducted at the Mahaveer Institute of Medical Sciences and Research (MIMSR), Bhopal, Madhya Pradesh. It is a tertiary care teaching hospital providing comprehensive mental health services to patients across central India.

Study Design and Population: This hospital-based cross-sectional observational study included three groups of participants—patients diagnosed with bipolar affective disorder (BPAD) who were in remission, their healthy first-degree relatives (FDRs) with no history of psychiatric illness, and normal healthy controls (NHCs) from the local community matched for age and sex. The BPAD group comprised individuals attending the inpatient wards or outpatient follow-up clinics of the Department of Psychiatry at MIMSR. The FDRs were biological relatives of these patients, and the NHCs were community volunteers without a personal or family history of psychiatric illness.

Study Duration and Sample Size: The study was carried out from January 2024 to December 2024. A total of 90 participants were enrolled, consisting of 30 BPAD patients in remission, 30 FDRs, and 30 NHCs. Although the estimated sample size by standard statistical formula was 126, a smaller sample was included due to the limited number of eligible patients without psychiatric comorbidities and the restricted time frame of the study.

Sampling Method: Participants were selected using purposive sampling based on the inclusion and exclusion criteria specified below.

Inclusion and Exclusion Criteria

For the BPAD group, participants were diagnosed according to ICD-10 criteria and were required to be in remission, confirmed by scores of ≤7 on both the Young Mania Rating Scale (YMRS) and the Hamilton Depression Rating Scale (HAM-D). Individuals aged between 18 and 60 years of either sex who provided written informed consent were included. The FDR group comprised first-degree relatives of BPAD patients who had no lifetime history of psychiatric disorders, within the same age range and with informed consent. The NHC group consisted of age- and sex-matched community volunteers with no family history of psychiatric illness who also provided written informed consent. Participants from all three groups were excluded if they had comorbid psychiatric, neurological, or major physical illnesses, intellectual disability, inability to read Hindi, English, or a history of substance dependence.

Assessment Tools: Socio-demographic and clinical details were collected using a semi-structured proforma designed for this study. It included information regarding age, sex, education, occupation, marital status, religion, place of residence, family type, and family history of psychiatric or major medical illness.

The Temperament Evaluation of Memphis, Pisa, Paris, and San Diego – Auto Questionnaire (TEMPS-A),[28] was used to assess affective temperaments. The short 50-item version, developed in San Diego, measures cyclothymic, dysthymic, irritable, and hyperthymic temperaments and has demonstrated high test–retest reliability ranging from 0.58 to 0.70. The Hindi version is validated for use in Indian populations.[29] Each temperament subscale has defined cutoff scores; for instance, a dysthymic score of ≥5 indicated dysthymic temperament. Participants were instructed to mark “true” for statements describing their general lifelong behavior patterns.

The Hamilton Depression Rating Scale (HAM-D), a 21-item scale used to assess the severity of depression, was administered, with scores ≤7 considered normal.[30,31] The Young Mania Rating Scale (YMRS),[32] an 11-item clinician-rated instrument, was used to assess manic symptoms over the previous 48 hours, with total scores ≤7 indicating remission.[31] Diagnostic confirmation was done

ISSN (O): 2687-5365; ISSN (P): 2753-6556

using the Mini International Neuropsychiatric Interview (M.I.N.I., Version 6.0.0), a structured diagnostic tool for major psychiatric disorders based on DSM-IV and ICD-10 criteria, known for its high reliability and short administration time of approximately 15–20 minutes.[32,33]

Study Procedure: After obtaining informed consent, participants were screened according to the inclusion and exclusion criteria. Diagnostic confirmation for BPAD was made using the M.I.N.I. questionnaire, and remission status was confirmed using the HAM-D and YMRS scales. All eligible participants, including BPAD patients, their first-degree relatives, and healthy controls, were administered the TEMPS-A questionnaire. Socio-demographic and clinical data were collected systematically for all participants.

Statistical Analysis: Data analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 20. Descriptive statistics, including mean, standard deviation, and percentage, were calculated for socio-demographic and clinical variables. The Chi-square test was used to compare categorical variables such as temperament distribution across the three study groups. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: Ethical approval for the study was obtained from the Institutional Ethics Committee of Mahaveer Institute of Medical Sciences and Research, Bhopal. Written informed consent was obtained from all participants prior to data collection. Confidentiality of participant information was maintained throughout the study, and each subject had the right to withdraw from the study at any point without any adverse consequence.

RESULTS

A total of 90 participants were included in the study—30 patients with bipolar affective disorder (BPAD) in remission, 30 healthy first-degree relatives (FDRs), and 30 normal healthy controls (NHCs). Statistical analysis was performed using SPSS version 20. The findings are presented under four major headings: (1) socio-demographic characteristics, (2) clinical profile of BPAD patients, (3) distribution of affective temperaments, and (4) intergroup comparison of temperamental traits.

Socio-Demographic Characteristics: The mean age of BPAD patients was 34.10 ± 11.42 years, and the mean years of education were 10.33 ± 2.48. The majority of patients were male (73.3%), Hindu (63.3%), and married (66.7%). Most participants were undergraduates (83.3%), employed or engaged in other occupations (63.4%), and belonged to nuclear families (66.7%). Most resided in rural or semi-urban areas (73.3%) and belonged to either middle (53.3%) or lower (46.7%) socioeconomic classes.

Table 1: Socio-Demographic Profile of BPAD Group

Variable	Category	n (%)
Sex	Male	22 (73.3)
	Female	8 (26.7)
Religion	Hindu	19 (63.3)
	Muslim	10 (33.3)
	Christian	1 (3.3)
Marital status	Single	9 (30.0)
	Married	20 (66.7)
	Others	1 (3.3)
Education	Up to middle school	8 (26.7)
	Up to high school	10 (33.3)
	Up to higher secondary	7 (23.3)
	Graduate and above	5 (16.7)
Occupation	Employed	14 (46.7)
	Unemployed	5 (16.7)
	Others	11 (36.7)
Socioeconomic status	Middle	16 (53.3)
	Lower	14 (46.7)
Residence	Rural	18 (60.0)
	Semi-urban	4 (13.3)
	Urban	8 (26.7)
Family type	Nuclear	20 (66.7)
	Joint	10 (33.3)

When compared with FDRs and NHCs, the mean age difference was not statistically significant (BPAD: 34.10 ± 11.42 vs. FDR/NHC: 41.83 ± 14.36; p = 0.053). However, a significant difference was found in sex distribution, with a higher proportion of females in the BPAD group (26.7%) compared to FDR/NHCs (3.3%; p = 0.011).

Clinical Profile of BPAD Patients

The mean age of onset of illness was 22.51 ± 9.09 years, with a mean illness duration of 11.65 ± 8.63 years. The average duration of remission was 11.16 ± 20.04 months, and the mean age at first hospitalization was 27.32 ± 9.64 years. Patients had an average of 2.8 ± 2.29 hospitalizations and 6.76 ± 4.98 total illness episodes, of which manic episodes were most frequent (5.23 ± 4.29).

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Ninety percent of patients had their first episode as mania, while 10% presented initially with depression. A family history of mania was observed in 6.7% of patients, and 3.3% had a family history of depression.

Table 2: Clinical Variables of BPAD Patients (n = 30)

Variable	Mean ± SD
Age of onset (years)	22.51 ± 9.09
Duration of illness (years)	11.65 ± 8.63
Duration of remission (months)	11.16 ± 20.04
Age at first hospitalization (years)	27.32 ± 9.64
Number of hospitalizations	2.80 ± 2.29
Total episodes of illness	6.76 ± 4.98
Total manic episodes	5.23 ± 4.29
Total depressive episodes	1.16 ± 2.12
Total mixed episodes	0.13 ± 0.43

Distribution of Affective Temperaments: The frequency distribution of affective temperaments assessed by the TEMPS-A questionnaire revealed that hyperthymic temperament was most common among BPAD patients (76.7%), followed by cyclothymic (56.7%), dysthymic (23.3%), and irritable (16.7%). Among FDRs, hyperthymic (60.0%) and cyclothymic (40.0%) temperaments were also common, while dysthymic and irritable temperaments were less frequent. In the NHC group, hyperthymic (40.0%) and dysthymic (23.3%) temperaments were predominant, whereas cyclothymic (10.0%) and irritable (0%) traits were rare.

Table 3: Frequency Distribution of Temperaments Across Study Groups

Temperament	BPAD n (%)	FDR n (%)	NHC n (%)
Dysthymic (≥ 5/9)	7 (23.3)	11 (36.7)	7 (23.3)
Cyclothymic (≥ 9/17)	17 (56.7)	12 (40.0)	3 (10.0)
Hyperthymic (≥ 7/13)	23 (76.7)	18 (60.0)	12 (40.0)
Irritable (≥ 6/11)	5 (16.7)	3 (10.0)	0 (0.0)

Overall, affective temperaments were more prevalent in BPAD patients than in their relatives or healthy controls. Dysthymic temperament, however, was most frequent among FDRs.

Comparison of Temperaments Between Groups

When comparing BPAD and FDR groups, hyperthymic temperament was present in 76.7% of BPAD patients versus 60% of FDRs, cyclothymic in 56.7% versus 40%, dysthymic in 23.3% versus 36.7%, and irritable in 16.7% versus 10%. None of these differences reached statistical significance ($p > 0.05$).

However, significant differences emerged when BPAD patients were compared with NHCs. Cyclothymic temperament (56.7% vs. 10%, $p < 0.001$), hyperthymic temperament (76.7% vs. 40%, $p = 0.004$), and irritable temperament (16.7% vs. 0%, $p = 0.020$) were significantly higher among BPAD patients.

Comparison between FDRs and NHCs also revealed a significant difference for cyclothymic temperament (40% vs. 10%, $p = 0.007$), while other temperaments showed no significant variation.

Table 4: Comparison of Affective Temperaments Between Study Groups

Comparison	Temperament	χ^2	df	p-value	Significance
BPAD vs FDR	Cyclothymic	1.669	1	0.196	NS
	Hyperthymic	1.926	1	0.165	NS
	Dysthymic	1.270	1	0.260	NS
	Irritable	0.577	1	0.448	NS
BPAD vs NHC	Cyclothymic	14.70	1	0.000	S
	Hyperthymic	8.297	1	0.004	S
	Irritable	5.455	1	0.020	S
FDR vs NHC	Cyclothymic	7.200	1	0.007	S
	Dysthymic	1.270	1	0.260	NS
	Hyperthymic	2.400	1	0.121	NS
	Irritable	3.158	1	0.076	NS

Overall, affective temperaments were more prevalent among patients with bipolar affective disorder and their first-degree relatives compared to healthy controls. Hyperthymic and cyclothymic temperaments showed the strongest association with bipolar affective disorder, while dysthymic and irritable traits were less frequent. Significant intergroup differences were observed for cyclothymic, hyperthymic, and irritable temperaments between BPAD patients and healthy controls, and for cyclothymic temperament between relatives and controls, suggesting a possible heritable link.

DISCUSSION

The present study explored the socio-demographic, clinical, and temperamental characteristics of

ISSN (O): 2687-5365; ISSN (P): 2753-6556

patients with bipolar affective disorder (BPAD) in remission, their first-degree relatives (FDRs), and healthy controls (NHCs). The findings were compared with previous studies to evaluate whether affective temperaments could serve as potential endophenotypic markers for BPAD. The mean age of BPAD patients in this study was 34.10 ± 11.42 years, with a predominance of males (73.3%), and most participants were married, Hindu, and from nuclear families. These observations are comparable with the demographic pattern reported by Ramdurg and Kumar.[34] The mean age of onset (22.5 ± 9.1 years) aligns with findings from previous studies that suggest the typical onset of bipolar disorder occurs in the mid-twenties.[35,36] In the present study, 90% of patients experienced mania as their first episode, similar to Indian studies by Khanna et al,[35] and Khess et al,[36] while Western research, including that of Denicoff,[37] and Judd,[38] reported a higher prevalence of depressive episodes. This difference could be attributed to sociocultural factors, as depressive states are often underrecognized in India, whereas manic symptoms attract more clinical attention due to their overt behavioral changes.[39,40] Moreover, the predominance of manic polarity and male representation observed in this study corresponds with findings from other developing countries.[41]

Affective temperament assessment using the TEMPS-A revealed that hyperthymic (76.7%) and cyclothymic (56.7%) temperaments were most common among BPAD patients, followed by dysthymic and irritable types. These results are in agreement with previous reports showing that hyperthymic and cyclothymic temperaments are strongly associated with bipolar illness.[42,43] Among FDRs, hyperthymic (60%) and cyclothymic (40%) temperaments were also frequent, whereas these traits were considerably lower among NHCs (40% and 10%, respectively). This gradient pattern supports the hypothesis that affective temperaments may act as heritable, state-independent traits linked to bipolarity, thus fulfilling the endophenotype criteria described by Gottesman and Gould.[3] When BPAD patients were compared with healthy controls, cyclothymic ($p < 0.001$), hyperthymic ($p = 0.004$), and irritable ($p = 0.02$) temperaments were significantly higher in patients, consistent with the findings of Vohringer et al,[44] and Gandotra et al,[29] who demonstrated that such temperaments often coexist with bipolar spectrum conditions. Although differences between BPAD patients and their relatives were not statistically significant, the elevated rates of cyclothymic traits among FDRs further reinforce their familial nature. Similar findings were reported by Mendlowicz et al,[25] and Chiaroni et al,[43] who observed increased cyclothymic traits among unaffected relatives of bipolar probands, suggesting that this temperament may represent a behavioral endophenotype with a genetic basis.

Previous literature also supports these observations, with multiple studies identifying hyperthymic and cyclothymic temperaments as stable markers of vulnerability to bipolarity.[42–46] Cyclothymic temperament, characterized by rapid fluctuations in mood and energy levels, is often regarded as a subclinical or prodromal expression of bipolar disorder, while hyperthymic temperament is typically associated with greater functional recovery and resilience during euthymic phases. Vazquez et al,[45] and Evans et al,[46] emphasized the familial clustering of these traits across generations. The present findings extend this evidence within an Indian population, thereby contributing valuable cross-cultural validation of the heritable nature of affective temperaments.

Clinically, these findings underscore the significance of temperament assessment in identifying individuals at genetic risk for BPAD even before illness onset. Early screening of family members using structured tools such as TEMPS-A could aid in psychoeducation, lifestyle modification, and closer psychiatric follow-up, potentially delaying or preventing the manifestation of the disorder. Understanding an individual's temperament profile may also help clinicians personalize treatment approaches, predict relapse patterns, and improve therapeutic adherence.

However, certain limitations must be acknowledged. The sample size was modest, and participants were recruited using purposive sampling from a single tertiary center, which may limit generalizability. The cross-sectional design precluded evaluation of longitudinal changes in temperament. Moreover, temperament assessment relied on self-reported questionnaires, which may introduce recall and response bias. Future studies should adopt larger, multicentric samples and longitudinal designs, integrating genetic and neurobiological correlates to strengthen the evidence for affective temperaments as endophenotypic markers.

In summary, this study demonstrates that hyperthymic and cyclothymic temperaments are more prevalent among BPAD patients and their first-degree relatives compared to healthy controls. The persistence of cyclothymic traits in unaffected relatives suggests that this temperament may serve as a stable, heritable endophenotype linking genetic predisposition and clinical expression of bipolar disorder. These findings reinforce the importance of temperament-based assessment in the understanding, early identification, and prevention of bipolar spectrum conditions.

CONCLUSION

The present study demonstrated that specific affective temperaments, particularly hyperthymic and cyclothymic traits, are more prevalent among patients with bipolar affective disorder and their first-degree relatives compared to healthy controls. The

ISSN (O): 2687-5365; ISSN (P): 2753-6556

presence of cyclothymic temperament among unaffected relatives supports its potential role as an endophenotypic marker for bipolar disorder. These findings reaffirm the familial and heritable nature of temperamental predispositions in mood disorders and provide further evidence for the continuum model of bipolar spectrum illness. Recognizing these temperamental patterns may assist in early identification of at-risk individuals, guide preventive interventions, and enhance understanding of the genetic and biological basis of bipolar affective disorder.

Future research with larger, longitudinal, and multi-centric samples is recommended to validate these results and explore the neurobiological and molecular correlates of affective temperaments in bipolar spectrum conditions.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556

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ISSN (O): 2687-5365; ISSN (P): 2753-6556