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Autistic spectrum disorder, attention deficit hyperactivity disorder, and allergy: Is there a link? A nationwide study



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ABSTRACT

Previous studies showed that both attention deficit hyperactivity disorder (ADHD) and autistic spectrum disorder (ASD) were associated separately with a higher risk of allergic diseases. However, the comorbid effect of ADHD and ASD on the risk of allergic diseases is still unknown. Using the Taiwan National Health Insurance Research Database, 5386 children aged less than 18 years with ADHD alone, 578 with ASD alone, 458 with ADHD + ASD, and 25,688 non-ADHD/ASD age- and sex-matched (1:4) controls were enrolled in our study. The prevalence of allergic diseases, including asthma, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis, was evaluated among the four groups. Logistic regression analysis showed that the ADHD + ASD group (odds ratio [OR]: 2.26, 95% confidence interval [CI]: 1.83–2.79), ADHD-alone group (OR: 1.81, 95% CI: 1.70–1.93), and ASD-alone group (OR: 1.24, 95% CI: 1.04–1.48) had an increased risk of allergic comorbidities compared to the control after adjusting age, sex, and level of urbanization. ASD children with more allergic comorbidities (≥ 3 : OR: 2.57, 95% CI: 1.74–3.79; 2: OR: 2.00, 95% CI: 1.41–2.84; 1: OR: 1.60, 95% CI: 1.16–2.22) were associated with a greater likelihood of ADHD. Children with ADHD or ASD had an increased risk of allergic comorbidities, and those with both ADHD and ASD had the highest. These results may inspire more research to clarify the underlying mechanisms among ASD, ADHD, and allergic diseases.

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1. Background

Autistic spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) are neurodevelopment disorders that occur in childhood, and usually co-occur in the same individual although their symptoms are very different: ASD

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involves impaired social cognition and interaction, restricted interests, and stereotyped behaviors; ADHD manifests as hyperactivity, inattention, and inability to modulate activities. Some studies have reported that about 20% of ASD patients met ADHD criteria (Hanson, Cerban, et al., 2013; Musser, Hawkey, et al., 2014), and others indicated that ASD and ADHD have an overlapping diathesis (Musser et al., 2014; Taurines, Schwenck, et al., 2012), although the pathophysiology of both diseases remains unclear. Evidence also has shown that patients with dual diagnoses of ASD and ADHD had a greater severity of illness and impairment of functioning (Kotte, Joshi, et al., 2013; Sprenger, Buhler, et al., 2013).

Previous studies suggested an association between ADHD and allergic diseases. A prospective birth cohort study of 770 children included at baseline between 2000 and 2001 with follow-up to age 11 years reported that the association of atopic dermatitis with ADHD was strong (relative risk [RR]: 5.17, 95% confidence interval [CI]: 2.18; 12.28) (Genuneit, Braig, et al., 2014). Hak, de Vries, et al. (2013) demonstrated that the risk of asthma (odds ratio [OR]: 1.6, 95% CI: 1.3–1.9) and any allergic diseases (OR: 1.6, 95% CI: 1.3–1.8) was significantly elevated in the ADHD group compared to the control group. Some studies also found an association between ASD and allergic diseases. Chen et al. (2013b) revealed that patients with ASD had an increased risk of asthma (OR: 1.74, 95%CI: 1.51–1.99), allergic rhinitis (OR: 1.70, 95%CI: 1.51–1.91), and atopic dermatitis (OR: 1.52, 95%CI: 1.30–1.78). Mostafa and Al-Ayadhi (2013) showed that among 42 ASD patients more than 40% exhibited allergic manifestations (asthma, atopic dermatitis, and allergic rhinitis).

Taking the above evidence together, both ADHD and ASD were associated separately with allergic diseases. However, the association between the ADHD/ASD comorbidity and allergic diseases is still unknown. Using the Taiwan National Health Insurance Research Database (NHIRD) with a large sample size, we investigated the comorbid effect of ADHD and ASD on the risk of allergic diseases, and hypothesized that patients with dual diagnoses of ADHD and ASD had an increased risk of allergic diseases compared to those with ASD or ADHD alone and the control group.

2. Methods

2.1. Data source

This study was based on the data from the NHIRD audited and released by the National Health Research Institute. Taiwan's National Health Insurance (NHI) program was implemented in 1995, and now covers up to 99% of all 23,000,000 residents (<http://www.nhi.gov.tw/>). Subjects included in the NHIRD are anonymous to protect individual privacy. Comprehensive information on insured subjects is included in the database, including demographic data, dates of clinical visits, and diagnoses. The diagnostic codes used were based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). The NHIRD has been used extensively in many epidemiologic studies in Taiwan (Chen et al., 2013b, 2014; Shen, Tsai, et al., 2013; Wu, Wang, et al., 2011).

2.2. Inclusion criteria for the ADHD-alone group, ASD-alone group, ADHD + ASD group, and the control group

Subjects aged under 18 years and identified as having “ADHD” (ICD-9-CM code: 314) or “ASD” (ICD-9-CM code: 299) by psychiatrists were included as the study group. The study group was divided into three subgroups: ADHD-alone, ASD-alone, and ADHD + ASD groups. The age- and sex-matched control group (four for every patient in the study cohort) was randomly identified from among the subjects in the database after eliminating patients who had been given a diagnosis of ADHD or ASD at any time. Comorbidities of asthma (ICD-9-CM codes: 493, 493.0, 493.1, or 493.9), allergic rhinitis (ICD-9-CM code: 477), atopic dermatitis (ICD-9-CM codes: 691 or 691.8), and allergic conjunctivitis (ICD-9-CM codes: 372.05 and 372.14) were identified by internists/pulmonologists/rheumatologists/pediatricians, internists/family physicians/pediatricians, dermatologists/pediatricians, and ophthalmologists. All diagnoses were given at least twice by corresponding physicians for diagnostic validity. Level of urbanization was also assessed in our study (Liu, Hung, et al., 2006).

2.3. Statistical analysis

In comparing the differences between the four groups (ADHD-alone, ASD-alone, ADHD + ASD, and control group), analysis of variance (ANOVA) was used for continuous variables and Pearson's χ^2 test was applied for nominal variables. Post hoc analysis was performed. In order to investigate the risk of allergic comorbidities among the four groups, multiple logistic regression analysis was used to calculate the OR with 95% CI after adjusting for age, sex, and level of urbanization. Furthermore, we also evaluated the risk of ADHD among ASD patients with allergic comorbidities and those without. A two-tailed *P*-value of less than 0.05 was considered statistically significant. All data processing and statistical analyses were performed with Statistical Package for Social Science (SPSS) version 17 software (SPSS Inc.) and Statistical Analysis Software (SAS) version 9.1 (SAS Institute, Cary, NC).

3. Results

3.1. Demographic characteristics of the participants with ADHD alone, ASD alone, ADHD + ASD, and control group

In all, 5386 children were diagnosed as having ADHD alone, 578 as having ASD alone, and 458 as having ADHD + ASD. Children with both ASD and ADHD, those with ADHD alone, and those with ASD alone had a higher prevalence of allergic

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