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Frequency of ragweed sensitization and allergy among patients with respiratory allergy

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Abstract

Pollen is well known to cause seasonal allergy. Ragweed sensitization and allergy represent a worldwide challenge for allergists. *Ambrosia* is one of the major genera in the *Asteraceae* family which includes at least 51 species known as "ragweed". The current study aimed at determining frequency of ragweed sensitization and allergy among patients with respiratory allergy. The study included 220 subjects selected from patients attended the Allergy Clinic, Ain Shams University. All patients were subjected to detailed medical history, clinical examination, asthma severity grading according to the Global Initiative for Asthma (GINA) guidelines, allergic rhinitis severity grading according to the allergic rhinitis and its impact on asthma (ARIA) guidelines, pulmonary function tests for asthmatic patients, complete blood count with differential for detection of eosinophilia, serum total IgE and skin prick testing (SPT) to ragweed pollen together with common inhalants and common food allergens. Specific IgE for *Ambrosia artemisiifolia* was done for patients who showed positive SPT to ragweed pollen. About 34% of patients had positive SPT to ragweed, 30.5% were sensitized to ragweed and 3.2% allergic. Specific IgE for *A. artemisiifolia* was positive in 33.8%. There was a statistically significant association between ragweed sensitization and level of asthma control and disease duration. We concluded that ragweed sensitization is less common as the frequency of *Ambrosia* pollen sensitization was about one third of the studied allergic patients.

Keywords: Allergic Rhinitis, Bronchial Asthma, Pollen, *Ambrosia*, Ragweed, Skin Prick Test, Specific IgE.

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Introduction

Respiratory allergies are chronic diseases with high social impact worldwide. [1] Epidemiological data has shown an increase in their incidence and prevalence. Specific clinical manifestations could be extremely unpleasant, affecting the patient's quality of life.[1]

Asthma is a heterogeneous, chronic inflammatory and obstructive lung disease which can be associated with many comorbidities in both children and adults.[2] The

phenotype of asthma including clinical features of the disease and their underlying mechanisms represent a host–environment interactions.[3]

Allergic rhinitis is the most common form of non-infectious rhinitis and is one of the most common chronic diseases globally.[4] It is characterized by rhinorrhea, nasal congestion, sneezing and nasal itching.[5] These symptoms have a significant impact on work activities.[6]
Pollen is well known to cause seasonal allergic respiratory diseases.[7] It is recognized that more than 150 pollen allergens play a significant role in an allergic process originating from weeds, grasses, and trees.[8]

Ambrosia is one of the major genera in the *Asteraceae* family which includes at least 51 species known as "ragweed". Ragweed pollen evokes allergic symptoms at low concentrations (about 10 pollen/m^3).[9] *Ambrosia* pollen can lead to type I hypersensitivity reactions in late summer and autumn. Ragweed pollen sensitization can result into respiratory diseases such as allergic rhinitis, asthma, allergic conjunctivitis, and less skin symptoms. High exposure to pollen or increased pollen concentration over a certain period of time results in high sensitization rate and symptoms.[10] Sensitization rates to ragweed were studied in many European countries and stated that Denmark was most heavily affected with a prevalence of 19.8%, and the prevalence in the Netherlands and Germany was 15.2% and 14.2%, respectively.[11]

Skin prick tests (SPT) and specific IgE detection using crude pollen extracts are currently performed in routine diagnosis. Allergen extracts however contain a variety of allergenic and non-allergenic components, and standardization of pollen extracts is difficult due to varying source material and product preparations.[8]

Molecular diagnosis using well-characterized purified allergen components from natural source or produced as recombinant molecules allows clinicians to obtain detailed information on sensitization profiles and thus supports improved patient's management.[12]

This study aimed at identifying the frequency of ragweed sensitization and allergy among patients with respiratory allergy.

Materials and Methods

The current cross-sectional study included 220 adult patients having allergic rhinitis, bronchial asthma, or both, and attending the allergy clinic at Ain Shams University hospitals during the period from October 2019 to October 2021.

Sample size calculation

Considering that the attendance rate of patients in the Allergy Clinic, Ain Shams University for 3 months was 532, and the prevalence rate of ragweed sensitization was 41%[13], the sample size was calculated to be 220 patients at a confidence level of 95%, effect size=1 and power of study 80%.

Inclusion criteria were patients above 16 years of age with seasonal symptoms. Diagnosis of asthma was made based on the Global Initiative for Asthma (GINA 2019 update) guidlines.[14] Diagnosis of allergic rhinitis was made according to the Allergic Rhinitis and its impact on asthma (ARIA) guidelines report (ARIA 2019 update).[15]

Exclusion criteria included patients with autoimmune diseases, pregnant and lactating females, patients on specific allergen immunotherapy, patients currently on oral antihistamines or any other drugs that inhibit the SPT reaction and patients with dermographism.

Patients included in the study were subjected to detailed allergic history, clinical examination, characterization according to age, gender, body mass index (BMI), residence, type of respiratory allergy, severity of allergy, duration of allergy and seasonal variation. Asthma severity was assessed according to the GINA Guidelines and Allergic Rhinitis severity was assessed according to ARIA Guidelines. Spirometry was performed to asthmatic patients.

SPT with standardized ragweed pollen was done in addition to common inhalants and cross-reactive food. Complete blood count for detection of eosinophilic count and serum total IgE were performed for all patients. Serum specific IgE to *A. artemisiifolia* was performed for patients with positive SPT to ragweed.

Assessment of pulmonary functions

Spirometry was performed at the Pulmonary Functions Laboratory at Ain Shams University Hospital, using the Flowmate V Plus spirometer (Spirometrics, Gray, ME, USA). Tests were completed while the patient was in the sitting position. The tests followed the criteria and standards of the European Respiratory Society (ERS) and the American Thoracic Society (ATS).[16] Evidence of variation in lung function or documentation of increased forced expiratory volume in 1 second (FEV1) greater than 12% during the bronchodilator reversibility test is diagnostic for asthma.[14]

Skin Prick Test

Antihistamines were discontinued for 5-7 days prior to testing. The skin was punctured using a calibrated lancet (1 mm) held vertically while introducing a drop of diluted purified allergen. Allergen extracts included Ragweed, Straw, Hay, Mites, Wool, Mixed Pollens, Profilins, *Alternaria*, *Artemisia*, Cockroach, House Dust, Horsehair, Mixed Molds, Rabbit, *Aspergillus*, Candida, Pigeon Feather, Tobacco, Cat, Dog, Grass, Latex, Aspirin, Penicillium, Peanuts, Maize, Egg, Milk, Wheat, Fish, Banana, Zucchini and Cucumber (Extracts were obtained from Omega, Canada – Allergy Overseas Consultants Inc., 82 Toor St, Port Said, Egypt). A drop of histamine (10 mg/ml) and saline solution were used as a positive and negative control, respectively. The maximum or mean diameter of the wheal to various allergens was read at 20 minutes. A wheal of 3 mm or more in diameter was considered positive, indicating sensitization to the allergen.[17]

Sensitization to ragweed was defined by a positive SPT with a wheal diameter of ≥3 mm and ragweed allergy was diagnosed on the concordance between a typical history of allergic seasonal symptoms and a positive SPT result to ragweed.

Laboratory investigations

Two venous blood samples (5 ml each) were obtained by venipuncture from each participant. The first sample was collected into a gel Vacutainer tube (Becton Dickinson, Oxford, UK). Blood was allowed to be clotted and serum was separated by centrifugation at 1200 g for 15 minutes at 25 °C. Separated sera were stored in aliquots at −20 °C until used for measurement of serum total IgE levels by an enzyme linked immunosorbent assay (ELISA) and specific IgE by an enzyme allegro-sorbent test (EAST). The second sample was collected on a K3EDTA Vacutainer tube (Becton Dickinson) for complete blood count (CBC) using a Coulter Counter (T660; Beckman Coulter, Brea, CA, USA).

Estimation of total IgE levels (IU/ml) was done using an ELISA kit (Catalog number: A0141, RIDASCREEN; R-Biopharm, Darmstadt, Germany) and performed according to the manufacturer's instructions. This procedure has a sensitivity of 1 IU/ml. The normal level of total IgE in adults is less than 100 IU/ml. In addition, detection of IgE (IU/ml) specific for *A. artemisiifolia* was performed by EAST (Catalog number: A0041, supplied by R-Biopharm, Germany). Specific IgE levels of 0.00-0.34 IU/ml were considered EAST class zero (0), 0.35-0.69 IU/ml were considered EAST class 1 (low), 0.70-3.49 IU/ml were considered EAST class 2 (increased), and 3.50-17.49 IU/ml were considered EAST class 3 (significantly increased).

Statistical analysis

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 20. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies and compared using chi square and Fisher exact test when appropriate. Kolmogorov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests were used to verify assumptions for use in parametric tests. To compare quantitative data between two groups, Mann Whitney test (for abnormally distributed data) and independent sample t test (for normally distributed data) were used. The level of statistical significance was set at $P<0.05$.

Results

The study included 220 patients with respiratory allergy (atopic asthma and allergic rhinitis). Out

of the 220 patients, 74 patients (33.6%) had positive SPT to ragweed. Of these, 67 patients (30.45%) were sensitized to ragweed and 7 patients (3.18%) were allergic to it (Figure 1).

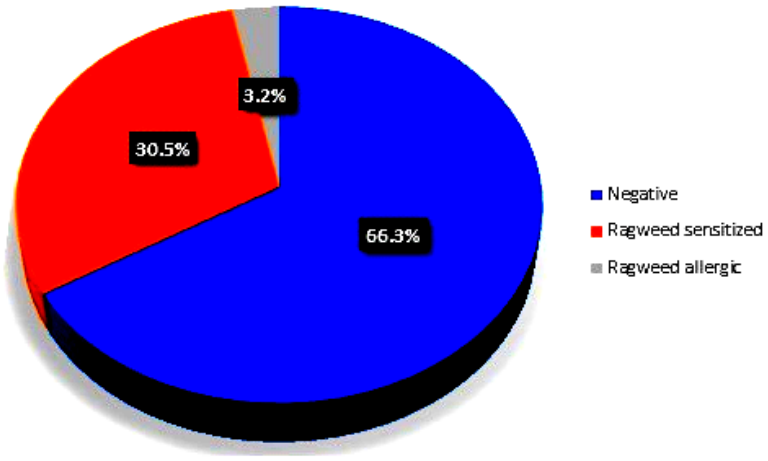

Figure 1. Pie chart showing distribution of patients with allergy and sensitization

The mean age of the 74 patients was 37.5 years. Males represented 51.4% of them. Larger percentage of patients had no special habits of medical importance. Of the studied patients, 40% had familial history of ragweed allergy (Table 1).

Of the studied patients, 90.5% had allergic rhinitis (AR), 17.6% bronchial asthma and 6.8% had both. The duration of the disease ranged from 3 to 38 years with a median of 13 years. Oral allergy syndrome (OAS) was illustrated in 16.2% of study patients (Table 1).

There was no relation between presence of ragweed allergy and either age, gender, residence, special habits, family history, presence of bronchial asthma, allergic rhinitis, or both. Yet, disease duration was significantly higher in those with ragweed sensitization and allergy (Table 1, Figure 2).

Table 1. Demographic data and characteristics of ragweed patients.

Parameter	Total	Ragweed		*P* value
	N=220 (%)	Negative N=146 (%)	Positive N=74 (%)	
Age: Mean ± SD	35.5 ± 12.38	34.67±12.3	37.12 ± 1.45	NS
Gender				
Male	127 (57.7%)	89 (61)	38 (51.4)	NS
Female	93 (42.3%)	57 (39)	36 (48.6)	
Family history:				
Negative	146 (66.4%)	102 (69.9)	44 (59.5)	NS
Positive	74 (33.6%)	44 (30.1)	30 (40.5)	
Residency:				
Urban	122 (55.5%)	2(56.2%)	40 (54.1%)	NS
Rural	98 (45.5%)	64(43.8%)	34 (45.9%)	

Table 1. Continued.

Parameter	Total	Ragweed		*P* value
	N=220 (%)	Negative N=146 (%)	Positive N=74 (%)	
Special habits:				
Non-smoker	195(88.6%)	133 (91.1)	62 (83.8)	NS
Ex-smokers	12 (5.5%)	8 (5.5)	4 (5.4)	
Smokers	13 (5.9%)	5 (3.4)	8 (10.8)	
AR				
Negative	20 (9.1%)	13 (8.9)	7 (9.5)	NS
Positive	200 (90.9%)	133 (91.1)	67 (90.5)	
Bronchial asthma				
Negative	186(84.5%)	125(85.6)	61 (82.4)	NS
Positive	34 (15.5%)	21 (14.4)	13 (17.6)	
Combined				
Positive	15 (6.8%)	9 (6.2)	6 (8.1)	NS
OAS				
Negative	184 (83.6%)	122 (83.6)	62 (83.8)	NS
Positive	36 (16.4%)	24 (16.4)	12 (16.2)	
Disease duration				
Median	11	10	13	0.016*
Range	(1 – 45)	(1 – 45)	(3 – 38)	

χ^2Chi square test AR: allergic rhinitis; OAS: Oral Allergy Syndrome

P > 0.05 is not significant (NS).

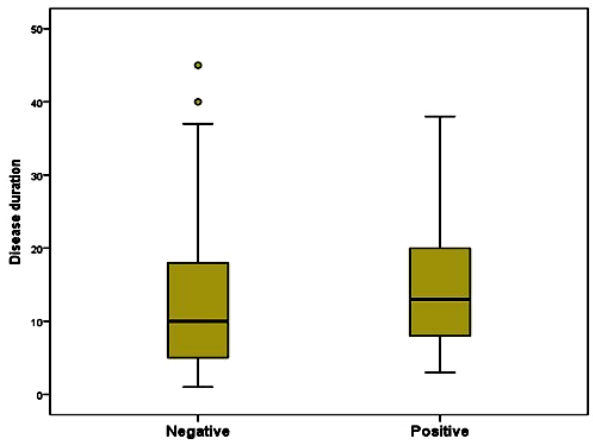

Figure 2. Boxplot showing relation between ragweed (sensitization and allergy) and duration of allergic respiratory disease (in years)

The 67 patients with AR were classified according to AR1A (2017). Of these, 35.8% had mild persistent disease, 34.3% moderate to severe persistent disease, 26.9% mild intermittent disease and 3% moderate to severe intermittent disease. There was no relation between ragweed (allergy and sensitization) and severity of allergic rhinitis (Table 2).

According to GINA (2021) classification 13 patients had bronchial asthma. Of these, 69.2% had partially controlled disease and 30.8% controlled disease. Our study demonstrated that there was a statistically significant relation between ragweed and level of control of asthma, i.e., all uncontrolled patients had neither ragweed sensitization nor allergy (Table 2).

Table 2. Relation between ragweed and severity of bronchial asthma and allergic rhinitis.

	Total	Ragweed sensitization and allergy		*P value
	N= (%)	Negative	Positive	
GINA 2021	N=34 (%)	N=21 (%)	N=13 (%)	
Uncontrolled	6 (17.6%)	6 (28.6)	0 (0)	0.007
Partially controlled	23 (67.6%)	14 (66.7)	9 (69.2)	
Controlled	5 (14.7%)	1 (4.8)	4 (30.8)	
AR1A 2017	N=200 (%)	N=133 (%)	N=67 (%)	
Mild intermittent	55 (25%)	37 (27.8)	18 (26.9)	
Mild persistent	90 (45%)	66 (49.6)	24 (35.8)	NS
Moderate/severe intermittent	3 (1.5%)	1 (0.8)	2 (3)	
Moderate/severe persistent	52 (26%)	29 (21.8)	23 (34.3)	

GINA: Global Initiative for Asthma, ARIA: Allergic Rhinitis and It's Impact on Asthma.

χ^2chi square for trend test. *P* > 0.05 is not significant (NS).

Serum total IgE level ranged from 4 to 1700 IU/ml (median 60 IU/ml). Serum specific IgE level was negative in 66.2% of patients. The specific IgE was positive in 25 patients (33.8%), low in 6.8%, increased in 21.6% and significantly increased in 5.4% (Figure 3). Serum absolute eosinophilia appeared in 13.6% of patients. Eosinophilia refers to an absolute eosinophil count in the peripheral blood of 0.5 × 10 9/L which is considered abnormal in most laboratories.[18]

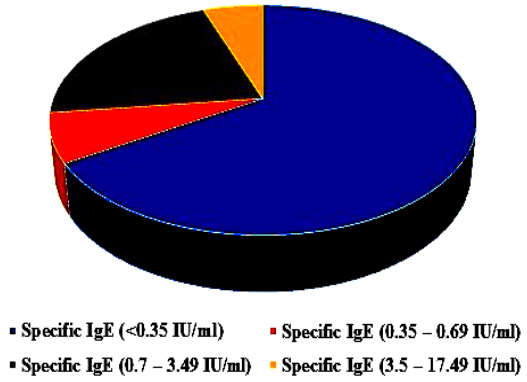

Figure 3. Pie chart showing serum specific IgE levels in patients with positive skin prick test to ragweed.

Regarding precipitating factors, there was statistically significant inverse relation between ragweed and exercise. Of 45 patients who reported pets as precipitating factors, 37 (82.2%) were not sensitized to ragweed. In addition, 6.8% of patients sensitized to ragweed reported exercise as precipitating factor (Table 3).

About other inhalant and cross-reactive food that were performed in SPT, 10.8% of patients with positive SPT to ragweed were sensitized to rabbit and 25.7% sensitized to pigeon. Also, there was statistically significant relation between ragweed and banana as 14.9% of patients with positive SPT to ragweed were cross reacted to banana (Table 3).

Table 3. Precipitating factors and frequency of other inhalants and cross-reactive foods in ragweed patients.

	Ragweed sensitization and allergy		*P* value
	Negative	Positive	
	N=146 (%)	N=74 (%)	
Pets	37 (25.3)	8 (10.8)	0.013
Chemicals	45 (30.8)	32 (43.2)	NS
Cold	67 (45.9)	32 (43.2)	NS
Exercise	2 (1.4)	5 (6.8)	0.044
Dust	91 (62.3)	51 (68.9)	NS
Smoking	42 (28.8)	31 (41.9)	NS
Peanut	3 (2.1)	4 (5.4)	NS
Maize	4 (2.7)	2 (2.7)	NS
Egg	5 (3.4)	4 (5.4)	NS
Milk	6 (4.1)	4 (5.4)	NS
Wheat	6 (4.1)	2 (2.7)	NS
Fish	2 (1.4)	1 (4.1)	NS
Banana	3 (2.1)	11 (14.9)	0.001
Zucchini	6 (4.1)	8 (10.1)	NS
Cucumber	2 (1.4)	3 (4.1)	NS
Dust	25 (17.1%)	18 (24.3%)	NS
Horsehair	11 (7.5%)	9 (12.2%)	NS
M molds	28 (19.2%)	14 (18.9%)	NS
Rabbit	5 (3.4%)	8 (10.8%)	0.028
Aspergillus	14 (9.6%)	5 (6.8%)	NS
Candida	10 (6.8%)	3 (4.1%)	NS
Pigeon	19 (13%)	19 (25.7%)	0.019

χ^2chi square test. $P > 0.05$ is not significant (NS).

Discussion

Allergic rhinitis is associated with considerable morbidity.[19] Bronchial asthma is increasingly prevalent particularly in developing countries and associated with a high level of social burden.[20] This study aimed to determine the frequency of ragweed sensitization and allergy among patients with respiratory allergy. To the best of our knowledge, this is the first study in Egypt to determine frequency of ragweed in adult patients with respiratory allergy. The study included 220 adult patients attending the allergy clinic at Ain Shams University hospitals.

Findings from this study showed that 67 patients (30.45%) were sensitized to ragweed and 7 patients (3.18%) were allergic. Recently, Hosney et al., 2021, published the first data

regarding sensitization to ragweed in children with bronchial asthma in Egypt. They reported a higher percentage of sensitization (41%) compared to our study. Most of asthmatic patients included in the current study had controlled or partially controlled disease. The disease duration was longer in patients with no ragweed allergy or sensitization.[13]

In a previous study in Romania, ragweed allergy was reported in 27% and 20.7% in two centers. They also reported that there was no correlation between environment (rural-urban), age, sex, family, or personal allergic history and sensitization to ragweed pollen which comes in agreement with findings of the current study.[21] The present study demonstrated the high frequency of ragweed sensitization compared to lower frequency of allergy. In general, the concept regarding the link between allergen exposure and symptom occurrence is a cornerstone in allergy.[22] Different countries experience has revealed the notion that *Ambrosia* infestation lasts for years before allergic sensitization begins to appear in an area.[23] Our findings are consistent with previous studies in different countries in Europe.[11, 21, 24, 25]

Measurement of specific IgE in serum is currently the most widely used as vitro method for allergy diagnosis.[26] Specific IgE to *A. artemisiifolia* was positive in 33.8% of patients with positive SPT to ragweed. Similarly, in a previous study, the prevalence of IgE antibodies specific to *A. artemisiifolia* and *A. artemisiifolia* allergen 1 (Amb a 1) were 14.7% and 11.2% in the studied patients with positive skin prick test respectively.[27] Similar results were obtained by a study of Boehme et al., 2009, who found that specific IgE antibodies to extracts of common ragweed pollen were present in 10 - 17 % of sera of 1,323 10-years old children.[28]

The present study demonstrated that 16.2% of ragweed patients had OAS. This comes in line with previous studies.[29, 30] OAS occurs in patients previously sensitized to pollens.[31] It is a type I cross-reaction mediated by IgE antibodies between an aeroallergen and a plant-derived antigen that mainly occurs on oral contact with raw fruit, vegetables, or nuts. Symptoms include itching of the lips, tongue, and throat, and sometimes accompanied by swelling of the lips and tongue.[29]

In our opinion this work has two limitations. It was conducted in a single center with relatively small sample size. Larger sample size and performance in more than one center may add more solid information. Also using molecular based specific IgE methods (e.g., Amb a 1 and Amb a 11) would help in more accurate diagnosis.

In conclusion, our study findings indicated that although ragweed pollen is one of the most frequent reasons for plant related allergenic reactions, ragweed sensitization was less common as the frequency of *Ambrosia* pollen sensitization was about one third of the studied allergic patients.

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Author Contributions

ZAA and DSS contributed to the study conception and design. NAM and AMA contributed to material preparation, data collection and analysis. ARE and OMZ provided clinical support. DHE wrote the manuscript draft. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

The study protocol was reviewed and approved by the Research Ethical Committee, Faculty of Medicine, Ain Shams University (approval number FMASU MD 363/2019).

Informed consent

An informed written consent was obtained from all participants at the time of recruitment.

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