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Lower prevalence of asthma and atopy in Turkish children living in Germany

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ABSTRACT: Ethnic origin has been reported to affect the prevalence of atopic diseases in several studies in different parts of the world. However, little is known about the prevalence of asthma and atopy in immigrants living in Europe. The objective of this study was to evaluate the prevalence of asthma and atopy in Turkish children living in Germany and to investigate the role of ethnic origin on the development of asthma and atopy in this population.

In a cross-sectional survey the prevalence of physician-diagnosed asthma, atopy, skin-prick tests and bronchial hyperresponsiveness (BHR) to cold dry air challenge was assessed in 7,445 school children aged 9–11 yrs, living in Munich, south Germany. Questionnaires were distributed to the parents for self-completion and children underwent skin prick tests and cold air hyperventilation challenge.

The Turkish children showed a significantly lower prevalence of asthma (5.3 *versus* 9.4%, $p<0.05$) than their German peers. Furthermore, atopy, as assessed by skin prick tests (24.7 *versus* 36.7%, $p<0.001$) and BHR (3.9 *versus* 7.7%, $p<0.001$), was less common in Turkish children. In multivariate regression models controlling for potential explanatory factors, Turkish origin still showed a significantly lower risk of developing asthma, atopic sensitization and BHR.

The prevalence of childhood asthma was therefore shown to be lower in Turkish children living in Germany than in Turkey. These findings suggest that the lower prevalence of asthma and allergy in Turkish children living in Germany might be attributable to a selection bias affecting the parents of these children, as healthy individuals may have decided to come to Germany for work.

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The difference in the prevalence of asthma in various parts of the world cannot entirely be explained by differences in methodology. Studies in children rather suggest a high prevalence of asthma in the UK, Australia and New Zealand compared with moderate prevalence rates in most Western European countries [1, 2] and low prevalence rates in Eastern Europe [3–5] and developing countries [6]. Moreover, the prevalence of asthma varies not only between countries but also between centres within the same country [7]. Even within study centres there are differences in the prevalence rates of atopic diseases as has been demonstrated in the USA [8], New Zealand [9] and Australia [10].

Among other explanatory factors, ethnicity was found to be associated with different prevalence rates of asthma and atopy in childhood. The reasons for these differences are still obscure. Genetic, lifestyle or environmental factors may account for these variations [8, 10–13]. In Europe, immigration for political or economical reasons from all over the world to countries such as France, the UK, Germany and the Netherlands leads to significant changes in the population structure. However, very little is known about the impact of ethnicity on the development of asthma and atopic diseases in Europe.

The aim of this analysis was to evaluate the prevalence of asthma and atopic diseases in Turkish children living in Germany and to study the relevance of associated risk. The methods used in this study have been published previously [3]. Only methods pertaining to this analysis are given below.

Subjects and methods

Subjects

Between September 1989 and July 1990 fourth-grade pupils, mainly 9–11 yrs of age, at all primary schools in Munich, south Germany, were enrolled in a cross-sectional survey. Questionnaires were sent through the schools to 7,445 families for self-completion. Children underwent skin prick testing, pulmonary function testing and bronchial challenge to cold air. Informed written consent was obtained from parents separately for skin prick testing, lung function testing and cold air challenge. All study methods were approved by the Ethics Committee of the Bavarian Medical Association.

Questionnaire

A self-administered questionnaire according to international standards was distributed to the parents of all children. Questions concerning ethnic origin, sociodemographic characteristics, symptoms and diagnosis of respiratory and allergic disorders and their possible risk

factors were included. The questionnaire was translated into Turkish and given to parents of Turkish children.

Ethnic origin was assessed by asking the question "What is the child's nationality?" In Germany, in contrast to many other countries, a child's nationality depends on the parental citizenship regardless of the child's place of birth. Children whose parents reported either asthma, recurrent spastic or recurrent asthmatic bronchitis were classified as having asthma, also referred to as "asthma ever" in the text and tables. Asthma with symptoms in the last 12 months was defined as current asthma. Children whose parents reported recurrent bronchitis without asthma were classified as having bronchitis. The occurrence of hay fever and atopic dermatitis was assessed by asking the questions: "Has a doctor ever diagnosed hay fever in your child?" and "Has your child ever had atopic dermatitis?" A child was considered wheezy if recurrent symptoms of wheeze were reported by the parents. Questions used to assess other symptoms were: "Has your child ever had attacks of shortness of breath?", "Does your child frequently cough at night without having a cold?" and "Does your child frequently cough after exercise or during foggy or cold weather?"

The family history of atopic diseases was assessed by the question: "Did you or a family member ever suffer from asthma, hay fever or atopic dermatitis?" Children with one or more nearest of kin (*i.e.* parents or siblings) with at least one of these allergic diseases were defined as having a positive family history of atopy. Further questions concerning possible risk factors for the development of asthma and atopic diseases were asked. These questions included: "How many siblings has your child?", "What is the mean number of cigarettes smoked daily in your household?", "Has your home been damaged by dampness?", "Which heating system is mainly used in your household?" and "Do you have pets in your home and if yes, which pets are these?" To evaluate the socioeconomic status of the families, parental education was assessed by asking about the highest degree earned by either the father or the mother.

Skin prick test

Sensitivity to six common aeroallergens (*Dermatophagoides pteronyssinus*, mixed grasses, birch and hazel pollen, cat and dog dander) was assessed by a multitest device (Stallerkit®; Stallergènes, Lyon, France). All allergen extracts were standardized in biological units. Results obtained using this device had been validated in a pilot study in Munich [14].

A child was considered sensitized if a weal reaction of >3 mm was present to a specific allergen after subtraction of the negative control. A child was considered atopic if a positive weal reaction to at least one of the six allergens tested was present.

Pulmonary function test and bronchial challenge

Pulmonary function testing was performed with the pneumoscope II (Jäger, Würzburg, Germany). Forced flow–volume curves were repeated until three reproducible loops were obtained. Isocapnic hyperventilation of cold, dry air was applied as the bronchial provocation method. To perform the cold air challenge a respiratory heat-exchange system (Jäger) was used. The test consisted of 4 min of isocapnic (5% CO_2) hyperventilation (*i.e.* (22 × FEV1)/min) of dry cold air (-15°C, measured at the mouthpiece). A target balloon guided the ventilatory effort. It was constantly filled with air at a predetermined rate and had to be held in the constant filling state throughout the provocation test by the child's respiratory effort. Lung function tests were performed before and 2–4 min after the cold air hyperventilation challenge.

To compare baseline lung function between German and Turkish children, predicted values were calculated. A reference population of German and Turkish children without a diagnosis of asthma and without wheeze and shortness of breath ever was identified. Within this reference population, baseline lung function values, which had been transformed on a logarithmic scale, were regressed with weight and height as logarithmically transformed covariates for Turkish and German males and females separately.

To assess bronchial hyperresponsiveness (BHR), changes in forced expiratory volume in one second (FEV1; in %) were calculated as: (FEV1 after inhalation -FEV1 before inhalation) × 100/FEV1 before inhalation (ΔFEV1). BHR was defined as a drop in FEV1 as large as or larger than the value of the 95th percentile (9% fall in FEV1) of the reference population (German children without asthma, hay fever or atopy), as reported in a previous work [15].

Statistical analysis

The Wilcoxon test was used to compare the distribution of age, height and weight in Turkish and German children. Prevalence rates were calculated and Chi-squared tests were used to assess differences between the two groups. A multivariate logistic regression analysis was computed to assess the independent effects of several potential determinants of asthma and atopic sensitization. The drop in FEV1 after cold air challenge was adjusted in a multivariate linear regression model for the following variables: height, nationality, family history of atopy, number of positive weal reactions, passive smoking and the FEV1/forced vital capacity (FVC) ratio. The SAS software package version 6.12 (SAS Institute, Cary, NC, USA) was used for all calculations.

Results

Of the 7,445 families sent questionnaires 6,490 responded (87%). Of the responders, 5,030 (77.5%) were of German origin, 451 (7%) were of Turkish origin and 1,009 (15.5%) were of various other ethnic origins (435 Yugoslavian, 21 Greek and 456 from nationalities not further specified in the questionnaire). As Yugoslavian nationality comprises children from different ethnic origins (Bosnia, Serbia, Croatia and Slovenia), the analysis of these data is not presented. However, the results followed the same trends as those described for Turkish children (data not shown).

Turkish children were slightly older, smaller in size and weighed slightly more than their German peers (table 1). There was no significant difference between the two groups in the percentage of children who were either born

Table 1. – Demographic characteristics of the study population

	German (n=5030)	Turkish (n=451)
Males %	48.6	49.7
Age yrs	9.8	10.0***
Born in Munich %†	77.8	78.2
Height cm	143.2	141.8***
Weight kg	34.6	36.3***

***: p<0.001 by Wilcoxon test. †: children who were born in Munich or moved to Munich in their first year of life.

in Munich or moved to Munich in their first year of life. Most of the children in the fourth-grade of primary school were between 9 and 11 yrs of age when they were tested. Of those children for whom the questionnaire was returned by their parents, 4,840 (4,451 German and 389 Turkish) underwent skin prick tests and 4,865 (4,505 German, 360 Turkish) underwent baseline lung function testing and cold air challenge.

There was a significant difference in the prevalence of asthma and asthma-related symptoms between Turkish and German children (table 2). The prevalence of asthma was lower in Turkish than in German children (5.3 *versus* 9.4%). Furthermore, fewer Turkish parents reported symptoms of current asthma in their children. The frequency of wheezing and shortness of breath was significantly lower in Turkish than in German children, while Turkish parents reported cough with exercise, during foggy or cold weather more often in their children than did German parents.

There was no significant difference in the prevalence of hay fever between Turkish and German children. However, atopic dermatitis differed greatly between the two groups. Only 1.6% of Turkish parents reported atopic dermatitis in their children, whereas atopic dermatitis was reported to occur in 13.9% of German children.

Atopic sensitization, as assessed by skin prick tests, was significantly less frequent in Turkish children than in their German peers (table 2). Only 24.7% of Turkish school children presented a weal reaction of ≥3 mm to at least one allergen tested, compared with 36.7% of the German pupils. When choosing different cut-off points (2 mm and 4 mm) for positivity of skin prick test reactions and when calculating the sum of all weal reactions as another measure of atopy, the difference between the two groups of children remained significant (data not shown). When analysing weal reactions to each allergen separately, significant differences were found for each allergen, although the difference in sensitization to house dust mites did not reach statistical significance (table 2).

Table 2. – Prevalence (%) of symptoms and diagnosis of respiratory and atopic diseases among children of German and Turkish nationality

	German (n=5030)	Turkish (n=451)
Asthma ever	9.4	5.3*
Current asthma	5.9	4.7
Wheezing	17.0	8.6***
Shortness of breath	8.7	4.2*
Cough with exercise	11.7	18.4***
Hay fever	8.6	10.0
Atopic dermatitis	13.9	1.6***
Bronchitis	15.9	6.4***
Atopic sensitization†	36.7	24.7***
Dermatophagoides pteronyssinus	10.3	9.3
Pollen (grass, birch, hazel)	31.0	19.3***
Cat and dog dander	24.7	1.9***
Bronchial hyperresponsiveness‡	7.7	3.9***

†: assessed by skin prick test (German n=4,451, Turkish n=339). ‡: assessed by cold air challenge (German n=4,505, Turkish n=360). *: p<0.05, ***: p<0.001 by Chi-squared test.

No significant difference in baseline lung function was observed between Turkish and German school children when adjusting for sex, height and weight. The mean±SD FVC was 100.6±10.6% predicted in Turkish *versus* 100.4 ±10.3% pred in German children, whereas the mean FEV_1 was 100.6±10.9% pred in Turkish *versus* 100.1±10.1% pred in German children. The prevalence of BHR was lower in the Turkish group (table 2). Of the Turkish children only 3.9% reacted to the cold air hyperventilation challenge, whereas 7.7% of their German peers had a significant drop in FEV_1 after the challenge.

To explore whether genetic or environmental differences between the study groups accounted for the observed variations in prevalence, potential risk factors for the development of atopic diseases were assessed (table 3). The family history of atopy, family size, passive smoke exposure, socioeconomic status, housing conditions, pet ownership and low birth weight were evaluated. A larger sibship size and higher passive smoke exposure were found in Turkish children, while a higher socioeconomic status (assessed by parental education), more pets at home and a higher prevalence of atopic dermatitis and hay fever in first-degree relatives were seen in German families (table 3). In contrast, there was no difference between Turkish and German children for a positive family history of asthma, housing conditions (heating and dampness at home) and birthweight (data not shown).

In multivariate analyses (tables 4 and 5) the relation of these potential risk factors to asthma (doctor′s diagnosis of asthma ever), atopy and BHR was assessed. The crude odds ratio (OR) of Turkish nationality for asthma ever was 0.54 (confidence interval (CI) 0.34–0.87, p<0.01) and 0.57 (CI 0.44–0.72, p<0.001) for atopic sensitization. A positive family history for atopy was significantly

Table 3. – Prevalence (%) of potential risk factors for the development of atopic diseases

		German (n=5030)	Turkish (n=451)
Family history	Asthma	9.7	11.5
	Hay fever	26.6	10.4*
	Atopic dermatitis	18.4	5.3*
Number of siblings	0	25.6	7.8*
	1	50.8	36.5*
	2	17.0	31.9*
	3	6.5	23.9*
Passive smoking		41.8	62.3*
Parental education	<8 yrs	0.4	9.2*
	8 yrs	22.3	51.7*
	10 yrs	26.5	23.6
	>10 yrs	47.2	10.5*
Pets at home	Cats or dogs	24.7	1.9*

*: p<0.05 by Chi-squared test.

Table 4. – Results of a multivariate logistic regression analysis with asthma ever and atopic sensitization as outcomes

	Asthma ever			Atopic sensitization		
	OR	95% CI	p-value	OR	95% CI	p-value
Turkish nationality	0.53	(0.30–0.94)	0.03	0.73	(0.55–0.96)	0.03
Family history atopy	1.64	(1.33–2.02)	0.0001	1.64	(1.44–1.87)	0.0001
Education† <8 yrs	0.24	(0.03–1.82)	0.2	0.85	(0.43–1.70)	0.7
8 yrs	0.82	(0.61–1.09)	0.2	0.87	(0.73–1.04)	0.1
10 yrs	1.00	–	–	1.00	–	–
>10 yrs	0.81	(0.64–1.03)	0.09	0.94	(0.81–1.09)	0.4
Number of siblings	1.04	(0.94–1.16)	0.5	0.91	(0.85–0.98)	0.01
Passive smoking	1.15	(0.93–1.43)	0.2	–	–	–
Dog or cat	1.01	(0.79–1.30)	0.9	0.91	(0.78–1.06)	0.2

†: Highest level of father′s or mother′s education. OR: odds ratio; CI: confidence interval.

associated with a higher risk for asthma and atopy. Neither the number of siblings, passive smoking, pet ownership nor father′s or mother′s education showed a significant effect on the diagnosis of asthma and atopic sensitization. When Turkish nationality was added to the model, it still showed a significant negative association with asthma, atopic sensitization and BHR, suggesting that the risk factors included in the regression models did not explain the association between Turkish ethnicity and both asthma and atopic sensitization.

Discussion

The results of this study demonstrate that the prevalence of asthma and other atopic diseases differs between ethnic groups in Germany. Asthma and other atopic diseases were significantly less common in Turkish children living in Munich than in a comparable group of German children. When assessing risk factors for the development of asthma and other atopic diseases, significant differences between the two study groups were found (table 3). However, in multivariate regression models, none of these factors explained the lower prevalence of asthma, atopic sensitization and BHR in Turkish children.

Some methodological problems may exist with this study. It is possible that some Turkish children of this age group living in Munich were missed because of language or reading problems, even though the questionnaire was translated into Turkish. However, population counts in Munich, a city of 1.2 million inhabitants in the south of Germany, showed that of all children aged 9–11 yrs, 8.6% are of Turkish nationality [16]. Therefore, an identification rate of ~7% represents the proportion of Turkish children in this age group. Questions concerning the lifetime prevalence and doctor′s diagnoses of atopic diseases are subject to recall bias and also reflect the attitude toward health issues and the accessibility of healthcare facilities, which may differ between German and Turkish families. In Turkish families, more fathers, who might not have the same insight into the children′s health as the mother, filled out the questionnaire than in German families (31.1 *versus* 6.8%, p<0.0001). When additionally controlling for the responding parent the effect of Turkish ethnicity on asthma decreased slightly (OR=0.59, 95% CI 0.33–1.05, p=0.07), but did not disappear. A similar prevalence of hay fever was found in Turkish and German children, although sensitization to pollen occurred less frequently in the Turkish subjects. This discrepancy might be attributable to translation problems, since the term hay fever is not a very commonly used expression in Turkish. This wording may thus have resulted in an overreporting of common cold symptoms rather than of symptoms of seasonal allergic rhinoconjunctivitis in the Turkish children. However, the differences in objective measures such as skin prick test results and BHR between Turkish and German children strongly suggest that the lower prevalence of asthma and atopy is real.

Table 5. – Results of a multivariate linear regression analysis with per cent change in forced expiratory volume in one second (FEV_1) after cold air challenge as the dependent variable†

	β-Coefficient	p-value
Turkish nationality	-0.70	0.02
Family history atopy	+0.15	0.35
Sum of atopy‡	+0.58	0.001
Passive smoking	-0.06	0.7
Ratio FEV_1/FVC	-10.97	0.0001

FVC: forced vital capacity. †: additionally adjusted for height; ‡: number of positive weal reactions.

The present findings are consistent with the results reported from other studies stressing the important role of ethnicity for the development of asthma and atopic diseases in children [8–11, 13, 17]. The results of the present study demonstrate that ethnicity should be taken into consideration when performing epidemiological surveys in Europe as prevalence rates of atopic diseases may vary significantly between immigrant and indigenous populations. Similar results have previously been reported in studies of Asian immigrants to Australia [10], of Maoris [9] and South Pacific Islanders [11] who had immigrated to New Zealand, of Puerto Ricans [8] and Mexicans [17] living in the USA and of Asian children living in the UK [13]. Belonging to a certain ethnic group may lead to higher [8, 9] or lower [10, 11, 13, 17] prevalence rates of asthma and atopy compared with the indigenous population.

Genetic and environmental factors might account for the difference in the prevalence of asthma and other atopic diseases between ethnic groups. While atopic sensitization became increasingly frequent with the length of stay in a new environment [10, 12], such effects cannot explain the results of the present survey. Because most of the Turkish

Table 6. – Comparison of asthma prevalence in Turkish children living in Germany and Turkey

First author	[Ref.]	Place	Location	Urban/rural	n	Ageyrs	Asthma prevalence%†
This study		Munich	Inland	Urban	451	9–11	5.3
KALYONCU	[28]	Ankara	Inland	Urban	1226	6–12	17.4
ONES	[30]	Istanbul	Coastal	Urban	2340	6–12	9.8
KUCUKODUK	[29]	Bursa	Coastal	Rural	3500	6–14	10.2
SELCUK	[31]	Edirne	Inland	Rural	4522	7–12	16.4

†: self-reported lifetime prevalence of physician-diagnosed asthma.

children enrolled in this study were either born in Munich or moved to Munich in their first year of life (78.2%), it can be assumed that the majority of these children represent the second generation of Turkish immigrants living in Germany. This suggests that Turkish and German children grew up in similar outdoor environments.

Moreover, indoor factors and lifestyle may differ. Therefore, potential risk factors were evaluated, which had shown an association with childhood asthma and other atopic diseases in previous studies: a positive family history of atopy [18], fewer siblings [19], exposure to environmental tobacco smoke [20], low socioeconomic status [20], poor housing conditions [21], pet ownership [22] and low birthweight [23]. Apart from a positive family history of atopy, which significantly increased the risk of asthma and atopic sensitization, only Turkish origin was significantly negatively associated with asthma, atopy and BHR. These findings indicate that either environmental factors closely related to Turkish ethnicity that were not assessed, or genetic factors account for the effect of Turkish origin in these data. Since Turkish and German children grow up in different social and cultural settings, different dietary habits [24] or differences in exposure to car traffic [25] or indoor pollutants may be factors that were not evaluated but which may have contributed to the development of different diseases. The higher prevalence of cough with exercise, foggy or cold weather in Turkish children (table 2) might, for example, be attributable to the higher exposure to environmental tobacco smoke of the Turkish children. Since cough without wheezing has been shown to be independent of childhood asthma and atopic diseases [26], the higher prevalence of cough in the present data reflecting bronchitic rather than asthmatic symptoms is consistent with an overall lower prevalence of asthma, BHR and atopy in the Turkish population.

Variations in the genetic background of different ethnic groups [27] may also explain the differences in the prevalence of childhood asthma and atopic diseases. If genetic differences were responsible for the reduced prevalence of asthma in Turkish children in Germany, one might expect that studies in Turkish children living in Turkey [28–31] would find the same low prevalence of asthma. Surprisingly, this is not the case (table 6). In Turkey, self-reported prevalence rates for physician-diagnosed asthma using comparable definitions varied between 7.9 [29] and 17.4% [28] and were similar to those found in German children living in Munich.

Therefore, it is proposed that the lower prevalence of asthma and allergic diseases in this Turkish study group is in part owing to a selection bias associated with immigration. Healthy individuals may have chosen to leave their country of origin and work abroad. In Germany, most positions offered to immigrants are of low quality and are physically demanding. This effect of preselecting healthy individuals for physically demanding jobs is well known in occupational medicine, where it is referred to as a "pre-employment healthy worker effect" [32]. As a consequence of migration selection, the offspring of Turkish immigrants may have a lower risk of asthma and atopic diseases. In fact, the prevalence of hay fever and atopic dermatitis was significantly lower in Turkish than in German families, although asthma occurred with a similar frequency. The assessment of a history of asthma in the parents is prone to misclassification since only a crude question asking for the presence of asthma in first-degree relatives was used. Since Turkish fathers smoked more frequently than German fathers (56.0 *versus* 30.0%, $p< 0.001$) a misclassification of chronic obstructive pulmonary disease as asthma may have occurred more frequently in the Turkish fathers, thus preferentially overestimating the familial predisposition for asthma in Turkish families. Owing to this possible bias, the true overall genetic predisposition for atopic diseases might be lower in Turkish families living in Munich than in German families.

In conclusion, the results of this study show that Turkish children living in Germany have a lower prevalence of asthma and atopic diseases than their German peers. These differences may be attributable to a genetic selection effect of healthy families migrating to Germany or unknown environmental factors related to the lifestyle of these Turkish families living in Germany. The importance of evaluating ethnic differences when studying childhood atopic diseases in Europe should be emphasized.

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