

The Role of Home Fungal Exposure in Allergic Fungal Rhinosinusitis

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Abstract

Background: Allergic fungal rhinosinusitis (AFRS) is disproportionately identified in patients of low socioeconomic status living in warm, humid climates, and is thought to occur in response to environmental fungal species.

Objective: We hypothesized that micro-geographic differences in fungal exposure contribute to the pathogenesis of AFRS, and compared home fungal exposure of patients with AFRS to normative data and controls.

Methods: Comprehensive prospective enrollment and data capture was completed in 70 patients. Patients with AFRS were compared to a control population with chronic rhinosinusitis with nasal polyposis (CRSwNP) and comorbid atopy. Comprehensive demographics, 22-item sino-nasal outcomes test (SNOT-22) questionnaires, and endoscopy scores were compiled. Using a test strip collection system, a home fungal assessment was completed for each patient, along with detailed questions related to home condition.

Results: Patients with AFRS were more likely to be younger ($p < .001$), African American ($p < .001$), from a lower income bracket ($p < .012$), and less likely to own their home ($p < .001$). There were no differences in prior surgeries ($p = .432$), endoscopy scores ($p = .409$) or SNOT-22 scores ($p = .110$) between the groups. There were no differences in overall fungal counts between patients with AFRS and controls ($p = .981$). AFRS patients had a higher prevalence of Basidiospores than controls ($p = .034$).

Conclusion: This study failed to detect differences in total home fungal exposure levels between those with AFRS and atopic CRSwNP, despite differences in socioeconomic status. This suggests that absolute fungal levels may not be the primary driver in development of AFRS, or that the fungal detection strategies utilized were not representative of patients' overall fungal exposure.

Keywords

allergic fungal rhinoallergic fungal sinusitis, allergy, chronic rhinosinusitis, fungus, nasal polyps, public health, sinusitis, sinusitis sinus surgery

Introduction

Allergic fungal rhinosinusitis (AFRS) is an inflammatory disease process of the paranasal sinuses that typically presents at an advanced stage, often with orbital and skull base involvement. In contradistinction to other forms of chronic rhinosinusitis (CRS) in the United States (US), AFRS is traditionally most commonly identified in patients from the southern US¹ and disproportionately in African Americans,² though this disease process is increasingly recognized in international cohorts and likely more ubiquitous than previously thought.^{3–6} Although the pathophysiology of AFRS has been debated since its original description 3 decades ago, it is generally believed to involve a type I

hypersensitivity reaction to ubiquitous fungal species.⁷ Current treatment of AFRS involves a combination of surgical and postoperative steroid-based therapy,

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however, postoperative recurrence rates are significantly higher than other forms of CRS.^{8–10} The high recurrence rates may be attributed to persisting immune dysregulation in patients with AFRS; however, we suspect that ongoing environmental exposure contributes to the refractory nature of this disease.

On an immunologic level, patients with AFRS share many similarities to those diagnosed more broadly with CRS with nasal polypsis (CRSwNP) and comorbid atopy.¹¹ While two distinct phenotypes, both disease processes appear to have underlying type 2 dysregulation. However, the combination of geographic localization and a unique set of patient demographics suggest that extrinsic factors beyond the underlying immune dysfunction contribute to the clinical course of AFRS. The geographic localization of AFRS is commonly attributed to the concept that increased fungal counts are higher in the southern US. However, patients with AFRS are not geographically spread in a homogenous or random fashion across the South. Instead, there is an increased prevalence of AFRS in counties with increased poverty and lower mean household income.^{2,12} This finding suggests that there may be micro-geographic differences in fungal exposure across the southern US. Evidence examining the relationship of mold exposure and socioeconomic factors in asthma support the concept that the local environment (e.g. home, work, or school) can serve as a disease modifier in type 2 inflammation.^{13–17} To our knowledge, there have been no prior investigations directly measuring fungal exposure in patients with AFRS, despite the apparent causal association. If in fact micro-geographic differences are present, eradication of fungal antigen burden in the micro-environment (e.g. home or school) would offer a potentially novel management strategy and would have substantial public health implications.

We hypothesize that micro-geographic differences in fungal exposure, in at-risk individuals, contributes to the clinical course of AFRS. In this study, we sought to directly quantify and characterize fungal exposure in the homes of patients with AFRS. Furthermore, we aimed to compare the fungal burden in homes of patients with AFRS to that identified in the homes of patients with CRSwNP and comorbid atopy. Finally, we sought to perform an exploratory analysis examining the relationship between micro-geographic fungal burden and clinical outcome measures in patients with AFRS.

Methods

Study Population

Study participants were prospectively enrolled in a cross-sectional fashion from tertiary care rhinology clinics at the Medical University of South Carolina

(MUSC; Charleston, SC). Study approval was granted by the MUSC Institutional Review Board and written informed consent was obtained from all included patients. All participants were English-speaking. All included AFRS patients met the diagnostic criteria for AFRS¹⁸ that requires the presence of 1) nasal polypsis, 2) type I hypersensitivity to fungi as determined by skin prick or radioallergosorbent test, 3) presence of noninvasive fungi on staining, 4) eosinophilic mucin without fungal invasion into sinus tissue and 5) characteristic radiographic findings including double density opacifications on CT scan. In an effort to most closely approximate both the underlying immunologic response and phenotypic presentation of the study population, control patients all had a diagnosis of CRSwNP according to the International Consensus Statement on Allergy and Rhinology diagnostic criteria¹⁹ as well as comorbid atopy by skin prick or radioallergosorbent testing. Immunocompromised patients, those that changed their place of residence in the year prior to enrollment, and patients with incomplete follow-up were excluded. In addition to standard and CRS-related clinical demographics (Table 1), enrolled patients were specifically queried regarding socioeconomic status and their housing conditions including the type of home, age of the home, materials the home is made from and the presence or absence of witnessed mold or flooding in or around the home. A complete summary of the specific questions are listed in Table 2. Participants who changed homes were excluded.

At the time of enrollment, endoscopic severity of disease and sinonasal quality of life was assessed for each patient. Endoscopic disease severity was depicted by Lund-Kennedy endoscopic scores. This metric is an endoscopic scoring system used to quantify the degree of visualized sinonasal pathology as it relates to CRS. The scoring system reports, on a score of 0–2, nasal polypsis, edema, discharge, crusting and scarring, for each side of the nasal cavity.²⁰ The Sino-Nasal Outcome Test (SNOT-22) was used to assess sinonasal quality of life. The SNOT-22 is a validated survey used to assess and report the symptom severity in patients with CRS and other sinonasal disorders. Symptoms are rated on a Likert scale from 0–5, with a level of 0 representing “no problem,” and 5 representing “problem as bad as it can be.”²¹

Home Mold Assessment

Commercially available, home mold testing kits were purchased from Pure Air Control Services (Clearwater, FL). Following enrollment, patients were given verbal and written instructions on how to use the testing kit and test strips were mailed to patients' homes. Patients were instructed to carry out testing in their bedroom, or

Table 1. Patient Demographics and Clinical Characteristics.

	AFRS		CRSwNP with Atopy		p-value
	Mean $\pm$ SD	n (%)	Mean $\pm$ SD	n (%)	
Age (years)	31.7 $\pm$ 13.8		57.8 $\pm$ 12.4		<.001
Race					
White		11 (35.5%)		32 (82.1%)	<.001
African American		20 (64.5%)		7 (17.9%)	
Sex					
Male		15 (48.4%)		30 (76.9%)	.013
Female		16 (51.6%)		9 (23.1%)	
Number of prior sinus surgeries	2.2 $\pm$ 1.7		2.6 $\pm$ 1.9		.432
Number of courses of oral antibiotics in the past year	2.3 $\pm$ 1.7		2.6 $\pm$ 1.8		.425
Number of courses of oral steroids in the past year	2.4 $\pm$ 1.7		2.3 $\pm$ 2.0		.961
Current subcutaneous immunotherapy		7 (22.6%)		8 (20.5%)	.834
Current sublingual immunotherapy		4 (12.9%)		1 (2.6%)	.163
Lund-Kennedy endoscopy score (n = 53)	8.0 $\pm$ 3.7		7.0 $\pm$ 3.9		.409
SNOT-22 (n = 66)	36.5 $\pm$ 21.8		45.4 $\pm$ 21.6		.110

AFRS = allergic fungal rhinosinusitis, CRSwNP = chronic rhinosinusitis with nasal polyposis, SD = standard deviation, n = number, % = percentage.

another location where they commonly spend time in order to obtain a representative sample. Completion of home testing required the removal of a wax paper backing from a test strip, firm and complete application of the test strip to a linear surface (e.g. wall or nightstand) to capture surface material, and then placement of the test strip into a small plastic container before submitting in postal mail in a pre-paid envelope. Test strips were requested to be sent for analysis immediately status post collection. All surface analysis specimens were interpreted by Environmental Diagnostics Laboratory (Clearwater, FL), which has demonstrated reliability to the standard of International Organization for Standardization (ISO) ISO/IEC 17025:2005 guidelines. Each test strip was analyzed for fungal presence and raw counts of fungal elements/spores. Results were compared to normative data as determined by Sahay et al.²² Test strips assessed total mold counts, fungal hyphal elements counts, and total counts of individual genera and species, including: *Dematiaceous* hyphal and spore elements, *Cladosporium* species, *Ascospores*, *Bipolaris* species, *Nigrospora* species, *Epicoccum* species, *Aspergillus/Penicillium*-like spores, *Basidiospores*, *Xylaria* species, *Tetraploa* species, *Rust* spores, *Curvularia* species and *Chaetomium* species (Table 3).

Statistical Analyses

Statistical analyses were completed using SPSS 25.0 (IBM Corporation, Armonk, New York). Despite lack of pilot data and the exploratory nature of this study, unpublished data was used for sample size calculations, assuming a national mean of 50 counts/cm², and an AFRS mean of 61.44 counts/cm² with a standard

deviation of 48 counts/cm²; at a sample size of 50, the study would be powered to show an effect size (Cohen's D) of 0.24. A Mann Whitney U test was used to compare the total mold measure between cases and controls. Because of the non-normal distribution, and skewness of the overall counts, the total mold measure was also categorized into "detectable" and "not detectable" categories and a Pearson Chi Squared test was conducted. Comparison of other independent categorical variables between cases and controls also used the Pearson's Chi-Squared test or the Fisher's Exact Test when any cells had an expected value of less than 5. The Welch's t-test was used to test differences between cases and controls for continuous variables. P values of $\leq .05$ were considered statistically significant.

Results

Study Population, Demographics and Clinic Characteristics

Eighty-nine total patients were enrolled in this study, though complete data and home fungal assessments were achieved in only 70 patients, despite multiple attempts for comprehensive data collection. Thirty-one patients with AFRS and 39 patients with CRSwNP and comorbid atopy had comprehensive data available. A complete comparison of patient demographics and clinical characteristics between patients with AFRS and the control population is demonstrated in Table 1. In this study population, patients with AFRS were more likely to be younger than patients with CRSwNP and comorbid atopy (mean age 31.7 $\pm$ 13.8 years vs. 57.8 $\pm$ 12.4, $p < .001$), more likely to be African American (64.5%

Table 2. Socioeconomic Characteristics and Home Conditions Between Patients With AFRS and CRSwNP Controls.

		AFRS n (%)	CRSwNP and Atopy n (%)	p-value
Highest level of education	Less than high school diploma	1 (3.1%)	1 (2.6%)	.076
	High school diploma or GED	5 (15.6%)	5 (12.8%)	
	Some college	9 (28.1%)	9 (23.1%)	
	Bachelor's degree	8 (25.0%)	12 (30.8%)	
	Graduate degree	4 (12.5%)	12 (30.8%)	
Employment status	Less than 18 years of age	3 (9.4%)	0 (0.0%)	<.001
	Unemployed and looking for work	2 (6.3%)	0 (0.0%)	
	Employed part-time	4 (12.5%)	3 (7.7%)	
	Employed full time	18 (56.3%)	17 (43.6%)	
	Disabled	1 (3.1%)	2 (5.1%)	
	Student	3 (9.4%)	0 (0.0%)	
	Retired	1 (3.1%)	17 (43.6%)	
Marital status	Married	12 (37.5%)	31 (79.5%)	<.001
	Widowed	0 (0.0%)	1 (2.6%)	
	Divorced or separated	0 (0.0%)	4 (10.3%)	
	Never married	17 (53.1%)	3 (7.7%)	
	Living with a partner	3 (9.4%)	0 (0.0%)	
Family/household income	Less than \$35,000	9 (28.1%)	4 (10.3%)	.009
	\$35,000–\$49,999	7 (21.9%)	6 (15.4%)	
	\$50,000–\$74,999	4 (12.5%)	8 (20.5%)	
	\$75,000–\$99,999	6 (18.8%)	5 (12.8%)	
	\$1,00,000 or more	3 (9.4%)	16 (41.0%)	
	Declined to answer	3 (9.4%)	0 (0%)	
Type of residence	House	22 (68.8%)	32 (82.1%)	.083
	Apartment	4 (12.5%)	2 (5.1%)	
	Townhouse	0 (0.0%)	3 (7.7%)	
	Mobile home or trailer	6 (18.8%)	2 (5.1%)	
Home ownership		14 (43.8%)	33 (84.6%)	<.001
Age of home	0 to 10.99 years	6 (18.8%)	12 (30.8%)	.090
	11 to 30.99 years	21 (65.6%)	14 (35.9%)	
	31 to 50 years	2 (6.3%)	7 (17.9%)	
	More than 50	3 (9.4%)	6 (15.4%)	
Home interior materials	Wood	18 (56.3%)	28 (71.8%)	.326
	Brick	4 (12.5%)	3 (7.7%)	
	Concrete	2 (6.3%)	0 (0.0%)	
	Other	8 (25.0%)	8 (20.5%)	
Have physically seen mold growing in home		9 (28.1%)	7 (17.9%)	.395
Had flooding in or around home in the past 3 years		9 (28.1%)	10 (25.6%)	1.00

AFRS=allergic fungal rhinosinusitis, CRSwNP = chronic rhinosinusitis with nasal polyposis, n = number, % = percentage.

vs. 17.9%, $p < .001$) and more likely to be female (51.6% vs. 23.1%, $p = .009$). There were no differences in number of prior sinus surgeries ($p = 0.432$), number of courses of antibiotics ($p = .425$) or oral steroids ($p = .961$) in the past year, the frequency of subcutaneous immunotherapy usage ($p = .834$) or sublingual immunotherapy ($p = .163$). There was no detectable difference in Lund-Kennedy endoscopic scores ($p = .409$) between the two groups. SNOT-22 scores were higher in the CRSwNP group (45.4 ± 21.6) as compared to patients with AFRS (36.5 ± 21.7 ; $p = .110$) however, this was not statistically significant.

Socioeconomic Characteristics and Home Conditions

Complete socioeconomic and home conditions of patients with AFRS compared to those with CRSwNP and atopy are listed in Table 2. As compared to patients with CRSwNP and atopy, patients with AFRS were less likely to be retired ($p < .001$), more likely to not be married ($p < .001$), and more likely to have a lower family/household income ($p = .012$). Similarly, when examining home ownership, patients with AFRS were less likely to own their home, with 14 (42.5%) of patients with AFRS reporting home ownership as compared to 33

Table 3. Comparison of Detectable Fungus and Mold Between Patients With AFRS and Patients With CRSwNP and Comorbid Atopy.

	AFRS n (%)	CRSwNP with Atopy n (%)	p-value
Presence of mold	22 (68.75%)	25 (64.1%)	.680
Total fungal hyphal elements	0 (0%)	2 (5.1%)	.498
Total fungal spore elements	3 (9.4%)	3 (7.7%)	1.00
Dematiaceous fungal hyphae	12 (37.5%)	16 (41.0%)	.762
Dematiaceous fungal spore elements	17 (53.1%)	15 (38.5%)	.217
Cladosporium species	1 (3.1%)	5 (12.8%)	.213
Ascospores	2 (6.25%)	2 (5.1%)	1.00
Bipolaris species	0 (0%)	1 (2.6%)	1.00
Nigrospora species	0 (0%)	1 (2.6%)	1.00
Epicoccum species	0 (0%)	1 (2.6%)	1.00
Aspergillus/Penicillium-like spores	4 (12.5%)	1 (2.6%)	.167
Basidiospores	4 (12.5%)	0 (0%)	.037*
Xylaria species	0 (0%)	1 (2.6%)	1.00
Tetraploa species	0 (0%)	1 (2.6%)	1.00
Rust spores	0 (0%)	1 (2.6%)	1.00
Curvularia species	2 (6.3%)	3 (7.7%)	1.00
Chaetomium species	1 (3.1%)	0 (0%)	.451

AFRS = allergic fungal rhinosinusitis, CRSwNP = chronic rhinosinusitis with nasal polyposis, n = number, % = percentage, *statistical significance at $p \leq .05$.

(84.6%) patients with CRSwNP ($p < .001$). Five patients under the age of 18 were enrolled in the AFRS cohort, and there was a trend towards higher education levels in the CRSwNP and atopy group, but this was not statistically significant. There were no differences in types of residence ($p = .096$), age of the home ($p = .069$) or materials the home was made of ($p = .348$). Patients from both study groups had physically seen mold growing on the inside of their home (28.1% AFRS and 17.9% CRSwNP) or had flooding in or around their home in the past 3 years (AFRS 28.1% and CRSwNP 25.6%), however, there were no differences in the frequency of reporting of these events between the 2 groups ($p = .273$ and $p = .751$ respectively).

Home Fungal Assessment

Using normative data, total fungal levels in homes of patients with AFRS were characterized as low (93.5%), moderate (0%), or high (6.5%). The majority of specimens were collected from the bedroom (67%), while 14% were captured from a living area, 8.5% from a bathroom, and 7% from an unknown location. No differences in counts were detected amongst different locations within the home. Similarly, there were no differences in overall fungal counts between patients with AFRS and the atopic CRSwNP group ($p = .981$; analysis not shown) or the presence of mold between these 2 patient populations ($p = 0.680$; Table 3). Moreover, when compared on the basis of fungal detection, no differences were identified in the presence or absence of

fungal hyphal or spore elements ($p = .499$ and 1.0 , respectively; Table 3) in the homes of patients with AFRS as compared to those with CRSwNP and comorbid atopy. Meanwhile, homes of patients with AFRS had a slightly higher prevalence of Basidiospores than controls ($p = .034$), but otherwise there were no detectable differences in fungal counts or fungal detection between patients with AFRS or those with CRSwNP and comorbid atopy at any taxonomic rank. Complete analysis of home fungal assessments, between patients with AFRS as compared to patients with CRSwNP and comorbid atopy, categorized by presence of each individual fungal assessment, is detailed in Table 3.

Discussion

Allergic fungal rhinosinusitis (AFRS) commonly occurs in the southern United States (US)¹ and socioeconomically-disadvantaged patient populations, though the breadth of this disease across socioeconomic statuses, patient populations, and its international relevance is increasingly recognized.^{2–5,12,23} The disease is characterized by high recurrence rates as compared to other forms of chronic rhinosinusitis (CRS)^{8–10} and is thought to be a manifestation of a type I hypersensitivity, IgE-mediated reaction to ubiquitous fungal species.^{6,7} In this exploratory study, we hypothesized that ongoing environmental exposures to common fungi in the homes of patients with AFRS may be associated with the clinical presentation of this disease. Despite enrolling a characteristic AFRS population, and a

control population with a similar severity of disease and immunologic dysfunction, we could not elicit a difference in home fungal exposures between the two CRS patient populations.

Since the diagnostic criteria of AFRS were defined by Bent and Kuhn,¹⁸ there have been major advances in the medical management and surgical techniques for AFRS, however, the understanding of the underlying pathophysiologic mechanism of this disease process remains somewhat elusive. The basic tenet of this disease is that environmental fungal exposure contributes to the development of AFRS. While initial evidence suggested that AFRS was a manifestation of fungal-specific IgE and IgG, or local IgE and type 2 inflammatory mediators such as IL-4, IL-5 and IL-13, follow-up investigations have failed to demonstrate differences in these markers between patients with AFRS and CRSwNP.⁶ More recent investigations propose that dysregulation of innate immune function, specifically in the epithelial barrier of the paranasal sinuses^{24–26} and the local antifungal response,^{27–29} may contribute to the pathogenesis of AFRS, however, the exact immunologic mechanism of this disease has yet to be elucidated.

In the search for the molecular pathogenesis of AFRS, it is increasingly clear that there are many similarities between AFRS and CRSwNP when compared on an immunologic level,^{6,11} especially when examining the subset of patients with CRSwNP and comorbid atopy. Despite these similarities, there are notable differences in the clinical presentation of these 2 disease processes. First, it is not uncommon for AFRS to present somewhat more dramatically than CRSwNP, with extensive bony destruction of the orbit(s) or skull base.^{30,31} Moreover, AFRS typically presents at younger ages, and is more common in African Americans, with a male preponderance. These studies have also demonstrated an association between AFRS and lower socioeconomic status.^{2,12,23}

In this current investigation, we compared patients with AFRS to those with CRSwNP and comorbid atopy. Patients with AFRS were more likely to be younger and African American as compared to their CRSwNP and atopy counterparts. In contradistinction to typical AFRS patient demographics, there was an equal distribution of sex in the cohort with AFRS, and meanwhile, a higher proportion of males in the cohort with CRSwNP and atopy, which may be representative of the relatively small sample size in this current study. Other than age, race and patient sex, the enrolled patients with AFRS and patients with CRSwNP were similar in regards to their surgical history, frequency oral antibiotics and oral steroids, current immunotherapy, endoscopic severity of disease, and disruptions of their sinonasal quality of life.

Beyond the clinical presentation, patients with AFRS in this study were more likely to be socioeconomically disadvantaged, and were more commonly from a lower income bracket, less likely to own their own home or be married. Meanwhile, patients with CRSwNP were more likely to be retired. Intuitively, some of these findings may be reflective of patient age, though this was not controlled for. Furthermore, when comparing living conditions between patient populations, there were no differences in type of residence, age of the home or materials that the home was constructed of. Interestingly, in both cohorts, patients reported having physically seen mold growing in their home or had flooding in or around their home.

After examining the clinical and socioeconomic characteristics of the 2 groups of patients evaluated in this study, it does seem that these 2 groups are largely representative of the anticipated AFRS and CRSwNP with comorbid atopy patient populations. Nonetheless, despite the basic assumption that fungal exposure contributes to the pathogenesis of AFRS, there were no differences in the comparison of 17 different measures of fungus in each patients' home, with the exception of Basidiospores, which was more common in the AFRS population. Given the large number of fungal assessments and overwhelming lack of difference between the two populations, we did not control for multiple comparisons, and suspect that the difference in Basidiospores most likely represents a Type I statistical error.

The lack of difference in fungal exposure levels between patients with AFRS and those with CRSwNP and comorbid atopy has several potential explanations. First, it may be that regardless of a longstanding correlation between patients with AFRS and increased levels of fungal exposure, such as those found in the southern US, micro-geographic differences, such as those potentially identified in patients' home, are not important in the development of this disease. It may be that other potential exposures such as at schools or the workplace are more important. Furthermore, it is even possible that a general threshold of fungal exposure, which is commonly encountered in the southern US, is all that is necessary for development of the disease, or even that fungal exposure altogether is not important, though this latter supposition is unlikely. Certainly, these findings suggest that the patient's underlying biology and immune response, rather than environment alone plays an important role in the distinction between development of AFRS or CRSwNP and comorbid atopy. Disruptions in patients' immune and antifungal response, such as dysfunction of the TLR-4 dependent pathways as described in the development of allergic asthma, may have implications in the understanding of AFRS.^{27,32}

Another potential explanation of the lack of difference in detected fungal levels between the 2 groups is that home fungal test kit used in this investigation is not representative of patient fungal exposure levels. The lack of difference between the two groups may suggest a lack of sensitivity in fungal detection of the employed test, or it may be that the isolated time point that was tested is not illustrative of cumulative or total fungal exposures. Broader measures of fungal exposure (e.g. additional locations collected over longer periods of time) may have been more likely to detect differences in this exploratory study.

Despite the lack of differences in fungal levels between these two populations, the socioeconomic differences in patients with AFRS as compared to patients with CRSwNP detected in this study and several others suggest that environment is important. Moreover, analogous findings in the asthma literature suggest that local environment can play a significant role in disease presentation.^{13–17,33} Thus, the combination of the hot and humid climate of the southern United States, along with the systemic inequalities of underserved populations may help to explain why AFRS disproportionately affects patients of minority populations. Further contributing to patient presentation, is the possibility that the lower socioeconomic status detected in this current patient population, may have contributed to limited patient access to care.

Overall, this study has many strengths, including its prospective nature, novelty and direct investigation into a scientific question with broad implications. This “negative” study raises further questions regarding the pathophysiology of AFRS as well as the socioeconomic disparities of the AFRS population. Nonetheless, the relatively small sample size and limited racial diversity of this current investigation limits the implications of our findings. Though patients were enrolled over a year-long period and patients had not recently moved from their home, future studies should include larger sample sizes and consider the potential impact of seasonal variation on fungal growth, as well as overall fungal exposure at the original time of diagnosis to investigate the possibility of an “inciting” event. Fungal detection sensitivity is another potential weakness of this study, and the use of more sophisticated next-generation sequencing fungal detection techniques, such as internal transcribed spacer (ITS) sequencing, could be used during future endeavors. Though use of modern sequencing techniques or investigator travel to patients’ homes to collect specimens, would have been prohibitively expensive for this pilot study, enhanced methods could allow for a finer resolution and characterization of the composition of fungal burden in these patients’ local environments.

Conclusion

This study failed to detect differences in total home fungal exposure levels between patients with AFRS and patients with CRSwNP and comorbid atopy, despite differences in socioeconomic status. This suggests that absolute fungal levels may not be the primary driver in development of AFRS, or that the fungal detection strategies utilized in this study are not representative of patients’ overall fungal exposure. Understanding the relationship amongst environmental exposures, socioeconomic disparities and immunologic dysregulation in AFRS remains obscure.

Presentation

This manuscript was presented as an oral presentation and was awarded first prize for top clinical abstract at the American Academy of Otolaryngic Allergy Annual Meeting in New Orleans, LA on September 15, 2019.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: ZMS is a consultant for Olympus, Optinose, Novartis and Healthy Humming; and has received grant support from Healthy Humming. RJS is consultant for Olympus, Stryker, Optinose, Sanofi and Healthy Humming; and has received grant support from Astra Zeneca, Sanofi, Roche, Optinose and Healthy Humming. There are no other financial disclosures or conflicts of interest for any other author.

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