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Epidemiologic characteristics of rhinitis in Turkish Children: the International Study of Asthma and Allergies in Childhood (ISAAC) phase 2

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Rhinitis is a common problem with important comorbidities. In order to search the association between rhinitis, allergic phenotypes and other risk factors in Turkish children, a parental questionnaire about allergic diseases and risk factors, and skin prick test (SPT) with 13 inhalant allergens were performed in a population-based sample of 2774 children aged 9–11 yr. Bronchoprovocation testing with hypertonic saline (HS)and total IgE analysis were limited to a subsample of 350 children. Rhinitis was defined as a problem with sneezing, rhinorrhea, or nasal congestion when the child did not have a viral respiratory infection. The prevalences of ever rhinitis, current (last 12 months) rhinitis (CR), and ever hay fever were 36.3%, 30.6%, and 8.3%, respectively. SPT positivity rate was 20.4% among children with CR. Current wheezing and flexural dermatitis were significantly associated with CR. CR significantly increased the risk of asthma among both atopic and non-atopic subjects [odds ratio (OR), 3.98; 95% CI, 1.81–8.76; and OR, 2.79; 95% CI, 1.82–4.26, respectively]. The association between CR and bronchial hyperreactivity (BHR) was not significant. The multiple logistic regression analysis revealed family atopy (OR = 2.25, 95% CI = 1.79–2.83, $p < 0.001$), current indoor heating with gas stove (OR = 1.78, 95% CI = 1.18–2.64, $p = 0.006$) and dampness/molds at home during the first year of life (OR = 1.70, 95% CI = 1.25–2.31, $p = 0.001$) as significant risk factors for CR. Turkish school children showed a high prevalence of rhinitis with a preponderance of non-atopics. The highly significant association between rhinitis and asthma independent of atopic sensitization emphasize the importance of non-atopic forms of rhinitis.

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Rhinitis is defined as the inflammation of the nose characterized by one or more of the following symptoms, nasal congestion, rhinorrhea, sneezing, and/or itching. There are various forms of rhinitis such as infectious, vasomotor, irritant-induced, and eosinophilic nasal disease such as non-allergic rhinitis with eosinophilia syndrome (NARES), in addition to allergic. It is considered to be allergic if shown to be associated with an IgE-mediated hypersensitivity to an allergen (1, 2). It is more difficult to define allergic rhinitis in epidemiological studies of large populations where individual assessment is not possible (2, 3). Both overestimation and underestimation of the real prevalences can occur according to the screening methodology and the population studied (4, 5). The International Study of Asthma and Allergies in Childhood

(ISAAC) was initiated to develop a standardized methodology in epidemiologic research of asthma and allergies. It revealed great variations in prevalence figures of allergic diseases both between and within countries (6). As a further step, ISAAC Phase II study was conducted in a substantial number of representative countries in order to explore for the reasons of these variations with the help of objective tests (7). The ISAAC core questions on rhinitis was previously validated in different populations (5, 8).

Recent epidemiologic studies have revealed that besides being a very common health problem, rhinitis may be an independent risk factor for asthma, even in the absence of atopy (9, 10). To date, no population-based studies have examined the relation among rhinitis, objective allergy markers and asthma in Turkish children. The present study was conducted to explore the prevalence and risk factors for rhinitis and also to search for its relationship with asthma, atopic dermatitis and allergic sensitization in a population-based sample of Turkish school children.

Methods

This study was conducted according to ISAAC Phase-II guidelines (11). The details of the study area, population, design, and procedures were described in detail elsewhere (12, 13). These will be described briefly here.

Study population and design

The study was conducted in Ankara, the capital of Turkey, between October 1999 and April 2000. This metropolitan city, harboring approximately four million inhabitants, receives a number of immigration from mostly rural portions of Anatolia every year. In the last few years, outdoor air pollution has substantially increased, especially in some underprivileged districts of the city, owing to the usage of bad quality charcoal for heating. Additionally, heavy car traffic with motor vehicle exhaust immissions contribute much to the air pollution during winter and summer. Outdoor air pollution due to sulfur dioxide (SO_2) and particulate matter (PM) has been routinely monitorized by stations located within administrative districts. These pollution data were available as mean daily, and yearly values.

Three months before the ISAAC study, a pilot study including parental self-administered ISAAC questionnaire and skin prick tests (SPT) was performed in a single school. The validity of parent-filled questions was evaluated by face-to-face interview with parents and found to be concordant.

The sampling method was two-stepped. In the first step of the study (prevalence study) the eight administrative districts of Ankara were accepted as the strata and weighted number of schools were selected in a stratified random manner from a complete list of primary schools in Ankara. All school children attending the fourth grade in 22 schools ($n = 3426$) were selected, primary schools being the sampling unit. A parent-filled questionnaire and SPT were administered in this population.In the second step (case–control study), these children were stratifed according to the presence or absence of wheezing in the last 12 months based on questionnaire responses. One hundred and seventy-five children from 'current wheezers' stratum and 175 children from 'current non-wheezers' stratum were randomly selected by block randomization method. These 350 children were recruited to blood sampling for serum specific and total IgE measurements, spirometric measurements, and bronchial challenge tests.

Questionnaires and definitions

The ISAAC Phase-II questionnaire modules including questions about demographic characteristics, rhinitis, wheezing, eczema, and risk factors were employed (11).Rhinitis was defined as a problem with sneezing, or a runny or blocked nose, when the child did not have a cold or flu. It is labeled as current if present in the last 12 months, and current rhinocunjunctivitis, if accompanied by eye symptoms. Hay fever was sought by the question 'has your child ever had hay fever?'. In our country general practitionaires and some pediatricians generally prefer to use the diagnostic term 'allergic bronchitis' instead of 'asthma', in order to avoid mislabeling or family demoralization. Hence, children whose parents reported either asthma, asthmatic bronchitis, or allergic bronchitis at least once were classified as having physician-diagnosed (PD) asthma. 'Current wheeze' was defined as a positive response to 'has your child had wheezing or whistling in the chest in the last 12 months?' Children whose parents reported an itchy rash which was coming and going for at least 6 months and involving any of the flexural areas in the last 12 months were labeled as having current flexural rash. In our population atopic dermatitis is generally diagnosed as 'eczema', or less commonly 'allergic eczema' by the physicians. Hence, children who ever had an diagnosis of eczema were classified as PD eczema. The risk factor questionnaire included 31 questions about socioeconomic and

demographic characteristics, gestational factors, feeding practices, family history, siblings, childhood infections, household conditions (heating, dampness, bedroom, etc.), animal contacts, tobacco smoke exposure (pre-natal and post-natal), for both current time and first year of life. Family atopy was defined as a positive history of asthma, rhinitis, and/or eczema in one or both of the parents.

Procedures

The SPT were performed with six 'core' allergen extracts recommended in ISAAC phase II module (11); *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Alternaria alternata*, cat epithelium, mixed grasses (*Phleum pratense, Poa pratensis, Dactylis glomerata*, *Lolium perennae*, *Festuca pratensis*, *Avena eliator*), and mixed trees (Tree mixed St: *Betula verrucosa*, *Alnus glutinosa*, *Coryllus avellena*). Seven additional allergens of local relevance were also added; *Parieteria officinalis*, *Cladosporium herbarum*, *Olea europea*, mixed feathers, mixed weeds (*Artemisia vulgaris*, *Chenopodium*, *Plantago*, *Salsola kali*), mixed local trees (Tree mixed L: *Quercus alba*, *Ulmus americana*, *Platanus*, *Salix*, *Populus)*, and *Blatella germanica*. Histamine 10 mg/ml and diluent were used as positive and negative controls, respectively. The standardized core allergen extracts and controls were provided by ALK-Abello (Hørsholm, Denmark), and standardized local allergens were provided by ALK-Abello, Allergopharma (Reinbek, Germany), and Center Pharmaceuticals Inc. (FL, USA). SPT was performed as recommended in ISAAC Phase-II module on the volar side of the forearm (11). A positive skin reaction was defined as a wheal size ≥3 mm, after substraction of the negative control. Atopy was defined as the presence of at least one positive skin reaction to any allergen tested.

Serum total IgE levels were measured in 350 children forming the case–control group by fluoroenzymeimmunoassay method (UniCAP, Pharmacia and Upjohn, Uppsala, Sweden). Levels of serum specific IgE for *D. pteronyssinus*, *D. farinae*, cat, cockroach, grass mix, tree mix, weed mix, olea, and *Cladosporium* were measured by fluoroenzymeimmunoassay method (UniCAP) in 80 children that were selected at random from those with and without a positive skin prick test.

Spirometry and bronchial challenge test with hypertonic saline (HS) were performed according to the standardized protocols (11) of ISAAC Phase II. Lung function was measured by a portable spirometer, Masterscope Version 4.1 (Jager, Germany). Subjects were excluded from the bronchial challenge test if the baseline FEV1 value was $<75\%$ of the predicted or in the case of non-compliance. The HS challenge test was performed with 4.5% saline delivered via a De Vilbiss ultrasonic nebuliser (De Vilbiss, Langen, Germany) Bronchial hyperreactivity (BHR) was defined when there was a fall of 15% or more in FEV1 from baseline during the procedure.

Statistical analysis

The SPSS software package version 10.0 was used for all calculations. Comparisons were done using Student's *t*-test for continous variables and the x^2-test for proportions.Test for trends was done using the Mantel–Haenszel test statistic.

The strength of association between rhinitis and comorbidities was expressed by odds ratio (OR), with their 95% confidence interval, unadjusted, and adjusted by age, sex, family atopy, and atopic sensitization.

The association between demographic and environmental risk factors and current rhinitis were analyzed with x^2-test, and univariate and multivariate logistic regression analysis. Major independent variables were: maternal and paternal atopic disease histories; maternal and paternal education levels (two categories; <8 yr, >8 yr); family income (two categories; <350 and ≥350 $/month); total number of siblings (two categories; 0–1, 2+ siblings); birth weight (two categories; <2500 g, ≥2500 g); month of birth (two categories; pollen season, winter months); gestational age (three categories; 3 wk earlier than the calculated date, within 3 wk of the calculated date, 3 wk later than the calculated date); duration of breast feeding (three categories; none, 1–6 months, more than 6 months or two categories; none to 6 months, more than 6 months); attendance at day care; current passive smoking; maternal smoking during pregnancy; maternal smoking during the first year of life; measles history; current and first 12 months exposures to: heating systems (classified as none, indoor wood/coal burning stove, indoor gas (methane) stove, indoor electric heating, central heating), bedding/pillows, mold/dampness at home, pets, cockroaches, poultry, and livestock. Initially, the crude association between risk factors and independent variables was analyzed. Variables that were associated with the outcomes in the univariate analysis at a p-value of less than 0.25 were examined in the multivariate logistic regression models. A backward reduction modeling strategy was used. Backward elimination started with all of the variables in the model. Then, at each step, variables were evaluated for

entry and removal. The score statistic was always used for determining whether variables should be added to the model.Wald statistic was used to select variables for removal (by default 0.10).The size of the effect of each of the risk factors was measured by using the ORs and 95% confidence intervals (CIs).

Ethical considerations

All study methods had been approved by the Ethics Committee of the Turkish Ministery of Health and the Ethics Committee of Hacettepe University, Faculty of Medicine. Informed written consent was obtained from the parents for all tests at one time at the beginning of prevalence study.

Results

Parents of 3056 (89.2%) children returned the questionnaire. Among those returned, 3041 (88.7%) questionnaires were taken into evaluation. Written consent for the tests were obtained from guardians in 2858 (92.5%) children. Of the eligible children SPT were performed and taken into evaluation in 2774 (97.1%). The analyses including serum total IgE and bronchial challenge test results were performed in subgroups of 347 and 329 children, respectively.

The demographic characteristics of the population were previously reported (12). Male/female ratio was 50.5/49.5%. Age of the children ranged between 8 and 11 yr (mean ± s.d., 9.14 ± 0.50). The prevalence of ever rhinitis, current rhinitis, current rhinoconjunctivitis, rhinitis, or conjunctivitis in pollen season and ever hay fever were 36.3%, 30.6%, 12.4%, 6.3%, and 8.3%, respectively. The association of rhinitis symptoms and diagnosis with allergy markers is shown in Table 1. Among subjects with current rhinitis skin test reactivity to at least one allergen was present in 20.4% and to any pollen allergen in 13.5% of children. Allergic sensitization rate was not significantly higher in children with rhinitis symptoms or diagnosis than those without. The most common sensitizing allergens were grass pollens, mites, and cockroach.The percentage of children with a serum total IgE level >100 kU/l was significantly higher among subjects with a previous history of hay fever ($p = 0.03$). Among children with atopic sensitization, 35.3% had ever rhinitis, 30.0% had current rhinitis, 4.0% had rhinitis in pollen season, and 7.1% had hay fever.

The SPT results were compared with the serum specific IgE results.The correlation between SPT and specific IgE was best for mite and grass allergens (81.2%, 93.8%, and 89.6%, respectively), while the lowest values were for weed mix (59.4%) and cat (62.6%) allergens. The specifity of SPT in relation to specific IgE measurements was over 90% for all antigens.

The association between current rhinitis and comorbidities is shown in Table 2. Children with a history of rhinitis in the last 12 months showed a significant association with PD asthma [adjusted odds ratio (aOR) = 3.00, 95% CI = 2.07–4.34], current wheezing (aOR = 3.16, 95% CI = 2.46–4.05), PD eczema (aOR = 1.89, 95% CI = 1.10–3.23), and current flexural rash (aOR = 3.50, 95% CI = 2.48–4.92) independent from age, sex, family atopy, and atopic sensitization. The association between current rhinitis and BHR and total IgE levels were analyzed in subsamples of 329 and 347 children. There was not any significant association between current rhinitis and total IgE levels ($p = 0.67$), or having high (>100 kU/l) IgE values ($p = 0.07$). The association between current rhinitis and BHR was also non-significant.

The association between rhinitis and asthma was further evaluated according to allergy markers. Current rhinitis significantly increased the risk of PD asthma both among those with atopic sensitization (OR = 3.98, 95% CI = 1.81–8.76) and those without sensitization (OR = 2.79,

Table 1. Association between rhinitis symptoms/diagnosis and allergy markers

	Skin test reactivity to				
Symptom/diagnosis	At least one allergen (n = 551) (%)	Mite (n = 171) (%)	Any pollen (n = 341) (%)	Cockroach (n = 152) (%)	Total IgE † >100 kU/l (n = 85) (%)
Current rhinitis	20.4	7.4	13.5	5.3	21.8
Current rhinoconjunctivitis	18.6	7.4	13.0	5.0	21.0
Current R or C in pollen season	14.2	6.3	8.0	3.4	20.8
Ever hay fever	18.2	4.1	14.5	3.2	39.1*

R: rhinitis; C: conjunctivitis.
*Significantly higher compared to subjects without a diagnosis, $p = 0.039$.
†Analyzed in a subgroup of 347 children.

Table 2. Association between current rhinitis and comorbidities

Comorbidity	Rhinitis		Crude OR	95% CI	Adjusted OR †	95% CI
	No (n = 1775) (%)	Yes (n = 781) (%)				
PD asthma	4.1	13.8	3.70	2.62–5.22	3.00	2.07–4.34
Current wheezing	7.3	21.5	3.50	2.77–4.42	3.16	2.46–4.05
Current flexural rash	3.3	10.8	3.57	2.56–4.98	3.50	2.48–4.92
PD eczema	1.7	3.4	2.02	1.21–3.36	1.89	1.10–3.23
STR ≥ 1 to aeroallergens	20.9	20.4	0.96	0.78–1.17	0.97	0.76–1.20
STR to pollens	12.6	13.5	1.08	0.85–1.38	1.10	0.85–1.42
STR to mites	6.0	7.4	1.25	0.90–1.73	1.34	0.95–1.90
STR to cockroach	5.9	5.3	0.90	0.62–1.29	0.81	0.55–1.19
Serum total IgE >100 kU/l ‡	29.2	21.8	0.74	0.41–1.10	0.61	0.35–1.05
Bronchial hyper-responsiveness ‡	24.6	25.9	1.07	0.64–1.78	0.99	0.58–1.70

†Adjusted for atopic sensitization (only for the first four comorbidities), age, sex, and family atopy.
STR: skin test reactivity; PD: physician-diagnosed.
‡Studied in subgroups of 347 and 329 children, respectively.

Table 3. Multiple logistic regression analysis of risk factors† for current rhinitis

	p-Value	Odds ratio (OR)	95% CI
Family atopy	0.000	2.25	1.79–2.84
Current heating with gas stove	0.006	1.76	1.18–2.64
Dampness/mold at 1 yr of age	0.001	1.70	1.25–2.31

†Final model is presented. Factors included in the first model of backward analysis: age, sex, family atopy, number of siblings, maternal smoking, previous measles, and parasitic infection, current and first year exposure to; heating systems (wood/coal stove, gas stove), furry pets, dampness/molds at home, and cotton pillow.
CI: confidence interval.

Table 4. Multiple logistic regression analysis of risk factors for current rhinitis in subjects with negative SPT

	p-Value	Odds ratio (OR)	95% CI
Family atopy	0.000	2.22	1.69–2.93
Current heating with gas stove	0.002	2.01	1.29–3.13
Dampness/mold at 1 yr of age	0.000	2.00	1.42–2.82

Factors included in the first model of analysis include age, sex, family atopy, number of siblings, maternal smoking, previous measles, and parasitic infection, current and first year exposure to; heating systems (wood/coal stove, gas stove), dampness/molds at home.
CI: confidence interval; SPT: skin prick test.

95% CI = 1.82–4.26). In a multivariate model, current rhinitis was still significantly associated with PD asthma after adjusting for age, sex, atopic sensitization, and total IgE levels (OR = 2.43, 95% CI = 1.20–4.92, p = 0.013).

The multiple logistic regression analysis revealed family atopy (OR = 2.25, 95% CI = 1.79–2.83, p = 0.000), current indoor heating with gas stove (OR = 1.76, 95% CI = 1.18–2.64, p = 0.006) and dampness/molds at home during the first year of life (OR = 1.70, 95% CI = 1.25–2.31, p = 0.001) as significant independent factors (Table 3). In order to find out if any multicollinearity was existing between independent variables, we examined the correlations and associations between independent variables, additionally we examined the changes in beta, SE of beta and related p-values by adding interaction terms into the model. As a result we found that there were collinearities between parental education level and a variety of environmental risk factors, and decided not to enter the family education in this model.

We also investigated the association between current rhinitis and risk factors in a subgroup of children without any SPT positivity in a similar manner with backward logistic regression analysis (Table 4). The same risk factors; family atopy (OR = 2.22, 95% CI = 1.69–2.91, p = 0.000), current indoor heating with gas stove (OR = 2.01, 95% CI = 1.29–3.13, p = 0.002) and dampness/molds at home during the first year of life (OR = 2.00, 95% CI = 1.42–2.82, p = 0.000) were found to be significantly associated with current rhinitis and the strength of associations were stronger than the original group.

Discussion

The present study showed that rhinitis, defined as sneezing, rhinorrhea, or nasal congestion apart from viral respiratory infection in the last 12 months affected almost a third of 9 to 11-year-old children. In previous prevalence studies the figures for rhinitis ranged between 6.3% and 39.9% in different regions of Turkey in school-aged children (14–16). Worldwide ISAAC Phase-I study revealed that allergic rhinoconjunctivitis symptoms ranged from 0.8% to 14.9% in the 6–7-year olds and from 1.4% to 39.7% in the 13–14-year olds from 91 to 155 centers,

respectively (6, 17). The highest prevalences of allergic rhinoconjunctivitis symptoms were reported from scattered centers in the world and showed discrepancy with asthma symptom distribution pattern. Our prevalence figure for current rhinoconjunctivitis was of moderate level among worldwide values. The large variations in prevalence values of rhinitis questions between centers is believed to be affected, at least in part, by cultural, and linguistic differences and hence validity of written questionnaires (6).

It is generally agreed that the prevalence of atopy can only partly explain differences in the prevalence of allergic diseases (18). In the present study, the associations between atopic sensitization and rhinitis symptoms, or PD hay fever were not significant. In some population studies there was a close correlation between the number of skin test reactivity to aeroallergens and allergic rhinitis (19). On the other hand, other studies conducted in different parts of the world found no significant, or limited association between rhinitis symptoms and atopic sensitization (18, 20, 21). These results and our data show that allergic rhinitis presents some diagnostic challenges in epidemiologic studies. Presumably, non-allergic forms of rhinitis and some forms of infectious rhinitis are also included among the cases, in different proportions according to the population studied. When we analyzed the relation between rhinitis and atopic sensitization in different districts belonging to different socioeconomic strata, we found that in some districts there was a significant association between current rhinitis and atopic sensitization, whilst in others not (data not shown). This suggests that cultural, educational and language factors underlying the difference of populations may influence the accuracy of questionnaire studies (17).

Chronic nasal symptoms without allergic causation are known as non-allergic rhinitis. Among a wide variety of etiological factors infections, chronic sinusitis, structurally related ones such as adenoid hypertrophy and septal deviation, irritant-induced (such as indoor and outdoor air pollution, passive smoking) rhinitis, and eosinophilic nasal disease such as NARES are most commonly encountered, especially among children (22). Epidemiologic data about the prevalance values for non-allergic rhinitis are scarce in childhood populations. In different series, frequency of non-allergic rhinitis was reported between 17% and 50% of rhinitis sufferers (10, 23, 24). The Joint Task Force points out that data regarding the true prevalance of rhinitis are difficult to interpret (23). Although Togias (24) has observed a predominance of adults among cases with non-allergic rhinitis, the same association was not observed by other authors (2, 25). Agius et al. (25) have examined the epidemiological characteristics of Maltese chronic rhinitis cases aged 5 to >70 yr in an outpatient clinic. Approximately half of the patients were skin test negative. Overall age difference between atopic and non-atopic rhinitis cases was not significant. Childhood prevalance studies where subjects with rhinitis had low atopic sensitization rates, point out that non-allergic rhinitis may be more frequent than expected in some populations (18, 20, 21). In Tucson study, 63% of children had rhinitis of some type by age 6, of whom only 34.2% were skin test positive (26). It is possible that in populations with a high incidence of infections and indoor–outdoor pollution, non-allergic forms of rhinitis, or rhinosinusitis increase. In the present study, we found that environmental factors such as dampness/molds at home, and indoor heating with gas stove, in addition to family atopy, were significant risk factors for rhinitis in multivariate logistic regression analysis. Additionally, there was an inverse association, though not reaching statistical significance, between rhinitis symptoms and paternal education level, which is a good predictor of SES. On contrary, we found a significant positive correlation between atopic sensitization and paternal education level in a previous study (13). High frequency of infections, poor living conditions such as dampness and indoor/outdoor pollution may be underlying reasons of the association between rhinitis and low SES. In previous studies low SES (27), dampness/molds at home (28), outdoor air pollution (29), and household gas stoving/cooking (28, 30) were found as significant risk factors for questionnaire based rhinitis symptoms among child populations. Especially dampness at home and use of domestic gas appliances may have pronounced effects on different respiratory health symptoms among both atopics and non-atopics (31). Gas stoves release respiratory irritants such as nitrogen dioxide and other combustion by-products. Gas stove exposure was found to be a significant risk factor for respiratory symptoms even after adjusting for nitrogen dioxide levels, although short term peak levels were not taken into account (32). It is not possible to speak of the type of pollutant(s) that may have resulted in this association between gas stove and current rhinitis, since we did not measure levels of any type of indoor pollutants.

In another study conducted in İstanbul, Turkey, authors have found that residence in a highly polluted area significantly increased the

risk of symptoms of allergic rhinitis among both atopics and non-atopics (29). According to the formal data provided by the Refik Saydam Hygiene Center in Ankara, mean annual (1999) outdoor air concentrations of SO2 and PM were 57.8 and 76.4 $\mu g/m^3$ for Ankara as a whole, while those annual figures reached to 77.7 and 98.7 $\mu g/m^3$, respectively, in some heavily polluted districts of the city. Some of these values were higher than the primary air quality standarts for different countries (33). Bad quality charcoal usage in central heating systems contributes to the increase in levels of these pollutants. These outdoor pollutants may be one of the reasons that resulted in an increased prevalence of rhinitis symptoms in Ankara school children. However, assesment of individual exposures to pollutants would be an ideal method in order to make conclusions about the exact role of SO_2 and PM in the development of rhinitis in children.

One of the most striking findings of this study was the significant association between asthma and rhinitis symptoms, among both atopic and non-atopic cases. This was also valid for the association between rhinitis and eczema symptoms and diagnosis. A number of cross-sectional studies have demonstrated that allergic rhinitis and asthma commonly occur together (16, 26, 34). Our study showed that 56.3% of cases with a previous diagnosis of PD asthma had rhinitis. The PD asthma was present in 13.8% of those with rhinitis and 4.1% of those without rhinitis. There was a significant relationship between rhinitis and diagnosed asthma, eczema, current rash and current wheezing. The significant association between rhinitis and asthma did not change among different socioeconomic groups (data not shown). Moreover, this significant association was, albeit higher in atopics, independent of atopic sensitization, family atopy, and IgE values. In recent years, a limited number of population studies involving mostly adults have revealed rhinitis as an independent risk factor for asthma among non-atopic subjects (9, 10, 35). Leynaert et al. (35) on behalf of the ECRHS group have shown that the strong (OR = 6.63, CI = 5.44–8.08) association between asthma and rhinitis detected in all participating countries was independent of smoking, allergic sensitization, total IgE, and parental history of asthma. The OR was found to be higher among non-atopic individuals.The reasons underlying this association are not clear yet. A number of theories regarding the mechanisms underlying connections between the upper and lower airways are proposed such as nasal-bronchial reflex mechanisms, loss of nasal air conditioning functions, chronic mouth breathing and dissemination of inflammatory mediators or cells via nasal drainage or the systemic circulation (36). Our results have confirmed previous studies in that the strong association between rhinitis and asthma is an universal phenomenon, also in children.

Since this is a cross-sectional study, it is impossible to make causal inferences. Another limitation of the present study was that the relationship between rhinitis and other comorbidities was questionnaire-based. We could not find a significant association between rhinitis and BHR measured by HS challenge. In ECRHS study, there was a significant relation between allergic rhinitis and BHR apart from an asthma diagnosis in adults (35). In contrast, non-asthmatic children with allergic rhinitis did not show a higher degree of BHR than asymptomatic atopic or non-atopic controls in German MAS study involving 7-year-old children (37). It seems possible that the development of BHR in subjects with rhinitis may be an age-related issue.Of course, methodologic problems such as reporting bias should not be overlooked.

In conclusion, the present cross-sectional epidemiologic study has shown that non-infectious rhinitis was a common problem and not significantly related to atopic sensitization in 9 to 11-year-old Turkish children. However, it showed a strong association with asthma independent of atopic sensitization. Environmental risk factors such as indoor dampness and gas stoving were significant risk factors for rhinitis, besides parental atopy.

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References

1. International Consensus Report on the Diagnosis and Management of Rhinitis. Allergy 1994: 49 (Suppl. 9): 5–34.

2. Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: clinical presentation and medical history. Thorax 1991: 46: 895–901.
3. Bousquet J, van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. ARIA Workshop Report. J Allergy Clin Immunol 2001: 108: S147–276.
4. Gruchalla RS, Gan V, Roy L, Bokovoy J, Mcdermott S, Lawrence G, et al. Results of an inner-city school-based asthma and allergy screening pilot study: a combined approach using written questionnaires and step testing. Ann Allergy Asthma Immunol 2003: 90: 491–99.
5. Braun-Fahrlander C, Wuthrich B, Gassner M, Grize L, Sennhauser FH, Varonier HS, Vuille JC. Validation of a rhinitis symptom questionnaire in a population of Swiss school children visiting the school health services. SCARPOL-team. Swiss study on childhood allergy and respiratory symptom with respect to air pollution and climate. International study of asthma and allergies in childhood. Pediatr Allergy Immunol 1997: 8: 75–82.
6. International Study of Asthma and Allergies in Childhood Steering Committee. Worldwide variations in the prevalance of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema. the International Study of Asthma and Allergies in Childhood (ISAAC). Lancet 1998: 351: 1225–32.
7. Weiland SK, Bjorsten B, Brunekreef B, Cookson WO, von Mutius E, Strachan DP. Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC II): rationale and methods. Eur Respir J 2004: 24: 406–12.
8. Vana AT, Yamada E, Arruda LK, Naspitz CK, Sole D. International Study of Asthma and Allergies in Chilhood: validation of the rhinitis symptom questionnaire and prevalence of rhinitis in School children in Sao Paulo, Brazil. Pediatr Allergy Immunol 2001: 12: 95–101.
9. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. J Allergy Clin Immunol 2002: 109: 419–25.
10. Leynaert B, Bousquet J, Neukirch C, Liard R, Neukirch F. Perennial rhinitis: an independent risk factor for asthma in nonatopic subjects: results from the European Community Respiratory Health Survey. J Allergy Clin Immunol 1999: 104: 301–4.
11. ISAAC Steering Committee. Phase II Modules of the Intenational Study of Asthma and Allergies in Childhood (ISAAC). Münster, 1998.
12. Saraclar Y, Kuyucu S, Tuncer A, Sekerel B, Sackesen C, Kocabas C. Prevalence of asthmatic phenotypes and bronchial hyperresponsiveness in Turkish schoolchildren: an International Study of Asthma and Allergies in Childhood (ISAAC) phase 2 study. Ann Allergy Asthma Immunol 2003: 91: 477–84.
13. Kuyucu S, Saraclar Y, Tuncer A, Sackesen C, Adalioglu G, Sumbuloglu V, Sekerel BE. Determinants of atopic sensitization in Turkish school children: effects of pre- and post-natal events and maternal atopy. Pediatr Allergy Immunol 2004: 15: 62–71.
14. Karaman O, Turkmen M, Uzuner N. Allergic disease prevalence in İzmir. Allergy 1997: 52: 689–90.
15. Ece A, Ceylan A, Saraçlar Y, Saka G, Gurkan F, Haspolat K. Prevalence of asthma and other allergic disorders among schoolchildren in Diyarbakır, Turkey. Turk J Pediatr 2001: 43: 286–92.
16. Kalyoncu AF, Selçuk ZT, Enünlü T, Demir A, Çöplü L, Şahin AA, Artvinli M. Prevalence of asthma and allergic diseases in primary school children in Ankara, Turkey: two cross-sectional studies, five years apart. Pediatr Allergy Immunol 1999: 10: 261–65.
17. Strachan D, Sibbald B, Weiland S, et al. Worldwide variations in prevalence of symptoms of allergic rhinoconjuctivitis in children: the International Study of Asthma and Allergies in Chilhood. Pediatr Allergy Immunol 1997: 8: 161–76.
18. Vartiainen E, Petays T, Haahtela T, Jousilahti P, Pekkanen J. Allergic diseases, skin prick test responses, and IgE levels in North Karelia, Finland, and the Republic of Karelia, Russia. J Allergy Clin Immunol 2002: 109: 643–8.
19. Celedon JC, Soto-Quiros ME, Hanson LA, Weiss ST. The relationship among markers of allergy, asthma, allergic rhinitis, and eczema in Costa Rica. Pediatr Allergy Immunol 2002: 13: 91–7.
20. Leung R, Ho P, Lam CWK, Lai CWK. Sensitization to inhaled allergens as a risk factor for asthma and allergic diseases in Chinese population. J Allergy Clin Immunol 1997: 99: 594–9.
21. Crimi P, Minale P, Tazzer C, Zanarda S, Ciprandi G. Asthma and rhinitis in school children; the impact of allergic sensitization to aeroallergens. J Investig Allergol Clin Immunol 2001: 11: 103–6.
22. Settipane RA, Lieberman P. Update on nonallergic rhinitis. Ann Allergy Asthma Immunol 2001: 86: 494–508.
23. Dykewicz MS, Fineman S, Skoner DP. Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. American Academy of Allergy, Asthma and Immunology. Ann Allergy Asthma Immunol 1998: 81: 478–518.
24. Togias A. Noninfectious, nonallergic rhinitis (NINAR): considerations on possible mechanisms. Am J Rhinol 1998: 12: 65–72.
25. Agius AM, Cordina M, Callega N. The role of atopy in Maltese patients with chronic rhinitis. Clin Otolaryngol 2004: 29: 247–53.
26. Wright AL, Holberg CJ, Martinez FD, Halonen M, Morgan W, Taussig LM. Epidemiology of physician-diagnosed allergic rhinitis in childhood. Pediatrics 1994: 94: 895–901.
27. Saraçlar Y, Yiğit Ş, Adalioğlu G, Tuncer A, Tunçbilek E. Prevalence of allergic diseases and influencing factors in primary school children in the Ankara region of Turkey. J Asthma 1997: 34: 23–30.
28. Zacharasiewicz A, Zidek T, Haidinger G, Waldhor T, Vutuc C, Goetz M, Pearce N. Symptoms suggestive of atopic rhinitis in children aged 6–9 years and the indoor environment. Allergy 2000: 55: 945–50.
29. Keles N, Ilicali C. The impact of outdoor pollution on upper respiratory diseases. Rhinology 1998: 36: 24–7.
30. Wong TW, Yu TS, Liu HJ, Wong AH. Household gas cooking: a risk factor for respiratory illnesses in preschool children. Arch Dis Child 2004: 89: 631–6.
31. Bornehag CG, Sundell J, Bonini S, Custovic A, Malmberg P, Skerfuing S, et al. Dampness in buildings as a risk factor for health effects, EUROEXPO: a multidisciplinary review of the literature (1998–2000) on

dampness and mite exposure in buildings and health effects. Indoor Air 2004: 14: 243–57.
32. Garrett MH, Hooper MA, Hooper BM, Abramson MJ. Respiratory symptoms in children and indoor exposure to nitrogen dioxide and gas stoves. Am J Respir Crit Care Med 1998: 158: 891–5.
33. Lippmann M, Maynard RL. Air quality guidelines and standarts. In: Holgate ST, Samet JM, Koren HS, et al., eds. Air pollution and health. San Diego: Academic Press 1999.
34. Peroni DG, Piacentini GL, Alfonsi L, Zerman L, Blasi PD, Visona G, Nottegar T. Rhinitis in pre-school children: prevalence, association with allergic diseases and risk factors. Clin Exp Allergy 2003: 33: 1349–54.
35. Leynaert B, Neukirch C, Kony S, Guenegou A, Bousquet J, Aubier M, Neukirch F. Association between asthma and rhinitis according to atopic sensitization in a population-based study. J Allergy Clin Immunol 2004: 113: 86–93.
36. Togias A. Mechanisms of nose-lung interaction. Allergy 1999: 54 (Suppl. 57): 94–105.
37. Nickel R, Lau S, Niggeman B, Sommerfeld C, Wahn U. German Multicenter Allergy Study Group. Comparison of bronchial responsiveness to histamine in asthma, allergic rhinitis and allergic sensitization at the age of 7 years. Clin Exp Allergy 2002: 32: 1274–7.