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The Relationship Between Early Onset Bipolar I Disorder with Clinical Features and Alexithymia

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Abstract

Introduction: This study aimed to investigate the correlation between the early onset (EO) of Bipolar I Disorder (BD-I) and alexithymia, as well as the association between alexithymia and the clinical features of BD.

Materials and Methods: A total of 83 individuals diagnosed with BD-I under remission were randomly selected for inclusion in the study. Among them, 39 were diagnosed before (EO) and 44 were diagnosed after 18 years of age. The participants were assessed with the Socio-demographic Data Form, Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (HAM-D), and Toronto Alexithymia Scale (TAS).

Results: In the EO group, the TAS total score, difficulty describing feelings subscale score, difficulty identifying feeling score, and externally oriented thinking score were significantly higher compared to the group diagnosed after age 18. Furthermore, the EO group exhibited a higher number of hospitalizations, a greater total number of attacks, an increased number of depressive attacks, manic attacks, extended disease duration, along with a higher incidence of suicide attempts and self-harm.

Conclusion: Our results indicate that early-onset in BD-I is correlated with elevated alexithymia levels, and is associated with prolonged disease duration, increased episode frequency, and a heightened incidence of suicide attempts among the affected individuals.

Key words: Bipolar disorder type I; age of onset; alexithymia; clinical characteristics.

Introduction

Bipolar Disorder (BD) is a persistent and incapacitating psychiatric disorder that entails recurrent episodes of manic and depressive moods, and can impact emotional regulation, cognitive function, and overall quality of life for affected individuals (1). Although our understanding encompasses social factors, genetics, trauma, and potential biological causes in the etiology of bipolar disorder, its exact origin remains incompletely understood (2). Despite accessible therapeutic interventions and the potential for extended remission, BD endures as a protracted ailment lacking a conclusive remedy (3). The estimated worldwide lifetime prevalence stands at approximately 1%, though documented rates have extended it to 2.6% (4). The onset of BD type I (BD-I) typically transpires around the age of 18, with the peak occurrence of the initial manic episode typically observed between the ages of 21 and 23 years (3). Given the conceivable antecedence of depressive episodes preceding manic manifestations, it is imperative to acknowledge that the commencement of BD during adolescence is not an infrequent phenomenon. A comprehensive clarification of the etiological underpinnings of BD remains elusive; nevertheless, it is recognized that its pathogenesis entails a complex interplay of multifaceted contributing factors. While a definitive characterization is absent from the existing literature, early onset (EO) in BD is delineated as the manifestation of symptoms before attaining 18 years of age (5). This designation assumes significance due to its discernible impact on the trajectory and severity of the ailment, as well as its influence on treatment response. Research findings indicate that EO BD is associated with an extended duration of episodes, increased frequency of mood swings, rapid cycling, and prolonged time to attain remission. These factors associated with EO BD can contribute significantly to poor prognosis (6). Introduced by Sifneos in 1973, alexithymia signifies a deficiency in recognizing, comprehending, and expressing one's own emotional experiences (7). Alexithymia is characterized by an inability to distinguish between bodily sensations and emotions and can result in difficulties in describing emotions to others as well as an overall limited capacity for self-observation regarding emotional experiences (8). Numerous studies have documented that

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individuals exhibiting alexithymia experience elevated stress levels, manifest more pronounced somatic symptoms, and demonstrate heightened severity in anxiety and depression compared to those lacking alexithymia (9). Although the relationship between alexithymia and diverse psychiatric disorders has been studied, there is a lack of explicit investigations into an association with BD. Individuals with BD and alexithymia are reported to experience more severe mood symptoms, cognitive impairment, and difficulties in emotional regulation (10). Emotional dysregulation is characterized by erratic, disordered, and rapidly fluctuating changes in affect, encompassing frequent shifts in emotional tone, heightened intensity of affect, accelerated emotional transitions, delayed return to baseline emotional states, and exaggerated responses to psychosocial stimuli (11). In the neuroanatomical context, alexithymia is primarily associated with deficits in the corpus callosum, indicating diminished interhemispheric communication and frontal hypoactivation. An An Functional magnetic resonance imaging (fMRI) investigation conducted on individuals diagnosed with BD indicated diminished activation within the anterior cingulate regions and medial prefrontal cortex. Consequently, these neuroanatomical regions were posited to exhibit a potential association with alexithymia (12). Moreover, alexithymia was linked to cingulate cortex hypofunction, which can impact the regulation and perception of affect, and insula dysfunction, which is crucial for the awareness of internal bodily states (13). On the other hand, a close relationship between alexithymia and regulation of emotion has been demonstrated in individuals with BD, with emotion perception correlated with emotion regulation. Additionally, high alexithymia scores are associated with diminished ability for emotional regulation (14). A neurobiological relationship is likely to exist between alexithymia and recurrent episodes as well as psychosocial stress factors in BD. Disruptions during critical neurodevelopmental periods such as adolescence and early adulthood, when the brain undergoes significant structural and functional changes, may shape the course and outcomes of BD, potentially influencing the clinical presentation and disease outcome (15). The existing data about the correlation between conditions that can be implicated in an unfavorable clinical course, such as alexithymia in BD, and an EO of the disease is currently insufficient. A recognition of comorbid conditions linked to the EO of illness in BD is imperative for appropriate intervention in a disorder that is generally associated with unfavorable clinical outcomes. Accordingly, the current study aimed to evaluate and compare clinical features and the levels of alexithymia in individuals diagnosed with early-onset BD and those diagnosed with BD after age 18. We hypothesized that the trajectory and outcomes of BD manifested in childhood and early adolescence would be significantly more severe compared to adult-onset BD.

Materials and Methods

Study design: A total of 83 patients with BD in remission were randomly selected between October 1, 2023 and January 31, 2024 for participation in this cross-sectional cohort study. The participants were assigned into two groups: 39 individuals who were diagnosed with Bipolar I disorder (BD-I) before the age of 18 and 44 individuals who were diagnosed after reaching the age of 18. The diagnosis of BD was carried out by a specialized psychiatrist using the Structured Clinical Interview for DSM-5 for all patients, with adherence to DSM-5 criteria being the primary inclusion criterion. Additional inclusion criteria were as follows: being in remission defined by scores of <8 on both the Hamilton Depression Rating Scale (Ham-D) and the Young Mania Rating Scale (YMRS), literacy, absence of concurrent psychiatric and neurological disorders, and voluntary provision of both verbal and written consent to participate in the study. All participants were using mood stabilizers and antipsychotic medications. The exclusion criteria were as follows: age below 18 years, presence of alcohol/substance use disorder, presence of mental retardation, and a history of any neurological disease that may prevent communication, such as organic mental disorders, dementia, head trauma, or epilepsy. The participants filled a Semi-Structured Sociodemographic and Clinical Data Form, YMRS, the HAM-D and the Toronto Alexithymia Scale (TAS). Sociodemographic and Clinical Data Form: Patient characteristics such as age, gender, clinical features of the illness, and the number of episodes were collected using a Semi-Structured Sociodemographic and Clinical Data Form. Hamilton Depression Rating Scale: HAM-D, developed by Hamilton, serves as a widely utilized tool to assess the severity of depressive symptoms in individuals with BD. HAM-D is recognized globally as the primary observer-rated depression scale, and is considered to be critical for research on depression. The scale encompasses various domains, including sleep, somatic symptoms,

genital symptoms, weight loss, and insight, with each item scored between 0 and 2, while others range from 0 to 4. The maximum attainable score is 53; scores falling within different ranges are indicative of varying degrees of severity of depression. The scale has undergone validation and reliability studies in the Turkish context, demonstrating favorable results with a reported Cronbach's alpha value of 0.75 and a reliability coefficient of 0.76 in internal consistency assessments (16). Young Mania Rating Scale: YMRS, developed by Young et al. in 1978, is a tool that is used to assess the severity of mania symptoms. The scale has 11 items, each measuring five levels of symptom severity. The scale therefore covers symptoms characteristic of the manic phase of bipolar disorder, ranging from mild to severe. It is administered by an interviewer, and considers the patient's condition within the last 48 hours and at the time of the interview. In this context, remission is defined as a score of ≤7.9 points. The overall scale score is obtained by summing the individual scores of each item. Validation and reliability studies for the YMRS have been conducted for the Turkish population, with the scale demonstrating favorable results, including an internal consistency coefficient of 0.79 (17). Toronto Alexithymia Scale (TAS): TAS-20, developed by Bagby et al. in 1994, was used to assess the alexithymic characteristics of the participants. The original scale demonstrated a Cronbach alpha value of 0.81. TAS comprises of 20 questions, utilizing a 5-point Likert scale. In the Turkish validity and reliability study conducted by Sayar et al. in 2001, it was suggested that scores equal to or less than 51 be categorized as "non-alexithymic," scores between 52 and 58 as "borderline," and scores equal to or greater than 59 as "alexithymic." Güleç and colleagues have conducted a validation and reliability study of the TAS-20 for the Turkish population and the internal reliability evaluation yielded a Cronbach alpha coefficient of 0.78 (18). Ethical Approval: Written consent was obtained from all patients participating in the current study, in accordance with the Declaration of Helsinki. An Ethical Committee permission was obtained from Unıversıty Of Health Scıences Erzurum Medical Faculty Clinical Research Ethics Committee.

Statistical analysis: Statistical analysis was carried out using SPSS 26.0 program. The clinical characteristics and demographics of the participants were analyzed using descriptive

Table 1: Clinical and demographic characteristics of the sample

	Bipolar I Disorder (n=83)			
	Early Onset (n=39)	Diagnosed after ag 18 (n=44)		
	Mean ± SD	Mean ± SD	t	*p*
Age	30.17 ± 10.74	30.97 ± 6.46	-2.898	0.687
Education (years)	10.82 ± 3.71	12.06 ± 3.84	-1.499	0.138
Age of Diagnosis	20.43 ± 4.44	25.79 ± 4.77	-5.269	0.001
Age at First Hospitalization	20.78 ± 4.89	26.10 ± 5.14	-4.434	0.001
Number of Hospitalizations	3.15 ± 4.84	1.54 ± 1.33	2.138	0.036
Total Number of Episodes	6.85 ± 7.88	3.40 ± 2.83	2.501	0.014
Number of Depressive Episodes	2.66 ± 3.33	1.40 ± 1.55	2.241	0.028
Number of Manic Episodes	3.92 ± 5.66	2.00 ± 1.76	2.138	0.036
Duration of Illness (years)	10.74 ± 9.54	6.18 ± 4.80	2.798	0.006
	n (%)	n (%)	χ^2	*p*
Gender (female)	18 (46.2)	19 (43.2)	-	-
Marital status (married)	39 (100)	44 (100)	-	-
Employment (no/irregular)	12 (30.8)	11 (25.0)	0.344	0.558
Smoking (yes)	22 (56.4)	21 (47.7)	0.624	0.429
History of AUD/SUD (yes)	4 (10.3)	4 (9.1)	0.032	0.857
Family History of BD (yes)	6 (15.4)	6 (13.6)	0.051	0.821
History of Suicide Attempt (yes)	12 (30.8)	4 (19.3)	6.244	0.012
History of Self-Harm (yes)	9 (23.1)	1 (2.3)	8.445	0.004
TAS score ≤58	21 (53.8)	8 (18.2)	11.568	0.001

Abbreviations: SD, Standard deviation; SUD, Non-alcohol substance use disorder; AUD, Alcohol use disorder; TAS, Toronto Alexithymia Scale; BD, Bipolar Disorder; χ^2, Chi-squared test. $p<0.05$ statistically significant (bold values). Parametric variables were compared with the Independent t-test.

statistical methods (percentage, number, standard deviation, and mean). The presence of a normal distribution was assessed with the Kolmogorov-Smirnov test. The Independent t-test or Spearman's rank correlation coefficient were used for variables that did not show normal distribution while Pearson's correlation coefficient was used for normally distributed variables. $p< 0.05$ was considered to be significant.

Results

Table 1 presents a comparative analysis of the demographic and clinical characteristics of the sample. The patients with EO BD-I (n=39) had a mean age of 30.17±10.74 years, while the mean age of the group diagnosed with BD-I after age 18 (n=44) was 30.97±6.46 years. The EO group exhibited a statistically significantly lower age at diagnosis (t=-5.269, p<0.001) and first hospitalization (t=-4.434, p<0.001) compared to the group diagnosed after age 18. Furthermore, the EO group demonstrated significantly higher number of hospitalizations (t=2.138, p=0.036), total number of episodes (t=2.501, p=0.014), number of depressive episodes (t=2.241, p=0.028), number of manic episodes (t=2.138, p=0.036), and duration of illness (t=2.798, p=0.006). Additionally, the EO group exhibited a more frequent history of suicide attempts (χ^2=6.244, p=0.012) and self-harm (χ^2=8.445, p=0.004) compared to the group diagnosed after age 18. Table 2 provides a comparative assessment of TAS scores between the EO group and the group diagnosed after age 18.

Table 2: Comparative evaluation of Toronto alexithymia scale

	Bipolar Disorder (n=83)			
	Early Onset (n=39)	**Diagnosed after age 18 (n=44)**		
	Mean ± SD	Mean ± SD	t	p
Toronto Alexithymia Scale Total	58.92 ± 8.80	51.61 ± 9.62	3.594	0.001
Difficulty Describing Feelings	19.66 ± 3.64	17.45 ± 3.93	2.645	0.010
Difficulty Identifying Feeling	16.10 ± 2.83	14.63 ± 1.97	2.757	0.007
Externally-Oriented Thinking	23.15 ± 5.39	19.45 ± 5.41	3.111	0.003

Abbreviation: SD, Standard deviation; TAS, Toronto Alexithymia Scale. Statistical significance ($p < 0.05$) is indicated by bold values. Parametric variables were assessed using the Independent t-test.

Table 3: Correlation analysis of Sociovirtualization perception scale score and clinical characteristics

r	**Difficulty Describing Feelings**	**Difficulty Identifying Feeling**	**Externally-Oriented Thinking**	**TAS Total**
[a]History of Suicide Attempts	0.120	0.197	0.276*	0.256*
[a]History of Self-Harm	0.251*	0.015	0.175	0.186
[b]Age at Diagnosis	-0.223*	-0.274**	-0.050	-0.192
[b]Number of Hospitalization	0.092	-0.063	0.184	0.114
[b]Number of Depressive Episodes	0.197	0.230*	0.177	0.241**
[b]Number of Manic Episodes	0.193	0.101	0.174	0.189
[b]Total Number of Episodes	0.222*	0.171	0.200	0.238**

r: correlation coefficient. **Abbreviation:** SD, Standard deviation; TAS, Toronto Alexithymia Scale. **a**Spearman's rank correlation coefficient **b**Pearson correlation coefficient ***The correlation is significant (two-tailed) at the 0.05 level.
****** The correlation is statistically significant at the 0.01 level (two-tailed).

The TAS Total score (t=3.594, p=0.001), Difficulty Describing Feelings subscale score (t=2.645, p<0.010), Difficulty Identifying Feeling subscale score (t=2.757, p<0.007), and Externally-Oriented Thinking subscale score (t=3.111, p<0.003) were all significantly higher in the EO group. The TAS total score demonstrated a statistically significant positive correlation with the number of suicide attempts (p<0.05), number of depressive episodes (p<0.001), and total number of episodes (p<0.001) (Table 3). Furthermore, the Difficulty Identifying Feeling subscale score exhibited a statistically significant positive correlation with age at diagnosis (p<0.001).

Discussion

The current study marks the first attempt in the existing literature to explore a link between alexithymia and the age of onset in BD-I. Our results revealed higher alexithymia scores in the EO BD-I group compared to BD-I patients with a later age (>18 years) of onset. The TAS scores in the EO group exhibited statistically significant increases across all sub-scales, indicating that individuals in this category may encounter heightened challenges in recognizing and comprehending emotions, accompanied by a propensity toward extroverted thinking. These findings are corroborated by previous studies (10). Our data suggest that alexithymia may be implicated in the heterogeneity associated with BD-I, and indicates for the first time that it may also have a relationship with the early age of onset of disease. Longitudinal studies spanning up to 20 years reveal the highly chronic nature of BD-I (19). Diagnosis at a younger age poses challenges due to the non-specificity of symptoms and overlap with other disorders (20). Delayed recognition and treatment contribute significantly to the burden and mortality associated with bipolar disorder (21). Evidence suggests that functional deficits and anomalies typically manifest after the onset of BD, differing from the developmental trajectory of schizophrenia (22). Early detection of the disorder is therefore crucial for preventing illness progression. Moreover, EO bipolar disorder often correlates with more severe outcomes, such as heightened rapid cycling and resistance to treatment, underscoring the importance of tailored interventions for this subgroup (23). We observed a heightened frequency of hospitalizations, more episodes, and an extended duration of illness in individuals with EO compared to those diagnosed after age 18. Our findings are well aligned with previously published research (24). Emotional dysregulation is a foundational aspect of BD, persisting even during periods of remission and contributing to greater relapse frequencies (25). This difficulty in regulating emotions has been consistently observed in BD patients compared to healthy controls (26). Moreover, studies indicate that emotional dysregulation during euthymic periods is associated with increased severity of symptoms in manic, depressive, and mixed states, further underscoring its clinical significance (25). Additionally, alexithymia, characterized by challenges in recognizing and expressing emotions, is prevalent among individuals with BD-1, with higher scores reported compared to control groups (27). Notably, recent studies have linked higher alexithymia scores with decreased social functionality in BD patients (28). Our study extends these findings by demonstrating elevated levels of alexithymia specifically in early-onset BD-I individuals, alongside a greater prevalence of suicide attempts and incidents of self-harm. These results are in good agreement with previous research highlighting the association between alexithymia and EO BD, emphasizing the importance of addressing emotional dysregulation in the management of BD to mitigate adverse outcomes such as suicide attempts (27). Somatic symptoms, encompassing bodily sensations like sleep and appetite disturbances, are prevalent in individuals with BD, akin to those with unipolar depression. These patients experience such symptoms at approximately twice the rate seen in the general population. Recent research indicates that BD-1 patients with higher somatization scores, indicative of greater severity of somatic symptoms, exhibit a higher prevalence of rapid cycling and worse disease prognosis (14). This further highlights the urgent need for targeted interventions and support that is tailored to address emotional dysregulation in this vulnerable subgroup. A high alexithymia score was reported to be correlated with a low ability for emotional regulation in BD patients (29); additionally, a close relationship between alexithymia and emotional regulation in BD has been reported (14). Therefore, a common neurobiological relationship between alexithymia and BD is highly probable. The recognition of alexithymia in EO BD cases, its integration into treatment plans, and its evaluation as a treatment dimension are likely to improve the clinical outcomes of these patients.

The current literature lacks data on the relationship between the age of onset of BD and its clinical course and comorbidities, which makes our study important. Our findings underscore a strong association between EO in BD-I and heightened levels of alexithymia. Although it is known that alexithymia is more common in BD patients, our study suggests that its strong relationship with early onset age should be considered in the etiology of the disease. The established correlation between alexithymia and a more severe disease course, including an elevated risk of hospitalizations and suicide, emphasizes an urgent need for targeted interventions. Furthermore, our results suggest that alexithymia should be considered in the treatment plans, which may positively influence the clinical trajectory of EO BD-I.

Study limitations: The current study has certain limitations. The study sample was recruited from a

clinical setting, which can introduce a potential limitation in generalizing the findings to a broader population of individuals with BD. The use of drugs, and antipsychotic drugs in particular, may cause emotional blunting. We have tried to minimize this factor by including patients in the remission period; nonetheless, it should be considered as a limitation of the study. Future longitudinal investigations are necessary, specifically to elucidate the temporal dynamics associated with the development of alexithymia in individuals with EO BD. Additionally, further exploration is warranted to comprehend potential mechanisms underpinning this relationship, considering the impact of neurobiological foundations and psychosocial stress factors.

Conclusion

The EO of BD-I is associated with various comorbid conditions. The current study is the first to reveal a significant association between an early age of onset of BD-I and alexithymia. Our data suggest that clinicians should be cognizant of the presence of alexithymia in individuals with early onset BD-I when formulating treatment plans and interventions. Such awareness may contribute to an improvement in the clinical trajectory of the disease. Additionally, future studies including patients with Bipolar II Disorder should also be designed.

Ethical approval: Written consent was obtained from all the patients participating in our study, in accordance with the Declaration of Helsinki. Ethical Committee approval was obtained from Written consent was obtained from all patients participating in the current study, in accordance with the Declaration of Helsinki. An Ethical Committee permission was obtained from Unıversıty Of Health Scıences Erzurum Medical Faculty Clinical Research Ethics Committee.

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