

# Comorbidity of attention deficit hyperactivity disorder in young adults who had major depressive disorder

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**BACKGROUND:** The comorbidity of Major Depressive Disorder (MDD) and Attention Deficit Hyperactivity Disorder (ADHD) in adults is well recognized. The role of ADHD in the etiology of MDD, as well as the overlap of genetic and environmental factors between these two disorders, is an area of research. ADHD symptoms are considered risk factors for MDD.

**OBJECTIVES:** The study aimed to examine the relationship between MDD in young adults with history of ADHD.

**DESIGN:** Retrospective and observational study

**SETTINGS:** Outpatient clinic of a tertiary hospital

**PATIENTS AND METHODS:** Data of young adults diagnosed with MDD, aged 18-25 years and seen between January 2017 and May 2023, were included. Individuals with comorbidities other than ADHD in adulthood were excluded from the study. The sociodemographic and clinical data of a total of 489 cases, as well as data on childhood psychiatric referrals, diagnoses, and treatment histories, were retrospectively examined.

**MAIN OUTCOME MEASURES:** ADHD diagnosis history and clinical impact in adults diagnosed with MDD

**SAMPLE SIZE:** 489

**RESULTS:** A total of 489 cases (68.9% female) with a mean age of 21.14 years were included in the study. It was determined that 8% of the cases had ADHD in adulthood, 13.3% in childhood, and 31.9% had at least one mental health diagnosis during childhood. The rate of ADHD diagnosis was significantly higher in males than females in both adulthood and childhood. Additionally, the age of diagnosis of MDD was lower in individuals with ADHD diagnosis and/or those who have discontinued ADHD treatment.

**CONCLUSIONS:** In young adults diagnosed with MDD, the comorbidity of ADHD should also be considered. It is important to acknowledge that ADHD is not just a childhood disorder but a lifelong disorder due to its negative consequences, and to develop appropriate strategies in this regard.

**LIMITATIONS:** Retrospective observational design and the single-center setting, which may affect the generalizability of the findings.

**CONFLICT OF INTEREST:** None.

**M**ajor Depressive Disorder (MDD) is a psychiatric disorder characterized by a depressed mood, loss of interest or pleasure in almost all activities, and a range of cognitive and physical symptoms.<sup>1</sup> It has been reported that the prevalence of MDD varies worldwide and lifetime prevalence rates are between 2.2% and 20%.<sup>2</sup> Although MDD can occur in children and adolescents, the onset age is most commonly reported to be between 20 and 25 years.<sup>3,4</sup> Attention Deficit Hyperactivity Disorder (ADHD), on the other hand, is a neurodevelopmental disorder that begins in childhood, is characterized by symptoms of inattention and hyperactivity/impulsivity, and can also persist in adulthood.<sup>5</sup> It is reported that prevalence rates for ADHD in children and adolescents are between 5-10%, while its prevalence in adults is around 2-5%.<sup>6,7</sup> ADHD can lead to problems in many different areas of individuals' lives, such as family relationships, academic achievement, social relationships, work, and career.<sup>8</sup> Individuals with ADHD often experience difficulties due to the core symptoms of the disorder, poor social skills, and risky behaviors, and this disorder may be accompanied by other psychiatric disorders such as anxiety, mood, eating, and substance abuse.<sup>9,10</sup> It has been reported that most adults with ADHD do not receive a diagnosis or treatment, and many visit clinics due to different mental health diagnoses, including MDD, and take treatment.<sup>11</sup> In addition, it has been revealed that ADHD is often untreated in individuals with mood disorders.<sup>12</sup> Studies on the prevalence of ADHD in adults with MDD have reported rates ranging from 5% to 22%.<sup>13-16</sup> On the other hand, it has been reported that 50% of individuals with ADHD receive a diagnosis of depression during their lifetime.<sup>17</sup>

There is evidence supporting the hypothesis of a strong genetic overlap between MDD and ADHD, that genetic and familial risk factors are shared, and ADHD is causally related to MDD.<sup>18-20</sup> In a follow-up study focusing on the relationship between MDD and ADHD, more than six-fold increased risk of MDD was reported in the first year of ADHD diagnosis.<sup>21</sup> Another study revealed that an ADHD diagnosis led to a more than two-fold increase in the risk of MDD after the age of 25 years.<sup>22</sup> Two different longitudinal follow-up studies have also reported that childhood ADHD was independent of depression in childhood and was associated with adult depression.<sup>23,24</sup> In one longitudinal study, depressive symptoms were assessed using self-report scales in participants aged 18-25 years, and it was found that a childhood history of ADHD predicted more severe depressive symptoms, and that ADHD

diagnosis was associated with an increase in severity of symptoms over time.<sup>25</sup> Additionally, it has been reported that a comorbid diagnosis of MDD and ADHD may be associated with greater clinical impairment and completed suicide risk than having a diagnosis of either disorder.<sup>26-28</sup>

Except for a few studies that investigated the prevalence of ADHD in patients with MDD,<sup>16,29</sup> it was observed that there were limited studies with smaller sample sizes that investigated only ADHD in adulthood or childhood ADHD.<sup>11,13,14,30-32</sup> This study aimed to investigate whether childhood ADHD, treated or not, affects the clinical characteristics of MDD in young adults diagnosed with MDD. For this purpose, the seven-year data of a tertiary-level hospital were screened, and individuals diagnosed with MDD were examined. The obtained sociodemographic and clinical data were discussed in the light of the literature.

## MATERIALS AND METHODS

This study included adults aged 18-25 years who applied to the Psychiatry Outpatient Clinic between January 2017 and May 2023, and diagnosed with depressive disorders. The patients' files were retrospectively examined using the hospital's record system. Patients diagnosed with Depressive episode (F32), Major depressive disorder, single episode, mild (F32.0), Major depressive disorder, single episode, moderate (F32.1), Major depressive disorder, single episode, severe without psychotic features (F32.2), Major depressive disorder, single episode, severe with psychotic features (F32.3), Other depressive episodes (F32.8), Major depressive disorder, single episode, unspecified (F32.9) ICD- 10 (International Classification of Diseases) codes were included in the study. Individuals diagnosed with neurodevelopmental disorders such as intellectual disability, specific learning disorder, autism spectrum disorder, those with hearing or visual impairments, and those with concomitant additional mental disorders in adulthood (obsessive-compulsive disorder, personality disorder, substance use disorder, etc.), chronic illnesses, and neurodegenerative diseases were excluded. A total of 731 files were examined, and 489 cases met the inclusion criteria.

Age, gender, age at first diagnosis of depression, follow-up duration, treatments for adult depression diagnosis, comorbid ADHD diagnosis in adulthood and their treatments, ADHD diagnosis in childhood, concomitant mental disorder diagnosis in childhood, and their follow-up statuses were collected and investigated. For treatments initiated in childhood, discontinuation of treatment outside of physician control and treatment

duration of less than six months in the hospital record system were considered as "treatment abandonment". Ethical approval was obtained from the institution's ethics committee (Ethics committee date: 12.09.2023; decision no: 2023/199) and all procedures related to the human participants in the study were performed in accordance with the ethical standards of the institutional and/or national research committee, as well as the 1964 Helsinki Declaration and its later versions.

### Statistical analysis

Statistical analysis was performed using SPSS version 25 (IBM Corp, Armonk, N.Y. USA). Descriptive statistics were presented in tables as minimum, maximum, number, percentage, mean, and standard deviation (SD) values. Normality was evaluated using the Kolmogorov-Smirnov test, skewness and kurtosis values, and histograms. The chi-square test was used for comparison of categorical data. Independent Student t-test was used to evaluate the mean difference normally distributed between groups. Statistical significance was set at  $P < .05$ .

## RESULTS

A total of 489 patients (mean age 21.14 [SD 2.27]

years), 68.9% (n=337) were females and 31.1% (n=152) were males, were included in the study. It was found that 87.3% (n=427) of the patients used only antidepressants for the diagnosis of MDD, while 12.7% (n=62) used antipsychotic treatment with antidepressant treatment. The most commonly used antidepressant (34.8%) was fluoxetine, and the most commonly used antipsychotic medication (3.7%) was risperidone. In 8% (n=39) of the patients, ADHD diagnosis accompanied the MDD diagnosis in adulthood, and 6.7% (n=33) used medication for ADHD diagnosis (**Table 1**). It was observed that the most commonly prescribed medication for ADHD treatment in adulthood was methylphenidate (81.8%).

It was determined that 21.9% (n=107) of patients were diagnosed with at least mental illness other than ADHD during childhood, and 13.3% (n=65) were diagnosed with ADHD alone in childhood. It was also observed that 58 of the 65 patients (89.2%) diagnosed with ADHD used medications for ADHD in childhood, and the most frequently prescribed medicine was methylphenidate (79.3%). The mean age at first diagnosis of ADHD was 12.95 [2.49]. Also, 67.2% (n=39) of patients diagnosed with ADHD during childhood had abandoned treatment. A total of 107 (n=21.9%)

**Table 1.** Sociodemographic and clinical data of the patients.

	Minimum-Maximum	Mean (SD)
Age (years)	18-25	21.14 (2.27)
Age of first diagnosis of depression (years)	13-25	19.72 (2.34)
Follow-up period with depression diagnosis (months)	1-85	17.95 (16.58)
	n	%
Gender		
Female	337	68.9
Male	152	31.1
Use of medication to treat depression		
Antidepressant treatment	427	87.3
Antidepressant and antipsychotic medication	62	12.7
ADHD comorbidity in Adulthood		
Yes	39	8
No	450	92
Those receiving ADHD treatment in adulthood		
Yes	33	6.7
No	456	93.3

ADHD: Attention deficit hyperactivity disorder, SD: Standard deviation.

**Table 2.** Childhood clinical data of patients.

	Min-Max	Mean (SD)
Childhood-ADHD age of first diagnosis	7-17	12.95 (2.49)
Childhood-ADHD treatment duration (months)	1-95	30.24 (26.35)
	n	%
Childhood-Presence of mental illness		
Yes	156	31.9
No	333	68.1
Childhood-Presence of ADHD diagnosis		
Yes	65	13.3
No	424	86.7
Childhood-Presence of mental illness other than ADHD		
Yes	107	21.9
No	322	78.1
Childhood-Other mental illness diagnoses		
Anxiety disorders	18	3.7
Depressive disorders	87	17.8
Obsessive compulsive disorder	4	0.8
Childhood-Medicine use		
Yes	144	29.4
No	345	70.6
Childhood - Medicine use for ADHD		
Yes	58	11.9
No	435	88.1
Childhood - Medicine use (non-ADHD)		
Yes	95	19.4
No	394	72.6
Childhood-Treatment Abandonment (ADHD)		
Yes	39	67.2
No	19	32.8

ADHD: Attention deficit hyperactivity disorder, SD: Standard deviation

of the cases had a different mental health diagnosis other than ADHD in childhood, and the most common disorder was depression with a prevalence of 17.8% (n=87). Detailed data on the mental health diagnoses and medication use of the patients are given in **Table 2**.

When stratified according to gender, it was found that the rate of comorbid ADHD diagnosis in adulthood was significantly higher in males (12.5%, n=19) than females (5.9%, n=20) ( $P=.021$ ). Similarly, it was observed that males had a significantly higher rate of childhood ADHD diagnosis (21%, n=32) than females (9.7%, n=33) ( $P=.001$ ) (**Table 3**).

Accordingly, it was found that 37% (n=24) of patients diagnosed with ADHD in childhood had persistence of ADHD in adulthood. Furthermore, patients with a history of ADHD had a significantly lower age of MDD diagnosis (mean=19.12 [1.91]) than those without a history of ADHD (mean=19.81 [2.4]) ( $P=.010$ ) (**Table 4**).

In **Table 5**, results showed that patients who discontinued ADHD treatment (74.3%, n=29) had a higher rate of comorbid ADHD in adulthood than those who continued ADHD treatment (25.7%, n=10) ( $P=.001$ ). Similarly, treatment abandonment cases (84.6%, n=33) used medications for ADHD treatment more than the patients who continued ADHD treatment (15.4%, n=6) ( $P<.001$ ). Lastly, the age of depression diagnosis in the treatment abandonment group (mean=18.21 [1.40]) was significantly lower than the group without a history of treatment abandonment (mean=19.62 [2.08]) ( $P=.032$ ).

## DISCUSSION

In this study, young adults diagnosed with MDD were retrospectively examined. Our results revealed that the number of females with MDD was higher, with 87.3% of cases on medication treatment, and in 8% of the cases, ADHD diagnosis accompanied the diagnosis of depression. At least one mental health diagnosis was found in 31.9% of the cases during childhood and an ADHD diagnosis was found in 13.3%. ADHD diagnosis was significantly higher in males in both childhood and adulthood than females. Additionally, the age of onset of MDD was lower in groups with an ADHD diagnosis and/or those considered to have ADHD treatment abandonment.

It is generally accepted that the prevalence of MDD is twice as high in adult females compared to males worldwide,<sup>1,33</sup> and our results are consistent with this. However, adult ADHD comorbidity was higher in males. Some studies showed that depressive disorder and ADHD comorbidity in adulthood were either not different between genders, or were higher in

females.<sup>11,14</sup> In our study, ADHD diagnosis was found to be significantly higher in males (21%) than females (9.7%). The accepted view regarding the distribution of ADHD among children is that the ratio of boys to girls is approximately 3:1-2:1.<sup>7,34</sup> Our results are consistent with this view. The male/female ratio reported in adults with ADHD is lower than childhood and adolescence period.<sup>7,35,36</sup> While there is no clear consensus on the differences occurring between genders in ADHD as age changes, it has been reported that hyperactivity/impulsivity symptoms, which are more common in males than females, tend to decrease as age increases, while inattentive symptoms persist for a longer duration.<sup>34,37</sup> This may arguably lead to prevalence differences between genders in childhood and adulthood.<sup>37,38</sup> In contrast, a review study examining gender differences in adult patients with ADHD diagnosis reported that gender differences could be attributed to methodological differences, or social and cultural influences rather than fundamental differences in the expression of ADHD in males and females.<sup>39</sup>

In this study, the persistence rate of ADHD diagnosis into adulthood was found to be 63%, and no difference was found in terms of persistence rates between genders. Similarly, a community-based twin study focusing on the persistence of ADHD diagnosis into adulthood reported a persistence rate of 55.3%, and no difference between genders.<sup>40</sup> A meta-analysis of follow-up studies published in 2005 reported that one-third of childhood ADHD cases continued to meet full diagnostic criteria until twenties, and approximately 65% continued to experience symptoms impairing functionality.<sup>41</sup> In another follow-up study conducted in Europe, childhood ADHD diagnosis persisted at a rate of 86.5% in adolescents and young adults.<sup>42</sup> Other studies include a 10-year follow-up study reporting a 60% persistence of ADHD in females diagnosed with ADHD,<sup>43</sup> while an 11-year follow-up study found a 62% persistence.<sup>44</sup> In males with ADHD, a persistence rate of 63% was reported.<sup>45</sup>

In the current study, it was found that 8% of the cases were diagnosed with ADHD and the rate of individuals receiving treatment for ADHD was 6.3%. Studies conducted on the prevalence of ADHD in individuals with MDD have reported varying rates. While some reported rates determined by self-report scales, others reported cases diagnosed through structured interviews. In one study conducted in female patients that had recurrent depression, Powell et al reported that 12.8% of the cases had ADHD symptoms and 3.4% met the diagnostic criteria for ADHD.<sup>22</sup> In terms of ADHD rate, Sadeghian et al reported 13.3%

**Table 3.** Comparison of clinical data by gender.

	Gender		P
	Female (n=337) n (%)	Male (n=152) n (%)	
Depression treatment			
Those receiving AD treatment	304 (90.2)	130 (85.5)	.173
Those receiving strengthening therapy	33 (9.8)	22 (14.5)	
Adult ADHD			
Yes	20 (5.9)	19 (12.5)	.021 <sup>a</sup>
No	317 (94.1)	134 (87.5)	
Adult ADHD treatment			
Yes	15 (4.5)	16 (10.5)	.019 <sup>a</sup>
No	322 (95.5)	138 (89.5)	
Presence of childhood ADHD			
Yes	33 (9.7)	32 (21)	.001 <sup>a</sup>
No	306 (90.3)	123 (79)	
Childhood ADHD treatment history			
Yes	27 (8)	27 (17.8)	.002 <sup>a</sup>
No	309 (92)	122 (82.2)	
Presence of childhood mental illness (except ADHD)			
Yes	75 (22.2)	32 (21.1)	.858
No	262 (76.8)	120 (78.9)	
	<b>Mean (SD)</b>	<b>Mean (SD)</b>	
Age	21.23 (2.29)	20.95 (2.19)	.193
Age of depression diagnosis	19.72 (2.42)	19.73 (2.15)	.956

ADHD: Attention deficit hyperactivity disorder, AD: Antidepressant, AP: Antipsychotic MDD: Major depressive disorder SD: Standard deviation,

Chi square test, independent sample t test, <sup>a</sup>P<.05

in a clinical evaluation study, Dunlop et al reported 12.5% using a self-report scale, Alpert et al reported 12%, and McIntyre et al reported 5.4%.<sup>11,13,14,46</sup> In a study conducted in MDD patients in Japan, the ADHD rate evaluated with a self-report scale was reported as 19.9%.<sup>31</sup> In Türkiye, the ADHD rate in the control group was reported as 12%, while this rate was 25% in the group diagnosed with MDD.<sup>30</sup> A recent meta-analysis study including 52 studies reported that the

**Table 4.** Relationship of ADHD diagnosis in childhood with sociodemographic and clinical data.

	Previous history of ADHD		P <sup>a</sup>
	Yes (n=65) n (%)	No (n=424) n (%)	
Gender			
Female (n=337)	33 (9.8)	304 (90.2)	.001
Male (n=152)	32 (21)	120 (79)	
MDD treatment			
AD treatment recipients	52 (80)	375 (87.4)	.088
Those receiving strengthening therapy	13 (20)	49 (12.6)	
Adult ADHD diagnosis			
Yes	24 (37)	15 (3.5)	<.001
No	41 (63)	409 (96.5)	
	Mean (SD)	Mean (SD)	
Age of onset of MDD (years)	19.12 (1.91)	19.81 (2.4)	.010 <sup>b</sup>

ADHD: Attention deficit hyperactivity disorder, AD: Antidepressant, AP: Antipsychotic MDD: Major depressive disorder SD: Standard deviation,

<sup>a</sup>Chi square test, <sup>b</sup>Independent sample t test.

**Table 5.** Relationship between treatment abandonment in childhood and clinical data.

	Presence of previous ADHD treatment abandonment		P <sup>a</sup>
	Yes (n=39) n (%)	No (n=19) n (%)	
Gender			
Female (n=28)	19 (48.7)	9 (47.3)	.923
Male (n=30)	20 (51.3)	10 (52.7)	
MDD treatment			
AD treatment recipients	33 (84.6)	12 (63.1)	.066
Those receiving strengthening therapy	6 (15.4)	7 (36.9)	
Adult ADHD diagnosis			
Yes	29 (74.3)	14 (73.7)	.001
No	10 (25.7)	5 (26.3)	
Adult ADHD treatment			
Yes	33 (84.6)	11 (47.9)	<.002
No	6 (15.4)	8 (42.1)	
	Mean (SD)	Mean (SD)	
Age of onset of MDD	18.21 (1.40)	19.62 (2.08)	.032 <sup>b</sup>

ADHD: Attention deficit hyperactivity disorder, AD: Antidepressant, AP: Antipsychotic MDD: Major depressive disorder SD: Standard deviation

<sup>a</sup>Chi square test, <sup>b</sup>Independent sample t test

prevalence of ADHD in MDD is 7% in adults.<sup>15</sup> The ADHD diagnosis rate of 8% obtained in our study for adults is lower than some of the studies using self-report scales, but similar to results obtained from diagnostic interviews.<sup>11,13,14,30,46</sup>

Additionally, in our study, it was determined that 12.5% of the cases received an ADHD diagnosis in childhood. Alpert et al reported that 16% of individuals with MDD met childhood ADHD criteria fully or subthreshold.<sup>14</sup> In a meta-analysis of 52 studies, the prevalence of ADHD in MDD was reported to be 28% in childhood and 17% in adolescence.<sup>15</sup> Genetic risk factors may partially explain the increased prevalence of ADHD.<sup>18,19,47,48,49</sup> Another related factor may be environmental risk factors such as child abuse and poverty.<sup>50</sup> Finally, as a more indirect effect, factors such as decreased self-esteem, poor social skills, peer bullying, and academic and occupational failure, which may develop secondary to the core symptoms of ADHD and their negative consequences in daily life, have been shown.<sup>51,52</sup>

In this study, it was found that the mean age at which participants were diagnosed with ADHD was approximately 13 years. Contrary to this finding, it is known that ADHD symptoms predominantly begin in early childhood, and applications to hospitals often occur during the elementary school years, when negative impacts on functioning are observed by parents and educators. In a study on the age of onset and diagnosis of ADHD, the mean age of diagnosis was reported to be around 7 years.<sup>53</sup> In our study, the childhood ADHD diagnosis ages of individuals with MDD were found to be later onset compared to the literature. Delayed hospital application and treatment for ADHD diagnosis can lead to an increase in the severity of symptoms and the frequency of comorbid diagnoses.<sup>54,55</sup>

In our study, no association was found between childhood ADHD diagnosis and antipsychotic use in adulthood. Individuals with both ADHD and depression have a higher risk of antidepressant treatment resistance than individuals with only depression.<sup>16,56</sup> However, there are also studies that report no differences in the number and duration of MDD episodes in the presence of a comorbid ADHD diagnosis.<sup>14</sup> The differences in the results can be attributed to a number of factors, such as patient inclusion criteria, age range of the study, methods used for diagnosis, and other comorbidities.

Our results showed that individuals diagnosed with ADHD in childhood received their MDD diagnosis at an earlier age compared to those without ADHD



diagnosis in childhood. Similarly, within the ADHD group, those who discontinued treatment had younger MDD diagnosis ages than those who continued treatment. Consistent with our findings, some studies have also reported younger MDD diagnosis ages for individuals with ADHD.<sup>11,13,16,29</sup> However, there are also studies that found no difference in MDD age of onset between individuals with and without ADHD.<sup>14</sup> Developing a more detailed and frequent screening, risk identification, appropriate parental information, and intervention strategies to enable early diagnosis and treatment of ADHD is crucial for the course of disorders such as MDD.

A strength of our study is that it includes individuals who received diagnoses of both MDD and ADHD based on structured clinical interviews instead of self-reported scales. In Türkiye, diagnosis and treatment for both MDD and ADHD are exclusively performed by psychiatrists. This eliminates potential diagnostic issues related to the validity of the data used, such as reporting bias, follow-up loss, and recall bias. Another strength of the present study is the wide duration of clinical data from childhood to adulthood with detailed data on treatment histories. Few studies have examined data from different periods. Our results may be a guide for clinicians in this regard. Additionally, our study excluded individuals with comorbid pathologies other than ADHD in adulthood, those with repeated suicide attempts, and those with a history of substance

use. Findings of the present study do not apply to these mentioned groups.

### **LIMITATIONS**

The study has limitations. First, the data was obtained retrospectively. Retrospective determination of ADHD diagnosis did not allow for a breakdown into ADHD subtypes, and therefore, it was not possible to evaluate whether there were differences in clinical data across subtypes in the context of MDD and ADHD comorbidity. Another limitation is that the data used in the study came from a single center.

In summary, the high comorbidity rates of MDD and ADHD, and the earlier onset age for MDD appear to be clinically significant. Based on this, clinicians should have a better understanding of ADHD in adults diagnosed with MDD, be familiar with the clinical characteristics of ADHD, facilitate accurate diagnosis, and implement appropriate interventions that can improve disease management and reduce negative impacts. Screening for ADHD may be included as part of the initial assessment of individuals with MDD. Future comparative studies focusing on anxiety disorders could provide additional information on the prevalence of ADHD in these disorders and whether it affects the treatment process for clinicians.

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