

## Original article

# Screening for attention deficit hyperactivity disorder among a group of allergic school-aged children

**Background:** There are rising estimations for the prevalence of allergic diseases and attention deficit hyperactivity disorder (ADHD) among children. Both disorders have their impact on the quality of life. We sought to assess ADHD symptoms among a group of school-aged allergic children. **Patients and Methods:** A group of 120 children with physician diagnosed allergies and another 120 age and sex matched healthy children were enrolled. Patients were recruited from the Pediatric Allergy, Immunology and Rheumatology Unit, Children's Hospital, Ain Shams University, during the period from May 2022 to November 2022. Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria for ADHD, Conners scale and strengths and difficulties questionnaire (SDQ) were measured through valid translated questionnaire. Medical records were revised for the results of absolute eosinophil count (AEC), total IgE level and skin prick test (SPT) if available. **Results:** Patients included 77 (64.2%) males and 43 (35.8%) females with ages ranging from 6 to 12 years. Allergic diseases were distributed as follows: 50% with urticaria, 35% with allergic rhinitis/asthma and 35% with atopic dermatitis. Allergic patients had higher scores in SDQ subscales, total difficulties ( $p=0.001$ ), emotional problems ( $p=0.006$ ), conduct problems ( $p=0.007$ ), hyperactivity ( $p=0.001$ ) and conners' subscales oppositional ( $p=0.045$ ), inattentive ( $0.001$ ), hyperactive ( $p<0.001$ ), anxiety ( $p<0.001$ ), perfectionism ( $p<0.001$ ), psychosomatic aspects ( $p<0.001$ ), social problems, emotional liability ( $p<0.001$ ), conners' global index ( $p=0.007$ ) and total DSM-IV ( $p<0.001$ ) in comparison to controls. **Conclusion:** ADHD symptoms are more common among allergic children compared to healthy controls. Regular psychiatric assessment of the allergic children is recommended for early detection and management of possible behavioral changes. Further studies are warranted to investigate the impact of allergy medications and the control of allergic disease on ADHD symptoms.

**Key words:** ADHD, hyperactivity, Allergic, children, behavior, control

Salwa A. Abd Elhamid, Eman A. Abdel Aziz, Azza M. Youssef, Amira S. Mohamed\*, Ghada A. Shousha\*\*

Pediatric Developmental and Behavioral Unit, \*Pediatric Department, \*\*Pediatric Allergy, Immunology and Rheumatology Unit, Children's Hospital, Ain Shams University, Cairo, Egypt

### Correspondence:

Amira Said Mohamed  
Email: amirasaid700@gmail.com  
Phone: 01010206062

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## INTRODUCTION

Children frequently suffer from chronic allergy diseases, such as atopic dermatitis (AD), asthma, and allergic rhinitis (AR), and their frequency has significantly increased in the recent years. Allergic children's daily activities and sleep patterns may be negatively impacted by the symptoms, which can result in behavioral and mental health issues.<sup>1</sup> One of the most prevalent neuropsychiatric illnesses in children is ADHD. To be diagnosed with ADHD, a person must exhibit six or more symptoms of inattention, hyperactivity, and impulsivity over the course of at least six months with negative impact on the daily activities and functioning, as per the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria.<sup>2</sup>

ADHD and allergic disorders are multifactorial in nature, involving gene-environment interactions and may have a common biological background.

Children with allergic diseases may also have hyperactive and impulsive behavior, thought to be secondary to the chronic illness or its management.<sup>3</sup> It is thought that the relationship between psychological problems and allergic diseases could be bidirectional.<sup>4</sup> Immune dysregulation is a cornerstone of both allergic and possibly neurodevelopmental conditions. The inflammatory markers released in allergic diseases were also found to be elevated in ADHD, attributed to the permeation of peripheral immune cells such as macrophages across the blood-brain barrier, which alter neural functions, leading to the development of psychiatric disorders.<sup>2</sup> Chronically increased oxidative stress may cause immunological malfunction and elevated IgE levels. Additionally, atopic patients have a 30–50% higher risk of developing ADHD.<sup>5</sup>

Studies investigating the frequency of ADHD symptoms among Egyptian children with allergies are lacking. ADHD, if present, could significantly

impact the quality of life of allergic children.<sup>2</sup> Therefore, this work aimed to screen for the symptoms of ADHD among a group of Egyptian school-aged allergic children to explore the burden of the problem.

## METHODS

This cross-sectional study was conducted on 120 allergic patients aged from 6 to 12 years, in addition to 120 apparently healthy age and sex matched children as a control group. Patients with allergy were recruited from Allergy, Immunology and Rheumatology Unit, Children's Hospital, Ain Shams University Hospitals, in the period from May 2022 till November 2022. An informed consent was taken from all the caregivers of the participants after explaining the aim and methods of the study. The protocol of the study gained the approval of the Research Ethics Committee, Faculty of Medicine, Ain Shams University. Ethical approval number is 000017585.

**Study population:** Allergic children were recruited consecutively during their follow up visits. Different forms of allergy were included such as allergic rhinitis (AR), bronchial asthma, urticaria and atopic dermatitis (AD). The healthy control group was recruited from the outpatients clinic of the same hospital, presenting with a minor illness (e.g. common cold, tonsillitis, acute bronchitis or acute gastroenteritis). Siblings of the patients, patients with major sensory and motor disorders and patients with metabolic diseases were excluded from the study.

### Study tools:

All patients were subjected to history taking from caregivers including the demographic data, family history of allergy or neurodevelopmental disorders, history of the allergic disease: duration of illness, adherence to treatment, disease control, controller therapy, duration of treatment. Clinical examination for assessment of the concurrent status of illness, assessment of severity using European Forum for Research and Education in Allergy and Airways diseases (EUFOREA), 2021 for allergic rhinitis,<sup>6</sup> the American academy of allergy asthma and immunology (AAAAI) criteria for urticaria,<sup>7</sup> the American Academy of Dermatology criteria for AD.<sup>8</sup> Bronchial asthma diagnosis, flare ups and remissions were assessed according to the 2021 update of the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) main report.<sup>9</sup> Medical records were revised for results of absolute eosinophil count,

serum total IgE level, results of skin prick test for assessment of atopy if available.<sup>10</sup>

The following scales were measured in both patients and control group:

**The Arabic version of Strengths and Difficulties Questionnaire (SDQ):** Emotional Symptoms, Conduct Issues, Hyperactivity/Inattention, Peer Relationship Issues, and Prosocial Behavior make up its five measures.<sup>11</sup> It consists of 25 items on strengths and difficulties and impact supplement. We used the validated Arabic version of SDQ.<sup>12</sup> For each of the five scales the scores can range from 0-10. Total score 0-13 close to average, 14-16 slightly raised, 17-19 high and 20-40 very high.

### DSM V criteria for the diagnosis of ADHD:<sup>13</sup>

Patients were screened for total 18 symptoms: 9 for inattention and 9 for hyperactivity and impulsivity. Six or more symptoms of inattention and/or hyperactivity and impulsivity for children are sufficient for ADHD diagnosis.

**Assessment of severity of ADHD symptoms, if present, was done using the Arabic version of the Conners' Parent Rating Scale-Revised, Long Version (CPRS-R-L):<sup>14</sup>** It consists of 80 items for different subscales from A to N (oppositional, cognitive inattention problems, hyperactivity, anxiety, perfectionism, social problems, psychosomatic, emotional liability, impulsivity). Each item scored from 0-3. Then T score measured according to age and sex with score higher than 60 indicates ADHD and T score higher than 70 means ADHD symptoms are serious.

### Statistical methods:

The Statistical Package for Social Science (SPSS) version 23 was used. Parametric data were presented as mean, standard deviations, and ranges, whereas nonparametric data were displayed as median with interquartile range (IQR). Using the Mann Whitney U test and independent-samples t-test of significance, respectively, parametric and non-parametric data were compared. The analysis of variance (ANOVA) in one direction was used to compare more than two means. Tukey's test was employed as a post hoc analysis. Only when the predicted count in any cell was less than 5 was the Chi-square test and Fisher's exact test used to compare groups using qualitative data. The allowable margin of error was set at 5%, while the confidence interval was set at 95%. The following is how the p-value was deemed significant: P value > 0.05 indicates non-significant (NS), P value 0.05 indicates significant (S), and P value 0.01 indicates highly significant (HS).

## RESULTS

### *Descriptive Data of the studied populations:*

The studied population included 77 (64.2%) males and 43 (35.8%) females, with male to female ratio 1.7:1. The majority (60%) were living in urban areas (Table 1). Allergic diseases were distributed as follows: 60 (50%) patients had the diagnosis of urticaria, 35 (29%) allergic rhinitis/ asthma and 35 (29.2%) patients had AD. The duration of allergy diagnosis ranged between 1 and 11 years with mean  $4.94 \pm 2.54$  years. Family history of allergy was positive among 82 patients (68.3%). Allergy was mild in 60% of patients, moderate in 32.5% and severe in 7.5% of patients. Adherence to treatment was the rule among 98 patients (81.7%). Controller therapies included mainly LTRA (60%) and oral antihistamines (56%) (Table 2). The absolute eosinophilic count ranged from  $0.01-5.6 \times 10^3/\mu\text{l}$ , total IgE serum levels were elevated among 19 (15.8%) patients and SPT showed positive sensitization among 103 (85.8%) of the patients.

### *Comparative Data of the studied population:*

The frequencies of ADHD symptoms among the allergic group were significantly higher compared

to the healthy control ( $p < 0.001$ ), with predominant hyperactive subtype representing 20% of patients, followed by combined type among 19% and predominant inattentive type among 7.5% of patients (Table 3). There were statistically significant differences between patients and controls regarding oppositional, inattentive, hyperactive, anxious, perfectionism, psychosomatic aspects, social problems, emotional liability, conners' global index and total DSM-IV, using Conner's scale (table 4). Total difficulties, emotional problems, conduct problems, hyperactivity and prosocial problems were significantly more detectable among allergic children using SDQ (Table 5).

### *The effect of allergic disease severity:*

In patients with urticaria, DSM-V total score and SDQ total difficulties were positively correlated to the severity of the condition ( $p < 0.003$ ,  $p < 0.001$ , respectively). Similarly, severity of AD was positively correlated with DSM-V total and SDQ total difficulties ( $p < 0.001$  both). Severity of AR/asthma was positively correlated to DSM-IV total and SDQ total difficulties ( $p < 0.001$ ,  $p = 0.024$ , respectively) (Table 6).

**Table 1.** Demographic data for the studied patients

Baseline characteristics		Patients group (n=120)
Age (years)	Mean $\pm$ SD	8.88 $\pm$ 2.07
	Range	6-12
Gender	Female	43 (35.8%)
	Male	77 (64.2%)
Age of diagnosis (years)	Mean $\pm$ SD	3.95 $\pm$ 2.79
	Range	1-11
Residency	Rural	29 (24.2%)
	Suburban	19 (15.8%)
	Urban	72 (60.0%)

**Table 2.** Clinical data of the allergic disease of the studied patients

Medical History	Patients group (n=120)
<b>Duration of allergic disease (years)</b>	
Mean $\pm$ SD	4.94 $\pm$ 2.54
Range	1-11
<b>Severity</b>	
Mild	72 (60.0%)
Moderate	39 (32.5%)
Severe	9 (7.5%)
<b>Family history of allergy</b>	
Negative	38 (31.7%)
Positive	82 (68.3%)
<b>Medications</b>	
LTRA	72 (60.0%)
Oral Anti histamines	68 (56.7%)
Inhalers	32 (26.7%)
Topical	32 (26.7%)
SABA	1 (0.8%)
Systemic corticosteroids	1 (0.8%)
<b>Allergic disease control</b>	
No	44 (36.7%)
Yes	76 (63.3%)

SABA short acting beta 2 agonist; LTRA: leukotriene receptor antagonist

**Table 3.** Comparison between the studied groups as regards DSM-V criteria of ADHD

DSM score	Patients group (n=120)	Control group (n=120)	Test value	P-value
<b>Inattentive</b>				
Median (IQR)	2 (1-5)	1 (0-2)	-7.215	<0.001
Range	0-6	0-5		
<b>Hyperactive</b>				
Median (IQR)	2 (1-5)	1 (1-2)	-5.142	<0.001
Range	0-6	0-6		
<b>DSM-V classification</b>				
Combined n (%)	23 (19.2%)	2 (1.7%)	41.350	<0.001
Hyperactive n (%)	24 (20%)	8 (6.7%)		
Inattentive n (%)	9 (7.5%)	2 (1.7%)		
Negative n (%)	64 (53.3%)	108 (90%)		

IQR: Interquartile range, U=Mann-Whitney test,  $\chi^2$ : Chi-square test or FE: Fisher's Exact test, when appropriate

**Table 4.** Comparison between allergic patients and healthy controls as regards Conner's score

Conner's score		Patients group (n=120)	Control group (n=120)	Test value t	P-value
<b>Oppositional</b>	Mean $\pm$ SD	67.51 $\pm$ 11.22	60.19 $\pm$ 5.67	2.018	0.045
	Range	43-90	46-70		
<b>Inattentive</b>	Mean $\pm$ SD	58.23 $\pm$ 9.67	53.91 $\pm$ 7.10	3.942	<0.001
	Range	40-90	43-86		
<b>Hyperactivity</b>	Mean $\pm$ SD	66.29 $\pm$ 10.04	59.08 $\pm$ 7.93	6.171	<0.001
	Range	45-90	44-86		
<b>Anxious</b>	Mean $\pm$ SD	65.21 $\pm$ 11.82	57.53 $\pm$ 7.66	5.970	<0.001
	Range	46-90	44-73		
<b>Perfectionism</b>	Mean $\pm$ SD	50.30 $\pm$ 8.94	55.47 $\pm$ 9.04	-4.451	<0.001
	Range	40-90	40-71		
<b>Social problem</b>	Mean $\pm$ SD	61.41 $\pm$ 12.40	56.41 $\pm$ 8.15	3.690	<0.001
	Range	45-90	40-76		
<b>Psychosomatic</b>	Mean $\pm$ SD	65.11 $\pm$ 14.38	56.04 $\pm$ 7.67	6.094	<0.001
	Range	42-90	43-69		
<b>ADHD index</b>	Mean $\pm$ SD	56.81 $\pm$ 10.60	56.83 $\pm$ 7.60	-0.014	0.989
	Range	30-90	40-73		
<b>CGI-Impulsive</b>	Mean $\pm$ SD	61.89 $\pm$ 12.55	60.50 $\pm$ 8.83	0.994	0.321
	Range	41-90	43-84		
<b>Emotional liability</b>	Mean $\pm$ SD	64.46 $\pm$ 12.38	57.94 $\pm$ 6.31	5.139	<0.001
	Range	41-90	42-72		
<b>CGI Total</b>	Mean $\pm$ SD	63.14 $\pm$ 11.64	59.59 $\pm$ 8.11	2.741	0.007
	Range	44-90	42-83		
<b>DSM-V Inattentive</b>	Mean $\pm$ SD	60.04 $\pm$ 11.32	53.50 $\pm$ 8.16	5.135	<0.001
	Range	40-89	41-80		
<b>DSM-V Hyperactive, impulsive</b>	Mean $\pm$ SD	63.57 $\pm$ 11.04	57.88 $\pm$ 8.43	4.488	<0.001
	Range	43-90	43-83		
<b>DSM-V total</b>	Mean $\pm$ SD	62.43 $\pm$ 9.93	56.66 $\pm$ 6.82	5.244	<0.001
	Range	41-90	45-72		

CGI: Conner's Global Index; ADHD: Attention Deficit Hyperactivity Disorder, DSM-V: Diagnostic and Statistical of mental Disorder fifth edition

**Table 5.** Comparison between allergic and healthy groups according to strengths and difficulties questionnaire (SDQ)

SDQ		Patients group (n=120)	Control group (n=120)	Test value	P-value
<b>Total difficulties</b>	Mean $\pm$ SD	10.11 $\pm$ 4.81	7.82 $\pm$ 4.14	t= 5.632	<0.001
	Range	10-35	8-29		
<b>Externalizing</b>	Median (IQR)	5 (4-8)	4 (2-5)	U= -4.452	<0.001
	Range	2-15	1-14		
<b>Internalization</b>	Median (IQR)	3 (2-6)	3 (3-4)	U= -1.239	0.215
	Range	0-12	1-11		
<b>Emotional problems</b>	Median (IQR)	2 (2-3)	2 (1-2)	U= -3.901	<0.001
	Range	0-9	0-5		
<b>Conduct problem</b>	Median (IQR)	2 (1-2)	1 (1-2)	U= -2.362	0.017
	Range	0-6	0-5		
<b>Hyperactivity</b>	Median (IQR)	3 (3-6)	3 (1-4)	U= -5.650	<0.001
	Range	1-10	0-9		
<b>Peer problem</b>	Median (IQR)	1 (0-3)	2 (1-2)	U= -1.569	0.381
	Range	0-5	0-6		
<b>Prosocial</b>	Mean $\pm$ SD	6.59 $\pm$ 1.52	7.59 $\pm$ 1.26	t= -5.548	<0.001
	Range	2-10	5-10		

U=Mann-Whitney test; " t= Independent Sample t-test, SDQ: Strengths and Difficulties Questionnaire, IQR: Interquartile range

**Table 6.** Correlations between allergy and ADHD severity

Parameters	DSM-V total		Total difficulties	
	r	p-value	r	p-value
Urticaria Severity	0.381	0.003	0.464	<0.001
AD Severity	0.490	<0.001	0.468	<0.001
AR/asthma severity	0.359	<0.001	0.261	0.024

AD: atopic dermatitis; DSM-V: Diagnostic and Statistical of mental Disorder fifth edition

## DISCUSSION

In this study, allergic patients were evaluated using DSM-V, strengths and difficulties questionnaire (SDQ), Conners' Parent Rating Scale-Revised, Long Version (CPRS-R-L) to pick up the patients with ADHD symptoms. ADHD symptoms, through DSM-V criteria, were more prevalent in the studied allergic patients compared to healthy controls. This might be attributed to sleep disturbance, nasal obstruction and hypoxia in patients with AR; and to also skin disfigurement and lack of sleep because of itching in patients with AD. Moreover, allergic children had more behavioral and emotional problems, through SDQ, than healthy controls.

There were statistically significant differences towards the allergic group, regarding the total difficulties score ( $p=0.001$ ), emotional problems (22% of patients compared to 7% of the control group), conduct problems (29% of patents compared to 9% of the control group) and hyperactivity problems (36% of patients compared to 17% of control). No problems with peer interactions were detected. Similarly, *Hammer-Helmich et al.* showed that while there were no peer issues, allergic children had more emotional, conduct, and hyperactivity problems.<sup>15</sup> *Keller et al.* assessed behavioral problems through using SDQ on 2701 participants aged from 3-18 years with atopic diseases. They discovered that children with AD were more likely to experience emotional, conduct, and hyperactivity/inattention issues due to scratching and persistent sleep disturbances, which raise the likelihood of neurodevelopmental abnormalities.<sup>16</sup> The itching itself may also result in restless and anxious behavior. However, in contrast to our findings, another study found that AR was associated with internalizing problems.<sup>17</sup>

Further evaluation by Conners' score revealed significant differences between patients and controls as regards oppositional, inattentive, hyperactive, anxious, perfectionism, psychosomatic, social problems, emotional liability with higher ranges of scores in patients ( $p=0.001$ ). This agrees with *Camfferman et al.* who assessed behavioral problems in children (6-16 y) with AD and found that AD was associated with higher

hyperactivity, and oppositional behavior scores, and lower quality of life scores.<sup>18</sup> Through their detrimental effects on sleep, the coexisting atopic illnesses rhinitis and asthma also showed independent impacts on behavior. Also, *Feng et al.* observed that children with AR had more behavioral issues associated to ADHD than the control group. According to some theories, cognitive distraction and inattention are directly caused by AR symptoms.<sup>19</sup>

On evaluation of the allergic patients by DSM-V criteria, we found that the hyperactive type was more prevalent in allergic patients, followed by the combined type of hyperactivity impulsivity and inattention and the inattentive type. This goes in agreement with *Yang et al.* who suggested that AR kids' impulsivity was a bigger problem than their lack of focus.<sup>20</sup> However, according to the Child Behavior Checklist (CBCL) and the ADHD rating scale score, *Lee et al.* found that children with AR showed noticeably greater ADHD-related behavioral issues in all spheres of behavior.<sup>21</sup> Cognitive impairment and inattention caused by AR symptoms including nasal blockage, rhinorrhea, and sneezing can be explained by these symptoms. Besides, *Madulara and Andaya* evaluated youngsters between the ages of 6 and 12 who attend school and have allergies determined by a physician and found that the combined and the inattentive types were of the same prevalence followed by the hyperactive type.<sup>22</sup> *Brawely et al.* demonstrated that there is a high prevalence of AR symptoms among children with ADHD. Some of the cognitive and behavioral patterns seen in ADHD may be explained by nasal obstruction, which causes sleep disturbances and associated learning disabilities.<sup>23</sup> Also, *Schmitt et al.* found that children with AD experience more mental health issues in a variety of pertinent areas, such as anxiety/depression, social disengagement and difficulty with others, thought and attention difficulties, as well as externalizing issues.<sup>24</sup>

In this study, there was a positive correlation between the severity of allergic diseases and the total difficulties, score of strength and total DSM-V in Conners' parenting scale. This goes in agreement

with *Lee et al.* who examined parenting stress and ADHD-like behavioral symptoms in pediatric AR and found that there was a strong correlation between the severity of AR and the overall ADHD Rating Scale score.<sup>21</sup> However, *Schmitt et al.* did not notice a connection between the signs of ADHD and clinical severity of AD.<sup>24</sup>

**In conclusion**, allergic patients scored higher than their healthy peers as regards ADHD assessment scales through DSM-V criteria, strengths and difficulties scale (SDQ), Conners' parent rating scale-revised, long version (CPRS-R-L) scale. There was a significant correlation between severity of the allergic disease and the behavioral and mental health problems. Therefore, periodic behavioral and mental assessment of allergic children is recommended for early detection of any ADHD symptoms, hence, soothing the overall effect on the patients and their families. Our study is limited by its cross-sectional design and the dependence upon mothers to report their children's behavior which might be influenced by their educational level.

## CONFLICTS OF INTEREST

Authors declare they have no conflicts of interest.

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