

Prevalence, Demographic and environmental factors of allergic fungal sinusitis among chronic sinusitis patients with nasal polyps in western Saudi Arabia

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Objectives: To detect the prevalence of allergic fungal sinusitis (AFRS), the demographic and environmental risk factors for AFRS and to predict AFRS among chronic sinusitis with nasal polyps (CRSwNP) patients.

Patients and Methods: A multicenter retrospective case-control study was conducted from March 2010 to October 2018 on 262 CRSwNP patients. Assessment of patients was conducted using nasal endoscopy, Computed Tomography (CT) of paranasal sinuses and Immunoglobulin E (IgE). All patients were operated under general anesthesia and underwent endoscopic sinus surgery with histopathology. Patients were assigned into two groups: AFRS (118 patients) and non-fungal CRSwNP (144 patients). All demographic and environmental factors of both groups were compared.

Results: The mean age of patients in the AFRS and non-fungal CRSwNP groups were 22.5 and 41.2 years respectively. Statistical significant differences were detected in most of the demographic and environmental factors compared between both groups.

Conclusions: The prevalence of AFRS is 45% of patients with nasal polyps in the western area of Saudi Arabia. Patients with nasal polyps who have the following characteristics; of being young adult, having low socioeconomic growth, having low education level, having been exposed to birds, exposed to dust from infrequent air conditioning (AC) filter cleaning at home, having carpet at home, residents in old or over crowded house, living in hot humid areas or being passive smoker are more likely to had AFRS.

Keywords: Sinusitis, nasal polyp, allergic, fungal, prevalence, demographic factors, environmental.

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Introduction

Chronic rhinosinusitis (CRS) is an inflammation of the lining membranes of one or more of the sinuses for more than 12 weeks with at least 2 characteristic symptoms (facial pain, nasal discharge, nasal blockage, reduced smell) along with endoscopic or radiographic disease confirmation. [1] CRS is classified into two types confirmed through nasal endoscopy: chronic rhinosinusitis without nasal polyps (CRSsNP) and chronic rhinosinusitis with nasal polyps (CRSwNP). [2] This separation is useful in clinical practice, since the majority of nasal polyps in western countries are eosinophilic and steroid responsive, which helps to guide disease management. In addition, CRSwNP patients are thought to have more severe sinonasal symptoms than CRSsNP patients. [3]

CRS with nasal polyps (CRSwNP) is a chronic inflammatory disease of the mucous membrane of the nose and paranasal sinuses which manifests itself as peduncle shaped masses of inflamed mucosa prolapsing into the nose. [4] Although, there is no single etiological factor that is responsible for the development of CRSwNP, allergy, viral, bacterial or fungal infections have all been suggested as possible initial triggers that may stimulate inflammation of the sinus mucosa and develop nasal polyp. [5]

Allergic fungal rhinosinusitis (AFRS) was first appreciated in 1981 by Millar et al who noted a histologic similarity between the sinus contents recovered from chronic sinusitis patients and the typical pathologic appearance of allergic

bronchopulmonary aspergillosis. [6] Since this first description of AFRS, the pathophysiology, etiology and diagnostic criteria of AFRS have been the topic of much debate, Bent and Kuhn [7] developed the current diagnostic criteria for AFRS based on radiographic, histologic, and immunologic characteristics.

The prevalence of nasal polyps most likely varies by geography and environment, although large studies of the prevalence of polyps across different geographic areas are lacking. [8] In a multicentric study done in China, it was reported that some occupational and environmental exposures are strongly associated with CRS. [9] In Reviewing the literature, some socioeconomic, [10] and geographical factors [11] were found to predict AFRS in certain populations. On the other hand, in the literatures, no consistent evidence was found in CRS patients to link the disease severity with the socioeconomic status. [12]

Most of the epidemiological data regarding CRS are mainly from studies conducted in western countries, and little is known regarding the potential role of socio-economic factors in the Middle East area.

It is well known that the nasal polyposis is a constant finding in AFRS patients as described by Bent and Kuhn, [7] but the final diagnosis of AFRS is delayed until histopathology is done post-operatively. Also, given that unilateral nasal polyp is not unique for AFRS patients as it was reported that only 37% of AFRS patients present with unilateral polyp, [13]

so, it is of great importance to find any factors that predict the diagnosis of AFRS preoperatively. To that extent this study was conducted to detect the prevalence of AFRS in chronic sinusitis patients with nasal polyps and detect the potential role of demographics and environmental factors as predisposing or risk factors for AFRS, also to predict AFRS preoperatively among chronic sinusitis patients with nasal polyps.

Patients and Methods

This study is a multicenter retrospective case-control study done from March 2010 to October 2018 in Saudi German Hospital, Saudi airlines medical services and Al jeddaani hospital, Jeddah, Saudi Arabia. The study protocol was approved by the local ethical committee of these hospitals and all study participants signed a written fully informed consent.

The study was done on 262 chronic rhinosinusitis patients with nasal polyps (CRSwNP) patients selected from patients with chronic sinusitis presented at ENT clinics in the previously mentioned hospitals. Assessment of patients included: taking detailed history, full ENT examination including nasal endoscopy, complete blood count (CBC) to detect serum eosinophilia, radiologic assessment with CT paranasal sinuses (PNS) to confirm the diagnosis of chronic sinusitis with polyps or allergic fungal sinusitis and to also detect any bone erosion, orbital or intracranial affection. Total and serum specific IgE were done using radioallergosorbent test (RAST) for all patients.

All patients must fulfil the following criteria of chronic sinusitis as suggested in the European position paper: [14] (A) presence of two or more symptoms one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip): \pm facial pain/pressure; \pm reduction or loss of smell; for $>$ 12 weeks; (B) either (1) Endoscopic signs of: polyps and/or; mucopurulent discharge primarily from middle meatus and/or; oedema/mucosal obstruction primarily in middle meatus (2) And/or CT changes: mucosal changes within the ostiomeatal complex and/or sinuses.

The following patients were excluded from the study: patients under 18 years old, patients with invasive fungal sinusitis, nasal tumors, and patients with genetic disorder accompanied by ciliary dysfunction.

All demographic data of patients in the form of age, sex, nationality, medical history (chest asthma), insurance class, occupation related allergy and educational attainment were documented. Also, environmental factors in the form of in-house domestic pets (cats, dogs or birds), cockroaches in house, carpets, plants or exposure to dust at home or workplace, residency, poor exposure to sun, infrequent AC filter cleaning, geographic areas and smoking were documented.

All patients undergone routine preoperative assessment and were operated under general anesthesia with endoscopic sinus surgery. The presence or absence of allergic mucin intraoperative was documented. Grossly, allergic fungal mucin is thick, tenacious, and highly viscous in consistency; its color may vary from light tan to brown or dark green. 15 Nasal polyps and allergic mucin were collected intraoperative; the specimens were immediately placed in sterile normal saline and 10% formalin bottles and sent to the microbiology and histopathology laboratories respectively.

Patients who met the major diagnostic criteria (the minor criteria serve to support the diagnosis) as set by Bent and

Kuhn [7] (**Table 1**) were designated as allergic fungal sinusitis (AFRS or group A), while the rest of the patients were designated as non-fungal chronic sinusitis with polyp (non-fungal CRSwNP or group B).

Statistical analysis:

All the demographic and environmental data of groups A and B were calculated, tabulated and statistically analyzed. Statistical analysis was conducted using SPSS version 17 for windows. P value was considered significant if $<$ 0.05.

Results

This study was conducted on 262 chronic rhinosinusitis patients with nasal polyps divided into allergic fungal rhinosinusitis (group A) and non-fungal chronic sinusitis with nasal polyps (group B). AFRS patients included 118 patients with the age ranged from 14 to 35 years with a mean of 22.5 ± 6.4 years, while non-fungal CRSwNP (group B) included 144 patients with the age ranged from 23 to 57 years with a mean of 41.2 ± 9.3 years. No significant differences in male to female ratio between both groups as p value was 0.626 (**Table 2**).

The percentage of Saudi patients was more in group A (81.4%) than in group B (52.8%) with a statistically significant difference. On the other hand, The percentage of non-Saudi patients was more in group B (47.2%) than in group A (18.6%) with a statistically significant difference. The percentage of asthmatic patients was more in group B (67.4%) than in group A (48.3%) with statistically significant difference. The percentage of patients with high insurance class was more in group B (85.4%) than in group A (28.9%) with a statistically significant difference. On the other hand, the percentage of patients with low insurance class was more in group A (71.1%) than in group B (14.6%) with a statistically significant difference. Also, the percentage of patients with low educational level was more in group A (53.4%) than in groups B (25%) with a statistically significant difference. No significant difference was found between both groups in occupation related allergy as p value was 0.207 (**Table 2**).

No significant differences were found between groups A and B in the percentages of patients who had cats or dogs or were exposed to cockroaches as p values were 0.190 and 0.416 respectively. While, the percentage of patients who had birds was more in group A (29.6%) than in group B (7.6%) with a statistically significant difference. Also, the percentages of patients who had carpets or exposed to dust at home or workplace were more in group A (70.3% and 58.5% respectively) than in group B (21.5% and 8.3% respectively) with statistically significant differences (**Table 3**).

Patients with residency in old houses, overcrowded houses, poor sun exposure or infrequent AC cleaning were more in group A (22.1%, 22.9%, 78.8% and 47.5% respectively) than in group B (1.4%, 1.4%, 32.6% and 9.7% respectively) with statistically significant differences seen between both groups. The percentage of patients from hot humid areas (Jeddah and Rabigh) was more in group A (83.9%) than in group B (25.7%) with significant difference. On the other hand, the percentages of patients from hot dry (Makah) or high altitude (Taif) areas were more in group B (34.7% and 39.6% respectively) than in group A (15.3% and 0.8% respectively) with statistically significant differences. No significant difference were detected in the percentages of smoker, ex-smoker or non-smoker patients between both groups as p values were not significant, while passive smoking was more in group A (20.3%) than in group B (10.4%) with a statistically significant difference (**Table 3**).

Table 1. Bent and Kuhn Diagnostic Criteria.⁷

Major criteria	Minor criteria
Type I hypersensitivity	Asthma
Nasal polyposis	Unilateral disease
Characteristic CT findings	Bone erosion
Eosinophilic mucin without invasion	Fungal cultures
Positive fungal stain	Charcot-Leyden crystals
	Serum eosinophilia

Table 2. Comparison of demographic factors between allergic fungal sinusitis (group A) and non-fungal chronic sinusitis with polyps (group B).

Parameter		Group A	Group B	P value
		Number (Percentage)	Number (Percentage)	
Gender	Male	68 (57.6%)	80 (55.6%)	0.626
	Female	50 (42.4%)	64 (44.4%)	0.626
Nationality	Saudi	96 (81.4%)	76 (52.8%)	0.000
	Non Saudi	22 (18.6%)	68 (47.2%)	0.000
Medical History	Asthma	57 (48.3%)	97 (67.4)	0.000
Socioeconomic Growth	Insurance class A	34 (28.9%)	123 (85.4%)	0.000
	Insurance class B	84 (71.1%)	21 (14.6%)	0.000
Occupation Related allergy		15 (12.7%)	24 (16.7%)	0.207
Educational Attainment	Secondary and Low Level	63 (53.4%)	36 (25%)	0.000
	University and Post	55 (46.6%)	108 (75%)	0.000

Table 3. Comparison of environmental factors between allergic fungal sinusitis (group A) and non-fungal chronic sinusitis with polyps (group B).

Parameter		Group A	Group B	P value
		Number (Percentage)	Number (Percentage)	
Pets (cats or dogs)		28 (23.7%)	41 (28.5%)	0.190
Pets (birds)		35 (29.6%)	11 (7.6%)	0.000
Cockroaches		37 (31.3%)	40 (27.8%)	0.416
Carpet at home or workplace		83 (70.3%)	31 (21.5%)	0.000
Plants at home or workplace		10 (8.5%)	62 (43.1%)	0.000
Resident in >30 y old house		26 (22.1%)	2 (1.4%)	0.000
Resident in overcrowded house Floor space per person below ≤26 meter		27 (22.9%)	2 (1.4%)	0.000
Exposure to dust at home or workplace		69 (58.5%)	12 (8.3%)	0.000
Poor exposure to sun		93 (78.8%)	47 (32.6%)	0.000
Infrequent AC filter cleaning		56 (47.5%)	14 (9.7%)	0.000
Geographic areas	Jeddah, Rabigh (Hot, Humid)	99 (83.9%)	37 (25.7%)	0.000
	Makah (Hot, Dry)	18 (15.3%)	50 (34.7%)	0.000
	Taif (High altitude)	1 (0.8%)	57 (39.6%)	0.000
Smoking	Cigarettes Smoker	21 (17.8%)	30 (20.8%)	0.369
	Passive smoker	24 (20.3%)	15 (10.4%)	0.002
	Ex-smoker	4 (3.4%)	6 (4.2%)	0.795
	Non Smokers	69 (58.5%)	93 (64.6%)	0.149

Discussion

Chronic Sinusitis is a big health problem and one of the most common chronic inflammatory disease worldwide, the global prevalence rate was reported to be in the range of 12-15%, [4] with the prevalence in western world was estimated to be about 10% of the population. [1] It was reported that, an increase in the prevalence of chronic rhinosinusitis is in the eastern areas of Saudi Arabia had been noticed. [16]

In a study done in northern India, the prevalence rate of AFRS is 89.3% of patients with CRSwNP, [17] in the present study, the prevalence rate of AFRS is 45 % of patients with CRSwNP, which is due to being in different geographic areas. In a study done 2009 in eastern Saudi Arabia [18] on 91 patients, the prevalence of AFRS was 12% of patients with CRSwNP which is lower than the current study, which is due to the large number in our study (262), the different geographic area, the change of climate and population habits with time.

In the current study, the mean age of patients with AFRS was 22.5 years while the mean age of non-fungal CRSwNP was 41.2 years and this difference is statistically significant, this finding is similar with a retrospective review study by Wise et al, [10] who found the average age of CRSwNP and AFRS at diagnosis was 48 and 28 years respectively.

In the current study, AFRS is more common in Saudi patients, while non-fungal CRSwNP is more common in non-Saudi patients, with statistically significant between both groups. Similarly, it was reported in a 2015 study that first-degree relatives of a patient with CRSwNP have a 4.1-fold increased risk of developing nasal polyps. [19] On the other hand, in our study, no statistically significant difference in male to female ratio between AFRS and non-fungal CRSwNP.

In the present study, chest asthma was detected in 48.5% of AFRS patients, similarly, it was reported in literature that, around 50% of AFRS patients suffer from asthma, [20] but, in the current study chest asthma is more common in non-fungal CRSwNP than in AFRS with a statistically significant difference.

In the current study, low socioeconomic level and low educational level are more common in AFRS than non-fungal CRSwNP patients with statistically significant differences, on the same line it was reported that CRS patients were more likely to have higher income and better access to primary care providers compared with AFRS patients. [12]

It was reported in a 2016 study done in Egypt [21] that no statistically significant differences in exposure to plants, animals or allergy related occupations between AFRS and control groups. Similarly, in the present study, no statistically significant differences were detected in the occupational related allergy, exposure to pets (cats, dogs) and cockroaches between AFRS and non-fungal CRSwNP patients as p values were not significant. On the other hand, in our study exposure to birds is more common in AFRS than in non-fungal CRSwNP patients, while exposure to plants is more common in non-fungal CRSwNP than AFRS patients with a statistically significant differences, this due to the fact that the soil in the plants acts as a reservoir of fungi in non-ventilated rooms. [22]

In the present study, AFRS patients had carpets at home, exposed to dust at home or work place with infrequent AC cleaning more than non-fungal CRSwNP patients with statistically significant differences. The effect of dust on AFRS can be explained by the study done by Benoliel [23] who stated that fungi adhere to dust particles and are inhaled,

the warm moist environment of the upper respiratory tract is a favorable environment for proliferation of fungi, however they are rarely pathogenic because of the host resistance except in highly susceptible individuals. Also, it was reported that fungal contamination is promoted inside the AC but suppressed outside it. [24]

In the current study, AFRS patients are resident of old houses or overcrowded houses and had poor sun exposure more than non-fungal CRSwNP patients with statistically significant differences. This is due to the effect of high relative humidity which is a good environment for fungal proliferation in old or overcrowded houses.

Review of literatures reveals that the majority of cases of AFRS are located in more temperate regions where relative humidity is high. [25] Similarly, in our study, most of the cases of AFRS were from hot humid areas (Jeddah and Rabigh), while non-fungal CRSwNP patients were more from hot dry (Makkah) or high altitude (Taif) areas than AFRS patients.

In the present study, no statistically significant difference were detected in cigarette smoking, ex smoking or no smoking patients between AFRS and non-fungal CRSwNP, while passive smoking was seen more in AFRS patients than non-fungal CRSwNP patients, but, these findings must be taken with caution due to small numbers of smokers or ex-smokers in both groups.

It was reported in literature that, bone erosion and extension of AFRS into adjacent anatomic areas encountered in 20% of the AFRS patients especially in bilateral or advanced disease, also, expansion or thinning of involved sinus walls is common in AFRS due to the expansile nature of the accumulating mucin and demineralization of bone. [26] This raises the importance of prediction of AFRS in CRSwNP patients, is that surgical option can be offered more to AFRS than CRSwNP, as there is incidence of bone erosion of orbit and skull base in longstanding AFRS. Also, in predicted patients of AFRS, the endoscopic tissue-sparing techniques can be adopted, but with complete removal of polyps, allergic mucin and debris to eliminate the antigenic-iciting factor [27] to decrease the recurrence of AFRS.

From the previous findings in our study, the incidence of AFRS can be decreased in hot humid areas if the educational and socioeconomic level is raised, also if the environmental risk factors are avoided such as having pets (birds) at home, carpets at home or workplace, exposure to dust, residency in old or overcrowded houses and poor sun exposure.

The current study was done in the western Saudi Arabia; further studies are needed on large numbers of patients in wide geographic areas of the middle east countries to detect the prevalence, the demographics and environmental factors of AFRS among CRSwNP patients.

Conclusions

The prevalence of AFRS is 45% of patients with nasal polyps in western area of Saudi Arabia. AFRS is more common in young adult, those with low socioeconomic growth and those with low education level. Patients with nasal polyps who were exposed to birds, exposed to dust, had carpet at home, residing in an old or over crowded house, had infrequent AC cleaning at home, living in hot humid areas or were passive smoker are more likely to had AFRS.

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Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Standards

The authors assert that research protocol was approved by the appropriate ethical committee. In line with the Declaration of Helsinki 1975, revised Hong Kong 1989.

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