RESEARCH ARTICLE

Editorial Process: Submission:02/04/2024 Acceptance:08/03/2024

The Association between Allergy and Cancer: A Case-Control Study

Mohammad Aryaie[1], Vahid Moazed[2], Ali-Akbar Haghdoost[3], Sima Saljughi[4], Andishe Hamedi[5], Zahra Jaafari[5], Reza Sadeghi[6], Hossein Mirshekarpour[7], Mitra Samareh-Fekri[8], Ahmad Naghibzadeh-Tahami[9]*

Abstract

Background: Allergies may either have a protective or a promoting effect on cancers. This study seeks to explore the relationship between various types of allergies and three specific cancer types: lung, breast, and colorectal cancer, thereby adding fresh insights to the existing scientific. **Methods:** Among the 556 patients, there were 115 cases of colorectal cancer, 305 cases of breast cancer, and 136 cases of lung cancer. The ratio of the case group to the control group was 1:1. We assessed the association between various variables, such as family history of allergy, allergies since the age of 10, pet allergies, seasonal flu, night and activity-related coughing, food allergies, itching or urticaria, childhood respiratory infections, and common colds, with the aforementioned cancers. The data were also analyzed using conditional logistic regression. **Results:** The results showed a protective association between itching or urticaria due to environmental factors and colorectal cancer (adjusted odds ratio [AOR]: 0.4, 95% CI: 0.17-0.94), as well as lung cancer (AOR: 0.26, 95% CI: 0.09-0.75). Additionally, a borderline association was observed between itching or urticaria and breast cancer (AOR: 0.54, 95% CI: 0.28-1.03). Allergy to pets also exhibited an inverse borderline association with breast cancer (AOR: 0.44, 95% CI: 0.18-1.05) and lung cancer (AOR: 0.25, 95% CI: 0.06-1.14). Furthermore, night coughing and allergies since the age of 10 were found to increase the odds of developing breast cancer (AOR: 2.38, 95% CI: 1.44-3.92; AOR: 5.10, 95% CI: 2.56-10.56, respectively) and lung cancer (AOR: 2.40, 95% CI: 1.29-4.46; AOR: 8.71, 95% CI: 3.29-23.03, respectively). **Conclusion:** allergies and cancer have a site-specific assciation . To confirm these findings and understand the reasons behind these associations, more investigation is required.

Keywords: Allergy- neoplasm- case-control- Iran

Asian Pac J Cancer Prev, **25 (8)**, 2787-2795

Introduction

Cancer is a significant leading cause of death globally. In 2018, there were 18.1 million new cases of cancer and 9.6 million reported deaths. Approximately one in five men and one in six women develop cancer during their lifetime, with one in eight men and one in eleven women ultimately succumbing to the disease [1, 2].

Various factors, including biological, lifestyle, and environmental influences, have been studied in relation to the development of cancer [3]. Immunoglobulin E (IgE)-mediated allergic diseases (hereon called allergies) are frequently reported, particularly in developed countries, and result in high morbidity and significant costs for healthcare systems [4, 5]. Previous studies have suggested a potential inverse association between allergies and cancer [6-8]. The most commonly reported allergies are atopic diseases, including allergic rhinitis, asthma, and eczema, as well as food allergies [9]. Currently, the association between allergy and oncology is of high interest. The European Academy of Allergy and Clinical Immunology (EAACI) has established a task force to better understand basic immune responses in both fields [10].

Given the high prevalence of allergies in the general population, their association with cancers has been noted.

*[1]Department of Primary Care and Public Health, School of Public Health, Imperial College London, London, UK. [2]Physiology Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran. [3]HIV/STI Surveillance Research Center, and WHO Collaborating Center for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. [4]Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran. [5]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran. [6]Sirjan School of Medical Sciences, Sirjan, Iran. [7]Nuclear Medicine Department of Shafa Hospital, Kerman University of medical Sciences and Health Services, Kerman, Iran. [8]Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences Kerman, Iran. [9]Health Services Management Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. *For Correspondence: anaghibzadeh61@gmail.com*

However, the relationship between allergies and cancer whether protective or promotinghas been controversial, giving rise to various hypotheses [4, 11]. In general, two distinct hypotheses have been proposed, First, the immune surveillance hypothesis suggests that allergies reflect an enhanced ability of the immune system to recognize and eliminate malignant cells. For example, an inverse association between asthma, allergies, or high serum IgE levels and cancer has been reported. Second, another hypothesis proposes that chronic inflammation, caused by long-term immune system stimulation, may be a factor. Persistent allergies may produce oxygen-free radicals that could promote carcinogenesis [12-14].

Despite this field's research, no study has shown that one hypothesis is superior to the other [15, 16]. Recent studies have revealed that the relationship between allergy and cancer varies depending on the type of cancer [17, 1]. On one hand, an inverse association between allergy and colorectal, pancreatic, and laryngeal cancers has been reported, so that the risk of these cancers is reduced in relation to allergies. On the other hand, a direct association between allergy and lymphoma, myeloma, prostate, breast, and lung cancers has been observed, this means that the risk of these cancers has increased in relation to allergies [14, 18-20]. This despite the fact that colorectal, breast, and lung cancers are common worldwide [21] and their association with allergy has been conflicting. For instance, a higher prevalence of allergic rhinitis has been reported among patients with breast and lung cancers compared to the general population, while the protective role of allergy in colon carcinogenesis has been suggested.

Moreover, the findings suggest that the relationship between allergy and cancer is influenced not only by the type of cancer but also by the type of allergic disorders [22].

Therefore, based on the existing contradictions and contravesies about the effect of allergy on cancer, the present study was conducted with the aim of investigating the effect of allergy on three cancers, including lung, breast, and colorectal cancers, in order to contribute new evidence to the scientific literature.

Materials and Methods

Subjects

Case selection

This research was a matched case-control study conducted between November 2017 and July 2018. Eligible cases included 556 Iranian patients aged 30 years and above, who were referred to Shahid Bahonar Hospital and Javad Al-Aimeh Clinic in Kerman City. These patients were diagnosed with breast, lung, and colorectal cancers within the past year and their diagnoses were confirmed by pathology.The exclusion criteria included lack of information, non-cooperation, and having cancers other than the desired types.

Control Selection

For each case, a healthy control was selected from among the companions of patients in wards other than oncology and emergency departments (with a 1:1 ratio of cases to controls). Individual matching was conducted based on age (±5 years) and gender between the case and control groups. Controls had no history of any type of cancer, and other exclusion criteria were similar to those of the case group. Using the cancer registry system to check the control information, we were able to determine that the controls had no history of cancer.

Primary analyses focused on history of allergies (irrespective of asthma) and any history of asthma (irrespective of allergies). In the baseline questionnaire, participants were asked if "a doctor ever told you that you have had, or have you ever been treated for hay fever, skin allergy, food allergy, or other allergy." Participants reporting "yes" were classified as having a history of allergies, while those who reported "no" were classified as having no history; those who refused to answer the question or reported "don't know" were classified as missing. Participants were also asked if "a doctor ever told you that you have had, or have you ever been treated for asthma." Participants who reported "yes" were classified as having a history of asthma, while those who reported "no" were classified as not having a history of asthma; those who refused or reported "don't know" were classified as missing.

Exposure, instruments and data collection procedures

A researcher-made checklist consisting of two sections was used to collect data. The first part of this checklist includes demographic variables such as age, gender, and education level. Exposure assessment was done based on questions from the patient, review of medical records and the patient's history of clinical symptoms that verified in accordance with ARIA recommendations [23]. Based on previous studies, the validity of asthma and allergy assessment using questions from patients has been confirmed [24].

So second part include of a question on a doctor ever telling you that you have had, or have you ever been treated for hay fever, skin allergy, food allergy, or other alleries (pet allergies, seasonal allergies, night and activity-related coughing, food allergies, itching or urticaria, childhood respiratory infections and common colds). Individuals who replied "yes" were categorized as having a history of allergies, "no" respondents were categorized as having no history, and "don't know" respondents were categorized as missing. furthormore, in order to increase validity and confirmation, the patient's medical documents were reviewed if available. Also the second part of the data collection form includes questions about person's lifestyle habits (alcohol consumption and cigarette smoking).

In order to reduce the inter-observer error observers all interviews were conducted by one trained interviewer. Also to reduce information bias (recall bias), interviewer assured the participants that all information gathered anonymously and data would be stored confidential. A family representative helped us fill out the in case of any problems.

Statistical analysis

Conditional logistic regression models were used to calculate the odds ratio (OR) and 95% confidence

interval (95% CI). Potential risk factors for cancer occurrence were considered in both crude and adjusted odds ratios (AORs) using a stepwise approach. All analyses were conducted using STATA (version 14.0, StataCorp). Statistical significance levels less than 0.05 were considered significant.

Results

In the present study, a total of 556 cases were included, comprising 115 patients with colorectal cancer, 305 patients with breast cancer, and 136 patients with lung cancer. Most participants in case group were men (71.54%), Controls and cases' mean age was 51.64± 13.26 and 52.24± 13.20 (P = 0.45). In the case group, most of the participants had an education level Under diploma (51.25%), while in the control group, they often had an education above the diploma (65.95%), and and had statistically significant differences (P < 0.001). Other demographic information about the cases and controls are presented in Table 1.

Among the cancer cases , 60 (57.14%) cases with colorectal cancer, 140 (59.32%) cases with breast cancer, and 47 (34.31%) cases with lung cancer had an education level of less than a diploma. This was compared to 45 (26.86%), 96 (40.68%), and 90 (56.69%) in their respective matched controls.

The number and percentage of allergy types according to the type of cancer are summarized in Tables 2-4

The crude and AORs between allergy and colorectal cancer are presented in Table 2. The crude odds ratio for seasonal cruise was 0.54 (95% confidence interval [CI]: 0.29-1.00), for active cough it was 0.41 (95% CI: 0.21-0.77), for food itching and urticaria it was 0.42 (95% CI: 0.21-0.86), and for matter itching and urticaria it was 0.31 (95% CI: 0.14-0.68). In the adjusted model, matter itching and urticaria (AOR: 0.40, 95% CI: 0.17-0.94), and active cough (AOR: 0.42, 95% CI: 0.21-0.84) were found to be significant.

Crude and AORs between allergy and breast cancer are shown in Table 3. The crude odds ratio for pet allergy was 0.28 (95% CI: 0.13-0.59), for childhood cold it was 0.56 (95% CI: 0.35-0.88), for food itching and urticaria it was 0.67 (95% CI: 0.46-0.98), and for matter itching and urticaria it was 0.51 (95% CI: 0.33-0.77). Furthermore, the crude odds ratio for night cough was 2.1 (95% CI: 1.37-3.22), and it was 1.46 (95% CI: 1.04-2.04) for a history of allergy since age 10. In multiple logistic models, night cough (AOR: 2.38, 95% CI: 1.44-3.92), and a history of allergy since age 10 (AOR: 5.11, 95% CI: 2.56-10.56) were significant. Moreover, the inverse association between food itching and urticaria (AOR: 0.54, 95% CI: 0.29-1.02), matter itching and urticaria (AOR: 0.54, 95% CI: 0.28-1.03), allergy to pets (AOR: 0.44, 95% CI: 0.18-1.05), seasonal cruise (AOR: 0.40, 95% CI: 0.21-0.76), and childhood colds (AOR: 0.56, 95% CI: 0.33-0.97) were borderline significant in multiple logistic regression.

Crude and AORs between allergy and lung cancer are shown in Table 4. The crude odds ratio for allergy since age 10 was 3.75 (95% CI: 1.98-7.09), for seasonal cruise it was 2.06 (95% CI: 1.14-3.75), for night cough it was 2.48 (95% CI: 1.56-3.95), and for active cough it was 2.04 (95% CI: 1.29-3.23). In adjusted model , allergy since age 10 (AOR: 8.71, 95% CI: 3.29-23.03), night cough (AOR: 2.40, 95% CI: 1.29-4.46), and matter itching and urticaria (adjusted OR: 0.26, 95% CI: 0.09-0.75) were found to be significant.

Discussion

In the present study, we investigated the association between different types of allergies and three common cancers: colorectal, breast, and lung. The odds of developing these cancers varied depending on the type of allergy, with some similarities observed among them.Our findings revealed an inverse association between different types of allergies and colorectal cancer. The adjusted odds ratio (AOR) of colorectal cancer was significantly lower in patients with matter itching and urticaria, as well as in those with active cough, compared to the control group. A study conducted in Western Australia in 2003, in Busselton, also illustrated a reduced risk of colorectal cancer among individuals with a history of allergies. Although the exact mechanisms by which immunological factors influence cancer risk are not yet fully understood, it is suggested that patients with allergies may experience a

Table 1. Demographic and Basic Characteristics Variables in Case and Control Groups

Variables	Cases N (%)	Controls N (%)	P-value*
Total	556	556	-
Age			
≤50	260 (46.7)	258 (46.4)	0.92
>50	296 (53.23)	298 (53.6)	
Mean ± SD	52.24± 13.20	51.64± 13.26	0.45
Gender			
Women	160 (28.8)	160 (28.8)	0.96
Men	396 (71.2)	396 (71.2)	
Education			
Under diploma	285 (51.25)	193 (34.7)	<0.001
Diploma & above	271(48.75)	363 (65.95)	

Table 2. Association between Allergies and Colorectal Cancer

Variables	Control (%)	Case (%)	Crude OR (95% CI)	A OR (95% CI)
Education				
< diploma	45 (26.86)	60 (57.14)	2.07 (1.09-3.92)	2.39 (1.18-4.84)
≥ diploma	70 (56.00)	55 (44.00)	Reference	Reference
Smoking				
No	94 (46.53)	108 (53.47)	Reference	-
Yes	21 (75.00)	7 (25.00)		-
Family history of allergy				
No	61 (46.92)	69 (53.08)	Reference	-
Yes	54 (54.00)	46 (46.00)	0.76 (0.46-1.27)	-
Pet allergy				
No	109 (48.88)	114 (51.12)	0.17 (0.02-1.38)	-
Yes	6 (85.71)	1 (14.29)		-
Allergy since age 10				
No	80 (49.38)	82 (50.62)	Reference	-
Yes	35 (51.47)	33 (48.53)	0.91 (0.51-1.65)	-
Seasonal cruise				
No	80 (46.24)	93 (53.76)	Reference	-
Yes	35 (61.40)	22 (38.60)	0.54 (0.29-1.00)	-
Night cough				
No	84 (48.28)	90 (51.72)	Reference	-
Yes	31 (55.36)	25 (44.64)	0.77 (0.43-1.38)	-
Activity cough				
No	72 (44.17)	91 (55.83)	Reference	Reference
Yes	43 (64.18)	24 (35.82)	0.41 (0.21-0.77)	0.42 (0.21-0.84)
Food itching or urticaria				
No	81 (45.76)	96 (54.24)	Reference	-
Yes	34 (64.15)	19 (35.85)	0.42 (0.21-0.86)	-
Matter itching or urticaria				
No	84 (45.16)	102 (54.84)	Reference	Reference
Yes	31 (70.45)	13 (29.55)	0.31 (0.14-0.68)	0.40 (0.17-0.94)
Childhood common cold				
No	92 (48.17)	99 (51.83)	Reference	-
Yes	23 (58.97)	16 (41.03)	0.65 (0.32-1.31)	-
Childhood respiratory infection				
No	98 (47.08)	107 (52.20)	Reference	-
Yes	17 (68.00)	8 (32.00)	0.40 (0.16-1.03)	-

general protective effect against cancer due to altered and modulated immune responses [25]. The observed inverse association in various studies could be a reflection of the immune system's ability to identify and remove cancer cells before being clinically apparent [26, 20].

Various studies have shown that high eosinophil and mast cell counts could predict better survival in patients with colon cancer. Additionally, in allergic patients, a precursor of mutagens bind to mucus and are eliminated before they can become mutagens, providing a plausible explanation for the observed effects in colon cancer tissues [20, 13]. The observed contradictory results in different studies could be attributed to factors such as varying allergic conditions, inconsistent definitions of allergy, and a lack of adjustment for certain confounding variables [20, 27]. In the present study, no significant association was found between allergy for 10 years and colorectal cancer. However, a study conducted by Negri and colleagues demonstrated that an early diagnosis of allergy history reduces the risk of colorectal cancer [28]. Not only the type of allergy but also the type of cancer could determine the direction and strength of the association between cancer and allergy.

In our study, allergies since age 10 and night cough increased the odds of breast cancer; however, pet allergies and food or matter itching and urticaria lowered the odds of breast cancer. Previous research has also shown a significantly increased risk of breast cancer among women

Table 3. Association between Allergies and Breast Cancer

Variables	Control (%)	Case (%)	Crude OR (95% CI)	A OR (95% CI)
Education				
< diploma	96 (40.68)	140 (59.32)	1.94 (1.36-2.75)	1.93 (1.30-2.86)
≥ diploma	209 (55.88)	165 (44.12)	Reference	Reference
Family history of allergy				
No	186 (48.56)	197 (51.44)	Reference	-
Yes	119 (52.42)	108 (47.58)	0.86 (0.62-1.19)	-
Pet allergy				
No	273 (47.98)	296 (52.02)	Reference	Reference
Yes	32 (78.05)	9 (21.95)	0.28 (0.13-0.59)	0.44 (0.18-1.05)
Allergy since age 10				
No	210 (53.30)	184 (46.70)	Reference	Reference
Yes	95 (43.98)	121 (56.02)	1.46 (1.04-2.04)	5.10 (2.56-10.56)
Seasonal cruise				
No	210 (49.18)	217 (50.82)	Reference	Reference
Yes	95 (51.91)	88 (48.09)	0.90 (0.63-1.27)	0.40 (0.21-0.76)
Night cough				
No	260 (53.50)	226 (46.50)	Reference	Reference
Yes	45 (36.29)	79 (63.71)	2.10 (1.37-3.22)	2.38 (1.44-3.92)
Activity cough				
No	237 (50.43)	233 (49.57)	Reference	-
Yes	68 (48.57)	72 (51.43)	1.08 (0.74-1.56)	-
Food itching or urticaria				
No	229 (47.71)	251 (52.29)	Reference	Reference
Yes	76 (58.46)	54 (41.54)	0.67 (0.46-0.98)	0.54 (0.29-1.02)
Matter itching or urticaria				
No	227 (46.71)	259 (53.29)	Reference	Reference
Yes	78 (62.90)	46 (37.10)	0.51 (0.33-0.77)	0.54 (0.28-1.03)
Childhood common cold				
No	249 (47.79)	272 (52.21)	Reference	Reference
Yes	56 (62.92)	33 (37.08)	0.56 (0.35-0.88)	0.56 (0.33-0.97)
Childhood respiratory infection				
No	266 (49.17)	275 (50.83)	Reference	-
Yes	39 (56.52)	30 (43.48)	0.74 (0.44-1.23)	-

with a history of allergies [11, 19, 29]. Previous studies have reported that epithelial cells in atopic dermatitis secrete high levels of thymic stromal lymphopoietin (TSLP), an interleukin-17 (IL-17)-like cytokine. TSLP activates the migration of dendritic cells (DCs) into draining lymph nodes, leading to the differentiation of naive T cells into inflammatory Th2 cells and the secretion of type 2 cytokines. Research has demonstrated that TSLP promotes human breast tumor growth by inducing inflammation and creating a conducive environment for the establishment, growth, and metastasis of primary breast cancer cells through Th2 polarization [11]. Another possible mechanism is that mast cells can contribute to carcinogenesis by releasing several factors involved in gene instability, extracellular matrix degradation (protease), and immunosuppression (TGF-β) [30].

Some other studies suggest that allergies could reduce the risk of breast cancer [31-33]. In the study conducted by Talbot-Smith and colleagues, no association between breast cancer and allergies was found [25]. The small number of patients and the failure to adjust for possible confounding factors could have led to different findings in various studies [34]. In addition, each study employed a different diagnostic approach to identify allergic patients, which included assessing patients' symptoms. These varying approaches may have different sensitivities in identifying allergies, thus potentially affecting the reported results [35]. It could be argued that allergic patients may be more inclined to adopt healthier lifestyles due to their conditions, which could potentially moderate their risk of cancer.

Our study also demonstrated lower odds of lung cancer in patients with pet allergies and matter itching and urticaria. While some studies have indicated an

Table 4. Association between Allergies and Lung Cancer

Variables	Control (%)	Case (%)	Crude OR (95% CI)	AOR (95% CI)
Education				
< diploma	90 (56.69)	47 (34.31)	3.69 (2.12-6.41)	3.84 (1.94-7.61)
≥ diploma	46 (34.07)	89 (65.93)	Reference	Reference
Smoking				
No	110 (56.70)	84 (43.30)	Reference	-
Yes	26 (33.33)	52 (66.67)	3.36 (1.72-6.59)	-
Family history of allergy				
No	79 (50.32)	78 (49.68)	Reference	-
Yes	57 (49.57)	58 (50.43)	1.03 (0.63-1.71)	-
Pet allergy				
No	123 (49.00)	128 (51.00)	Reference	Reference
Yes	12 (60.00)	8 (40.00)	0.67 (0.27-1.63)	0.25 (0.06-1.14)
Allergy since age 10				
No	107 (59.12)	74 (40.88)	Reference	Reference
Yes	29 (31.87)	62 (68.13)	3.75 (1.98-7.09)	8.71 (3.29-23.03)
Seasonal cruise				
No	110 (54.19)	93 (45.81)	Reference	-
Yes	26 (37.68)	43 (62.32)	2.06 (1.14-3.75)	-
Night cough				
No	96 (61.94)	59 (38.06)	Reference	Reference
Yes	39 (33.62)	77 (66.38)	2.48 (1.56-3.95)	2.40 (1.29-4-46)
Activity cough				
No	92 (58.97)	64 (41.03)	Reference	-
Yes	43 (37.39)	72 (62.61)	2.04 (1.29-3.23)	-
Food itching or urticaria				
No	95 (47.74)	104 (52.26)	Reference	-
Yes	40 (56.34)	31 (43.66)	0.71 (0.41-1.23)	-
Matter itching or urticaria				
No	101 (47.42)	112 (52.58)	Reference	Reference
Yes	34 (58.62)	24 (41.38)	0.62 (0.33-1.15)	0.26 (0.09-0.75)
Childhood common cold				
No	100 (50.51)	98 (49.49)	Reference	-
Yes	35 (47.95)	136 (50.18)	1.12 (0.65-1.92)	-
Childhood respiratory infection				
No	113 (59.90)	109 (49.10)	Reference	-
Yes	22 (44.90)	27 (55.10)	1.26 (0.69-2.31)	-

increased risk of lung cancer in patients with asthma, limited research has explored the relationship between lung cancer and other types of allergic conditions [22]. A study conducted in Montreal on men and women aged 35 to 75 years revealed an inverse association between allergy history and lung cancer, whereas our study found that allergy since age 10 and night cough increase the odds of lung cancer. Additionally, a study by Mariam El-Zein and colleagues found a distinct difference in the risk of developing lung cancer based on the onset of allergic disease before or after the age of 20, with no observed difference regarding the time elapsed since the onset of the allergic disease [36]. Another study showed a higher risk of lung cancer in patients with asthma, yet it revealed an inverse association with allergy, where in the role of IgE was discussed. The associated allergic symptoms linked to IgE may confer a protective function, facilitating the rapid clearance of pathogens, harmful natural toxins, and other carcinogenic antigens before they initiate malignant neoplasia in tissues [13]. In IgE-mediated allergies, elevated levels of IgE can bind to tumor-specific antigens, facilitating antibody-dependent cytotoxicity and antibody-dependent cellular phagocytosis mechanisms. Additionally, IgE can stimulate the production of reactive

oxygen metabolites and nitric oxide, which play crucial roles in tumor eradication [37].

In general, allergic diseases may be inversely associated with colorectal cancer, but IgE reactivity may have different effects on cancers, as evidenced by the increased odds of breast and lung cancers in our study. Deviation of the immune system towards T helper type 2 (Th2) cells may play a significant role. Unlike Th2 cells, Th1 cells produce pro-inflammatory cytokines and play a central role in immunity against infections, the elimination of cancer cells, and autoimmune disorders [38]. Imbalance in Th1/Th2 pathways is responsible for numerous immune disorders, including allergies. Since Th1 and Th2 cells can have inhibitory effects on each other, overactivation of one system may exacerbate or alleviate symptoms caused by the otherOne of the strengths of our study is the consideration of different types of allergies and cancers; however, it should be noted that we could not collect information about patients' treatment [11].

In summary, we observed lower odds of colorectal cancer in patients with matter itching or urticaria and active cough. Lower odds of breast cancer were detected in patients with pet allergy, night cough, food and matter itching or urticaria, as well as childhood common cold. Additionally, pet allergy and matter itching or urticaria were protective against lung cancer. However, night cough and allergies since age 10 increased the odds of both breast and lung cancers.

One of the most crucial challenges for any case-control study is selecting the optimal control group. Most researchers agree, there is no ideal control group in a case-control study, and researchers must carefully consider the representativeness of the control group, because a biased control group can lead to wrong results [39]. In this study, we selected hospital controls, despite the well-documented tendency for the use of hospital controls to weaken or obscure relationships [40, 41] ,but the majority of our results remained statistically significant.

Furthermore case-control studies are subject to recall bias, although this is unlikely to be a significant issue when studying allergies because the relationship between allergy and disease is not well known. Also We measured variables as binary, so there might be measurement errors which affects the results.

In conclusion, our findings showed that pet allergy reduces the odds of developing breast and lung cancers, whereas night coughing and allergies since age 10 increase the odds of developing this cancers. Furthermore, itching or urticaria due to environmental factors demonstrates a protective role against all three cancers colorectal, breast, and lung cancers.Generally allergies and cancer have a site-specific assciatio . To confirm these findings and understand the reasons behind these associations, more investigation is required.

Author Contribution Statement

Ahmad Naghibzadeh-Tahami and Mohammad Aryaie framed the study design and data analysis and prepared the initial manuscript. Mohammad Aryaie, Vahid Moazed and Ali-Akbar Haghdoost cleaned the data and conducted the statistical analyses and drafted the results. Hosein Mirshekarpour, Sima Saljughi, Andishe Hamedi, Zahra Jaafari, Reza Sdeghi and Mitra samareh Fekri contributed by consultation and facilitating the data collection and helped supervise the project. They also provided mentoring and assisted in the preparation of the manuscript. All authors read and approved the final version of the manuscript.

Acknowledgements

We would like to thank the Vice Chancellor for Treatment and Research of Kerman University of Medical Sciences, as well as the staff and patients of Bahonar Hospital and Javad Al-Aimeh Clinic in Kerman, for their necessary collaboration.

Statement of Ethics

Written informed consent was obtained from all subjects involved in the study, and the research was conducted following the principles of the Declaration of Helsinki. Additionally, the study protocol was approved by the ethical committee of Kerman University of Medical Sciences. The Ethics approval Code is IR.KMU.REC.1398.072.

Fundings

This study was partly funded by the Clinical Research Development Unit, Shafa Hospital of Kerman University of Medical Sciences (KUMS) through grant number 98000069. The funding bodies were not involved in the study design, study implementation, or writing the manuscript.

Availability of data and materials

The datasets generated and/or analyzed during the present study can be requested from the corresponding author upon reasonable inquiry.

Conflict of interest

The authors declare no potential conflicts of interest.

References

1. Salameh L, Mahboub B, Khamis A, Alsharhan M, Tirmazy SH, Dairi Y, et al. Asthma severity as a contributing factor to cancer incidence: A cohort study. PloS one. 2021;16(5):e0250430. https://doi.org/10.1371/journal.pone.0250430.
2. Turner MC, Chen Y, Krewski D, Ghadirian P. An overview of the association between allergy and cancer. Int J cancer. 2006;118(12):3124-32. https://doi.org/10.1002/ijc.21752.
3. Naghibzadeh-Tahami A, Khosravi Y, Es'haghi M, Haghdoost AA. Scoping review of 5 common occupational cancers and their related exposures. Med J Islam Repub Iran. 2022;36:84. https://doi.org/10.47176/mjiri.36.84.
4. Fereidouni M, Ferns GA, Bahrami A. Current status and perspectives regarding the association between allergic disorders and cancer. IUBMB life. 2020;72(7):1322-39. https://doi.org/10.1002/iub.2285.
5. Hendaus MA, Jomha FA, Ehlayel M. Allergic diseases among

children: Nutritional prevention and intervention. Ther Clin Risk Manag. 2016;12:361-72. https://doi.org/10.2147/tcrm.S98100.
6. Zhao H, Cai W, Su S, Zhi D, Lu J, Liu S. Allergic conditions reduce the risk of glioma: A meta-analysis based on 128,936 subjects. Tumour Biol. 2014;35(4):3875-80. https://doi.org/10.1007/s13277-013-1514-4.
7. Helby J, Bojesen SE, Nielsen SF, Nordestgaard BG. Ige and risk of cancer in 37 747 individuals from the general population. Ann Oncol. 2015;26(8):1784-90. https://doi.org/10.1093/annonc/mdv231.
8. Rittmeyer D, Lorentz A. Relationship between allergy and cancer: An overview. Int Arch Allergy Immunol. 2012;159(3):216-25. https://doi.org/10.1159/000338994.
9. Brown EM, Arrieta MC, Finlay BB. A fresh look at the hygiene hypothesis: How intestinal microbial exposure drives immune effector responses in atopic disease. Semin Immunol. 2013;25(5):378-87. https://doi.org/10.1016/j.smim.2013.09.003.
10. Jensen-Jarolim E, Bax HJ, Bianchini R, Capron M, Corrigan C, Castells M, et al. Allergooncology - the impact of allergy in oncology: Eaaci position paper. Allergy. 2017;72(6):866-87. https://doi.org/10.1111/all.13119.
11. Sadeghi F, Shirkhoda M. Allergy-related diseases and risk of breast cancer: The role of skewed immune system on this association. Allergy Rhinol. 2019;10:2152656719860820. https://doi.org/10.1177/2152656719860820.
12. Siemes C, Visser LE, Coebergh J-WW, Splinter TA, Witteman JC, Uitterlinden AG, et al. C-reactive protein levels, variation in the c-reactive protein gene, and cancer risk: The rotterdam study. J Clin Oncol. 2006;24(33):5216-22. https://doi.org/10.1200/JCO.2006.07.1381.
13. Sherman PW, Holland E, Sherman JS. Allergies: Their role in cancer prevention. Q Rev Biol. 2008;83(4):339-62. https://doi.org/10.1086/592850.
14. Josephs D, Spicer J, Corrigan C, Gould H, Karagiannis S. Epidemiological associations of allergy, ige and cancer. Clin Exp Allergy. 2013;43(10):1110-23. https://doi.org/10.1111/cea.12178.
15. Arana A, Wentworth C, Fernández-Vidaurre C, Schlienger R, Conde E, Arellano F. Incidence of cancer in the general population and in patients with or without atopic dermatitis in the uk. Br J Dermatol. 2010;163(5):1036-43. https://doi.org/10.1111/j.1365-2133.2010.09887.x.
16. Heikkilä K, Harris R, Lowe G, Rumley A, Yarnell J, Gallacher J, et al. Associations of circulating c-reactive protein and interleukin-6 with cancer risk: Findings from two prospective cohorts and a meta-analysis. Cancer causes control. 2009;20(1):15-26. https://doi.org/10.1007/s10552-008-9212-z.
17. Vojtechova P, Martin RM. The association of atopic diseases with breast, prostate, and colorectal cancers: A meta-analysis. Cancer Causes Control. 2009;20(7):1091-105. https://doi.org/10.1007/s10552-009-9334-y.
18. Olson SH, Hsu M, Satagopan JM, Maisonneuve P, Silverman DT, Lucenteforte E, et al. Allergies and risk of pancreatic cancer: A pooled analysis from the pancreatic cancer case-control consortium. Am J Epidemiol. 2013;178(5):691-700. https://doi.org/10.1093/aje/kwt052.
19. Wang H, Rothenbacher D, Löw M, Stegmaier C, Brenner H, Diepgen TL. Atopic diseases, immunoglobulin e and risk of cancer of the prostate, breast, lung and colorectum. Int J cancer. 2006;119(3):695-701. https://doi.org/doi.org/10.1002/ijc.21883.
20. Prizment AE, Folsom AR, Cerhan JR, Flood A, Ross JA, Anderson KE. History of allergy and reduced incidence of colorectal cancer, iowa women's health study. Cancer Epidemiol Biomarkers Prev. 2007;16(11):2357-62. https://doi.org/10.1158/1055-9965.EPI-07-0468.
21. Pilleron S, Soto-Perez-de-Celis E, Vignat J, Ferlay J, Soerjomataram I, Bray F, et al. Estimated global cancer incidence in the oldest adults in 2018 and projections to 2050. Int J cancer. 2021;148(3):601-8. https://doi.org/10.1002/ijc.33232.
22. Cui Y, Hill AW. Atopy and specific cancer sites: A review of epidemiological studies. Clin Rev Allergy Immunol. 2016;51(3):338-52. https://doi.org/10.1007/s12016-016-8559-2.
23. Klimek L, Bachert C, Pfaar O, Becker S, Bieber T, Brehler R, et al. Aria guideline 2019: Treatment of allergic rhinitis in the german health system. Allergol Select. 2019;3(1):22-50. https://doi.org/10.5414/alx02120e.
24. Kantor ED, Hsu M, Du M, Signorello LB. Allergies and asthma in relation to cancer risk. Cancer Epidemiol Biomarkers Prev. 2019;28(8):1395-403. https://doi.org/10.1158/1055-9965.Epi-18-1330.
25. Talbot-Smith A, Fritschi L, Divitini ML, Mallon DF, Knuiman MW. Allergy, atopy, and cancer: A prospective study of the 1981 busselton cohort. Am J Epidemiol. 2003;157(7):606-12. https://doi.org/10.1093/aje/kwg020.
26. Tambe NA, Wilkens LR, Wan P, Stram DO, Gilliland F, Park SL, et al. Atopic allergic conditions and colorectal cancer risk in the multiethnic cohort study. Am J Epidemiol. 2015;181(11):889-97. https://doi.org/10.1093/aje/kwu361.
27. Wang H, Diepgen T. Is atopy a protective or a risk factor for cancer? A review of epidemiological studies. Allergy. 2005;60(9):1098-111. https://doi.org/10.1111/j.1398-9995.2005.00813.x.
28. Negri E, Bosetti C, La Vecchia C, Levi F, Tomei F, Franceschi S. Allergy and other selected diseases and risk of colorectal cancer. Eur J Cancer. 1999;35(13):1838-41. https://doi.org/10.1016/s0959-8049(99)00209-9.
29. Petridou E, Chavelas C, Dikalioti S, Dessypris N, Terzidis A, Nikoulis D, et al. Breast cancer risk in relation to most prevalent ige specific antibodies: A case control study in greece. Anticancer Res. 2007;27(3B):1709-13.
30. Varricchi G, Galdiero MR, Loffredo S, Marone G, Iannone R, Marone G, et al. Are mast cells masters in cancer? Front Immunol. 2017;8:424. https://doi.org/10.3389/fimmu.2017.00424.
31. Hedderson MM, Malone KE, Daling JR, White E. Allergy and risk of breast cancer among young women (united states). Cancer Causes Control. 2003;14(7):619-26. https://doi.org/10.1023/a:1025686913626.
32. Lowcock EC, Cotterchio M, Ahmad N. Association between allergies, asthma, and breast cancer risk among women in ontario, canada. Cancer Causes Control. 2013;24(5):1053-6. https://doi.org/10.1007/s10552-013-0177-1.
33. Engkilde K, Thyssen JP, Menné T, Johansen JD. Association between cancer and contact allergy: A linkage study. BMJ open. 2011;1(1):e000084. https://doi.org/10.1136/bmjopen-2011-000084.
34. Krishnamachari B, Il'yasova D, Scheurer ME, Bondy M, Zhou R, Wrensch M, et al. A pooled multisite analysis of the effects of atopic medical conditions in glioma risk in different ethnic groups. Ann Epidemiol. 2015;25(4):270-4. https://doi.org/10.1016/j.annepidem.2014.12.007.
35. Merrill RM, Isakson RT, Beck RE. The association between allergies and cancer: What is currently known? Ann Allergy Asthma Immunol. 2007;99(2):102-17. https://doi.org/10.1016/S1081-1206(10)60632-1.
36. El-Zein M, Parent M-E, Siemiatycki J, Rousseau M-C. History of allergic diseases and lung cancer risk. Ann Allergy Asthma Immunol. 2014;112(3):230-6. https://doi.

org/10.1016/j.anai.2013.12.021.
37. Di Gioacchino M, Della Valle L, Allegra A, Pioggia G, Gangemi S. Allergooncology: Role of immune cells and immune proteins. Clin Transl Allergy. 2022;12(3):e12133. https://doi.org/10.1002/clt2.12133.
38. Karim AF, Westenberg LEH, Eurelings LEM, Otten R, Gerth van Wijk R. The association between allergic diseases and cancer: A systematic review of the literature. Neth J Med. 2019;77(2):42-66.
39. Wacholder S, McLaughlin JK, Silverman DT, Mandel JS. Selection of controls in case-control studies. I. Principles. Am J Epidemiol. 1992;135(9):1019-28. https://doi.org/10.1093/oxfordjournals.aje.a116396.
40. Mohebbi E, Rashidian H, Naghibzadeh Tahami A, Haghdoost AA, Rahimi-Movaghar A, Seyyedsalehi MS, et al. Opium use reporting error in case-control studies: Neighborhood controls versus hospital visitor controls. Med J Islam Repub Iran. 2021;35:60. https://doi.org/10.47176/mjiri.35.60.
41. Shakeri R, Kamangar F, Nasrollahzadeh D, Nouraie M, Khademi H, Etemadi A, et al. Is opium a real risk factor for esophageal cancer or just a methodological artifact? Hospital and neighborhood controls in case-control studies. PLoS One. 2012;7(3):e32711. https://doi.org/10.1371/journal.pone.0032711.