

# Prevalence of comorbidities in children with attention deficit/hyperactivity disorder: Measured and systematic review of care health studies

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## Abstract

**Background and objectives:** Children and adolescents with a diagnosis of attention deficit hyperactivity disorder demonstrate a developmental delay in emotional and social functions, sleep difficulties, enuresis, and/or paroxysms in electroencephalographic measurements. The purpose of the study is to know if there is an association between comorbidities and ADHD. The second objective was to compare the results with previous studies in different countries. **Material and methods:** Retrospective analysis of a clinical database (CDB) was conducted identifying 1049 Spanish children and adolescents diagnosed with ADHD according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) in the Department of Pediatrics of the Hospital Universitario Dr. Peset. **Results:** In the 297 CDB aged 6 - 16 years children included, the comorbidities were statistically significant. This medical conditions in Spanish children with ADHD coexist outside of Spain and are statistically significant in all aspects analyzed except in anxiety, Asperger's syndrome and enuresis. **Conclusions:** Our results support the association between comorbidities and ADHD. It is important for professionals to make sure that they identify different comorbidities during the diagnostic process as during the clinical follow-up. The article is recommended to teachers, therapists and health professionals, for adopting a proactive and intermodal team approach in the detection and treatment of comorbidities in children and youth.

**Key words:** Attention deficit hyperactivity disorder. Comorbidities. Detection. Diagnosis.

## Prevalencia de comorbilidades en niños con trastorno por déficit de atención/hiperactividad: revisión medida y sistemática de estudios de salud asistencial

## Resumen

**Antecedentes y objetivos:** Los niños y adolescentes con diagnóstico de Trastorno por Déficit de Atención/Hiperactividad (TDAH) presentan un retraso en el desarrollo de las funciones sociales y emocionales, dificultades para dormir, enuresis y/o paroxismos en las mediciones electroencefalográficas (EEG). El propósito del estudio es saber si existe una asociación entre las comorbilidades y el TDAH. El segundo objetivo fue comparar los resultados con estudios previos en diferentes

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países. **Método:** Se realizó un análisis retrospectivo de una base de datos de historias clínicas (CDB) que identificó a 1049 niños y adolescentes españoles diagnosticados con TDAH de acuerdo con el DSM-IV (Manual diagnóstico y estadístico de trastornos mentales) en el Departamento de Pediatría del Hospital Universitario Dr. Peset. **Resultados:** En las 297 CDB de niños con edades entre los 6 a 16 años, las comorbilidades fueron estadísticamente significativas. Estas condiciones médicas en niños españoles con TDAH coexisten fuera de España y han sido estadísticamente significativos en todos los aspectos analizados, excepto en ansiedad, síndrome de Asperger y enuresis. **Conclusiones:** Nuestros resultados apoyan la asociación entre comorbilidades y TDAH. Es importante que los profesionales se aseguren de identificar las diferentes comorbilidades durante el proceso de diagnóstico y durante el seguimiento clínico. El artículo se recomienda a maestros, terapeutas y profesionales de la salud para que adopten un enfoque de equipo proactivo e intermodal en la detección y tratamiento de comorbilidades en niños y jóvenes.

**Palabras clave:** Trastorno por déficit de atención/hiperactividad. TDAH. Comorbilidades. Detección. Diagnóstico.

## Introduction

Attention deficit hyperactivity disorder (ADHD) is the most commonly diagnosed neurodevelopmental disorder of childhood, and it is associated with social and academic difficulties and psychiatric comorbidities such as depression, anxiety, low self-esteem, and pervasive across settings can cause problems in the daily activities of a child as well as later in their adult life<sup>1</sup>. In addition, studies detected difficulties in behavioral regulation and emotional stability in children younger than 2 years of age who were later diagnosed diagnosis with ADHD<sup>2</sup>. ADHD during childhood is one of the most common causes of school failure and social problems. It is a disorder that can persist and manifest in adulthood in more than 60% of cases. Several studies have found that the quality of life in adolescents and in adults who were diagnosed with ADHD during their childhood is clearly related to the severity of comorbidities symptoms<sup>3</sup>. In studies with adults who have a residual form of this disorder, the research has found a higher frequency of behavioral abnormalities in labor activities and in family relationships, substance abuse, accidents, and crime<sup>4</sup>. Depression during childhood and adolescence also predicts negative outcomes in adulthood such as stressful life events, low social support, and low satisfaction with life<sup>5</sup>. Maternal depression and concurrent symptoms at 4-6 years of age predict which children with ADHD are at greatest risk for depression and/or suicidality as adolescents<sup>6</sup>. A diagnosis of both ADHD and depression is associated with the most significant deficiencies for either disorder than one alone. For example, young people with ADHD and depression have an increased risk of developing bipolar disorder and oppositional defiant disorder, and require much more intensive interventions compared to young people with ADHD but without depression<sup>5</sup>. Interventions for both diagnoses also report more psychosocial and family problems as well as higher levels of

stress<sup>7,8</sup>. Despite the impact of ADHD and depressive symptoms in young people, few studies have examined the underlying mechanisms which contribute to the emergence of these symptoms<sup>9</sup>. One promising mechanism is emotion regulation (ER), as the deficit in the ability of ER has been associated with young children with ADHD and with depressive symptoms. This point is primarily relevant for young people with ADHD symptoms as it emphasizes the role of effort in control – the deliberate modulation of emotional states, emotional regulation, and subsequent behaviors, which involve the ability to focus deliberately, divert attention, hyperactivity, and inhibit or activate an appropriate behavior<sup>10-12</sup>. Several studies suggest that young people with ADHD demonstrate an inability to continue a task when frustrated or they have an inability to seek help from their parents. In extreme levels, when they are solving more limited problems, they focus more on negative aspects of a task compared to healthy controls. Young people with ADHD also have difficulties identifying and processing negative emotions and high-stress exposure between childhood and young adulthood is strongly intertwined with a persistent course of ADHD and with comorbid problems taking the form of severe and persistent emotion dysregulation (irritability, extreme reactivity, and frustration) or elevated and increasing irritability, anxiety, and depression<sup>13,14</sup>. Longitudinal research has shown that the ADHD diagnosis persists into adulthood, participants manifest higher levels of impulsive emotions (defined by symptoms such as low tolerance to frustration, impatience, and irritability) compared to those who do not have ADHD as an adult. This situation contributes to deficits in family, peer, financial, and labor relationships<sup>15</sup>. When comparing subtypes, children with inattentive ADHD have a higher rate in eating disorders, anxiety, and depression than in those with hyperactive and/or combined ADHD. In this both hyperactive and combined ADHD, children often have social problems, as they take things that do not belong to them,

do not wait their turn, and act without considering before the feelings of others. Children with ADHD inattentive type, rather, tend to be socially isolated, self-absorbed, and most likely have an introverted behavior<sup>16</sup> (Diamond, 2005). ADHD without hyperactivity and ADHD with hyperactivity are two different disorders with different cognitive and behavioral profiles, different patterns of comorbidities, different responses to medication, and different underlying neurobiology<sup>16</sup> characteristics that become chronic and progressively worse (i.e., findings support the diagnosis of ADHD in younger children by demonstrating that the symptoms and associated impairment are likely to persist well into elementary school)<sup>17</sup>. It is unclear whether the features of anxiety and ADHD are possible to identify very early of age; for example, in one child, his emotional deregulation at 18 months of age was associated with symptoms of anxiety and ADHD at 3 years of age. The study could not confirm if the emotional deregulation at 18 months predicts the cooccurrence of anxiety and ADHD symptoms. This implies that the identification risk at 18 months is a clinical challenge. By identifying early, there is a risk of over-identification and treatment of preschool children who are not going to develop ADHD or anxiety in their immediate future<sup>18</sup>. However, longitudinal studies in school-age children found continuity of symptoms for anxiety and ADHD<sup>19,20</sup>. In children with ADHD with an anxiety disorder have more than 50% of them also oppositional defiant disorder or conduct disorder<sup>21</sup>.

The relationship between ADHD and sleep disorders is unclear. According to a categorical approach, specific sleep disorders are a common comorbidity in children with ADHD. Those with ADHD more often display hypopnea and/or apnea, movements in peripheral limbs during sleep, insomnia, and narcolepsy which could result in significant functional impairments that affect mood, attention, behavior, and ultimately school/work performance and quality of life<sup>22</sup>. Polysomnography shows an increased latency in sleep onset of families ADHD children report less maintenance and duration of sleep, resistance by the child at bedtime, difficulties in sleep onset, difficult in nocturnal breathing, enuresis, nocturnal awakenings, and difficulty in waking up in the morning and daytime sleepiness<sup>23</sup>. In another multicenter cross-sectional study in 12 Spanish hospitals, neurologists reported that sleep disorder affects less than a quarter of patients (24.5%) and up to 23% stated that the prevalence was < 10%, while between 58% and 92% of parents of patients attending consultations in pediatric neurology report that their children have some aspect disturbed in the sleep. Although most

neurologists appreciate the importance of diagnosis and treatment of sleep disorders in children with neurological disorders, it is often underestimated and therefore essential to include in ADHD evaluations as proper and early treatment would improve symptoms and the quality of life in patients and families<sup>24</sup>.

Moreover, many children with ADHD develop epilepsy. In one study of 23 patients with epilepsy, 19 of them had ADHD symptoms preceding the onset of seizures<sup>25</sup>. An epidemiological study showed that the risk of epilepsy is 2.5 times higher in children who have already developed symptoms of ADHD<sup>26</sup>. With regard to abnormal electroencephalographic (EEG) recordings outside epilepsy, a recent study found abnormal EEG readings in 19 of 50 children diagnosed with ADHD. The most abnormal results were in focal and generalized paroxysms of sharp waves in phase opposition and slow waves. The most frequent location of EEG abnormalities was in the temporal lobe (45%), although there were focal paroxysms in other lobes; 28% in the right temporal region, 17% in the left temporal region, and 22% in the left frontal lobe, followed by 11% in the left parietal region<sup>27</sup>.

In children's ADHD diagnosis, enuresis is a relatively new clinical aspect and is part of our ongoing effort to better understand comorbidities. Children with ADHD are more likely than their peers without ADHD to develop enuresis with a similar trend for encopresis and comorbid enuresis implying an immaturity in the developing nervous system of children who have this combination of problems<sup>28</sup>. Children with primary nocturnal enuresis (PNE) show a significant reduction in activity in the left posterior cerebellum compared to controls without PNE<sup>29</sup>. Similarly, functional magnetic resonance imaging (fMRI) demonstrated low activation in the right prefrontal cortex and increased activity in the left hemisphere during inhibition of motor response compared to controls without PNA, indicating abnormal network brain areas during response inhibition in children with PNE<sup>30</sup>.

Therefore, this study aims to characterize the diagnostic complexity of children and adolescents who receive a diagnosis of ADHD. These findings could be helpful to develop guidelines that reflect the needs of children with ADHD. We treat a review of the comorbidities in itself complex in the diagnosis of ADHD.

## Methods

### Participants

Retrospective analysis of a clinical database (CDB) was conducted identifying 1049 Spanish children and

**Table 1.** Total excluded and included

226 participants born since 1990 and 1998
379 participants without an interdisciplinary diagnosis
14 participants had ADS
47 participants had a neurological disease diagnosed as epilepsy, brain traumatic
9 participants had a genetic syndrome diagnosed as deletions
26 participants coming from national or international adoptions or born in Spain of foreign parents
39 participants had not neurophysiological studies (EEG, qEEG, and ERPs)
12 participants without approach less medical data
Total included
297 participants met the clinical criteria

ADS: autism spectrum disorder; EEG: electroencephalographic; qEEG: quantitative EEG; ERPs: event-related potentials.

adolescents diagnosed with ADHD according to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) in the Department of Pediatrics of the Hospital Universitario Dr. Peset. The comorbidities were diagnosed in the corresponding medical service (Pediatrics, Mental Health, Neurology). Personal and clinical data of patients were reviewed to determine those who met the clinical criteria previously established and described below. After eliminating patients who did not meet for the above, 297 CDB aged 6-16 years of children (79 females and 218 males; mean age, 09.10 years) diagnosed with ADHD were used for this study.

### Inclusion criteria

- Patients diagnosed with ADHD born in Spain from January 1999 to December 2009.
- Patients diagnosed with ADHD with intelligence quotient (IQ) of 80 or higher with Spanish parents.
- Patients diagnosed with ADHD who attended medical appointments.

### Exclusion criteria

- Patients diagnosed with ADHD born and raised from January 1999 to December 2009 in Spain with IQ below 80.
- Patients aged in or outside the range 6-15 years and 11 months adopted or born and raised in Spain of foreign parents

- Patients diagnosed with ADHD who not attended medical appointments.
- Patients diagnosed with ADHD who later acquired brain injury, surgery, and/or neurological diseases such as traumatic brain injury, epilepsy, and/or Gilles de la Tourette Syndrome (Table 1).

In the following table are described by the participants:

Medical data related to the child were recorded in a confidential database for exclusive use of the project. Data about diagnosis, treatments, personal circumstances, and about clinical evolution were collected according to the law 15/99 on protection of personal data.

### Statistical analysis

First, descriptive statistics as comorbidity prevalence of the different pathologies studies and their confidence interval 95% were calculated. The relationships between the categorical variables the prevalence of ADHD child's comorbidity with the ADHD child's without comorbidity were analyzed using the Chi-square test ( $p < 0.05$ ) by each comorbidity studied. Finally, a comparison of each comorbidity prevalence identify was also compared through the review of outside studies from other countries; it was analyzed using the Chi-square test ( $p < 0.05$ ). Statistical analyses were conducted using IBM SPSS Statistics 25.

### Results

Many children diagnosed with ADHD have comorbidities. In Spain, children and adolescents diagnosed with ADHD, the current study found that all potential comorbid conditions were statistically significant in the aspects analyzed ( $p \leq 0.001$ ) (Table 2). When examining outside studies, results on the presence or absence of conditions that coexist in children diagnosed with ADHD outside of Spain are statistically significant in all aspects analyzed ( $p \leq 0.001$ ), except in anxiety, and in Asperger's disease<sup>31</sup> and in female and male Enuresis<sup>32</sup> (Table 2a).

### Discussion

In this study in ADHD, 25% of patients showed social problems, 28% depression and/or anxiety, and 19% had difficulties in the maintenance of nighttime sleep. The results were associated with those obtained by Hoza<sup>12</sup>, Mellon<sup>28</sup>, and Sheerman<sup>32</sup> in United States of America, by Chou in China<sup>33</sup>, by Fonseca in Brazil<sup>34</sup>,

**Table 2.** Prevalence of comorbidities in children with attention deficit hyperactivity disorder for the sample (n = 297)

Variable	Frequency (n)	Prevalence (%)	Prevalence (95% CI)	Chi-square test (p)
Peer/dyadic relationship difficulties	74	25.00	20.18-30.31	≤ 0.001
Depression/anxiety	83	28.00	23.62-34.18	≤ 0.001
Anxiety	41	14.00	10.48-18.74	
Sleep disorders	56	18.90	15.87-25.31	≤ 0.001
Insomnia for lack of limits on family	7	2.35	1.25-5.44	≤ 0.001
Nocturnal enuresis	15	5.10	2.95-8.36	≤ 0.001
Snorer	3	1.01	0.26-3.17	≤ 0.001
Nighttime awakenings	11	3.70	1.95-6.71	≤ 0.001
Delay sleep onset syndrome	3	1.01	0.26-3.17	≤ 0.001
Restless leg syndrome	3	1.01	0.26-3.17	≤ 0.001
Bruxism	3	1.01	0.26-3.17	≤ 0.001
Catathrenia (night whimper)	4	1.70	0.43-3.64	≤ 0.001
Night terrors	2	0.70	0.11-2.67	≤ 0.001
Somniloquy	5	1.70	0.62-4.10	≤ 0.001
Epilepsy (EEG)	72	24.35	19.69-29.79	≤ 0.001
Primary nocturnal enuresis	10	3.37	1.72-6.29	
Female	2	0.67	0.11-2.67	
Male	8	2.70	1.25-5.44	0.055

ANOVA test: p &lt; 0.01. RF: relative frequency; %: proportion; 95% CI: Confidence Interval 95%; p: Fisher values; EEG: encephalogram.

**Table 2a.** Comorbidities in children with attention deficit hyperactivity disorder according to previous studies

Variable	Frequency (n)	Prevalence (%)	Prevalence (95% CI)	Chi-square test (p)	Previous studies
Peer/dyadic relationship difficulties	92	56.00	47.83-63.41	≤ 0.001	Hoza, 2005
Depression	10	6.70	3.59-12.82	0.029	Bauermeister, 2007
Depression	68	21.30	17.03-23.30	0.020	Silva, 2015
Anxiety	34	23.77	17.23-31.75	0.012	Bauermeister, 2007
Anxiety	169	52.60	47.34-58.54	≤ 0.001	Silva, 2015
Anxiety	12	11.90	6.55-20.20	0.665	Ogrim, 2012
Asperger syndrome (symptoms)	5	4.95	1.83-11.71	0.148	Ogrim, 2012
Sleep disorders	45	31.46	24.10-39.84	0.003	Bauermeister, 2007
Epilepsy 6-18 years old (EEG)	2843	15.63	15.10-16.17	≤ 0.001	Chou, 2013
Epilepsy 8-11 years old (EEG)	3	10.00	2.61-27.67	0.095	Fonseca, 2008
Primary nocturnal enuresis	100	9.00	7.25-10.63	0.044	Shreeram, 2009
Female	32	2.51	1.95-4.00	0.198	
Male	68	6.21	4.70-7.56	0.216	
Primary nocturnal enuresis	35	12.10	6.99-13.45	≤ 0.001	Mellon, 2013
Primary nocturnal enuresis	165	17.60	15.02-19.94	0.010	Joinson, 2007

ANOVA test: p &lt; 0.01 (11, 20, 8, 33, 34, 28, 35); p ≤ 0.05 (31, 32). RF: relative frequency; %: proportion; 95% CI: Confidence Interval 95%; p: Fisher values; EEG: electroencephalogram.



by Joinson in United Kingdom<sup>35</sup>, by Silva in Australia<sup>9</sup>, and by Bauermeister in Puerto Rico<sup>20</sup>.

Children with ADHD often have conflicts with adults and peers, and suffer from unpopularity, rejection by peers, and a lack of friendships, in part as a consequence of their ADHD symptoms. In summary, social relations are also one of the biggest problems in children with ADHD. Parents, teachers, and their own colleagues systematically report that those with ADHD can be aggressive, intrusive, disruptive, manipulative, and less able to communicate and socialize effectively<sup>11,13,36</sup>. Some studies reported little difference and related problems between genders<sup>20</sup>.

Parents with ADHD children compared with normative data reported more problems in terms of emotional-behavioral role function, behavior, mental health, and self-esteem. Children with multiple comorbidity disorders have poorer psychosocial health-related quality of life across a range of domains compared with children with none and one comorbid disorder<sup>4</sup>. In addition, compared to children who have no comorbidities, psychosocial health-related quality of life was significantly lower in children with comorbid oppositional defiant disorder or conduct disorder, but not in children with a comorbid learning disorder<sup>4</sup>. In summary, social relations are one of the biggest problems in children with ADHD.

Sleep disorders may also induce symptoms of ADHD and are believed to be the result of excessive daytime sleepiness. However, it may be difficult for the clinical professional to recognize differences between the comorbidity from one sleep disorder to similar symptoms in ADHD<sup>37,38</sup>. We found abnormal results in 24.35% of patients; therefore, the EEG is a valid study in the valuation process for test underlying or comorbid epilepsy in children with ADHD. Epilepsy and ADHD can affect social, educational, and emotional life. The association between ADHD and epilepsy is of great interest in many studies published recently because children with epilepsy have a significant risk in presenting ADHD, and often display deficits in the performance of working memory<sup>26,33,39</sup>. Studies have detected significant similarities between epilepsy and ADHD in males (citation). ADHD with or without epilepsy may share a common abnormal and underlying neurobiological cause<sup>40</sup>.

In our study, the PNE in children with ADHD was in 5.05%, we consider the increase of psychological problems reported by parents of children with enuresis compared to those children without enuresis, and the possible pathogenic etiological between ADHD and

incontinence according to neurophysiological and neuroimaging results<sup>30</sup>. However, enuresis is difficult to treat and show lower compliance. Given results in the treatment in incontinence are appreciated in the relevant clinical data regarding ADHD and enuresis, this appears to be a main comorbid condition that should be evaluated and specifically address in ADHD children<sup>40</sup>.

## Conclusions

The current study carried out a broad and comprehensive characterization of comorbidities in children and adolescents with ADHD in an effort to promote appropriate clinical decision making and reduced confusion. Detection and resolution of depressive symptoms, anxious symptoms, and/or difficulties in sleep in those diagnosed with ADHD may reduce emotional risk and morning fatigue. It is very important to detect these symptoms to decrease social and cognitive consequences. Finally, using EEG in this population provides greater assessment and diagnosis of complex developmental disorders such as ADHD.

## Study limitations

First, we recruited data about ADHD comorbidities from different medical specialties departments at the hospital. Our findings should be interpreted in light of limitations. Accordingly, we were unable to stratify symptoms according to high- and low-comorbidity. Second, we were not able to test whether comorbidities are unique to children with ADHD or are also observed in other disorders such as depression and learning delay. Future studies are needed about the relationship between comorbidities and ADHD.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that no patient data appear in this article.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

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