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Skin Prick Test Results and Total IgE Levels of Asthma Patients in Zagazig University Hospital (2015-2019)

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ABSTRACT

Background: Bronchial asthma is one of the relevant diseases of the respiratory tract, the asthma is one of the forms of respiratory allergy. The change in environment and aeroallergens are the main etiology of asthma. Allergy of asthma is thought to affect the bronchial region of the respiratory airway.

Objective: The current study aimed to compare the total IgE elevation and skin prick test (SPT) positivity to evaluate the IgE and SPT ability to assess the asthmatic severity.

Subjects and Methods: This retrospective case study was carried out on 3450 cases at the outpatient clinic and Chest Department at Zagazig University and did skin prick test and IgE in authorized centers were collected from 2015 -2019. The cases were already diagnosed asthmatic according to Global Initiative for Asthma (GINA) [9] guidelines and were divided according to severity into mild, moderate, and severe according to GINA guidelines.

Results: IgE has been tested for different aeroallergens and has strong significant elevation with (P< 0.001) in Alternaria, cat hair, cotton, birch, and helminths aeroallergen. Most of the cases with elevated IgE had moderate asthma severity followed by mild severity cases then severe cases.

Conclusion: Comparing the results of SPT and IgE, the SPT test is more accurate, reliable, and easy in detecting the aeroallergen sensitivity.

Keywords: Aeroallergen, IgE, Allergic asthma, Asthmatic severity, Skin prick test.

INTRODUCTION

Asthma is considered one of the most significant causes of mortality and morbidity, which is accompanied by an uncontrolled spasmatic narrowing of the bronchus and bronchioles as a result of bronchitis and bronchial myocytic contraction [1]. Allergy is considered an immune-mediated hypersensitivity reaction associated with expression of specific immunoglobulins mainly IgE caused by identification of antigens of specific allergen [2].

Patients with familial history of allergic diseases like allergic rhinitis, drug and food allergy, and eczema were diagnosed with allergic asthma. The atopic patients had elevated levels of IgE caused by natural aeroallergens. A previous study hypothesis that half of the allergic cases had symptoms, commonly manifest in the respiratory tract diagnosed as allergic sensitization [3].

Atopy is considered the most susceptible factor for allergic asthma. Atopy is also resulted from altered immunologic response for the activation of T-helper type 2 lymphocyte, causing chronic response correlated with the induced eosinophilia and IgE [4].

Aeroallergens exposure have a potential role in bronchial asthma pathogenesis. Regarding the locations within countries, the aeroallergens differ [5]. The treatment and diagnosis of bronchial asthma were determined by the type of aeroallergens [6].

A previous study on atopic disease, in vitro analysis using IgE and in vivo skin prick test (SPT) were carried out on inhalant and food extracts. The hypersensitivity type I was determined by IgE and SPT, and help in atopic diseases phenotypic diagnosis [7]. Both IgE and SPT can detect atopic status. The skin test is economic, rapid and sensitive that expression of IgE specific-antigen in the mast cells. The incidence of allergy is elevating worldwide with the trend of SPT positivity [8].

The current study was concerned with the evaluation of IgE and SPT ability to assess the asthmatic severity.

SUBJECTS AND METHODS

This retrospective case study was carried out on 3450 cases at the outpatient clinic and Chest Department at Zagazig University and did skin prick test and IgE in authorized centers were collected from 2015 -2019. The cases were already diagnosed asthmatic according to Global Initiative for Asthma (GINA) [9] guidelines and were divided according to severity into mild, moderate, and severe according to GINA guidelines.

The cases were diagnosed atopic bronchial asthma with raised serum IgE and peripheral blood eosinophilia and were above 18 years old, were included in this study.

The excluded cases included; all patients that had dermatological diseases other than allergic skin diseases or were not a resident of Sharkia.

Technique:

The records of all patients contain the following:

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Full history was taken from all patients including locality of the patient, family history of allergy, smoking history, and history of exposure to a certain allergen. The severity of asthma (mild, moderate, and severe) was included in all records. The records contain IgE results, which were performed on all patients simultaneously with SPT.

Droplets of allergen extracts were put on the forearm with 2 cm intervals and needles pricked the skin perpendicularly. The test was assessed after 20 min. The widest diameter of the edematous area, along with the diameter that is perpendicular to the widest diameter, were evaluated. These two values were added and the sum was divided by 2. If the negative control yielded no reaction and a positive result (2 + and above) to a specific allergen was indicated by a mean wheel diameter measuring 3 mm or more, greater than the negative control (buffered saline). A mean wheal diameter measuring 3 mm or greater than the negative control (buffered saline) but less than 5 mm was taken as 2+. Similarly, a mean wheel diameter measuring ≥5 mm and <7 mm was taken as 3+, ≥7 mm, and <9 mm as 4 +, and so on, respectively.

Before performing SPT, inhaled drugs were continued, oral drugs including antihistamines, steroids, and any drugs with effect on SPT were stopped 1 week before the tests. Oral short-acting anti-histaminic drugs were stopped one 1 week before, and long-acting anti-histamines were stopped 4 weeks before performing the tests.

The antigens that were used are (corn M, wheat M, Stemphylium, hay dust M, aspergillus F, aspergillus N, Fusarium, Alternaria, botrytis, horse hair, cat hair, dog H, goat H, cotton, wool, candida albicans, dandelion P, grass P, weed P, feather, cockroach, straw, tobacco, mixed mites, birch, helminth, epicoccus, Cladosporium, and ragweed).

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of sharing his/her information in such study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

All data were collected, tabulated, and statistically analyzed using SPSS 20 for windows (IBM Corp., Armonk, NY, USA). Continuous quantitative variables were expressed as the mean ± SD, and median (range), and categorical qualitative variables were expressed as absolute frequencies (number) and relative frequencies (percentage). Categorical data were compared using the Chi-square test or Fisher's exact test when appropriate. All tests were two-sided. P-value < 0.05 was considered statistically significant, p-value < 0.001 was considered highly statistically significant.

RESULTS

Our study included 50.2% females, mean age of our patients was 27.56 years. 58.1 of our patients were non-smokers. 51.6% of our patients had a positive family history **(Table 1).**

Table (1): Patients demographic characteristics

Demographic data	The studied bronchial asthma patients (N=3450)	
	Number	Percent
Gender		
Male	1719	49.8%
Female	1731	50.2%
Age (years)		
Mean±SD	7.56±9.20	
Median (Range)	25 (18 – 65)	
Age group		
<20 years	519	15%
>20-30 years	1906	55.2%
>30-40 years	637	18.5%
>40-50 years	242	7%
>50-60 years	96	2.8%
>60-70 years	50	1.4%
Family history		
Negative	1671	48.4%
Positive	1779	51.6%
Current smoking		
No	2003	58.1%
Yes	1447	41.9%

According to the current results, Alternaria, cat hair, cotton, birch, helminths had the most significant elevation of IgE among all tested aeroallergen **(Table 2a and b).**

Table (2a): Frequency of elevated IgE in different aeroallergens

		Total	Normal (N=1037)		Elevated (N=2413)		Chi^2	p-value
Aeroallergens	**PST result**		**No.**	**%**	**No.**	**%**		
Corn M	Negative	1088	304	27.9%	784	72.1%	3.387	0.066
	Positive	2362	733	31%	1629	69%		
Wheat M	Negative	3366	1010	30%	2356	70%	0.178	0.673
	Positive	84	27	32.1%	57	67.9%		
Stemphyllium	Negative	3166	952	30.1%	2214	69.9%	0.002	0.961
	Positive	284	85	29.9%	199	70.1%		
Hay Dust M	Negative	1524	457	30%	1067	70%	0.007	0.935
	Positive	1926	580	30.1%	1346	69.9%		
Aspergillus F.	Negative	1738	502	28.9%	1236	71.1%	2.297	0.130
	Positive	1712	535	31.2%	1177	68.8%		
Aspergillus N.	Negative	1940	599	30.9%	1341	69.1%	1.412	0.235
	Positive	1510	438	29%	1072	71%		
Fusarium	Negative	3263	983	30.1%	2280	69.9%	0.131	0.717
	Positive	187	54	28.9%	133	71.1%		
Alternaria	Negative	3194	985	30.8%	2209	69.2%	12.492	<0.001
	Positive	256	52	20.3%	204	79.7%		
Botrytis	Negative	3337	1002	30%	2335	70%	0.047	0.829
	Positive	113	35	31%	78	69%		
Horse H	Negative	3444	1037	30.1%	2407	69.9%	2.583	0.188
	Positive	6	0	0%	6	100%		
Cat H	Negative	3276	966	29.5%	2310	70.5%	10.066	0.002
	Positive	174	71	40.8%	103	59.2%		
Dog H	Negative	3396	1022	30.1%	2374	69.9%	0.136	0.713
	Positive	54	15	27.8%	39	72.2%		
Goat	Negative	3378	1016	30.1%	2362	69.9%	0.028	0.868
	Positive	72	21	29.2%	51	70.8%		
Cotton	Negative	3422	1035	30.2%	2387	69.8%	7.051	0.008
	Positive	28	2	7.1%	26	92.9%		
Wool	Negative	2623	799	30.5%	1824	69.5%	0.847	0.357
	Positive	827	238	28.8%	589	71.2%		

Table (2b): Frequency of elevated IgE in different aeroallergens

		Total	Normal (N=1037)		Elevated (N=2413)		Chi^2	p-value
Aeroallergens	**PST result**		**No.**	**%**	**No.**	**%**		
Candida Albicans	Negative	2915	865	29.7%	2050	70.3%	1.318	0.251
	Positive	535	172	32.1%	363	67.9%		
Dandelion P	Negative	1740	533	30.6%	1207	69.4%	0.551	0.458
	Positive	1710	504	29.5%	1206	70.5%		
GRASS P	Negative	2186	661	30.2%	1525	69.8%	0.092	0.762
	Positive	1264	376	29.7%	888	70.3%		
Weed P	Negative	3443	1035	30.1%	2408	69.9%	0.007	1.000
	Positive	7	2	28.6%	5	71.4%		
Feather	Negative	2758	838	30.4%	1920	69.6%	0.697	0.404
	Positive	692	199	28.8%	493	71.2%		
Cockroach	Negative	2523	774	30.7%	1749	69.3%	1.716	0.190
	Positive	927	263	28.4%	664	71.6%		
Straw	Negative	2179	645	29.6%	1534	70.4%	0.588	0.443
	Positive	1271	392	30.8%	879	69.2%		
Tobacco	Negative	1596	485	30.4%	1111	69.6%	0.154	0.694
	Positive	1854	552	29.8%	1302	70.2%		
Mixed Mites	Negative	727	240	33%	487	67%	3.824	0.051
	Positive	2723	797	29.3%	1926	70.7%		
Birch	Negative	3412	1033	30.3%	2379	69.7%	6.972	0.008
	Positive	38	4	10.5%	34	89.5%		
Helminthes	Negative	3392	1007	29.7%	2385	70.3%	13.172	<0.001
	Positive	58	30	51.7%	28	48.3%		
Epicoccus	Negative	2099	618	29.4%	1481	70.6%	0.966	0.326
	Positive	1351	419	31%	932	69%		
Cladosporium	Negative	2204	652	29.6%	1552	70.4%	0.656	0.418
	Positive	1246	385	30.9%	861	69.1%		
Ragweed	Negative	2365	694	29.3%	1671	70.7%	1.820	0.177
	Positive	1085	343	31.6%	742	68.4%		

The current study reported that the atopic cases with elevated IgE were moderate (35.8% of all atopic cases) followed by mild severity cases (35.6% of all atopic cases) then severe cases (28.6% of all atopic cases) with no significant difference between them **(Table 3).**

Table (3): Relationship between IgE and asthma severity

IgE	N	Mild (N=1232)		Moderate (N=1235)		Severe (N=983)	
		No.	%	No.	%	No.	%
Non-atopic	1037	373	36%	372	35.9%	292	28.2%
Atopic	2413	859	35.6%	863	35.8%	691	28.6%
Chi^2 p-value				0.088 0.957			

Correlation of the most frequent aeroallergen (mixed mites) with the severity of asthma in each region; severe cases were found in Zagazig (83.5% of all cases), Belbes (78.4% of all cases), Awlad Sakr (85.7% of all cases), Mashtol (88.2% of all cases), Diarb Negm (97.8% of all cases), Menia el quamh (75.4% of all cases). Mild cases were found in Abu Hamad (85.6% of all cases), El Asher mn Ramadan (82.7% of all cases), Hehia (87.5% of all cases), Ibrahemia (82.9% of all cases). Moderate severity was present in Fakos (87.4% of all cases), Abo-Keber (88.4% of all cases), Kafr Sakr (85.7% of all cases), El quenayat (81.2% of all cases). The predominance of mixed mites showed a significant correlation with moderate and severe cases while there was no significant relation in mild cases **(Table 4).**

Table (4): Distribution of aeroallergen (Weed pollen, feather, cockroach, straw, tobacco, mixed mites) in different Sharkia regions stratified by asthma severity

	Asthma severity	Positive SPT for						
Region		**N**	**Weed P**	**Feather**	**Cockroach**	**Straw**	**Tobacco**	**Mixed Mites**
Zagazig	Mild	205	0%	15.1%	30.7%	37.6%	56.6%	80%
	Moderate	209	0%	13.4%	25.8%	36.8%	63.6%	78.5%
	Severe	170	0%	14.1%	25.3%	33.5%	62.9%	83.5%
Belbes	Mild	287	0%	26.8%	29.6%	34.5%	53.3%	74.9%
	Moderate	278	0%	22.7%	33.8%	36%	49.3%	75.2%
	Severe	227	0%	22.5%	28.2%	38.3%	50.7%	78.4%
Fakos	Mild	79	0%	29.1%	24.1%	24.1%	48.1%	84.8%
	Moderate	87	0%	19.5%	31%	31%	43.7%	87.4%
	Severe	63	0%	28.6%	17.5%	30.2%	41.3%	85.7%
Abu Hamad	Mild	97	2.1%	20.6%	26.8%	36.1%	56.7%	85.6%
	Moderate	101	2%	14.9%	27.7%	39.6%	63.4%	82.2%
	Severe	74	0%	21.6%	35.1%	47.3%	77%	75.7%
Elasher Mn Rmdan	Mild	52	0%	21.2%	13.5%	40.4%	55.8%	82.7%
	Moderate	60	0%	8.3%	16.7%	38.3%	51.7%	80%
	Severe	34	0%	26.5%	29.4%	64.7%	61.8%	79.4%
Abo Keber	Mild	70	2.9%	22.9%	24.3%	35.7%	55.7%	84.3%
	Moderate	43	0%	18.6%	18.6%	30.2%	41.9%	88.4%
	Severe	51	2%	25.5%	19.6%	37.3%	52.9%	72.5%
Hehia	Mild	56	0%	25%	33.9%	39.3%	42.9%	87.5%
	Moderate	65	0%	21.5%	33.8%	33.8%	33.8%	86.2%
	Severe	71	0%	12.7%	21.1%	23.9%	25.4%	83.1%
Kafr Sakr	Mild	52	0%	19.2%	34.6%	46.2%	55.8%	76.9%
	Moderate	56	0%	23.2%	26.8%	48.2%	42.9%	85.7%
	Severe	44	0%	13.6%	31.8%	59.1%	52.3%	77.3%
Awlad Sakr	Mild	58	0%	25.9%	24.1%	34.5%	67.2%	72.4%
	Moderate	64	0%	25%	32.8%	34.4%	54.7%	67.2%
	Severe	42	0%	26.2%	21.4%	21.4%	69%	85.7%
Mashtol	Mild	51	0%	17.6%	19.6%	35.3%	64.7%	88.2%
	Moderate	42	0%	26.2%	19%	33.3%	57.1%	73.8%
	Severe	32	0%	28.1%	34.4%	34.4%	62.5%	81.2%
Diarb Negm	Mild	55	0%	9.1%	12.7%	30.9%	43.6%	80%
	Moderate	64	0%	23.4%	10.9%	31.2%	48.4%	79.7%
	Severe	45	0%	13.3%	22.2%	37.8%	66.7%	97.8%
Menia El-Kamah	Mild	99	0%	19.2%	30.3%	42.4%	52.5%	73.7%
	Moderate	98	0%	16.3%	26.5%	45.9%	53.1%	66.3%
	Severe	69	0%	17.4%	23.2%	42%	60.9%	75.4%
Ibrahemia	Mild	35	0%	8.6%	25.7%	42.9%	60%	71.4%
	Moderate	36	0%	22.2%	25%	33.3%	44.4%	80.6%
	Severe	37	0%	27%	29.7%	35.1%	40.5%	54.1%
El-Quenayat	Mild	36	0%	16.7%	22.2%	38.9%	47.2%	66.7%
	Moderate	32	0%	9.4%	40.6%	50%	56.2%	81.2%
	Severe	24	0%	29.2%	12.5%	16.7%	50%	75%
P-value	Mild		0.015	0.033	0.119	0.560	0.303	0.061
	Moderate		0.048	0.104	0.013	0.437	0.001	0.011
	Severe		0.147	0.132	0.375	<0.001	<0.001	0.002

DISCUSSION

Asthma is considered one of the most significant causes of mortality and morbidity, which is accompanied by an uncontrolled spasmatic narrowing of the bronchus and bronchioles as a result of bronchitis and bronchial myocytic contraction. Around 300 million cases are reported with asthma, and it is suggested that by 2025 more 100 million cases may be affected [10].

Asthma prevalence, mortality and severity varied according to geographical location. In countries with high income the asthma records were high, while in countries with low to middle income, the mortality related to asthma was high. Although the asthmatic medications had advances in the last decades, new diagnostic tools still needed [10,11].

In this study the results of skin prick test were taken from 3450 patients among 14 different regions in Sharkia including patients from Zagazig (584), Belbes (792), Fakos (229), Abu Hammad (272), Elasher Mn Rmdan (146), Abo-Kber (164), Hehia (192), Kafr Sakr (152), Awlad Sakr (164), Mashtol (125, Diarb Negm (164), Menia El-Quamh (266), Ibrahemia (108) and El-Quenayat (92).

Our study was single centre study and first study in Egypt to make pattern of aeroallergen sensitivity among Sharkia regions in adults above 18 years, it included 3450 SPT results, which were interpreted with the same method by measuring the average diameter method as we add both the longest diameter and the diameter perpendicular to it and divide them by 2. If the result was more than 3 mm, it indicated the positivity of the test.

There are three methods for interpretation of the SPT results (calculating the average diameter, area method measured by scanning device, HEP-index diameter method, which means allergen-induced average diameter divided by histamine-induced average diameter [12].

In the current study, there were 43.9 % of the tested population showed triple sensitization from the aeroallergen in the study, 27.2 % have allergy for four aeroallergen or more then only 17 % have mono-sensitivity from the aeroallergen and in the last place comes the 11.9 % who have double-sensitization. However, in China a study from 2011 to 2013 using SPT to detect the sensitivity panel showed that (17.0%) have mono-sensitization, (24.7%) with 2 sensitizations, (19.7%) with 3 sensitizations, (9.94%) with 4 sensitizations and (28.6%) with 5 or more sensitizations. The highest percentage in both studies ensured that most of the allergic patients have poly-sensitization. Poly-sensitization is considered a risk factor for the allergic disease development in sensitized cases. Multi-allergen sensitization may be a consequence of reactivity and sensitivity among allergens. The immune system cannot detect multiple allergens from each other because of their high homologic degree between these allergens [13].

The percentage of males was 49.8% and females 50.2% with positive family history in 51.6% as previous results reported that males and females reaction is correlated to different risk factors, females are susceptible to air pollutants [14], the positive family history comes in concordance with a study in Algeria in which a close percentage for familial atopy with 74% but in same study males were more common than females with a total percentage of (63.23%) and this supports the role of genes in allergic conditions [15].

The most affected age group is between (20-30) years (55.2%) followed by age group (30-40) years (18.5%) the least to be affected is (60-70) years (1.4%). This is the same result in **Kumar *et al.*** [5], which has been done in India where the most affected age group was between (20-30) years (52 %). Elderly patients are commonly diagnosed with asthma. Regarding asthma, dyspnea is a common symptom. Among elderly patients it is confused and considered normal [4].

Atopy is thought to respond to many allergens, leading to $CD4^+$ Th2 differentiation and overexpression of IgE, so we collected the results of IgE from all people who already have done SPT. Among 3450 IgE result, the patients with elevated IgE were 2413 with a percentage of 69.96%, which came in concordance with a study done in Colorado, in which **Knight *et al.*** [16] reported good concordance between both SPT and IgE with an overall >70% agreement between methods. If an IgE test is carried out and has results beyond expectation when considering the history, SPT should be carried out to confirm the diagnosis of an allergy. This is due to the IgE being evaluated is the free IgE; it does not assess the mast cells bound IgE from an existing sensitization. IgE serum testing is not associated with suspected allergies. So SPT is easy and more reliable with high yield results than IgE.

Our results showed that IgE had significant elevation in Alternaria (Ber black fruit spot), cat hair, cotton, birch and helminths eggs.

Allergies to cats are the prominent animal-origin allergy, and affect nearly 1 in 5 adults in the world. Fel d 1 is the common cat allergen, accounting for up to 96% of human allergic sensitization to cats and 60%-90% of the overall antigenicity of cats and cat dander [17]. Our result with significant elevation of IgE is reinforced by **Melén *et al.*** [18]**,** who demonstrated that sensitization to cat hair was correlated with asthma severity. Also another study in US population; **Shargorodsky *et al.*** [19] included 5138 patient tested by pets' exposure (cat H and dog H). There was a high association of allergic symptoms with higher levels of exposure regarding cat exposure.

The incidence of Alternaria alternata was recorded up to 30% in the survey in Aksu, China [20].

Birch and other related trees alder, oak, hornbeam hazel, beech, and chestnut were primarily based on the elevated IgE reactivity of these allergen homologs [21]. Our study with elevated IgE has similar reinforcement as **Biedermann *et al.*** [21] reported in their study that

birch pollen is the most relevant tree pollen in Central and Northern Europe and is a significant precursor of asthma symptoms. Levels of birch pollen have elevated and exposure period has significantly increased as a result of climate changes, giving rise to birch pollen sensitization.

Also, cotton dust was associated with significant elevation IgE result. This comes along with study in Pakistan where raw cotton account for 56.90% of total aeroallergen as Pakistan is the fourth largest county to produce cotton [(22)].

Helminths eggs represent a high significant elevation in IgE and a serious hazard in transmitting infection by aerosol such as enterobiasis is easily transmitted and by inhalation of these eggs through contaminated hands. Recent results have shown that it occurred more in over-crowded areas or families [(23)].

The current results reinforce the result of SPT as most of elevated IgE in atopy cases are of moderate severity with total percentage of 35.8% then mild type severity with a percentage of 35.6 % and finally come severe type with 28.6% percentage. Noting that patients with normal IgE have the same categorial pattern of elevated IgE; most of them have moderate severity then comes mild severity while severe cases have the lowest percentage. Our results come in concordance with a study in Algeria where the majority of atopic asthmatic people had moderate asthma severity (33.82%) then mild asthma (29.41%), and (23.53%) had severe asthma [(24)].

CONCLUSION

Our study concluded that IgE was tested for different aeroallergens and it had strong significant elevation with Alternaria, cat hair, cotton, birch and helminths aeroallergen. Most of cases with elevated IgE had moderate asthma severity followed by mild severity cases then severe cases. Comparing the results of SPT and IgE, SPT test is more accurate, reliable and easy in detecting the aeroallergen sensitivity.

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