

ORIGINAL ARTICLE

Frequency of allergy among patients with solid tumors

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ABSTRACT

Key words:

AllergoOncology, Allergy, Solid tumors

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Background: Since the introduction of the AllergoOncology term that investigates the relationship between allergy and cancer diseases, this relationship has gained intense interest. Additionally individual molecules that play key role in the allergic conditions had gain attention. However, researches had led to conflict results. **Objective:** The aim of this work is to find out the relation between the allergy and solid cancer. **Methodology:** This study included 50 cancer patients suffered from solid tumors and 50 healthy controls. Cancer was diagnosed and staged according to the NCCN guidelines. We diagnosed allergic conditions according to the international guidelines. To determine allergen sensitization, we performed skin prick testing (SPT) and measured serum-Specific IgE whenever SPT could not be preformed. **Results:** The incidence of allergy in control group was significantly higher than that in the patient group groups ($P=0.009$). Odds ratios between allergy and cancer specific site were insignificant. **Conclusion:** Allergy may be protective against solid tumors. However, no specific relation between allergy and cancer specific site has been detected.

INTRODUCTION

The term AllergoOncology officially rose in 2006 to address the field considered with studying the significance of IgE mediated allergic immune responses against tumors aiming to identify IgE-based treatment options against tumors¹.

The suggested relation between allergy and tumor rose in 1950². Since then, several studies tried to elucidate the nature of the association between allergy and cancer. These studies yield conflict results³.

Theoretically, allergy and oncology may represent two opposite concepts: whereas immune tolerance is desired in allergy, it is fatal in cancer. Thus, allergy might be accompanied by enhanced immune surveillance, leading to better detection and destruction of malignant cells, consequently, a decreased risk of cancer. In contrast, an increased incidence of cancer may result from recurrent tissue inflammation in atopic patients, which could be linked to repeatedly damaged tissues. On this basis, four different hypotheses have been proposed: antigen stimulation or chronic inflammation hypothesis⁴; Immunosurveillance; prophylaxis hypothesis and inappropriate Th2 response hypothesis⁵.

The chronic inflammation or antigen stimulation hypotheses and the inappropriate biased Th2 response hypothesis supports that allergy sufferers are more prone to develop cancer. On the contrary, the immunosurveillance and the prophylaxis hypotheses predict that allergic patients are less likely to develop cancer⁵.

This study aimed to detect the frequency of allergic diseases in controls versus patients suffering from solid cancers and the possible role of serum total IgE and IL-10 with the occurrence of solid cancers.

METHODOLOGY

This case-control study was conducted in Allergy and Clinical Immunology Department, Faculty of Medicine, Ain-Shams University and Medical Oncology Department, Faculty of Medicine, Zagazig University Egypt. It included 50 cancer patients suffered from solid tumors and 50 healthy controls in the period from November 2018 to July 2019. The study was reviewed and approved by the Institutional Review Board of Faculty of Medicine, Ain Shams University and Faculty of Medicine, Zagazig University, Egypt.

The study included patients treated from solid tumors and ended their treatment at least one year ago to avoid the immunosuppressive effects of chemotherapy or radiotherapy and early diagnosed cancer patients before starting chemo or radiotherapy. We excluded patients receiving immunotherapy or anti-IgE (Omalizumab) treatment, patients with end-organ failure and patients with hematological malignancies.

Diagnosis of cancer:

Cancer diseases were diagnosed and staged according to the National Comprehensive Cancer Network (NCCN) guidelines for Detection, Prevention, & Risk Reduction⁶.

Diagnosis of allergy:

We diagnosed allergic rhinitis according to the AIRA guidelines⁷. Diagnosis of bronchial asthma was made according to the GINA guidelines⁸. Chronic urticaria was scored according to Urticaria activity score 7 (UAS7) adopted by European Academy of Allergology and Clinical immunology/ Global Asthma and Allergy European Network/ European Dermatology Forum/ World Allergy Organization (EAACI/GA²LEN/EDF/WAO) for the definition, classification, diagnosis, and management of urticaria⁹. Atopic dermatitis cases were diagnosed according to Hanifin and Rajka's Criteria for Atopic Dermatitis¹⁰.

Skin prick testing:

We performed Skin prick test (SPT) according to European Academy of Allergy and Clinical Immunology (EAACI) guidelines¹¹. Different Coca's extracted antigens were used. Allergens extract was prepared by extracting the desired allergen to a final 1:10 w/v in Coca's solution (5 gram sodium chloride, 2.5 gram sodium bicarbonate, 5 gram phenol crystals and water for injection to make 1000ml water). The battery of allergens used included: (*Dermatophagoid farina*, *Dermatophagoid pycnissis*, *Aspergillus*, *Penicillium notatum*, *Cladosporium*, *Alternaria*, Timothy grass, Rye/Mugwort, Cat epithelium, Cockroach, and Feather extract) for aero allergens, while for food allergens we used extracts of fish, egg, milk, nuts, strawberry, mango, peach, beans, meat and seafood¹².

Measuring Serum-Specific IgE:

Specific IgE was measured using AlleisaScreen Pannel 30 Resp EGY (**MEDIWISS Analytic GmbH, Germany**). A trough contains a positive control and 30 different allergens were processed according to the manufacturer instructions. For investigating food allergens, Alleisa Screen Pannel 30 Food EGY (**MEDIWISS Analytic GmbH, Germany**) was used.

Statistical Analysis:

We used the Statistical Package for the Social Sciences for Windows (version 21.0; SPSS Inc., Chicago, IL, USA). Data were expressed using descriptive statistics (median, mean \pm standard deviation) and were analyzed using Chisquare. We used Mann Whitney for comparing two or more independent samples for parametric samples. A P value

of <0.05 was considered significant, with a 95% confidence interval (CI).

RESULTS**Demographic data of the included individuals**

The study included 50 cases 15 males and 35 females with age range from 29 - 76 Mean \pm SD (53.74 \pm 13.92) and 50 controls with age range from 27 - 68. Mean \pm SD (49.12 \pm 13.19). There was no statistical significance difference between the two studied groups in age or gender distribution.

Distribution of cancer types among the cancer group

In the included cancer patients, 23cases (46%) suffered from breast cancer, 9 (18%) cancer colon, four cases (8%) prostatic cancer, three ovarian cancer patients (6%) and two for each of gastric carcinoma, lung, mesothelioma, and esophageal cancer while the study included only one case of each of Gastrointestinal stromal tumors (GIST), endometrial carcinoma, and soft tissue carcinoma (table 1).

Table 1: Frequency of different types of cancer among the case group

Type of cancer	Cases	
	No (50)	%
Breast cancer	23	46
Colorectal cancer	9	18
Endometrial	1	2
Gastric cancer	2	4
GIST*	1	2
Lung cancer	2	4
Mesothelioma	2	4
Oseophgeal cancer	2	4
Ovarian	3	6
Prostate Cancer	4	8
Soft tissue carcinoma	1	2

Frequency of allergy between cases group and control

According to our results, 21 (42%) of individuals in the control group suffered from allergy, while, only nine cancer patients (18%) did. The difference of the frequency of allergy between the two studied groups was statistically significant ($P=0.009^{**}$) (table2).

Table 2: Difference of frequency of allergy among the two studied groups

Variable	Cases (n=50)		Control (n=50)		χ^2	P
	No	%	No	%		
Total Allergic individuals	9	18	21	42	6.86	0.009**

χ^2 : Chi square test

** : Highly significant (<0.01)

Effect of allergy on the occurrence of site specific cancer

Calculation of Odds ratio between the frequency of allergy and the occurrence of cancer at different sites reveals that all odds ratios were below 1 however they were statistically insignificant all P values were below 0.05. Thus allergy cannot be considered as a protective agent against cancer (table3).

Table 3: Odds ratio of allergy and site specific cancer in different groups of cancer patients

Cancer specific site	Allergy		
	Odds ratio	95% Confidence interval	P
Breast cancer	0.35	0.08-1.62	0.17 NS
Colorectal cancer	0.72	0.12-1.23	0.72 NS
Other cancers	0.0812	.0100-0.6591	0.09 NS

NS: Non significant (P>0.05)

*: Significant (P<0.05)

This table shows that although all Odds ratios were below 1, allergy cannot be considered as a protective factor, as all Odds ratios were statistically insignificant at 95% confidence interval.

DISCUSSION

Different studies which tried to find out the definite relation between allergies and cancer, had led controversial and contradictory results^{13,14,15,16}.

The aim of this work is to find out the relation between the allergy and solid cancer

The study included 50 healthy individuals and 50 patients with different types of solid cancers. According to our results, the most commonly encountered allergic disorder was allergic rhinitis; this was supported by Penagos et al.¹⁷, who concluded that allergic rhinitis is the most common allergic disease in adults. Meanwhile, atopic dermatitis was last ranked, which is also expected as the prevalence of atopic dermatitis ranged from 2.1% to 4.9% across countries¹⁸.

According to these results, allergy affected 21 (42%) individuals of the control group while the number was only 9(18%) in the cancer patient group. Thus the incidence of allergy in control group was significantly higher than that in the patient group groups (P=.009)

This result was supported by Ma et al.¹⁹ who concluded that there is an inverse association between allergic conditions on the one side and colorectal cancer on the other side. Also, Kozłowska et al.²⁰ found that

patients with cancer had a slightly but significantly lower risk of IgE-mediated allergic diseases than those in the control population. The odds ratio of a clinical manifestation of any allergy (i.e., allergic rhinitis, conjunctivitis, atopic dermatitis, and bronchial asthma) in patients diagnosed with solid tumors was 0.76 (95 % CI 0.63–0.84) compared to non-cancer patients.

Also, our results were supported by a large cohort study done in the USA, followed 1.1 million patients of allergic rhinitis and asthma for 18 years. The study concluded that there is a significant inverse association between a history of both allergic rhinitis and asthma, and all cancer mortality²¹.

Additionally, Vena et al.² found that there is a stronger evidence for a decreased risk of cancer associated with a history of hives and other allergy-related diseases. Reduced risks associated with a history of hives and other allergies are seen in males with oral cancer, cancers of the lung, larynx, digestive system, urinary system, and cancers of all sites combined and in females with cancers of the digestive system, reproductive system, in particular, cancer of the cervix, and cancers of all sites combined. These findings suggest that individuals with allergy-related disorders may be at a decreased risk of cancer.

By contrast, a meta-analysis evaluated the association between atopic diseases and breast, prostate, and colorectal cancers, found no significant association between atopic diseases and cancer²².

Additionally, Skaaby et al.²³ supported this side and found no association between atopy and cancer prevalence. The study included approximately 15,000 Danish patients.

These differences can be attributed to the failure to define specific mechanisms that can describe the relationship between allergy and cancer. In the absence of the framework of these mechanisms, investigation of this relation couldn't be precise and couldn't lead to a definite conclusion. Additionally, a larger sample of cancer patients must be included, so an association between a particular type of allergy and specific kind of cancer could be possible. Collectively consider all types of allergic diseases, and all sorts of tumors may lead to conflicting results.

Odds ratios were calculated to define the effect of allergy on each cancer site. Odds ratios for three groups were (0.38, 0.46 and 0.09) respectively. Although all three Odds ratios were below 1, allergy cannot be considered as a protective factor for any cancer, as all Odds ratios were statistically insignificant at 95% confidence interval

Small sample size may be the cause behind this insignificance. In a study led by Hedderson et al.²⁴ they conclude that history of allergy was associated with a reduced risk of breast cancer for women who develop breast cancer between 35 and 45 years. Also, Turner et

al.²⁵ concluded that allergy might be protective against colorectal cancer. Furthermore, other authors found that there is a potential inverse association between allergic status and site-specific cancers, including pancreatic, glioma, and head and neck tumors. The magnitude of the effect ranged from approximately 30–40% reductions in risk^{26,27,28,29}.

On the other hand, other researchers showed that allergic conditions might increase the risk of prostate cancer, compared with the general population^{30,31}. Additionally, a meta-analysis suggested that asthma might be a risk factor for lung cancer³². This study didn't include any patient with pancreatic cancer and only two cases of lung cancer, so the relation of these site-specific cancers and allergy cannot be discussed here.

CONCLUSION

Finally, we conclude that allergy may be a protective factor against solid cancer, however we found no association between occurrence of allergy and tissue specific cancers. We therefore foresee the importance of similar studies including larger number of patient and stratify them regarding the site of cancer and also the cancer stage.

Conflict of interest:

- The authors declare that they have no financial or non financial conflicts of interest related to the work done in the manuscript.
- Each author listed in the manuscript had seen and approved the submission of this version of the manuscript and takes full responsibility for it.
- This article had not been published anywhere and is not currently under consideration by another journal or a publisher.

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