

Comparison of two different questionnaire techniques: the parent-reported and doctor guided-parent reported questionnaires-in determining the risk factors for allergic diseases among school-age children in the East Mediterranean Region

İki farklı anket tekniğinin karşılaştırılması: Doğu Akdeniz Bölgesi okul çağı çocuklarında ailenin doldurduğu ile doktor kılavuzluğunda ailenin doldurduğu anketlerin allerjik hastalıklarda risk faktörlerini belirlemedeki değeri

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ABSTRACT

Objective: We carried out three consecutive projects in our region over the last 15 years in order to assess changes in the prevalence of asthma and allergic diseases and to investigate the relationship between the allergic diseases and possible risk factors. In the last survey, we compared two different questionnaire techniques - the direct parent-reported and the doctor guided-parent reported questi-

ÖZET

Giriş: Astım ve allerjik hastalıkların prevalansındaki değişiklikleri değerlendirmek ve allerjik hastalıklar ile olası risk faktörleri arasındaki ilişkiyi incelemek için son 15 yılda bölgemizde birbirini izleyen üç proje yürüttük. Son araştırmada, okul çağı çocuklarında allerjik hastalıkların risk faktörlerini belirlemede iki farklı anket tekniğini karşılaştırdık; doğrudan ebeveynin yanıtladığı ve dok-

onnares-in determining the risk factors for allergic diseases among school-age children.

Materials and Methods: ISAAC questionnaires were given to 5150 school-age children (6-14 years) and 3470 (67.3%) of these were returned. The parents completed a simple two-page written questionnaire about asthma, allergic rhinoconjunctivitis and atopic eczema and a one-page questionnaire about the risk factors. According to the questionnaire results, we constituted an atopic group of 100 children, and 100 children with no allergic symptoms were chosen randomly as the control group. Skin prick test, pulmonary function tests and specific IgE levels were evaluated in those 200 children.

Results: 11.6-41.8% of the parents denied their answers in the second questionnaire, even though they were living under the same conditions. 17.8-52.8% of the parents accepted some of the questions regarding the risk factors in the second questionnaire after denial in the first. There were differences between the two questionnaires regarding the risk factors for asthma and other allergic diseases. History of varicella and history of recurrent lower respiratory tract infection were found as major risk factors both in the first and second questionnaire. Family history of allergic rhinitis was the major risk factor for the development of allergic rhinitis in both questionnaires.

Conclusion: In order to obtain a reliable cause-result relationship between the risk factors and the prevalence of allergic diseases, we suggest that detailed serologic and immunologic laboratory tests should be performed in addition to the questionnaire studies, especially in populations with lower socioeconomic status.

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Key words: ISAAC, questionnaires, parents, risk factors, epidemiology

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INTRODUCTION

Asthma is a common chronic disorder, the prevalence of which is increasing rapidly. We carried out three consecutive projects in our region, which carries typical Mediterranean features both climatically and geographically, over the last 15 years in order to assess changes in the prevalence of asthma and allergic dise-

tor tarafından yönlendirilerek ebeveynin yanıtladığı anketler.

Materyal ve Metod: ISAAC anketi 5150 okul-çağı çocuğuna (6-14 yaş) verildi ve bu anketlerden 3470 (%67.3) tanesi geri getirildi. Ebeveynler, astım, allerjik rinokonjunktivit ve atopik egzema hakkında basit iki sayfalık bir anketi ve risk faktörleri hakkında bir sayfalık bir anketi yanıtladılar. Anket sonuçlarına göre 100 çocuktan oluşan bir atopik grup oluşturduk ve allerjik semptomları olmayan 100 çocuk rastgele kontrol olarak seçildi. Bu 200 çocuğun deri testi, solunum fonksiyon testleri ve spesifik IgE düzeyleri değerlendirildi.

Bulgular: Ebeveynlerin %11.6-41.8'i, aynı koşullarda yaşamalarına karşın, ikinci ankette yanıtlarını kabul etmediler. Ebeveynlerin %17.8-52.8'i ilk ankette kabul etmedikleri risk faktörü sorularının bazılarını ikinci ankette kabul ettiler. Astım ve diğer allerjik hastalıklar için risk faktörleri anketleri arasında farklılıklar vardı. Suçiçeği öyküsü, yineleyen alt solunum yolu infeksiyonu öyküsü hem ilk hem de ikinci ankette temel risk faktörleri olarak belirlendi. Her iki ankette de, ailede allerjik rinit öyküsü olması allerjik rinit gelişimi için temel risk faktörüydü.

Sonuç: Risk faktörleri ve allerjik hastalıkların prevalansı arasında güvenilir neden-sonuç ilişkisi elde edebilmek için, özellikle düşük sosyoekonomik durumu olan toplumlarda, anket çalışmalarına ek olarak ayrıntılı serolojik ve immünolojik laboratuvar testlerinin yapılması gerektiğini öneriyoruz.

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Anahtar kelimeler: ISAAC, anket, ebeveyn, risk faktörleri, epidemiyoloji

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ases and to investigate the relationship between the allergic diseases and possible environmental (pollen and spore counts, air pollution, nutrition, immunization, indoor pollution [house dust mites], endotoxin) risk factors^[1-4].

These studies were performed with five-year intervals using the data obtained from the parent-reported ISAAC (International Study

of Asthma and Allergies in Childhood) questionnaires for allergic diseases among school-age children. The ISAAC questionnaire is being used in more than 40 countries for investigating asthma. This important study will define geographical variation in asthma prevalence and permit exploration of the reasons for these variations. Because of the differences in the sociocultural status of populations, an epidemiological survey with written questionnaires may result in some perception problems^[5-10].

We found similar results in our first two studies (24.7% and 24.9%); however, the recent 2004 study pointed out a significant increase (33.9%) in the prevalence of the allergic diseases^[1,2]. In this study, we aimed to compare two different questionnaire techniques-the direct parent-reported and the doctor guided-parent reported questionnaires-in determining the risk factors for allergic diseases among school-age children. In addition, we evaluated the relationship between risk factors and objective criteria of allergic diseases and asthma (specific IgE, skin prick test and pulmonary function tests).

MATERIALS and METHODS

Five thousand one-hundred and fifty ISAAC questionnaires were given to school-age children (6-14 years), and 3470 (67.3%) of these were returned^[3]. The parents completed a simple two-page written questionnaire about asthma, allergic rhinoconjunctivitis and atopic eczema and a one-page questionnaire about the risk factors (Part of ISAAC questionnaire is given in Appendix 1). One hundred children with no allergic symptoms were chosen randomly as the control group (Figure 1). According to the questionnaire results, we constituted an atopic group of 100 children.

The atopic group was composed of children with at least one allergic symptom (n= 51) from the three allergic diseases (asthma, allergic rhinitis, and atopic dermatitis) according to the direct parent questionnaire (n= 49).

The ISAAC questions were applied to the same parents a second time by a doctor who also filled in the forms and examined the children. Pulmonary function and skin prick tests were performed. Skin prick tests were performed on the forearm, with aeroallergens manufactured by ALK-Abello (tree pollen mixture, grass pollen

Appendix 1. Core questionnaire for wheezing and asthma (ISAAC)

1. Have you (has your child) ever had wheezing or whistling in the chest at any time in the past? <i>If you have answered "No" please skip to question 6</i>	Yes/No
2. Have you (has your child) had wheezing or whistling in the chest in the last 12 months? <i>If you have answered "No" please skip to question 6</i>	Yes/No
3. How many attacks of wheezing have you (has your child) had in the last 12 months?	None/1-3/4-12/> 12
4. In the last 12 months, how often on the average, has your (your child) sleep been disturbed due to wheezing?	Never woken with wheezing/ less than one night per week/ one or more nights per week
5. In the last 12 months, has wheezing ever been severe enough to limit your (your child's) speech to only one or two words at a time between breaths?	Yes/No
6. Have you (has your child) ever had asthma?	Yes/No
7. In the last 12 months, has your (your child's) chest sounded wheezy during or after exercise?	Yes/No
8. In the last 12 months, have you (your child) had a dry cough at night apart from a cough associated with a cold or flu?	Yes/No

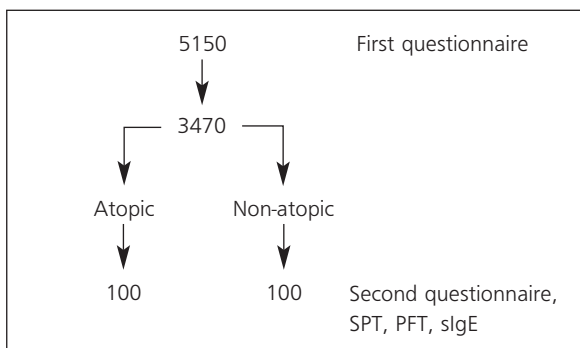


Figure 1. Description of the study population.

mixture, mites, cat and dog dander, mold mixture). Negative (saline solution) and positive (histamine 1 mg/mL) controls were used. After 15 minutes, the diameter was measured in millimeters (mm). Skin prick test was considered positive when the mean wheal size was greater than 3 mm in relation to a negative control. Specific IgE was analyzed by ImmunoCAP, Pharmacia®. This panel was used to analyze specific IgE to a combination of common inhalant allergens: cat, dog, birch, mugwort, Parieteria, mold fungus (*Alternaria* and *Cladosporium*), and house dust mite (*Der p1* and *Der p2*), and food allergens (milk, egg, peanut and wheat). The test was performed according to the manufacturer's instructions, and results are expressed in kU/L. The environmental, nutritional and genetic factors and the medical history of the children (past infectious diseases, parasites and immunization) were also evaluated. Both the first (3470 children) and the second (100 atopic and 100 non-atopic children) groups were given the risk factor questionnaires individually. We compared the differences between the answers of the direct parent-reported and the doctor guided-parent reported questionnaires. We also compared the results of the second group of 200 children according to the risk factors in the doctor guided-parent reported questionnaires and the laboratory evaluations that were also performed.

In statistical analysis, Cochran-Armitage Trend test was used to evaluate the trend of prevalence in different years. The crude association between asthma and allergic diseases and potential risk factors were analyzed via chi-squ-

are test after continuity correction, using the data from the 2004 survey. Multiple logistic regression analysis models were constructed to examine the independent association between the potential risk factors and current wheeze, doctor-diagnosed asthma, current rhinitis, doctor-diagnosed rhinitis, atopic eczema, general allergic diseases, and asthma. Statistical significance was defined as $p < 0.05$. The p values less than 0.01 and 0.001 were also noted.

RESULTS

Differences Between the Results of the Direct Parent-Reported Questionnaire and the Doctor Guided-Parent Reported Questionnaire

After evaluating the data obtained from the two questionnaires, we observed statistically significant differences in the answers to several questions. For example; while 11.6% of parents reported insufficient sunlight in the first (parent-reported) questionnaire, they denied it in the second (doctor-guided). 37.1% of parents reported sufficient sunlight in the house in the first questionnaire and denied it in the second, though they still lived in the same house. According to the first report, 41.8% who reported presence of indoor humidity denied it in the second questionnaire. Likewise, 19.3% who claimed having fungi on their indoor walls denied it in the second doctor-guided questionnaire. 24.8% of the parents who marked "cockroach indoors" denied it in the second questionnaire, and vice versa, 52.8% who reported the presence of cockroach indoors in the second questionnaire denied it in the first (Table 1).

Risk Factors

The risk factors for asthma and other allergic diseases and differences between the two questionnaires are shown in Tables 2-5. In the first questionnaire, smoking during pregnancy, having pets at home, and family history of allergic diseases and asthma were determined as risk factors for asthma. History of varicella and history of recurrent lower respiratory tract infection were found as major risk factors both in first

Table 1. Differences between two questionnaires

	% change
Insufficient sunlight in the house	11.6*
Sufficient sunlight in the house	37.1*
Presence of indoor humidity	41.8*
Visible fungi on the wall	19.3*
Presence of cockroach	24.8*
	52.8**
Earth or concrete floor	35.7*
Family history of asthma	32.0*
	17.8**

* Denied in the second questionnaire.

** Accepted in the second questionnaire.

and second questionnaires. Having a bird at home during pregnancy was found as a risk factor according to the second questionnaire, but not according to the first. Family history of allergic rhinitis was the major risk factor for the development of allergic rhinitis in both questionnaires. Similarly, family history of atopic der-

matitis was found to be the major risk factor for atopic dermatitis in the first and second questionnaire. Presence of parasites was found as a risk factor for allergic rhinitis and atopic dermatitis according to the first questionnaire.

Laboratory

The first step was to evaluate the ISAAC questions and the lab results. The group with allergic signs (100 atopic patients) was compared with the control group (100 non-atopic controls) according to the answers from the doctor guided-parent reported questionnaires. The comparison was based on their positive response to at least one lab test (skin prick test and specific IgE panel). There was no significant difference between these two groups ($p > 0.05$). Similarly, no statistically significant difference was found between these two groups according to pulmonary functions. In the second step of the study, the answers were matched with the lab parameters individually. The positive lab results were found

Table 2. Differences between two questionnaires for risk factors for allergic rhinitis

	First questionnaire				Second questionnaire			
	Exp (B)	95% CI		p	Exp (B)	95% CI		p
Lower		Upper	Lower			Upper		
Yogurt consumption								
Home made	0.532	0.307	0.921	0.024	-	-	-	NS
Commercial	0.916	0.576	1.455	0.709	-	-	-	NS
Insufficient sunlight in the house	1.506	1.063	2.133	0.21	11.056	1.925	63.505	0.001
Lower respiratory tract infection during 1-3 age								
None				0.000	-	-	-	NS
1-3 times	3.478	2.276	5.315	0.000	-	-	-	NS
> 4 times	2.115	1.354	3.302	0.001	-	-	-	NS
Presence of parasitizes	1.496	1.005	2.226	0.047	-	-	-	NS
Positive test for echinococcus	1.780	1.047	3.028	0.033	-	-	-	NS
Family history of allergic rhinitis	2.833	2.099	3.822	0.000	18.364	4.071	82.840	0.001
Family history of allergic conjunctivitis	1.781	1.245	2.547	0.002	-	-	-	NS
Family history of drug allergy	2.407	1.481	3.914	0.000	-	-	-	NS
History of mump	-	-	-	NS	18.364	1.519	222.01	0.001
History of varicella	-	-	-	NS	8.115	1.491	44.18	0.014
Varicella vaccine	-	-	-	NS	7.794	1.421	42.73	0.032
Attending to day care during infancy	-	-	-	NS	41.874	4.786	366.32	0.001

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Table 3. Differences between two questionnaires for risk factors for asthma

	First questionnaire				Second questionnaire			
	Exp (B)	95% CI		p	Exp (B)	95% CI		p
		Lower	Upper			Lower	Upper	
Smoking during pregnancy	1.606	1.060	2.434	0.026	-	-	-	NS
History of varicella	1.659	1.138	2.417	0.008	4.068	1.063	15.562	0.040
Lower respiratory tract infection during 1-3 age								
None				0.000				0.15
1-3 times	5.815	3.564	9.487	0.000	1.268	0.395	4.069	0.690
> 4 times	3.272	1.959	5.464	0.000	5.779	1.624	20.565	0.007
Having pet during the first year of life	2.255	1.465	3.471	0.000	-	-	-	NS
Family history of allergic diseases	1.770	1.115	2.810	0.015	-	-	-	NS
Family history of asthma	3.744	2.398	5.848	0.000	-	-	-	NS
Central heating	2.832	1.436	5.584	0.003	-	-	-	NS
Having bird at home during pregnancy	-	-	-	NS	3.816	1.204	12.098	0.023

Table 4. Differences between two questionnaires for risk factors for atopic dermatitis

	First questionnaire				Second questionnaire			
	Exp (B)	95% CI		p	Exp (B)	95% CI		p
		Lower	Upper			Lower	Upper	
Passive smoking during pregnancy	1.427	1.061	1.917	0.019	-	-	-	NS
Cheese consumption								
None				0.015	-	-	-	NS
Every other day	0.654	0.481	0.889	0.007	-	-	-	NS
Every day	0.735	0.543	0.994	0.046	-	-	-	NS
Presence of parasitizes	1.563	1.090	2.243	0.015	-	-	-	NS
Heating with electric	1.680	1.259	2.241	0.000	-	-	-	NS
Central heating	1.745	1.058	2.877	0.029	-	-	-	NS
Family history of allergic diseases	1.787	1.359	2.352	0.000	-	-	-	NS
Family history of atopic dermatitis	2.191	1.508	3.182	0.000	7.169	2.103	24.438	0.002
Family history of allergic rhinitis	-	-	-	NS	5.840	1.692	20.155	0.005
Visible fungi on the wall	1.488	1.149	1.926	0.003	-	-	-	NS
Attending to day care during infancy	-	-	-	NS	6.060	1.115	32.929	0.037
Having pet during pregnancy and/or at present	-	-	-	NS	4.702	1.212	18.236	0.025

Table 5. Risk factors for skin prick test/specific IgE positivity.

	Exp (B)	95% CI		p
		Lower	Upper	
MMR vaccine	6.595	1.461	29.766	0.014
Having pet during pregnancy	5.397	1.272	22.889	0.022
Having pet at present	2.630	1.264	5.473	0.10

significantly higher among the children who responded positively to the doctor-diagnosed asthma or rhinitis questions ($p < 0.05$).

DISCUSSION

It is reported that allergic diseases and asthma have increased rapidly worldwide especially in the last two decades^[3,4]. We have performed three consecutive researches in our clinic with five-year intervals since 1995 to determine the prevalence of allergic diseases among school-age children. The prevalence of cumulative allergic diseases was close in the first two surveys (24.7% and 24.9%). However, we found a significant increase in the prevalence of allergic diseases in the third 2005 survey (33.9%). While investigating the cause of this unexpected and significant increase in the last five years, some questions arose over the reliability and validity of the questionnaire technique used in such studies.

In ISAAC studies, the data are always obtained from the direct parent-reported or video-supported questionnaires^[3]. However, in the literature, there are some reports of false-positive or false-negative answers in underdeveloped countries like sub-Saharan Africa, due to the social or language insufficiencies^[5-7].

In this study, we used a second ISAAC questionnaire, which was directed to the parents of the randomly selected 200 patients by a doctor. We determined three major significant differences between the answers obtained from the questionnaires. Since the literature reports several cases of falsely perceived questions, we assumed that the changes in the answers might have been due to not only the social and lingu-

al factors but also to factors such as motivation, mood and duration of the questionnaire^[5-9]. Today, there is a tendency to use parameters like exhaled NO level for diagnosis and genetic analysis for determination of risk factors^[11,12].

In our study, we compared the laboratory results and the answers to the questionnaires of children with asthmatic symptoms, including those with doctor-diagnosed asthma, with the asymptomatic group. We found no difference between these two groups. We believe that the result is related to this fact, which brings forth the importance of confirming asthma by bronchoprovocation tests. Therefore, allergic diseases should be supported by laboratory evaluations in order to define final questionnaires. We believe that this result may be related to the fact that three-fourths of childhood asthma is mild intermittent asthma and pulmonary function test is normal^[8,9]. On the other hand, the other lab parameters showed significant correlation only for the doctor-diagnosed asthma and doctor-diagnosed rhinitis cases. These statistical results support the fact that the other questions might also be open to misunderstanding, which would consequently lead to false answers.

These results increased our suspicion about the marked increase in asthma in our allergy survey. We aimed at solving the problem of obtaining false answers by applying the same questionnaire for a second time under doctor supervision. We thus formed two groups, each of which included 100 children selected randomly among the children who were evaluated as allergic or non-allergic according to the direct parent-reported questionnaire, and administered the questionnaire again under doctor guidance. The results of the second application were surprisingly different in the risk factors part of the questionnaire, by nearly 50%. For example, although cockroach was a major risk factor in the parent-reported questionnaire, it was not found significant in the second questionnaire (doctor guided-parent reported). Another contradiction was regarding the presence of oxiur or ascaris in feces, which was found significant in the first result and insignificant in the second. Recent li-

terature indicates that the presence of parasites in the intestines is an increasing risk factor for allergic diseases in subtropical regions, but a preventative factor in the tropical regions^[10-15]. This difference was explained by the amount of parasites in the intestines (worm type) and the amount of the antigens.

This could also be compatible with our results since the city of our survey showed characteristics of subtropic regions. However, there should be more reliable evidence to postulate the presence of parasites in feces as a major risk factor for allergy.

In conclusion, we suggest that the ISAAC questionnaire technique should not be used alone if valid results are aimed at evaluating the prevalence and risk factors for allergy globally. We believe that not only direct parent-reported but also doctor guided-parent reported questionnaires may lead to significant false-positive or false-negative results in such studies, especially in populations with lower socioeconomic status, unless they are supported by some practical and inexpensive lab tests for more reliable and valid results. Furthermore, as reported often in the recent literature, the risk factors determined by the ISAAC questionnaire should be asked with the "doctor-diagnosed asthma or rhinitis" question instead of the "current wheeze" question^[3,4,12,13].

In order to obtain a reliable cause-result relationship between the risk factors and the prevalence of allergic diseases, we suggest that detailed serologic and immunologic lab tests should be performed in addition to the questionnaire studies, especially in populations with lower socioeconomic status.

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