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Allergic Rhinitis and Self- Reported Allergic Diseases in Doctor- Diagnosed Attention Deficit Hyperactivity Disorder (ADHD) Paediatric Patients

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Abstract

Allergic rhinitis (AR) as other allergic diseases (AD), e.g; asthma, eczema and food allergy, is common in children. Characteristic symptoms of AR may result in daytime inattention, irritability, and hyperactivity, which are also components of Attention Deficit Hyperactivity Disorder (ADHD). Conflicting data in previous studies exist regarding the relationship between ADHD and AD. The aim of this study was to examine the prevalence and risk of AR and self- reported allergic diseases in doctor- diagnosed ADHD pediatric patients.

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We conducted a case- control study, where 78 patients and 103 non-ADHD controls were included. Skin prick test to common aeroallergens was done to all participant as a test for the presence of allergic rhinitis disease besides self- report questionnaires were distributed among them where they self-reported the presence of AD. The results shows that the prevalence of any positive skin prick test (SPT) in ADHD patients was higher than in the control group, at 25.6 % and 13.6%, respectively (p = 0.04).Whilst the frequency of self-reported allergic rhinitis was 3.6 times higher in the ADHD patients than among the non-ADHD controls (p = 0.004). The prevalence of any self- reported atopic disease was similar among the groups (≈ 49%, p< 0.05), The factors that best predict the presence of ADHD disease were positive skin prick test, self-reports of allergic rhinitis and family reports of asthma (p< 0.05). As a conclusion**;** This study has provided the first population-based case-control study of the prevalence of allergic rhinitis and self- reported AD among pediatric patients with ADHD in Jordan. According to our findings, the rates of any positive skin prick test to aero- allergens and allergic rhinitis in ADHD children are greater compared to healthy cohort. Therefore, assessment of allergic diseases may be beneficial in children diagnosed with ADHD.

Keywords: Attention Deficit Hyperactivity Disorder; Allergic rhinitis; Allergic Disease; Skin Prick Test.

1. Introduction

Despite significant advances in disease prevention and treatment during the last few decades, there has been a significant increase in the prevalence of eczema, asthma, and rhinitis worldwide [1], as well as in Jordan [2].The development of allergic disease (AD) depends on a complex interaction between genetic and several environmental factors, such as environmental exposure to food and inhalant allergens, and nonspecific adjuvant factors, e.g., air pollution and tobacco smoke [3].Evidence reported in the extant literature indicates that comorbidity of eczema, asthma, and rhinitis is not limited to allergic diseases. Some authors posit that, owing to ADs, affected individuals and their families can experience significant problems in everyday life. Moreover, the treatment of these conditions and associated ailments constitutes a significant economic burden and represents a major public health concern, with significant implications on adult health[4, 5]. Patients affected by ADs frequently experience high levels of social stress and anxiety [6, 7]. For example, many individuals suffering from eczema feel stigmatized because of itchy lesions on visible sites [8] and have sleeping problems in early life [9].

Attention Deficit Hyperactivity Disorder (ADHD) is the most common behavioral disorder in children and adolescents [10], and is typically diagnosed at (pre-) school age. Although the ADHD worldwide prevalence rate is around 5%[10],it is slightly higher in Jordan (6.24%),with a male to female ratio of 2.4:1[11]. The condition typically manifests as difficulties with retaining attention, as well as impulsivity and hyperactivity [12]. ADHD is a genetically complex disorder. However, many authors point towards a strong interaction between genetic makeup and the environmental factors [13].

As ADHD is associated with sleeping problems, disruption in family communication, impaired social functioning, and sub optimal school performance, it results in a significantly diminished quality of life [14, 15].The prevalence of ADHD is increasing worldwide, and there is growing body of evidence linking it to the

increase in prevalence of ADs (i.e., eczema, asthma, allergic rhinitis and food allergy).Several studies have demonstrated the link between mental health problems, including ADHD, and common atopy [16, 17].

The causal association between ADHD and allergies has been a matter of debate for quite a long time[18-20].Aiming to test this hypothesis, several authors have investigated the co-existence of atopy and ADHD, failing to identify a significant relationship [21, 22]. On the other hand, in some recently published studies, a significant link between the presence of allergic diseases—such as eczema, allergic rhinitis and asthma—and ADHD was established [23-26]. While some children affected by ADHD exhibit more pronounced symptoms after consuming certain foods, artificial colors or a sodium benzoate preservative[27], or after pollen exposure [28], it is likely that this reaction is due to their hypersensitivity. A better understanding of the relationship between AD prevalence and the development of ADHD is of significant public health relevance, as it may lead to the development of targeted treatments and improved preventive measures. This would greatly benefit children diagnosed with AD, who are at an increased risk of developing ADHD.

The purpose of this study was to determine the prevalence of allergic rhinitis—indicated by at least one positive skin reaction to any aeroallergen tested—and self- reported ADs that are associated with physician-diagnosed ADHD.

2. Patients and Methods

2.1. Study Design and Ethical Considerations

This case-control study was conducted between October 2013 and June 2014 at Al-karak Governate Hospital, Al-karak, Jordan. The study participants included 78children aged 2.5 to 16 years, all of whom had pediatrician-diagnosed ADHD and met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for ADHD [29]. In addition, 103 non-ADHD children (2.5-14 years old),recruited within 9 months from dental, ophthalmic and ENT outpatient clinics, formed the control group. Children with psychotic disorders, schizophrenia or pervasive developmental disorder were excluded from this study. The study protocol was approved by the Ethics Committee on the medical faculty of Mutah University prior to commencing the research.

Once the informed consent was obtained from the parents (or the study participants, where age-appropriate), both the treatment and the control group members were asked to complete a self-report questionnaire. The items included aimed to gather the demographic data and home environmental characteristics of the subjects, as well as personal and family history of eczema, asthma, allergic rhinitis and food allergy. Subsequently, the skin prick tests were performed on all patients, using the standardized aeroallergen extracts from a commercial test kit (Stallergenes, France), in accordance with published guidelines [30]. As some of the standardized allergen extracts were mixtures, approximately25 allergens were tested in this study. SPTs for common allergens were used. More specifically, we tested for *Dermatophagoidespteronyssinus (Dp)* and *Dermatophagoidesfarinae (Df)* house dust mite, as well as olive, cat dander, dog dander, compositae, wall pellitory, salsola kali, 4 cereals, 12 grasses, and mould, along with positive control (histamine) and negative control (vehicle). The allergens used in

this study were chosen according to the common regional plant species [31]. The patients had not taken any antihistaminic drugs within ten days prior to skin testing, as recommended prior to and verified on the day of testing.

2.2. Statistical Analysis

Parametric analysis was performed as the data was normally distributed. Mean and standard deviation were calculated, in addition, Chi-square and Fisher's Exact test were performed for prevalence comparisons. Multi-logistic regressions were used to calculate Adjusted Odds Ratio (AOR), and 95% confidence intervals (95% CI) to assess the relationship between risk factors and ADHD disease, including the potential confounders. A p-value < 0.05 was considered statistically significant. All the analyses were performed using SPSS software version 16.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Characteristics of the Study Population

The study participants included 78 ADHD and 103 non-ADHD control subjects, with the latter recruited from a dental, ophthalmic and ENT outpatient clinics.The characteristics of the study population are summarized in Table 1. As can be seen, while the mean age of the entire study sample was 6.83 ± 3.52 years, it was slightly lower for the ADHD group (6.54±3.23 years), which comprised56males, 22 females, with7.25±3.9 years measured for the control group (59 males, 44 females).

Males were more prevalent (63.5%) in the entire sample, and this gender disparity was even more pronounced in the ADHD group (71.8%), compared to57.3% in non-ADHD controls. However, this is to be expected as empirical evidence indicates that the ADHD disease is more prevalent among males ($p< 0.05$).The mean birth weight for the entire study sample was 3.05kg, with little difference between ADHD patients and the controls. Moreover, 70.7% of the participating children were breastfed exclusively for 4 months, with this percentage being somewhat higher (78.2%) among the ADHD children, compared to those in the control group (65%) ($p> 0.05$). The analysis of the questionnaire responses pertaining to the allergic symptoms indicated that

The personal and family history of self-reported asthma and personal history of allergic rhinitis were significantly higher in the ADHD group compared to the non-ADHD controls ($p< 0.05$). On the other hand, while the prevalence of other allergic diseases—as indicated by the personal and family history of eczema and food allergy and family history of allergic rhinitis—was higher in non-ADHD controls, the difference was not statistically significant.

3.2. Prevalence of Skin Prick test and allergic diseases in ADHD Patients and non- ADHD Controls

The percentages of positive skin test, self-reports of at least one atopic disease and the incidence of both were analyzed in ADHD and non- ADHD groups and presented in Figure 1. In the ADHD group, 20 patients (25.6%) had at least one positive skin test, compared to14 (13.6%) in the control group. This difference was statistically significant ($p =0.04$).

Table 1: The key characteristics of the study population.

Characteristics	ADHD Cases N=78	Non-ADHD Controls N=103	Total N=181	P-value
Age (year) mean±(SD)	7.25(3.9)	6.54(3.23)	6.83(3.52)	**0.220****
Birth weight (kg) mean±(SD)	3.1(0.69)	3.0(0.48)	3.046(0.58)	**0.824****
Sex, no (%)				
Male	56(71.8%)	59(57.3%)	115(63.5%)	**0.045*†**
Female	22(28.2%)	44(42.7%)	66(36.5%)	
Breast feeding, no (%)	61(78.2%)	67(65%)	128 (70.7%)	**0.54***
Personal history of				
Asthma, no (%)	7(8.9%)	2(1.9%)	9 (5%)	**0.031*†**
Allergic Rhinitis, no (%)	29(37.2%)	24(23.3%)	53(29.3%)	**0.042*†**
Eczema, no (%)	14(17.9%)	20(19.4%)	34(18.8%)	**0.8***
Food allergy, no (%)	8(10.3%)	16(15.5%)	24(13.3%)	**0.3***
Family history of				
Asthma, no (%)	9(11.5%)	3(2.9%)	12(6.6%)	**0.021*†**
Allergic Rhinitis, no (%)	31(39.7%)	45(43.7%)	76(42%)	**0.59***
Eczema, no (%)	14(17.9%)	20(19.4%)	34(18.8%)	**0.8***
Food Allergy, no (%)	9(11.5%)	16(15.5%)	25(13.8%)	**0.44***

*****Chi-square. **t-test**.** †P-value < 0.05

While the self-reports of at least one atopic disease in ADHD patients was 48.7% and 48.5% in non- ADHD controls, the percentages were similar and did not reflect the significant difference in the prevalence of positive skin prick tests between both groups.

The percentage of individuals who reported atopic disease and showed a positive skin prick test was 12.8% in ADHD group and 9.7% in non- ADHD group, the difference was insignificant.

3.3. Frequency of positive skin prick test by aeroallergen types

The relative frequency of the sensitizing allergens in the ADHD and non- ADHD groups by allergen types was analyzed and the results were presented in Figure 2. As can be seen; olive pollens produced reaction in 14.1% ADHD children, *Df* and *Dp* resulted in 10.3% followed by cat dander and 4 cereals (8.9%). Whereas, in non-ADHD controls; mould, olive pollens and cat dander represent the most sensitizing agents (4.9%) and the second most are *Df*, *Dp*, salsola kali, and wall pellitory (3.4%). The ADHD cases were more likely to have positive skin prick tests to olive pollens than the non-ADHD controls ($p< 0.05$). The incidence of two or more positive skin prick test among the total was more in the ADHD group (21.8%) than non- ADHD group (9.7%),

the difference was insignificant.

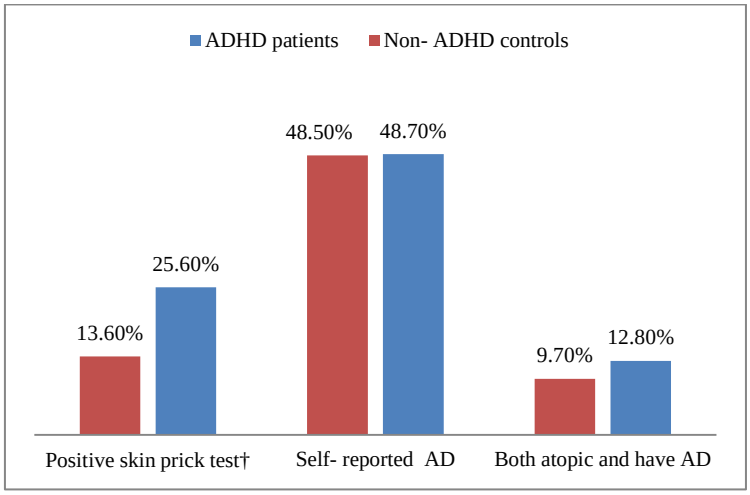

Figure 1: Prevalence of positive skin prick test, self-reports of at least one atopic disease and both in ADHD patients and non- ADHD controls. (Total no. = 78 for ADHD, 103 for Non- ADHD).

†P-value < 0.05. P-value by Chi-square. AD= Atopic Disease.

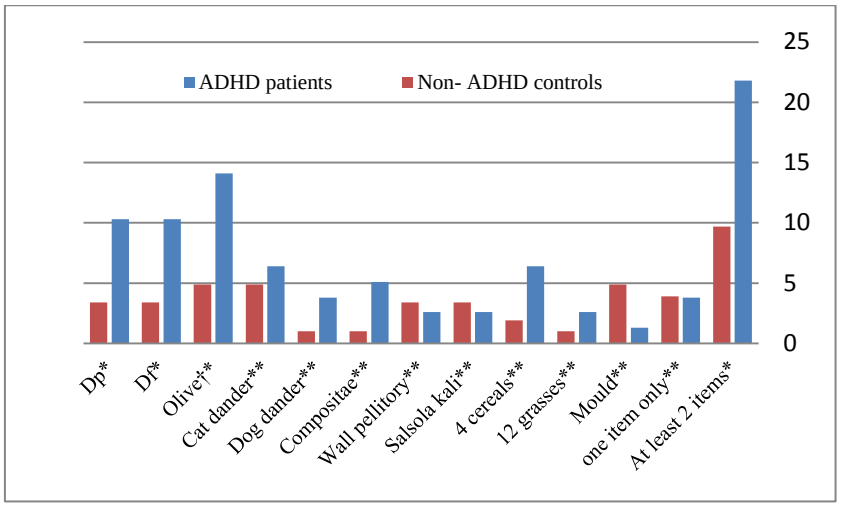

Figure 2: The percentages of the positive skin prick tests for the most common sensitizing allergens in ADHD and non-ADHD groups. (Total no. = 78 for ADHD, 103 for Non- ADHD).

†P-value < 0.05. * P-value by Chi-square, ** P-value by Fisher's Exact Test. (Dp)= Dermatophagoidespteronyssinus. (Df)= Dermatophagoides

3.4. The Factors that are Associated with the ADHD Disease

To identify the characteristics that best predict the presence of ADHD disease within the target population, a stepwise multiple logistic regressions with backward entry of each type of personal or family history of AD

(asthma, eczema, allergic rhinitis and food allergy), sex, birth weight and breastfeeding as independent variables, with health status (ADHD or non-ADHD) as the dependent variable (Table 3), was used. The findings the aforementioned analyses yielded indicate that, among the ADHD children, the rate of allergic sensitization is about 2.4 times higher compared to the non-ADHD controls, while the rates for self-reports of allergic rhinitis and family reports of asthma and allergic rhinitis are about 2.7-4.6 times higher.

Table 2: Adjusted odds ratios of allergic sensitization and allergic diseases in the ADHD and the control group

Variables	AOR* (95% CI)	P-value	Chi square
Allergic sensitization	2.44 (1.05-5.66)	0.038†	4.324
Personal history of allergic rhinitis	3.6 (1.5-8.47)	0.004†	8.318
Family history of asthma	4.61 (1.1-19.6)	0.037†	4.342

*****(Adjusted odds ratios with 95%confidence intervals) (n = 181)**,** †P-value < 0.05

4. Discussion

The purpose of this study was to investigate the possible relationship between atopy, atopic diseases and ADHD. The male-to-female ratio among the study participants was 1.7:1. The gender distribution in the ADHD group was in line with the extant evidence, suggesting that the prevalence of physician-diagnosed ADHD is higher in boys than in girls, and this difference was statistically significant [32].

For the purpose of this study, we asked for self- reported atopic diseases as eczema, asthma, allergic rhinitis, and food allergy besides doing skin prick test to all participant. The results showed that the ADHD cases were more likely to have positive skin prick tests than the non-ADHD controls ($p< 0.05$). Whereas the prevalence of at least one self- reported atopic disease was similar between ADHD and non- ADHD groups. In addition, nearly quarter to one fifth of the individuals with atopic disease had positive skin test in ADHD and non- ADHD groups, respectively. The reasons behind this incongruence between the perceived atopic disease and the positive skin prick test may be due to the fact that not all individuals reported these diseases are truly atopic, i.e. have specific IgE antibodies against environmental allergens [33] or even are truly aware of the atopic diseases

symptoms.

In our study, most children with positive skin prick test were reactive to 2 or more allergens. Similar findings were also obtained from a study in Jordan[2]. Poly-sensitization is very common and might be the result of genetic factors or factors related to the allergen such as cross-reactivity between the aero- allergens epitopes.

The most common allergens causing sensitization in both groups were olive pollens, *Df*, *Dp* and cat dander. This result is in agreement with the findings from a previous study on allergic sensitization of allergic rhinitis patients from Jordan, where olive tree pollens were the most common allergens in this group of patients (all seasonal). Cat allergen was the most common perennial allergen, followed by dust mite. These findings could be attributed to multiple factors, including the fact that olive trees are widely cultivated all over Jordan for ornamental and business purposes[2],while dust mite is a common aeroallergen worldwide [34].In addition, as cats can be found in almost every area of Jordan, it is known that cat allergy can be a major problem even for individuals that do not own them[35]. Finally, according to our findings, no significant difference in the rate of sensitization to any allergen exists between the ADHD and the control group.

Currently available research data concerning the causal association between ADHD and allergies are conflicting [36]. The findings yielded by our study indicate that the allergic sensitization and allergic rhinitis are important risk factors for the development of the ADHD, with the affected individuals being 2.4 times more likely to have been sensitized to aeroallergen and 3.6 times more likely to report allergic rhinitis than are the members of the non-ADHD control group. This result is in line with the findings reported by Suwan et al., indicating that most patients with ADHD had allergic rhinitis symptoms and positive skin prick test results to common aeroallergens[37].This highlights that assessment of atopy to aero-allergens may be beneficial to children diagnosed with atopic disease who are at increased risk to develop ADHD and it may lead to target treatment and improve low cost preventive measures which would be of public health relevance especially in poor country as Jordan.

Furthermore, ADHD patients were 4.6 times more likely to have family history of asthma than non-ADHD controls, which may be due to the familial association of atopy[38], prevalent in ADHD patients.

The link between other factors examined in this study, such as breastfeeding and birth weight is still controversial [39, 40] and was not established in our study.

The results reported in this work provide strong support for the hypothesized relationship between atopy and atopic diseases in childhood and ADHD [20]. Nonetheless, whether allergic sensitization may affect the development of ADHD later in life remains unclear. One hypothesis is that the increased levels of pro-inflammatory cytokines and mediators released during the atopic response may pass the blood brain barrier [41] activate neuro-immune mechanisms that involve behaviorally and emotionally relevant circuits [42].According to another hypothesis, the prefrontal cortex that is known to subserve executive cognitive functions such as planned behavior, decision making, motivation and attention may be affected by the pro- inflammatory mediators [43]. Aside this neuro-immunologic pathway, other mechanisms such as stress may be involved. The

misery of living with atopic disease during early infancy is associated with high levels of sleep disturbances that may lead to long-term alterations of the behavioral and physiological repertoire in children increasing their vulnerability to psychopathological conditions [44].

It may also be speculated that treatment of atopic disease with oral corticosteroids may pharmacologically induce ADHD symptoms [45]. The underlying pathophysiological mechanisms of this finding are unclear.

4.1. Strengths and Limitations of the Study

The strength of this study is that it is the first attempt to establish an association between ADHD and atopy in Jordan. Based on *Diagnostic and Statistical Manual of Mental Disorders,* criteria, all children in the ADHD group were diagnosed by developmental and behavioral pediatricians. Moreover, all study participants were tested by the skin prick tests to confirm presence of atopy. This is an improvement with respect to most of the extant studies, which used inadequate criteria to define atopy and ADHD, as these were usually self-reported by the participants' parents or based on secondary data from routine practice, rather than validated diagnostic criteria [25, 46]. Furthermore, findings of several cross-sectional studies indicate that the highest ADHD-associated incremental costs are incurred in mental health services and pharmaceutical therapy. Thus, this study provides cost-efficient and convenient survey method, enabling us to gain a better understanding of the relationship between atopic diseases and the development of ADHD. The aim is to assist in the development of targeted treatments and improvements in the preventive measures for children that are at an increased risk of developing ADHD.

As any other study, this work is also subject to some limitations, most notably the fact that the children included in the control group were not randomly selected. However, the prevalence of allergic diseases in the control group is likely to be similar to that in the Jordanian general population[2]. Moreover, the data utilized in the analyses was obtained through a questionnaire-based survey, which carries a potential to introduce subjectivity to the data, as all information is provided from the perspective of the participant/parent. Reliance on self-reports of allergic diseases can lead to problems arising from variability in the perception of symptoms and memory bias. Thus, in future studies, it would be highly beneficial to recruit all study participants from multiple sites and populations and include a more reliable measure of their AD symptoms.

5. Conclusion

This case control study was the first attempt to analyze the relationship allergic rhinitis and self- reported atopic diseases might have with physician- diagnosed ADHD disease. In most of the children diagnosed with ADHD, there was a higher presence of any positive skin prick test and allergic rhinitis than other non- ADHD controls. Thus, we posit that greater awareness of these comorbidities may help clinicians to provide better comprehensive management and reduce the burden of the disease both on the affected families and the society as a whole.

References

[1] M. I. Asher, S. Montefort, B. Björkstén, C. K. Lai, D. P. Strachan, S. K. Weiland, *et al.*, "Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys," *The Lancet*, vol. 368, pp. 733-743, 2006.

[2] S. Aburuz, N. Bulatova, and M. Tawalbeh, "Skin prick test reactivity to aeroallergens in Jordanian allergic rhinitis patients," *EMHJ*, vol. 17, pp. 604-610. 2011.

[3] S. Halken, " Prevention of allergic disease in childhood: clinical and epidemiological aspects of primary and secondary allergy prevention," *Blackwell Munksgaard*, pp. 2270, 2004.

[4] J. Schmitt, M. Romanos, N. M. Schmitt, M. Meurer, and W. Kirch, "Atopic eczema and attention-deficit/hyperactivity disorder in a population-based sample of children and adolescents," *JAMA*, vol. 301, pp. 724-726, 2009.

[5] H. Chen, M. K. Gould, P. D. Blanc, D. P. Miller, T. V. Kamath, J. H. Lee, *et al.*, "Asthma control, severity, and quality of life: quantifying the effect of uncontrolled disease," *Journal of Allergy and Clinical Immunology*, vol. 120, pp. 396-402, 2007.

[6] D. R. Williams, M. Sternthal, and R. J. Wright, "Social determinants: taking the social context of asthma seriously," *Pediatrics*, vol. 123, pp. S174-S184, 2009.

[7] J. Arndt, N. Smith, and F. Tausk, "Stress and atopic dermatitis," *Current allergy and asthma reports*, vol. 8, pp. 312-317, 2008.

[8] G. Schmid-Ott, R. Burchard, H. Niederauer, F. Lamprecht, and H. Künsebeck, "Stigmatization and quality of life of patients with psoriasis and atopic dermatitis," *Der Hautarzt; Zeitschrift fur Dermatologie, Venerologie, und verwandte Gebiete*, vol. 54, pp. 852-857, 2003.

[9] A. Smaldone, J. C. Honig, and M. W. Byrne, "Sleepless in America: inadequate sleep and relationships to health and well-being of our nation's children," *Pediatrics*, vol. 119, pp. S29-S37, 2007.

[10] G. Polanczyk, M. de Lima, B. Horta, J. Biederman, and L. Rohde, "The worldwide prevalence of ADHD: a systematic review and metaregression analysis," *American journal of psychiatry*, vol. 164, pp. 942-948, 2007.

[11] A. Shaheen and O. Nafi, "Prevalence of Attention Deficit Hyperactive Disorder (ADHD) in School Children in Al-Qaser District Jordan," *J Med J*, vol. 45, pp. 37-43, 2011.

[12] J. B. Schweitzer, T. K. Cummins, and C. A. Kant, "Attention-deficit/hyperactivity disorder," *Medical Clinics of North America*, vol. 85, pp. 757-777, 2001.

[13] J. Buitelaar, "ADHD: strategies to unravel its genetic architecture," in *Neurodevelopmental Disorders*, ed: Springer, 2005, pp. 1-17.

[14] S. Cortese, E. Konofal, N. Yateman, M. Mouren, and M. Lecendreux, "Sleep and alertness in children with attention-deficit/hyperactivity disorder: a systematic review of the literature," *SLEEP-NEW YORK THEN WESTCHESTER-*, vol. 29, p. 504, 2006.

[15] E. J. Paavonen, K. Räikkönen, J. Lahti, N. Komsi, K. Heinonen, A.-K. Pesonen, *et al.*, "Short sleep duration and behavioral symptoms of attention-deficit/hyperactivity disorder in healthy 7-to 8-year-old children," *Pediatrics*, vol. 123, pp. e857-e864, 2009.

[16] S. Moussavi, S. Chatterji, E. Verdes, A. Tandon, V. Patel, and B. Ustun, "Depression, chronic diseases, and decrements in health: results from the World Health Surveys," *The Lancet*, vol. 370, pp. 851-858, 2007.

[17] M. Al-Nsour, M. Zindah, A. Belbeisi, I. V. Rolle, H. Walke, T. Strine, *et al.*, "Peer Reviewed: Frequent Mental Distress, Chronic Conditions, and Adverse Health Behaviors in the Behavioral Risk Factor Surveillance Survey, Jordan, 2007," *Preventing chronic disease*, vol. 10, 2013.

[18] A. E. Meuret, J. T. Ehrenreich, D. B. Pincus, and T. Ritz, "Prevalence and correlates of asthma in children with internalizing psychopathology," *Depression and anxiety*, vol. 23, pp. 502-508, 2006.

[19] J. Stevenson and E. S. Group, "Relationship between behavior and asthma in children with atopic dermatitis," *Psychosomatic Medicine*, vol. 65, pp. 971-975, 2003.

[20] L. M. Pelsser, J. K. Buitelaar, and H. F. Savelkoul, "ADHD as a (non) allergic hypersensitivity disorder: a hypothesis," *Pediatric Allergy and Immunology*, vol. 20, pp. 107-112, 2009.

[21] J. Biederman, S. Milberger, S. V. Faraone, K. A. Lapey, E. D. Reed, and L. J. Seidman, "No confirmation of Geschwind's hypothesis of associations between reading disability, immune disorders, and motor preference in ADHD," *Journal of abnormal child psychology*, vol. 23, pp. 545-552, 1995.

[22] T. Gaitens, B. J. Kaplan, and B. Freigang, "Absence of an association between IgE-mediated atopic responsiveness and ADHD symptomatology," *Journal of Child Psychology and Psychiatry*, vol. 39, pp. 427-431, 1998.

[23] J. Schmitt, C. Apfelbacher, J. Heinrich, S. Weidinger, and M. Romanos, "Association of atopic eczema and attention-deficit/hyperactivity disorder-meta-analysis of epidemiologic studies," *Zeitschrift fur Kinder-und Jugendpsychiatrie und Psychotherapie*, vol. 41, pp. 35-42; quiz 42-4, 2013.

[24] A. Brawley, B. Silverman, S. Kearney, D. Guanzon, M. Owens, H. Bennett, *et al.*, "Allergic rhinitis in children with attention-deficit/hyperactivity disorder," *Annals of Allergy, Asthma & Immunology*, vol. 92, pp. 663-667, 2004.

[25] C.-S. Shyu, H.-K. Lin, C.-H. Lin, and L.-S. Fu, "Prevalence of attention-deficit/hyperactivity disorder in patients with pediatric allergic disorders: a nationwide, population-based study," *Journal of Microbiology, Immunology and Infection*, vol. 45, pp. 237-242, 2012.

[26] H. J. Kwon, M. Y. Lee, M. Ha, S. J. Yoo, K. C. Paik, J.-H. Lim, *et al.*, "The associations between ADHD and asthma in Korean children," *BMC psychiatry*, vol. 14, p. 70, 2014.

[27] M. Boris and F. S. Mandel, "Foods and additives are common causes of the attention deficit hyperactive disorder in children," *Annals of Allergy*, vol. 72, pp. 462-467, 1994.

[28] M. Boris and A. Goldblatt, "Pollen exposure as a cause for the deterioration of neurobehavioral function in children with autism and attention deficit hyperactive disorder: nasal pollen challenge," *Journal of Nutritional and Environmental Medicine*, vol. 14, pp. 47-54, 2004.

[29] A. P. Association, " *The Diagnostic and Statistical Manual of Mental Disorders,* " *DSM 5*: bookpointUS, 2013.

[30] S. Dreborg and A. Frew, "Position paper: allergen standardization and skin tests," *Allergy*, vol. 48, pp. 49-54, 1993.

[31] M. Tawalbeh, N. Bulatova, and S. Aburuz, "Investigation of the Impact of Aeroallergens Sensitization on Allergic Rhinitis Severity**," *J Med J*, vol. 45, pp. 18-28, 2011.

[32] J. Biederman, E. Mick, S. V. Faraone, E. Braaten, A. Doyle, T. Spencer, *et al.*, "Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic," *American Journal of Psychiatry*, vol. 159, pp. 36-42, 2002.

[33] S. Johansson, T. Bieber, R. Dahl, P. S. Friedmann, B. Q. Lanier, R. F. Lockey, *et al.*, "Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003," *Journal of allergy and clinical immunology*, vol. 113, pp. 832-836, 2004.

[34] L. P. Boulet, H. Turcotte, C. Laprise, C. Lavertu, P. M. BEDARD, A. Lavoie, *et al.*, "Comparative degree and type of sensitization to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma," *Clinical & Experimental Allergy*, vol. 27, pp. 52-59, 1997.

[35] T. A. Platts-Mills, J. W. Vaughan, M. C. Carter, and J. A. Woodfolk, "The role of intervention in established allergy: avoidance of indoor allergens in the treatment of chronic allergic disease," *Journal of allergy and clinical immunology*, vol. 106, pp. 787-804, 2000.

[36] J. Schmitt, A. Buske-Kirschbaum, and V. Roessner, "Is atopic disease a risk factor for attention-deficit/hyperactivity disorder? A systematic review," *Allergy*, vol. 65, pp. 1506-1524, 2010.

[37] P. Suwan, D. Akaramethathip, and P. Noipayak, "Association between allergic sensitization and

attention deficit hyperactivity disorder (ADHD)," *Asian Pacific Journal of Allergy and Immunology*, vol. 29, pp. 57-65, 2011.

[38] T. L. Diepgen and M. Blettner, "Analysis of familial aggregation of atopic eczema and other atopic diseases by ODDS RATIO regression models," *Journal of investigative dermatology*, vol. 106, 1996.

[39] H. Kadziela-Olech and J. Piotrowska-Jastrzebska, "The duration of breastfeeding and attention deficit hyperactivity disorder," *Roczniki Akademii Medycznej w Bialymstoku (1995)*, vol. 50, pp. 302-306, 2004.

[40] E. Mick, J. Biederman, J. Prince, M. J. Fischer, and S. V. Faraone, "Impact of low birth weight on attention-deficit hyperactivity disorder," *Journal of Developmental & Behavioral Pediatrics*, vol. 23, pp. 16-22, 2002.

[41] A. Yarlagadda, E. Alfson, and A. H. Clayton, "The blood brain barrier and the role of cytokines in neuropsychiatry," *Psychiatry (Edgmont)*, vol. 6, p. 18, 2009.

[42] C. L. Raison, L. Capuron, and A. H. Miller, "Cytokines sing the blues: inflammation and the pathogenesis of depression," *Trends in immunology*, vol. 27, pp. 24-31, 2006.

[43] M. A. Rosenkranz, W. W. Busse, T. Johnstone, C. A. Swenson, G. M. Crisafi, M. M. Jackson, *et al.*, "Neural circuitry underlying the interaction between emotion and asthma symptom exacerbation," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 102, pp. 13319-13324, 2005.

[44] M. Ednick, A. P. Cohen, G. L. McPhail, D. Beebe, N. Simakajornboon, and R. S. Amin, "A review of the effects of sleep during the first year of life on cognitive, psychomotor, and temperament development," *Sleep*, vol. 32, p. 1449, 2009.

[45] S. Kayani and D. C. Shannon, "Adverse Behavioral Effects of Treatment for Acute Exacerbation of Asthma in ChildrenA Comparison of Two Doses of Oral Steroids," *CHEST Journal*, vol. 122, pp. 624-628, 2002.

[46] J.-D. Tsai, S.-N. Chang, C.-H. Mou, F.-C. Sung, and K.-H. Lue, "Association between atopic diseases and attention-deficit/hyperactivity disorder in childhood: a population-based case-control study," *Annals of epidemiology*, vol. 23, pp. 185-188, 2013.