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Allergies and Lung Cancer: Exploring the Association with Allergic Rhinitis

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ABSTRACT

Allergy and lung cancer are two distinct health concerns. While allergies are typically associated with heightened immune activity, such immune responses may also influence the tumor microenvironment. This study aimed to investigate a potential link between allergic conditions and the risk of lung cancer.

We conducted a case-control study analyzing 82 histologically confirmed lung cancer patients and 82 healthy controls from 2019 to 2022. Data were collected through structured questionnaires assessing asthma, allergic rhinitis (AR), food/drug allergies, and chronic urticaria. Statistical analyses included independent samples t-tests and chi-square tests, with significance set at a predetermined threshold.

We observed a significant inverse association between AR and lung cancer (8.54% vs 47.56% in controls; OR=0.14, 95% CI: 0.06–0.32). No significant associations were found for asthma (7.32% vs 3.66%), chronic urticaria (3.66% vs 3.66%), drug allergy (4.88% vs 1.22%), or food allergy (2.44% vs 6.10%). The association between AR and lung cancer remained robust after adjustment for demographic factors.

AR demonstrated a strong negative association with lung cancer, suggesting potential protective mechanisms distinct from other allergic conditions. These findings support the growing evidence for allergy-cancer immunomodulatory interactions and highlight the need for mechanistic studies on AR-specific pathways in oncogenesis.

Keywords: Allergic rhinitis; Asthma; Cancer immunology; Hypersensitivity; Lung cancer

INTRODUCTION

Lung cancer (LC) is the most frequently diagnosed cancer globally, with around 2.2 million new cases reported in 2020. It is the leading cause of cancer-related deaths, accounting for over 1.8 million fatalities annually.[1–4] LC is often linked to multiple risk factors, with smoking being the primary cause responsible for the majority of cases. Secondhand smoke exposure, environmental factors such as radon, asbestos, air pollution, and genetic predispositions, also contribute significantly to LC risk.[5,6]

Allergic diseases affect a considerable portion of the population, with estimates indicating that up to 30% of

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adults experience allergic conditions.[7] Allergies represent a spectrum of disorders characterized by exaggerated immune responses to otherwise harmless allergens. In allergic diseases, the immune response stimulates B cells to produce immunoglobulin E (IgE) antibodies specific to the allergen. Upon re-exposure to the same allergens, IgE binds to the allergen, forming an allergen-IgE complex that attaches to mast cells and basophils. This interaction triggers their degranulation and the release of various cytokines.[8]

The relationship between allergies and lung cancer is complex and sometimes contradictory. One hypothesis proposes that allergies may have a protective role against cancer, as certain IgE antibodies could exert cytotoxic effects on malignant cells.[9,10] Conversely, other hypotheses suggest that allergies may increase cancer risk through prolonged immune stimulation and chronic inflammation.[11,12] Chronic infections associated with allergies could lead to the production of free oxygen radicals, potentially encouraging oncogenesis.[13] Research focusing on asthma and chronic rhinosinusitis has indicated a possible association with an increased risk of lung cancer.[14,15] Additionally, some studies propose that while allergies may not have a direct link to lung cancer, they could influence the development of lung metastases in breast cancer patients.[16]

Although allergies and lung cancer are distinct health issues, their interactions, particularly through chronic inflammation, shared risk factors, and immune responses, warrant further investigation. This study aims to investigate the relationship between self-reported allergic diseases and lung cancer, utilizing data from a population-based study from 2019 to 2022.

MATERIALS AND METHODS

Study Design and Setting

Ethical approval for this study was obtained from the Research Ethics Committee of Shiraz University of Medical Sciences (Approval Code: IR.SUMS.REC.1403.584, Date: March, 2025). This case-control study utilized data from 435 lung cancer patients from 2019 to 2022.

Data Collection and Patient Eligibility

Initially, medical records of 435 patients with histologically confirmed lung cancer (2019–2022) were reviewed. Patients were included if they were alive at the time of recruitment, and had complete medical records. Patients were excluded if they had deceased before data collection (n=210), or declined/failed to respond to follow-up contact (n=143). After applying these criteria, 82 patients were eligible and included in the final analysis.

After identifying the included cases, healthy controls (n=82) were recruited from the community and consisted of unrelated volunteers with no history of any type of cancer by randomization. These individuals were matched to cases by ethnicity and geographic region. Controls were not recruited from hospital clinics to minimize potential selection bias. Only individuals who provided consent and completed the questionnaire were included.

A custom questionnaire was developed to gather demographic information, including age, sex, age at cancer diagnosis, and history of allergy in parents, education level, and parental consanguinity. This questionnaire was primarily based on the Global Allergy and Asthma Network of Excellence (GA2LEN) questionnaire and aimed to collect information about allergic rhinitis (AR), asthma, food allergies, drug allergies, and chronic spontaneous urticaria (CSU).[17]

A participant was considered to have AR if they reported one or more of the following symptoms on at least four consecutive days for a minimum of four weeks: sneezing, itching, nasal congestion, and rhinorrhea. Diagnosis for asthma was based on a positive response to the questions, “Have you ever had asthma?” along with at least one affirmative answer to the following questions: Have you had wheezing or whistling in your chest at any time in the last 12 months? Have you woken up with a feeling of tightness in your chest at any time in the last 12 months? Have you been woken by an attack of shortness of breath at any time in the last 12 months? Have you been woken by a flare-up of coughing at any time in the last 12 months? Have you had wheezing or whistling without cold? Diagnosis of food allergy and drug allergy was based on adverse reactions reported by the patient and confirmed by a physician based on the patient’s history. CSU was defined as the presence of wheals, angioedema, or both, accompanied by itchiness lasting more than six weeks.

We added additional questions regarding participants' smoking habits, including: whether the participant smokes, the average number of cigarettes smoked daily, whether the participant smokes cigarettes or uses a water pipe, and whether there is a smoker in participant’s the home.

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Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics (#). Normally distributed variables (age) were expressed as mean±standard deviation and compared using independent samples t-tests. Categorical variables were presented as frequencies and percentages and analyzed using Pearson's χ^2 tests or Fisher's exact tests when expected cell counts were <5. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated from 2×2 contingency tables.

RESULTS

Table 1 summarizes the demographic and clinical characteristics of lung cancer patients (n=82) and healthy controls (n=82). The mean age of lung cancer patients was 54.81±12.44 years, comparable to that of controls (51.63±13.10 years; p=0.07). The sex distribution was balanced between groups (51.22% male cases vs. 54.88% male controls; p=0.63). Significant differences were observed in education level, with a higher proportion of illiteracy (25.61% vs. 0%) and lower college attainment (19.51% vs. 85.36%) among cases (p<0.001). Parental allergy history was less frequent in lung cancer patients (13.41% vs. 42.68%; p < 0.001), while parental consanguinity showed no difference (p=0.73). Smoking status differed markedly: 36.59% of cases were active smokers versus 1.22% of controls (p<0.001), and 47.56% of cases reported secondhand smoke exposure (vs. 0% controls; p<0.001). Among smokers, cigarette use ranged from 5 to 100 per day, and four patients used water pipes daily.

Table 1. Characteristic data of patients with lung cancer and the control group

Characteristic data	Cases with lung cancer n=82	Healthy control n=82	*p*
Age, year Mean ± SD	54.81±12.44	51.63±13.10	0.07
Sex, no. (%)			0.63
Female	40 (48.78)	37 (45.12)	
Male	42 (51.22)	45 (54.88)	
Educational level, no. (%)			<0.001
Illiterate	21 (25.61)	0 (0)	
Under diploma	12 (14.61)	3 (3.67)	
Diploma	33 (40.24)	9 (10.97)	
College	16 (19.51)	70 (85.36)	
Parental allergy, no. (%)			<0.001
Yes	11 (13.41)	35 (42.68)	
No	71 (86.59)	47 (57.32)	
Parental consanguinity, no. (%)			0.73
Yes	25 (30.49)	27 (32.93)	
No	57 (69.51)	55 (67.07)	
Smoking in case, no. (%)			<0.001
Yes	30 (36.59)	1 (1.22)	
No	52 (63.41)	81 (98.78)	
Secondhand smoker, no. (%)			<0.001
Yes	39 (47.56)	0 (0)	
No	43 (52.44)	82 (100)	

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The prevalence of allergic conditions among lung cancer cases and healthy controls is presented in Table 2. A statistically significant inverse association was observed between AR and lung cancer status. Specifically, 7 of 82 lung cancer patients (8.54%) reported AR, compared with 39 of 82 controls (47.56%), yielding an unadjusted odds ratio of 0.14 (95% CI: 0.06–0.32; $p < 0.001$). Among AR-positive individuals, seasonal AR was more common (n=35) than perennial AR (n=11). Other allergic conditions showed no significant relationship with cancer status in this cohort. These findings suggest a potentially specific protective mechanism related to AR rather than a generalized allergy-cancer association.

Table 2. Allergy diseases in patients with lung cancer and the control group

Type of allergy	Cases with lung cancer n=82	Healthy control n=82	*p*
Asthma, no. (%)			0.30
Yes	6 (7.32)	3 (3.66)	
No	76 (92.68)	79 (96.34)	
Allergic rhinitis, no. (%)			<0.001
Yes	7 (8.54)	39 (47.56)	
No	75 (91.46)	43 (52.44)	
Chronic urticaria, no. (%)			1.00
Yes	3 (3.66)	3 (3.66)	
No	79 (96.34)	79 (96.34)	
Drug allergy, no. (%)			0.17
Yes	4 (4.88)	1 (1.22)	
No	78 (95.12)	81 (98.78)	
Food allergy, no. (%)			0.24
Yes	2 (2.44)	5 (6.10)	
No	80 (97.56)	77 (93.90)	

DISCUSSION

The relationship between lung cancer and allergic conditions remains a significant area of interest and investigation. Our study demonstrated a significant inverse association between AR and lung cancer. While, other allergic diseases did not differ significantly between the groups.

Several studies have suggested that individuals with a history of allergies may have a lower risk of developing lung cancer. A Canadian study by El-Zein et al reported that asthma, eczema, and AR are less likely to be associated with lung cancer, with AR showing the strongest inverse correlation. [18] A recent systematic review and meta-analysis covering seven studies(five from the United States and two from Canada and Germany) demonstrated a protective association between AR and lung cancer, reporting an OR of 0.55 (95% CI: 0.45–0.68; p value < 0.001).[19] This protective effect might be attributed to enhanced immune activity: allergies trigger an immune response that leads to increased production of certain antibodies (like IgE) and immune cells (like eosinophils). This heightened immune activity could help identify and destroy abnormal cells, potentially reducing cancer risks.[9,20] On the other hand, chronic inflammation associated with allergic conditions may create an environment that is hostile to cancer cell development.[21] Additionally, some genetic predisposition linked to allergic disorders may confer protective effects against the development of cancer.

The present study found no significant direct correlation between asthma and an increased risk of lung cancer. Although chronic inflammation is a shared

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feature, the specific pathways and outcomes differ. Asthma-related inflammation primarily affects airway function, whereas lung cancer involves complex cellular changes that lead to tumor development. Some evidence suggests that certain asthma medications, such as corticosteroids, may offer some protective effects against lung cancer, but this remains a topic of ongoing research.[22] Several studies have indicated a significant association between asthma and an increased risk of lung cancer, with a meta-analysis study suggesting that individuals with asthma might face a higher risk, potentially due to chronic inflammation or other underlying factors.[14,23,24] Future studies, extensive multicenter studies, should be conducted further to assess the association between asthma and lung cancer.

Other allergic diseases, including food allergy, drug allergy, and CSU, did not differ significantly between the groups in our study. Due to the low prevalence of these allergic conditions in our sample, no definitive conclusions can be drawn; larger multicenter studies are needed clarify these associations.

Low educational attainment is often associated with lower socioeconomic status, which can influence living conditions, nutrition, access to healthcare, preventive services, and overall health, thereby contributing to cancer risk. Targeted educational initiatives may help bridge the gap by providing resources and information to individuals at higher risk due to educational levels.

Allergic diseases often run in families. Genetic factors significantly contribute to the risk of developing allergic diseases. These findings suggest that genetic factors may play a role in the protective association between AR and lung cancer.

Lung cancer and smoking are closely linked, with tobacco use being a major global cause of the disease.[25] Tobacco smoke contains numerous harmful chemicals, including carcinogens that damage lung cells and lead to cancer development. The risk increases with greater exposure. Smoking is responsible for approximately 85% of all lung cancer cases worldwide; this rate in our patients with lung cancer was 65.9%. The lower rate in our study likely reflects the inclusion of only surviving patients with lung cancer.[26,27] When studying asthma or other respiratory conditions, it is crucial to control smoking status, as confounding by smoking can influence observed associations with lung cancer.

Beyond smoking, occupational exposures such as asbestos, silica, diesel exhaust, and other workplace carcinogens are well-recognized contributors to lung cancer risk. Although our study did not systematically capture occupational history, these exposures may act as potential confounders in interpreting the relationship between allergic conditions and lung cancer. Future research should incorporate detailed occupational exposure assessments to better clarify these interactions.

All patients were recruited from the Cancer Research Center as part of a retrospective study, which explains the high number of patients who have unfortunately passed away. Prospective research is needed to more fully elucidate the relationship between allergies and lung cancer. In prospective studies, we can measure IgE levels and various cytokines. This approach will enable a more comprehensive understanding of how allergies may impact lung cancer. One limitation of our study is the lack of comprehensive data on occupational exposures (e.g., asbestos, silica, and other carcinogens), which are established risk factors for lung cancer. This absence may have limited our ability to fully adjust for all relevant confounders.

In conclusion, this study suggests that AR may confer a protective effect against lung cancer. Understanding this interplay could provide novel insights into cancer prevention and immunotherapy strategies.

STATEMENT OF ETHICS

Ethical approval for this study was obtained from the Research Ethics Committee of Shiraz University of Medical Sciences (Approval Code: IR.SUMS.REC.1403.584, Date: March, 2025).

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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DATA AVAILABILITY

Data are available upon reasonable request (zkanannejad@gmail.com, mozhgan.moghtaderi96@gmail.com).

AI ASSISTANCE DISCLOSURE

Not applicable

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