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TOTAL IGE AND INHALANTS ALLERGY SCREENING IN PATIENTS WITH RESPIRATORY DISEASE LIVING IN THE SYRIAN COAST REGION

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ABSTRACT

Respiratory allergy affect noticeably the life quality of patients, and increase the pressure on the health system, detecting undiagnosed allergy and identification of allergens, play a major role in both avoidance and pharmaceutical management of the patients. This research hope to answer two basic questions: To what degree allergy could be a comorbid in patients who are not diagnosed with asthma or allergic rhinitis? And what are the inhalant allergens that mostly affecting the respiratory ill patient in the east Mediterranean region? A total of 840 patients diagnosed with asthma, allergic rhinitis or other respiratory conditions were tested for total IgE and inhalant specific IgE, a retrospective collection of the patient's diagnosis and laboratory results were statically analyzed. Treating the data has given the following results: 1- respiratory patients diagnosed with other than asthma or allergic rhinitis showed a relatively high level of total IgE justifying more regular screening, 2- Pet`s epithelia, mites and cockroaches (all indoor allergens) are by far the mostly findings in respiratory ill patients, 3- no significant variation in specific IgE found with different diagnosis.

KEYWORDS: Respiratory allergy affect noticeably the life quality of patients, and increase the pressure on the health system, detecting undiagnosed allergy and identification of allergens, play a major role in both avoidance and pharmaceutical management of the patients.

INTRODUCTION

Respiratory system allergy diseases: asthma and allergic rhinitis are widely common, estimating 30% of the general population has either asthma, allergic rhinitis or both, this means that at least one member of 80% of the families is affected.[1]

Allergic rhinitis and asthma cost individuals 90% higher mean drugs cost and 35% higher mean number of physician's visits compared to control[2], the compound economic cost of treating respiratory allergic conditions exceeds $80 billion a year in the United States.[3]

Management of respiratory allergic diseases, asthma and allergic rhinitis, is a combination of three approaches: identification and avoidance of allergens, pharmaceuticals, and immunotherapy.[4]

Allergens varies by time and seasons, and also by different countries and geographic environments, screening for inhalant allergens in patients with respiratory illness in the east Mediterranean region aim to helps the identification of allergens that potentially have a significant impact on public health, at the hope that this will help guiding doctors interrogation, and raise the awareness of methods to control the environment and avoid exposure.

Allergy diseases are often underdiagnosed or undertreated[1], detecting the level of total IgE in respiratory patients who are not diagnosed with asthma/allergic rhinitis, will determine if allergy is a comorbidity in this group of patients, the specific IgE aim to highlight allergens with the most impact on respiratory patients in the Syrian coast, should also show the proportion of each allergen by diagnosis.

METHOD

Patients

The study has been taken at Al Kenndy hospital, this is a major private hospital of multi specialties, it has a wide reputation in treating patients with respiratory conditions and as a result, a relatively high number of patients with allergy are received.

The screened patients were visiting either the pulmonology clinic and/or the otolaryngology clinic, so the sample reflects patients frequenting respiratory clinics.

840 patients were tested with an in-vitro total igE test and inhalants specific IgE allergy test, the tests were performed between June 2022 and October 2023, the analysis performed in retrospective.

The study involved patients who are 5 years old and above, making sure that all analyzed patients has a mature immune system.

Before starting the study was presented and approved by the medical manager and the ethical committee, as the study is purely observational, no medical intervention in any kind was conducted on the patients, it is retrospective, the data has been collected from the archive, and patient's identity does not show in any way.

Consents has been taken, the patients are completely anonyms, and file numbers has been replaced with codes.

In order to try to obtain correlation between the degree of total igE / specific allergens and the diagnosis, patients were divided in 4 groups.

- Group AS: asthmatic patients, diagnosed asthma by the pulmonology consultant.
- Group AR: allergic rhinitis, diagnosed by the otolaryngology consultant.
- Group AS/AR: association of diagnosed asthma and allergic rhinitis.
- Group NON: none of the former diagnosis has been confirmed, this group are visiting for other conditions as bronchitis, sinusitis, nasal polyposis.., the test was ordered for suspected allergy, a family history of allergy, upon the patient's own request, or any other reason.

The test

Blood sample was collected from all patients in serum separator tubes (SSTs) that contain gel with clot activator. Serum has been used to measure the total IgE and Inhalant specific IgE (sIgE).

For total IgE we used Vidas[6] machine and reagents, form (Biomerieux, France), which uses enzyme immunoassay sandwich method (ELFA: Enzyme-Linked Fluorescent Assay).

We followed the manufacturer instructions for calibration (once with every new reagent lot or every 14 days maximally) and control (once with every single run). The measuring values of total IgE (0.5 to 1000 KIU/L), and sample can be diluted for results more 1000 KIU/L using the ready-to-use diluent included inside the kit.

For measuring inhalant specific IgE (AP-Blot Elite) machine form (das, Italy) and Polycheck Allergy Diagnostic reagents from (Biocheck GmpH, Germany)[7] have been used, with a fully automated immunoblot ELISA (Enzyme-Linked Immunoassay) method the manufacturer instructions for calibration has been followed (internal four calibrator lines with each strip, making a calibration curve for each strip) and control (once with every run). This method uses the color intensity of the lines on the strip to determine the quantitative sIgE comparing with the calibration curve. The measuring range of sIgE (0.15 to 100 KIU/L).

Specific igE tested 6 groups of inhalant allergens.

1- Plants: Timothy grass Pollen, Sweet Vernel Grass pollen, Rye pollen, cultivated oat pollen, 6 Grass Mix, Mugwort pollen, Goosefoot pollen, Pigweed pollen, Ragweed pollen, Alder pollen, Birch pollen, Date palm pollen and Pine pollen.
2- Animal's epithelia: Cat epithelia, Dog epithelia, Horse epithelia, Cow epithelia, Camel epithelia and Sheep epithelia.
3- Fungus: Penicillium notatum, Cladosporium herbarum, Aspergillus fumigatus, Alternaria alternate and Candida albicans.
4- Mites: House dust, D. pteronyssinus/ D. farinae Mix.
5- Insects: Cockroach Mix.
6- Birds: Cage Birds Mix, Feathers Mix II

Results are classified into 6 levels depending on the level of IgE of each specific allergen.
Level 0 for IgE less than 0.35 KU/l
Level 1 for IgE 0.35 to 0.7 KU/l
Level 2 for IgE 0.7 to 3.5 KU/l
Level 3 for IgE 3.5 to 17.5 KU/l
Level 4 for IgE 17.5 to 50 KU/l
Level 5 for IgE 50 to 100 KU/l
And level 6 for IgE over 100 KU/l

In order to obtain a better reflection of the effect of each allergen on the health of patients, the mean of each allergen was calculated using two variants: the number of patient`s positive/negative, and the level of severity of allergy, rather than only calculating the frequency of positive results alone.

Statistical Analysis

The data analysis was performed with Datatab online statistics calculator**8**, the program used to calculate and compare the frequency, mean, standard deviation, minimum and maximum values of different groups, it has also provided the illustration charts, regarding the hypothesis tests and P value: it used ANOVA

with/without replication measures, the significance level for all tests was set at $p < 0.05$.

RESULTS

I- Patients

Over a sample of 840 patient the male to female ratio was 35.24% males to 64.76% females.

The starting accepted age is 5 y/o, the maximum age of a patient participated was 89 y/o, the mean age of the sample is 35.11, and the standard deviation is 19.43(table 2).

Patients diagnosed with asthma (AS group) made 42.98% a total of 361 patients, patients with allergic rhinitis (AR group) made 7.98% a total of 67 patients, patients diagnosed with both asthma and allergic rhinitis made 9.4% a total of 79patients, and finally patients attended the pulmonology clinic or the ENT clinic and diagnosed of any other diagnosis (NON group) made 39.64% a total of 333 patients (table 1).

Table1: diagnosis distribution.

Diagnosis	Frequency	Valid %
AS	361	42.98%
NON	333	39.64%
AS/AR	79	9.4%
AR	67	7.98%
Total	840	100%
Invalid	0	
Total	840	

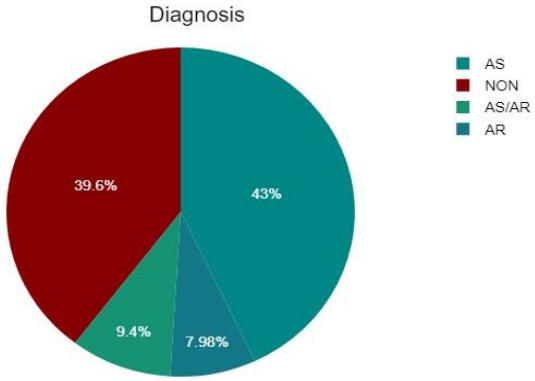

Diagram 1: diagnosis distribution.

II- Total IgE test

Total IgE was checked for all patients, the minimum value 1 ku/l and the maximum was 1000, mean value was 123.35, and the std.deviation 200.04.

Total IgE compared of each patient group separately: the mean is by group: AS: 148.13, AR: 148.33, AS/AR: 172.81 and NON: 79.74, (table 2).

Table2: mean IgE by diagnosis.

		Frequency	Mean	Std. Deviation	Minimum	Maximum
IgE Total	AS	361	148.13	233.8	1	1000
	NON	333	79.74	94.01	1	598
	AS/AR	79	172.81	297.27	2	1000
	AR	67	148.33	212.46	3	1000

Diagram 2 will illustrate the difference of mean IgE between groups.

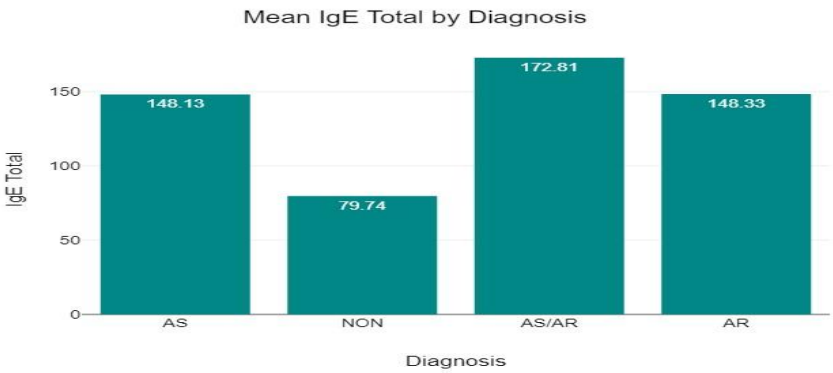

Diagram 2: mean IgE by diagnosis.

The P value was inferior to the level of significance set at the beginning of the research, the null hypothesis is: There is no difference between the 4 categories of the independent variable *Diagnosis* with respect to the dependent variable IgE Total, P value calculated <.001 (table 3).

Table 3: p value IgE by diagnosis.

	Sum of Squares	df	Mean Squares	F	p
Diagnosis	1090032.65	3	363344.22	9.35	<.001
Residual	32484193.34	836	38856.69		
Total	33574225.99	839			

III- Specific IgE

5 allergens had high mean results: Cockroach Mix 0.43, House dust 0.56, Dog epithelia 0.67, Mites: D. pteronyssinus/ D. farinae Mix 0.76, and Cat epithelia 0.89 (diagram 3).

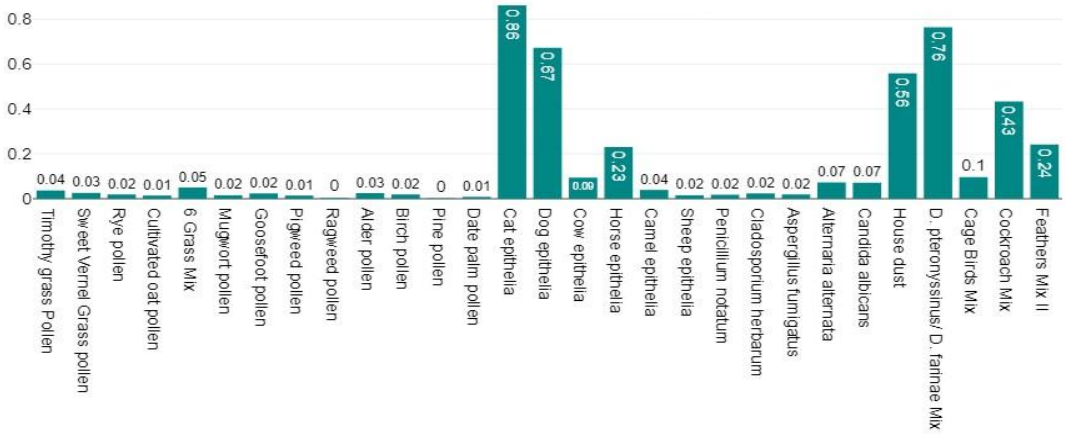

Diagram 3: mean specific IgE by allergen.

When comparing the distribution of different allergens over the 4 group of patients we have the mean of each allergen by diagnosis, illustrated in the following diagram.

All 4 diagnosis group were found in all allergens, the variation of the mean of each diagnosis by group was insignificant (diagram 4).

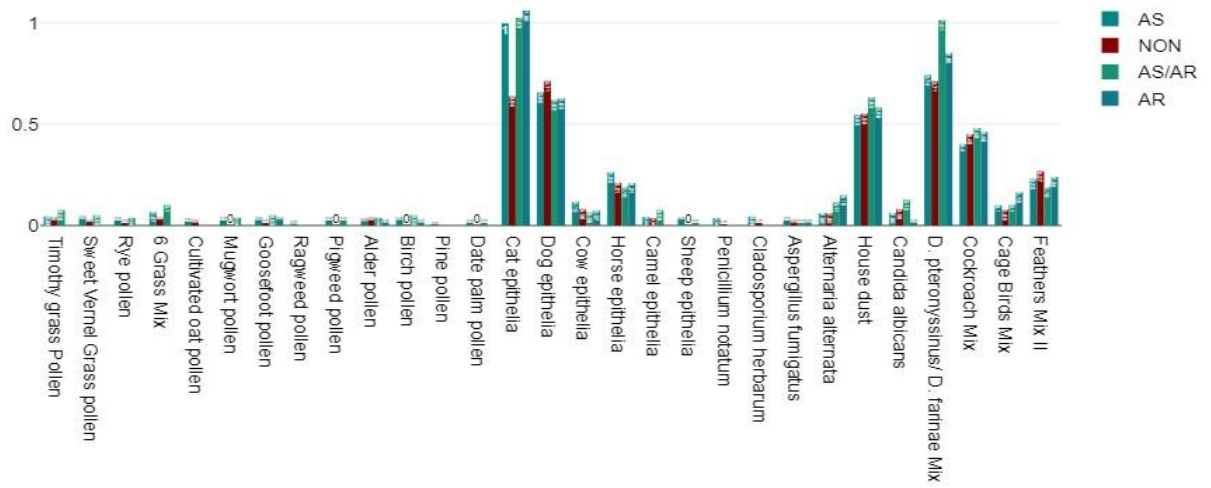

Diagram 4: mean specific IgE by diagnosis.

Also the P value calculated inferior to 0.001 indicated high reliability, the null hypostasis is the absence of significant difference between the groups of the first factor allergens as well as the second factor *Diagnosis* in relation to the dependent variable (table 6).

Table 6: p value allergen by diagnosis.

	Sum of squares	df	Mean Squares	F	p
allergens	1462.41	28	52.23	155.08	<.001
Diagnosis	3.73	3	1.24	1.08	.357
A x B	38.89	84	0.46	1.37	.013
Between	966.74	839	1.15		
Within the sample	963.01	836	1.15		
Residuum	7883.53	23408	0.34		
Within	9384.83	23520	0.4		
Total	10351.56	24359	0.42		

DISCUSSION

It is expected that more female were tested (64.76%, table1), as respiratory allergies (and asthma in particularly) are more common in females aged over 13y/o, which make the majority of the tested patients.[9]

Patients with asthma or allergic rhinitis had a similar level total IgE mean 148.13, 148.33 respectively (table 2) indicating the expected high level of allergy, Patients with both had higher mean level 172.81, reflecting expected higher level of allergy(diagram 2).

Group NON (diagnosed with none allergic respiratory conditions) had lower mean level 79.74, compared to the rest, nonetheless, it still a high number to be found in a group of patients where allergy is uncertain, this is an indicator of underdiagnoses of allergy as a comorbid.

Expanding indications for total IgE testing in this group of patients seems justified, further studies needs to be done to divide this group into different diagnosis: COPD, nasal polyposis, URTI etc., to obtain more precision and less unnecessary negative results.

Regarding specific IgE: the leading cause of respiratory allergy in the Syrian coast found to be pet's epithelia both cats and dogs, cat epithelia had the higher mean for frequency and severity, followed by house dust and mites, then allergy to cockroach(diagram 3).

All these allergens are perennial and not seasonal, they are also indoor allergens with the exception of cockroaches which is considered both indoor and outdoor, This information should facilitate doctor's interrogation and affect the education and management of patients, avoidance of these allergens is possible: pet's eviction or frequent wash, acaricids and other means for the mites, insect control by the city… Plants, pollen, molds and fungus detected rarely in all groups (diagram…), this information is very encouraging public health wise, as these allergens are more difficult to eradicate, and their avoidance could be challenging.

When observing the distribution of specific IgE by diagnosis, all 4 groups had insignificant difference by allergens, cats, dogs, mites and cockroaches remained the leading allergens regardless of the diagnosis (diagram 4).

CONCLUSION

Both patients with allergic respiratory illness and patients with non-allergic respiratory illness has showed high total IgE levels, although the level in the second group was lower, it still high enough to justify expanding total IgE screening.

All groups of patients with respiratory illness were affected mostly by 3 allergens: Pet`s` epithelia, house dust and mites, and cockroach, all indoor perennial allergens, a need to raise awareness, in both doctors and patients, to how to manage and avoid these allergens.

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