AGE-RELATED CHANGES OF SENSIBILIZATION PROFILES TO INDOOR INHALATION ALLERGENS IN THE PATIENTS OF THE SOUTHERN REGION OF UKRAINE

Kurtova M.M.[1], Koltsova I.H.[1], Tarasov Ye.V.[2], Blazhevich O.O.[1]

[1]Odessa State Medical University
[2]State institution «The Filatov Institute of Eye Diseases and tissue therapy of the NAMS of Ukraine»

Introduction: It is known that epidemiology of allergic diseases is affected by many factors, such as the range of plants, animal and insect allergens, social and living conditions, nature of food habits of certain populations, sex and age of patients. In addition, age-related changes in immunological sensitization profiles may also be geographically dependent. Thus, it is important to have epidemiological data that characterizes a set of primary importance allergens for different age groups for each particular geographic region. This will allow doctors to narrow down the amount of target allergens in different age groups, make diagnosing and prescription of specific treatment quicker.

The purpose of the study: Identify profiles of sensitization to household allergens, which often cause respiratory manifestations of allergic diseases throughout the year in patients of different age groups in the Southern region of Ukraine.

Materials and methods: Patients from Southern Region of Ukraine aged 1 to 84 years were included in the study. During 2015-2018 years, we examined 2197 patients living in the Southern region of Ukraine (Odessa and Mykolaiv regions) with suspected respiratory allergic diseases and/or proven allergic diagnosis (pollinosis, allergic rhinconjunctivitis and bronchial asthma) for presence of IgE antibodies to household respiratory allergens by immunoblotting method (Alleisa Screen, manufactured by Mediwiss (Germany). Blot strips included the following indoor markers: epithelium – cat (e1), dog (e5), horse (e3), rabbit (e82), golden hamster (e84), guinea pig (e6), mouse (e88) and rat (e87); allergens of domestic dust ticks – D. pteronyssinus (d1), D. farinae (d2) and flour tick Acarus siro (d70); allergens of cockroach Blatella germanica (i6); moulds - Penicillium notatum (m1), Cladosporium herbarum (m2), Aspergillus fumigatus (m3), Alternaria alternata (m6); mixture of parrot's feathers (ex8). Immunoblotting with double-labeled system was performed with the whole blood serum of the patient according to the manufacturer's instructions. Statistics was performed with the help of program package StatPlus:mac, AnalystSoft Inc. - Version 6. (StatSoft Inc, USA) and Microsoft Excel.

Results: Among 2197 examined patients 86,6%±0,7% had antibodies to at least one of the allergens present on the blots. All patients were divided on age groups with 5 years interval from birth up to 40 years and older. In each group calculation was done by next manner: in group 0-5 were present persons from 6 month up to completed 5 years, in group 5-10 were present persons from 5years and month up to completed 10 years, and so on later. Analysis of percentage of positive patients in each age group showed that sensitization are slowly increasing from age group 0-5 up to age group 25-30 and then slowly decreasing in older groups, difference between seropositivy in age group 0-5, 40 and older and medium groups 10-15 to 25-30 was statistically significant ($p<0,05$) (figure 1).

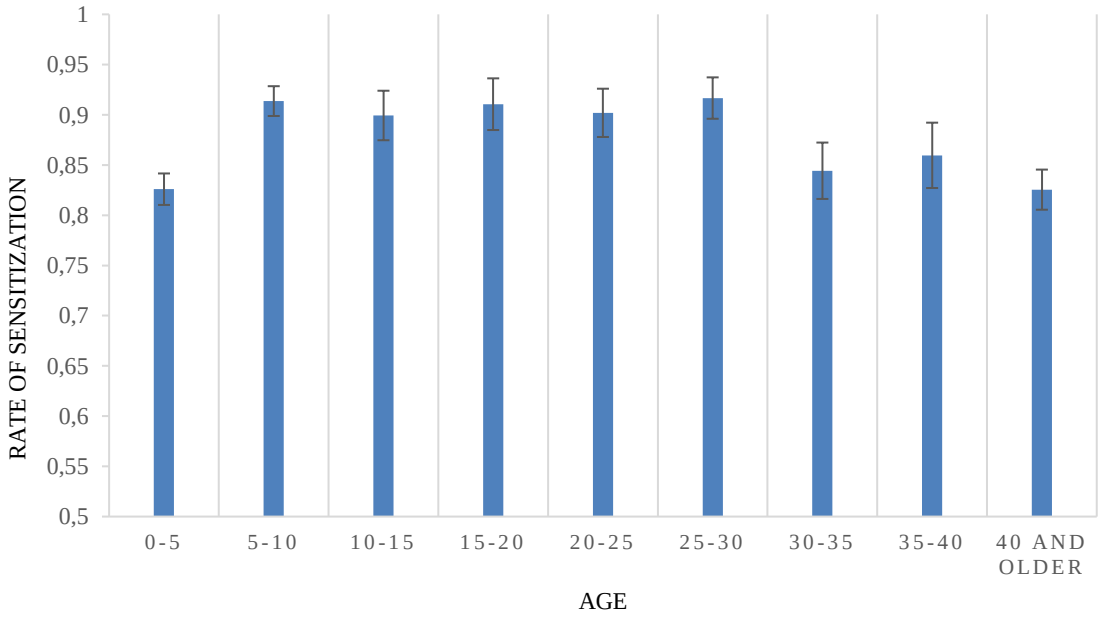

Fig.1. Rate of positive patients in each age group.

The highest percentage of positive reactions in whole pool of patients was shown to mould Alternaria alternata (40,7%±1,0%), storage mite Acarus siro (38,7%±1,3%) and domestic dust mite D.pteronyssinus (28,3%±0,9%). Approximately in one quarter of the patients were registered antibodies to Cladosporium herbarum (25,3%±0,9%), rat epithelium (24,9%±1,9%), home dust mite D.farinae (23,8%±0,9%). Antibodies to

DOI: 10.5281/zenodo.2547466

cat, mouse and dog epithelium were demonstrated in 19,0%±0,8%, 19,0%±1,7% and 18,4%±0,8% respectively. From 11,8%±0,7% to 9,1%±0,6% of the patients were seropositive to the allergens of mould Aspergillus fumigatus, epithelium of horse, hamster and German cockroach (see figure 2, table 1).

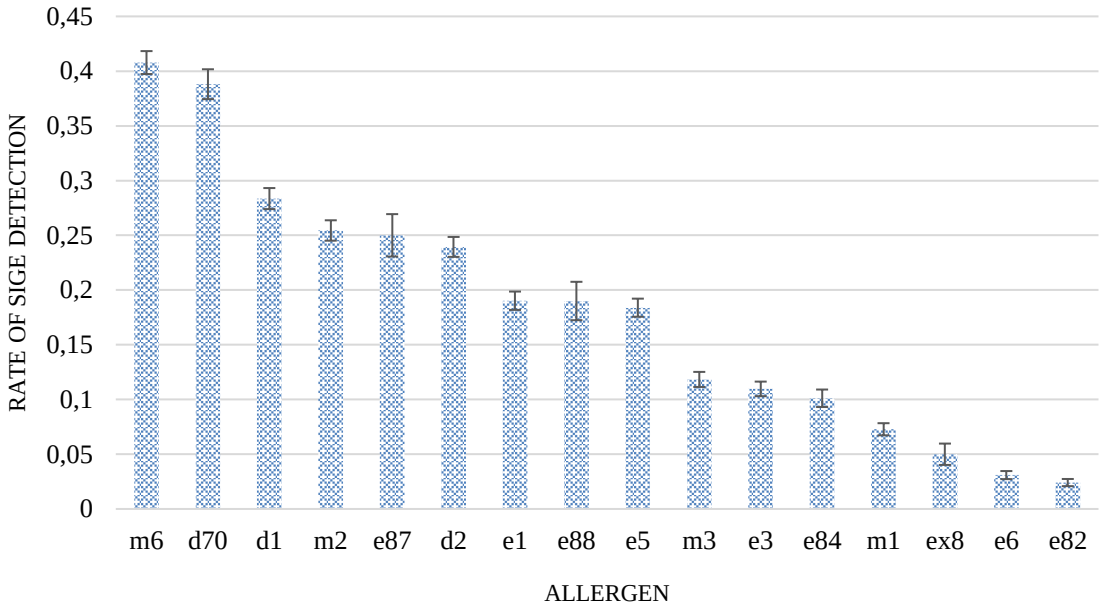

Fig. 1. Rate of sensibilized patients to different indoor allergens.

But precise analysis showed significant fluctuations in different age groups to particular allergens (figure 3).

It was shown that first increasing of positive reactions to many allergens was detected from age groups 0-5 and 5-10, what is logic, because children during this time have exposure to many unknown antigens, but abrupt statistically significant increasing was registered to next indoor allergens: mites of domestic dust – D. pteronyssinus (d1), D. farinae (d2), storage mite Acarus siro (d70), cat epithelium (e1) ($p< 0,01$). That's what was interesting – levels of antibodies to dust mites and cat epithelium were gradually decreased with age, at the same time levels of antibodies to storage mites were gradually increased and reached the highest percentage at the age 20-30 years (48,6%±4,2%) ($p< 0,05$).

According to studies, which we managed to find in the literature, it was big diversity in seroprevalence to house dust mites and storage mite in different part of the world. For example, in children living in Russia (Moscow region), antibodies to house dust mites were detected only in 7%, and rose up to 16% in children from 13 to 17 years old [1]. Among 1,145 patients in Taiwan in 3-6 years age group antibodies to D. farinae were registered in 63,3%, to D. pteronyssinus in 59%; in 7-18 year old group – to D. farinae in 64.1%, D. pteronyssinus in 67%, and in group ≥19 years old – to D. farinae in 59,4%, to D. pteronyssinus in 50,5% [2]. Among children living in the Netherlands, antibodies to the house dust mite were detected in 22,2% [3]. In Kataya, Turkey, antibodies to Acarus siro were registered in 13,79%, children living on the territory of Egypt, had antibodies to Acarus siro only in 4%, patients living in the territory of Bavaria in 7% [4, 5, 6]. Korean authors showed that it was a strong correlation in the sIgE value between house dust mites (D. pteronyssinus and D. farinae) and between storage mites (A. siro and T. putrescentiae). Their data showed that D. farinae is a source of primary sensitization and IgE reactivity to other mites is due to cross-reactivity [7].

Level of antibodies to mould Alternaria alternata (m6) in the Southern region of Ukraine was unexpectedly high. It was the highest comparing to data from other countries. So, Alternaria alternata antibodies were registered from 0,8% to 10,3% in the UK, Finland, Italy, Belgium, Switzerland, Holland, Poland, Austria, Denmark, Portugal and France; in 11% in Germany, 18,8% in Hungary; in Italy (Champagne region) in patients aged 14-18 antibodies were registered in 8,1% of cases; in the Northeast Greece among schoolchildren in 34,6%, total on the territory of Greece in 23,8%, the average level on the territory of Canada was 10,3%, Malaysia – 17,6%, in Mexico (Mexico City), the percentage of detection in children younger than 6 years was 11,3% and more than 6 years – 15,3% [8, 9, 10, 11, 12, 13].

First boost of antibodies to Alternaria alternata was also registered from age 0-5 to 5-10 (46,3%±2,0% to 54,2%±2,6% respectively, $p<0,05$) and then were gradually decreased up to age group 20-25 (35,4%±3,7%, $p< 0,01$).

The same regularity was seen concerning antibodies to Cladosporium herbarum (m2), allergens of German cockroach Blatella germanica (i6) and guinea pig epithelium (e6). It was statistically significant raise of antibodies from age 0-5 to 5-10 ($p<0,05$). Then level of antibodies to Blatella germanica increased twice from age 10-15 and 15-20 ($p<0,05$) and stay on this range almost whole life. At the same time levels of antibodies to guinea pig epithelium after first raise were present without changes up to age group 35-40 and then fall down after 40 years.

DOI: 10.5281/zenodo.2547466

We didn't find any information about sensitization to mouse and rat epithelium as in Ukrainian, as in the world literature. But our study showed that in the Southern region of Ukraine it was registered high levels of antibodies to both allergens from very early age. For example, antibodies to rat epithelium (e87) and mouse epithelium (e88) were registered in 37,1%±4,5% and 24,1±4,0% respectively in age group 0-5. Antibodies to rat epithelium were fixed on this high level up to 15-20 years, then slowly decreased up to 20-25 years, and it was statistically significant fall ($p<0,05$) at the age 25-30 and later. Concerning antibodies to mouse epithelium there was not statistically significant raise, even if percentage of positive patients was higher at the age 10-15 (29,7%±7,5%), and in groups 25 and older did not exceed the limit of 12,9%±6,0%.

Conclusions:

1. The highest percentage of positive reactions in whole pool of patients was shown to mould Alternaria alternata (40,7%±1,0%), storage mite Acarus siro (38,7%±1,3%) and domestic dust mite D.pteronyssinus (28,3%±0,9%).
2. First rise of antibodies to Alternaria alternata was registered from age 0-5 to 5-10 (46,3%±2,0% to 54,2%±2,6% respectively, $p<0,05$) and then were gradually decreased up to age group 20-25 and stay at the same level during life.
3. Antibodies to dust mites and cat epithelium were gradually decreased with age, in the same time antibodies to storage mites were gradually increased and reached the highest percentage at the age 20-30 years (48,6%±4,2%).
4. Our study showed that in the Southern region of Ukraine antibodies to mouse and rat epithelium was registered from early age in high levels: 37,1%±4,5% and 24,1±4,0% respectively.
5. On the base of our data could be proposed main target-allergens for examination of allergic patients in different ages.

References

1. Voloshin S., et al. Patterns of sensitization to inhalant and food allergens among pediatric patients from the Moscow region (Russian Federation) PLOS ONE. 2018. P. 2-11 URL: https://doi.org/10.1371/journal.pone.0194775
2. Yong S.B., et al. Different profiles of allergen sensitization in different ages and geographic areas in Changhua, Taiwan. J Microbiol Immunol Infect. 2013. Vol.46.P.295-301. URL: https://doi.org/10.1016/j.jmii.2012.07.002
3. De Jong A.B., Dikkeschei L.D., Brand P.L. Sensitization patterns to food and inhalant allergens in childhood: a comparison of non-sensitized, monosensitized, and polysensitized children. Pediatr Allergy Immunol. 2011.Vol. 22.P.166-171. https://doi.org/10.1111/j.1399-3038.2010.00993.x
4. Akdemir C. et al. House dust mite in Kutahya, Turkey. Turkiye Parazitol Derg. 2005. 29(2). P.110-115
5. Hossny E. et al. Sensitivity to Five Types of House Dust Mite in a Group of Allergic Egyptian . Pediatr Allergy Immunol Pulmonol. 2014. 27(3). C.133-137.
6. Rasp G. Sensitization against storage mites in allergic rhinopathy. [German] Laryngorhinootologie. 1991. 70(12). 678-680
7. Son M. et al. Ige reactivity to Acarus siro extract in Korean dust mite allergic patients. Exp Appl Acarol. 2014. 63(1). P. 57-64.
8. Liccardi G. Allergy in adolescent population (14-18 years) living in Campania region (Southern Italy). A multicenter study. Eur Ann Allergy Clin Immunol. 2018. doi.org/10.23822/EurAnnACI.1764-1489.65
9. Fernández-Soto R. Et al. Fungal Allergy: Pattern of sensitization over the past11 years years. Allergol Immunopathol (Madr). 2018 May 5.
10. Katotomichelakis M. Et al. Allergic sensitization prevalence in a children and adolescent population of northeastern Greece region. Int J Pediatr Otorhinolaryngol. 2016. Vol. 89. – P.33-37
11. Chan-Yeung M. et al. Geographical variations in the prevalence of atopic sensitization in six study sites across Canada. Epidemiology and genetics. Allergy. 2010. N. 65. P. 1404–1413
12. Wan Ishlah L. Et al. Skin prick test reactivity to common airborne pollens and molds in allergic rhinitis patients. Med J Malaysia. 2005. 60(2). P. 194-200.
13. Heinzerling L. M. et al. GA2LEN skin test study I: GA2LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe // John Wiley & Sons A\S. Allergy. 2009. N. 64. P. 1498-1506.

AGE-RELATED CHANGES OF SENSIBILIZATION PROFILES TO INDOOR INHALATION ALLERGENS IN THE PATIENTS OF THE SOUTHERN REGION OF UKRAINE

Kurtova M.M., Koltsova I.H., Tarasov Ye.V., Blazhevich O.O.

Introduction: It is known that epidemiology of allergic diseases is affected by range of plants, animal and insect allergens, social and living conditions, nature of food habits of certain populations, sex and age of patients. Age-related changes in immunological sensitization profiles may also be geographically dependent. Thus, it is important to have epidemiological data that characterizes a set of primary importance allergens for different age groups for each particular geographic region. **The purpose of the study:** Identify profiles of sensitization to household allergens, which often cause respiratory manifestations of allergic diseases throughout the year in patients of different age groups in the Southern region of Ukraine. **Materials and methods**: Patients from Southern Region of Ukraine aged 1 to 84 years were included in the study. During 2015-2018 years, we examined 2197 patients living in the Southern region of Ukraine (Odessa and Mykolaiv regions) with suspected respiratory allergic diseases and/or proven allergic diagnosis (pollinosis, allergic rhinconjunctivitis and bronchial asthma) for presence of IgE antibodies to household respiratory allergens by immunoblotting method. **Results & discussion:** The highest percentage of positive reactions in whole pool of patients was shown to mould Alternaria alternata (40,7%±1,0%), storage mite Acarus siro (38,7%±1,3%) and domestic dust mite

DOI: 10.5281/zenodo.2547466

D.pteronyssinus (28,3%±0,9%). First rise of antibodies to Alternaria alternata was registered from age 0-5 to 5-10 (46,3%±2,0% to 54,2%±2,6% respectively, p<0,05) and then were gradually decreased up to age group 20-25 and stay at the same level during life. Antibodies to dust mites and cat epithelium were gradually decreased with age, in the same time antibodies to storage mites were gradually increased and reached the highest percentage at the age 20-30 years (48,6%±4,2%). **Conclusion:** Our study showed that in the Southern region of Ukraine antibodies to mouse and rat epithelium was registered from early age in high levels: 37,1%±4,5% and 24,1±4,0% respectively. Level of antibodies to mould Alternaria alternata (m6) in the Southern region of Ukraine was unexpectedly high. It was the highest comparing to data from other countries. On the base of our data could be proposed main target-allergens for examination of allergic patients in different ages. **Keywords:** allergy, indoor allergens, household allergens, epidemiology of allergic diseases, sensibilization profiles

DOI: 10.5281/zenodo.2547466

Table 1. Percentage of positive patients to different allergens in each age group

Group of allergens	Allergen	Pool data	Groups by age								
			0-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40 and older
		%±m n									
Arthropods	d1	28,3±0,9 2197	17,3±1,6 585	39,7±2,6 358	36,5±4,0 148	35,5±4,3 124	35,4±3,8 161	33,9±3,5 180	28,7±3,5 167	26,3±4,1 114	23,6±2,2 360
	d2	23,8±0,9 2197	14,2±1,4 585	38,8±2,6 358	30,4±3,8 148	26,6±4,0 124	26,1±3,5 161	29,4±3,4 180	20,4±3,1 167	20,2±3,8 114	19,7±2,1 360
	d70	38,7±1,3 1268	23,9±3,0 205	35,0±3,8 157	34,5±5,2 84	32,9±5,0 88	48,2±4,8 110	48,6±4,2 144	41,9±4,3 129	44,9±5,3 87	42,8±3,0 264
	i6	10,7±0,9 1268	3,9±1,3 205	7,6±2,1 157	5,95±2,6 84	11,4±3,4 88	10,9±3,0 110	14,6±2,9 144	14,7±3,1 129	14,9±3,8 87	13,6±2,1 264
Moulds	m1	7,3±0,6 2197	6,8±1,0 585	6,7±1,3 358	10,8±2,6 148	7,3±2,3 124	5,6±1,8 161	5,0±1,6 180	4,2±1,6 167	7,9±2,5 114	10,3±1,6 360
	m2	25,3±0,9 2197	26,0±1,8 585	33,2±2,5 358	31,1±3,8 148	19,35±3,6 124	21,1±3,2 161	21,1±3,0 180	23,35±3,3 167	20,2±3,8 114	22,5±2,2 360
	m3	11,8±0,7 2197	12,3±1,4 585	14,2±1,9 358	12,2±2,7 148	8,1±2,5 124	6,8±2,0 161	11,1±2,3 180	12,6±2,6 167	8,8±2,7 114	12,8±1,8 360
	m6	40,7±1,0 2197	46,3±2,0 585	54,2±2,6 358	48,7±4,1 148	45,2±4,5 124	35,4±3,7 161	30,6±3,4 180	31,1±3,6 167	28,9±4,2 114	29,2±2,4 360
Animals epithelium and its derivates	e1	19,0±0,84 2197	18,1±1,6 585	30,2±2,4 358	26,3±3,6 148	21,8±3,7 124	21,1±3,2 161	20,0±3,0 180	14,4±2,7 167	11,4±3,0 114	8,3±1,5 360
	e3	11,0±0,7 2197	13,8±1,4 585	14,2±1,8 358	15,5±3,0 148	12,1±2,9 124	14,3±2,8 161	6,1±1,8 180	6,6±1,9 167	7,0±2,4 114	5,3±1,2 360
	e5	18,4±0,8 2197	20,3±1,7 585	25,7±2,3 358	22,3±3,4 148	26,6±4,0 124	13,7±2,7 161	15,6±2,7 180	10,2±2,3 167	15,8±3,4 114	11,4±1,67 360
	e6	3,1±0,4 2197	1,7±0,5 585	4,2±1,1 358	4,7±1,7 148	4,8±1,9 124	4,3±1,6 161	3,3±1,3 180	4,2±1,5 167	5,3±2,1 114	1,4±0,6 360
	e82	2,4±0,3 2197	1,9±0,6 585	2,8±0,9 358	4,0±1,6 148	3,2±1,6 124	3,1±1,4 161	1,7±0,9 180	1,2±0,8 167	1,7±1,2 114	2,8±0,9 360
	e84	9,1±0,6 2197	13,3±1,4 585	11,4±1,7 358	11,5±2,6 148	8,9±2,5 124	11,8±2,5 161	4,4±1,5 180	3,0±1,3 167	6,2±2,2 114	3,9±1,0 360
	e87	24,9±1,9 501	37,1±4,5 116	36,2±5,4 80	35,1±7,9 37	27,9±7,8 33	22,5±6,6 40	8,3±4,6 36	9,8±4,6 41	16,1±6,6 31	11,5±3,4 87
	e88	19,0±1,7 501	24,1±4,0 116	28,7±5,0 80	29,7±7,5 37	24,2±7,5 33	20,0±6,3 40	5,6±3,8 36	9,8±4,6 41	12,9±6,0 31	8,0±2,9 87
	ex8	5,0±1,0 501	0,9±0,9 116	5,0±2,4 80	5,4±3,7 37	3,0±3,0 33	5,0±3,4 40	8,3±4,6 36	12,2±5,1 41	3,2±3,2 31	6,9±2,7 87

Fig. 3. Age-related changes of sensibilization to different indoor allergens

DOI: 10.5281/zenodo.2547466