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Relationship Between Adult Separation Anxiety Disorder and Suicide in Patients with Bipolar Disorder

Bipolar Bozukluk Tanılı Hastalarda Yetişkin Ayrılma Anksiyete Bozukluğu ve İntihar Arasındaki İlişki

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ABSTRACT

The present study aimed to investigate the comorbidity of adult separation anxiety disorder (ASAD) and the relationship between this comorbidity and suicide in patients with bipolar disorder (BD). A total of 138 outpatients with BD at remission between the ages of 18-65 years and 63 healthy controls were included in our study. All participants were administered a sociodemographic data form, Hamilton Depression Scale (HMDS), Young Mania Rating Scale (YMRS), Adult Separation Anxiety Questionnaire, and Structured Clinical Interview for Separation Anxiety Symptoms (ASAD-SCI). The age and gender of the participants did not differ significantly between the control group, the BD and BD+ASAD groups. The mean age of the participants was 42.3±11.9 years. When categorized according to gender, 42.3% of the participants were male and 57.7% were female. ASAD was detected in 46.3% of the participants. The suicide attempt rate was significantly higher in the BD and BD+ASAD groups than in the control group. The rate of suicide attempt was significantly higher in the BD+ASAD group than in the BD group. We demonstrated that the comorbidity of ASAD was associated with previous suicide attempts in patients with BD. Recognizing and treating ASAD in patients with BD may reduce suicide attempts in these patients.

Keywords: Bipolar disorder, suicidality, separation anxiety

ÖZ

Çalışmamızda bipolar bozukluk (BB) tanılı hastalarda yetişkin ayrılma anksiyete bozukluğu (YAAB) komorbiditesi ve bu komorbiditenin intihar ile ilişkisinin araştırılması amaçlanmıştır. Çalışmamıza ayaktan izlenen remisyonda BB tanılı 18-65 yaşları arasındaki 138 hasta ve 63 sağlıklı kontrol alınmıştır. Tüm katılımcılara tarafımızca hazırlanmış sosyodemografik veri formu, Hamilton Depresyon Ölçeği (HMDÖ), Young Mani Derecelendirme Ölçeği (YMDÖ), Yetişkin ayrılma anksiyete anketi, Ayrılma Anksiyetesi Belirtileri için Yapılandırılmış Klinik Görüşme (AAB-YKG) verilmiştir. Kontrol grubu, BB ve BB+YAAB grupları arasında katılımcıların yaşları ve cinsiyetleri anlamlı farklılık göstermemiştir. Katılımcıların yaş ortalaması 42,3±11,9 olarak tespit edilmiştir. Cinsiyet durumuna göre kategorize edildiğinde katılımcıların % 42,3'ü erkek olup % 57,7'si kadınlardan oluşmaktadır. Katılımcıların % 46,3'ünde YAAB tepit edilmiştir.BB ve BB+YAAB gruplarında intihar girişim oranı kontrol grubundan anlamlı olarak daha yüksekti. BB+YAAB olan grupta intihar girişim oranı BB grubundan anlamlı olarak daha yüksekti. Sonuçlarımız, BB tanılı hastalarda YAAB komorbiditesinin önceki intihar girişimleriyle ilişkili olduğunu göstermiştir. BB tanılı hastalarda YAAB'nin tanınması ve tedavi edilmesi bu hastalarda intihar girişimini azaltabilir.

Anahtar sözcükler: Bipolar bozukluk, intihar, ayrılma anksiyetesi

Introduction

Suicide attempts are acts of individuals harming themselves or ending their lives. World Health Organizastion (WHO) states that suicidal behavior is a series of behaviors that include thinking, planning and attempting suicide (WHO 2014). Some studies have shown that 10% to 19% of patients diagnosed with bipolar disorder (BD) die by suicide (Goodwin and Jamison 2007). It is widely accepted that there is a relationship between suicidal behavior in BD and variables such as age of onset, family history of BD, type of first episode, panic spectrum symptoms and sociodemographic characteristics of patients (Swann et al. 2005).

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Adult Separation Anxiety Disorder (ASAD) causes clinically significant distress or impairment in social, academic, occupational and other important areas in adults who have an unexpectedly severe fear or anxiety about separation from people to whom they feel intense attachment (APA 2013). In addition, in a study examining comorbidity and clinical features in patients with ASAD, more than half of these patients were found to have suicidal ideation at any point in their lives (Karaytuğ et al. 2021). ASAD symptoms can often be confused with dependent personality disorder. Therefore, it is important to make a distinction. While the source of anxiety in ASAD is directed towards losing the attachment figure, the source of anxiety in dependent personality disorder is directed towards the person himself/herself (Namlı et al. 2022).

An epidemiological study conducted in 2006 showed that 19.4% of ASAD was comorbid with bipolar disorder (Shear et al. 2006). In a study, 15.9% of patients with bipolar disorder had Childhood Separation Anxiety Disorder (CSAD) and 7.7% had ASAD (Pini et al. 2005). In another study of Pini et al (2012) 454 participants with mood and anxiety disorders were included and the rate of ASAD was found to be 40.7% (Pini et al. 2012). Furthermore, CSAD and ASAD were detected in 46.1% of individuals in a study of patients with Panic Disorder and BD II. (Toni et al. 2008). ASAD symptoms were reported to have a detrimental impact on functionality in a study investigating the comorbidity of ASAD in patients with BD (Sahin et al. 2019).

Although there is limited data on the comorbidity of BD in ASAD, recent epidemiologic studies show that separation anxiety disorder (SAD) occurs in a large part of the adult population and negatively affects the course, prognosis and treatment of BD, as in the comorbidity of other psychiatric disorders (Pini et al. 2005, 2010). SAD may be an indicator of early-onset BD and CSAD is thought to be associated with personality disorders in adulthood (Tasdemir et al. 2016). In this context, accompanying SAD in patients diagnosed with BD may worsen the course of the disease and cause impairment in functionality when left untreated.

The aim of our study was to determine whether there is a relationship between ASAD comorbidity and suicide in patients diagnosed with BD. Our hypothesis is that there will be an increase in suicide rate in patients with ASAD comorbidity.

Method

Sample

In the present study, 152 literate patients diagnosed with BD who were examined in Çukurova University Faculty of Medicine (CUFM) Department of Mental Health and Diseases between 02.01.2022-15.08.2022, aged between 18-65, without comorbid dementia and mental retardation were included. Seventy-four people who stated that they did not have a known mental illness, were similar to the patient group in terms of age and gender, and graduated from at least primary school were voluntarily randomly included in the study as the control group.

The ethics committee approval of the study was obtained from Cukurova University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Decision No. 115/15 dated 1.10.2021). Written informed consent was obtained from all participants before the study. The study was conducted in accordance with the Declaration of Helsinki. The case and control groups underwent psychiatric interview by the first author according to DSM-5 (Diagnostic and Statistical Manual of Mental Disorders) diagnostic criteria (APA 2013).

Only patients with BD in remission were included in the patient group. Patients who scored seven points or less on the Hamilton Depression Scale (HMDS) and twelve points or less on the Young Mania Rating Scale (YMDS) and who had not had an episode for at least the last three months and had no history of inpatient treatment were considered to be in remission (Israel 2006, Patel et al. 2007). In the patient group, six patients who were found to have had a recent mood episode and who scored above 12 on the YMDS, three patients who scored above 7 on the HMDS, and five patients who were diagnosed with any personality disorder according to the psychological examination were excluded from the study. In the control group, six people who did not want to fill out the scales and seven people who were found to have psychiatric disorders as a result of mental examination were excluded from the study. The study was conducted with 138 patients diagnosed with BD and 63 healthy controls. With the G Power program (version 3.1.9.2), the required sample size was calculated as 112 with a medium effect size (Cohen's d = 0.30), power of 0.95 and error of 0.05 (p = 0.05). According to this result, it was concluded that the sample in our study had sufficient power.

Procedure

Each patient was given approximately 1 hour for psychological examination and filling out the forms. Information on whether they had attempted suicide at any point in their lives was collected with the help of a data form created by us. Any action attempted to end life throughout life was considered as a suicide attempt. The parts that the participants did not understand were explained by the interviewer upon their request.

Data Collection Tools

Sociodemographic and Clinical Data Form

This form includes sociodemographic data such as marital status, gender, education level, age, occupation, and information about the disease process such as duration of illness, number of hospitalizations, and suicidal acts.

Adult Separation Anxiety Questionnaire (ASAQ)

This self-report questionnaire consists of 27 items. It evaluates the symptoms of separation anxiety present after the age of 18 (Manicavasagar et al. 2003). The higher the score obtained from the questionnaire, the higher the probability of ASAD diagnosis. The reliability and validity study of the Turkish version was conducted by Diriöz et al. A score of 25 and above on this version leads to a diagnosis of ASAD (Diriöz et al. 2012).

Structured Clinical Interview for Separation Anxiety Symptoms (SAD-SCI)

This form consists of two sections and 8 items. In the first part, separation anxiety symptoms from childhood are questioned. In the second part, symptoms from the period after the age of 18 are questioned. For both sections, the presence of three of the eight items leads to a diagnosis of SAD. For the first part, Cronbach's alpha value is 0.56, and for the second part, Cronbach's alpha value is 0.57. The scale has been adapted into Turkish (Cyranowski et al. 2002, Diriöz et al. 2002).

Young Mania Rating Scale (YMRS)

It is an 11-item scale that is scored based on the clinician's observations during the examination and the patient's narratives. However, the clinician's opinion is prioritized (Young et al. 1978). Cronbach's alpha value was found to be 0.79 in the Turkish reliability and validity study (Karadağ et al. 2002).

Hamilton Depression Rating Scale (HDRS)

It is a scale that evaluates depressive symptoms consisting of 17 items. As the score obtained from this scale increases, it shows that the severity of depressive symptoms increases. It is completed by clinicians (Zimmerman et al. 2013). Cronbach's alpha value was found to be 0.75 in the Turkish reliability and validity study (Akdemir et al. 1996).

Statistical Analysis

Mean, standard deviation, median minimum, maximum, frequency and ratio values were used in the data obtained by descriptive analysis. Distribution between variables was tested with the Kolmogorov Smirnov test. The Kruskal-Wallis test was used to examine independent quantitative data such as age and ASAD, and the Mann-Whitney U test was used to examine quantitative data such as years of illness, number of depressive episodes, number of manic episodes, and number of hospitalizations. Independent qualitative data such as gender, educational status, marital status, occupation, place of residence, dominant episode, social support, suicide attempt, and family history of mental illness were analyzed using chi-square test. Fischer test was used when Chi-square test conditions were not met. SPSS 28.0 program was used in the analyses.

Results

The average age of the participants was 42.3±11.9 years. When categorized according to gender, 42.3% of the participants were male and 57.7% were female. The age of the patients did not differ significantly ($p > 0.05$) between the control group, BD and BD + ASAD groups (Table 1). Smoking, alcohol and substance use, employment status, place of residence, marital status, educational status, gender distribution did not differ significantly ($p > 0.05$) between the groups (Table 1, Table 2).

The number of depressive episodes, number of manic episodes, length of hospitalization, and duration of illness did not differ significantly ($p > 0.05$) between the BD and BD+ASAD groups. (Table 3) Adult separation anxiety questionnaire score and separation anxiety symptom inventory score were significantly ($p < 0.05$) higher in the BD and BD+ASAD groups than in the control group. In addition, adult separation anxiety questionnaire score and separation anxiety symptom inventory score did not differ significantly ($p > 0.05$) between the BD and BD+ASAD groups. (Table 3)

The rate of history of physical illness was significantly ($p < 0.05$) higher in the BD+ASAD group than in the control group. The rate of history of physical illness did not differ significantly ($p > 0.05$) between the BD, control and BD+ASAD groups. (Table 3) The rate of family history of mental illness was significantly ($p < 0.05$) higher in the BD and BD+ASAD groups than in the control group. The rate of family history of mental illness did not differ significantly ($p > 0.05$) between the BD and BD+ASAD groups. (Table 3)

The suicide attempt rate was significantly ($p < 0.05$) higher in the BD and BD+ASAD groups than in the control group. The suicide attempt rate was significantly ($p < 0.05$) higher in the BD+ASAD group than in the BD group (Table 3).

The distribution of predominant episode types did not differ significantly ($p > 0.05$) between BD and BD+ASAD groups. The rate of social support did not differ significantly ($p > 0.05$) between the control group, BD, BD+ASAD groups. (Table 3) The rate of childhood separation anxiety was significantly ($p < 0.05$) higher in the BD+ASAD group than in the control and BD groups. The rate of childhood separation anxiety did not differ significantly ($p > 0.05$) between the BD and control groups. (Table 3)

Discussion

The most important finding of the study is the high rate of suicidal behavior in patients with BD accompanied by ASAD. It is estimated that the prevalence of ASAD is high among adults, and its rate is higher in those with mood and anxiety disorders (Pini et al. 2012). Our study revealed that ASAD is quite common in patients with BD, and approximately 45% of patients have ASAD. Anxiety disorders are frequently seen at a high rate in patients with BD. In one study, 500 participants with a diagnosis of BD were included, and it was revealed that approximately half of the participants had a lifelong anxiety disorder (Simon et al. 2004). Taşdemir et al. showed that ASAD accompanies approximately half of the patients with BD, consistent with our study (Tasdemir et al. 2016). The association of SAD with other psychiatric disorders, especially anxiety disorders, has been investigated in the literature. While the worsening effect of these disorders on the prognosis is well known, studies on the comorbidity of SAD in BD are limited. As with other anxiety disorders, such as panic disorder and agoraphobia, SAD is thought to be associated with more psychopathology in BD. In this context, underdiagnosed and untreated SAD in patients with BD may adversely affect the prognosis of the disease.

In our study, the number of suicide attempts was significantly higher in the ASAD group. Many studies in the literature show that SAD comorbidity is associated with suicidality in psychiatric disorders and that the related disorder can be considered a severity index (Gesi et al. 2013, Pini et al. 2013). When the patients with BD with and without anxiety disorder were compared in Simon et al.'s study (2004), comorbid anxiety disorders are shown to increase the risk of suicide attempts. Among the patients with any existing anxiety disorder, 60.3% had a history of suicide attempts, while 27.4% of the patients without an existing anxiety disorder had the highest number of suicide attempts. Lifetime comorbid anxiety disorders also significantly increased rates of suicide attempts. While 22.1% of bipolar patients without lifetime anxiety disorder attempted suicide, this rate was 52.1% in patients with a lifetime anxiety disorder (Simon et al. 2004). In another study, comorbidity of ASAD was examined in patients diagnosed with major depressive disorder and findings indicated that these patients showed more anxiety symptoms and had a lower response to antidepressant treatment compared to the group

Table-1 Sociodemographic and Clinical Characteristics of the Participants

		Min-Max			**Median**	**Mean±Sd/n-%**		
Age		22.0	-	67.0	43.0	42.3	±	11.9
Gender	Male					85		42.3%
	Female					116		57.7%
Educational Status	Primary school					57		28.4%
	High school					99		49.3%
	University					45		22.4%
Marital status	Single					106		52.7%
	Married					95		47.3%
Employment Status	Employed					71		35.3%
	Unemployed					130		64.7%
Smoking						88		43.8%
Alcohol use						57		28.4%
Substance use						201		100.0%
Residence	Urban					90		44.8%
	Rural					111		55.2%
Disorder duration, year		1.0	-	30.0	8.0	9.6	±	7.1
Number of Depressive Episodes		0.0	-	10.0	2.0	2.0	±	1.7
Number of Manic Episodes		1.0	-	6.0	1.0	1.8	±	1.0
Number of Hospitalizations		0.0	-	8.0	2.0	1.9	±	1.2
Adult Separation Anxiety Questionnaire		10.0	-	44.0	15.0	19.4	±	8.9
Separation Anxiety Symptom Inventory		0.0	-	27.0	14.0	16.6	±	6.0
Physical Illness History	Presence					73		36.3%
	Absence					128		63.7%
Family History of Mental Disorder	Presence					95		47.3%
	Absence					106		52.7%
Suicide Attempt	Presence					30		14.9%
	Absence					171		85.1%
Predominant polarity	Manic					57		41.3%
	Depressive					81		58.7%
Social support	Presence					199		99.0%
	Absence					2		1.0%
Adult Separation Anxiety Disorder	Presence					93		46.3%
	Absence					108		53.7%

Min: minimum; Max: maximum; Sd: standart deviation

not accompanied by ASAD (Elbay et al. 2021). In the light of these results, the inclusion of SAD in the clinical evaluation of patients diagnosed with BD may create a new intervention area for suicide in some of the patients.

The age of onset of BD may be affected by comorbid anxiety disorders. In one study, the mean age at onset was found to be 19.4 years in 500 patients diagnosed with BD without lifetime anxiety disorder (Simon et al. 2004). However, patients with lifetime anxiety disorders experienced their first episode at an average age of 15.6 years (Simon et al. 2004, Baldassano 2006). Early age of onset is associated with a poor prognosis in BD and suicide risk is also seen at higher rates in these patients. In the study by Taşdemir et al. there was no difference in the age at onset of the disease between the BD group with ASAD and the group without ASAD (Tasdemir et al. 2016). In the present study, no difference was found between the groups in terms of age at onset of BD. The number of patients in the study of Simon et al. may be the reason for the difference between the groups. For a more accurate determination of this parameter in future studies, increasing the number of patients included in the study is recommended.

The rate of physical illness in the patients diagnosed with BD with ASAD was significantly higher in this study than in the control group. In addition, the rate of family history of mental illness was also significantly higher in patients with BD and patients with BD comorbid with ASAD compared to the control group. Physical disorders are reported to be more common in patients diagnosed with BD due to treatment side effects. In addition, family history for mental disorders appears to be more frequent compared to the healthy population due to genetic transmission (Kelsoe 2003, Correl 2008).

This study has several limitations. First, the study was conducted on a small sample group in a tertiary care hospital. The diagnosis of SAD was based on the narrative history of adult patients. Although patient selection was based on strict criteria, the effects of other comorbid anxiety disorders could not be ruled out. Because of these limitations, it is difficult to generalize our results. In the present study, patients diagnosed with BD were not categorized as BD-I, BD-II and cyclothymic in accordance with the classification in DSM-5; therefore, data on each disorder could not be obtained and our study is limited in this respect. Another limitation of the study is that DSM-5 based structured clinical interview guidelines were not used in psychiatric interviews.

Conclusion

The results of the present study suggest that ASAD is prevalent in a large proportion of patients diagnosed with BD and has a

Table-2 Comparison of the Groups' Sociodemographic Characteristics

			Control			Bipolar Disorder(BD)			BD+Adult Separation Anxiety Disorder			p	
Age		mean.±Sd	42.2	±	11.6	42.5	±	11.0	42.1	±	13.0	0.935	K
		Median	37.0			43.0			43.0				
Gender	Male	n-%	26		41.3%	31		48.4%	28		37.8%	0.445	X^2
	Female	n-%	37		58.7%	33		51.6%	46		62.2%		
Educational Status													
Primary school		n-%	22		34.9%	20		31.3%	15		20.3%	0.227	X^2
High school		n-%	29		46.0%	27		42.2%	43		58.1%		
University		n-%	12		19.0%	17		26.6%	16		21.6%		
Marital status													
Single		n-%	28		44.4%	32		50.0%	46		62.2%	0.102	X^2
Married		n-%	35		55.6%	32		50.0%	28		37.8%		
Employment Status													
Employed		n-%	29		46.0%	21		32.8%	21		28.4%	0.086	X^2
Unemployed		n-%	34		54.0%	43		67.2%	53		71.6%		
Smoking		n-%	22		34.9%	30		46.9%	36		48.6%	0.226	X^2
Alcohol use		n-%	19		30.2%	21		32.8%	17		23.0%	0.410	X^2
Substance use		n-%	63		100.0%	64		100.0%	74		100.0%	1.000	X^2
Residence													
Urban		n-%	25		39.7%	30		46.9%	35		47.3%	0.617	X^2
Rural		n-%	38		60.3%	34		53.1%	39		52.7%		

^{K} Kruskal-wallis (Mann-Whitney U test) / $^{X^2}$ Chi-square test (Fischer test)
sd: standard deviation

Table-3 Comparison of the Participants' Clinical Characteristics

			Control			Bipolar Disorder(BD)			BD+Adult Separation Anxiety Disorder			p	
Disorder duration, year		Mean±Sd				9.5	±	7.1	9.8	±	7.1	0.832	m
		Median				8.0			8.5				
Number of Depressive Episodes		Mean±Sd				2.0	±	1.5	2.0	±	1.8	0.594	m
		Median				2.0			1.0				
Number of Manic Episodes		Mean±Sd				1.7	±	1.0	1.8	±	1.0	0.388	m
		Median				1.0			2.0				
Number of Hospitalizations		Mean±Sd				1.8	±	1.1	2.0	±	1.3	0.502	m
		Median				1.5			2.0				
Adult Separation Anxiety Questionnaire		Mean±Sd	14.4	±	2.2	19.5	±	7.9	23.7	±	10.9	***0.000***	K
		Median	15.0			16.0			21.0				
Separation Anxiety Symptom Inventory		Mean±Sd	12.3	±	2.8	17.8	±	6.1	19.1	±	6.0	***0.000***	K
		Median	12.0			15.0			22.0				
Physical Illness History	Presence	n-%	18		28.6%	20		31.3%	35		47.3%	***0.045***	X^2
	Absence	n-%	45		71.4%	44		68.8%	39		52.7%		
Family History of Mental Illness	Presence	n-%	17		27.0%	36		56.3%	42		56.8%	***0.001***	X^2
	Absence	n-%	46		73.0%	28		43.8%	32		43.2%		
Suicide Attempt	Presence	n-%	0		0.0%	8		12.5%	22		29.7%	***0.000***	X^2
	Absence	n-%	63		100.0%	56		87.5%	52		70.3%		
Predominant polarity													
Manic		n-%				24		37.5%	33		44.6%	0.399	X^2
Depressive		n-%				40		62.5%	41		55.4%		
Social Support	Presence	n-%	63		100.0%	62		96.9%	74		100.0%	p>0.05	X^2
	Absence	n-%	0		0.0%	2		3.1%	0		0.0%		

[K] Kruskal-Wallis (m Mann-whitney u test) / [X²] chi-square test (Fischer test)
Sd: standart deviation

close link with suicidal behavior. In the follow-up of patients diagnosed with BD, it seems necessary to question symptoms related to anxiety disorders as well as typical symptoms of the disorder such as unhappiness, insomnia, increased energy and euphoria, especially in terms of suicidal phenomenon. Further research on this subject will raise awareness for ASAD and lead to more attention and time being devoted to the assessment and diagnosis of SAD in psychiatric interviews. Thus, therapeutic interventions for SAD in a patient population with a high risk of suicide like BD, may prevent at least some of the suicides. Since there are few studies examining both disorders together, the effects of ASAD comorbidity on the course of BD are still unclear. We suggest that future studies should explore the effects of comorbidity of ASAD on quality of life, functioning, prognosis, types and frequency of episedsn patients with BD.

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