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Review Article

**THE LINK BETWEEN ALLERGIC RHINITIS AND RHEUMATIC DISORDERS: FROM AVICENNA'S VIEW TO RECENT FINDINGS**Ali Reza Derakhshan<sup>1\*</sup>, Mahmood Khodadoost<sup>2</sup>, Mostafa Ghanei<sup>3</sup>, Sohrab Dehghan<sup>4</sup><sup>1</sup> Student Research Committee, School of Traditional Medicine, Department of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. ar.derakhshan@sbmu.ac.ir<sup>2</sup> School of Traditional Medicine, Department of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: mkhodadoost@sbmu.ac.ir<sup>3</sup> Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran. m.ghanei@bmsu.ac.ir.<sup>4</sup> Shahid Beheshti University of Medical Sciences, School of Traditional Medicine, Department of Traditional Medicine, Tehran, Iran. sohrabdehghan@yahoo.com**Abstract:**

Allergic rhinitis (AR) is one of the most prevalent allergic disorder across the globe which has significant socioeconomic costs. In addition to direct and indirect costs, the disease also has hidden direct costs related to comorbid conditions. AR can result in several complications such as pharyngitis, sinusitis, asthma, otitis media, eczema and lymphoid hypertrophy. Although associations between AR and other airway disorders have been investigated for years, less attention has been focused on the association of this disease with non-respiratory disorders. Considering the fact that AR is rarely found in isolation and reports of traditional Persian medical literatures on the relationship between rhinitis and joint disorders, this study aimed to investigate the link between AR and rheumatic disorders. In this regard, Avicenna's Canon of Medicine which was a well known medical textbook until 17<sup>th</sup> century was reviewed. Modern medical databases were searched as well. The results of this study showed that as mentioned in the teachings of Avicenna, allergic rhinitis may have association with some rheumatic disorders such as rheumatoid arthritis, low back pain and gout. Findings that support this hypothesis include the wide range of symptoms and complications of allergic rhinitis, emphasizing the association by prominent medical scholars of the past like Rhazes and Avicenna, studies found an association between AR or chronic rhinosinusitis with rheumatic diseases and common cytokines and inflammatory biomarkers that serve similar roles in both allergic rhinitis and rheumatic diseases like IL-4, IL-6, IL-8, IL-17 and TNF-alpha. It is suggested that studies be conducted with the main aim of investigating the relationship between these diseases and evaluating underlying mechanisms. The result of such research can be helpful in finding new treatment modalities in both groups.

**Keywords:** allergic rhinitis; rheumatic disorder; comorbidity, traditional medicine; Persian medicine; Avicenna**Corresponding author:**

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**INTRODUCTION:**

Allergic Rhinitis (AR) is one of the commonest allergic disorders affecting the world's population. It is inflammation of nasal mucosa which is characterized by rhinorrhea, nasal itching, sneezing and nasal congestion. These symptoms are mainly initiated by inhalant allergens(1). Current treatment modalities for AR are anti-histamines and corticosteroids(2). AR prevalence has been increasing during the past decades. Although usually it is not considered a serious disorder, its socioeconomic costs are significant(3).

AR costs is divided into two categories: direct costs which include disease management costs and indirect costs which is due to absenteeism and decreased productivity associated with AR(4). There are also hidden direct cost which is referred to costs due to comorbid conditions such as asthma, sinusitis and chronic otitis media. It has been shown that treatment costs in AR patients increase if they have concomitant asthma. On the other hand, costs of patients with asthma and associated AR were significantly higher than patients with asthma alone(4, 5).

AR can lead to fatigue, headache, cognitive impairment, sleep disturbance, and other systemic symptoms. In addition it is rarely found in isolation and it can result in numerous comorbid disorders such as pharyngitis, sinusitis, asthma, otitis media, eczema and lymphoid hypertrophy(6). Although associations between AR and other upper and lower airway diseases have been investigated for years, less attention has been focused on the association of this disease with rheumatic disorders (3).

In recent years, the use of complementary and alternative medicine in management of AR has increased. Persian medicine is a type of complementary and alternative medicine which has attracted the attention of researchers in recently(7). This system of medicine was founded in old Persia and flourished in Islamic lands(8). Ibn-Sina (Avicenna 980–1037 AD) was the most distinguished physician of Persian medicine, who had a major role in development of medical sciences. His master work, the *Canon of Medicine*, summarized and systematized medical knowledge of the time and also contained his own teachings which was taught in western universities until the 17<sup>th</sup> century(9, 10).

Due to high prevalence of AR and importance of comorbidities in predicting disease complications and costs and also lack of sufficient attention to non-respiratory comorbidities of AR, this study aimed to investigate the link between AR and rheumatic disorders. The hypothesis of this study is based on Ibn-Sina's teachings on rhinitis. In this regard, the authors

first reviewed the *Canon of Medicine* of Ibn-Sina. Then, databases including Pubmed and Google Scholar were searched as well in order to find related evidence on the link between rhinitis and rheumatic disorders.

**RESULTS:**

Ibn-Sina devoted a special chapter of his book to two diseases named *Zokam* and *Nazleh* in which he explained the physiopathology, symptoms, diagnosis and management of these diseases. The predominant symptom in *Zokam* is rhinitis and the main characteristic in *Nazleh* is catarrh. Ibn-Sina believed that *Zokam* and *Nazleh* can be considered as a same disease because they have a common origin and can transform to each other and if left untreated, they can surpass the nose, sinuses and throat and affect the whole body(11). Persian scholars have given great importance to *Zokam and Nazleh* and have considered this disease as "Mother of all diseases" and have highlighted its role in the development of various ailments(12).

The symptoms of AR in modern medicine are close to symptoms of a type of *Zokam* and *Nazleh* known as *warm Zokam* and *Nazleh*. According to Canon of medicine, some of the rheumatic disorders can be the result of persistence of *Zokam* and *Nazleh*(11, 13). In this book Ibn-Sina mentioned *Zokam* and *Nazleh* as a causative factor for development of some rheumatic diseases including arthritis, low back pain, sciatica and gout(13).

The link between AR and rheumatic diseases have been investigated in several studies. A cohort study of 170570 patients with age of 20 years and older diagnosed with allergic diseases, including asthma, AR, or atopic dermatitis found significant association between common allergic diseases and incident of rheumatoid arthritis. The authors conclude that AR and rheumatoid arthritis might share a common underlying etiologic pathway related to chronic inflammatory responses(14).

A population based study among 329 children with juvenile idiopathic arthritis (JIA) showed that children with onset of allergic diseases like allergic conjunctivitis, AR or asthma were at increased risk of developing JIA. The increased risk was associated with the cumulative effect of concurrent allergic diseases(15). Similar study among 344 adult JIA patients indicated that AR is the second most common comorbid condition after uveitis(16). Another study determined the coincidence of the major Th2-mediated atopic diseases; asthma, eczema and AR, with the Th1-mediated autoimmune conditions; type I diabetes, rheumatoid arthritis and psoriasis and concluded that

Th1- and Th2-mediated diseases are significantly associated in a large general practice population(17). Besides, two studies show that history of AR and low back pain are linked together(18, 19).

As we already know AR and chronic rhinosinusitis(CRS) are associated together and may represent a spectrum of the same disease entity through the concept of united allergic airways(20). On the other hand, despite the lack of research on the association of AR and gout, relation between CRS and gout have been discussed in two studies. Fu et al. in a study which was conducted in China to evaluate the effect of CRS on health-related quality of life indicated that individuals suffering from CRS showed an increased prevalence of AR, asthma and gout compared to individuals without CRS(21). Another study included a total of 10636 respondents indicated that individuals with history of COPD or gout were more susceptible to development of CRS compared to those without such history(22).

#### DISCUSSION:

Several studies found the relationship between some rheumatic disorders and AR or CRS. In this regard, it can be expected that untreated AR may play a causal role in development of these rheumatoid disorders. The evidence supporting this hypothesis is as follows:

- AR is not just a runny nose. It can lead to fatigue, headache, cognitive impairment, sleep disturbance, and other systemic symptoms(23).
- AR is rarely found in isolation. It has several comorbidities such as asthma, sinusitis, otitis media, lymphoid hypertrophy, eczema, atopic dermatitis, migraine and some psychiatric disorders. These comorbid condition are not limited to respiratory system and can affect other systems such as skin, skeletal and nervous system too(24-27).
- Several studies showed an association between AR and some rheumatic disorders such as arthritis, back pain and gout(14-22).
- Historical and traditional medicine literatures from prominent scholars of Persia like Rhazes and Avicenna have emphasized the relationship between rhinitis or sinusitis and some rheumatic disorders. The treatment plan of this disorders covers the treatment of rhinitis/sinusitis too(11, 28).
- Some biomarkers play the same role in AR and rheumatic disorders. For example, IL-4 and IL-17 have been linked to disease pathogenesis in AR and rheumatoid arthritis(29, 30). Furthermore therapeutic blockade of TNF- $\alpha$  improve clinical signs in both diseases(31, 32). IL-6, IL-8 and IL-18 are associated with inflammatory activity in AR

and gout(29, 33, 34). It has also been proven that patients with chronic low back pain due to disc herniation have higher levels of IL-6 and TNF- $\alpha$ (35). Besides, TNF- $\alpha$ , IL-6 and IL-17 are known as major contributor in intervertebral disc degeneration and related radicular pain(36). Taken these facts together, it seems that AR may share a similar mechanism in its inflammatory actions with these rheumatic disorders. Also, positive therapeutic effects of some drugs like quercetin which have been proven in RA and gout as well as AR, are consistent with this theory.

#### CONCLUSION:

Based on systemic symptoms of AR and several comorbidities associated with this disease and literature and articles which showed the association between AR and some rheumatic disorders, the authors of current study concluded that untreated AR may play a role as a predisposing factor for these rheumatic disorders. Avicenna has highlighted this relationship many centuries ago. Exploring the ideas of complementary and alternative medical systems especially eastern traditional systems of medicine which provide holistic view to human body in order to implementing these ideas in future clinical researches around the link between AR and non-respiratory disorders. From this perspective, the researchers of this study suggest conducting future studies on this topic with the main goal of identifying the exact relationship between AR and rheumatic disorders and underlying mechanisms. Also we suggest additional studies for exploring the other non-respiratory complications of AR.

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#### Conflict of Interest:

The authors declare that they have no conflict of interest.

#### Ethical approval:

This article does not contain any studies with human participants or animals performed by any of the authors.

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