Comorbidity of Adult Attention Deficit and Hyperactivity Disorder in Bipolar Patients: Prevalence, Sociodemographic and Clinical Correlates

Yetişkin Bipolar Bozuklukta Erişkin Dikkat Eksikliği ve Hiperaktivite Bozukluğu: Sıklık, Sosyodemografik ve Klinik İlişkiler

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ABSTRACT

Introduction: The aims of this study were to determine the frequency of adult attention deficit and hyperactivity disorder (ADHD) comorbidity in bipolar patients and to investigate the influence of this comorbidity on the clinical characteristics of bipolar disorder (BD).

Method: A total of 135 patients with BD type I and II and BD not otherwise specified were included in this study. First, the Adult ADD/ADHD DSM-IV-Based Diagnostic Screening and Rating Scale (ADHD scale) was administered to all patients, and all of the patients were also interviewed for the diagnosis. Patients who were diagnosed as having ADHD comorbidity (n=23) on the basis of DSM-IV and those who were not diagnosed to have ADHD comorbidity (n=32) were compared in terms of sociodemographic and clinical correlates.

Results: Twenty-three of 135 patients (17%) were found to have ADHD comorbidity. In the ADHD comorbidity group, the level of education and the number of suicide attempts were higher (p=.011 and .043, respectively). Although not significant, sub-threshold depressive symptoms in interepisodic periods, the lifetime history of antidepressant use and the total number of lifetime depressive episodes tended to be more frequent in bipolar disorder with ADHD comorbidity group than in the control group.

Conclusion: Bipolar disorder has a frequent comorbidity with ADHD, and contrary to expectations, it might be related to the depressive aspect, rather than the manic aspect, of bipolar disorder. Early diagnosis of ADHD comorbidity in bipolar patients might help to prevent serious risk factors. (Archives of Neuropsychiatry 2014; 51: 97-102)

Key words: Adult attention deficit and hyperactivity disorder, bipolar disorder, comorbidity, depressive symptoms

Conflict of interest: The authors reported no conflict of interest related to this article.

ÖZET

Giriş: Bu çalışmanın amacı bipolar hastalarda yetişkin dikkat eksikliği ve hiperaktivite bozukluğu (DEHB) eştanısı sıklığını tespit etmek ve bu eştanının, bipolar bozukluğun (BB) klinik özellikleri üzerine etkisini araştırmaktır.

Yöntem: Çalışmaya toplam 135 bipolar I, II veya BTA BB tanılı hasta alınmıştır. Öncelikle, Yetişkin DEB/DEHB DSM-IV'e Dayalı Teşhis Tarama ve Değerlendirme Ölçeği (DEHB ölçeği) tüm hastalara uygulandı, buna bağlı tüm hastalarla tanı için görüşüldü. DSM-IV'e göre DEHB eştanısı tespit edilen hasta grubu (23 hasta) ile bu eştanının tespit edilmediği hasta grubu (32 hasta) sosyodemografik ve klinik özellikleri açısından karşılaştırılmıştır.

Bulgular: Yüz otuz beş bipolar hastanın 23'ünde (%17) DEHB eştanısı bulundu. DEHB eştanısı olan bipolar grupta eğitim seviyesi daha yüksek ve intihar girişimi öyküsü daha sık (p=0,011, p=0,043) idi. Anlamlılık düzeyine ulaşmamakla birlikte, DEHB'nin eşlik ettiği grupta eşikaltı depresif belirtiler, toplam depresif epizod ve antidepresan kullanma öyküleri oransal olarak daha fazlaydı.

Sonuç: Dikkat eksikliği ve hiperaktivite bozukluğu (DEHB), bipolar hastalarda sık görülen bir eştanıdır ve beklenilen tersine bipolar bozukluğun manikten öte depresif yanı ile ilişkili olabilir. Bipolar hastalarda DEHB eştanısı olasılığını erken değerlendirmek ciddi risklerin önlenmesinde yardımcı olabilir. (Nöropsikiyatri Arşivi 2014; 51: 97-102)

Anahtar kelimeler: Yetişkin dikkat eksikliği ve hiperaktivite bozukluğu, bipolar bozukluk, eştanı, depresif belirtiler

Çıkar çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

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Introduction

Bipolar disorder (BD), especially manic symptoms, and attention deficit and hyperactivity disorder (ADHD) are thought to have a specific association or transaction because of their overlapping symptoms (including impulsivity, talkativeness, irritability, distractibility, and increased motor activity). Therefore, the association between these two disorders has recently been emphasized (1). Although studies have differed on the basis of samples and diagnostic criteria, the prevalence of ADHD in childhood was found to be 3-9% (2,3), and other studies have indicated that approximately half of these children maintain this diagnosis into adulthood (1,4,5,6). However, BD generally has its onset in adulthood. Therefore, it has been suggested that studying the association between adult ADHD and BD could contribute to understanding the links and differences between the two disorders, thus, clarifying the psychopathological characteristics of the two disorders.

Comorbidity of BD and ADHD in childhood and adolescence has been reported to be frequent (1,7,8,9,10). It has also been suggested that more than half of bipolar children and adolescents might have ADHD comorbidity (1,7,8,9,10). However, one important consideration is the age group of bipolar children who have ADHD comorbidity because as age increases, comorbidity tends to decrease. For example, while ADHD comorbidity is diagnosed in almost all pre-pubertal patients (10), the rate of comorbidity decreases to one third of late adolescents (7). Additionally, family studies suggest that ADHD and BD might have a family link. Increased frequency of ADHD in children of parents with BD and of BD in families of children with ADHD was reported (11).

Contrary to these studies in children, data are scarce on the frequency of ADHD comorbidity in adult bipolar patients and on possible outcomes of this comorbidity. A limited number of studies have reported that ADHD in adult bipolar patients is more frequent than expected and might be correlated with poor outcomes (1,12). Studies have reported variable rates of comorbidity between ADHD and BD from 9 to 35% (1,12,13,14). A review reported that the prevalence might be approximately 15% and that it is higher than the ADHD prevalence in adulthood (6).

It has also been reported that in bipolar patients with ADHD comorbidity, the onset of BD is earlier (1,12,13,14), the total number of affective and depressive episodes is higher (1,12), other psychiatric comorbidities, including alcoholism and substance abuse, are more frequent (1,12), the duration of wellness periods is shorter, and the response to mood stabilizers is poorer (15) than in patients without ADHD comorbidity.

The aims of this study were to determine the frequency of ADHD comorbidity in bipolar patients and to investigate the effects of ADHD comorbidity on the clinical course of BD.

Methods

A total of 135 bipolar patients followed at the Mood Disorders Unit of the Psychiatry Department at Istanbul Faculty of Medicine, Istanbul University, were included in this study. The included patients were part of the Bipolar Disorder Prospective Follow-up Program, which also covers the treatment of the patients. The

Mood Disorders Unit works mainly as an outpatient clinic; it has an inpatient unit and is also connected to an emergency unit. BD diagnoses were made by two experienced clinicians through a detailed semi-structured clinical assessment, in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) (16), when the patients were first referred to the unit. A semi-structured interview that assessed sociodemographic and clinical features (for example, family history, presence of psychotic features, age of onset, predominant episode type, number and type of episodes, ratio of episode types, total number of episodes, number of hospitalizations, and duration and outcome of prophylactic treatment) of the patients was used to record the data obtained from the patients and their families on admission, as well as previous medical records and a "mood chart," which includes graphical records for the outcome of the disorder and the outcomes of treatments since the onset of BD. These charts were updated at every follow-up visit. During follow-up, the patients and their accompanying relatives were interviewed once per month during the first 6 months, once every 2 months for the second 6 months and once every 3 months for the remainder of the maintenance period in remitted patients. In cases of recurrence, more frequent visits were scheduled according to the necessities of the treatment. The life charts and all of the records of the patients were screened for the present study, and missing parts were completed at update visits when necessary. Age of onset was the age at which the patient met the mood episode criteria of the DSM-IV for the first time, and the predominant episode type was the most frequent of all episodes.

This study was conducted between August 2007 and August 2008. Our study had approval, with file number 2008/3198, from the Istanbul University Faculty of Medicine's local ethics committee. In this study, bipolar patients who were followed at the Mood Disorders Unit of the Psychiatry Department at Istanbul Faculty of Medicine, Istanbul University, were enrolled into the study consecutively during their applications for routine control, and the files of these patients were analyzed retrospectively. A total of 123 subjects were diagnosed with bipolar I, six were diagnosed with bipolar II, and the remaining six were diagnosed with BD not otherwise specified (BD NOS). BD NOS was the diagnosis of six patients who developed manic or hypomanic episodes while on antidepressant medication. However, there was insufficient evidence to determine whether the affective symptoms were primary or were due to medication. In addition, during the interviews with the patients, only one patient was found to have used methylphenidate for a short time, and it was surmised that this medication did not have any significant effect on the patient's BD course.

Included in this study were patients older than 18 years old who were diagnosed with BD according to the DSM-IV criteria (16) and who were symptomatically in remission (Young Mania Rating scale (17) score <12, Hamilton Depression Scale (18) score <8), as determined during the month prior to the study. Patients with substance abuse disorders due to general medical conditions were excluded. To participate in the study, all patients provided written informed consent.

The Adult ADHD DSM-IV-Based Diagnostic Screening and Rating Scale (ADHD-Scale) (19) was administered to all subjects

to assess for the presence of ADHD symptoms; the language equivalence, validity and reliability of the Turkish version of the scale were previously reported (20). The ADHD scale is a five-point Likert scale with three sub-scales: an inattention section (a total of nine items composed on the basis of the DSM-IV inattention symptoms); a hyperactivity/impulsivity section (a total of nine items composed on the basis of the DSM-IV hyperactivity symptoms); and an ADHD characteristics and problems section (thirty items composed on the basis of clinical experience and observations). A total of 135 patients were divided into two groups according to their adult ADHD-Scale scores:

1. Patients whose inattention or hyperactivity/impulsivity sub-scale score was equal to or greater than 11 (40 patients); and
2. Patients whose inattention and hyperactivity/impulsivity sub-scale scores were less than 11 (95 patients).

Additionally, a semi-structured interview was conducted with each patient to assess for ADHD on the basis of the DSM-IV criteria, and the mood disorders module of the Structured Clinical Interview for DSM-IV/Clinical Version (SCID-I/CV) (21) was applied. While 23 of the first group patients were diagnosed with ADHD comorbidity, none of the second group patients received this diagnosis.

For the next phase, we aimed to compare bipolar patients with ADHD comorbidity to patients without ADHD comorbidity. However, we planned to exclude patients who had sub-threshold ADHD symptoms from the group without ADHD comorbidity. Sixty-three patients who had scores of 6-11 on the ADHD scale were excluded, with the goal of enrolling in the control group bipolar patients who did not have ADHD symptoms as much as possible. Statistically, 63 patients who were excluded did not have significant differences from the 32 control patients in terms of their clinical and sociodemographic characteristics. Therefore, we formed two groups with the following characteristics:

- a) Twenty-three bipolar patients who met the DSM-IV-TR criteria for ADHD were assigned to the "BD with ADHD group" (BD-ADHD); and
- b) Thirty-two bipolar patients who both had inattention and hyperactivity/impulsivity sub-scale scores lower than six and who did not meet the ADHD criteria based on the clinical interview were assigned to the "BD without ADHD group" (control group).

In the BD-ADHD group, 21 patients had BD-I, and 2 patients had BD-II, whereas in the control group, 30 patients had BD-I, 2 patients had BD-II; in both groups, none of the patients had BD NOS. There was no significant difference between the two groups in terms of polarity. The two groups were compared in terms of sociodemographic and clinical characteristics.

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 11.0. Fisher's exact test/ χ^2 test was employed to compare categorical variables. Continuous variables were analyzed with the independent samples t-test and the Mann-Whitney U test when necessary. All p values were 2-tailed, and statistical significance was set at $p < .05$.

Results

The proportions of the 135 patients diagnosed with BD-I, BD-II, and BD-NOS were 91% ($n=123$), 4% ($n=6$), and 4% ($n=6$), respectively. Twenty-three of 135 patients with BD (17%), who were included in the present study, met the diagnostic criteria for current adult ADHD. ADHD comorbidity was diagnosed in 17% (21/123 patients), 33% (2/6 patients) and 0% (0/6 patients) of the patients with BD-I, BD-II and BD-NOS, respectively. Only one of the patients with ADHD comorbidity had been diagnosed with ADHD before the study and had undergone short-term methylphenidate treatment.

The sociodemographic and clinical characteristics of the patient groups with and without ADHD comorbidity are presented in Table 1. The level of education and number of suicide attempts were higher in the BD with ADHD group than in the control group ($p=.011$ and $.043$, respectively). Additionally, although not significant, dysthymic courses in interepisodic periods, a lifetime history of antidepressant use and the total number of lifetime depressive episodes had the tendency to be more frequent in the BD with ADHD comorbidity group than in the control group ($p=.057$, $.066$, and $.059$, respectively).

There were no significant differences between the two groups in terms of mean age, sex distribution, polarity, marital status, age at onset of BD, cycling interval, psychiatric history in first-degree relatives, mean episode severity, lifetime history of psychotic features, rapid cycling, hospitalization, total number of lifetime episodes, or first and predominant episode types.

Discussion

There are many studies in the literature on ADHD and BD, however, most of these studies focused on childhood and adolescent ADHD. Furthermore, previous studies commonly assessed the comorbidity of BD among patients with ADHD. On the other hand, in the present study, we evaluated the rate of ADHD in adult patients with BD, and sociodemographic and clinical characteristics of patients with comorbid ADHD and BD.

Our findings showed that 17% of the patients with BD included in this study had a current diagnosis of adult ADHD. This rate was significantly higher than the rate reported for ADHD in the general adult population (1-6%) (22). However, it is in line with the findings of studies conducted in adult bipolar patients (1,6,12,13). Nierenberg et al. (12) found a rate of lifetime ADHD comorbidity of 9.5% in 1000 adult bipolar patients, in their study conducted to determine ADHD frequency and its consequences in adult bipolar patients. The comorbidity rate we found in the present study was similar to those reported in similar studies conducted in Turkey (15% and 16%, respectively) (1,13). Our study sample might have been composed of patients with more severe symptoms than the general bipolar population because the sample included patients followed at a specialized mood disorders unit. This fact might have been a factor in the higher rate of ADHD comorbidity here than in a study by Nierenberg et al. (12) conducted on a general bipolar population. Additionally, it was reported that patients followed by specialized units sought treatment more frequently than the general population and that the probability of a higher

frequency of comorbidity might increase for these patients (23). All these findings support the idea that adult ADHD rates are higher in patients with BD than in the general population.

Generally, as the number of comorbid disorders increases, an adverse impact on academic performance might be expected. In particular, a disorder such as ADHD, which has its onset in childhood, is more likely to have such consequences. There have been many studies reporting that ADHD patients have poorer academic performance than people without ADHD (24,25,26). It was reported that impairment in the general level of functionality, including academic performance, increased in the presence of ADHD comorbidity in child and adolescent bipolar patients (8). However, the specific effect of ADHD comorbidity on academic performance in adult bipolar patients has not been investigated widely. A study conducted in Turkey did not find a difference between bipolar groups with and without ADHD comorbidity in terms of total years of education (1). However, our study indicated that bipolar patients with ADHD comorbidity were more educated than patients without ADHD comorbidity ($p=0.011$). Further studies are needed to explain this finding.

Weiss and Hechtman (27) reported that 75% of adults diagnosed with ADHD experienced interpersonal problems. The same study reported that 10% of patients attempted suicide, and 5% died accidentally or intentionally. This finding might be related to the presence of a tendency toward depressive symptoms (28,29) and impulsivity, the latter of which is one of the primary symptoms of ADHD. A study conducted in adult ADHD patients reported that the most significant symptoms were distractibility, impulsivity and activity, and in addition, these patients experience difficulties in

establishing close relationships and suffer from decreases in self-esteem (31). In cases of ADHD comorbidity in BD, increases in impulsivity, intensification of interpersonal problems and conflicts could lead to an increase in the frequency of suicide attempts, which is a significant risk in bipolar patients. Our finding that a history of suicide attempt was more frequent in the ADHD comorbidity group than in the control group ($p=0.043$) supports this notion. Although some studies have not revealed similar findings (1), other studies have similarly found a high frequency of suicide attempts in the presence of ADHD comorbidity in bipolar patients (12). This finding implies the importance of the recognition and proper treatment of ADHD in bipolar patients.

In our view, one of the most significant findings of the present study was the marginally higher total number of depressive episodes in the bipolar group with ADHD comorbidity compared to the control group ($p=.059$). Given that the mean age of the BD with ADHD group was younger than that of the group without ADHD (35 and 41 years, respectively) and that the total duration of illness was shorter in the former group (approximately 4.18 years); it might be assumed that the difference between the two groups, in terms of total number of depressive episodes, was significant. This finding is consistent with the findings of previous studies (1,12,13,30). Additionally, a tendency toward a dysthymic course during interepisodic intervals and a higher frequency of antidepressant use were found in the BD with ADHD group. These tendencies, together with the higher frequency of suicide attempts in the ADHD group, support the idea that ADHD comorbidity is correlated with the depressive part of bipolar disorder. We think of ADHD patients as "talkative,

Table 1. Comparison of the groups in terms of sociodemographic and clinical features

	BD with ADHD n=23 (%)	BD without ADHD n=32 (%)	p
Gender (female)	14 (60.9)	20 (62.5)	NS
Polarity			
BD-I	21 (91.3)	30 (93.8)	
BD-II	2 (8.7)	2 (6.3)	NS
Mean episode severity (severe)	11 (47.8)	19 (59.4)	NS
Suicide attempts	11 (47.8)	7 (21.9)	.043
Psychotic features	17 (73.9)	27 (84.4)	NS
Dysthymia in interepisodic interval	6 (26.1)	2 (6.3)	.057
Lifetime antidepressant use (yes)	19 (82.6)	19 (59.4)	.066
	(SD)	(SD)	
Age	35.1 (10.7)	41.3 (13.0)	NS
Age of onset	20.6 (5.4)	22.6 (7.0)	NS
Education (year)	12.8 (1.9)	11.2 (2.3)	.011+
Total number of episodes	11.6 (10.4)	9.5 (6.7)	NS
Number of manic episodes	4.7 (6.1)	4.7 (5.3)	NS
Number of hypomanic episodes	1.6 (2.1)	1.2 (2.3)	NS
Number of mix episodes	.7 (.9)	.6 (1.4)	NS
Number of depressive episodes	4.6 (4.3)	2.8 (2.9)	.059+
Number of hospitalization	1.8 (1.6)	2.9 (2.9)	NS

ADHD: attention-deficit hyperactivity disorder, BD: bipolar disorder, MDD: major depressive disorder, NS: not significant.

* Mann Whitney U test

vigorous, cheerful, active" people. However, according to many studies conducted on this domain, as well as similar findings of the present study, bipolar patients with ADHD are unhappy, more prone to stress and more frequently in need of anti-depressants than patients with BD only.

There have been various studies indicating that there is a close relationship between ADHD and depression. Epidemiological and clinical studies conducted in children and adolescents have reported that 9-38% of cases have both ADHD and major depressive disorder (MDD) (31). Sixteen to thirty-one percent of adults with diagnoses of ADHD have MDD comorbidity (32,33). In another study, 16% of adult MDD patients were reported to meet the childhood ADHD diagnostic criteria, and 75% of these patients continued to meet these criteria into adulthood (34). Additionally, molecular studies have indicated that the dopamine D2 receptor gene has a role in both ADHD and MDD (35). It was found that stress factors, such as the presence of maternal depression, a dysfunctional family environment and parental conflict, were common psychosocial risk factors for both disorders (36). Based on these and similar findings, some researchers have suggested that ADHD and MDD might be different aspects of a common etiology (37). In contrast, some authors have noted that ADHD and depression have some common genetic and environmental risk factors, but other risk factors might determine the differences between ADHD with and without depression comorbidity (36).

First mood disorder episodes have been reported to be earlier in bipolar patients with ADHD comorbidity (1,8,12,14,30,38). Although this finding was not supported by the present study, it might be important to understanding the relationship between the two disorders because it appears as a common point in many studies. For example, in a study of 16 patients, Sachs et al. (14) compared bipolar patients with (n=8) and without (n=8) ADHD comorbidity, and they reported that the patients with ADHD comorbidity had an earlier onset among bipolar patients. Nierenberg et al. (12) found that the rate of ADHD comorbidity was 13% in the group with onset of BD before 18 years of age, whereas the rate was 5% for the group with onset after age 18. They reported that the group with ADHD comorbidity had the onset of BD approximately five years earlier (12). Although not significant, the present study indicated that the group with ADHD comorbidity had the onset of BD approximately two years earlier. Additionally, a study conducted in Turkey reported that 65% of patients with ADHD comorbidity had the onset of BD before age 18, whereas only 20% of those without ADHD had the onset of BD before 18 years of age (1). In another study, it was found that the rate of ADHD in manic adolescents, who had the onset of BD in childhood, and the rate of manic children were similar, at 90%, whereas the rate of ADHD in manic adolescents, who had the onset in adolescence was 60% (39). These findings suggest that there is a relationship between earlier age at onset of BD and ADHD comorbidity. There have been many studies reporting that families with a high frequency of BD had earlier ages of onset of the disease (40,41,42,43). It was suggested that BD with early onset might be a subtype with a significant genetic component, and it might be related to both early onset BD and other early onset psychopathologies (14).

The main limitation of the present study is its retrospective method for the assessment of data of BD such as the number and severity of previous bipolar episodes, and presence of psychotic features. However, the life charts of the patients were completed prospectively as part of the follow-up program, although the assessment was performed retrospectively. The life chart method is often used in studies of the long-term course of BD. The reliability and validity of the life chart method has been confirmed in the literature (44). Another limitation is the nature of the sample: The bipolar patients included in the study were followed by a specialized mood disorders clinic, thus, limiting the generalization of our findings to all bipolar patients and to population-based samples. Another limitation of BD and ADHD studies is the two-way overlap of symptoms for both disorders, perhaps contributing over-identification of these two disorders (12,45). Still, many studies have suggested that most patients continue to meet their original diagnoses of BD and ADHD, even after statistical correction for symptom overlap (45,46).

ADHD is frequent in BD patients, but this comorbidity might be overlooked in clinical practice (even in specialized units). However, the presence of this comorbidity could increase serious risks, such as suicide attempts, and could intensify the depressive course of BD. Considering the diagnosis of ADHD as an option in BD patients, together with close follow-up and screening using appropriate scales, could help to prevent possible complications.

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