



LETTER TO THE EDITOR

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Aeroallergen sensitization and upper respiratory allergies among patients living in rural and urban areas: Real-life exploration of the hygiene hypothesis

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INTRODUCTION

The number of people experiencing allergies has been increasing in the last decades. However, the increase in the global incidence of allergies observed is too fast and steady to be due to a genetic mutation. It may be due to environmental changes acting on some individual susceptibilities. According to what experts call “the hygiene theory”, the “excessive cleanliness” has been implied in reduced “microbial stimulation needed to enable normal development of the immune system”.¹ Specialists in allergy and immunology explored this concept; it evolved into the broader notion that declining microbial exposure is a major causative factor in the increasing incidence of atopy in recent years. Thus, children living in rural areas are subject to less sanitized environment and a greater exposure to infections and endotoxins, thus, they would develop fewer allergies than others by a likely production of a suppressive mechanism via Th1.² Yet, the question remains whether the association between cleanliness and development of asthma and allergies can be substantiated in human

populations.³ Family structure and exposure to infections were found to have the most impact on asthma, atopic sensitization and wheeze in childhood.⁴ Moreover, children raised in modern styles of metropolitan life, relatively free of this natural microbial load, and treated with antibiotics during childhood,⁵ may have an under-stimulated immune system, thus, promoting a model of pro-allergic immune development. Previous studies conducted in Lebanon showed that the prevalence of allergic disease was 39.6% in children aged 5-12 years, 5.6% of diagnosed asthma, 32.7% of allergic rhinitis and 11.5% of eczema in children aged 13-14 years⁶.

Differences in the prevalence of allergic disease between urban and rural areas have been observed in many parts of the world. Previous findings from Africa showed that populations living in rural areas experienced a very low burden of allergic disease.⁷ To the best of our knowledge, this hypothesis has not yet been explored in Lebanon. As part of the evaluation of the hygiene hypothesis, we conducted a retrospective observational study comparing patients with allergic rhinitis living in two different areas of Lebanon, the capital Beirut (urban city), and a rural area in Southern Lebanon.

METHODS

Study design

This is a retrospective, observational study, enrolling patients with allergic rhinitis. Data were collected randomly from medical records at several allergy clinics from two governorates in

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Lebanon (Beirut and Southern). The inclusion criteria included all patients aged between 3 and 65 years. One hundred files were selected from the clinics in Beirut (group A) and another 100 files from Southern Lebanon clinics (group B), with equal number of patients from each gender.

Ethical considerations

The Institutional Review Board of the Lebanese University at the Faculty of Pharmacy waived the need for an approval based on the facts that it was an observational study that respected participants' autonomy and confidentiality, induced minimal harm, and followed the principles set out in the Declaration of Helsinki for such studies.

Statistical analysis

Data entry and analysis were performed on Statistical Package for the Social Sciences (SPSS) software version 23. The independent-sample t-test was used to compare means between two groups (negative/positive sensitization to dust mites and to pollen). For categorical variables, the χ^2 and Fisher exact tests were used when applicable. Multivariate analysis logistic regressions were carried out using variables that showed a $p < 0.2$ in the bivariate analysis; potential confounders may be eliminated only if $p > 0.2$, in order to protect against residual confounding. In the logistic regression, the dichotomous negative/positive sensitization to dust mites and negative/positive sensitization to pollen were used as dependent variables. Significance was defined as a p-value less than 0.05.

RESULTS

A significantly higher mean age was found in patients consulting in Beirut (23.4 years) compared to those living in Southern Lebanon (14.2 years)

($p < 0.0001$). A significantly higher proportion of patients in group A (12%) had gastro-esophageal reflux, compared to 3% in group B ($p = 0.03$). 33% of patients with allergic rhinitis living in Beirut were exposed to tobacco smoke, compared to 31% of those living in South Lebanon, with no significance difference between both groups ($p = 0.88$). 21% of group A patients admitted the presence of carpet in their bedroom versus 18% in group B, with no significant difference between the two groups ($p = 0.7$). No significant difference was found between both groups concerning a family history of atopy (59% in group A vs 60% in group B; $p = 1$), family history of asthma (9% in group A vs 15% in group B; $p = 0.27$) and a family history of allergic rhinitis (7% in group A vs 9% in group B; $p = 0.79$).

A significantly higher percentage of patients in Group A (62%) underwent an allergy test, skin prick test and/or specific IgE compared to those in group B (36%) ($p = 0.0004$). A significantly higher percentage of patients living in Beirut was sensitized to pollen (56.45%) compared to those living in South Lebanon (33.33%) ($p = 0.036$). However, no significant difference was found between the two groups concerning the sensitization to mites ($p = 1$), co-sensitization to mites and pollen ($p = 0.07$) (see [Table 1](#)).

No significant difference was found between group A and B regarding the antibiotic therapy received during childhood (25% vs 32%; $p = 0.34$). A significantly higher percentage of people with positive reaction to dust mites had atopic dermatitis, positive allergy testing and lived in an urban city.

The bivariate analysis showed that a significantly higher percentage of patients with positive reaction to pollen had a positive allergy testing, lived in an urban city and had a higher mean age ($p < 0.05$

	Beirut (n = 62)	South Lebanon (n = 36)	p-value
Sensitization to mites	45 (72.58%)	27 (75%)	1
Sensitization to pollen	35 (56.45%)	12 (33.33%)	0036
Co-sensitization to mites and pollen	24 (38.71%)	7 (19.44%)	0.07
No testing done	6 (9.67%)	4 (11.11%)	1

Table 1. Patients' diagnostic profile

for all variables). The bivariate analysis, taking the absence/presence of sinusitis as the dependent variable, showed that a lower percentage of patients with sinusitis had a positive reaction to dust mites, compared to those without sinusitis (8.3% vs 37.9%).

Multivariable analysis

The results of a first logistic regression, taking the sensitization to dust mites as the dependent variable, showed that living in an urban city was significantly associated with higher odds of a positive reaction to dust mites ($OR_a = 2.3$). A second logistic regression taking the sensitization to pollen as the dependent variable showed that living in an urban city ($OR_a = 2.7$) and an increased age ($OR_a = 1.032$) were significantly associated with higher odds of having a positive reaction to pollen.

DISCUSSION

Our results showed that living in Beirut (urban city) would increase the odds of sensitization to both pollen and dust by two folds.

In recent decades, increasing sensitization and prevalence rates of allergic diseases attracted worldwide attention and concern.⁸ The connection between urbanization and allergy appears to be a complex puzzle, and there is currently no simple explanation or unique hypothesis that would be applicable. However, the study of Bryce et al.⁹ suggests a direct impact of air pollution on allergen carriers. Recent findings suggested also that living in Beirut was significantly associated with a higher risk of asthma versus Mount Lebanon while there was no significant difference between the 2 districts with probable asthma.¹⁰ The principles of hygiene hypothesis may be a possible theory to understand the reasons behind the rise of allergic diseases in order to try to prevent further increase in the future.

Limitations

Our study has some limitations. The sample size is small. It was withdrawn from two governorates in Lebanon, and thus cannot be extrapolated to the whole population.

CONCLUSION

Our findings confirm that residing in rural area is associated with a significantly lower sensitization to allergens and symptoms in our small sample. Larger studies across different parts of the country are needed. Health care professionals should counsel their patients about how to avoid environmental risk factors associated with allergic diseases.

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