

# Meta-analysis of the comorbidity rate of allergic rhinitis and asthma in Chinese children

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## ABSTRACT

**Objectives:** Allergic rhinitis (AR) and asthma often occur concomitantly and are the two most common inflammatory conditions of the airways in children. Large-scale studies investigating the comorbidity of asthma and AR in children are rare. So, we performed a meta-analysis to describe the comorbidity rate of asthma and AR in Chinese children.

**Methods:** We retrieved related studies from Pubmed, Science, Springer, Elsevier, Embase, BMJ, and four Chinese biomedical databases, including Wanfang Data, VIP, CBM, and CNKI. From these individual studies, the comorbidity rate of asthma and AR in Chinese children was extracted and pooled to generate summary effect estimates in R version 3.2.3.

**Results:** The meta-analysis included 25 cross-sectional studies. The results indicated that in China, the incidence of asthma in children with AR is 35.01% (95% CI: 32.32%–37.70%) and the incidence of AR in children with asthma is 54.93% (95% CI: 53.05%–56.80%).

**Conclusions:** The comorbidity of AR and asthma is high in Chinese children. Statistically, the prevalence of AR was higher in children with asthma, as opposed to the prevalence of asthma in children with AR. The comorbidity rate of AR and asthma signifies the importance of improving the recognition and treatment under both conditions by respiratory physicians and otolaryngologists.

## 1. Introduction

Childhood allergic respiratory diseases, allergic rhinitis (AR) and asthma, are rightly called the 21st century epidemic. Although the conditions affect different parts of the respiratory tract, they are similar in etiology pathogenesis and pathological changes [1]. Childhood AR and asthma are generally perceived as separate disorders in clinical treatment, and they are diagnosed by pediatric otolaryngologists and respiratory physicians, respectively. However, if a doctor only treats AR or asthma in children with comorbidity of both disorders, the treatments are less effective [2,3]. Therefore, to effectively control both diseases, the incidence of asthma in children with AR and the incidence of AR in children with asthma must be better understood. This in turn would improve pediatric respiratory physicians' and otolaryngologists' abilities to provide clinical treatment and medical advice for children with both conditions.

To date, there have been few large-scale, multi-center studies investigating the association between childhood AR and asthma. Thus, we sought to determine the prevalence of asthma in children with AR and AR in children with asthma. By collecting clinical epidemiology studies

on childhood asthma and AR from the last 10 years, we performed a meta-analysis to provide a more scientific basis for the diagnosis and treatment of children with the comorbidity of asthma and AR.

## 2. Methods

A protocol for the review was devised in accordance with PRISMA guidelines [4]. Searches of *Pubmed*, *Science*, *Springer*, *Elsevier*, *Embase*, *BMJ Journals* electronic databases, and four Chinese biomedical databases, including Wanfang Data, VIP, CBM, and CNKI were performed from January 2006 to May 2016 for articles reporting the comorbidity prevalence of asthma and AR in children. The search terms used were “(allergic rhinitis) AND (asthma) and (epidemiology OR prevalence OR morbidity OR incidence OR attack rate) AND (children OR childhood OR adolescent OR pediatric)”. The titles and abstracts of the articles were browsed, and papers with relevant information were identified and included in the meta-analysis. Reference lists of included articles and other relevant studies were scanned to find additional studies.

To meet the analysis requirement and reduce systematic and random error, the included literature fulfilled the following criteria: (1)

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**Table 1**

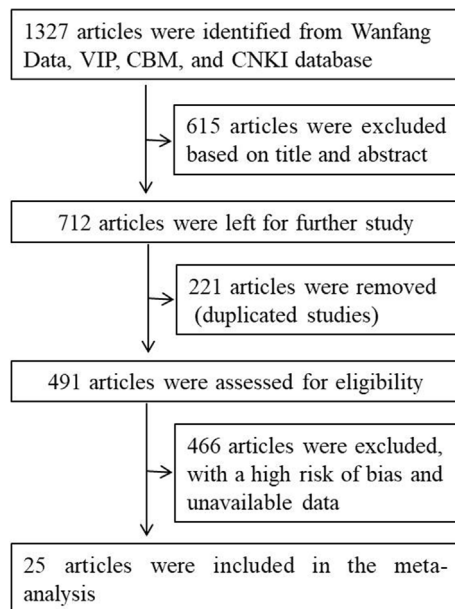
Overview of the studies included in systematic review.

| Study                     | Study Design          | Age Range(Y) | Criteria | AR(n) | AR with Asthma (n) |
|---------------------------|-----------------------|--------------|----------|-------|--------------------|
| Wang Yuan et al.,2015     | Cross-sectional study | 7–15         | ARIA     | 467   | 152                |
| Su liang et al.,2015      | Cross-sectional study | 3–7          | ARIA     | 802   | 312                |
| Huang Yanping et al.,2012 | Cross-sectional study | 7–11         | ARIA     | 151   | 38                 |
| Huang Sui et al.,2011     | Cross-sectional study | 0–14         | ISAAC    | 319   | 111                |
| Chen Yan et al.,2012      | Cross-sectional study | 13–14        | ARIA     | 2104  | 738                |
| Wu Jun et al.,2008        | Cross-sectional study | 7–11         | ARIA     | 131   | 43                 |
| Jiang Manjie et al.,2006  | Cross-sectional study | 9–10         | ARIA     | 48    | 19                 |
| Lu Diqing et al.,2006     | Cross-sectional study | 2–12         | ARIR     | 472   | 186                |

**Table 2**

Overview of the studies included in systematic review.

| Study                     | Study Design          | Age Range(Y) | Criteria | Asthma(n) | Asthma with AR (n) |
|---------------------------|-----------------------|--------------|----------|-----------|--------------------|
| Lu Xu et al.,2015         | Cross-sectional study | 0–14         | ARIA     | 47        | 28                 |
| Ning Lihua et al.,2014    | Cross-sectional study | 0–14         | ISAAC    | 127       | 75                 |
| Yang Yungang et al.,2013  | Cross-sectional study | 0–14         | ISAAC    | 368       | 219                |
| Gu Jiali et al.,2013      | Cross-sectional study | 0–14         | ARIA     | 169       | 97                 |
| Li Min et al.,2013        | Cross-sectional study | 0–14         | ARIA     | 551       | 286                |
| Liu Chuanhe et al.,2013   | Cross-sectional study | 0–14         | ISAAC    | 497       | 261                |
| Wei Qing et al.,2013      | Cross-sectional study | 0–14         | ARIA     | 370       | 208                |
| Ding Yanxia et al.,2012   | Cross-sectional study | 0–14         | ARIA     | 338       | 162                |
| Lu Gen et al.,2012        | Cross-sectional study | 0–14         | ISAAC    | 215       | 121                |
| Xiong Mei et al.,2012     | Cross-sectional study | 0–14         | ARIA     | 495       | 272                |
| Liu Jixian et al.,2012    | Cross-sectional study | 0–14         | ARIA     | 540       | 332                |
| Jin ke et al.,2012        | Cross-sectional study | 0–14         | ISAAC    | 132       | 74                 |
| Lei Xingli et al.,2012    | Cross-sectional study | 2–7          | ISAAC    | 791       | 430                |
| Sun Libin et al.,2009     | Cross-sectional study | 0–14         | ISAAC    | 348       | 172                |
| Shen Chunlin et al.,2007  | Cross-sectional study | 6–14         | ISAAC    | 422       | 219                |
| Kong Yun et al.,2006      | Cross-sectional study | 0–14         | ISAAC    | 324       | 172                |
| Liu Changpeng et al.,2006 | Cross-sectional study | 0–14         | ARIA     | 320       | 188                |

**Fig. 1.** The figure displayed the information retrieval process for valuable articles and exclusion process of irrelative articles for the study.

The research subjects were under the age of 16; (2) The studies met the clinical diagnostic criteria for children with AR and asthma [5]; (3) The research reported the comorbidity prevalence of asthma and AR in children, or, contained data that could be used to calculate the incidence; (4) The studies were cross-sectional surveys; (5) The research had an appropriate study design and statistical treatment. Studies were excluded if they (1) presented data collected prior to 2006; (2) presented data of inferior quality; (3) presented data on a study population

that had already been included in the study.

Two authors independently screened all the articles by title and abstract to identify those that met the inclusion criteria. If studies were shortlisted, their full text was assessed for eligibility. Articles likely to contain data on the incidence of asthma in children with AR were then retrieved. Any disagreements regarding the suitability of individual studies were resolved through appraisal by a third author.

Two reviewers independently evaluated the literature quality and bias risks according to Combie criteria for cross-sectional studies which include the following seven domains [5]: (1) The study's design is scientific. (2) The data collection strategy is reasonable. (3) The research reports sample response rates. (4) The population's representation of samples is very good. (5) The research purpose and method are reasonable. (6) The study reports the statistical power of the data.

The data analysis was conducted using R version 3.2.3. The prevalence of asthma in children with AR at 95% confidence intervals (CIs) was counted, and heterogeneity across studies was also determined. If  $P > 0.1$  and  $I^2 < 50\%$ , the fixed effects model was used for meta-analysis; otherwise, the random effects model was used. In our study, the random effects model was used for meta-analysis as a result of the heterogeneity test.

### 3. Results

After the removal of duplicates, our initial search generated 491 studies. Studies were excluded if they presented a high risk of bias. Articles were mainly excluded if they surveyed populations unrepresentative of the general population. In total, 25 cross-sectional studies were included in the meta-analysis (Table 1 and Table 2). The flow chart of the studies screening process is shown in Fig. 1.

Seventeen studies (6054 Chinese children with asthma) reported prevalence of AR in children with asthma [6–13]. After determining heterogeneity across all studies, the random effects model was used for

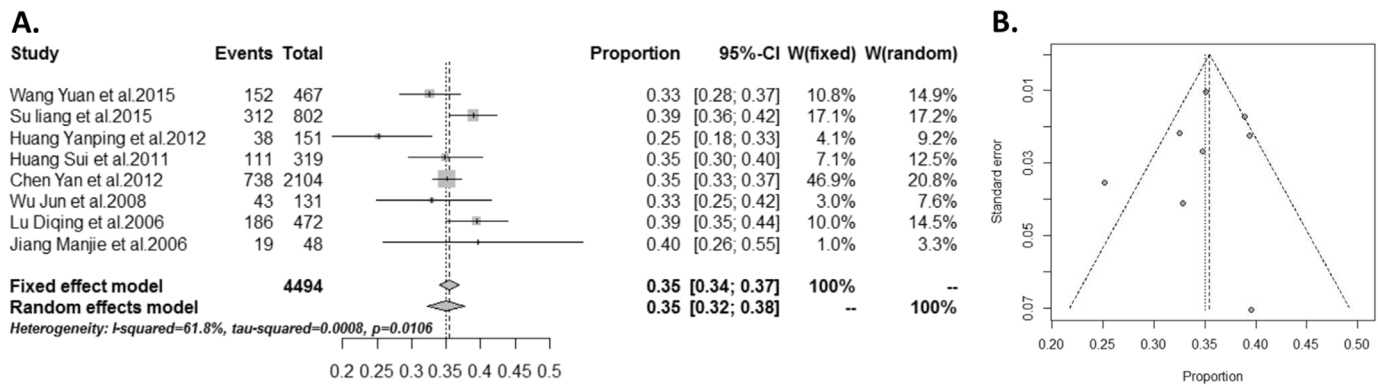


Fig. 2. Prevalence of asthma in Chinese children with AR. (A) Forest plot (B) Funnel plot.

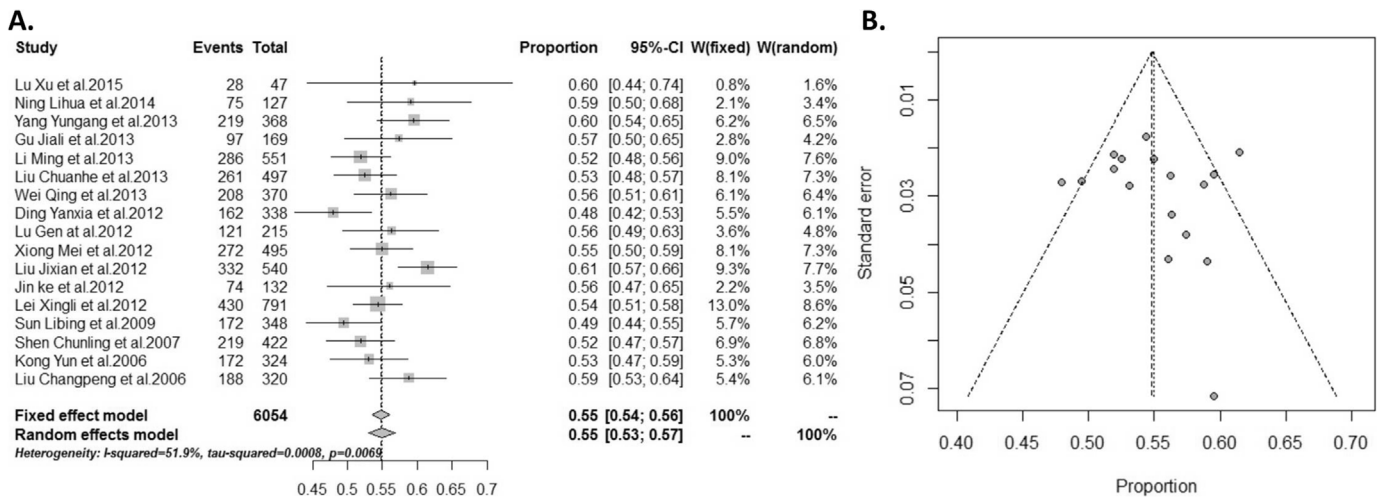


Fig. 3. Prevalence of AR in Chinese children with asthma. (A) Forest plot (B) Funnel plot.

meta-analysis. The results revealed that the comorbidity of AR in children with asthma is 54.93% (95% CI: 53.05%–56.80%) (Fig. 2).

Eight studies (4494 Chinese children with AR) reported incidences of asthma in children with AR [14–30]. After determining heterogeneity across all studies, the random effects model was used for meta-analysis. The results of the study showed that the comorbidity of asthma in Chinese children with AR is as high as 35.01% (95% CI: 32.32%–37.70%) (Fig. 3). Therefore, the comorbidity of AR and asthma in Chinese children is high. Yet, the comorbidity of AR in children with asthma is statistically higher than that of asthma in children with AR.

#### 4. Discussion

From the general population studies included in this survey, the estimated comorbidity of asthma in Chinese children with AR is 35.01% and the estimated comorbidity of AR in Chinese children with asthma is as high as 54.93%. The ratio of the comorbidity of asthma in children with AR appears to be lower than that of AR in children with asthma.

The ISAAC study also revealed the presence of asthma in 25%–35% subjects with AR, and rhinitis symptoms in 75%–90% of asthmatics [31]. Zvezdin *et al* reported that in those diagnosed with allergic asthma, the frequency of concomitant AR was 64%. Conversely, in those diagnosed with non-allergic asthma, the frequency of concomitant AR was 28% [32]. The symptoms of AR usually precede those of asthma. Peat *et al* have demonstrated that the age of onset of atopy was an important factor for the development of asthma and AR or AR alone [33]. The follow-up study by Settupane *et al* discovered the patients with nasal symptoms and a positive skin prick tests, reporting that in ten years, 50% of the tested patients had the same symptoms,

while 20% developed asthma [34]. The children with asthma included both atopic and non-atopic patients. Asthma's comorbidity with AR is considered to be more frequent among atopic patients than among non-atopic patients [35]. Thus, the ratio of AR's comorbidity among children with asthma may actually depend on the ratio of children with atopic asthma. Additionally, the differences between the ratios may also be attributed to the distribution of allergens, which varying from place to place in China due to it depends on geographical features, climate and vegetation [36].

An increasing number of studies have found that environmental factors play an important role in the etiology of AR and the comorbidity of allergic diseases. The exposure to tobacco smoke in childhood is significant risk factor. Lundback *et al* have confirmed that both smokers and ex-smokers with a positive family history of atopy have seven times increased risk to develop AR and/or asthma [37]. Moreover, a rise in levels of air pollutants, such as  $\text{NO}_2$  or  $\text{PM}_{2.5}$ , could be responsible for the current increase in the prevalence of allergic diseases [38]. Ouyang *et al* reported that oak pollen exposing to high concentrations of  $\text{SO}_2$  or  $\text{NO}_2$  could significantly increase their crispness and dissociation, leading to subsequent release of pollen cytoplasmic granules into the atmosphere, which increased the incidence of susceptible population via accelerating the bioavailability of airborne allergens [39].

Our study reveals a close relationship between AR and asthma as well, which supports the use of the term the “united airway disease”. This term was coined based on the evidence that AR is an independent risk factor for the development of asthma. Adams *et al* found that treatment of asthmatic patients with intranasal corticosteroids confers protection against emergency department visits for asthma exacerbations under the population-based studies [40]. Aubier *et al* suggested

that a protective nasal effect of antihistamines against BHR after nasal allergen challenge in AR patients can be illustrated by an effect of the drug on the airways and by protection concerned with the control of AR [41]. This therapeutic strategy can also reduce the subsequent development of asthma in children with atopic diseases [42]. So, an integrated and unified strategy combining the treatment of both AR and asthma appears to be optimal.

A limitation of this study is the fact that many of the included surveys did not contain age stratification and gender classification of the children with AR and comorbid asthma. As a result, our study did not include an age hierarchical analysis or gender classification analysis. Furthermore, the data was collected from different district hospital with various levels of research competency; thus, there may be discrepancies in specific study methods that would contribute to inherent biases.

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## Disclosure

The authors declare that no financial or other conflicts of interest exist in relation to the content of this article.

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