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# Original contribution

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## Development and health in the diagnosis of attention-deficit/hyperactivity disorder

Desarrollo y Salud en el diagnóstico en Trastorno por Déficit de Atención/Hiperactividad

### Abstract

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**Introduction:** The purpose of the study was to describe the health status in children diagnosed with Attention Deficit/Hyperactivity Disorder (ADHD), to know possible diseases and the clinical interdisciplinary intervention.

**Method:** This retrospective cohort study included 297 medical histories of patients from both genders diagnosed with ADHD (DSM IV) meeting the clinical criteria previously established in a public hospital of the Community of Valencia.

**Results:** The otorhinolaryngology, ophthalmology, and allergology results in children diagnosed with ADHD and those obtained by several previous studies were statistically significant, except in obesity at 16 years of age for Khalife, in diabetes mellitus and in asthma for Guerrero-Prado, and in asthma for Calam.

**Conclusions:** The general health difficulties for patients diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD) can be treated, and there is a significant correlation in the remission of symptoms after treatment. Finally, it will be interesting to develop further research on whether the optimization in the management of these processes influences or not the evolution of the ADHD-diagnosed child.

### Keywords

ADHD, Pediatric, ORL, OPD, ALG.

## Resumen

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**Introducción:** El propósito del estudio fue describir la salud en los niños con diagnóstico en Trastorno por Déficit de Atención/Hiperactividad (TDAH), conocer posibles enfermedades y su intervención clínica interdisciplinaria.

**Método:** Estudio cohorte retrospectivo de 297 historias clínicas (HC) de pacientes de ambos géneros con diagnóstico en Trastorno por Déficit de Atención/Hiperactividad (TDAH) en un Servicio de Pediatría en un hospital público de la Comunidad de Valencia.

**Resultados:** Los resultados en Otorrinolaringología (ORL), Oftalmología (OFT) y Alergología (ALG) en los niños diagnosticados TDAH y en los obtenidos por diversos estudios previos, fueron estadísticamente significativos, exceptuando en obesidad a los 16 años de edad por Khalife, en Diabetes Mellitus y en asma por Guerro-Prado y en asma por Calam.

**Conclusiones:** Las dificultades generales en la salud en los pacientes con diagnóstico en Trastorno por Déficit de Atención/Hiperactividad (TDAH) del estudio son atendidos por los demás servicios médicos del hospital (ORL, OFT, ALG) comprobándose una correlación significativa en la remisión de los síntomas luego de su tratamiento. Finalmente, será interesante desarrollar más investigaciones sobre si la optimización en el manejo de estos procesos influye o no en la evolución del niño con diagnóstico en TDAH.

### Palabras clave

TDAH, Pediatría, ORL, OFT, ALG.

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## Introduction

According to the epidemiological studies of the American Academy of Pediatrics, Attention-Deficit/Hyperactivity Disorder (ADHD) is the most frequently diagnosed neurobiological disorder in childhood and adolescence.<sup>1</sup> The scientific literature has studied the common pathologies at a pediatric age in ADHD and they confirm there has been an increase in recent decades in prevalence and burden of atopic diseases such as eczema, atopic dermatitis, rhinitis, and asthma accompanied by a global increase in diagnosis of ADHD.<sup>2-7</sup> One of the most studied medical conditions is allergy in ADHD.

A recent study conducted by the National Health Insurance Research Database (NHIRD) showed that pediatric patients with allergic disorders had a substantial increase in odds of developing ADHD. Eczema and asthma are diagnosed more frequently in children with ADHD than in children without diagnosis of ADHD—however, asthma does not represent a greater risk for ADHD.<sup>8</sup> Furthermore, ADHD-diagnosed children in the following consultations report: dysphonia and laryngeal nodules in the Otorhinolaryngology department,<sup>9</sup> hyperopia, myopia, strabismus, and amblyopia (“lazy eye”) in Ophthalmology,<sup>10,11</sup> headaches and febrile seizures in Neurology,<sup>10-14</sup> and in Pediatric Nephrology, nocturnal enuresis—which causes a great problem in emotional behavior.<sup>15-18</sup> Cardiology has reported the presence of congenital heart murmurs and heart disease,<sup>19</sup> and Endocrinology reports the existence of overweight and obesity in children and adolescents with ADHD, which, similarly to nocturnal enuresis, brings with it important affective consequences, and, if compounded by academic difficulties, results in an even more complex situation.<sup>20,21</sup>

High-quality interdisciplinary prospective research should continue to advance to better understand the mechanisms underlying these diseases and ADHD and to establish prevention and treatment strategies directed at ADHD.<sup>21</sup>

## Methods

During the first semester of 2015, one researcher made a cohort study of retrospective analysis of 1,049 clinical histories (CH) of children and adolescents diagnosed with ADHD according to the criteria of DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) in the Pediatric Service of the Dr. Peset University Hospital, selecting and analyzing the clinical data statistically. The search and statistical analysis of personal and clinical data of children diagnosed with ADHD who met the previously-established clinical criteria was performed. The profiles of the children with the CH included in the study did not present significant differences in terms of clinical, psychological, or social variables. Based on the homogeneity present in all participants, 297 CH were selected (79 girls and 218 boys) with Spanish nationality aged  $\geq 6$  to  $\leq 16$  years old (mean age in years: 09.10), meeting the established clinical criteria.

Description of the selection of the study subjects:

### Total excluded

226	Born between 1990 and 1998
379	Were not diagnosed in an interdisciplinary way
14	Presented ASD
47	Presented a previously-diagnosed neurological pathology = comorbid ADHD (e.g., epilepsy, TBI, CVA)
09	Presented diagnosed genetic syndromes (e.g., deletions)
26	Were adopted at the national or international level, in foster care and/or born in Spain from parents of foreign origin
39	Presented neurophysiological studies but were no longer patients of the Pediatric Service of the hospital
12	Inaccessible data

### TOTAL INCLUDED

N=297 met the clinical criteria

## Selection criteria

**Inclusion criteria:** 1- patients of either gender born with a diagnosis of ADHD, aged between  $\geq 6$  and  $\leq 16$  years old, with an IQ over 80, and born and raised in Spain by Spanish parents; 2- patients who met the requirements of the previous point and have attended pediatric check-ups correctly; 3- patients who met both previous requirements and who have complied with the pertinent medical indications.

**Exclusion criteria:** 1- patients of either gender diagnosed with ADHD aged  $\geq 6$  to  $\leq 16$  years old, born and raised in Spain by parents with IQ under 80 and/or illiteracy; 2- patients of either gender diagnosed with ADHD, aged between  $\geq 6$  and  $\leq 16$  years old, born in Spain but brought up abroad, or brought up by foreign parents, or adopted regardless of being reared inside or outside of Spain; 3- patients of either gender diagnosed with ADHD, aged  $\geq 6$  to  $\leq 16$  years old, with no attendance at pediatric check-ups, failure to comply with the pertinent medical indications, or diagnosed with ADHD after acquired brain damage, surgeries, and/or neurological disease.

The study was carried out without financial funding and was approved by the Ethics Committee for Clinical Research of the Dr. Peset University Hospital in the city of Valencia. The records related to the children were gathered in a confidential database, for the sole and exclusive use in the project. The data related to the diagnosis of each child, treatments, and personal circumstances, as well as those that refer to their evolution, were collected according to the Law 15/99 on Protection of Personal Data.

For the descriptive data, dispersion measures were used in order to evaluate the extent to which the data differed from each other by establishing frequencies (FR), percentages (%), and p value, to indicate the significant statistical level, considering  $>0.05$  not significant and  $\leq 0.001$  statistically significant. In bivariate analysis of the quantitative variables, Pearson's test ( $\chi^2$ ) was used.

## Results

**Development and general health history.** Regarding general health history in children diagnosed with ADHD, statistically significant results were obtained in all the types analyzed ( $p \leq 0.001$ ). **Table 1.**

In the general health history in children diagnosed with ADHD studied by the authors, the results are statistically significant in headaches/migraines ( $p \leq 0.001$ ) from Guerro-Prado,<sup>39</sup> Arruda,<sup>13</sup> and Genizi,<sup>14</sup> and from Khalife<sup>40</sup> in obesity/overweight, except for obesity at 16 years of age ( $p = 0.146$ ) which coincides with our total data, as well as with the data obtained by Guerro-Prado in asthma ( $p = 0.705$ ) and diabetes mellitus ( $p = 0.889$ ). **Table 1 (a).**

Otorhinolaryngology history. Regarding the ENT history in children diagnosed with ADHD, the results are statistically significant in all the clinical aspects analyzed ( $p \leq 0.001$ ). **Table 2.** Six pathologies have  $\chi^2$  values of  $p \leq 0.001$ .

In the ENT history of laryngeal nodules = dysphonia in children diagnosed with ADHD, the results of Barona-Lleo<sup>9</sup> are statistically significant with respect to the present study ( $p \leq 0.001$ ). **Table 2 (a).**

Ophthalmology history. Regarding the ophthalmology history of children diagnosed with ADHD, the results are statistically significant in all the clinical aspects analyzed ( $p \leq 0.001$ ) as well as among the five diagnoses ( $\chi^2 p = 0.003$ ). **Table 3.**

In the ophthalmology medical history of children diagnosed with ADHD studied by the authors, the results are statistically significant with the present study in all the clinical aspects analyzed ( $p \leq 0.001$ ). **Table 3 (a).**

Allergology history. In the allergology history of children diagnosed with ADHD, the results are statistically significant in all the clinical aspects analyzed ( $p \leq 0.001$ ). **Table 4.**

In the allergology history of children diagnosed with ADHD obtained by the authors, the results have been statistically significant in atopy ( $p = 0.002$ ) and

**Table 1.** Development and Health.

Variable	FR	%	IC 95%	p
Presents health history	127	42.76	37.09-48.61	
Deficits in motor development	37	12.46	9.02-16.88	<0.001
Bronchospasms in childhood	6	2.02	0.82-4.56	<0.001
Resp. insufficiency upper airways	31	10.43	7.30-14.62	<0.001
Febrile convulsions in childhood	4	1.34	0.42-3.64	<0.001
Primary nocturnal enuresis	15	5.05	2.95-8.36	<0.001
Pneumonia	4	1.34	0.42-3.64	<0.001
Cryptorchidism	4	1.34	0.11-2.67	<0.001
Juvenile idiopathic arthritis	1	0.33	0.01-2.15	<0.001
Childhood viral meningitis	1	0.33	0.01-2.15	<0.001
Headaches/Migraines	24	8.08	5.35-11.93	<0.001
Asthma	9	3.03	1.48-5.87	<0.001
Obesity/Overweight	6	2.02	0.82-4.56	<0.001
Diabetes Mellitus	2	0.67	0.11-2.67	<0.001

**Table 1a.** ADHD child's health according to previous studies.

Variable	FR	%	CI 95%	p	
Headaches/Migraines	2	0.5	0.08-1.86	<0.001	Guerro-Prado D. 2014*
Headaches/Migraines	21	19.80	22.26-46.44	0.003	Genizi J. 2013*
Headaches/Migraines	114	4.80	3.97-5.73	0.015	Arruda MA. 2010*
Asthma	11	2.68	1.35-4.67	0.705	Guerro-Prado D. 2014
Overweight at 8 y/o	916	13.20	10.63-12.01	<0.001	Khalife N. 2014*
Overweight at 16 y/o	288	4.10	3.16-3.98	0.073	
Obesity at 8 y/o	787	11.80	9.09-10.37	<0.001	
Obesity at 16 y/o	238	3.60	2.58-3.33	0.146	
Diabetes Mellitus	2	0.50	0.08-1.86	0.889	Guerro-Prado D. 2014

RF: Relative frequency. %: proportion, CI 95%: Confidence interval 95%, p: Fisher values \*39, 14, 13, 40.

**Table 2.** ENT History of the ADHD child.

Variable	FR	%	CI 95%	p
Presents history Total	77	26	21.11-31.37	
Tonsil/adenoidectomy	34	12.10	8.16-15.76	<0.001
Otitis 1/2	4	1.40	0.42-3.64	<0.001
Recurrent laryngitis	10	3.50	1.72-6.29	<0.001
Otitis ½ + recurrent laryngitis	2	0.70	0.11-2.67	<0.001
Sinusitis	1	0.30	0.01-2.15	<0.001
Laryngeal nodules = dysphonia	26	8.75	5.90-12.71	<0.001

**Table 2a.** ENT history of the ADHD child according to previous studies.

Variable	FR	%	CI 95%	p	
Laryngeal nodules = dysphonia	25	78.12	59.55-90.05	<0.001	Barona-Lleo L. 2015*

RF: relative frequency, %: proportion, CI 95%: Confidence interval 95%, p: Fisher values.

$\chi^2$ = Pearson's test \*9.

**Table 3.** Ophthalmology History of the ADHD child.

Variable	FR	%	CI 95%	p
Presents history Total	37	12.45	9.09-16.88	
Myopia	21	7.07	4.53-10.76	0.026
Astigmatism	4	1.40	0.42-3.64	<0.001
Strabismus	7	2.35	1.03-5.00	0.003
Hyperopia	3	1.01	0.26-3.17	<0.001
Astigmatism/Hyperopia	2	0.67	0.11-2.67	<0.001

**Table 3a.** Ophthalmology history of the ADHD child according to previous studies.

Variable	FR	%	CI 95%	p	
Myopia	22	43.00	29.62-57.67	<0.001	Mezer E. 2012*
Myopia	8	19.00	9.14-34.62	0.021	Grönlund MA. 2007*
Astigmatism	10	19.60	10.28-33.54	<0.001	Mezer E. 2012
Astigmatism	10	24.00	12.58-39.80	<0.001	Grönlund MA. 2007
Strabismus	3	5.88	1.53-17.22	<0.001	Mezer E. 2012
Strabismus	10	24.00	12.58-39.80	<0.001	Grönlund MA. 2007
Hyperopia	10	19.60	10.28-33.54	<0.001	Mezer E. 2012
Hyperopia	10	24.00	12.58-39.80	<0.001	Grönlund MA. 2007

RF: relative frequency, %: proportion, CI 95%: Confidence interval 95%, p: Fisher values.  
 $\chi^2$ = Pearson's test \*10, 11.

**Table 4.** Allergology History of the ADHD child.

Variable	FR	%	CI 95%	p
Presents history Total	48	16.16	12.26-20.95	
Atopy	23	7.74	5.07-11.54	<0.001
Asthma	6	2.02	0.82-4.56	<0.001
Rhinitis	7	2.36	1.03-5.00	<0.001
Inverse psoriasis	2	0.67	0.11-2.67	<0.001
Food allergy	6	2.02	0.82-4.56	<0.001
Various allergies*	3	1.01	0.26-3.17	<0.001

**Table 4a.** Allergology history of the ADHD child according to previous studies.

Variable	FR	%	CI 95%	p	
Atopy 3-10 years	73	15.08	12.07-18.65	0.002	Schmitt J. 2010*
Atopy	4	0.97	0.31-2.65	0.002	Guerro-Prado D. 2014*
Asthma	11	2.68	1.41-4.89	0.633	Guerro-Prado D. 2014
Asthma	13	9.28	2.80-8.60	<0.001	Biederman J. 1995*
Asthma	30	2.00	1.37-2.87	0.970	Calam R. 2005*
Asthma	5	0.22	0.08-0.54	0.007	Secnik K 2005

RF: relative frequency, %: proportion, CI 95%: Confidence interval 95%, p: Fisher values.  
\*8 Biederman J and Secnik K according to a review by Schmitt J, 2. \*animals/grasses/olives/mites.

in asthma by Biederman ( $p \leq 0.001$ ) and by Secnik ( $p = 0.007$ ), while the results in asthma by Guerro-Prado ( $p = 0.633$ ) and by Calam ( $p = 0.970$ ) correspond to those obtained in the present study. [Table 4 \(a\)](#).

## Discussion

The study highlights the conditions of psychophysical development and general health in children diagnosed with ADHD. A percentage of 12.46 observed difficulties in motor development was reported, which was clinically corroborated with the detection of limited fine and gross motor skills and a poor manual and exploratory game. During childhood, movement experiences are essential because they provide opportunities for learning and promoting the development of important everyday skills such as the correct use of cutlery, drawing, and playing with toys and games. The recognition of the importance of the evolution of motor competence for social and emotional development is also increasing due to the numerous studies that show a significant relationship between these domains.<sup>22</sup> In addition, the hypothesis arising is that psychosocial problems are secondary consequences of problems in motor development,<sup>23</sup> and these deficits tend to appear increasingly highlighted for the child through social demands and classmates in school years.<sup>24</sup> Problems in the social domain in children with motor difficulties have also been communicated by the parents, and the deficit in the level of skill is verified in the clinic.<sup>25</sup> Nowadays, if cognitive difficulties presented by children with ADHD are added to disability in sports and/or games, these can trigger emotional consequences. Therefore, it is vital to evaluate, guide, and encourage physical activity and/or playfulness, as they are essential to improve the motor skills, in general, and to develop positive emotions resulting from both activities, in particular.

Another health condition for children with ADHD is the presence of headaches in 8.08%. Although the prevalence of headaches in children with ADHD, as well as its association with the duration

and frequency of headaches are contradictory data, both create difficulties in concentration, hyperactivity, behavior, and in the family and/or school environment.<sup>26,27</sup> In summary, frequent headaches can increase distraction<sup>28</sup> and deteriorate school learning.<sup>13</sup>

Regarding 5.05% of primary nocturnal enuresis (PNE) in the clinical histories of the study, it represents a valid clinical datum within the anamnesis that should be evaluated considering the psychological problems reported by the parents of these children, compared to those who do not present enuresis.<sup>29</sup> A study with functional magnetic resonance imaging (fMRI) in working memory with children with PNE showed a significant reduction of activity in the left posterior cerebellum compared to controls.<sup>30</sup> Another fMRI study showed a low activation in the right prefrontal cortex and an increase in activity in the left hemisphere in children with PNE compared to healthy controls during the inhibition of motor response, indicating an abnormal network in these areas of the brain during the inhibition response in children with PNE.<sup>31</sup> In another investigation in children with PNE, they detected that the results in the latency measurements were prolonged or the amplitude was reduced in the parietal area (Pz) in the neurophysiological studies called Cognitive Evoked Potentials (p300)<sup>32,33</sup> providing evidence of deficit in the uniform maturation of cortical structures mainly in the motor cortex circuit.<sup>34</sup>

With regard to Otorhinolaryngology history, there is 10.43% of respiratory failure due to obstruction of the upper airways and 12.10% of tonsillectomy and/or adenoidectomy. This represents interesting data considering that a previous investigation reported a decrease in ADHD symptoms 2-13 months after surgery to remove tonsils and adenoids, suggesting that the improvement post-adenotonsillectomy indicates that the symptoms of ADHD are also related to sleep disturbances due to breathing difficulties.<sup>35</sup>

Regarding Ophthalmology history, 12.45% of the ADHD-diagnosed children have ocular convergence failure, a relevant result because it

shows that ocular deficits often accompany poor reading skills and poor school performance, both of which exist in the clinical histories of analyzed ADHD-diagnosed children. It has even been postulated that the treatment of an insufficient and/or underlying anomaly in ocular convergence could improve the functioning of children diagnosed with ADHD.<sup>11</sup> Although the range and spectrum of ocular alterations vary substantially between studies, their existence together with other neurological and behavioral difficulties may hinder the overall development of children with ADHD. Since ametropia and heterotropia can be easily treated to potentially improve the functioning of these children, it is advisable to perform an ophthalmological examination as part of the routine evaluation.<sup>10</sup>

Finally, 16.16% of allergic pathologies were reported in children with ADHD, 7.74% of which were characterized by the presence of atopies, diseases which, together with asthma, have been associated with ADHD, although their underlying mechanisms require greater clarification.<sup>7</sup> Eczema and asthma are diagnosed more frequently in children with ADHD than in children without ADHD, though asthma does not represent an increased risk for ADHD.<sup>8</sup> Recent studies have provided some possible explanations for the association between asthma and ADHD. First, inflammatory cytokines released during atopy can pass the blood-brain barrier<sup>36</sup> and activate neuro-immune mechanisms that involve the brain circuits of ADHD-related behavior and emotions.<sup>37</sup> Images in fMRI show that the anterior cingulate cortex and the insula are involved in the evaluation of sensory affective stimulation, in the regulation of homeostatic responses, and in visceral perception. In people with asthma and other stress-related conditions, these regions of the brain may be hypersensitive to the afferent emotional and physiological signals specific to the disease, which may contribute to the deregulation of peripheral processes, as occurs during atopic episodes.<sup>38</sup>

## Conclusions

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Regarding general health in children diagnosed with ADHD, the results are statistically significant by themselves as well as compared to the results obtained by Guerro-Prado in Spain, Genizi in Israel, Arruda in Brazil, and Khalife in Finland, the ENT results by Barona-Light in Spain, the Ophthalmological results by Mezer in Israel and Grönlund in Sweden, and the Allergy results from Schmitt in Germany, Biederman and Secnik in the USA, and Calam in the United Kingdom.

In short, the rapid detection of health problems in children diagnosed with ADHD after a successful pediatric examination and its subsequent referral to specialist clinicians (ENT, Ophthalmologist, Allergologist), not only represents the cure of the ailment or malaise, but also a positive change in the psychosocial behavior of the child in the school and family environment, aspects which are essential to correct in order to avoid aggravating the symptoms of ADHD. Finally, it will be interesting to develop more research on whether optimization in the management of these processes influences or not the evolution of the patient with ADHD.

### Conflicts of interest

The authors of the research state there are no conflicts of interest in this study.

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