



The association between allergic rhinitis with migraine: A systematic review and meta-analysis study

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General Note



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ABSTRACT

Background: Allergic rhinitis (AR) and migraine are two diseases with high rates in the population that can effect on quality of life. We aimed to assess the migraine frequency in patients with AR compared with controls in a meta-analysis study. **Materials and Methods:** Four databases including PubMed, Web of Science, Scopus, and Cochrane Library were searched up to January 2018. A random-effects meta-analysis was used by Review Manager 5.3 using odds ratio (OR) and 95% confidence intervals. **Results:** Out of 310 studies found in data based, 5 studies were included and analyzed in meta-analysis study. The pooled OR reporting the prevalence of migraine in patients was compared with controls was 3.83 (65%CI: 2.40, 6.11; $P < 0.00001$). The pooled OR reporting the prevalence of migraine with aura and without aura in patients compared with controls was 4.35 (65%CI: 3.34, 5.69; $P < 0.00001$), and 3.54 (65%CI: 2.110, 5.94; $P < 0.00001$), respectively. **Conclusion:** AR patients were at higher risk to develop the migraine compared with nAR subjects, suggesting that physicians need to pay more attention when complaints of the headache in the patients.

Keywords: Allergic rhinitis, migraine, prevalence

1. INTRODUCTION

Migraine [1,2] and allergic rhinitis (AR) [1] have adverse consequences for quality of life. The prevalence of AR ranges from approximately 10% of the USA population to as high as 30% among adults and 40% among children [3]. Patients with AR often have complaints of fatigue, irritability, mood swings, and cognitive disturbances [4]. The migraine can begin in childhood and increase in the prevalence of 3% in young children to 15% in adolescents [5]. Migraine prevalence is approximately 35 to 50% among AR patients; this high rate causes in frequent AR patient referrals to neurology clinics with headaches that are treated unsuccessfully [6,7]. The migraine is a neurovascular pain syndrome [8], which includes alteration of brain excitability, sensitization of the trigeminovascular system, intracranial arterial dilatation, and neurogenic inflammation in genetically susceptible subjects [9]. The migraine was frequently accompanied by sinus-associated symptoms, such as a runny nose, congestion, and ocular symptoms [10]. The migraine and AR may occur with a sinus headache, nasal congestion, and lacrimation and may worsen with weather changes and exposure to allergens [11]. Therefore, the proper diagnosis and treatment of headache patients should be a priority [11]. With respect to almost same pathogenic mechanisms in AR and migraine, we aimed to assess the migraine frequency in patients with AR compared with non-allergic rhinitis (nAR) in a meta-analysis study.

2. MATERIALS AND METHODS

Search strategies & Study selection

A comprehensive search was done using databases of PubMed, Web of Science, Scopus, and Cochrane Library up to January 2018. We searched the databases by a combination of terms "allergic rhinitis" and "migraine. The studies were selected for assessment of the prevalence of migraine in the patients with AR compared with the nAR (controls) in English abstract. The studies included in the meta-analysis had to: (I) use a case-control design; (II) report the number of patients with the migraine in AR and nAR subjects.

Data extraction

One author (M.S) searched and two authors (R.F & H.R.M) reviewed independently the articles for relevant publications. The data extracted for each study was the first author's name, the year of publication, the country which the study was conducted, type of the study, the mean age/male (%) of the AR patients and controls, the number of the AR patients and controls.

Statistical analysis

To evaluate the prevalence of migraine in AR patients compared with controls, a random-effects meta-analysis was used by Review Manager 5.3 (RevMan 5.3, The Cochrane Collaboration, Oxford, United Kingdom) using odds ratio (OR) and 95% confidence intervals (CIs). Heterogeneity among studies was evaluated with the Q and the I^2 statistic and results were defined as heterogeneous for $P < 0.10$ or $I^2 > 50\%$ [12] and P -value (2-sided) < 0.05 was considered statistically significant in this meta-analysis. In addition, the publication bias was evaluated by funnel plot with Begg's and Egger's tests [13].

3. RESULTS

Search strategy

Out of 310 studies found in data based, after removing duplicate studies, 236 studies were screened that 225 studies were excluded because they were not relevant (Figure 1). After that, 11 studies were evaluated that 6 studies were excluded with reasons. At last, 5 studies were included and analyzed in meta-analysis study.

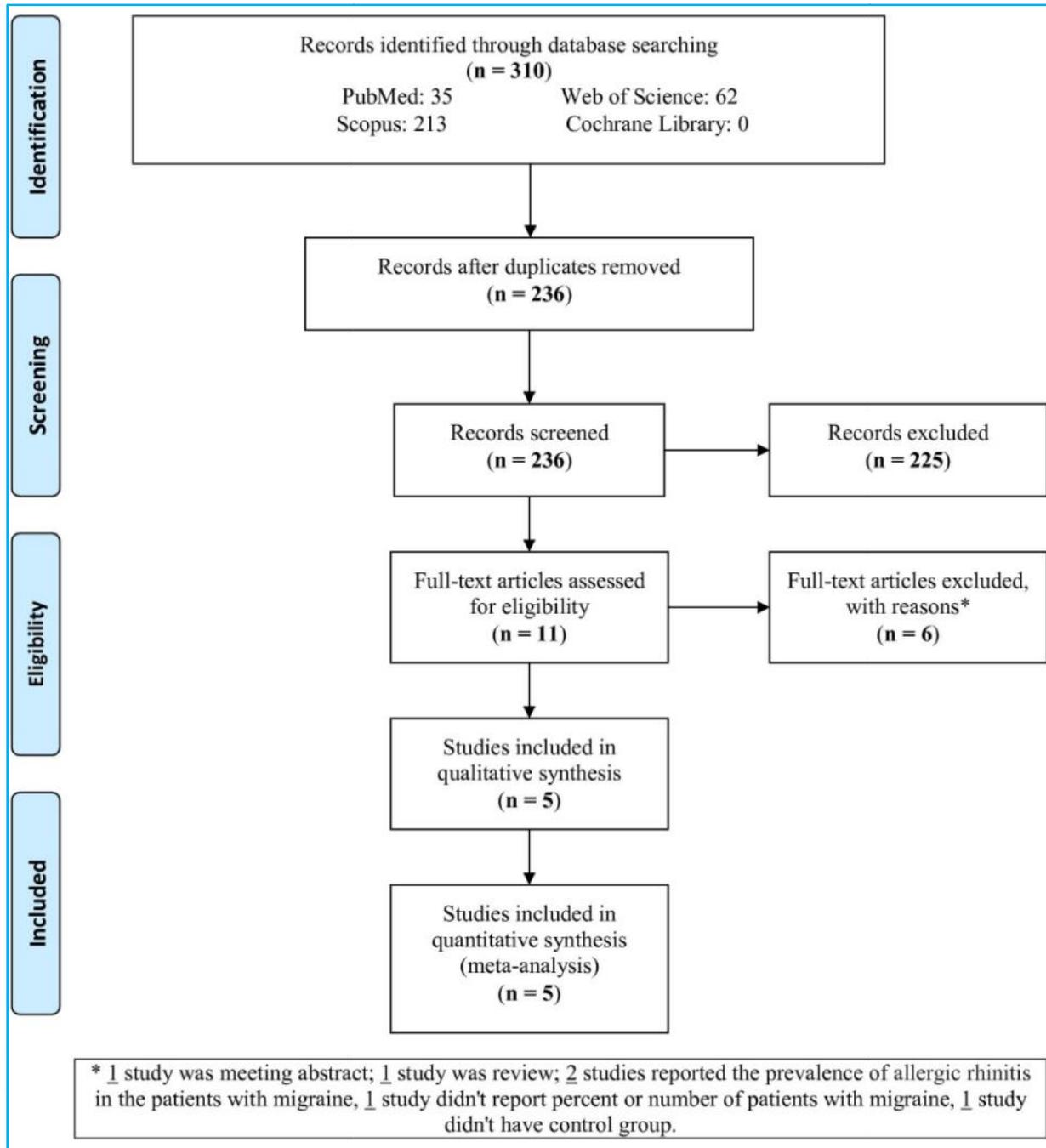


Figure 1 Flowchart of the study

Characteristics of the studies

The characteristics of five studies included in meta-analysis have been shown in Table 1. One study was reported in the USA [7], one in Iran [14], one Turkey [4], one in Taiwan [15], and one in Sweden [16]. Four studies were case-control study [4,7,14,15] and one study was nested case-cohort [16]. The number of patients was 462350 and controls 463788. The mean age and percent of males in two groups are other variables in Table 1.

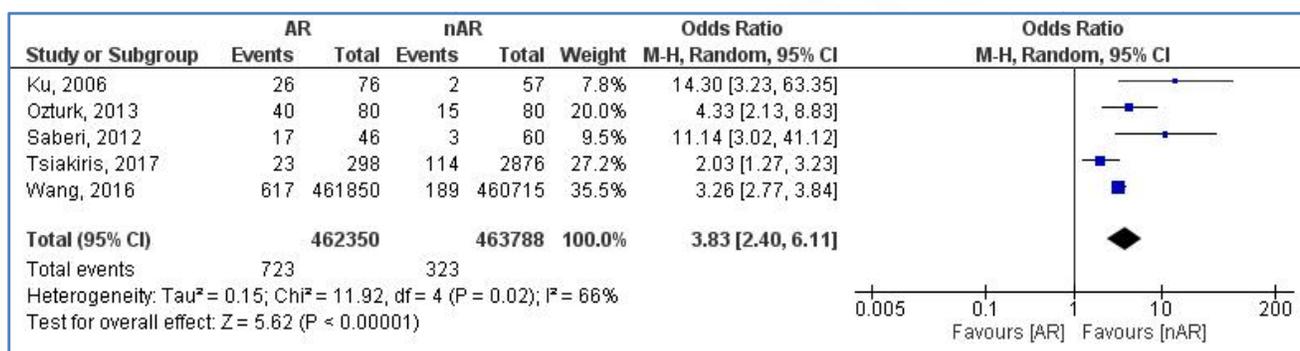
Table 1 The characteristics of the studies included with AR patients and nAR or controls (n=5)

The first author, year	Country	Type of study	Number of AR subjects	Number of nAR subjects	Mean age(year)/male % of AR subjects	Mean age (year)/male % of nAR subjects
Ku, 2006 [7]	USA	Case-control	76	57	40/21	45/23
Saberi, 2012 [14]	Iran	Case-control	46	60	31.2/30.4	37.6/38.3
Ozturk, 2013 [4]	Turkey	Case-control	80	80	32.3/37.5	34.1/42.5
Wang, 2016 [15]	Taiwan	Case-control	461850	460718	6.1/59.1	6.1/59.2
Tsiakiris, 2017 [16]	Sweden	Case-cohort	298	2876	47/45	51.7/44.6

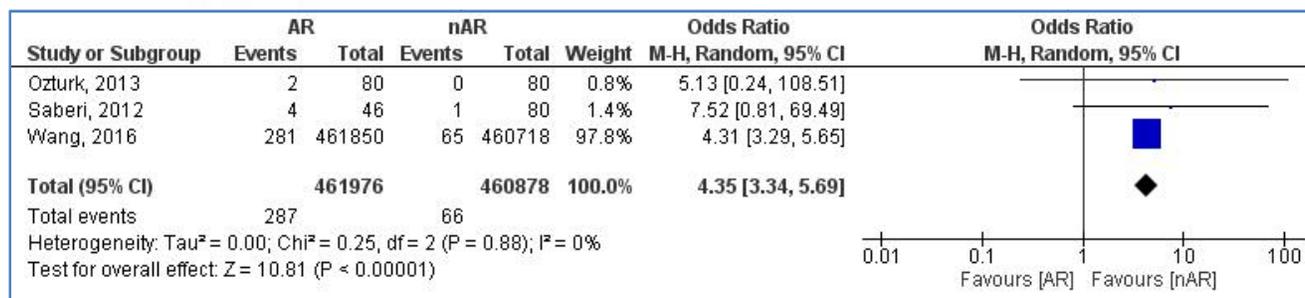
Abbreviations: AR, allergic rhinitis; nAR, non-allergic rhinitis.

The prevalence of migraine in patients of AR compared controls has been shown in **Figure 2**. The pooled OR was 3.83 (65%CI: 2.40, 6.11; $P < 0.00001$) that the prevalence of migraine in patients was significantly higher than controls with $I^2 = 66%$ ($P = 0.02$).

Prevalence of migraine

**Figure 2** Forest plot of odds ratio of the prevalence of migraine in patients of allergic rhinitis (AR) compared with non-allergic rhinitis (nAR) or controls.

The prevalence of migraine with aura in patients of AR compared controls has been shown in Figure 3. The pooled OR was 4.35 (65%CI: 3.34, 5.69; $P < 0.00001$) that the prevalence of migraine with aura in patients was significantly higher than controls without heterogeneity ($I^2 = 0%$).

**Figure 3** Forest plot of odds ratio of the prevalence of migraine with aura in patients of allergic rhinitis (AR) compared with non-allergic rhinitis (nAR) or controls.

The prevalence of migraine without aura in patients of AR compared controls has been shown in Figure 4. The pooled OR was 3.54 (65%CI: 2.110, 5.94; $P < 0.00001$) that the prevalence of migraine in patients was significantly higher than controls with $I^2 = 47\%$ ($P = 0.15$).

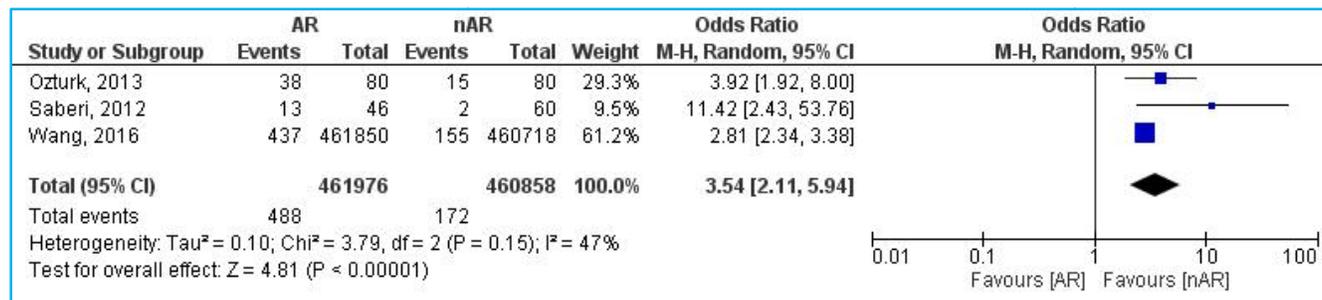


Figure 4 Forest plot of odds ratio of the prevalence of migraine without aura in patients of allergic rhinitis (AR) compared with non-allergic rhinitis (nAR) or controls.

Publication bias

Begg's and Egger's tests didn't reveal a significant evidence of publication bias among the included studies (Figures 5B, 5B, and 5C).

4. DISCUSSION

The meta-analysis study reported that the prevalence of migraine in patients was significantly higher than controls (around 4-fold) that migraine with aura was more than 4-fold, but the migraine without aura was around 3.5-fold. It is considered that the resetting of hypothalamic hormones plays an important role in the increased prevalence of migraine at puberty, [17] and alters the trigeminovascular system, which is the main neural pathway involved in the migraine [18]. AR is a chronic disease of seasonal and/or perennial course, determined by antibody immunoglobulin E (IgE)-mediated inflammation of the nasal mucosa, happened by allergens [4]. Serum IgE [4] and histamine levels [4,19] increased in migraine patients with and without allergy compared with healthy controls. Immune response determined with histamine and nitric oxide (NO) mediated inflammation is considered as the fundamental factor of AR pathogenesis [20]. Exposure to allergens in urban populations leads to increased migraine symptom frequency and severity, which is in accordance with our observation of an association between AR and migraine prevalence and intensity [2]. Calcitonin gene-related peptide and NO are other factors that play an important role in the pathophysiology of migraine [19]. Therefore, the existence of communication mechanisms between the migraine and AR may indicate that there is a close relationship between two diseases that the more prevalence of migraine in the AR patients compared with the controls in this meta-analysis could confirm it.

The migraine is a well-studied disorder that causes from the interaction of several genes with environmental events. Genomic regions that increase the individual risk to the migraine have been known in the neurological, vascular and hormonal pathways [21]. Many epidemiological studies have shown that environmental exposure to endotoxin may have a crucial role in the progression of tolerance to allergens found in natural environments [22]. The findings support the concept of lessening features of migraine over time resulting in a less prevalence of migraine in elderly patients [23]. Migraines due to AR are easily confused because the symptoms of both conditions often overlap [11]. Topical nasal corticosteroids may be important in the treatment and prevention of the migraines in AR patients and migraine headaches [7]. Therefore, the presence of several factors involved in the two diseases can indicate that the complete treatment of these diseases is very difficult or even impossible, but strategies such as awareness of the risk factors for any disease and the selection of best treatment for the AR patients with early signs of migraine by clinicians can reduce the severity and duration of them.

Limitation

1) The few studies. 2) Unmatched age between studies.

Strength

1) Low heterogeneity in meta-analysis. 2) Lack of bias

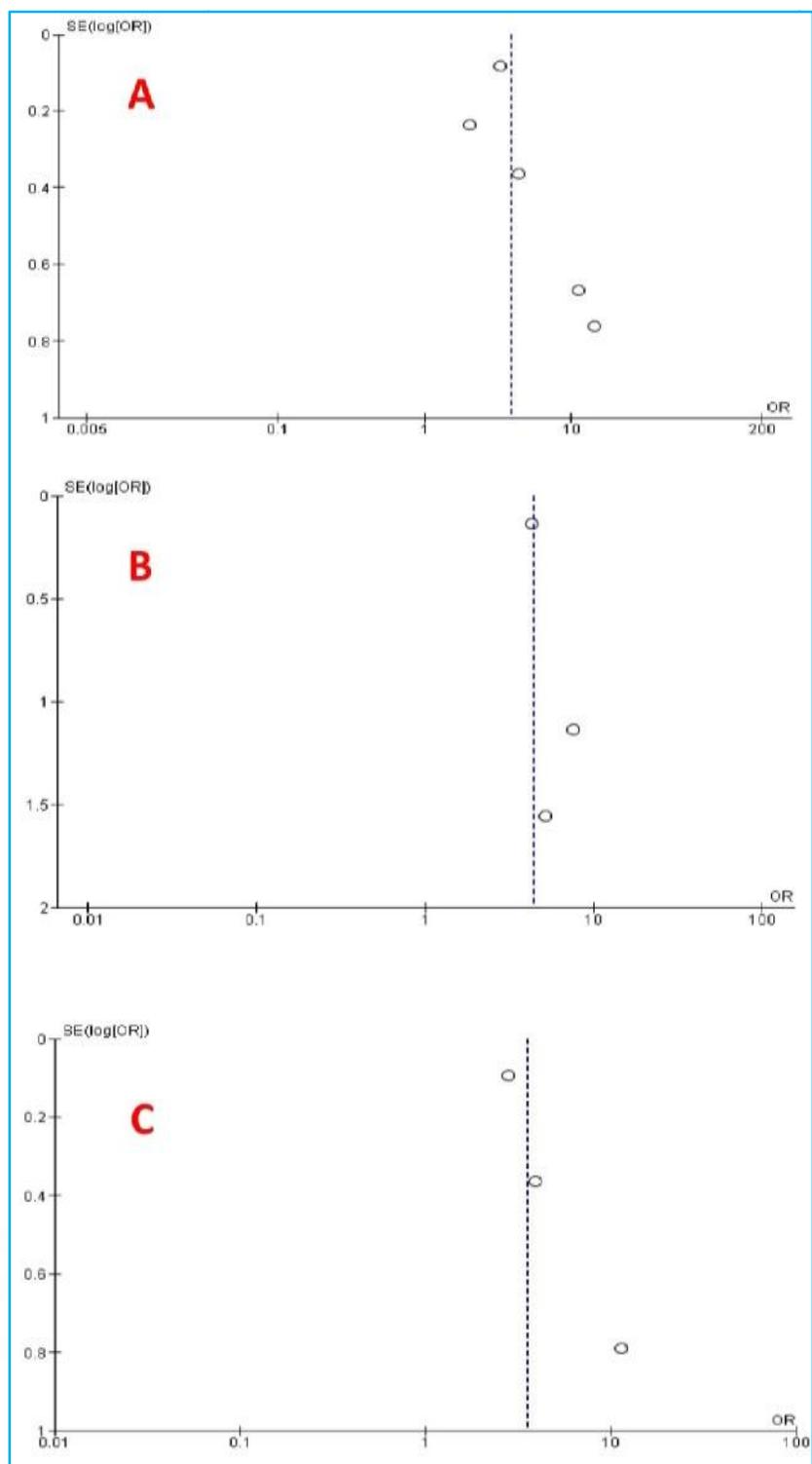


Figure 5 Funnel plot of the incidence of (A) migraine, (B) migraine with aura, and (C) migraine with aura in patients of allergic rhinitis compared with non-allergic rhinitis or controls.

5. CONCLUSION

Our study showed that AR patients were at higher risk to develop the migraine compared with nAR subjects, suggesting that physicians need to pay more attention when complains of headache in the patients. Therefore, the clinician must be aware of the possible presence of the migraine in the future follow-up of the patients so that an early and correct diagnosis and effective treatment can control complaints of the migraine.

CONFLICT OF INTEREST

The authors have declared that there was no conflict of interest.

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