Original Article

Prevalence of Asthma and Allergic Diseases in Sanliurfa, Turkey, and the Relation to Environmental and Socioeconomic Factors: Is the Hygiene Hypothesis Enough?

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Abstract. *Background:* The prevalence of asthma and allergic diseases has been reported to be higher in urban than in rural areas between developed and underdeveloped countries and within any given country. Studies in Turkey have yielded different results for different regions. This study aimed to investigate the prevalence of asthma and atopy in Sanliurfa, Turkey, and the influence of environmental factors.
Materials and Methods: We recruited 1108 children from different areas of Sanliurfa and administered the questionnaire of the International Study of Asthma and Allergies in Childhood. Items asking for socioeconomic data were also included. Skin prick and purified protein derivative tests were performed on the children. Measles antibodies were determined and feces were analyzed for parasites.
Results: The total prevalence of atopic diseases was 8.6% (n=95/1108), asthma 1.9% (n=21/1108), allergic rhinitis 2.9% (n=32/1108), and allergic conjunctivitis 3.8% (n=42/1108). The rate of atopic diseases was 5.6% (n=32/573) in children attending schools in peripheral, less urban, slum areas while it was 11.8% (n=63/535) in those attending city-center schools (OR, 2.2; 95% confidence interval [CI]; 1.4-3.5; $P<.001$). Skin prick test positivity was observed in 3.9% (n =43/1108) overall; at schools in slum areas it was 1.9% (n =11/573), whereas at central schools the rate was 6% (n=32/535) (OR, 4.08; 95% CI, 2.03-8.20; $P<.001$). The prevalence of asthma and atopic diseases was significantly higher in children who have a family history of atopy, attend a central school, live in an apartment, have more rooms in their homes, and enjoy better economic conditions.
Conclusion: We found associations between various factors suggested by the hygiene hypothesis and asthma, and very low rates of prevalence of asthma and atopic diseases both in Sanliurfa in comparison with the more developed western regions and in the peripheral slum areas. The hygiene hypothesis is helpful in explaining these observations.

Keywords: Asthma. Atopy. Prevalence. Turkey.

Resumen. *Antecedentes:* Se ha demostrado que la prevalencia de asma y enfermedades alérgicas es mayor en países desarrollados que en aquéllos en vías de desarrollo; y también en zonas urbanas que en zonas rurales. Los resultados de varios estudios en Turquía oscilaron según la región. Este estudio tiene como objetivo investigar la prevalencia de asma y atopia en Sanliurfa, Turquía, y la influencia de factores medioambientales.
Materiales y Métodos: Se reclutaron 1108 niños de diferentes zonas de Sanliurfa y cumplimentaron el cuestionario del Estudio Internacional de Asma y Alergia en la Infancia. En el cuestionario se incluyeron preguntas de índole socioeconómica. A los niños se les practicaron pruebas cutáneas de prick y de proteína purificada. Se determinaron los anticuerpos antisarampión y se recogieron heces para análisis de parásitos.

Resultados: La prevalencia total de enfermedades fue de 8,6 % (n = 95/1108); 1,9 % de asma (n = 21/1108), 2,9 % de rinitis alérgica (n = 32/1108) y 3,8% de conjuntivitis alérgica (n = 42/1108). La prevalencia de enfermedades atópicas fue del 5,6% (n = 32 / 573) en niños escolarizados en zonas periféricas menos urbanas (de clase social baja), mientras que la misma prevalencia fue del 11,8% (n = 63/535) en niños escolarizados en el centro de las ciudades (OR, 2,2; intervalo de confianza [CI] 95%; 1,4-3,5; $P < 0,001$). Se observaron resultados positivos en pruebas cutáneas de prick de un total de 3,9 % (n = 43/1108); la frecuencia en colegios en zonas de clase baja fue de 1,9 % (n = 11/573), mientras que la tasa en colegios céntricos fue del 6% (n = 32/535) (OR, 4,08; CI 95%, 2,03-8,20; $P < 0,001$). La prevalencia de asma y enfermedades atópicas fue mucho mayor en aquellos niños con historia de atopia en la familia, escolarizados en colegios céntricos, que viven en apartamentos, tienen más habitaciones en las casas y gozan de unas condiciones económicas más favorables.
Conclusión: Encontramos asociaciones entre varios factores sugeridos por la hipótesis de higiene y asma, y por una tasa de prevalencia de asma y enfermedades atópicas muy baja en Sanliurfa, en comparación con las regiones occidentales más desarrolladas y en las zonas periféricas de clase baja de la ciudad en comparación con el centro de la ciudad. La hipótesis de la higiene es útil para explicar estas observaciones.

Palabras clave: Asma. Atopia . Prevalencia. Turquía.

Introduction

Most studies from Western countries suggest that there has been a significant increase in the incidence and prevalence of atopic diseases in recent years [1-3]. It has been suggested that this increase can not be explained by genetic factors and improvements in diagnostic methods alone but that environmental factors, especially a Western lifestyle, play a role. Higher prevalences in urban areas of any given country as compared to rural areas also suggest that different environmental conditions and more hygienic conditions have a role in the emergence of atopic diseases [4]. Studies carried out in different parts of Turkey using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire have reported quite different results. In developed western parts of the country, the prevalence of asthma ranges from 6.9 % to12.6% [5-8] and the prevalences of allergic rhinitis varies from 7.2% to 17.6% [9-11] according to different studies.

The Turkish city of Sanliurfa, with its hot, dry climate, poor socioeconomic conditions, high rates of infectious and parasitic diseases, and widespread marriage between relatives, is different in many ways from developed regions of Turkey. This study was planned to determine the prevalence of childhood asthma and atopic diseases in Sanliurfa and the influence of socioeconomic conditions and environmental factors.

Materials and Methods

According to the census for the year 2000, approximately 385 000 people live in the metropolitan area of Sanliurfa and two thirds of them live in outlying poor neighborhoods with deficient infrastructure. A sample of 1108 children was randomly chosen from 5 primary schools located in different parts of the metropolitan area (both central and suburban slum areas) with different socioeconomic conditions. After consent was given by the children and their families, we administered the standard ISAAC questionnaire used in epidemiological studies all over the world. A child's classification of having asthma was defined by a positive answer to 2 out of 3 questions related to doctor-diagnosed asthma, asthma treatment, and admission to a hospital for asthma. A classification of having allergic rhinitis was based on a positive answer to questions about having had a problem with sneezing or blocked nose during the last 6 months when the child did not have a cold or flu or ever having had hay fever.

In addition, subjects were asked about the blood relationship between the mother and father (marriage between cousins), presence of pet animals in the home, number of persons living at home (0-4 or > 4), smoking, the type of house (slum dwelling on the outskirts of the city or a city-center apartment), number of rooms (0-4 or >4), economic status of the family (low income, moderate income, and good income), and atopic diseases in the family (asthma, rhinitis, and allergic conjunctivitis). Prick tests were administered to 930 (83.9 %) cases out of the 1108; 21 did not undergo such testing because they were using antihistamines or had acute illnesses, and 157 did not give their consent. Eleven allergens (*Dermatophagoides pteronyssinus, Dermatophagoides farinae*, 12 grasses mix, *Festuca elatior*, cereals mix, *Artemisia* species mix, *Alternaria* species mix, Betulaceae, tree mix, latex, and cockroach) (Stallergenes SA, Paris, France) were applied along with negative and positive control pricks on the volar surface of the subjects' forearms. A wheal response at least 3 mm in diameter larger than that produced by the negative control was regarded as a positive response. The presence of positive skin prick tests to at least 1 common aeroallergen was defined as atopy.

A purified protein derivative (PPD) test was performed on 600 subjects participating in the study. A wheal ≥ 15 mm or ≥ 10 mm was accepted as positive in bacille Calmette-Guerin (BCG)-vaccinated and unvaccinated subjects, respectively. BCG vaccine positivity was detected in BCG-vaccinated subjects by checking for a

vaccination scar. In 360 subjects measles antibody level was tested. All blood samples drawn from children were stored at –80 °C and measles-specific IgG antibodies were measured qualitatively by using a microenzyme linked immune assay (RIDASCREEN, R-Biopharm GmbH, Darmstadt, Germany). Levels above 12 IU/mL were considered as per instructions. Moreover, because the children had had only 1 measles vaccination we used the cutoff value of 100 IU/mL as an indication of having had an infection, as per the method of Rawat et al [12]. For 473 children, feces were stained with Lugol's iodine solution and concentrated with formol ethyl acetate to detect parasites.

Statistics

Statistical analysis was performed with the SPSS computing program (version 10.0) for Windows. Prevalence of atopic diseases in children who live in slum areas and central areas was assessed by a χ^2 test. The influence of the socioeconomic variables on the prevalence of asthma and atopic diseases was evaluated by calculating the odds ratio (OR) and 95% confidence intervals. A *P* value less than .05 was considered significant.

Results

Of a total of 1108 children recruited, 535 (48.3%) were from 2 schools attended by those following an urban lifestyle in better socioeconomic conditions and 573 (51.7%) were from 3 schools attended by those living a rural lifestyle in poor socioeconomic conditions. The mean (±SD) age of the children was 13.1 ± 1.2 years (range, 10-18 years); 32.8% were female and 67.2% were male. The total prevalence of atopic diseases (asthma, allergic rhinitis, and allergic conjunctivitis) was 8.6% (n=95/1108), according to the ISAAC questionnaire results. Individual prevalence rates were as follows; asthma 1.9% (n=21/1108), allergic rhinitis 2.9 % (n = 32 /1108), and allergic conjunctivitis 3.8 % (n = 42/1108). According to the ISAAC questionnaire results the prevalence rates of all atopic diseases overall was 5.6% (n =32/573) in children attending schools in slum areas while it was 11.8 % (n = 63/535) in those attending central schools and the difference was significant (OR, 2.2; 95 % CI, 1.4-3.5; *P* < .001). The overall prevalence rates of skin prick test positivity were found to be 3.9 % (n = 43 / 1108): 1.9 % (n = 11 / 573) in children attending schools in slum areas and 6 % (n = 32 / 535) in those attending central schools. This difference was also significant (OR, 4.08; 95% CI, 2.03-8.20; *P* < .001). In both groups, the most frequent sensitivity was to grass pollen. Table 1 shows the distribution of skin prick positivity in the 2 groups.

The positivity rate in cases for which the skin prick test was performed was 25.4 % (15 / 59) in subjects with atopic disease and 3.2 % (28 / 871) in those without atopic disease.

Risk Factors for Asthma

Genetic sensitivity. Atopy was more common in children with a family history of atopy *P* < .001; OR, 10.5; 95% CI, 6.6-16.6); although the rate of parents who were first degree relatives was high at 28.8%, no relation was found between that factor and the prevalence of atopic diseases (*P* > .05; OR, 0.6; 95 % CI, 0.1-2.2) (Table 2).

Environmental conditions. The prevalence of asthma and atopic diseases was significantly higher at central city schools in comparison to peripheral slum schools (*P* < .001; OR, 2.2; 95 % CI,1.4-3.5). Allergic diseases were also significantly more common in children living in apartments (*P* < .001; OR, 3.4; 95 % CI, 2.1-5.4).

No relationship was detected between keeping pets or stabled animals and the development of asthma or an atopic disease. Nor was there a relationship between smoking at home and development of atopic diseases. The relationship between the number of rooms (0-4 or >4) and atopy was found to be significant. No relationship was found between the number of persons at home (0-4, >4) and atopy.

Table 1. Distribution of Skin Prick Positivity in Children Attending Schools in Slum Areas and in the City Center*

	Peripheral Slum Areas, n = 529	City Center, n = 401	*P*	OR (95% CI)
1 or more positive test†	11 (2%)	32 (8%)	< .001	4.0 (2.0-8.2)
Dp/Df	5	9		
Grass pollen	7	29		
Tree pollen	0	2		
Cockroach	0	3		
Fungus	1	0		

*ISAAC indicates International Study of Asthma and Allergies in Childhood; CI, confidence interval; Dp, *Dermatophagoides pteronyssinus*; Df, *Dermatophagoides farinae.* † Sensitivity to more than 1 allergen was detected in some patients.

Table 2. Risk Factors for Atopic Diseases*

	Subjects Diagnosed With Asthma and Atopic Diseases, n = 95	Subjects Diagnosed With Asthma but Without Atopic Diseases, n = 1013	*P*	Odds Ratio (95% CI)
SPT positivity, n = 930	15	28	< .001	0.12 (0.07-0.22)
Genetic sensitivity				
Marriage of first degree relatives	17	269	NS	0.63 (0.18-2.27)
Atopy history in the family	62	153	< .001	10.5 (6.6-16.6)
Socioeconomic conditions				
City-center school	63	472	< .001	2.2 (1.4-3.5)
Apartment living	69	444	< .001	3.4 (2.1-5.4)
Pets in the home	20	165	NS	1.37 (0.81-2.30)
Stabled animals	7	62	NS	1.07 (0.57-2.01)
Smoking at home	71	736	NS	0.97 (0.86-1.09)
Number of rooms (≤ 4)	30	504	< 0.001	1.5 (1.1-2.1)
Crowded living (> 4)	83	903	NS	1.02 (0.94-1.10)
Economic well-being	8	16	< .001	0.18 (0.08-0.42
Infection factors				
Seroprevalence of measles (+), n = 360	12/15	262/345	NS	0.94 (0.73-1.23)
Parasite (+), n = 473	11/15	282/458	NS	0.84 (0.61-1.14)
BCG (+), n = 600	11/16	289/584	NS	2.24 (0.77-6.54)
PPD (+), n = 600	0/16	40/584	NS	0.93 (0.91-0.95)

* CI indicates confidence interval; SPT, skin prick test; BCG, bacillus Calmette-Guerin; PPD, purified protein derivative.

We detected a significant relationship between economic well-being of the family and development of asthma and atopic diseases (OR, 0.18; 95% CI, 0.08-0.42; *P* < .001).

Infection. No relationship was found between seroprevalence of measles, parasitic positivity, or BCG positivity and the prevalence of asthma and atopic diseases. However, the risk of asthma and atopic diseases was found to be lower in children with a negative PPD test whether they had been vaccinated or not (OR, 0.93; 95% CI, 0.91-0.95; *P* = .27).

Discussion

Asthma and atopic diseases are reported to occur at higher rates in developed Western countries compared to developing countries; similarly, they are more frequent in urban areas of a given country compared to rural areas [13, 14]. High urban prevalence in developed Western countries or in a developed area of a given country indicates that environmental factors play an important role in the development of atopic diseases [13, 14]. This situation is explained by the hygiene hypothesis [4, 15]. Turkey is a country where there is great difference between the western and eastern parts in terms of development and socioeconomic conditions. The eastern and southeastern Anatolian regions, which include Sanliurfa, are less industrially developed and agriculture is the primary economic activity.

Although the reported prevalence of asthma and allergic rhinitis in developed western parts of Turkey ranges between 6.9% and 14.8% [5-8] and 7.2% to 17.6% [9-11], respectively, we have found a prevalence of 1.6% for asthma and of allergic rhinitis of 2.9% in Sanliurfa. These results are not only much lower than those in developed western countries, but also lower than those reported for developed parts of our own country.

Asthma and atopic diseases develop against a genetic background [16]. Because of the high rate (30%) of marriage between close relatives in our region [17], we assessed the relationship between the prevalence of atopic diseases and parents who are first degree relatives but found no link. Various studies suggest that the existence of an atopic disease in a family is influential in the development of asthma or atopic diseases in children [18, 19], however; yet we also found significant presence of atopic disease in the families of atopic children.

We did find the prevalence of atopic disease in central city schools with better socioeconomic conditions

significantly higher. Furthermore, a strong relationship was found between atopy and signs of good socioeconomic status in our region, higher status being associated with living in the town center, in an apartment, and in a dwelling with a larger number of rooms. Various studies have reported that the prevalence of atopic disease is higher in children with a higher socioeconomic level [20, 21]. Our findings support that in general differences in living conditions influence the prevalence of asthma and atopic disease.

Environmental conditions, among them the home quality, have been suggested to influence atopic disease. Because apartment dwellers may stay indoors for long periods, exposure to mites and cockroaches may have an effect of increasing the incidence of atopic disease. However, different findings have been reported [22, 23]. We also found apartment living to be highly significant.

Contact with animals has been reported to be related to the development of asthma and atopic disease [24, 25]. We found no relationship between keeping animals at home and atopic disease, however. In slum areas, breeding stabled animals was significantly more common, but no relationship between this factor and the prevalence of atopic diseases was found. We could not assess how long or how intensely the children were in contact with the stable animals, however, as ours was merely a cross-sectional survey.

The hygiene hypothesis postulates that more infections will have been suffered by individuals with many siblings and that such infections may protect against the development of asthma and atopic diseases [26, 27]. Various groups have reported the existence of an inverse relation between crowded family conditions and the development of asthma [28, 29]. A study carried out in England and New Zealand, however, suggested that large family size has no significant effect on the prevalence of asthma and atopic diseases [30]. Despite the presence of a large number of families living in crowded conditions, we found no relationship between that factor and the prevalence of atopic diseases.

Exposure to cigarette smoke in the early years of life is said to be a risk factor for the development of asthma [31]. In both groups we studied, the rate of passive smoking was found to be high, but no association with atopy prevalence emerged.

Different results are reported for the effect of measles infection on the development of atopic disease. Shaheen et al [32] in their studies carried out in Guinea Bissau reported that having had measles infection lowers the risk of developing asthma, but a study in Finland found no such association [33]. We also found no relationship between measles seroprevalence and atopic diseases.

Shirakawa et al [34] have suggested that BCG vaccination decreases the risk of developing atopic disease by stimulating the type 1 helper T cell (T_H1) response [34]. However, 2 studies carried out to date have not confirmed such a relationship between BCG vaccination and asthma or atopy [35, 36]. We also failed to observe a relationship between BCG positivity, prevalence of atopy, and skin prick test positivity. However, we did observe that the risk of atopic disease was lower in PPD positive patients, whether positivity was due to vaccination or not. This finding may indicate that natural infection, by further stimulating the T_h1 response, is more successful in preventing atopy development.

Two studies have suggested that parasitic infections decrease skin prick test sensitivity and the prevalence of atopic diseases [37, 38], but our findings were not consistent with that suggestion. This may be because the prevalence of parasitic infections is as high as 62 % in Sanliurfa [39]. In addition, the rate of atopy is significantly lower than in regions where the prevalence of parasitic infection is low. Not all children recruited were screened for parasites, however, and our observations may therefore not reflect the real situation. This relationship may not persist in longer cross-sectional studies.

We found that the prevalence of asthma and atopic disease is lower in Sanliurfa than in developed communities. A family history of atopic disease, living in an apartment, economic well-being, and having more rooms in the house were determined to be risk factors for the development of asthma and atopic disease. However, no relationship was found for having closely related parents, passive smoking, stabled animals or pets in the home, or parasitic or other infections. We found associations with various factors suggested by the hygiene hypothesis and asthma, and the very low rates of prevalence of asthma and atopic diseases both in Sanliurfa in comparison with the more developed western regions and in the peripheral slum areas (where socioeconomic conditions are worse than in the center of the city): the hygiene hypothesis is helpful in explaining these observations. Differences between our results and others' may be attributed to study design and regional differences.

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