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Clinical and Treatment Profile of Late-Onset Bipolar Disorder: A Retrospective Evaluation

Geç Başlangıçlı Bipolar Bozuklukta Klinik ve Tedavi Profili: Retrospektif Bir Değerlendirme

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ABSTRACT

Aim: This study aims to compare the sociodemographic characteristics, clinical course, and treatment approaches of patients diagnosed with early-onset bipolar disorder (EOBD, <50 years) and late-onset bipolar disorder (LOBD, ≥50 years) based on age at disease onset.

Methods: This retrospective, observational study included 87 patients (EOBD: 52; LOBD: 35). Data were obtained from patient files and a digital tracking system. Normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Group comparisons were performed using independent-samples t-tests and chi-square tests.

Results: No significant differences were observed in sociodemographic characteristics between the groups (p>0.05), except for employment status (p=0.007). The EOBD group had a higher number of manic episodes (p=0.006). Lithium use was more frequent in LOBD patients, although not statistically significant (p=0.295), while olanzapine use was statistically significant (p=0.010). Antidepressant use was low in both groups (p=0.156).

Conclusion: Late-onset bipolar disorder may present with distinct clinical features and treatment preferences compared to early-onset cases. Age at onset is a key determinant for clinical management and treatment planning.

Keywords: Bipolar Disorder; Early-Onset; Late-Onset; Clinical Features, Treatment Approaches

ÖZ

Amaç: Bu çalışma, hastalık başlangıç yaşına göre; erken başlangıçlı bipolar bozukluk (EBBB <50 yaş) ve geç başlangıçlı bipolar bozukluk (GBBB ≥50 yaş) tanısı almış hastaların sosyodemografik özellikleri, klinik seyirlerini ve tedavi yaklaşımlarını karşılaştırmayı amaçlamaktadır.

Yöntemler: Retrospektif, gözlemsel bir çalışmadır. Toplam 87 hasta (EBBB: 52, GBBB: 35) değerlendirilmiş, hasta dosyalarından ve dijital takip sisteminden veriler alınmıştır. Sürekli değişkenlerin normal dağılımı Kolmogorov-Smirnov testi ile değerlendirilmiş, gruplar arası karşılaştırmalar için bağımsız örneklem t-testi ve Ki-kare testi kullanılmıştır.

Bulgular: Gruplar arasında sosyodemografik özellikler açısından anlamlı fark yoktu (p>0.05), ancak istihdam durumu açısından fark gözlendi (p=0.007). EBBB grubunda manik atak sayısı daha yüksek bulundu (p=0.006), GBBB grubunda lityum kullanımı daha sık tercih edildi (p=0.295, anlamlı değil), olanzapin kullanımı istatistiksel olarak anlamlıydı (p=0.010). Her iki grupta antidepresan kullanımı düşüktü (p=0.156).

Sonuç: Geç başlangıçlı bipolar bozukluk, erken başlangıçlı hastalardan farklı klinik özellikler ve tedavi tercihleri sergileyebilir. Hastalık başlangıç yaşı, tedavi stratejileri ve klinik değerlendirmelerde önemli bir belirleyicidir.

Anahtar kelimeler: Bipolar Bozukluk; Erken Başlangıç, Geç Başlangıç; Klinik Özellikler, Tedavi Yaklaşımları

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Introduction

Bipolar disorder (BD) is a severe, lifelong mood disorder characterised by manic, hypomanic, and depressive episodes [1]. Although BD usually begins in young adulthood, it can also be seen in older individuals [2]. There is no definitive consensus on the concept of "older age" in bipolar disorder. While the age limit of 60 or 65 is generally discussed in geriatric psychiatry, some drug trials have used the age limit of 55. Furthermore, when considering the lifelong course of bipolar disorder, due to its early onset, sometimes 50 or 40 years of age is also regarded as old age. Actual late-onset bipolar disorder (LOBD), on the other hand, is rare and refers to conditions in which the first manic, hypomanic, or mixed episode begins after age 50 [3].

Approximately 90% of bipolar disorder diagnoses have been reported to begin before age 50, suggesting a prevalence of LOBD of 10% [4]. Although the prevalence of BD in the geriatric population is lower than in the general population, it is a significant clinical problem due to treatment resistance, increased medical comorbidities, cognitive decline, and increased mortality risk [5]. In older individuals, BD generally presents with less pronounced manic symptoms and longer and more persistent depressive episodes [6]. Furthermore, the onset of the disease in older age may be influenced by underlying vascular pathologies, neurodegenerative processes, or medical illnesses [7]. LOBD is characterised by more white matter lesions, increased cerebrovascular risk, and age-related structural brain changes compared to early-onset bipolar disorder (EOBD), suggesting that different neurobiological mechanisms may play a role between the two subtypes [8].

One study reported that although LOBD is clinically similar to early-onset cases, it may have a different pathophysiological basis due to its association with underlying organic brain pathologies [9]. Factors such as decreased neuroplasticity with age, pharmacokinetic changes, and polypharmacy can complicate treatment response to LOBD and increase the risk of adverse effects [10]. For all these reasons, geriatric BD should be considered not only as a subtype of BD seen in older individuals but also as a condition requiring unique clinical, neurobiological, and therapeutic approaches [11]. Within the scope of this research, we aimed to elucidate the differences in clinical features and treatment responses between patients with LOBD and those with EOBD. Thus, the aim is to obtain data that will shed light on the diagnostic and treatment processes of LOBD.

Method

Study Design and Participants

This is a retrospective, comparative, observational study based on a chart review method. A total of 87 patients diagnosed with bipolar disorder were admitted to the psychiatry outpatient clinic of Alanya Education and Research Hospital between 2019 and 2024, and were followed up with the ICD-10 classification system, with diagnosis codes F31, F31.1, F31.2, F31.3, F31.4, F31.5, F31.6, F31.7, F31.8, and F31.9. The diagnoses were established by psychiatrists through comprehensive clinical interviews, in accordance with ICD-10 diagnostic criteria.

Patients with incomplete charts were excluded from the study. Patients included in the study were divided into two groups based on age at onset of illness:

- Late-Onset Bipolar Disorder (LOBD): Patients with a first episode of bipolar disorder aged 50 years or older
- Early-Onset Bipolar Disorder (EOBD): Patients with a first episode of bipolar disorder aged under 50 years

Sociodemographic characteristics, clinical courses, and treatments of both groups were comparatively examined.

Data Collection

Data were obtained from patient files and a digital patient tracking system. The following variables were analysed:

- Demographic data: age, gender, marital status, residence
- Clinical variables: age at first episode, episode type, episode frequency, number of hospitalisations

- Treatment information: Mood stabilisers, antipsychotics, antidepressants, benzodiazepines, and other treatments used.

Due to the retrospective nature of the study, patients with missing data in their medical records or digital patient tracking files, as well as those identified as not attending regular follow-up visits, were excluded from the study.

Statistical Analysis

Patient data collected within the scope of the study were analysed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data, and mean and standard deviation for continuous data, were provided as descriptive statistics. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test prior to group comparisons. For comparisons between groups, the "Independent Sample T-test" was used for two groups, and the "Pearson Chi-Square Test" was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

Results

When the sociodemographic characteristics of EOBD and LOBD patients were compared, no significant differences were found between the groups in terms of gender, marital status, and education level. Women and married individuals predominated in both groups. A significant difference was found in terms of occupational status (p =0.007), with a higher proportion of employed/student individuals in the under-50 age group. In comparison, the proportion of unemployed individuals in the over-50 age group was significantly higher. As expected, the mean age was significantly higher in the LOBD group (p <0.001). The sociodemographic characteristics of EOBD and LOBD patients are presented in Table 1. Sociodemographic Characteristics of Bipolar Disorder Patients According to Age of Onset (EOBD vs. LOBD).

Onset was significantly earlier in the EOBD group (p <0.001), and the number of manic (p =0.006), hypomanic (p =0.035), and total episodes (p =0.041), as well as the number of hospitalisations (p =0.002), were statistically significantly higher in this group. The number of depressive episodes did not differ significantly between the groups (p =0.900). Clinical variables of EOBD and LOBD patients are presented in Table 2.

Pharmacological treatment approaches were compared in patients diagnosed with EOBD (n = 52) and LOBD (n = 35). Regarding overall treatment approaches, Mood Stabiliser (MS) monotherapy was used in 20.0% of the LOBD group, while this rate was 7.7% in the EOBD group. Antipsychotic (AP) monotherapy was preferred with similar frequency in both groups (EOBD: 15.4%; LOBD: 14.3%). The most frequently preferred treatment modality was the combination of MS and AP, with 48.1% use in the EOBD group and 42.9% in the LOBD group. Furthermore, the combination of MS, AP, and AD was also used at 21.2% in the EOBD group and 14.3% in the LOBD group.

When looking at the detailed distribution of mood-stabilising agents, lithium was used at 42.9% in the LOBD group and 23.8% in the EOBD group. Valproate use was similar in both groups (EOBD: 38.1%; LOBD: 35.7%). The combination of lithium and valproate was preferred at 16.7% in the EOBD group and 3.6% in the LOBD group. Lamotrigine was used at a similar rate in both groups (EOBD: 7.1%; LOBD: 10.7%). Valproate and lamotrigine, or lithium and lamotrigine combinations, were administered at lower rates.

Regarding antipsychotic medications, quetiapine was the most commonly used antipsychotic in both groups (EOBD: 30.4%; LOBD: 36.0%). Aripiprazole (EOBD: 21.7%; LOBD: 32.0%) and olanzapine (EOBD: 15.2%; LOBD: 28.0%) were other frequently preferred agents. Olanzapine use was particularly high in the LOBD group. Risperidone, paliperidone, amisulpride, and long-acting injectable antipsychotics were used at lower rates, and these agents were generally preferred only in the EOBD group.

Regarding antidepressant use, SSRIs were used only in the EOBD group (54.5%). SNRI use was 27.3% in the EOBD group and 50.0% in the LOBD group. Other antidepressants were administered at similar rates in both groups (EOBD: 18.2%; LOBD: 50.0%). A difference in SSRI use was

Table 1. Sociodemographic Characteristics of Bipolar Disorder Patients According to Age of Onset (EOBD vs. LOBD).

Variable	EOBD (n, %)	LOBD (n, %)	p-value
Age (Mean ± SD)	**53.94 ± 7.14**	**59.11 ± 6.37**	**p <0.001****
Sex			
Female	35 (67.3%)	23 (65.7%)	0.877*
Male	17 (32.7%)	12 (34.3%)	
Marital Status			
Single	3 (5.8%)	2 (5.7%)	0.495*
Married	38 (73.1%)	29 (82.9%)	
Widowed/Divorced	11 (21.2%)	4 (11.4%)	
Educational Level			
Primary Education	22 (42.3%)	21 (60.0%)	0.398*
Secondary Education	9 (17.3%)	3 (8.6%)	
High School	12 (23.1%)	6 (17.1%)	
Bachelor's and above	9 (17.3%)	5 (14.3%)	
Occupation Status			
Working/Student	15 (28.8%)	4 (11.4%)	0.007*
Not Working	4 (7.7%)	11 (31.4%)	
Retired	33 (63.5%)	20 (57.1%)	

Note: Column percentages are presented. *chi-square test , ** mann-witney u

Abbreviations: EOBD: Early onset bipolar disorder LOBD: Late onset bipolar disorder

Table 2. Comparison of Clinical Variables by Age of Onset (EOBD vs. LOBD).

Clinical Variable	Group	N	Mean	SD	p-value
Age at illness onset (years)	EOBD	52	29.46	8.11	**< .001**
	LOBD	35	53.63	3.62	
Number of manic episodes	EOBD	52	3.06	2.88	**.006**
	LOBD	35	1.69	1.66	
Number of hypomanic episodes	EOBD	52	1.50	3.23	.035
	LOBD	35	0.49	0.85	
Number of depressive episodes	EOBD	52	3.12	3.34	**.900**
	LOBD	35	3.00	4.67	
Total number of episodes	EOBD	52	7.67	5.92	.041
	LOBD	35	5.14	5.33	
Number of hospitalizations	EOBD	52	2.62	2.71	**.002**
	LOBD	34	1.21	1.37	

Note: Independent samples t-test results, based on "Equal variances not assumed"

Abbreviations: EOBD: Early onset bipolar disorder, LOBD: Late onset bipolar disorder

notable between the groups.

According to the statistical analysis results, no significant difference was found between the two groups in terms of lithium use. (p = 0.295*) but a significant difference was found between the groups in terms of olanzapine use. (p = 0.010*). The difference in SSRI use was not statistically significant, but it was marginally significant (p =0.156**). The treatment regimens of EOBD and LOBD patients are presented in Table 3.

No individuals used regular benzodiazepine treatment or other psychotropic medications among the patients included in the study.

Discussion

This study compared the sociodemographic characteristics, clinical courses, and treatment approaches of patients diagnosed with BD based on age at disease onset (<50 years and ≥50 years). No significant differences were observed between the groups in terms of sociodemographic characteristics, gender, marital status, and education level. However, a significant difference was found between the groups in terms of employment status. This may be since age

Table 3. Treatment Distribution by Age of Onset (EOBD vs. LOBD).

Treatment	EOBD (n=52)	LOBD (n=35)	Total (n=87)	p
MS Monotherapy	4 (7.7%)	7 (20.0%)	11 (12.6%)	0.664*
AP Monotherapy	8 (15.4%)	5 (14.3%)	13 (14.9%)	
MS + AP Combination	25 (48.1%)	15 (42.9%)	40 (46.0%)	
MS Combination	1 (1.9%)	1 (2.9%)	2 (2.3%)	
MS + AD Combination	1 (1.9%)	0 (0.0%)	1 (1.1%)	
MS + AP + AD Combination	11 (21.2%)	5 (14.3%)	16 (18.4%)	
No medication	2 (3.8%)	2 (5.7%)	4 (4.6%)	
Mood Stabilizers (MS)				
Lithium (Li)	10 (23.8%)	12 (42.9%)	22 (31.4%)	0.295*
Valproate (VPA)	16 (38.1%)	10 (35.7%)	26 (37.1%)	
Li + VPA	7 (16.7%)	1 (3.6%)	8 (11.4%)	
Lamotrigine	3 (7.1%)	3 (10.7%)	6 (8.6%)	
VPA + Lamotrigine	1 (2.4%)	0 (0.0%)	1 (1.4%)	
Li + Lamotrigine	5 (11.9%)	2 (7.1%)	7 (10.0%)	
Antipsychotics (AP)				
Olanzapine	7 (15.2%)	7 (28.0%)	14 (19.7%)	0.010*
Quetiapine	14 (30.4%)	9 (36.0%)	23 (32.4%)	
Risperidone	4 (8.7%)	1 (4.0%)	5 (7.0%)	
Aripiprazole	10 (21.7%)	8 (32.0%)	18 (25.4%)	
Paliperidone	6 (13.0%)	0 (0.0%)	6 (8.5%)	
Amisulpride	1 (2.2%)	0 (0.0%)	1 (1.4%)	
Long-acting injectables	4 (8.7%)	0 (0.0%)	4 (5.6%)	
Antidepressants (AD)				
SSRI	6 (54.5%)	0 (0.0%)	6 (40.0%)	0.156**
SNRI	3 (27.3%)	2 (50.0%)	5 (33.3%)	
Other	2 (18.2%)	2 (50.0%)	4 (26.7%)	

Note: *Independent samples t-test results, ** chi-square test. Column percentages are presented.

Abbreviations: EOBD: Early onset bipolar disorder, LOBD: Late onset bipolar disorder, MS: Mood Stabilizer, AP: Antipsychotic, AD: Antidepressant, Li: Lithium, VPA:Valproate , SSRI: Selective Serotonin Reuptake Inhibitor, SNRI: Serotonin-Norepinephrine Reuptake Inhibitor

Table 4. Clinical and treatment differences between early-onset and late-onset bipolar disorder

Feature / Treatment	EOBD (Early-Onset BD)	LOBD (Late-Onset BD)
Episode Severity	More severe	Milder
Rapid Cycling	High	Low
Psychotic Symptoms	More frequent	Less frequent
Treatment Variety	Greater	More limited
Long-Acting Formulations	Preferred	Less commonly used
Lithium Use	Less frequent	More frequent, not statistically significant
Olanzapine Use	Less frequent	More frequent, statistically significant

Note.This visual diagram was created based on the current study's data, summarizing the clinical features and treatment preferences of patients with early-onset and late-onset bipolar disorder.

directly affects occupational status, and older age groups are often in retirement. One study reported that the severity of depressive symptoms was higher in older individuals, which may be strongly associated with poorer functioning [5].

This study observed that the disease tended to be more severe and episodic in the EOBD group. EOBD patients generally experience more severe, atypical, and psychotic symptoms in their first manic episode, and they also have a higher rate of rapid cycling. In contrast, LOBD patients have

milder symptoms during their manic episode, but treatment resistance and mortality rates have been reported to be higher [12]. Another study also noted that the disease is more severe and recurrent episodes are more common in EOBD [13]. There may be differences between the clinical courses of patients with early- and late-onset BD. Similar to our study results, early-onset BD has been shown to have a more severe clinical course and higher comorbidity [14]. Depressive episodes can be more common with age than manic and hypomanic episodes in BD [6]. Another study provides essential data demonstrating that LOBD is clinically similar to early-onset BD, with only a minor difference in terms of endocrine diseases. Therefore, both forms are different manifestations of the same disease, and considering them as separate subtypes may not be appropriate [15]. This study found that lithium monotherapy was more frequently preferred in LOBD patients, and fewer drug combinations were used. This is consistent with previous reports that treatment regimens should be kept simpler in older patients, considering drug tolerance and side effect profiles [16].

In drug trials, the distinction between EOBD and LOBD has not been made in most studies, and it remains unclear whether there are differences between these two groups in terms of treatment response and side effect profile [12]. Studies have reported that treatment options for LOBD patients may include lithium, valproate, carbamazepine, lamotrigine, atypical antipsychotics, antidepressants, benzodiazepines, electroconvulsive therapy (ECT), and psychotherapies [17]. Although lithium's effectiveness in the elderly is similar to that in younger patients, lower doses and serum level monitoring are recommended due to pharmacokinetic changes, decreased renal function, and the risk of side effects. Lower serum lithium levels (0.4 –0.6 mmol/L) are generally recommended in the elderly [3]. Antiepileptics such as valproate and lamotrigine have been reported to be better tolerated in the elderly, and ECT may be a safe and effective option, especially in refractory cases [17].

In this study, it is noteworthy that second-generation antipsychotics (aripiprazole, olanzapine, quetiapine) were used more frequently in the LOBD group, while the EOBD group showed a wider variety of medications and a preference for longer-acting formulations. Atypical antipsychotics are commonly used pharmacological agents in patients with bipolar disorder; similar to our study results, the most frequently preferred medications in this group are quetiapine and olanzapine. However, the risk of metabolic syndrome, weight gain, hyperglycemia, dyslipidemia, and cardiovascular disease increases in older individuals with the use of these drugs. Furthermore, some large-scale observational studies have reported that second-generation antipsychotics may increase mortality rates in older patients. This increase is attributed to both cardiovascular complications and complications such as sedation, fall risk, and aspiration. Therefore, the use of antipsychotics in older bipolar patients should be carefully evaluated, and it is recommended that mood stabilisers be preferred over antipsychotics whenever possible [17]. In this study, on the other hand, olanzapine use was found to be statistically significant among LOBD patients. This may be attributed to olanzapine’s relatively favorable cardiac side effect profile [18] and the potential benefit of its sedative properties [19].

Our study found very low rates of antidepressant use in both groups (n = 15). The limited use of antidepressants in both groups emphasises the need for cautious use of antidepressants in the management of depressive episodes in bipolar disorder. Studies recommend short-term use of antidepressants in conjunction with mood stabilisers in bipolar disorder, and it has been reported that long-term use may increase the risk of mania [20]. As a summary of the present study, Table 4 synthesizes the key clinical characteristics and treatment differences between early-onset and late-onset bipolar disorder.

Limitations

Limitations of the study include missing data due to the retrospective design and the inability to assess details regarding medication doses and treatment duration. Furthermore, comorbid medical conditions in older patients and their impact on treatment choices could not be

thoroughly addressed. Prospective examination of these factors in future studies will provide more in-depth information on age-specific management of bipolar disorder.

Conclusion

The findings highlight the importance of individualizing treatment plans in clinical practice based on patient age and age at disease onset. In particular, the use of olanzapine and lithium in LOBD patients should be carefully considered in terms of both efficacy and safety. In early-onset patients, greater variability in treatment and the more frequent use of long-acting formulations necessitate that medication selection be guided by the patient's symptom profile and treatment response. Accordingly, clinicians should perform age-specific assessments and develop individualized treatment strategies.

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