

Association between atopic dermatitis and attention deficit hyperactivity disorder in children and adolescents: A meta-analysis

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Liu, HZ; Huang, M; Yang, Lj; Li, XN.

Corresponding author:

Li Xuening

lixuening1988@163.com

Author Affiliation:The Fourth Affiliated Hospital of
China Medical University.**ADMINISTRATIVE INFORMATION****Support** - The authors received no funding to perform this study.**Review Stage at time of this submission** - The review has not yet started.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202460013**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 June 2024 and was last updated on 04 June 2024.**INTRODUCTION**

Review question / Objective This meta-analysis aims to summarize, quantify and explore the published literature to determine the relationship between AD and ADHD.

Condition being studied Previous studies have shown that the relationship between the proinflammatory cytokines reactivity found to be triggered by allergic response and the central nervous system may predispose some children to impulsive behavior, autism, or ADHD. However, studies have found a lack of correlation between atopic dermatitis (AD) and ADHD. A recent meta-analysis analyzed the association between AD and ADHD, however, some studies on the relationship between AD and ADHD were published within the last year, therefore, many recent articles were not included in this meta-analysis. In order to further explore the correlation between AD and ADHD, this study carried out updated meta-analysis based on observational studies including cohort, case-control, cross-sectional studies, to provide

evidence-based medicine basis for the etiological research and prevention and control of ADHD. The relationship between atopic dermatitis (AD) and attention deficit hyperactivity disorder (ADHD) in children and adolescents is unclear. This meta-analysis aims to summarize, quantify and explore the published literature to determine the relationship between AD and ADHD.

METHODS

Search strategy PubMed, Web of Science and Scopus were searched for observational studies on the relationship between AD and ADHD. In addition, we manually reviewed the list of references included in the article to avoid the potential omission of relevant articles. The search time was from establishment date of database to April, 2023. We used the following search strategy. 1) PubMed: (("atopic dermatitis"[tiab]) OR ("eczema"[tiab]) OR ("atopic eczema"[tiab])) AND (("attention deficit hyperactivity disorder"[tiab]) OR ("ADHD"[tiab]) OR ("hyperactivity disorder"[tiab]) OR ("hyperactivity"[tiab]))

II) Web of Science: TS= (“atopic dermatitis”) OR (“eczema”) OR (“atopic eczema”) AND (“attention deficit hyperactivity disorder”) OR (“ADHD”) OR (“hyperactivity disorder”) OR (“hyperactivity”)

III) Scopus: (TITLE-ABS-KEY (“atopic dermatitis”) OR TITLE-ABS-KEY (“eczema”) OR TITLE-ABS-KEY (“atopic eczema”) AND (TITLE-ABS-KEY (“attention deficit hyperactivity disorder”) OR TITLE-ABS-KEY (“ADHD”) OR TITLE-ABS-KEY (“hyperactivity disorder”) OR TITLE-ABS-KEY (“hyperactivity”)).

Participant or population The subjects were children and adolescents.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included Observational study design.

Eligibility criteria For eligible studies, studies must meet the following criteria: 1) observational studies, including cohort, case-control or cross-sectional study; 2) observational study design on association between AD and ADHD; 3) the subjects were children and adolescents; 4) the study data are complete, and the OR value and 95% CI can be extracted, or the basic data can be calculated. Exclusion criteria for the articles included: reviews, meta-analyses, animal studies, duplicate literature, conference abstract, letters, notes, editorials and incomplete data.

Information sources PubMed, Web of Science and Scopus were searched for observational studies on the relationship between AD and ADHD. In addition, we manually reviewed the list of references included in the article to avoid the potential omission of relevant articles.

Main outcome(s) The statistically relationship was observed between AD and ADHD (OR=1.38 95%CI:1.23-1.55). Meanwhile, sensitivity analysis using the metaninf test confirmed the robustness of the results as removing some of the studies would not make a significant impact on the overall conclusions.

Quality assessment / Risk of bias analysis The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of the included studies. NOS total score was 9. The total score of 7-9 is high quality, 4-6 is medium quality, and ≤ 3 is low quality.

Strategy of data synthesis For binary variables, OR was used as the effect analysis statistic, and the 95% CI of each effect size was provided. The heterogeneity test of included studies was judged together with the results of Q test and I2 test. $P < 0.05$ and $I^2 > 50\%$ indicated that the heterogeneity among studies was high, and a random-effects model was used to calculate the combined effect size.

Subgroup analysis The source of heterogeneity was explored by subgroup analysis according to study type (cohort, case-control, cross-sectional), area (Asia, Europe, America), sample size (≤ 1000 , > 1000) and age (0-6 year, 0-18 year, 7-12 year).

Sensitivity analysis Sensitivity analyses were performed using the metaninf test to assess the impact of each individual study on the overall result. Egger's test was used to evaluate publication bias.

Country(ies) involved China (The Fourth Affiliated Hospital of China Medical University).

Keywords Attention deficit hyperactivity disorder; Children; Adolescent; Atopic dermatitis; Meta-analysis.

Contributions of each author

Author 1 - Liu Hezuo.

Email: 13605785301@163.com

Author 2 - Huang Minhui.

Author 3 - Yang Lingjie.

Author 4 - Li Xuening.