

Original article

Prevalence of asthma in a large group of Israeli adolescents: influence of country of birth and age at migration

Background: The occurrence of asthma has geographic variations and is lower in developing compared with industrialized countries. Both environmental and genetic factors may influence its prevalence. We aimed to evaluate the importance and effect of immigration (country of birth and age at immigration to Israel) on the prevalence of asthma in a large group of Israeli adolescents.

Methods: Computerized medical records of 17-year-old adolescents, who underwent routine examination before military recruitment, were studied. The sample comprised both native-born Israelis (NBI) and immigrants from Ethiopia, the Former Soviet Union (FSU), and Western countries (WC). Asthma was defined as clinical symptoms and signs compatible with the disease accompanied by abnormal spirometry or documented chronic use of inhaled steroids.

Results: Our cohort consisted of 1 466 654 adolescents, including 1 317 556 (89.8%) NBI and 149 098 (10.2%) immigrants. The prevalence of asthma at age 17 was higher in NBI compared with Ethiopian immigrants [4.7% (61 921) vs 2.6% (418), respectively, $P < 0.0005$], lower compared with immigrants from WC [5.6% (2177), $P < 0.0005$], and similar to immigrants from the FSU. Further analysis of the association between age at immigration and the risk for developing asthma showed that the younger immigrants from the FSU and Ethiopia arrived to Israel, the higher their prevalence of asthma at the age of 17 was.

Conclusions: Both environmental and genetic factors seem to influence the prevalence of asthma in 17-year-old adolescents. However, the higher risk for developing asthma associated with young age of immigration points toward an environmental predominance.

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The incidence and prevalence of asthma are increasing worldwide making it a global health concern (1). The International Study of Asthma and Allergy in Childhood (ISAAC) reported major geographic variations in the prevalence of asthma in more than 50 countries (2).

Both environmental and genetic factors are thought to influence the prevalence and severity of asthma. Environmental factors may include viral infections (3, 4), allergen sensitization (5), air pollution (6, 7), and inner-city habitat (8). As to genetic factors, similar to hypertension and diabetes mellitus, the inheritance pattern of asthma is complex and cannot be characterized by a single gene. Moreover, varying disease-modifying genes have been linked to asthma in different populations and geographic zones (9–11). Studying the effect of immigra-

tion on the prevalence of asthma may help to identify the reasons for the geographic variations and the effects of the environmental and genetic factors on this disease. Immigration involves exposure to new allergens and pollutants and socioeconomic issues such as changes in living conditions and availability of medical services. It has been found that the prevalence of asthma and allergy is relatively low in developing compared with industrialized countries (2, 12, 13). Recently, it has been shown that immigration from developing to industrialized countries increases the risk of having asthma and allergy (14–23). Several studies have also demonstrated a possible correlation between duration of residency in the new country and increased risk for developing asthma and allergy (15, 18–20). Evidence also exists suggesting that the risk of developing asthma increases even within months after immigration (19). Although all these studies have demonstrated similar trends, several limitations need to be considered. First, most studies were held on relatively small populations of both immigrants and controls.

Second, given that the diagnosis of asthma was mainly based on self-reported symptoms without objective confirmation of the diagnosis, nonasthmatic transient wheezing or other respiratory diseases could have been mistaken for asthma. Finally, there were insufficient data regarding the possible correlation between duration of residency in the new country and the risk for developing asthma.

Two major factors make the Israeli population ideal for evaluating the effect of immigration on the prevalence of asthma. For many years, Israel has been a destination for Jewish immigrants from all over the world. During the last 20 years more than one million immigrants arrived in Israel, most of them from the FSU, others from other parts of Europe, North America and Ethiopia. Furthermore, at the age of 17, most Israeli adolescents undergo a complete medical evaluation as part of a routine health assessment before mandatory military service. This provides a unique opportunity to study the effects of immigration on the prevalence of asthma in a large group of Israeli adolescents.

Accordingly, we aimed to study the effect of age at immigration and the country of birth on the prevalence of asthma in 17 years old Israeli adolescents.

Methods

Study population and procedures

We studied the computerized draft medical records of 17-year-old male and female adolescents born between 1963 and 1987, who had a routine health assessment between 1980 and 2004 at the Army Draft Office before mandatory service in the Israeli Defense Forces (IDF). The health assessment included an interview and a complete physical examination by an experienced physician as well as revision of all past medical records. Demographic data comprised country of birth of each examinee and that of his father as well as the age of immigration to Israel when applicable. Pulmonary function test was recorded during the routine health assessment if the history or physical examination raised any suspicion of asthma.

The study population consisted of both native-born Israelis (NBI) and immigrants. The latter were from Ethiopia, the Former Soviet Union (FSU), and Western countries (WC) (defined as immigrants from North America and Western Europe). Immigrants from other countries were not included because their numbers were too low for meaningful analysis. While the number of immigrants from the WC and Ethiopia, examined at the age of 17 remained constant during the study period, among the immigrants from the FSU, who consisted the largest group, more than 80% were examined after 1989.

Precluded were Moslem Arab adolescents who comprise 21% of the general population and 25% of Jewish women who are exempt from military service for religious reasons. Altogether, the detailed medical records of approximately 70% of the population of interest were available for epidemiological study.

Definition of asthma

Asthma was defined as clinical symptoms and signs compatible with the disease at least during the last 12 months. Symptoms included:

attacks of dyspnea, cough, wheezing, chest tightness, nocturnal awakening with dyspnea and/or wheezing. Signs included wheezing, prolonged expiration and tachypnea. The clinical findings had to be accompanied by at least one of the following: (1) forced expiratory volume in one second (FEV_1) of less than 80% of normal values or (2) at least 10% decrease in FEV_1 in exercise test, or (3) increase of 10% in FEV_1 after treatment with bronchodilators or (4) documented chronic use of inhaled steroids at the time of the medical assessment.

Ethical considerations

The Institutional Review Board of the IDF Medical Corps approved this study on the basis that the anonymity of the participants is strictly protected. Given that data were recorded anonymously, no individual informed consent was obtained.

Statistical analysis

Chi-square test was used to compare the prevalence of asthma among the different groups. Pearson correlation was used to assess the link between the prevalence of asthma and the duration of residency in Israel. A test was considered significant when a P value was ≤ 0.05 ($\alpha = 0.05$). Odds ratio (OR) and 95% confidence intervals (CIs) were calculated to measure the risk of having asthma at age 17 in immigrants compared with NBI.

Results

Sample and subpopulations

The sample included 1 466 654 adolescents aged 17, of whom 1 317 556 (89.8%) were NBI and 149 098 (10.2%) were immigrants. No significant difference was found in the prevalence of asthma at the age of 17 between the two groups (4.7% and 4.8%, respectively, $P = 0.342$). Of the latter group, 93 982 (63%) emigrated from the FSU, 39 109 (26.3%) from WC, and 16 007 (10.7%) from Ethiopia.

Comparison of the prevalence of asthma between immigrants and NBI

Table 1 shows the prevalence of asthma at age 17 according to place of birth. The prevalence of asthma was found to be significantly lower in Ethiopian immigrants compared with NBI (2.6% and 4.7%, respectively, $P < 0.0005$), and significantly higher in immigrants from

Table 1. The prevalence of asthma at age 17 in immigrants from the FSU, WC, and Ethiopia compared with NBI*

Place of birth	Size of population (%)	Cases with asthma (%)	P-value
FSU	93 982 (63)	4544 (4.8)	0.155
WC	39 109 (26.3)	2177 (5.6)	<0.0005
Ethiopia	16 007 (10.7)	418 (2.6)	<0.0005

FSU, Former Soviet Union; WC, Western countries; NBI, native-born Israelis.

*The prevalence of asthma for NBI was 4.7%.

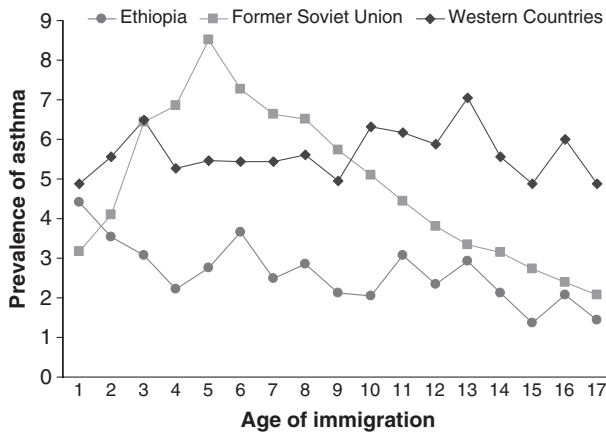


Figure 1. The prevalence of asthma at age 17 in immigrants from Ethiopia, the Former Soviet Union, and Western countries, according to age at immigration to Israel.

WC compared with NBI (5.6% and 4.7%, respectively, $P < 0.0005$). There was no significant difference in the prevalence of asthma between immigrants from the FSU and NBI (4.8% and 4.7%, respectively, $P = 0.155$).

As most immigrants from the FSU immigrated after 1989, we did a separate comparison of the prevalence of asthma at the age of 17 in immigrants from the FSU and NBI examined between 1990 and 2004. In this analysis, the prevalence of asthma was found to be significantly higher in the NBI compared with immigrants from the FSU (5.3% and 4.8%, respectively, $P < 0.0001$).

Prevalence of asthma according to the age at immigration to Israel

Figure 1 describes the prevalence of asthma at age 17 among immigrants according to the age at migration to Israel. A negative correlation was found between the immigration age and the prevalence of asthma among immigrants from Ethiopia and the FSU (P for trend = 0.006 and $P < 0.0005$, respectively). No association was found between duration of residency in Israel and prevalence of asthma among immigrants from WC ($P = 0.563$).

The risk for developing asthma within the same ethnic group

As can be seen in Table 2, the prevalence of asthma was significantly lower in immigrants from the FSU compared with NBI whose fathers were born in the FSU (4.8% and 5.6%, respectively, $P < 0.0005$). A similar relationship was found between Ethiopian immigrants and NBI whose fathers were born in Ethiopia (2.6% and 3.9%, respectively, $P = 0.001$). There was no difference in the prevalence of asthma in immigrants from WC when compared with NBI whose fathers were born in the same country.

The immigrants from the FSU and Ethiopia were further divided into three groups according to the age at

Table 2. The prevalence of asthma at age 17 in immigrants compared with NBI whose father was born in the same country

Place of birth	Prevalence of asthma (no. of adolescents)		P-value
	Immigrants	NBI whose father was born in the same country	
FSU	4.8% (93 982)	5.6% (81 409)	<0.0001
WC	5.6% (39 109)	5.6% (403 407)	0.627
Ethiopia	2.6% (16 007)	3.9% (2206)	0.001

NBI, native-born Israelis; FSU, Former Soviet Union; WC, Western countries.

immigration (1–5, 6–10, and 11–17 years). The OR and 95% CIs for the risk of having asthma at the age of 17 were calculated and compared with those of NBI adolescents whose father was born in the same country (Table 3). The within-ethnic difference tended to decrease the longer the immigrants stayed in Israel.

Discussion

The striking variation in the prevalence of asthma across the world and its changing occurrence over time has raised many hypotheses regarding the underlying factors of this disorder. The current study examined the prevalence of asthma in a very large group of 17-year-old adolescents and showed wide variations in the prevalence of asthma between Israeli born adolescents and their counterparts born in FSU and Ethiopia and living in Israel. The younger these immigrants arrived to Israel, the higher the risk of having asthma at age 17 was, suggesting the possibility that an environmental effect is considerably different in Israel and in their countries of origin. To a lesser extent, differences in the prevalence of asthma between these immigrants and NBI still existed after 12 years of residence in Israel, pointing towards possible persistent ethnic or genetic factors.

Asthma among Ethiopian immigrants

Asthma was diagnosed in 2.6% of Ethiopian immigrants. This prevalence is comparable with data reported for Ethiopians in Ethiopia (8) but is significantly lower than that of our 17-year-old NBI. While Ethiopia is a developing country, Israel is considered a Western urbanized country. It is hypothesized that moving from Ethiopia to Israel had a pro-asthmatic effect on this group of immigrants. Our results are supported by Rosenberg et al. who were the first to report an increased prevalence of asthma among Ethiopian immigrants to Israel (16). This study that was based on a small cohort and was dealing with adults (the immigrants' mean age was 42.7) revealed the same trends reported by us. Similar data were reported for Asian immigrants in Australia (24) and in extra-European immigrants in Italy (22). These data support the hygiene theory assuming that factors

Table 3. The odds ratio (OR) of having asthma at age 17 in immigrants from the FSU and Ethiopia compared with NBI whose father was born in the same according to years of residency in Israel

	Age at immigration	Prevalence of asthma (number of cases)	OR (95% CI) of immigrants compared with NBI whose father was born in the same country*	P-value
Immigrants from FSU	1–5	7% (871)	1.28 (1.19–1.38)	<0.0001
	6–10	6.2% (2209)	1.119 (1.06–1.18)	<0.0001
	11–17	3.2% (1464)	0.56 (0.53–0.60)	<0.0001
Immigrants from Ethiopia	1–5	3.1% (114)	0.78 (0.59–1.04)	0.09
	6–10	2.7% (167)	0.67 (0.52–0.88)	0.003
	11–17	2.3% (137)	0.58 (0.44–0.76)	

FSU, Former Soviet Union; NBI, native-born Israelis.

*The prevalence of asthma for NBI whose father was born in the FSU and Ethiopia was 5.6% and 3.9%, respectively.

associated with very early life experiences are significant determinants of risk for developing asthma. Indeed, the difference became less pronounced the earlier Ethiopian immigrants came to Israel.

Asthma among immigrants from the FSU

The prevalence of asthma was found to be significantly lower in immigrants from the FSU compared with NBI. This prevalence was low and comparable to that reported in different east European countries (25). The longer immigrants from the FSU lived in Israel, the higher the prevalence of asthma was. Apparently, living in Israel constituted a risk factor for developing asthma in this group. This interesting finding can be attributed to genuine environmental effects as well as to known differences between medical systems in the FSU and the Western world, supporting the assumption that asthma has been under diagnosed in the FSU according to the current criteria.

Asthma among immigrants from WC

Adolescents who immigrated from WC to Israel present the opposite tendency, with significantly higher rates of asthma than NBI. This finding is unique, as most immigrants move from poor countries to more prosperous ones. Therefore, no data exist regarding the effects of immigration from one WC to another. Moreover, wide variations in the prevalence of asthma were found in neighboring European countries. For example, the prevalence of asthma in German and Danish teenagers is 7.9% and 5.6%, respectively (26, 27). Israel is considered a WC in terms of quality of health services, life expectancy, and percentage of population living in urbanized areas. Thus, the differences between NBI and immigrants from WC can be attributed to variations found between WCs.

The data presented concerning all three groups of immigrants reflect the between-ethnic differences in asthma prevalence. For immigrants from Ethiopia and FSU, but not for immigrants from WC, moving to Israel increased the risk of developing asthma. The relative

importance of genes *vs* environmental effects explaining these differences remains to be investigated.

Immigration and the prevalence of asthma within the same ethnic group

There is a paucity of data regarding the effects of immigration on the prevalence of asthma within the same ethnic group. The prevalence of asthma for immigrants from Ethiopia was significantly different between recently arrived immigrants and NBI whose father was born in Ethiopia. When Ethiopian immigrants arrived to Israel younger than 5 years of age, the difference within the same ethnic group decreased and lost its significance. The prevalence of asthma for immigrants from FSU was significantly lower in recently arrived immigrants compared with NBI whose father was born in the FSU. This within-ethnic difference tended to decrease the longer immigrants stayed in Israel and then changed direction, showing that immigrants from the FSU that came to Israel during early childhood had a significantly higher prevalence of asthma than NBI whose father was born in the FSU. These findings are consistent with recently published reports showing higher rates of asthma in US-born Mexican American adults compared with Mexican American adults born in Mexico (21). A similar trend for Mexican-American children has been reported by Eldeirawi et al. (20). The within-ethnic differences in asthma rates depend not only on the place of birth but also on residence duration in the new country. The possible role of each one of the two potential groups of environmental factors: early childhood residency in developing countries *vs* long stay in industrial environment is unresolved at this point. Nevertheless, the interesting dichotomy between within-ethnic and between-ethnic differences may hint to a genetic effect that is not totally abolished by the long and strong environmental influences.

Study limitations

Studies dealing with the prevalence of asthma among various populations have to use similar definitions of

asthma. Most large multicenter surveys have used video or a written questionnaire (2). Although most of the questionnaires have been validated, lack of objective confirmation of the diagnosis may have influenced the results. To avoid these biases, our diagnosis of asthma depended on physician diagnosis supported by objective findings. On one hand the strict definition may have, to some extent, diminished the percentage of examinees defined as asthmatics. On the other hand, the moderate spirometric criteria allowed us to include patients with very mild asthma and increased the sensitivity of the diagnosis. Overall, we believe that these criteria validated the diagnosis of asthma and minimized the possibility of confusing it with other respiratory diseases. The fact that all participants were examined and diagnosed according to the same written guidelines further reduced bias contributed to varying diagnostic customs. Thus, taken together the precise diagnosis and the very large size of our population make the data presented particularly powerful.

When analyzing the data we considered the father's and adolescent's country of birth as indicators of ethnic origin. Our database did not include information regarding the mother's country of birth. However, the vast majority of immigrants from Ethiopia and from the FSU get married within the same ethnic community. Therefore, we believe that the division into the different ethnic

groups based on the father's country of birth is still precise.

This study is subject to the limitations inherent in any cross-sectional survey. To evaluate whether and which environmental factors are involved in disease evolution would require detailed information regarding smoking, pet ownership, exposure to endotoxin in early childhood, rural or urban place of birth, body mass index, level of education, area of residence and income – all suspected to play a role in asthma pathogenesis. Furthermore, adaptation to a new culture in the host society might be associated with stress, changes in diet, access to health services, and changes in economic and social status – all risk factors that were not available for analysis.

Conclusions

In conclusion, this study is, to our knowledge, the largest ever conducted in a single country. We showed extensive variations in the prevalence of asthma between NBI and immigrants to Israel from different parts of the world. Both environmental and genetic factors contribute to these variations. However, our findings may suggest that the environmental effect is more pronounced. This work provides a framework for further research that is warranted to better understand the pathogenesis of asthma.

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