

Attention Deficit Hyperactivity Disorder and Psychiatric Comorbidities

Mengühan Araz Altay, Işık Görker, Begüm Demirci Şipka, Leyla Bozatlı, Tuğçe Atas

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AUTHORS / YAZARLAR

Mengühan Araz Altay
(Corresponding Author)

menguhanarazaltay@gmail.com

Department of Child and
Adolescent Psychiatry,
Trakya University School of
Medicine, Edirne, Turkey
ORCID iD:
0000-0001-9433-050X

Işık Görker

Department of Child and
Adolescent Psychiatry,
Trakya University School of
Medicine, Edirne, Turkey
ORCID iD:
0000-0003-0859-4221

Begüm Demirci Şipka

Department of Child and
Adolescent Psychiatry,
Trakya University School of
Medicine, Edirne, Turkey
ORCID iD:
0000-0001-7490-3366

Leyla Bozatlı

Department of Child and
Adolescent Psychiatry,
Trakya University School of
Medicine, Edirne, Turkey
ORCID iD:
0000-0002-4701-4835

Tuğçe Atas

Department of Child and
Adolescent Psychiatry,
Trakya University School of
Medicine, Edirne, Turkey
ORCID iD:
0000-0003-3642-8079

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ABSTRACT

Aim: This study aims to obtain current information on the clinical features of attention deficit hyperactivity disorder cases, comorbid psychiatric disorders and psychiatric drug use.

Methods: All patients between the ages of 6 and 18 years who were admitted to our outpatient clinic and diagnosed with attention deficit hyperactivity disorder were included in the study. The files of the patients were examined and their demographic characteristics, symptoms, psychiatric diagnoses and drug profiles were recorded. The pattern of the psychiatric disorders accompanied by attention deficit hyperactivity disorder cases and the differences according to age and gender were analyzed. The differences were determined in patients with psychiatric comorbidity compared to those without.

Result: The mean age of the 777 patients included in the study was 11.1±2.94 and 76.6% were boys. 60.9% of attention deficit hyperactivity disorder patients had comorbid psychiatric disorders. The most common psychiatric comorbidities were specific learning disability (23.6%), oppositional defiant disorder (12.9%) and conduct disorder (12.1%). There was no difference between the genders in terms of the incidence of psychiatric comorbidities. The rate of psychiatric comorbidity was significantly higher in adolescents than in children. A psychotropic medication was used in 86.4% of the cases and psychotropic polypharmacy was present in 31.5%. The rate of polypharmacy was significantly higher in the group with psychiatric comorbidity.

Conclusion: Attention deficit hyperactivity disorder is frequently accompanied by other psychiatric disorders and the psychiatric comorbidity leads to a more complicated clinical profile. Approximately one-third of attention deficit hyperactivity disorder patients have psychiatric polypharmacy and these patients should be carefully monitored. Primary care physicians who are frequently confronted with attention deficit hyperactivity disorder cases should be careful about psychiatric comorbidities.

Keywords: Child psychiatry, attention deficit hyperactivity disorder, mental disorders, Family practice

Dikkat Eksikliği Hiperaktivite Bozukluğu ve Psikiyatrik Eştanılar

ÖZ

Amaç: Bu çalışmamızda amacımız dikkat eksikliği hiperaktivite bozukluğu olgularının klinik özellikleri, eşlik eden psikiyatrik bozukluklar ve psikiyatrik ilaç tedavisi kullanımlarıyla ilgili güncel bilgiler elde etmektir.

Yöntem: Bir yıllık süre boyunca polikliniğimize başvurup dikkat eksikliği hiperaktivite bozukluğu tanısı konulan 6-18 yaş arasında tüm olgular çalışmaya alındı. Hastaların dosyaları incelenmiş, demografik özellikler, başvuru yakınmaları, psikiyatrik tanıları, başlanılan psikotropik ilaç profili kaydedilmiştir. Dikkat eksikliği hiperaktivite bozukluğu olgularına eşlik eden psikiyatrik bozuklukların paterni, yaş ve cinsiyete göre farklılıkları analiz edildi. Psikiyatrik eştanı olanlarda olmayanlara göre farklılıkları belirlendi.

Bulgular: Çalışmaya alınan 777 olgunun yaş ortalaması 11,1±2,94 olup %76,6'sı erkekti. Dikkat eksikliği hiperaktivite bozukluğu olgularının %60,9'una eşlik eden psikiyatrik bozukluk saptandı. En sık saptanan psikiyatrik eştanılar özgül öğrenme bozukluğu (%23,6), karşıt olma karşı gelme bozukluğu (%12,9) ve davranım bozukluğuydu (%12,1). Psikiyatrik eştanıların görülme sıklıkları açısından cinsiyetler arası fark izlenmedi. Ergenlerde çocuklara göre psikiyatrik eştanı oranı anlamlı olarak daha yüksekti. Olguların %86,4'ünde psikiyatrik ilaç kullanılmakta olup %31,5'inde psikiyatrik polifarmasi mevcuttu. Psikiyatrik eştanı olan grupta polifarmasi oranı anlamlı olarak yüksek bulundu.

Sonuç: Dikkat eksikliği hiperaktivite bozukluğu, sıklıkla diğer psikiyatrik bozuklukların eşlik etmekte olup, psikiyatrik eştanı daha kompleks klinik tabloya yol açmaktadır. Dikkat eksikliği hiperaktivite bozukluğu bulunan olguların yaklaşık üçte birinde psikiyatrik polifarmasi olup bu olguların dikkatle takip edilmesi gerekir. Dikkat eksikliği hiperaktivite bozukluğuna sıklıkla diğer psikiyatrik bozuklukları eşlik etmekte olup, psikiyatrik eştanı daha kompleks klinik tabloya yol açmaktadır.

Anahtar kelimeler: Çocuk Psikiyatrisi, dikkat eksikliği hiperaktivite bozukluğu, mental hastalıklar, Aile Hekimliği

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Introduction

In recent years, there has been a significant increase in the diagnosis rates of psychiatric disorders and psychiatric drug treatment in children and adolescents (1,2). In developing countries, the incidence of psychiatric disorders in children and adolescents has been reported to be between 7-35% (4,5). Attention deficit and hyperactivity disorder (ADHD) has an important place among these psychiatric diseases. In the large-scale multicenter study conducted in our country, ADHD was the most commonly diagnosed psychiatric disorder in children and adolescents (6). ADHD is a disorder in which symptoms such as inattention, inability to focus, excessive movement and impulsivity are observed which adversely affect the individual's academic, work and social functioning (7).

ADHD is one of the most prevalent psychiatric disorder in children and adolescents in our country and the world (1-3). The prevalence of ADHD in Diagnostic and Statistical Manual of Mental Disorders (DSM-5) was reported to be 5% in children and adolescents (8). The prevalence of ADHD in our country was found to be 8.1% in a study conducted in 2004, 12.7% in a study conducted in 2014 and 12.4% in a study conducted in 2018 (6,9,10). The changes in diagnostic criteria and public awareness works have played an important role in increasing the incidence of ADHD in recent years.

Many views have been put forward regarding the etiology of ADHD. Studies have shown that this disorder has a genetic basis (11). The relative risk was found to be 5-9 times higher in children having a first-degree relative with ADHD (12). In addition, there are many recent evidence that perinatal factors, toxins, dietary characteristics, psychosocial factors, neurodevelopmental disorders and inflammation may play a role (13-15). It is known that ADHD starts in childhood, continues in adulthood and the risk of familial transmission is higher in those who have ongoing ADHD in adulthood (8). ADHD has also been shown to be associated with other organic disorders (15,16). ADHD can affect the functioning of individuals in childhood and adulthood. In addition,

the association of ADHD with many psychiatric disorders has been reported (17).

This study aims to obtain current information on the clinical features, comorbid psychiatric disorders and psychiatric drug use of ADHD cases whose incidence has increased in recent years. The obtained data will inform all clinicians, especially primary care physicians, pediatricians and child and adolescent psychiatrists, about the current clinical pattern of ADHD.

Methods

The study was conducted in Trakya University Medical Faculty of Child and Adolescent Psychiatry which has the highest volume of patients in the Trakya region of Turkey. The study was a retrospective and cross-sectional study in which all patients aged 6-18 years who were admitted to the Child and Adolescent Psychiatry Outpatient Clinic between October 1, 2018 and October 1, 2019 were included. A total of 777 patients diagnosed with ADHD between these dates were included in the study. The files of all patients were examined in detail and demographic characteristics, admission symptoms, psychiatric diagnoses made according to the criteria of DSM-5 and psychotropic drug profile were recorded. Study protocol was approved by Trakya University Scientific Research Ethics Committee with TUTF-BAEK 2019/376 numbered decision.

Analyses were performed using Statistical Package for Social Sciences software, version 17.0 (SPSS; IBM, Armonk, New York, USA). Whether or not the distributions of continuous variables were normal was determined by the Kolmogorov–Smirnov test. Continuous variables with normal distribution were expressed as mean \pm SD and compared using one-way analysis of variance. Number of cases and percentages were used for categorical data. Mean differences between groups were compared by Student's t-test, whereas the Mann–Whitney U test was applied for comparisons of the not normally distributed data. Categorical variables were expressed as numbers and percentages and Pearson's chi-square or Fisher's exact tests were used to evaluate the

differences. Statistical significance was accepted as $p < 0.05$.

Results

The mean age of 777 patients between the ages of 6-18 was 11.1 ± 2.94 and 76.6% were boys. The most frequent symptoms of the patients admitted to the child and adolescent outpatient clinic were inattention (39.3%), hyperactivity (37.5%), irritability (12.4%) and poorer school performance (10.4%). Inattention rates were similar in both genders, while hyperactivity (40.8% vs. 26.4%, $p=0.01$) and irritability (13.6% vs. 8.2%, $p=0.045$) were higher in boys; and poorer school performance rate (14.8% vs. 9.1%, $p=0.037$) was higher in girls.

ADHD subtypes were examined, 62.3% of them were combined type, 32.0% were predominantly inattentive type and 5.7% were predominantly

hyperactive and impulsive type.

In 60.9% of the cases, psychiatric disorder accompanying ADHD was diagnosed. There was no additional psychiatric disorder in 39.1% of the cases, while 48.8% had one, 10.6% had two, 1.5% had three or more psychiatric disorders. The most common psychiatric comorbidities diagnosed in ADHD cases were specific learning disability (SLD) (23.6%), oppositional defiant disorder (ODD) (12.9%), and conduct disorder (12.1%). 61.0% of boys and 60.4% of girls had psychiatric comorbidity and no difference was observed between genders in terms of comorbidity frequency ($p=0.93$). The distribution of psychiatric disorders by gender was examined, SLD was the most common comorbidity in both genders. There was no statistically significant difference between the genders in terms of the incidence of psychiatric disorders accompanying ADHD cases (Table 1).

Table 1. Distribution of psychiatric comorbidity accompanying ADHD by gender

DSM-5 Disorders	Total (n=777)	Male (n=595)	Female (n=182)	p
Specific learning disorder, n(%)	186 (23.6)	134 (22.5)	52 (28.6)	0.11
Oppositional defiant disorder, n(%)	100 (12.9)	81 (13.6)	19 (10.4)	0.31
Conduct disorder, n(%)	94 (12.1)	75 (12.6)	19 (8.1)	0.51
Intellectual disability, n(%)	70 (9.0)	49 (8.2)	21 (11.5)	0.18
Autism Spectrum Disorder, n(%)	28 (4.7)	3 (1.6)	19 (2.5)	0.082
Anxiety disorder, n(%)	20 (2.6)	14 (2.4)	6 (3.3)	0.54
Motor disorders, n(%)	19 (2.4)	17 (2.9)	2 (1.1)	0.27
Elimination disorders, n(%)	17 (2.2)	15 (2.5)	2 (1.1)	0.38
Sleep-Wake disorders, n(%)	9 (1.2)	5 (0.8)	4 (2.2)	0.22
Depressive Disorders, n(%)	9 (1.2)	5 (0.8)	4 (2.2)	0.22
Communication disorders, n(%)	8 (1.0)	7 (1.2)	1 (0.5)	0.2
Obsessive-compulsive and related disorders, n(%)	5 (0.6)	4 (0.7)	1 (0.5)	0.94
Impulse control disorder, n(%)	3 (0.4)	1 (0.2)	2 (1.1)	0.13

In order to determine the relationship between psychiatric disorders accompanying ADHD with age, the patients were grouped as < 12 years (children) ($n=466$) and $12 \geq$ years (adolescents) ($n=311$) and then compared. 57.9% of the children and 65.3% of the adolescents had psychiatric comorbidity and the rate of psychiatric disorders accompanying ADHD was

significantly higher in adolescents ($p=0.043$). Elimination disorders were significantly higher in children, while conduct and anxiety disorders were significantly higher in adolescents and there was no significant difference in terms of other psychiatric disorders (Table 2).

Table 2. Distribution of psychiatric comorbidity accompanying ADHD by children and adolescents

DSM-5 Disorders	Children (n=466)	Adolescents (n=311)	p
Specific learning disorder, n(%)	113 (24.2)	73 (23.5)	0.86
Oppositional defiant disorder, n(%)	71 (15.2)	29 (9.3)	0.096
Conduct disorder, n(%)	39 (8.4)	55 (17.7)	<0.001
Mental retardation, n(%)	35 (7.5)	35 (11.3)	0.18
Autism Spectrum Disorder, n(%)	19 (4.1)	12 (3.9)	0.88
Elimination disorders, n(%)	14 (3.0)	3 (1.0)	0.044
Motor disorders, n(%)	9 (1.9)	10 (1.1)	0.27
Communication disorders, n(%)	6 (1.3)	2 (0.6)	0.48
Anxiety disorder, n(%)	5 (1.1)	15 (4.8)	0.002
Sleep-Wake disorders, n(%)	5 (1.1)	4 (1.3)	0.78
Bipolar disorders, n(%)	4 (0.3)	4 (0.5)	0.48
Depressive Disorders, n(%)	3 (0.6)	6 (3.2)	0.34
Impulse control disorder, n(%)	0 (0.0)	3 (1.0)	0.064
Obsessive-compulsive and related disorders, n(%)	1 (0.2)	4 (1.3)	0.087

The psychotropic drug use of ADHD cases was evaluated; 13.6% of the patients did not use any psychotropic drugs, while 54.6% were using single drug, 23.6% were using two drugs, 7.9% were using three or more drugs. The rate of polypharmacy expressing the use of two or more drugs was 31.5%. The most commonly used drugs were determined as long-acting psychostimulants (57.7%), atomoxetine (22.5%), and short-acting psychostimulants (13.8%) (Table 3).

Table 3. Distribution of psychotropic medications in the study population (n=777)

Drugs	n	%
Long acting psychostimulants	448	57.7
Short acting psychostimulants	107	13.8
Atomoxetine	175	22.5
Antidepressants	27	3.3
Antipsychotics	20	2.6
Antihistaminics	5	0.6

ADHD patients with and without psychiatric disorder were compared, there was no significant difference between the groups in terms of age, gender and ADHD subtypes. In the comorbid group, comorbid neurological disorder, polypharmacy, the number of hospital admissions within 1 year and the number of drugs used were found significantly higher than those without psychiatric comorbidity (Table 4).

Table 4. Clinical characteristics of patients with and without psychiatric comorbidity

Variables	With comorbidity (n=473)	Without comorbidity (n=304)	p
Age, years	11.0± 2.9	10.9± 2.8	0.84
Gender, male, n(%)	363 (76.7)	232 (76.3)	0.93
Admission number	5.7± 3.3	4.9± 2.5	0.001
ADHD combined type, n (%)	308 (65.1)	176 (57.9)	0.61
Neurological disorder, n(%)	25 (5.3)	7 (2.3)	0.04
Polypharmacy, n(%)	195 (41.2)	51 (16.8)	<0.001
Drug number	1.4± 0.9	1.0± 30.6	0.001

Discussion

Our study reveals the current clinical features, comorbid psychiatric disorders and the pattern of psychotropic drug use of ADHD diagnosed children and adolescents who were admitted to child and adolescent psychiatry clinics in Turkey. In the literature, the diagnosis of ADHD has been reported to be more common in boys. The boy-girl ratio has been reported to be 2:1 in some studies and 3-4:1 in other studies (8,18). In our study, it was observed that ADHD was seen 3 times more in boys than in girls in Turkey, similar to the literature. Girls showed predominantly attention deficit in the literature; however, distraction was similar in both genders in our study. Poorer school performance was more prominent

in girls, while hyperactivity and irritability were more prominent in boys (8). Therefore, ADHD should be considered especially for girls with poorer school performance. In our study, similar to previous studies, the combined type of ADHD was identified as the most common ADHD subtype (10,19).

Other psychiatric disorders are likely to accompany a significant proportion of children admitted to the clinic with the ADHD diagnosis and this increases the severity of the clinical profile and potentiates the social communication deficiency of children (20). The psychiatric disorders associated with ADHD vary widely according to the study design and the countries in which the study was conducted. The comorbidity rate was found to be 52% in the Danish cohort where 14,825 patients were analyzed, while it was 73% in the Iranian cohort (17,21). In three studies conducted in our country, comorbidity rates of 60%, 73.7% and 96.7% have been reported, which are quite different from each other (22-24). In these previous studies, the number of cases with ADHD was low which may have affected the results. In another study with a higher number of cases compared to these studies, the comorbidity rate was found to be 56.3% (19). In our study which shows the current trend with a high number of cases, the rate of psychiatric disorder accompanying ADHD in our country is 60.9% and it is similar to the world literature. The rate of two and more psychiatric disorders accompanying ADHD have been reported in the literature between 26-67% and found to be less in our study (23,24). Considering this result and the comorbidity rates reported in the previous years in our country, our study suggests that ADHD awareness and admission of uncomplicated cases at an early stage have been increased in our country.

In a large nationwide study by Jensen et al. (25), the most common comorbid psychiatric disorder in ADHD cases was found to be conduct disorder. The authors found neuropsychiatric disorders in boys and internalization disorders in girls more frequently. In many other studies, ODD has been reported as the most comorbid psychiatric disorder accompanying ADHD (26-29). In previous studies in our country,

destructive conduct disorder and ODD and anxiety disorders were found to be the most common comorbid disorders. In some of these studies, destructive conduct disorders were found to be predominant in boys, while in others, the frequency of psychiatric diagnoses did not differ between genders (10,19,23,24). Although ODD and conduct disorder are the most frequent diagnoses in our study, the most prominent result in our study is that SLD is also the most frequent comorbidity different from other studies. Studies on SLD have different rates in the literature due to differences in diagnostic criteria and the prevalence of SLD has been reported at a rate of 5-15% (8,30). It is thought that there is an increase in the diagnosis of SLD after changing DSM-5 SLD diagnostic criteria. SLD and ADHD are highly comorbid psychiatric disorders (31). There is even evidence that these two disorders are based on a common genetic basis (32). It has been reported that SLD cases are accompanied by ADHD at a rate of 10-90% and ADHD cases are accompanied by SLD at a rate of 7-92% (2,33,34). This result of our study suggests that in our society, when attention deficit is accompanied by learning disability, the clinic gets more important and specialists are consulted.

Psychotropic polypharmacy was detected in approximately one-third of children and adolescents with ADHD in our study. Cases using polypharmacy were significantly higher in the psychiatric comorbidity group, indicating that this group has complicated cases with difficulty in treatment. More frequent neurological disorders in the group with psychiatric comorbidity and the high number of hospital admissions support this finding. Our study shows that the psychiatric comorbidity of ADHD cases complicates the clinic and complicates the treatment.

In ADHD cases, early admission increases the functionality of the person as well as reduces comorbidity, thus decreasing the rate of polypharmacy. Early diagnosis and treatment also reduce the incidence of ADHD symptoms in adults (35,36). In our study, the higher comorbidity rates of older adolescents compared to children support this information. Therefore, the results of our study

highlight the importance of early diagnosis in ADHD cases.

It was found that 48% of the 6.1 million physician visits of children and adolescents with a primary diagnosis of ADHD in the USA between 2012 and 2013 were performed by pediatricians, 36% by psychiatrists and 12% by family practitioners (37). Family physicians are the physicians who are in the neighborhood of individuals and members of their families or who are easy to reach, who will be admitted first and provide preventive health services and primary care diagnosis services (38). Therefore, family physicians are the primary health professionals that children and adolescents with ADHD will admit for a symptom related to ADHD or any reason, especially preventive health services. It is important that family physicians refer patients with ADHD symptoms and those with learning difficulties to the children and adolescent psychiatry. It is important in this respect that primary care physicians are subject to current education programs on ADHD and other mental disorders as suggested by previous studies (39). It should be known that ADHD is a disorder frequently

associated with other psychiatric disorders and cases should be handled in this respect. Psychotropic polypharmacy rates are high in children and adolescents with a psychiatric disease accompanying ADHD and it is important to monitor these cases for potential side effects.

The most important limitations of the study were the use of single-center data and its retrospective nature. The fact that the center where the study was conducted was a tertiary center is another limitation as it may have affected the results.

Conclusion

The results of our study show that ADHD is often accompanied by other psychiatric disorders, especially SLD, and psychiatric comorbidity leads to a more complicated clinical profile. Psychotropic polypharmacy is present in approximately one-third of ADHD patients and these patients should be followed carefully. Primary care physicians and pediatricians who are frequently confronted with ADHD should be aware of ADHD symptoms and psychiatric comorbidity.

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