

Nasal Polyps: Heredity, Allergies, and Environmental and Occupational Exposure

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ABSTRACT

Objective: To determine the role of heredity, allergies, smoking, and environmental and occupational exposure in the epidemiology of nasal polyposis.

Study Design: A case-control study comprising 100 patients with nasal polyps admitted to three Athens hospitals and 102 controls from the general population. Gender, educational level, family history, allergies, smoking, occupational activities, and environmental exposure were examined as eventual determinants. The prevalence of each determinant was compared between cases and controls using multiple logistic regression, and odds ratios (ORs) were estimated.

Results: A total of 13.3% of the patients and none of the controls had a history of polyps in the family. According to multiple logistic regression, the OR for certain allergies was 19.1 and for probable allergy was 9.0, with the prevalence among patients being 64% and 12%, respectively. The OR for certain environmental exposures was 15.0 and for occupational exposures was 21.4. Occupational exposure to chemicals was a predominant factor among patients. No significant difference was found between nasal polyps and educational level or smoking habits.

Conclusions: The development of nasal polyps seems to be strongly related to family history and a history of allergies, but the role of smoking remains controversial. Occupational and environmental exposures probably enhance the appearance of the disease on the basis of genetic predisposition.

SOMMAIRE

Objectif: L'objet de l'étude était de déterminer le rôle de l'hérédité, des allergies, du tabac et des expositions environnementale et professionnelle dans l'épidémiologie de la polypose nasale.

Type d'étude: Il s'agit d'une étude cas témoins comparant 100 malades admis dans trois hôpitaux d'Athènes avec 102 témoins provenant de la population générale. Le sexe, le niveau d'instruction, les antécédents familiaux, les allergies, la consommation de tabac, la profession et l'exposition environnementale ont été considérés comme des déterminants possibles de la polypose. La prévalence de chaque paramètre a été comparée entre les cas et les témoins par une régression logistique multiple, qui a permis l'estimation des risques relatifs approchés (RRA).

Résultats: Dans l'ensemble, 13.3% des malades avaient des antécédents familiaux de polypes contre aucun témoin. Selon l'analyse de régression logistique, le RRA pour les allergies certaines était de 19.1 et celui pour les allergies probables, de 9.0, et la prévalence parmi les malades était de 64% et de 12%, respectivement. Le RRA pour les expositions environnementales certaines était de 15.0 et celui pour les expositions professionnelles, de 21.4. L'exposition professionnelle aux produits chimiques était un facteur très important parmi les malades. En ce qui concerne le niveau d'instruction et la consommation de tabac, on ne relève pas de différence significative.

Conclusions: L'apparition de polypes nasaux semble fortement associée à l'hérédité et aux allergies, mais le rôle du tabac est incertain. Les expositions professionnelle et environnementale favorisent probablement l'apparition de la polypose compte tenu de la prédisposition génétique.

Key words: allergy, case-control study, heredity, nasal polyposis, occupational or environmental exposure

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Nasal polyps are the most common tumours of the nasal cavity, and their prevalence is estimated to be about 2.1 to 4%.^{1,2} They can impair quality of life, causing nasal obstruction and leading to acute or chronic sinusitis, hyposmia or anosmia, sleep apnea, and nasal bone destruction.^{3,4}

There are several pathogenic theories,⁵ but the precise mechanism of nasal polyps is not completely understood. Nasal polyps or nasal polyposis is considered a subgroup of chronic rhinosinusitis. It is therefore related to a chronic inflammatory condition of the nasal cavity, where eosinophils have a predominant role.⁶

Hereditary and allergic mechanisms have been investigated and seem to play a significant role in the development of nasal polyps. Environmental determinants such as smoking, occupation, and pollution are not clear and are sometimes controversial.⁷ Taking into account the lack of sufficient epidemiologic data, we attempted with this study to investigate the frequency of eventual risk factors among patients with nasal polyps and to compare it to that of healthy controls.

Materials and Methods

This retrospective case-control study was carried out in Athens (Greece) from July 2007 to June 2009. One hundred patients with nasal polyps admitted to the otolaryngology department of three hospitals in Athens and 102 healthy controls matched for age participated in the study. Cases were selected by convenience sampling (consecutive cases during the study duration), and controls were selected following representative sampling criteria from the general population that had access to the orthopedic department following an accident at the same three hospitals.

Cases and controls were over 18 years old. Of the cases, 95 were operated on for nasal polyps and 5 were under noninvasive treatment. A questionnaire was completed by interview with both patients and controls by one of the researchers following obtaining written informed consent. All participants were interviewed on the onset of disease, their educational level as an index of the socioeconomic level, their smoking habits, their previous occupational activities, and the duration of each. They were also asked for their personal and family history of nasal polyposis as well as their history of food allergies; allergy to aspirin, other medication, or pollen; and other known or unknown factors, such as asthma, dermatitis, and seasonal or perennial rhinitis. Allergy was considered evident only in persons who had ever had a positive allergic test in the past. Owing to the design of the study, it was not possible

to differentiate between atopic and nonatopic asthma. Perennial rhinitis was not classified as an allergy because its allergic origin is not clear.

For evaluating environmental exposure, all participants were asked about their current and previous domiciles; the distance of their homes from environmental pollutant activities such as industries, wood-related activities, and dust-producing activities; and the use of a wood stove in their house. The degree and duration of environmental exposure were assessed blindly and independently by two experts, who took into account the environmental pollution of the participants' houses using Athens pollution maps, the proximity of the house to high traffic roads or other polluting activities, and the use of a wood stove. Relevant adjustments were made for those who had lived in rural areas or other cities. Environmental pollution was classified into three levels (none, not certain, evident). In case of disagreement between the two experts, a third expert was included for further concordance on the final classification. The same procedure was followed for occupational exposure. Occupation was also classified into the same categories. In addition, duration of occupational exposure, if any, was classified as long or short term. Given that there are no known occupational risk factors related to nasal polyps, activities considered high risk were those with exposure to dust, fumes, formaldehyde, chrome, nickel, arsenic, irritants, colours, solvents, and other volatile organic compounds.

Beyond atopy and allergy to acetylsalicylic acid, the overall history of allergies and/or asthma, even in childhood, was evaluated in the same manner as environmental or occupational exposure, assessing the answers provided by the participants. Each case or control was accordingly classified as nonallergic, probably allergic, or obviously allergic. Gender, educational level, classification of environmental or occupational exposure, smoking habits, and family history of allergy and of nasal polyposis were considered eventual determinants and were compared between cases and controls.

Continuous variables are presented as mean values $\pm$ standard deviation (SD). Categorical variables are presented as absolute and relative frequencies. Chi-square test and Pearson or Fisher exact test were used to test the differences between patients and controls in terms of gender, smoking status, educational level, heredity, history of allergy and nasal polyps, classification of environmental or occupational exposure, and duration. Student *t*-test was used to test differences in pack-years of cigarette smoking and the number of cigarettes smoked per day between patients and controls.

We applied multiple logistic regression to calculate odds ratios (ORs) and corresponding 95% confidence intervals for patients with nasal polyps compared to healthy controls. The set of independent variables comprised the severity of smoking (packages per year), heredity, allergy history (none, probable, or evident), environmental exposure (none, uncertain, and certain), occupational exposure (none, uncertain, and certain), and duration of occupational exposure (none, minimal to short, and long). ORs were adjusted for sex and education (medium, high, and superior).

All statistical tests were two-sided, and p values $< .05$ were considered statistically significant. Data analysis was performed using *PASW Statistics* software version 16.0 (SPSS Inc, Chicago, IL).

Results

The study population consisted of 202 participants with a mean (SD) age of 49 (16.8) years (100 patients with nasal polyps and 102 healthy controls). The distribution of patients and controls in terms of the various determinants is presented in Table 1. The distribution of gender, allergy history, heredity, environmental and occupational exposure, and duration of occupational exposure differed significantly between patients and controls ($p < .05$). More specifically, the percentage of women was higher among cases and that of men was higher among controls. The distribution of current smokers, previous smokers, and nonsmokers did not differ significantly between cases and controls, but the average number of cigarettes per day was higher among patients (10; SD 14.2) compared to controls (7; SD 11.1) (t -test: 1.39, $p = .08$). Also, when smoking habits were expressed as pack-years of cigarette smoking per year, they were found to be nearly significant (t -test: -1.39 , $p = .07$). The duration of environmental exposure did not differ between cases and controls when comparing short or long exposure to nonexposure.

Table 2 displays the distribution of the different kinds of allergies in patients and controls. More specifically, aspirin intolerance was mentioned by 5.5% of the patients. A history of seasonal rhinitis, asthma, and atopic dermatitis was much higher among cases, with some of them having more than one site of allergy.

Among 23 cases with evident occupational exposure, 11 (47.8%) were exposed mainly to dust and 12 (52.2%) mainly to chemicals. Among 9 controls, only 2 (22.2%) were exposed to chemicals and the rest (77.8%) to dust. Exposure to chemicals seems to be predominant among occupational factors.

In Table 3, the results of multiple logistic regression analysis are presented. A statistically significant increased risk of nasal polyps was observed for allergy history, occupational exposure, and duration of occupational exposure. More specifically, subjects with a probable or evident allergy history showed an elevated risk for nasal polyps compared to participants without allergies. Uncertain or evident occupational exposure was associated with increased risk for nasal polyps compared to no exposure. The results were similar when examining the duration of occupational exposure. A borderline significant association was found for gender, whereas a nonsignificant elevated risk of nasal polyps was observed for smoking habits and educational level. Heredity could not be included in the analysis because there was no reference to family history of polyps in the control group.

Discussion

In the present case-control study, we attempted to examine the predisposing factors that contribute to the manifestation of nasal polyposis. There is a male preponderance of polyps in some studies,^{2,8} but this is not a constant finding in all epidemiologic screening studies.^{1,9} In our study, there was an excess of women among the cases, but the selection of cases was not representative of the prevalence of nasal polyps in the population of reference.

According to the results of this study, nasal polyposis in the family was present in 13% of the patients and in none in the controls. The role of heredity is evident by the initial analysis because it was not possible to be included in the logistic regression model. Although a recall bias may underestimate family history among healthy controls, this is similar to the findings observed in other studies, which have also shown that about half of patients with a family history had more than one member with this problem in the family.¹⁰ The incidence of nasal polyps within some families suggests the possibility of an autosomal mode of inheritance.¹¹ The lack of family history does not exclude the possibility of a latent genetic predisposition. A genetic predisposition to nasal polyps is also evident among patients with chronic rhinosinusitis.^{7,9} Recent studies have focused on the role of genes in the growth of nasal polyps. Nasal polyps appear to have characteristic transcriptional signatures compared to normal sinonasal mucosa.¹²

The history of allergy among patients requiring treatment for nasal polyps varies from 48 to 84%. Perennial allergy seems to be of higher risk than seasonal allergy,¹³ although these are not independent conditions. Sensitivity to multiple environmental factors is found

Table 1. Distribution of the Various Determinants for Nasal Polyps in Patients and Controls

<i>Determinant</i>	<i>Patients (n = 100)</i>	<i>Controls (n = 102)</i>	<i>Total</i>	<i>p Value</i>
	<i>n (%)</i>	<i>n (%)</i>		
Gender				
Men	43 (43.0)	63 (61.8)	106	.008*
Women	57 (57.0)	39 (38.2)	96	
Smoking				
Yes	36 (36.0)	32 (31.4)	68	.58*
No	51 (51.1)	56 (54.9)	107	
Interrupted	13 (13.0)	14 (13.7)	27	
Heredity				
Yes	13 (13.3)	0 (0)	13	< .001*
No	87 (87.0)	102 (102.0)	180	
Educational level				
Lower	65 (65.0)	67 (65.7)	132	.63*
Medium	18 (18.0)	14 (13.7)	32	
High	17 (17.0)	21 (20.6)	38	
Allergy				
None	24 (24.0)	81 (79.4)	105	< .001*
Probable	12 (12.0)	6 (5.9)	18	
Evident	64 (64.0)	15 (14.7)	79	
Environmental exposure				
None	75 (75.0)	77 (75.7)	152	.03 [†]
Uncertain	17 (17.0)	24 (23.5)	41	
Evident	8 (8.0)	1 (1.0)	9	
Duration of environmental exposure				
None	75 (75.0)	77 (75.5)	152	.28 [†]
Short-medium	3 (3.0)	0 (0.0)	3	
Long	22 (22.0)	25 (24.5)	49	
Occupational exposure				
None	61 (61.0)	84 (82.2)	145	.003*
Uncertain	16 (16.0)	9 (8.8)	25	
Evident	23 (23.0)	9 (8.8)	32	
Duration of occupational exposure				
None	61 (61.0)	84 (84.4)	145	.001*
Short-medium	12 (12.0)	2 (2.0)	14	
Long	27 (27.0)	16 (15.7)	43	

*Pearson chi-square test.

[†]Fisher exact test.**Table 2.** Distribution of Allergy Types among Patients and Controls

<i>Type of Allergy</i>	<i>Patients, n (%)</i>	<i>Controls, n (%)</i>
Aspirin intolerance	5 (5.5)	1 (0.98)
Other pharmaceutical allergy	9 (9.9)	8 (7.84)
Asthma	35 (35.0)	4 (3.92)
Atopic dermatitis	20 (20.0)	4 (3.92)
Seasonal rhinitis	40 (40.0)	6 (5.88)
Total evident allergies	64 (64.0)	15 (14.70)

among patients, with dust mite, cat, and mould allergy playing a large role. Nasal allergy related to atopy is a predisposing factor, although, according to some authors, nasal polyps are more frequent among nonatopic than atopic asthmatic patients.¹⁴ Aspirin intolerance has been related to nasal polyposis; around 60% of individuals with aspirin intolerance have nasal polyps.^{13–16} In our study, the prevalence of certain allergy among patients was 64% and 11.2% had probable allergy. This determinant had the highest OR, whereas 5% of the patients had intolerance to

Table 3. Potential Nasal Polyp Risk Factors in the Study Population

<i>Factor</i>	<i>Odds Ratio</i>	<i>95% CI</i>	<i>p Value</i>
Gender (male vs female)	0.46	0.20–1.07	.072
Smoking habits (no. of cigarettes per day)	1.01	0.98–1.04	.516
Education			
Medium vs lower	1.52	0.54–4.22	.426
High vs lower	1.64	0.59–4.58	.341
Allergy history			
Probable vs none	8.98	2.49–32.45	.001
Evident vs none	19.12	7.85–46.58	< .001
Environmental exposure			
Uncertain vs none	1.14	0.45–2.89	.784
Evident vs none	15.0	1.20–186.91	.036
Occupational exposure			
Uncertain vs none	25.7	3.47–190.90	.001
Evident vs none	21.4	3.36–136.25	.001
Duration of occupational exposure			
Short/medium/long vs none	4.91	1.43–16.86	.012

acetylsalicylic acid. This is in concordance with most studies relating to allergies and nasal polyposis.

Occupational and environmental exposure has been found in some studies to play a significant role in the manifestation of nasal polyps. An analysis of about 1000 patients showed that around half had exposure to occupational dust and fumes.⁸ A case-control study showed that wood stoves are a determinant for nasal polyps.¹⁷ The same study showed an increased OR for occupational exposure. Wood stove exposure was included in our study; the only two cases found were classified as environmentally exposed. However, according to the literature, there is no sufficient evidence for the role of environmental and occupational exposure in the epidemiology of nasal polyps. In this study, environmental and occupational exposure seems to have an important role as a determinant of nasal polyps, independent of backup allergies or family history. Exposure to chemicals was the predominant exposure factor among patients. Chemicals were also found to play a role in other studies.^{8,17} The inconsistency in the duration of occupational exposure with nasal polyps can be explained by the healthy worker effect as a subject with nasal polyps is likely to quit an unhealthy occupational activity. Environmental pollution also seems to contribute to the etiology of nasal polyps. The pollution pattern in Athens is photochemical, with an

excess of nitrous oxides and ozone.¹⁸ These are chemicals with a known irritating effect to the nasal mucosa. In total, it seems reasonable that the inflammatory process, which is the main mechanism of nasal polyps, can be initiated or aggravated by environmental or occupational chemicals.

The role of smoking is not evident. Houser and Keen found that 30.2% of patients with nasal polyps were current smokers.¹³ These authors found a significant association between tobacco use and nasal polyps in a multivariate analysis, although the prevalence of subjects who had “ever smoked” did not differ significantly from that of those who had “never smoked.”¹⁹ Risk factors in this study were searched among patients with nasal polyps only. The prevalence of nasal polyps was much higher in patients with perennial allergy who were nonsmokers and light smokers, but in heavy smokers, the prevalence of polyps was greater in those without perennial allergy than those with perennial allergy.¹³ According to Theriault and colleagues, smoking may inhibit the inflammatory process and retard the growth of polyps.²⁰ There is, however, a problem of selection bias for all of these studies because individuals with nasal allergies or nasal polyposis may avoid smoking for reducing their nasal symptoms.¹³ In our study, 36% of the participants were smokers, but no significant difference in smoking prevalence was found between the two groups, although subjects with nasal polyps had higher smoking exposure.

Conclusion

The conclusion of this study is that family aggregations, allergies, and occupational and environmental exposure, independently viewed, are much more frequent among patients with nasal polyps in comparison to the general population. Patients in the present study were subjected to detailed examination prior to treatment, whereas controls were not, and this may have caused an overestimation of the role of eventual determinants owing to the fact that some patients may have had asymptomatic polyps.

The role of smoking remains unclear, and more sophisticated studies with larger samples are necessary for this purpose. The appearance of the disease beyond genetic factors depends on environmental factors inducing either allergic or irritating inflammatory effects. The findings of the study gave clear results in terms of the factors investigated for nasal polyposis but were based on history taking only. Future research could be improved if objective data are included, for example, regarding allergy, skin, or serum tests for IgE.

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