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To cite this article: Gokhan Umut, Mehtap Arslan Delice, Alparslan Cansiz, Aylin Can, Assoc. Prof. Erhan Kurt & Assoc. Prof. Cuneyt Evren (2016) Clinical Characteristics of Euthymic Bipolar Disorder Patients Comorbid with Alcohol and Drug Use Disorders and Psychometric Properties of the Assessment Tools, Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology, 26:1, 48-57, DOI: [10.5455/bcp.20150223052448](https://doi.org/10.5455/bcp.20150223052448)

To link to this article: <https://doi.org/10.5455/bcp.20150223052448>



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Published online: 08 Nov 2016.



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# Clinical Characteristics of Euthymic Bipolar Disorder Patients Comorbid with Alcohol and Drug Use Disorders and Psychometric Properties of the Assessment Tools

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## ABSTRACT:

Clinical characteristics of euthymic bipolar disorder patients comorbid with alcohol and drug use disorders and psychometric properties of the assessment tools

**Objective:** The primary objective of this study was to identify the frequency of alcohol and drug use disorder -abuse or dependence- (ADUD) in bipolar disorder patients who were followed in a specialized mood disorders unit and to investigate the clinical characteristics of the sample. Secondary aim of the study was to evaluate the psychometric properties of the scales related with alcohol and drug use disorder among bipolar patients in remission.

**Methods:** Alcohol Use Disorders Identification Test (AUDIT), Michigan Alcoholism Screening Test (MAST), Drug Use Disorders Identification Test (DUDIT), and Drug Abuse Screening Test (DAST-10) were applied to 292 bipolar disorder patients in the euthymic state, diagnosed by using mood disorder and alcohol/drug use disorder modules of the Structured Clinical Interview Form for DSM-IV Axis I Disorders (SCID-I) and monitored in our Mood Disorders Center.

**Results:** In our sample, frequency of bipolar disorder patients with ADUD was 6.16% (18/292). 15 of 18 patients with ADUD were men and 3 were women. ADUD in men (12.00%) was higher than in women (1.79%), and this difference was statistically significant ( $p<0.001$ ). Alcohol use disorder frequency was detected as 5.14% in general (15/292), 9.60% in men (12/125) and 1.79% in women (3/167). The frequency of drug use disorder was found as 4.11% in general (12/292), 8.00% in men (10/125) and 1.19% in women (2/167). Proportion of depressive, manic, hypomanic, and mixed episodes did not differ between patients with ADUD and those without ADUD, whereas the proportion of total episodes was higher in patients with ADUD and difference was statistically significant ( $p=0.016$ ).

**Conclusions:** Frequency of bipolar disorder patients comorbid with ADUD followed up in our center was found to be lower than those reported in the literature.

**Keywords:** bipolar disorder, alcohol and drug use disorder, mood disorders

Klinik Psikofarmakoloji Bulteni - Bulletin of Clinical Psychopharmacology 2016;26(1):48-57



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## Date of submission:

January 09, 2015

## Date of acceptance:

February 23, 2015

## Declaration of interest:

G.U., M.A.D., A.C., A.C., E.K., C.E.: The authors reported no conflicts of interest related to this article.

## INTRODUCTION

A community-based epidemiological field study reveals that alcohol use disorder proportion (abuse or alcohol dependence) was 13.5%, while drug use disorder was 6.1% within the whole population<sup>1</sup>. The same study demonstrates that any one of alcohol or drug use disorders in patients with

bipolar disorder (BD) was 56.1%, alcohol use disorder 44.7%, and drug use disorder 33.5%<sup>1</sup>. Similar results were obtained in clinical studies. In 392 inpatients treated due to manic or mixed episodes, lifelong psychoactive drug use disorder proportion was found as 48.5% for alcohol, 43.9% for other drugs and 59.4% for either of them<sup>2</sup>. High proportions of alcohol or drug use disorders in

bipolar disorder patients were suggested in other clinical studies as well<sup>3,4</sup>.

Comorbidity of bipolar disorder and alcohol and drug use disorder in such high proportions is explained by patient's tendency to drug use for treatment of signs and symptoms of the disease, non-compliance to treatment due to the increase in drug use and thus resulting in increased severity of symptoms or, apart from these, onset of drug use as a symptom of bipolar disorder<sup>5,6</sup>.

Alcohol or drug use disorders may occur prior to bipolar disorder as well as at any time following bipolar disorder<sup>5-7</sup>. Regardless of the period it occurs, alcohol or drug use disorder comorbidity in bipolar disorder affects the clinical outcome and changes the course of the disease negatively. Patients with bipolar disorder comorbid with alcohol and drug use disorder demonstrate higher proportions of mixed or dysphoric mania, rapid cycling, increased severity of manic and depressive symptoms, and higher proportions of impulsivity<sup>8</sup> and suicide attempts<sup>9</sup> when compared with patients without comorbidity. Furthermore, it has been reported that healing will be delayed, labor loss and mortality will increase due to relapses, need for hospitalization will be higher, treatment compliance will get harder<sup>2</sup>, and response to lithium treatment will decrease<sup>10</sup> upon occurrence of alcohol and drug use disorder.

Since treatment compliance would be better in bipolar disorder patients regularly monitored in a specialized center, we believed that lower proportions of alcohol and drug use disorder comorbidity would be observed. This study aimed to detect the frequency of alcohol and drug use disorder in bipolar disorder patients monitored in a specialized mood disorders unit in Turkey and to investigate the clinical features of bipolar disorder in these patients. Prior to the current study, psychometric properties of the AUDIT, MAST, DUDIT and DAST-10 were not assessed in a bipolar patients sample in Turkey. Therefore, we also aimed to evaluate the psychometric properties of these scales in a sample of bipolar patients in remission.

## METHODS

Our study was conducted between March 2012 and May 2013 in 292 bipolar disorder patients in euthymic state diagnosed by using modules of mood disorder and alcohol and drug use disorders of Structured Clinical Interview Form for DSM-IV Axis-I Disorders (SCID-I)<sup>11,12</sup> and monitored in Bakırköy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatry, Neurology, and Neurosurgery (BRSHH)'s Raşit Tahsin Mood Disorders Center for averagely about five years (ranging from two to ten years). SCID-I was applied by three psychiatrists. Patients monitored due to mood disorders and unipolar depression unexplainable otherwise and patients refusing to give informed consent form were not included in the study. Prior to the study, approval of ethical committee was received, all patients were informed thereon, and written consent forms were obtained from patients who accepted to participate in the study. Participants were administered socio-demographic data form in addition to Alcohol Use Disorders Test (AUDIT), Michigan Alcoholism Screening Test (MAST), Drug Use Disorders Identification Test (DUDIT), and Drug Abuse Disorders Identification Test (DAST).

### Materials

**Alcohol Use Disorders Identification Test (AUDIT):** A screening test with a total of 10 items developed by World Health Organization to detect hazardous and high-risk alcohol consumption in primary care, with a cut-off score recommendation of 8 or 9<sup>13</sup>. Saatcioglu et al.<sup>14</sup> reported that Turkish interview form of AUDIT was reported to be valid in diagnosis of alcohol dependence based on its relationship with MAST. Self-report form was used and cut-off score was accepted as 8 in this study.

**Michigan Alcoholism Screening Test (MAST):** This 25-item screening test is used to detect whether a person has experienced alcohol use problems or not, if yes, to measure the degree thereof. It can be applied to persons presenting to primary

healthcare services and believed to have problems with alcohol dependence. While filling the questionnaire, patients are asked to choose the option that fits themselves the most. It screens for - alcoholism, a non-diagnostic term, and is not based on the diagnostic criteria of the DSM-IV. Developed by Gibbs<sup>15</sup>, the validity and reliability of the Turkish version was reported by Coşkunol et al.<sup>16</sup>.

**Drug Use Disorder Identification Test (DUDIT):** It is an 11-item scale based on self-report and developed in order to screen drug use problems. It was developed by Berman et al.<sup>17</sup> as an analogue of ADUD including parallel questions with ADUD except for a few differences (2 items were deleted and 3 new items were added). The validity and reliability of Turkish version was established by Evren et al.<sup>18</sup> and it was reported to significantly distinguish drug use disorders from alcohol use disorders.

**Drug Abuse Screening Test (DAST-10):** 28-item DAST scale is one of the most frequently used tools to assess both alcohol- and drug-related problems. Skinner<sup>19</sup> developed a 10-item shortened DAST-10 scale from this 28-item DAST scale. DAST-10 detects the identifiable drug use disorders by focusing on drug use in the previous year and results regarding drug use. The validity and reliability of Turkish version was established by Evren et al.<sup>20</sup>.

### Statistical Analysis

Data were analyzed by using SPSS 15.0 for Windows (SPSS, Inc., Chicago, IL). In the assessment of study data, descriptive statistics (median, 25%-75% values, frequencies and percents) were used as well as chi-square test to assess the relationships between categorical variables, and Mann-Whitney U test for continuous variables in independent groups due to the absence of normal distribution. Significance value for all statistical analyses was accepted as  $p < 0.05$ . The following strategies were used to investigate

the psychometric properties of the AUDIT, the MAST, the DUDIT, and the DAST-10: (1) convergent validity was evaluated by calculating Pearson's product-moment correlation between the AUDIT and the MAST, also between the DUDIT and the DAST-10; (2) internal consistency was assessed using Cronbach's alpha values; (3) predictive validity, sensitivity, specificity, and optimal cut-off scores were estimated by constructing a Receiver Operating Characteristic (ROC) curve; (4) Cohen's kappa coefficient was performed to measure agreement between SCID-I diagnoses and alcohol or drug use disorder diagnoses according to the scales; and (5) discriminant validity was evaluated using Mann-Whitney U test of the AUDIT and the MAST scores for the groups with and without alcohol use disorder and of the DUDIT and the DAST-10 scores for the groups with and without drug use disorder.

## RESULTS

In our sample, 167 of the total 292 participants (57.19%) between the ages of 18-61 were women and 125 of them were men (42.81%). Median age was 36 (31.25-43), median duration of education was 11 (8-14), median age for BP onset was 21 (18-26), and median age for onset of alcohol-drug use was 20 (18-23) for the sample. Sociodemographic characteristics of participants are summarized in Table 1.

Proportion of subjects with psychiatric comorbidity was found as 8.90% ( $n=26$ ), 20 (76.92%) with obsessive compulsive disorder, three (11.54%) with panic disorder, and three with (11.54%) personality disorder diagnosis. Proportion of subjects with additional physical disorders was 17.12% ( $n=50$ ). Among additional physical disorders, hyperthyroidism was the most frequent disease with 23 subjects, followed by hypertension with 6 subjects. Highest number of episodes was 34 and median of total episodes was found as 6 (4-10). The median of manic episodes was 2 (1-4), the median of depressive episodes was 2 (1-3), the median of hypomanic episodes was 1 (0-2) and the median of mixed episodes was 0

(0-0). Information on clinical characteristics is demonstrated in Table 2.

In our sample, frequency of patients with bipolar disorder concomitant with ADUD was 6.16% (18/292). Fifteen of 18 patients with ADUD (83.33%) were men and three (16.67%) were

women. ADUD frequency was higher in men (12.00%) than in women (1.79%) and this difference was statistically significant ( $p < 0.001$ ). Alcohol use disorder frequency was found as 5.14% in the whole group (15/292), 9.60% in men (12/125) and 1.79% in women (3/167). The rate of

**Table 1: Sociodemographical features in bipolar patients with and without comorbid alcohol and drug use disorder**

	ADUD		p
	No (n=274) n (%)	Yes (n=18) n (%)	
<b>Gender</b>			<0.001*
Women	164 (59.85)	3 (16.67)	
Men	110 (40.15)	15 (83.33)	
<b>Marital status</b>			0.283
Single	147 (53.65)	12 (66.67)	
Married	127 (46.35)	6 (33.33)	
<b>Employment</b>			0.103
Employed	128 (46.72)	7 (38.89)	
Unemployed	67 (24.45)	8 (44.44)	
Retired	15 (5.47)	2 (11.11)	
Housewife	64 (23.36)	1 (5.56)	
	<b>*Median (25-75%)</b>	<b>*Median (25-75%)</b>	
<b>Age (years)</b>	36 (31-43)	36 (31-44.5)	0.933
<b>Duration of education (years)</b>	11 (8-14)	11 (8-12.25)	0.430

ADUD: Alcohol-Drug Use Disorder, Chi square Test, \*Mann-Whitney U Test,  $p < 0.05$ \*

**Table 2: Clinical features in bipolar patients with and without comorbid alcohol and drug use disorder**

	ADUD		p
	No (n=274) n (%)	Yes (n=18) n (%)	
<b>BD type</b>			0.706
BD-I	252 (91.97)	17 (94.44)	
BD-II	22 (8.03)	1 (5.56)	
<b>First episode type</b>			0.503
Depressive	136 (49.63)	7 (38.89)	
Manic	123 (44.89)	11 (61.11)	
Hypomanic	7 (2.56)	0 (0)	
Mixed	8 (2.92)	0 (0)	
<b>Psychotic features</b>	167 (60.95)	13 (72.22)	0.341
<b>Rapid cycling</b>	25 (9.12)	2 (11.11)	0.778
<b>Suicide attempt</b>	58 (21.16)	6 (33.33)	0.227
	<b>*Median (25-75%)</b>	<b>*Median (25-75%)</b>	
<b>Onset age of BD</b>	21 (18-27)	23 (19.25-24.50)	0.757
<b>Number of hospitalization</b>	2 (1-3.25)	3 (1.75-7.25)	0.060
<b>Age of first hospitalization</b>	23 (19-29)	23 (22-27)	0.787
<b>Number of episodes</b>			
Total	6 (4-10)	10 (5-15.25)	0.016*
Depressive	2 (1-3)	4 (0-6.25)	0.185
Manic	2 (1-4)	3 (2-6)	0.169
Hypomanic	1 (0-2)	1 (0-4)	0.380
Mixed	0 (0-0)	0 (0-1.25)	0.352

ADUD: Alcohol-Drug Use Disorder, BD: Bipolar disorder, Chi square Test, \*Mann-Whitney U Test,  $p < 0.05$ \*

**Table 3: Frequency of alcohol or drug use disorder, psychometric properties of the scales, and median of the scales**

	Yes		No	
	n	%	n	%
<b>AUD</b>	15	5.14	277	94.86
<b>DUD</b>	12	4.11	280	95.89
	<b>AUDIT</b>	<b>MAST</b>	<b>DUDIT</b>	<b>DAST-10</b>
<b>Cronbach's Alpha</b>	0.914	0.922	0.964	0.910
<b>Cut-off point<sup>a</sup></b>	3	3	2	2
<b>AUC</b>	0.996 (SE=0.002)	0.965 (SE=0.038)	0.958 (SE=0.047)	0.955 (SE=0.047)
<b>Sensitivity</b>	0.996	0.993	0.996	0.989
<b>Specificity</b>	0.778	0.765	1.000	0.900
<b>Kappa</b>	0.839	0.802	0.955	0.811
<b>PPV</b>	0.986	0.986	1.000	0.996
<b>NPV</b>	0.933	0.867	0.917	0.750
<b>Median (25%-75%) values</b>				
The group without UD	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
The group with UD	7 (2.75-15.5)	12 (0.75-17.5)	3.50 (0-14)	1.5 (0-4.5)

AUC: the area under curve, Kappa: Cohen's Kappa coefficient, PPP: positive predictive power, NPP: negative predictive power, SE: Standard Error, UD: Use disorder, AUD: Alcohol Use Disorder, DUD: Drug Use Disorder, Positive if Greater Than or Equal To<sup>a</sup>

alcohol use disorder was statistically significantly higher in male patients than female patients ( $p=0.003$ ). Drug use disorder frequency was observed as 4.11% in the whole group (12/292), 8.00% in men (10/125) and 1.19% in women (2/167). Similarly to alcohol use disorder, the rate of drug use disorder was statistically significantly higher in male patients than female patients ( $p=0.004$ ). Reported drugs were illicit drugs such as cannabis and ecstasy, prescription drugs like biperiden and volatile solvent, and cannabis was the most used drug with proportion of 2.39% (7/292). Nine patients (3.08%) were using both alcohol and drug while six patients (2.05%) were using only alcohol and three patients (1.02%) were using only drug. Proportion of patients having bipolar disorder with ADUD comorbidity was 4.89% ( $n=7$ ) in patients with the first-episode being a depressive episode, 8.20% ( $n=11$ ) in patients with the first episode being a manic episode. No patients having the first-episode as mixed or hypomanic were detected. No statistically significant difference was found between groups with and without ADUD based on first episode type ( $p=0.503$ ). The number of patients having an episode with psychotic features was 180, 13 (7.22%) of whom with ADUD, while the number of patients without an episode with psychotic features was 112, of which 5 (4.46%) was

comorbid with ADUD. No statistically significant differences were detected between the groups with or without ADUD in terms of episodes with psychotic features ( $p=0.340$ ). No statistically significant differences were present between the groups with and without ADUD in terms of employment ( $p=0.103$ ). No statistically significant differences were present between BP-I and BP-II groups in terms of ADUD proportions ( $p=0.706$ ). Twenty-seven patients had rapid cycling, and no statistically significant differences were found between patients with and without rapid cycling ( $p=0.778$ ). Proportion of patients attempting suicide was 21.91% ( $n=64$ ), of which 6 was comorbid with ADUD. Difference in ADUD proportions for suicide attempts was statistically insignificant ( $p=0.227$ ). No statistically significant differences were detected between the age of onset in patients with bipolar disorder with and without ADUD ( $p=0.750$ ).

No statistically significant differences were present between numbers of depressive, manic, hypomanic and mixed episodes of patients with and without ADUD ( $p=0.185$ ,  $p=0.169$ ,  $p=0.380$ ,  $p=0.352$ , respectively). There was a statistically significant difference in terms of total number of episodes ( $p=0.016$ ), and patients with ADUD were found to have higher number of episodes. Comparison of the groups with and without ADUD

for hospitalization revealed that the difference was statistically insignificant ( $p=0.060$ ). No statistically significant differences were found between the groups with and without ADUD in terms of age of onset and first hospitalization for bipolar disorder ( $p=0.757$ ,  $p=0.787$ , respectively).

### **Convergent Validity and Internal Consistency Reliability**

The Pearson's product-moment correlation between the AUDIT and MAST scores ( $r=0.936$ ,  $p<0.001$ ) and between the DUDIT and DAST-10 scores ( $r=0.776$ ,  $p<0.001$ ) were statistically significantly high.

Internal consistency for the AUDIT (coefficient  $\alpha=0.914$ ), for the MAST (coefficient  $\alpha=0.922$ ), for the DUDIT (coefficient  $\alpha=0.964$ ) and for the DAST-10 (coefficient  $\alpha=0.910$ ), examined by Cronbach's alpha, were also sufficiently high (Table 3).

### **Predictive Validity, Sensitivity, Specificity, Optimal Cut-Off Scores, and Cohen's Kappa Coefficients**

The predictive validity, sensitivity, and specificity of the four scales (DUDIT, DAST-10, AUDIT and MAST) were examined using a ROC curve that included all participants ( $n=292$ ). First participants were dichotomously classified according to the SCID-I as a group with alcohol use disorder or a group without alcohol use disorder. Then, participants were dichotomously classified according to the SCID-I as a group with drug use disorder or a group without drug use disorder. Results revealed that a score of 3 from AUDIT and MAST were the most critical value for identifying a participant as having a alcohol problem, whereas a score of 2 from DUDIT and DAST-10 were the most critical value for identifying a participant as having a drug problem (Table 3). Cohen's kappa coefficients found for AUDIT and MAST were 0.839 and 0.802 respectively, whereas these values for DUDIT and DAST were 0.955 and 0.811 respectively (Table 3). Statistically significance for all these coefficients were at the level of  $p<0.001$ .

### **Discriminant Validity**

To evaluate discriminant validity, Mann-Whitney U test was conducted. The mean scores of the AUDIT ( $p<0.001$ ) and the MAST ( $p<0.001$ ) were statistically significantly higher in the group with alcohol use disorder than the group without alcohol use disorder. The mean scores of the DUDIT ( $p<0.001$ ) and the DAST ( $p<0.001$ ) were statistically significantly higher in the group with drug use disorder than the group without drug use disorder (Table 3).

## **DISCUSSION**

In patients with bipolar disorder, drug abuse was reported to be between 34-60% (average 56%), and alcohol or drug abuse between 30-69% (mean 49%) in various studies<sup>1,2,21</sup>. When compared with general population, alcohol use disorder was found 3 times higher, whereas drug use disorder was 7 times higher in BD patients<sup>1</sup>. In a current comprehensive epidemiological study in the United States of America, compared to other psychiatric disorders, the highest relationship with alcohol-related disorders was detected in manic and hypomanic episodes of bipolar disorder<sup>4</sup>. Alcohol use disorder frequency was found as 5.14% in the whole group (15/292), 9.60% in men (12/125) and 1.79% in women (3/167) in our study. Drug use disorder frequency was observed to be 4.11% in the whole group (12/292), 8.00% in men (10/125) and 1.19% in women (2/167). In the 2012 report published by Turkish Statistical Institute (TurkStats)<sup>22</sup>, alcoholic drink use was reported to be 10.4% in general population, 17.2% in men and 3.8% in women. In 2013 report of Turkish Monitoring Center for Drugs and Drug Addiction (TUBİM)<sup>23</sup>, the proportion of persons in 15-64 age group trying any drug at least once (lifelong drug use prevalence) was reported to be 2.7% in general, 3.5% in men and 2.6% in women. When compared with TUBİM data drug use disorder was observed to be higher in the whole group and in men, and lower in women. Since users trying once are involved and so these proportions may not imply the proportion of drug use disorder,

the higher drug use disorder proportions according to the general population may have been over estimated. Similarly, how many of those individuals using alcohol has alcohol use disorder is not known. So we compared the results of our group with those of limited number of similar studies conducted in Turkey and Western countries. In The Report of Mental Health Profile of Turkey<sup>24</sup>, the prevalence of alcohol use disorder was stated as 0.8 in the general population, 1.7 in men and 0.1 in women. In a fieldwork conducted in the province of Sivas<sup>25</sup>, the prevalence of alcohol use disorder was found as 2.28 in the general population, 6.33 in men and no alcohol use disorder was detected in women. Lifelong alcohol abuse was found as 10% in a study conducted in Turkey assessing comorbidity incidence in 50 bipolar disorder patients<sup>26</sup>, and as 5.4% in a study conducted in a specialized mood center<sup>27</sup>. When compared with studies from Western countries, lower proportions of drug use disorder were detected in bipolar disorder patients in studies conducted in Turkey on drug use disorders. In a study, retrospective file screening was performed on 1370 bipolar disorder inpatients and drug use was found as 3.5%<sup>28</sup>. In addition, a study conducted by Akkaya et al.<sup>29</sup>, in 53 centers all around in seven different geographical regions of Turkey with participation of 584 manic attack patients reported psychoactive drug dependence as 3.2%, and alcohol dependence as 4.9%. Our findings of alcohol and drug use disorder proportions in the general population and BD patients were not similar with those of studies conducted in the Western countries, but were similar to results of other studies conducted in Turkey.

These differences in proportions may be due to data acquisition methods. Despite the differences in proportions, studies show that alcohol and drug use disorders are in high levels in BD patients. The differences in the results between the Western countries and our study as well as other studies conducted in Turkey on alcohol-drug use disorders may be a consequence of less consumption of alcohol and drugs compared to the western societies due to the social, cultural and religious

values of our country. Furthermore, since information on alcohol or drug use and scale results are obtained from self-reports of patients, deficiencies in these reports may have led to an under detection of alcohol and drug use proportion of patients in our center.

We found no relationship between alcohol and drug use disorder and age of onset of bipolar disorder in our study. Goldstein et al.<sup>30</sup> reported that onset of bipolar disorder during childhood or adolescence has no relationship with alcohol and drug use. While our study confirmed findings of this study, it reached opposite conclusions with studies demonstrating a relationship between age of onset of bipolar disorder and alcohol and drug use disorder. In these studies, Kesebir et al.<sup>31</sup> reported that age of onset of mood disorder was earlier in cases with comorbid drug use disorder; Fleck et al.<sup>32</sup>, on the other hand, reported that age of onset of bipolar disorder was later in cases with comorbid alcohol use disorder.

Various studies revealed that alcohol and drug use disorder proportion in bipolar disorder patients was higher in men<sup>2,3,27</sup>. Statistical significance of higher proportions of alcohol and drug use disorder in male patients in our sample complies with studies mentioned above. Same studies reported that healing will be delayed and relapses will increase in case of a comorbid drug use disorder<sup>2</sup>. Total number of episodes of bipolar disorder patients with alcohol and drug use disorder was found to be higher in our study. The study by Kesebir et al.<sup>31</sup> demonstrating that total number of attacks in bipolar disorder patients is higher in patients with comorbid drug use disorder is another study supporting findings in our sample. We found that there were more hospitalized bipolar disorder patients with alcohol and drug disorder compared to patients without comorbidity, however, the difference was statistically insignificant ( $p=0.060$ ). Cassidy et al.<sup>2</sup>, similarly, reported more hospitalizations in patients with drug use disorder comorbidity. In our study, proportion of patients having an attack with at least one psychotic feature was found as 61.64% (180/292). This proportion was detected to be 75%



in a study by Ozyildirim et al.<sup>27</sup> investigating alcohol use disorder comorbidity, 36% in a study by Kesebir et al.<sup>31</sup> investigating drug use disorder comorbidity and 80% in a study by Healey et al.<sup>33</sup> investigating drug use disorder comorbidity. Sampling characteristics of treatment centers may have caused these differences. For instance, the study by Kesebir et al.<sup>31</sup> comprises participants monitored in a specialized hospital, the study by Ozyildirim et al.<sup>27</sup> comprises participants monitored in a university hospital, and the study by Healey et al.<sup>33</sup> comprises only 15 participants. Referral of patients developing psychotic features to the training and research hospitals or especially to the tertiary level hospitals such as ours may also have led to these results.

In our study, no statistically significant differences were found between patients with and without alcohol and drug use disorder in terms of suicide attempt. In the study by Kesebir et al.<sup>31</sup>, suicide attempt was reported to be more frequent in patients with drug use disorder comorbidity. Another study is also available reporting that patients with drug use disorder have an increased risk of suicide attempt<sup>9</sup>, however, our findings conflict with these studies. Due to the very low number of patients using alcohol and drug in our sample, we may have not detected a significant relationship in terms of suicide attempts.

Overall, the AUDIT and the MAST were found to have satisfactory psychometric properties as alcohol abuse screening tests, whereas the DUDIT and the DAST-10 were found to have satisfactory psychometric properties as a drug abuse screening test in bipolar patients in remission. High correlations between the AUDIT and the MAST and between the DUDIT and the DAST-10 indicated good convergent validity. All the scales also showed good discriminant validity, as

evidenced by their ability to differentiate persons with alcohol use disorders (AUDIT and MAST) and drug use disorders (DUDIT and DAST-10) from those without. In terms of reliability, the Turkish version of the scales had high internal consistency scores. The ROC curve showed that the scales had good predictive validity as suggested by high sensitivity, specificity, and the AUC. Our results revealed that cut-off scores of 3 for the AUDIT and MAST and 2 for the DUDIT and DAST-10 were the most critical values for identifying participants who had an alcohol and drug use disorder according to the SCID-I respectively.

The present study had some limitations. In studies related to alcohol and drug use of participants, confirmation of self-reports with examinations of drug metabolites in urine and blood would lead to more accurate results. Therefore, not having done these lab examinations is the one of the limitations of the present study. Absence of a control group of bipolar disorder patients monitored from general psychiatry outpatient clinics is another limitation of the present study.

In conclusion, alcohol-drug morbidity proportion in bipolar disorder patients was observed to be much lower in our study compared to studies in other countries; however, it was found to be consistent with previous studies in Turkey. Multicenter studies with participation of larger number of patients comparing specialized mood disorders centers monitoring patients regularly and general psychiatry clinics would explain differences better and contribute to the current literature substantially.

**Acknowledgement:** *We would like to thank Cavide Cakmak and Aysel Ozer, the staff nurses of our center, for their valuable contribution in organizing the patients' charts.*

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