PROFESSIONAL PAPER

doi: 10.5455/medarh.2019.73.272-275
MED ARCH. 2019 AUG; 73(4): 272-275
RECEIVED: JUL 12, 2019 | ACCEPTED: AUG 25, 2019

Total and Specific Immunoglobulin E for Detection of Most Prevalent Aeroallergens in a Jordanian Cohort

Rame Khasawneh[1], Mansour Al-Hiary[2], Baheieh Al-Abadi[2], Ahmad Bani-Salameh[3], Sohaib Al-Momani[4]

[1]Department of Hematology, Princes Iman Center, Amman, Jordan
[2]Department of Immunology, Princes Iman Center, Amman, Jordan
[3]Department of Internal medicine, King Hussein Medical Center, Amman, Jordan
[4]Department of Otolaryngology, King Hussein Medical Center, Amman, Jordan

Corresponding author: Mansour, Al-Hiary, MD, consultant, Immunology Department, Princes Iman Center, Amman, Jordan. Phone #00962795697525, E-mail: mansourhiary1974@gmail.com. . ORCID ID: https://www.orcid.org/0000-0002-7507-6582.

ABSTRACT

Introduction: Allergies are defined as an immune response to non-microbial environmental antigens (allergens) that involve T_H2 cells, mast cells, eosinophils and immunoglobulin E (IgE). Atopic disorders such as urticaria, asthma, hay fever, and eczema exhibit a strong familial predisposition and specific IgE-mediated reaction after exposure to the allergens. Aeroallergens involved in the hypersensitivity reactions include pollens, animal dander, fungal spores and house dust mite. Frequency and type of aeroallergens vary in different countries based on climate, vegetation and geographic areas. **Aim:** Due to increased prevalence of allergic diseases, in vitro diagnostic tests are commonly utilized in our area. The aim of our study is to evaluate the association between total and specific IgE and to study frequency of different aeroallergens in the population. **Methods:** The study was conducted in a time period between 1/12/2017 and 15/11/2018 at King Hussein Medical Center, Amman, Jordan. A total of 80 patients with symptoms of allergic disorders were included, ages of individual's ranged between 1 year and 77 years, 58.8 % (n=47) of which male and 41.2 % (n=33) female. Blood samples from all patients were collected into a 10 ml gel separator (with clot activator) tubes and tested for total IgE and specific IgE. **Results:** A total of 80 patients aged 1-77 years were divided into 4 groups depending on the normal value of total IgE as follow: 1-5 years, 6-9 years, 10-15 years, and adult. A total of 43(53.75%) patients exhibited elevated total IgE level, and 37(46.25%) had normal level. 41(51.2%) patients had elevated total IgE and positive specific IgE. The sensitivity and specificity of total IgE when using specific IgE as standard test was 77.4% and 92.5% respectively. The accuracy rate of the total IgE test was 82.5%. The most common aeroallergens were dermatophagoides pteronyssinus (13.6%), followed by grass mix (12.8). **Conclusion:** Testing of specific IgE is an essential procedure that helps to detect the cause of allergy. Although negative specific IgE could not exclude allergen sensitization due to limitations of detection method and allergen selection, and positive total and specific IgE indicate probability of sensitization.

Keywords: Allergy, immunoglobulin E, aeroallergens.

1. INTRODUCTION

Allergies are defined as an immune response to non-microbial environmental antigens (allergens) that involve T_H2 cells, mast cells, eosinophils and immunoglobulin E (IgE). As a result of these responses the allergens induce CD+4 T_H2 cells that help B cells to produce IgE antibodies and bind to the Fc receptors on mast cells and basophils, eventually when these cells are cross-linked by allergens, they are activated and rapidly release multiple mediators including histamine, leukotrienes and various interleukins. These mediators cause vasodilatation, increased vascular permeability, bronchial and visceral smooth muscle contraction (immediate hypersensitivity reaction) (1). Atopic disorders such as urticaria, asthma, hay fever, and eczema exhibit a strong familial predisposition and specific IgE-mediated reaction after exposure to the allergens (2).

Aeroallergens involved in the hypersensitivity reactions include pollens, animal dander, fungal spores and house dust mite. Frequency and type of aeroallergens vary in different countries based on climate, vegetation and geographic areas (3). Other important allergens are domestic animals, insects, and body covering of animals (4). Depending on the sources of allergens there are indoors and outdoors allergens. The most common source of indoor allergens is house dust mite, where as pollens are the most frequent outdoors source of allergens (5). Regarding house dust mite species the Dermatophagoides

pteronyssinus, Dermatophagoides farinae, Euroglyphus maynei and Blomia tropicalis are most common worldwide (6). Allergenic pollens include grass, olive tree, oak tree, and orach tree pollens. In many countries of the world's grass pollens are the major cause of pollinosis (7). Olive trees pollens are known as most common cause of olive pollinosis (respiratory allergy), and they are widely distributed in Middle East (including Jordan), Mediterranean Europe and other parts of the worlds. In Jordan olive trees constitute about 36% of the all cultivated areas, and 72% of area planted with fruit trees (8). Another important cause of respiratory allergy is fungal allergens and there are about 1.5 million fungal species worldwide. Alternaria, aspergilluss, cladosporium, and penicillium are most frequently associated with development of allergy. International Allergen Nomenclature had approved 107 allergens from 28 fungal species, 20 of which are recognized as well characterized allergens and 87 less well characterized (9).

Diagnosis of respiratory allergic diseases caused by different aeroallergens begins by clinical presentation of the disease, historical situation, seasonality and chronicity of symptoms with focusing on upper and lower respiratory tract. Identifying patients with respiratory symptoms after exposure to aeroallergens using skin testing and serological testing (total and specific IgE) have similar diagnostic sensitivity (10). Skin test is an in vivo biologic method for medical diagnosis of allergies that provoke natural immediate hypersensitivity reaction after interaction between specific IgE antibodies on mast cells and allergen which leads to release of mediators and formation of wheal and flare. Radioallergosorbent assay (RAST) is an in vitro detection of specific IgE concentration in the serum (11). Regarding total IgE antibodies it is used as initial laboratory test for diagnosis of allergy and it has some limitations such as it is increased in allergic and non-allergic diseases (parasitic infestations) and not all allergic patients have increased level of IgE (12).

2. AIM

Due to increased prevalence of allergic diseases, in vitro diagnostic tests are commonly utilized in our area. The aim of our study is to evaluate the association between total and specific IgE and to study frequency of different aeroallergens in the population and to define the prevalence of aeroallergens in allergic patients and to assess the concordance between total IgE measurements with radioallergosorbent assay (RAST).

3. METHODS

Our retrospective study had been approved by the ethical committee of the Royal Medical Services, Amman, Jordan. The study was conducted in a time period between 1/12/2017 and 15/11/2018 at Princess Iman Center for research and laboratory sciences, King Hussein Medical Center. A total of 80 patients with symptoms of allergic disorders were included, ages of individuals ranged between 1 year and 77 years, 58.8 % (n=47) of which male and 41.2 % (n=33) female. Regarding age 40% (n=32) were children and 60% (n=48) were adult. Blood samples from all patients were collected into 10 ml gel separator (with clot activator) tubes and tested for total IgE and specific IgE. Total IgE immunoglobulin was assayed using cobas e-411 total IgE assay, which is a solid phase electrochemiluminescence immunoassay. According to manufacturer's protocol controls run every 24 hours and the calibration was performed once per reagent lot using fresh reagent (Roche diagnostics, USA). The measuring range between 0.200-2500 iu/ml. Another method used for detection total IgE was enzyme-linked immunosorbent assay (ELISA) by r-Biopharm kit, Germany. According to the results from Roche diagnostics, total serum IgE was divided into 6 levels depending on patient age (Table 1).

Age group	IU/ml
Neonates	≤ 1.5
Infants first year of life	≤ 15
1-5 years	≤ 60
6-9 years	≤ 90
10-15years	≤ 200
Adults	≤ 100

Table 1. Normal total IgE serum levels according Roche diagnostics-USA.

Radioallergosorbent assay test (RAST) was performed by immunoblot EUROLINE, Germany; measurement and evaluation of allergy screen immunoblot test strips by EUROLine Scan with software for archiving and documentation. The aeroallergens used include Dermatophagoides pteronyssinus, Dermatophagoides farinae, Alternaria, Aspergilluss fumigatus, cladosporium, penicillium notatum, cultivated rye, Olive, mulberry tree, Grass pollens, grass mix, tree mix, weed mix, flower mix, feather mix, Cat, Dog, Horse, cow, sheep, dog, hamster and cockroach. The sensitivity and specificity of the test are 90% and 97% respectively. For statistical analysis of results the MedCalc statistical software was used.

4. RESULTS

A total of 80 patients aged 1-77 years were divided into 4 groups depending on the normal value of total IgE as follow: 1-5 years, 6-9 years, 10-15 years, and adult (Figure 1). A total of 43(53.75%) patients exhibited elevated total IgE level, and 37(46.25%) had normal level. 41(51.2%) patients had elevated total IgE and positive specific IgE (Table 2). The sensitivity and specificity of total IgE when using specific IgE (RAST test) as standard test was 77.4% and 92.5% respectively. The accuracy rate of the total IgE test was 82.5% (Table 3). A total of 41 (from 43) patients with elevated total IgE immunoglobulin were positive specific IgE for one or more aeroallergens. 29.2% (12) were positive for one aeroallergen and 70.8% (12) were positive for two or more aeroallergens and when they sensitized to two or more allergens, the total IgE was more elevated. On the other hand, 37 patients had normal total IgE, 12 of which (32.4 %) had positive specific IgE and 25 (67.6%) were negative. 8 of 12 (66.6%) were positive for one allergen and 4 (33.3%) were positive for two or more allergens. A total of 53 (66.25%) patients

Total IgE	Specific IgE		Total
	Positive=N (%)	Negative N= (%)	
Elevated (positive)	41(51.2%)	2(2.5%)	43 (53.7%)
Normal (negative)	12 (15%)	25(31.3%)	37(46.3%)
Total	53 (66.2%)	27 (33.8%)	80(100%)

Table-2: Comparison of specific IgE and total IgE results in all patients

Statistics	%
Sensitivity	77.4
Specificity	92.5
Positive predictive value	95.3
Negative predictive value	67.3
Accuracy	82.5

Table 3. Statistical analysis of total IgE test when using specific IgE as a gold standard test for allergy diagnosis

fore identification of allergen and avoiding contact with it play a major role in prevention of allergic diseases and to achieve those goals by using total IgE and specific IgE are widely applied in clinical practice (15). In our study we estimated the frequency of aeroallergen, including pollens (grass. Tree), animal dander, fungal allergens, and house dust mite in allergic patients and compared the association with total IgE level. Most allergist initially order total IgE test for patients suspected to be having allergic disease and order specific IgE only in patients with high level of total IgE. Our study shows moderate sensitivity (77.4%) and high specificity (92.5%) of total IgE. Although we found that 2.5% of cases had elevated total IgE and no evidence of allergen sensitization (negative specific IgE), and 15% had normal level total IgE and did not rule out allergy (positive specific IgE). Study conducted in Saudi Arabia by Jamil Al-Mughales reported that the sensitivity and specificity of total IgE was 78.6%

Allergen group	Allergen	Winter (45)		Spring (29)		Summer (28)		Autumn (30)		Total (132)	
		N	%	N	%	N	%	N	%	N	%
Host dust mite	Dermatophagoides pteronyssinus	7(15.5%)		3(10.3%)		4 (14%)		4 (13.3%)		18 (13.6%)	
	Dermatophagoides farina	5 (11%)		3 (10.3%)		3 (10.8%)		3 (10%)		14 (10.6%)	
Animal	cat	5 (11%)		4 (13.8%)		3 (10.8%)		2 (6.6%)		14 (10.6%)	
	Cockroach	2 (4.4%)		3 (10.3%)		4 (14%)		3 (10%)		12 (9%)	
	horse	2 (4.4%)		1 (3.4%)		1 (3.6%)		0		4 (3%)	
	Feather mix	3 (6.6%)		0		0		0		3 (2.3%)	
Plants	Tree mix	6 (13.3%)		1 (3.4%)		4 (14%)		2 (6.6%)		13 (9.8%)	
	olive	3 (6.6%)		2 (6.9%)		0		2 (6.6%)		7 (5.3%)	
	Grass mix	4 (8.8%)		6 (20.6%)		2 (7.2%)		5 (16.6%)		17 (12.8%)	
	Grass pollen	3 (6.6%)		2 (6.9%)		1 (3.6%)		4 (13.3%)		10 (7.5%)	

Table 4. Seasonal frequency of allergens sensitivity in allergic patients.

were positive for specific IgE, whereas 33.75% were negative. 20 (37.7%) of 53 patients had positive specific IgE for one allergen, and 33 (62.3%) had positively for two or more allergens. The most common aeroallergens were dermatophagoides pteronyssinus (13.6%), followed by grass mix (12.8%), dermatophagoides farina (10.6%) and cat (10.6%). Sensitization to house dust mite was reported in 32 patients with slight increase in frequency of dermatophagoides pteronyssinus than dermatophagoides farina. Table 4 shows the frequency of all aeroallergens. Frequency of sensitization to aeroallergens during seasons was as follows: winter 78.2% (18/23), spring 50% (13/26), summer 66.6% (14/21) and autumn 80 % (8/10).

5. DISCUSSION

Allergy is defined as an allergen-specific hypersensitivity reaction type-1 and accurate diagnosis is important for correct management and treatment. In Jordanian populations the prevalence of allergy is 20% (1,200,000 of 6,000,000). However increase in the level of total IgE is not specific for allergy by itself because it is increased in other conditions such as parasitic infestations. Total IgE indicates allergy because it is associated with type-1 hypersensitivity reaction (allergy) (13, 14). Risk factors for allergy include contact and exposure to allergen. There-

and 41.8% respectively. Although he reported that up to 44% of cases with normal total IgE do not indicate absence of allergy, and 20% of cases with high level of total IgE do not indicate an allergy (16). Javad Ghaffari et al reported that 60.5% of patients with asthma and allergic rhinitis had elevated level of total IgE and this **is** almost in keeping with our results which is 51.2% (17). Another Study conducted in India by Md.Nawad Azam et al shows that 32 % of allergic cases had elevated level of total IgE (18). Regarding the concentration of total IgE and number of specific IgE positive we found that 70.8% of cases were positive for two or more aeroallergens in high level total IgE patients and 29.2% were positive for one aeroallergen. In patients with normal total IgE level 66.6% (n=8) were positive for one aeroallergen and 33.3% (n=4) were positive for two or more aeroallergens. Man-Li Chang et al reported that in 135 patients with normal total IgE, 17.8% of patients had two or more specific IgE positive and 82.2% had one specific IgE positive. They suggests that increased number of specific IgE may lead to increased total IgE, and that the total IgE stayed at normal level when the quantity of specific IgE did not increase enough (15). Our study shows that 62.3% of cases were polysensitized and 37.7% were monosensitized. One study in Jordan reported 81.4% of cases were poly-

sensitized and 9% were monosensitized (19). We reported that most common aeroallergens was house dust mite 24.2% (13.6%- dermatophagoides pteronyssinus, 10.6%- dermatophagoides farina) followed by grass mix and pollens 20.3% (grass mix- 12.8%, grass pollen- 7.5%) and cat 10.6%, and this is in accordance with results reported by Aburuz S, et al in 2011 in Jordan. They reported grass pollens mix, olive tree pollens, house dust mite and cat allergen were most common (20). Regarding tree pollens we found the frequency of sensitization to olive tree pollens was 5.3%.The frequency in Palestine was 37.2%, in Egypt 12.5%, Saudi Arabia 35.8% (21).Our results show sensitization to fungal allergen was least common with 3 % frequency rate. A review article conducted in Austria by Teresa Twaroch et al reported no exact frequency of fungal sensitization but is estimated to range from 3% to 10% in population. They report the frequency of fungal molds in European countries with highest prevalence in Spain (20%) and the lowest in Portugal (3%) (9). These data was in keeping with our results. Study conducted in Iran by Abdol Hussein et al shows high prevalence (23.7%) of fungal allergy (22). Further studies that include different geographic distribution in Jordan are recommended, in addition to expand the list of allergens to be tested. Moreover, Multi centric studies are recommended with a larger cohort in order to address the prevalence of aeroallergens in Jordan.

6. CONCLUSION

Total IgE is an important screening test for allergic diseases. Testing of specific IgE is an essential procedure that helps to detect the cause of allergy. Although negative specific IgE could not exclude allergen sensitization due to limitations of detection method and allergen selection, positive total and specific IgE indicate probability of sensitization. To make accurate diagnosis combination of clinical manifestations, disease history and laboratory tests are mandatory.

- **Acknowledgments:** Research ethics committee of Royal Medical Services, Amman, Jordan.
- **Authors contributions:** Conception and design: MA, RK; Analysis and interpretation of data: BA, MA, RK; Drafting the article: MA, BA, SA; Stringent revision for intellectual content: RK, AB; Approved final version of the article: BA, MA, RK, SA, AB.
- **Conflicts of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** Nil.

REFERENCES

1. John BZ. Essential clinical immunology 2009: 145-160.
2. Yaghoub MO, Reza FH, Hamid A. et al. Report of Common Aeroallergens among Allergic Patients in Northeastern Iran. Iranian Journal of Otorhinolaryngology. 2017; 29: 91.
3. Mozhgan M, Zinatosadat H, Niloofar K. et al. Sensitization to aeroallergens in patients with allergic rhinitis, asthma, and atopic dermatitis in Shiraz, Southwestern Iran. Indian Journal of Allergy and Immunology. 2015; 29: 79-83.
4. Manuchehr M, Ameneh B, Negin N. The Frequency of Common Allergens in Allergic Rhinitis among the Patients Referred to the Allergy Clinic of Qods Hospital in Qazvin during 2007-2010. Journal of allergy and therapy. 2013; 4: 1.
5. Mozhgan M, Saeed T, Shirin F. Sensitization to common allergens among patients with allergies in major Iranian cities: a systematic review and meta-analysis. Epidemiology Health. 2017; 39.
6. Moussa SA, Mehdi Z, Sayyed MA. et al. Species Identification and Prevalence of House Dust Mites as Respiratory Allergen in Kindergartens of the Bandar Abbas City. Iran J Allergy Asthma Immunology. 2017; 16: 133-139.
7. D'Amato G, Cecchi L, Bonini S. et al. Allergenic pollen and pollen allergy in Europe. Allergy 2007. doi: 10.1111/j.1398-9995.2007.01393.x.
8. Ziad WJ, Alaa AB, Qotaibah A. et al. Identification of allergenic pollen grains in 36 olive (Olea europaea) cultivars grown in Jordan. Food and Agricultural Immunology. 2012; 23(3): 255-264.
9. Teresa ET, Mirela C, Rudolf V. et al. Mold Allergens in Respiratory Allergy: From Structure to Therapy. Allergy Asthma Immunology Res. 2015; 7(3): 205-220.
10. Robert GH, John O. Serological IgE Analyses in the Diagnostic Algorithm for Allergic Disease. J Allergy Clin Immunol Pract. 2015; 3: 833-840.
11. Birjis C, Edgar Y, Sami LB. Skin testing versus radioallergosorbent testing for indoor allergens. Clinical and Molecular Allergy. 2005; 3(4): doi: 10.1186/1476-7961-3-4.
12. Motala C, Hawarden D. Diagnostic testing in allergy. SAMJ 2009; 99(7).
13. Hani Ababneh. Impact of olive pollens in allergy and asthma in Jordan. http://www.worldallergy.org.
14. Hani Ababneh. Concordance and relevance of total and specific IgE laboratory assays at a major Jordanian hospital. IJBMR. 2012; 3(3): 2199-2203.
15. Man-li C, Can C, Yan-Hong L. et al. Analysis of total immunoglobulin E and specific immunoglobulin E of 3,721 patients with allergic disease. Biomedical Reports. 2015; 3: 573-577.
16. Jamil AA. Diagnostic Utility of Total IgE in Foods, Inhalant, and Multiple Allergies in Saudi Arabia. Journal of Immunology Research. 2016; http://dx.doi.org/10.1155/2016/1058632
17. Javad G, Mohammad K, Mohammad JS. et al. Hypersensitivity to House Dust Mite and Cockroach Is the Most Common Allergy in North of Iran. Iran J Immunol. 2010; 7: (4).
18. Nwad Azam, Modi NP, Mohanty AK. Prevalence and Pattern of Allergic and Non Allergic Rhinitis in Hospitalized Patients in a Tertiary Health Care: A Cross Sectional Study. Journal of Dental and Medical Sciences. 2014; 13(1): 16-20.
19. Goronfolah L. Aeroallergens, atopy and allergic rhinitis in the Middle East. Eur Ann Allergy Clin Immunol. 2015; 48(1): 5-21.
20. Aburuz S. Skin prick test reactivity to aeroallergens in Jordanian allergic rhinitis patients. East Mediterr Health J. 201; 17(7): 604-610.
21. Hassan M, Farahzad JA, Mojtaba S. et al. The Most Common Allergenic Tree Pollen Grains in the Middle East: A Narrative Review. Iran J Med Sci. 2017; http://ijms.sums.ac.ir.
22. Abdoul Hussein S, Mohammad A, Akram A. et al. Prevalence of fungal allergens in respiratory allergic patients in Ahvaz city, Southwest Iran. Jundishapur journal of microbiology. 2013; 6(4).