Factors Associated with the Loss of Attention-Deficit Hyperactivity Disorder Diagnosis in Children

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ABSTRACT

Objective: Attention-deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood and is notable for its high persistence into adulthood. This study aimed to evaluate factors associated with the loss of an ADHD diagnosis in children.

Materials and Methods: Data from children diagnosed with ADHD who were evaluated at a university hospital between November 2017 and November 2022 were analyzed retrospectively. The study included 259 children with a persistent ADHD diagnosis and 117 children who lost the diagnosis during a 3–10 year follow-up period.

Results: No statistically significant associations were found between loss of ADHD diagnosis and gender, ADHD subtype, treatment discontinuation, ADHD treatment, use of additional psychiatric treatment, and treatment response, comorbidity, chronic disease status, and use of additional treatment. The diagnosis was lost in 17.54% of patients with a severe disorder according to the baseline Clinical Global Impression (CGI) – Severity scale, compared to 47.36% in those with moderate severity (p=0.023). Among patients who responded to ADHD treatment (CGI-Improvement ≤2), 42.85% lost the diagnosis, whereas only 24.15% of non-responders did so (p<0.001).

Conclusion: Disorder severity and treatment response were two factors associated with the loss of an ADHD diagnosis. Recognizing these factors may help clinicians better predict patient prognosis.

Keywords: ADHD, children, improvement, loss of diagnosis, persistence.

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by symptoms of inattention, impulsivity, and hyperactivity.[1] A recent meta-analysis reported its prevalence as 5.6% in adolescents and 7.6% in children aged 3–12 years.[2] ADHD can present with both overlapping and distinct symptoms across different age groups. Accidents, academic difficulties, peer problems, and risky behaviors are frequently observed from the preschool period through childhood, adolescence, and adulthood.[3–6] Early recognition of ADHD, the symptoms of which are associated with numerous adverse outcomes, is important. In this way, appropriate treatment and monitoring of ADHD and comorbid psychiatric disorders can help reduce potential problems.

Gul et al. The Loss of Attention-Deficit Hyperactivity Disorder in Children

J Clin Pract Res 2025;47(4):391–398

Studies in children, adolescents, and adults in both community and clinical populations have shown that ADHD is highly persistent. Many factors have been identified as predictors of ADHD persistence in these studies. In one community sample, ADHD symptoms were assessed through parent interviews four times a year for six years; seven attention deficit symptoms persisted from childhood into adolescence, while eight hyperactivity symptoms decreased by more than 50%.[7] In another study, symptoms persisted in 85% of boys with ADHD who were followed for four years, while 15% showed remission (half during childhood and half during adolescence). Comorbidities such as conduct disorder, anxiety disorders, and mood disorders, as well as the familial nature of ADHD and psychosocial adversities, were found to be predictors of persistence.[8] In a study with a follow-up period of 2–16 years, 30% of children with ADHD showed complete remission, but symptoms recurred in the majority (60%). A total of 9.1% of participants showed sustained improvement until the end of the study, and 10.8% showed persistence.[9] In another study, boys aged 6–17 years with ADHD were followed for 11 years, and it was observed that the symptoms persisted in 78% of them. Psychiatric comorbidity, severe ADHD-related impairment, and maternal psychopathology were identified as predictors of ADHD persistence in these patients.[10] The persistence of ADHD at age 25 was 15%, but increased to 65% when partial responders were included.[11] Adults with a mean age of 34.1 years were followed for seven years, and it was found that ADHD persisted in 66%; predictors of persistence were baseline ADHD symptom count and comorbid oppositional defiant disorder and social phobia.[12] In a meta-analysis, ADHD severity, ADHD treatment, comorbid depressive disorder, and comorbid conduct disorder were found to be predictors of the persistence of childhood ADHD into adulthood.[13] Childhood ADHD severity and comorbid conduct disorder were the most important predictors of negative outcomes in adulthood.[14] In a study in which youth with childhood ADHD were re-evaluated after six years, those with persistent ADHD had lower IQ scores than those whose ADHD had remitted.[15]

The common feature of all these studies is that they investigated factors predicting ADHD persistence. To the best of our knowledge, no study has evaluated the prognosis of any neurodevelopmental disorder, other than autism spectrum disorder (ASD), from the perspective of losing the diagnosis.[16] Therefore, the aim of this retrospective study was to investigate the rate of loss of diagnosis and the factors associated with the loss of ADHD diagnosis in children admitted to a university hospital over a five-year period. We hypothesized that the majority of patients would retain their diagnosis during the follow-up period. We also hypothesized that the severity of ADHD, treatment response, comorbidity, and medication use for this condition would be associated with the loss of diagnosis.

KEY MESSAGES

- 68.9% of the patients continued to meet the diagnostic criteria for attention-deficit hyperactivity disorder.
- A statistically significant association was found between disorder severity and loss of diagnosis.
- Response to ADHD treatment was also associated with loss of diagnosis.

MATERIALS AND METHODS

Participants and Study Center

Data from children with ADHD admitted to a university hospital in Türkiye between November 2017 and November 2022 were analyzed retrospectively. In our department, ADHD is diagnosed according to Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 criteria. Conners' Teacher Rating Scale, Conners' Parent Rating Scale and Atilla Turgay DSM-IV Based Child and Adolescent Disruptive Behaviour Disorders Rating Scale, and sometimes neuropsychological tests are used to support the clinical assessment. Patients' symptoms are also monitored with these scales. To further support clinical evaluation, IQ levels are assessed using the Wechsler Intelligence Scale for Children-Revised (WISC-R). Comorbidities are determined according to DSM-5 diagnostic criteria.

Inclusion and Exclusion Criteria

Data from 427 children with ADHD were included in the study. Forty-six patients who had already been diagnosed with ASD were excluded. Five patients were excluded due to missing data. The follow-up period ranged from 3 to 10 years. At their last follow-up, the patients' ages ranged from 8 to 18 years.

Procedure

Severity of the disorder and treatment response were assessed using the Clinical Global Impression (CGI) Scale. The following variables were recorded: gender, ADHD subtype, initial ADHD severity according to the CGI-Severity scale, initial ADHD treatment and treatment response (CGI-Improvement ≤2) for that medication, treatment interruption period, comorbidities and medications used for these conditions along with treatment response, chronic illnesses, and their treatments. Ethical approval for this study was obtained from the Ethics Committee of Erciyes University (2022/822). All procedures were conducted in accordance with the ethical standards outlined in the Declaration of Helsinki.

J Clin Pract Res 2025;47(4):391–398

Gul et al. The Loss of Attention-Deficit Hyperactivity Disorder in Children

Measures

Atilla Turgay DSM-IV-Based Child and Adolescent Disruptive Behavior Disorders Rating Scale

This 41-item scale, developed by Turgay, is completed by parents and teachers. It evaluates the presence of ADHD (18 items), conduct disorder (15 items), and oppositional defiant disorder (8 items) according to DSM-IV diagnostic criteria.[17] The Turkish translation and adaptation were performed by Ercan et al.[18]

Conners' Parent Rating Scale-48

This 4-point Likert-type scale, consisting of 48 items, includes subtests assessing learning problems, conduct problems, impulsive-hyperactive, psychosomatic, and anxiety symptoms.[19] The Turkish validity study was conducted by Dereboy et al.[20]

Conners' Teacher Rating Scale-28

This 28-item, 4-point Likert-type scale was developed to assess students' behavioral problems at school.[19] It has three subscales: Inattention, Hyperactivity, and Conduct Problems. The Turkish validity study was conducted by Dereboy et al.[20]

Clinical Global Impression (CGI) Scale

This three-dimensional scale was developed to assess the course of psychiatric disorders. It is used to evaluate the severity of the disorder, response to treatment, and severity of side effects.[21]

Wechsler Intelligence Scale for Children-Revised (WISC-R)

This test was developed to measure the intelligence of children aged 6–16 years. It provides three different scores: verbal intelligence, performance intelligence, and general intelligence.[22] The Turkish adaptation was performed by Savaşır and Şahin.[23]

Statistical Analysis

The IBM Statistical Program for the Social Sciences (IBM SPSS Statistics for Windows, Version 26.0; Armonk, NY: IBM Corp.) was used to analyze the data. Data are presented as number (n), percentage (%), mean, and standard deviation. The chi-square test was used to compare relationships between groups, and the Bonferroni correction was applied to reduce the risk of Type I error. The statistical significance level for all analyses was set at $p < 0.05$.

RESULTS

Seventy-nine percent of the patients were male and 21% were female. The mean age at the last examination was 12.07 ± 2.96 years. During the follow-up period, 259 patients (68.9%) continued to meet the diagnostic criteria for ADHD, while 117 patients lost the ADHD diagnosis according to clinical interviews and scale scores. Gender, duration of treatment interruption, subtypes, ADHD treatment, additional treatments, chronic illness status, and comorbidities are shown in Table 1.

A statistically significant difference was found between disorder severity and loss of diagnosis (Table 2). While 47.36% of patients with moderate disorder lost the ADHD diagnosis, the rate was 17.54% among patients with severe disorder. A statistically significant difference was also found between response to ADHD treatment and loss of diagnosis (Table 3). The diagnosis was lost in 42.85% of patients who responded to ADHD treatment, compared to 24.15% of non-responders. No statistically significant differences were found between loss of ADHD diagnosis and gender, subtype, treatment discontinuation, ADHD treatment, use of additional psychiatric treatments and treatment response, comorbidity, chronic illness status, and use of additional treatments ($p = 0.227$, $p = 0.920$, $p = 0.947$, $p = 0.780$, $p = 0.344$, $p = 0.582$, $p = 0.342$, $p = 0.149$, $p = 0.069$, respectively) (Table 1).

DISCUSSION

In this study, factors associated with the loss of ADHD diagnosis in children were investigated. The rate of loss of ADHD diagnosis was 31.1%, and the persistence rate was similar to that reported in other studies.[9,11,12] In the present study, a significant relationship was found between ADHD severity and loss of diagnosis. Previous studies on the predictive effect of disorder severity have focused more on diagnostic persistence. In a review, disorder severity was identified as one of the most important predictors of negative outcomes.[14] ADHD severity was also associated with diagnostic persistence in a meta-analysis evaluating predictors of ADHD persistence into adulthood.[13] Similarly, the presence of severe impairment in males was linked to persistence,[10] and baseline numbers of attention-deficit and hyperactivity symptoms predicted persistence in adults.[12] In a study following children diagnosed with ADHD between the ages of 4 and 6 until age 18, higher baseline levels of inattention and hyperactivity-impulsivity symptoms predicted higher levels of the same symptom dimensions later on. Additionally, higher baseline inattention symptoms predicted greater functional impairment.[24] Likewise, higher baseline ADHD-Rating Scale total scores predicted worse hyperactivity/impulsivity outcomes in children.[25] The dopamine-norepinephrine pathways, which are implicated in the etiology of ADHD and targeted by ADHD medications, may be more affected in severely ill patients. This could

Gul et al. The Loss of Attention-Deficit Hyperactivity Disorder in Children

J Clin Pract Res 2025;47(4):391–398

Table 1. Clinical characteristics of the patients and results of group comparisons

Variable	Diagnostic status				p
	Ongoing diagnosis		Lost diagnosis		
	n	%	n	%	
Gender					0.227
Male	209	80.69	88	75.21	
Female	50	19.30	29	24.78	
Subtypes					0.920
Inattentive	27	10.42	12	10.25	
Hyperactive-impulsive	19	7.33	10	8.54	
Combined	213	82.23	95	81.19	
Treatment discontinuation					0.947
No	123	47.49	56	47.86	
Yes	136	52.50	61	52.13	
Attention-deficit hyperactivity disorder medications					0.780
Methylphenidate	179	69.11	83	70.94	
Atomoxetine	67	25.86	30	25.64	
Combination of methylphenidate and atomoxetine	13	5.01	4	3.41	
Additional psychiatric treatment					0.344
Atypical antipsychotic	72	27.79	27	23.07	
Selective serotonin reuptake inhibitor	7	2.70	8	6.83	
Typical antipsychotic	4	1.54	2	1.70	
Combination of selective serotonin reuptake inhibitor and atypical antipsychotic	8	3.08	5	4.27	
None	168	64.86	75	64.10	
Additional psychiatric treatment response					0.582
Yes	43	47.25	22	52.38	
No	48	52.74	20	47.61	
Comorbidities					0.342
Mild mental retardation	56	21.62	21	17.94	
Conduct disorder	24	9.26	7	5.98	
Specific learning disorder	17	6.56	12	10.25	
Borderline intellectual functioning	22	8.49	8	6.83	
Enuresis	11	4.24	7	5.98	
Anxiety disorders	11	4.24	5	4.27	
Tic disorder	5	1.93	8	6.83	
Oppositional defiant disorder	6	2.31	2	1.70	
Adjustment disorder	6	2.31	4	3.41	
Communication disorders	4	1.54	1	0.85	
Obsessive-compulsive disorder	1	0.38	2	1.70	
Multiple comorbidities	14	5.40	9	7.69	
None	82	31.66	31	26.49	

Table 1 (cont). Clinical characteristics of the patients and results of group comparisons

Variable	Diagnostic status				p
	Ongoing diagnosis		Lost diagnosis		
	n	%	n	%	
Chronic illness					0.149
No	227	87.64	96	82.05	
Yes	32	12.35	21	17.94	
Additional treatment					0.069
No	244	94.20	104	88.88	
Yes	15	5.79	13	11.11	

n: Number.

Table 2. Comparison of diagnostic status by ADHD severity

	CGI-severity						p
	Moderate		Marked		Severe		
	n	%	n	%	n	%	
Ongoing	10	52.63[a]	202	67.33[a,b]	47	82.45[b]	0.023
Lost	9	47.36[a]	98	32.66[a,b]	10	17.54[b]	

ADHD: Attention-deficit hyperactivity disorder; CGI: Clinical Global Impression Scale; n: Number. Different superscript letters indicate statistically significant differences.

Table 3. Comparison of diagnostic status by treatment response

	CGI-I ≤2		CGI-I >2		p
	n	%	n	%	
Ongoing	80	57.14[a]	179	75.84[b]	<0.001
Lost	60	42.85[a]	57	24.15[b]	

CGI-I: Clinical Global Impression Scale – Improvement; n: Number. Different superscript letters indicate statistically significant differences.

reduce treatment response and, consequently, lower the likelihood of diagnosis loss. In the present study, treatment responders were more likely to lose the ADHD diagnosis: 42.85% treatment responders lost the diagnosis compared with 24.15% of non-responders. Similarly, in a previous study, children who responded to methylphenidate treatment at three weeks had lower ADHD-Rating Scale scores at three years compared to non-responders, with similar results observed at 12 weeks.[25] Failure to respond to initial ADHD treatment may be a factor that reduces the likelihood of losing the diagnosis, as it may require higher medication doses, more frequent medication changes, greater functional impairment, and longer follow-up. As mentioned above, the possible relationship between disorder severity and treatment response can also be considered a factor influencing the loss of diagnosis.

In our study, no significant difference was found between gender and loss of diagnosis. Two studies have reported that female gender is associated with poorer outcomes. Parent and interviewer Children's Global Assessment Scale scores of girls with ADHD at baseline were significantly lower in adolescence, indicating poor functioning.[24] Female gender also predicted worse outcomes at three years after the initiation of methylphenidate treatment.[25] These results may be due to the fact that predominant inattentive type of ADHD is more common in females, leading to later diagnosis and later initiation of treatment. However, a meta-analysis found that female gender was not a predictor of persistence into adulthood.[13]

Continuation of treatment in our study was defined as being followed for at least one year after drug initiation, and the rate of treatment interruption was 47.6%. In a large retrospective

Gul et al. The Loss of Attention-Deficit Hyperactivity Disorder in Children

J Clin Pract Res 2025;47(4):391–398

study using a population-based database, 65% of children and 47% of adolescents continued treatment within one year of initiation. At five-year follow-up, 30–40% of adolescents and adults, and 50–60% of children, were still receiving treatment in most countries.[26] In our study, no significant difference in loss of diagnosis was found between those who continued treatment and those who interrupted it. This shows that loss of diagnosis is not associated with treatment continuity. However, since the study period included the Coronavirus Disease 2019 (COVID-19) pandemic, the fact that some patients continued their medication through renewed medication reports without attending outpatient clinics may also have affected the results.

Comorbidities are known to worsen the prognosis of ADHD.[27] Comorbid psychiatric disorders, especially oppositional defiant disorder, conduct disorder, mood disorders, and social phobia, have been found to be associated with ADHD persistence.[8,10,12–14] Higher levels of anxiety, conduct, and oppositional symptoms at baseline have been shown to predict greater functional impairment.[24] In addition, having one or more comorbidities predicted worse hyperactivity/impulsivity outcome at three years of follow-up in children who used methylphenidate for 12 weeks.[25] In our study, no significant association was found between having a comorbidity, using additional psychotropic medications, treatment response to these medications, and loss of ADHD diagnosis. Although methylphenidate is known to be more effective than atomoxetine,[28,29] there was no significant difference between them in terms of loss of diagnosis. The lack of a relationship between these factors and loss of diagnosis suggests that the loss of ADHD diagnosis is more closely related to biological characteristics of ADHD, such as disorder severity and treatment response.

Limitations

This retrospective study had several limitations. First, the data were obtained from patient files. Semi-structured interviews were not conducted to determine diagnoses in all patients, and over this long period, evaluations were performed by different clinicians. The age of onset of the disorder was unknown, and the total duration of treatment was not included in the analysis. Furthermore, unlike in longitudinal studies, the sample did not consist solely of patients who were followed for a defined period. The present study had a long follow-up interval, and therefore standardization could not be achieved. In addition, the relationship between familial, educational, and sociodemographic factors and loss of diagnosis was not assessed. For these reasons, this study on losing ADHD diagnosis should be repeated with a longitudinal design and with a much larger sample and set of variables.

CONCLUSION

In this study, the severity of ADHD and response to treatment were found to be associated with the loss of ADHD diagnosis. ADHD is a highly persistent disorder, with symptoms continuing from childhood into adulthood. When comorbid psychiatric disorders are present, it can negatively affect academic success, school life, relationships, and work life. Understanding the individual and environmental factors that influence this disorder during the treatment period is important. Knowing the factors associated with losing the diagnosis can help predict a patient's prognosis. At the same time, by identifying patients at high risk for persistence early, follow-up visits can be scheduled more frequently for those requiring long-term monitoring, allowing the effectiveness of psychoeducation and medications to be assessed more often, thereby reducing functional impairment. Preventive measures and interventions targeting modifiable factors that negatively affect the likelihood of losing the diagnosis may also contribute to improved prognosis. The development of applications and measurement tools that can be used routinely in clinics worldwide will further assist clinicians in predicting the prognosis of ADHD in the future. However, it is clear that, to develop these methods effectively, numerous studies on predictive factors influencing prognosis are still needed.

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Gul et al. The Loss of Attention-Deficit Hyperactivity Disorder in Children

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