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Research Article

ASSOCIATION BETWEEN ALLERGIC FUNGAL SINUSITIS AND NASAL POLYPS

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Abstract:

Background: Nasal polyposis is a common problem. Since allergic fungal sinusitis (AFS) can present with unilateral or bilateral nasal polyps, it is important to be aware of the prevalence of AFS in patients with nasal polyps. This study was planned to evaluate the frequency of allergic fungal sinusitis. In the literature published nationally and internationally lies a controversy as they have stated variable results. This study may help all the clinicians to decide a good strategy if a high frequency of allergic sinusitis is noted in cases with nasal polyps.

Objective: The objective of this study was to:

determine the prevalence of allergic fungal sinusitis among patients with nasal polyps presenting in a tertiary care hospital

Duration of the study: From: 02-04-2017 to 05-10-2017

Study Design: Cross sectional study

Methodology: The patients fulfilling the inclusion criteria were enrolled after informed consent from OPD of ENT department Sheikh Zayed Hospital and FPGMI, LHR by the researcher. All patients with nasal polyps were advised CT scan and Paranasal sinuses with FESS protocol to be done from Radiology department of same institution. Findings of allergic fungal sinusitis were noted (as per operational definition). All information was gathered by a performa (attached).

Results: In our study, out of 100 cases of nasal polyps, 72%(n=72) were between 15-50 years of age while 28%(n=28) were between 51-70 years of age, mean±sd was calculated as 41.1±12.67 years, 55%(n=55) were females while 45%(n=45) were male patients, frequency of allergic fungal sinusitis among patients with nasal polyps was recorded in 18%(n=18) of the cases.

Conclusion: We concluded that the frequency of allergic fungal sinusitis is high among patients presenting with nasal polyps presenting in a tertiary care hospital. So, it is recommended that every patient who present with nasal polyps, should be sort out for allergic fungal sinusitis. However, it is also required that every setup should have their surveillance in order to know the frequency of the problem.

Keywords: Nasal polyps, allergic fungal sinusitis, frequency

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INTRODUCTION:

Fungal infections of the sinuses have recently been blamed for causing most cases of chronic sinusitis. The evidence, though, is still controversial. Most fungal sinus infections are benign or noninvasive, except when they occur in individuals who are immune compromised. Several reports are available that have shown invasive fungal infections in immune competent individuals.¹

Over the past 2 decades, allergic fungal sinusitis (AFS) has become increasingly defined.² Allergic fungal sinusitis (AFS) is a severe, chronic recalcitrant disease characterized by frequent relapses often necessitating surgical intervention. The pathogenesis of AFS is considered an IgE-mediated hypersensitivity response to an environmental fungal agent(s) with histologic and clinical manifestations similar to allergic broncho pulmonary aspergillosis (ABPA).⁹ This is in contrast to invasive fungal infections that affect immune compromised hosts, such as patients with diabetes mellitus and patients with AIDS.

Approximately 5-10% of patients affected by chronic sinusitis actually carry a diagnosis of allergic fungal sinusitis (AFS). Atopy is characteristic of the disease; approximately two thirds of patients report a history of allergic rhinitis, and 90% of patients demonstrate elevated specific IgE to one or more fungal antigens. Approximately 50% of patients in a series by Manning et al had asthma.

Incidence of allergic fungal sinusitis (AFS) appears to be impacted by geographic factors. Review of world literature reveals that most sites reporting cases of allergic fungal sinusitis (AFS) are located in temperate regions of relatively high humidity.

Allergic fungal sinusitis (AFS) is most common among adolescents and young adults; the mean age at diagnosis is 21.9 years. The male-to-female (M/F) ratio of allergic fungal sinusitis (AFS) differs slightly between published reports but is believed to be equal when all ages are evaluated together.

Nasal polyps are lesions arising from the nasal mucosa, occurring at any site in the nasal cavity or paranasal sinuses but most frequently seen in the clefts of the middle meatus.

Nasal polyps can be considered as part of the spectrum of chronic rhinosinusitis.^{8,9} The population prevalence of nasal polyps is reported as 2-4%, with no racial predilection.¹⁹ The male to female ratio has been reported at approximately 2:1.¹⁰

Symptoms of polyps include nasal congestion, sinusitis, anosmia (loss of smell), and secondary infection leading to headache.⁶ There was a significance direct relationship between the CT grading of nasal polyps and recurrence, with a recurrence rate of 60.7% (34 of 56) in patients with grade III nasal polyps.³

In another study done in Karachi, 100 patients with nasal polyps were evaluated and operated. Specimens were sent for histopathology and culture examination. The frequency of AFS was about 24%. Presence of gross deviation of nasal septum and bilateral inferior turbinate hypertrophy was seen in 4 (16.7%) and 5 (20.8%) patients respectively. On evaluating co-morbid conditions 5 (20%) patients were asthmatic and only 1 patient was diabetic.¹⁰

A total 324 cases of nasal polyposis were included in a study done in Jamshoro, out of which 159 were males and 165 were female. Underlying fungus was found in 224 (69.75%) subjects.¹¹

In another local study done in Peshawar, of 100 patients out of which 58 males and 42 were females, allergic fungal sinusitis was diagnosed in 13 (13%) patients.¹²

The rationale of this study is to evaluate the frequency of allergic fungal sinusitis. In the literature published nationally and internationally lies a controversy as they have stated variable results. This study will help all the clinicians to decide a good strategy if a high frequency of allergic sinusitis is noted in cases with nasal polyps.

OBJECTIVES:

The objective of this study was to:

- determine the prevalence of allergic fungal sinusitis among patients with nasal polyps presenting in a tertiary care hospital.

OPERATIONAL DEFINITIONS:**ALLERGIC FUNGAL SINUSITIS**

- It is a chronic infection of paranasal sinuses caused by allergic reaction to fungal debris which gives double density shadow (grey and white on CT Scan nose and paranasal sinuses).

NASAL POLYPS

- It is an unwanted growth arising from nasal cavity lining mostly bilateral causing nasal obstruction and nasal discharge, opacifies the air containing paranasal sinuses (on CT Scan and paranasal sinuses).

MATERIALS AND METHODS:**SETTING:**

- The study was conducted in ENT Department, Akhtar Saeed Hospital Lahore

DURATION OF THE STUDY:

- From: 02-04-2017 to 05-10-2017

SAMPLING TECHNIQUE:

- Non-probability consecutive sampling

STUDY DESIGN:

- Cross sectional study

SAMPLE SIZE:

- The sample size of 100 is estimated by using 95% Confidence level, 6% margin of error with expected percentage of AFS among patients with nasal polyps i.e. 9.45%.⁴

SAMPLE SELECTION:**Inclusion Criteria**

- Patients of ages between 15-70
- Patients of both genders
- Patients diagnosed of nasal polyps as per operational definition

Exclusion Criteria

- History of sinus surgery
- History of upper respiratory tract infection on presentation
- History of mechanical nasal airway obstruction
- Pregnant women
- History of lactation

DATA COLLECTION PROCEDURE:

The patients fulfilling the inclusion criteria were enrolled after informed consent from OPD of ENT department Sheikh Zayed Hospital and FPGMI, LHR by the researcher. All patients with nasal polyps were advised CT scan and Paranasal sinuses with FESS protocol to be done from Radiology department of same institution. Findings of allergic fungal sinusitis were noted (as per operational definition). All information was gathered by a performa (attached).

DATA ANALYSIS PROCEDURE:

Data was entered and analyzed using SPSS version 22.0. For descriptive statistics, the mean and standard deviation was shown for quantitative data like age and grading of polyps. Qualitative data like gender, allergic fungal sinusitis was presented by using frequency and percentages. Data was stratified for age, gender, CT Grading of polyps, asthma, nasal blockage to address modifiers. Post stratification chi-square test was applied to check the significance with P-value ≤ 0.05 as significant.

RESULTS:

A total of 100 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the prevalence of allergic fungal sinusitis among patients with nasal polyps.

AGE DISTRIBUTION

Age distribution of the patients was recorded, it shows that 72%(n=72) were between 15-50 years of age while 28%(n=28) were between 51-70 years of age, mean \pm sd was calculated as 41.1 \pm 12.67 years. (Table No. 1)

GENDER DISTRIBUTION

Gender distribution shows that majority of the patients were females by calculating 55%(n=55) while 45%(n=45) were male patients in this study. (Table No. 2)

FREQUENCY OF ALLERGIC FUNGAL SINUSITIS

Frequency of allergic fungal sinusitis among patients with nasal polyps was recorded in 18%(n=18) of the cases while 82%(n=82) had no findings of the morbidity. (Table No. 3)

DATA STRATIFICATION

The data was stratified for age, gender, CT Grading of polyps, asthma, nasal blockage to address modifiers. Post stratification chi-square test was applied to check the significance with P-value ≤ 0.05 as significant. (Table No. 4-8)

TABLE No. 1: AGE DISTRIBUTION
(n=100)

Age(in years)	No. of patients	%
15-50	72	72
51-70	28	28
Total	100	100
Mean\pmSD	41.1\pm12.67	

**TABLE No. 2: GENDER DISTRIBUTION
(n=100)**

Gender	No. of patients	%
Male	45	45
Female	55	55
Total	100	100

**TABLE No. 3: FREQUENCY OF ALLERGIC FUNGAL SINUSITIS AMONG PATIENTS WITH NASAL POLYPS
(n=100)**

Allergic fungal sinusitis	No. of patients	%
Yes	18	18
No	82	82
Total	100	100

TABLE No. 4: STRATIFICATION FOR FREQUENCY OF ALLERGIC FUNGAL SINUSITIS AMONG PATIENTS WITH NASAL POLYPS WITH REGARDS TO AGE

Age (in years)	Allergic Fungal Sinusitis (n=18)		P value
	Yes	No	
15-50	14	58	0.54
51-70	4	24	

TABLE No. 5: STRATIFICATION FOR FREQUENCY OF ALLERGIC FUNGAL SINUSITIS AMONG PATIENTS WITH NASAL POLYPS WITH REGARDS TO GENDER

Gender	Allergic Fungal Sinusitis (n=18)		P value
	Yes	No	
Male	10	35	0.31
Female	8	47	

TABLE No. 6: STRATIFICATION FOR FREQUENCY OF ALLERGIC FUNGAL SINUSITIS AMONG PATIENTS WITH NASAL POLYPS WITH REGARDS TO CT GRADING OF POLYPS

CT Grading	Allergic Fungal Sinusitis (n=18)		P value
	Yes	No	
I	4	16	0.955
II	5	25	
III	9	41	

TABLE No. 7: STRATIFICATION FOR FREQUENCY OF ALLERGIC FUNGAL SINUSITIS AMONG PATIENTS WITH NASAL POLYPS WITH REGARDS TO ASTHMA

Asthma	Allergic Fungal Sinusitis (n=18)		P value
	Yes	No	
Yes	5	10	0.09
No	13	72	

TABLE No. 8: STRATIFICATION FOR FREQUENCY OF ALLERGIC FUNGAL SINUSITIS AMONG PATIENTS WITH NASAL POLYPS WITH REGARDS TO NASAL BLOCKAGE

Nasal blockage	Allergic Fungal Sinusitis (n=18)		P value
	Yes	No	
Yes	15	71	0.48
No	3	11	

DISCUSSION:

Nasal polyposis is a common problem. Since allergic fungal sinusitis (AFS) can present with unilateral or bilateral nasal polyps, it is important to be aware of the prevalence of AFS in patients with nasal polyps. This study was planned to evaluate the frequency of allergic fungal sinusitis. In the literature published nationally and internationally lies a controversy as they have stated variable results. This study may help all the clinicians to decide a good strategy if a high frequency of allergic sinusitis is noted in cases with nasal polyps.

In our study, out of 100 cases of nasal polyps, 72% (n=72) were between 15-50 years of age while 28% (n=28) were between 51-70 years of age, mean±sd was calculated as 41.1±12.67 years, 55% (n=55) were females while 45% (n=45) were male patients, frequency of allergic fungal sinusitis among patients with nasal polyps was recorded in 18% (n=18) of the cases.

In a study done in Karachi, 100 patients with nasal polyps were evaluated and operated. Specimens were sent for histopathology and culture examination. The frequency of AFS was about 24%. Presence of gross deviation of nasal septum and bilateral inferior turbinate hypertrophy was seen in 4 (16.7%) and 5 (20.8%) patients respectively. On evaluating co-morbid conditions 5 (20%) patients were asthmatic and only 1 patient was diabetic.¹⁰

A total 324 cases of nasal polyposis were included in a study done in Jamshoro, out of which 159 were males and 165 were female. Underlying fungus was found in 224 (69.75%) subjects.¹¹

In another local study done in Peshawar, of 100 patients out of which 58 males and 42 were females, allergic fungal sinusitis was diagnosed in 13 (13%) patients.¹²

Our findings are in agreement with local studies^{10,12} where it ranges from 13-24% of the cases.

McClay JE and others are of the view that allergic fungal sinusitis (AFS) is most common among adolescents and young adults; the mean age at diagnosis is 21.9 years. The male-to-female (M/F) ratio of allergic fungal sinusitis (AFS) differs slightly between published reports but is believed to be equal when all ages are evaluated together. A literature review of 98 cases in the 1980s and early 1990s from 29 published journal articles reported an equal M/F incidence. A review by the author and colleagues of 151 patients at the University of Texas (UT) at Southwestern also revealed an equal M/F ratio, with ages ranging from 5-75 years.⁷⁷

A recent study by Abdur Rehman and others evaluated allergic fungal sinusitis occurrence in patients with nasal polyps and recorded that allergic fungal sinusitis (AFS) was found in 28/125 (22.4%) nasal polyp patients. In 28 cases of allergic fungal sinusitis, mean age was 30 years. Majority of patients (67.8%) were in the age range 20 – 40 years. Male to female ratio was 1.4:1. Most (53.5%) of AFS patients belonged to lower social class. Concomitant asthma was noted in 06 (21.4%) patients.⁷⁸ They concluded that allergic fungal sinusitis is common aetiology seen among nasal polyp patients. Slightly more than one fifth of cases with nasal polyp (22.4%) had AFS in this study, while treating chronic rhinosinusitis patients, this disease entity must be kept in mind. AFS was seen

to effect mainly young adults and middle aged poor people living in hot humid conditions. Aspergillus was the commonest organism responsible for AFS. Results are good if it is diagnosed early and treated properly.

Akhtar MR⁷⁹ reported 14% frequency whereas Irshad-ul-Haq M⁸⁰ reported 11% frequency of AFS among patients with nasal polyps. Another local study by Baloch ZA⁸¹ reported 38% frequency of AFS, which is quite high compared to our results. Internationally Telmesani LM,⁸² in his study found AFS in 12.1% of nasal polyp patients. These results show that there is great variation in AFS frequency among patients with chronic sinusitis with nasal polyp and it's increasing when compared to previously reported incidence of 7% in international literature.⁸³ However, our data is helpful for all the clinicians at local level to decide a good strategy for allergic sinusitis in cases with nasal polyps.

CONCLUSION:

- We concluded that the frequency of allergic fungal sinusitis is high among patients presenting with nasal polyps presenting in a tertiary care hospital. So, it is recommended that every patient who present with nasal polyps, should be sort out for allergic fungal sinusitis. However, it is also required that every setup should have their surveillance in order to know the frequency of the problem.

REFERENCES:

1. Siddiqui AA, Shah AA, Bashir SH. Craniocerebral aspergillosis of sinonasal origin in immunocompetent patients: clinical spectrum and outcome in 25 cases. *Neurosurgery*. 2004;55(3):602-11.
2. Glass D, Amedee RG. Allergic fungal rhinosinusitis: a review. *Ochsner J*. Fall 2011;11(3):271-5.
3. Robson JM, Hogan PG, Benn RA. Allergic fungal sinusitis presenting as a paranasal sinus tumour. *Aust N Z J Med*. 1989;19(4):351-3.
4. Ponikau UJ, Sherris AD, Kern BE, Homburge AH. The Diagnosis and Incidence of Allergic Fungal Sinusitis. *Mayo Clin Proc*. 1999;74:877-884
5. Laila M. Telmesani. Prevalence of allergic fungal sinusitis among patients with nasal polyps *Ann Saudi Med*. 2009;29(3):212-14.
6. Rehman A, Haq IU, Qadree SH, Aqil S. Frequency of Allergic Fungal Sinusitis in Patients with Nasal Polyps and Associated Risk Factors. *Pakistan Journal of Medical & Health Sciences*. 2009;3(2).
7. Bakhshae M, Fereidouni M, Mohajer MN, Majidi MR, Azad FJ, Moghiman T. The prevalence of allergic fungal rhinosinusitis in sinonasal polyps. *Eur Arch Otorhinolaryngol*. 2013;270(12):3095-8.
8. eMedicine - Nasal Polyps : Article by John E McClay. 2014.
9. Nsouli TM, Schluckebier C, Bellanti J. Allergic Fungal Sinusitis: A Challenging Disorder for the Clinician. *Journal of Allergy and Clinical Immunology*. 2013;131(2):224.
10. Fokkens WJ, Lund VJ, Mullol J. European Position Paper on Rhinosinusitis and Nasal Polyps. *Rhinol Suppl*. 2012.
11. Bachert C, Van Bruaene N, Toskala E. Important research questions in allergy and related diseases: 3-chronic Allergy. 2009;64(4):520-33.
12. Newton JR, Ah-See KW. A review of nasal polyposis. *Ther Clin Risk Manag*. 2008;4(2):507-12.
13. Ni-Ankh Sekhmed. Nasal Polyps - historical perspective. *Mag Otorhinolaryngol*. 2003 Nov;28:11-3.
14. Ślifirski JA, Parzyński S, Fal AM. Comparison of cytological evaluation of nasal polyps with postoperative histopathology. *Alergol Info*. 2008;4:120-6.
15. Jurkiewicz D. Nasal Polyps. *Mag Otorhinolaryngol*. 2003;11 3-9.
16. Vento S, Virkkula P. Nasal polyposis. *Duodecim*. 2012;128(2):219-24.
17. Aouad RK, Chiu AG. State of the art treatment of nasal polyposis. *Am J Rhinol Allergy*. 2011 Sep-Oct;25(5):291-8.
18. Caplin I, Haynes JT, Spahn J. Are nasal polyps an allergic phenomenon? *Ann Allergy*. 1970 Dec;29(12):631-4.
19. Perić A, Vojvodić D, Vukomanović-Durdević B, Baletić N. Eosinophilic inflammation in allergic rhinitis and nasal polyposis. *Arh Hig Rada Toksikol*. 2011 Dec;62(4): 341-8.
20. Bernstein JM, Gorfien J, Noble B. Role of allergy in nasal polyposis: a review. *Otolaryngol Head Neck Surg*. 1995 Dec. 113(6):724-32
21. Hamera-Słynarska M. Effects of glucocorticoids on the cytological picture of the nasal mucosa. *Mag Otorhinolaryngol*. 2007;6(2):55-8.
22. Bernstein JM, Kansal R. Super antigen hypothesis for the early development of chronic hyperplastic sinusitis with massive nasal polyposis. *Curr Opin Otolaryngol Head Neck Surg*. 2005 Feb;13(1):39-44.
23. Otto BA and Wenzel SE. The role of cytokines in chronic rhinosinusitis with nasal polyps. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:270-74.
24. Chen YS, Arab SF, Westhofen M. Expression of interleukin-5, interleukin-8, and interleukin-10 mRNA in the osteomeatal complex in nasal polyposis. *Am J Rhinol*. 2005;19:117-123

25. Van Zele T, Claeys S, Gevaert P. Differentiation of chronic sinus diseases by measurement of inflammatory mediators. *Allergy*. 2006;61:1280–89.
26. Sakaguchi S, Miyara M, Costantino CM. FOXP3+ regulatory T cells in the human immune system. *Nat Rev Immunol*. 2010;10:490–500.
27. Van Bruaene N, Pérez-Novo CA, Basinski TM. T-cell regulation in chronic paranasal sinus disease. *J Allergy Clin Immunol*. 2008;121:1435–41.
28. Wang QP. Myofibroblasts accumulation induced by transforming growth factor-beta is involved in pathogenesis of nasal polyps. *Laryngoscope*. 1997;107:926–31.
29. Little SC, Early SB, Woodard CR. Dual action of TGF-beta1 on nasal-polyp derived fibroblasts. *Laryngoscope*. 2008;118:320–24.
30. Glass D, Amedee RG. Allergic fungal sinusitis: a review. *Ochsner J*. 2011 Fall. 11(3):271-5.
31. Safirstein BH. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. *Chest*. 1976 Dec. 70(6):788-90.
32. Robson JM, Hogan PG, Benn RA. Allergic fungal sinusitis presenting as a paranasal sinus tumour. *Aust N Z J Med*. 1989 Aug. 19(4):351-3.
33. Allphin AL, Strauss M, Abdul-Karim FW. Allergic fungal sinusitis: problems in diagnosis and treatment. *Laryngoscope*. 1991 Aug. 101(8):815-20.
34. Loury MC, Leopold DA, Schaefer SD. Allergic Aspergillus sinusitis. *Arch Otolaryngol Head Neck Surg*. 1993 Sep. 119(9):1042-3.
35. Cody DT 2nd, Neel HB 3rd, Ferreiro JA. Allergic fungal sinusitis: the Mayo Clinic experience. *Laryngoscope*. 1994 Sep. 104(9):1074-9.
36. Bent JP 3rd, Kuhn FA. Allergic fungal sinusitis/polypoidosis. *Allergy Asthma Proc*. 1996 Sep-Oct. 17(5):259-68.
37. Deshpande RB, Shukla A, Kirtane MV. Allergic fungal sinusitis: incidence and clinical and pathological features of seven cases. *J Assoc Physicians India*. 1995 Feb. 43(2):98-100.
38. Kupferberg SB, Bent JP III, Kuhn FA (1997) Prognosis for allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 117(1):35–41.
39. Wise SK, Ghegan MD, Gorham E et al (2008) Socioeconomic factors in the diagnosis of allergic fungal rhinosinusitis. *Otolaryngol Head Neck Surg* 138:38–42
40. Ferguson BJ, Barnes L, Bernstein JM. Geographic variation in allergic fungal rhinosinusitis. *Otolaryngol Clin North Am* 2000;33:441.
41. Wise SK, Ghegan MD, Gorham E, Schlosser RJ. Socioeconomic factors in the diagnosis of allergic fungal rhinosinusitis. *Otolaryngol Head Neck Surg* 2008;138:38.
42. Lu-Myers Y, Deal AM, Miller JD. Comparison of Socioeconomic and Demographic Factors in Patients with Chronic Rhinosinusitis and Allergic Fungal Rhinosinusitis. *Otolaryngol Head Neck Surg* 2015;153:137.
43. Granville L, Chirala M, Cernoch P. Fungal sinusitis: histologic spectrum and correlation with culture. *Hum Pathol* 2004;35:474–81.
44. Wise SK, Ghegan MD, Gorham E. Socioeconomic factors in the diagnosis of allergic fungal rhinosinusitis. *Otolaryngol Head Neck Surg* 2008;138:38–42.
45. Saravanan K, Panda NK, Chakrabarti A. Allergic fungal rhinosinusitis: an attempt to resolve the diagnostic dilemma. *Arch Otolaryngol Head Neck Surg* 2006;132:173–8.
46. Singh NN, Bhalodiya NH. Allergic fungal sinusitis-earlier diagnosis and management. *J Laryngol Otol* 2005;119:875–81.
47. Manning SC, Holman M. Further evidence for allergic pathophysiology in allergic fungal sinusitis. *Laryngoscope* 1998;108(10):1485–96.
48. International Rhinosinusitis Advisory Board. Infectious rhinosinusitis in adults: Classification, etiology and management. *Ear Nose Throat J* 1997;76:5-22.
49. Ponikau JU, Sherris DA, Kern EB, Homburger HA, Frigas E, Gaffey TA. The diagnosis and incidence of allergic fungal sinusitis. *Mayo Clin Proc* 1999;74:877-84.
50. Ferguson BJ, Barnes L, Bernstein JM, Brown D, Clark III CE, Cook PR, DeWitt WS. Geographic variation in allergic fungal rhinosinusitis. *Otolaryngol Clin North Am* 2000;33:441-49.
51. Klossek JM, Serrano E, Peloquin L, Percodani J, Fontanel JP, Pessey JJ. Functional endoscopic sinus surgery and 109 mycetomas of paranasal sinus. *Laryngoscope* 1997;107:112-17.
52. Ghegan MD, Lee FS, Schlosser RJ. Incidence of skull base and orbital erosion in allergic fungal rhinosinusitis (AFRS) and non-AFRS. *Otolaryngol Head Neck Surg* 2006;134:592-95
53. Ghegan MD, Wise SK, Gorham E, Schlosser RJ. Socioeconomic factors in allergic fungal rhinosinusitis with bone erosion. *Am J Rhinol* 2007;21:560-63.
54. Gilespe MB, O'Mailey BW. An algorithmic approach to the diagnosis and management of invasive fungal rhinosinusitis in the immunocompromised patient. *Otolaryngol Clin North Am* 2000;33:323-34.

55. Saravanan K, Panda NK, Chakrabarti A, Bapuraj RJ. Allergic fungal rhinosinusitis: An attempt to resolve the diagnostic dilemma. *Arch Otolaryngol Head Neck Surg* 2006;132:173-78.
56. Michael RC, Michael JS, Ashbee RH, Mathews MS. Mycological profile of fungal sinusitis: An audit of specimens over a 7-year period in a tertiary care hospital in Tamil Nadu. *Indian J Pathol Microbiol* 2008;51:493-96.
57. Ferguson BJ. Fungus balls of the paranasal sinuses. *Otolaryngol Clin North Am* 2000;33:389-98.
58. Feger TA, Rupp NT, Kuhn FA. Local and systemic eosinophil activation in allergic fungal sinusitis. *Ann Allergy Asthma Immunol*. 1997 Sep. 79(3):221-5.
59. Lu-Myers Y, Deal AM, Miller JD. Comparison of Socioeconomic and Demographic Factors in Patients with Chronic Rhinosinusitis and Allergic Fungal Rhinosinusitis. *Otolaryngol Head Neck Surg*. 2015 Apr 27.
60. Marple BF, Gibbs SR, Newcomer MT, Mabry RL. Allergic fungal sinusitis-induced visual loss. *Am J Rhinol*. 1999 May-Jun. 13(3):191-5.
61. Stewart AE, Hunsaker DH. Fungus-specific IgG and IgE in allergic fungal rhinosinusitis. *Otolaryngol Head Neck Surg* 2002;127:324-32.
62. Pant H, Kette FE, Smith WB. Fungal-specific humoral response in eosinophilic mucus chronic rhinosinusitis. *Laryngoscope* 2005;115:601-6.
63. Luong A, Davis LS, Marple BF. Peripheral blood mononuclear cells from allergic fungal rhinosinusitis adults express a Th2 cytokine response to fungal antigens. *Am J Rhinol Allergy* 2009;23:281-7.
64. Pant H, Beroukas D, Kette FE. Nasal polyp cell populations and fungalspecific peripheral blood lymphocyte proliferation in allergic fungal sinusitis. *Am J Rhinol Allergy* 2009;23:453-60.
65. Manning SC, Schaefer SD, Close LG, Vuitch F. Culture-positive allergic fungal sinusitis. *Arch Otolaryngol Head Neck Surg* 1991;117:174.
66. Torres C, Ro JY, el-Naggar AK. Allergic fungal sinusitis: a clinicopathologic study of 16 cases. *Hum Pathol* 1996;27:793.
67. Cleland EJ, Bassiouni A, Boase S. The fungal microbiome in chronic rhinosinusitis: richness, diversity, postoperative changes and patient outcomes. *Int Forum Allergy Rhinol* 2014;4:259.
68. Al-Dousary SH. Allergic fungal sinusitis: radiological and microbiological features of 59 cases. *Ann Saudi Med* 2008;28:17.
69. Revankar SG, Sutton DA. Melanized fungi in human disease. *Clin Microbiol Rev* 2010;23:884.
70. Dematiaceous fungi. Mount Sinai Hospital. <http://microbiology.mtsinai.on.ca/mig/defungi/index.shtml> (Accessed on June 23, 2015).
71. Kimura M, McGinnis MR. Fontana-Masson--stained tissue from culture-proven mycoses. *Arch Pathol Lab Med* 1998;122:1107.
72. Shin SH, Ponikau JU, Sherris DA. Chronic rhinosinusitis: an enhanced immune response to ubiquitous airborne fungi. *J Allergy Clin Immunol* 2004;114:1369.
73. Okano M, Fujiwara T, Haruna T. Role of fungal antigens in eosinophilia-associated cellular responses in nasal polyps: a comparison with enterotoxin. *Clin Exp Allergy* 2011;41:171.
74. Clark DW, Wenaas A, Luong A. *Staphylococcus aureus* prevalence in allergic fungal rhinosinusitis vs other subsets of chronic rhinosinusitis with nasal polyps. *Int Forum Allergy Rhinol* 2013;3:89.
75. Dutre T, Al Dousary S, Zhang N, Bachert C. Allergic fungal rhinosinusitis-more than a fungal disease? *J Allergy Clin Immunol* 2013;132:487.
76. Collins M, Nair S, Smith W, Kette F, Gillis D, Wormald PJ. Role of local immunoglobulin E production in the pathophysiology of noninvasive fungal sinusitis. *Laryngoscope*. 2004;114(7):1242-46.
77. McClay JE, Marple B, Kapadia L, et al. Clinical presentation of allergic fungal sinusitis in children. *Laryngoscope*. 2002; 112(3):565-9.
78. Rehman A, Rafiq F, Uppal AA. Evaluation of Allergic Fungal Sinusitis Occurrence in Patients with Nasal Polyps. *PJMHS* 2015;9:875-8.
79. Akhtar MR, Ishaque M, Saadat ullah. Aetiology of nasal polyp. *Pak J Otolaryngol* 2004; 20: 9-11.
80. Irshad-ul-Haq M, Farooq M, Qadri SH. Prevalence of allergic fungal sinusitis among patients with nasal polyps. *JSZMC* 2014;5(4):690-2.
81. Baloch ZA, Ahmad AN, Mahmood Z, et al. Frequency of Allergic Fungal Sinusitis in Patients with Nasal Polyposis and its Causative Species. *Pakistan Journal of Otolaryngology* 2010; 26:76-77.
82. Telmesani LM. Prevalence of Allergic fungal sinusitis among patients with nasal polyps. *Ann Saudi Med* 2009;29:212-4.
83. Kumar N, Berry V. Allergic fungal sinusitis JK Science, *Journal of Medical Education & Research*, 2008;10(1):5-8