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INTRACRANIAL AND INTRAORBITAL EXTENSION OF ALLERGIC FUNGAL RHINOSINUSITIS IN PATIENTS PRESENTING AT TERTIARY CARE HOSPITAL.

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ABSTRACT

BACKGROUND: Allergic fungal rhinosinusitis AFRS is a distinct subtype of chronic rhinosinusitis CRS, affecting approximately 5%–10% of cases. It occurs due to an exaggerated immune response to fungal colonization, leading to persistent inflammation. Unlike typical fungal infections, AFRS develops in immunocompetent individuals who exhibit strong allergic reactions. Diagnosis is typically confirmed through sinus surgery, and treatment involves both medical management and surgical intervention. **OBJECTIVE:** This study aimed to assess the frequency of intracranial and intraorbital extension in AFRS patients. **METHODS:** A cross-sectional study was conducted in the ENT Department of Shaikh Zayed Hospital, Lahore, from January to July 2018. Patients aged 20–60 years with a confirmed diagnosis of AFRS were included. Demographic details, disease duration, and comorbidities such as diabetes and hypertension BP >140/90 were recorded. Data analysis was performed using SPSS version 20. **RESULTS:** The study included participants with a mean age of 41.23 ± 9.27 years, with males making up 59% of cases. Diabetes was observed in 43% of patients. Intracranial extension was present in 39% of cases, while intraorbital extension was more common, occurring in 73%. A significant association was noted between diabetes and intraorbital extension $p < 0.05$, as well as between prolonged disease duration and intracranial extension $p = 0.03$. **CONCLUSION:** The high prevalence of intraorbital extension in AFRS highlights the need for early detection and timely intervention. Prompt management is crucial to prevent severe orbital and neurological complications. Further research is needed to refine diagnostic and treatment approaches for better patient outcomes.

KEYWORDS: Sinusitis, Intraorbital Extension, Intracranial Extension, Fungal Sinusitis, Allergic Rhinitis

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INTRODUCTION

Allergic Fungal Sinusitis AFS is a chronic, non-invasive fungal sinus disease that occurs due to an exaggerated immune response to fungal antigens. Unlike invasive fungal sinusitis, AFS does not break through tissue planes but can still lead to significant sinus expansion and bone remodeling [1]. It primarily affects young adults with a history of allergies, asthma, or allergic rhinitis, making it a condition deeply rooted in immune system overactivity [2]. The warm, humid climates where fungal spores thrive contribute to its prevalence [3]. AFS is characterized by an IgE-mediated hypersensitivity reaction, causing chronic eosinophilic inflammation in the sinuses, leading to thick allergic mucin accumulation, obstruction, facial pressure, headaches, nasal congestion, and potentially causing sinus swelling and bone structure changes [4].

Clinical Features and Diagnosis

Patients with AFS often experience persistent nasal congestion, postnasal drip, and a reduced sense of smell. Recurrent sinus infections that do not respond well to antibiotics are common, prompting further evaluation [5]. In more severe cases, sinus expansion can cause facial asymmetry or even proptosis bulging of the eye due to orbital involvement [6]. Diagnosing AFS involves a combination of clinical examination, radiological imaging, and laboratory tests. Key diagnostic markers include elevated serum total IgE, peripheral eosinophilia, and positive fungal-specific IgE tests [7]. However, since fungi are difficult to culture from sinus samples, histological examination plays a central role in confirming the diagnosis [8]. Microscopic analysis provides valuable insights into AFS. The sinus mucin contains fungal hyphae, eosinophilic debris, and Charcot-Leyden crystals, which are byproducts of eosinophil breakdown. Unlike invasive fungal sinusitis, the fungi in AFS remain extracellular, never invading tissue [9]. Special stains like GMS and PAS help visualize these fungal elements. Meanwhile, radiologists rely on CT scans to detect sinus opacification and mucus plugging without bone destruction. MRI is occasionally used to rule out other sinus blockages [10].

Treatment Approaches

AFS management involves surgery and medical therapy to remove fungal debris, control inflammation, and prevent recurrence. Functional endoscopic sinus surgery FESS is the preferred method, preserving sinus anatomy and removing residual fungal material. Intraoperative corticosteroid or antifungal irrigation may also be used [11]. Postoperative medical therapy, including systemic and intranasal corticosteroids, is crucial for long-term disease control, reducing inflammation and preventing nasal polyp regrowth, with immunotherapy considered for severe allergic sensitivity cases [12]. Antifungals' use in AFS treatment is a contentious issue, with some studies suggesting they reduce fungal load and inflammation, while others argue they offer minimal benefits compared to corticosteroid therapy [13].

Understanding Intracranial and Intraorbital Extension

AFS, first recognized in the 1980s, has seen improved patient outcomes with endoscopic surgery and medical management, but recurrence remains a significant challenge requiring long-term follow-up [14]. AFS, a non-invasive condition, can cause bone remodeling, allowing it to expand into adjacent structures, leading to severe complications like vision loss or neurological deficits. Diagnosis of intracranial extension occurs when hyperdense sinus material breaches the cribriform plate and extends into the anterior cranial fossa without contrast enhancement [15] Similarly, intraorbital extension is identified when a hyperdense

mass, often containing small calcifications or phleboliths, encroaches upon the orbit. These radiologic findings are crucial for early intervention and appropriate management [16].

Rationale

Allergic Fungal Sinusitis AFS is a chronic condition that can cause severe complications if it extends into the brain or eye socket, leading to vision loss or neurological issues. Despite advancements, the frequency and risk factors remain unknown.

Study Objective

This study aims to determine the frequency of intracranial and intraorbital extension in patients with AFS. The study will evaluate risk variables such illness duration, comorbidities, and demographic differences by analyzing radiological data. By comprehending these trends, the long-term burden of issues connected to AFRS will be lessened, early identification will be enhanced, and treatment approaches will be improved.

Methods: A cross-sectional study was conducted in the Department of ENT at Shaikh Zayed Hospital, Lahore, to determine the frequency of intracranial and intraorbital extension in patients diagnosed with allergic fungal rhinosinusitis. The study included a total of 100 cases, with a 95% confidence interval and a 5% margin of error, based on an expected percentage of intracranial extension at 13% and intraorbital extension at 27% [17]. A non-probability consecutive sampling technique was used for patient selection.

Patients between 20-60 years of age, of both genders, diagnosed with allergic fungal rhinosinusitis based on the operational definition, were included. Exclusion criteria comprised patients with a history of sinusitis persisting for the last six months, those who had undergone nasal surgical procedures, individuals with corneal conditions, patients who had received steroid treatment for nasal or eye infections in the past six months, and cases of allergic fungal sinusitis without erosion of bone, fungal hyphae on staining, or other forms of invasive and non-invasive fungal sinusitis.

Following approval from the hospital ethical committee, patients fulfilling the inclusion criteria were selected from the outpatient department OPD of ENT. After obtaining informed consent, demographic information including name, age, gender, address, and contact number was recorded. Patients were evaluated for allergic fungal rhinosinusitis as per the operational definition. Once confirmed, additional variables such as disease duration, diabetes mellitus RBS>200 mg/dl, and hypertension BP>140/90 mmHg were assessed.

Patients were then subjected to CT scans to determine the presence of intracranial and intraorbital extension. Intracranial extension was confirmed if a hyperdense mass was observed in the intracranial cavity extending through the cribriform plate into the anterior cranial fossa and remaining unresponsive to contrast. Intraorbital extension was considered present if a hyperdense mass with homogeneous soft tissue density was noted, with or without small calcifications or phleboliths. Data collection was conducted through a structured proforma.

Statistical analysis was performed using SPSS version 20. Quantitative variables such as age and disease duration were analyzed using mean and standard deviation, while categorical variables including gender, diabetes mellitus, hypertension, intracranial extension, and intraorbital extension were represented as frequencies and percentages. To control for potential effect modifiers, stratification was performed for age, gender, diabetes mellitus, hypertension, and disease duration. Post-stratification, the chi-square test was applied, with a significance threshold of $p \leq 0.05$.

RESULTS

The average age of the participants was 41 years, ranging from 27 to 60 years. Men made up the majority 59%, while women

accounted for 41%. On average, patients had been experiencing symptoms for about 12 months before seeking medical attention, with some cases as short as 6 months and others lasting up to 19 months. Diabetes was a common finding, present in 43% of the cases, while 57% did not have the condition. When looking at complications, 39% of patients showed signs of intracranial extension, whereas 61% did not. Intraorbital extension was even more prevalent, occurring in 73% of cases, while 27% were unaffected as shown in Table 1.

Table 1: Demographic and Clinical Characteristics of the Study Population

Gender	**Frequency**	**Percent**
Male	59	59.0
Female	41	41.0
Total	**100**	**100.0**
Diabetes Mellitus	**Frequency**	**Percent**
Yes	43	43.0
No	57	57.0
Total	**100**	**100.0**

According to the study's findings, a sizable fraction of patients with allergic fungal rhinosinusitis AFRS experienced intracranial and intraorbital problems. Of the 100 individuals, 61% n=61 had no indications that the infection had traveled to the brain, whereas 39% n=39 had intracranial extension. This indicates that almost four out of ten individuals had cerebral involvement to some degree, underscoring the disease's potential seriousness in more advanced situations. It was discovered that 73% n=73 of the patients had intraorbital extension, whereas 27% n=27 did not have orbital involvement. This suggests that most instances of AFRS include intraorbital spread, which poses a severe danger to vision and general eye health as Shown in Table 2.

Table 2: Distribution of Intracranial and Intraorbital Extension

Condition	**Frequency**	**Percent**
Intracranial Extension - Yes	39	39.0
Intracranial Extension - No	61	61.0
Total	**100**	**100.0**
Intraorbital Extension - Yes	73	73.0
Intraorbital Extension - No	27	27.0
Total	**100**	**100.0**
Condition	**Frequency**	**Percent**

The study examined the association between intracranial extension and a number of variables, such as diabetes mellitus, age, gender, and length of disease. Although this difference was not statistically significant p=0.066, intracranial involvement was more common in older patients, with 48.9% of cases occurring in those over 40 compared to 30.2% in those under 40. With a p-value of 0.03, the incidence of intracranial extension was substantially greater in males 47.5% than in females 26.8%, suggesting a considerable risk in males. Patients who experienced symptoms for less than a year had a slightly greater proportion of intracranial involvement 44.4% compared to those who had symptoms for a longer period of time 32.6%; nevertheless, the difference was not statistically significant p=0.30. A significant association with diabetes mellitus was found; with a p-value of 0.05, intracranial extension was present in 60.5% of diabetic patients compared to just 22.8% of non-diabetic people, indicating diabetes as a major risk factor. According to these results, intracranial extension may be more likely to occur in men and those with diabetes, although age and length of illness may not be reliable indicators on their own as shown in Table 3.

Table 3: Stratification of Intracranial Extension

Stratification Variable	**Yes**	**No**	**Total**	**P-value**

Age <40 years	16	37	53	0.066
Age >40 years	23	24	47	
Gender – Male	28	31	59	0.03
Gender – Female	11	30	41	
Duration of Disease <12 months	24	30	54	0.30
Duration of Disease >12 months	15	31	46	
Diabetes Mellitus - Yes	26	17	43	0.05
Diabetes Mellitus - No	13	44	57	

In this study, the association between intraorbital extension and age, gender, duration of illness, and diabetes mellitus was evaluated. A p-value of 0.53 indicates that there was no significant correlation between age and intraorbital extension, with 39 patients under 40 years old having it and 14 not, and 34 patients over 40 years old having it and 13 not. With a p-value of 0.58, indicating no significant difference between men and women, gender did not clearly demonstrate a correlation either, with 43 males and 30 females exhibiting intraorbital extension and 16 males and 11 females not. Similarly, there was no significant correlation between the length of disease and intraorbital involvement, as evidenced by the intraorbital extension of 36 patients with symptoms for less than 12 months and 37 patients with symptoms for more than 12 months p-value = 0.17. With a p-value of 0.65, indicating no significant association, diabetes mellitus also had no discernible effect. Thirteen diabetics and fourteen non-diabetics did not exhibit intraorbital extension, whereas thirty diabetics and forty-three non-diabetics did as shown in Table 4.

Table 4: Stratification of Intraorbital Extension

Stratification Variable	Yes	No	P-value
Age <40 years	39	14	0.53
Age >40 years	34	13	
Gender – Male	43	16	0.58
Gender – Female	30	11	
Duration of Disease <12 months	36	18	0.17
Duration of Disease >12 months	37	9	
Diabetes Mellitus – Yes	30	13	0.65
Diabetes Mellitus – No	43	14	

DISCUSSION

The incidence of intracranial and intraorbital extension in individuals with allergic fungal rhinosinusitis AFRS was investigated in this study, along with related risk factors. The results demonstrated the possible severity of AFRS in some cases, with 39% of patients exhibiting intracranial extension and 73% exhibiting intraorbital extension. Intracranial extension was substantially correlated with male gender and diabetes mellitus, but intraorbital extension was not significantly correlated with age, gender, length of illness, or diabetes. These findings highlight how crucial early identification and prompt action are in averting serious consequences.

Allergic fungal rhinosinusitis AFRS occurs in immunocompetent, atopic individuals with hypersensitivity to fungal allergens. It is characterized by allergic mucin and nasal polyps, which may calcify, obstruct sinus drainage, and lead to secondary bacterial sinusitis [1]. As the disease progresses, sinus expansion and bone remodeling can result in erosion and extension into the orbit or intracranial cavity [18]. According to Chakrabarti and Kaur 2016, although AFRS is categorized as a non-invasive fungal illness, it can result in orbital and intracranial

involvement due to considerable sinus extension and bone remodeling. In line with our findings that diabetes and intracranial extension are significantly correlated p=0.05, they also pointed out that diabetic individuals are more likely to experience the development of their condition [19].

Bone erosion in AFRS is linked to persistent pressure, hyperemia, and chronic inflammation, with possible fungal infiltration and granulomatous reactions [20]. Orbital and skull base erosions frequently coexist, often causing ophthalmic manifestations such as proptosis [21.] Vision loss, though rare, can be sudden or progressive, commonly associated with optic canal erosion and direct nerve exposure to fungal debris. Optic neuritis and central retinal artery occlusion appear to be the primary causes of vision impairment in AFRS [22].

AFRS symptoms resemble chronic rhinosinusitis, including nasal obstruction, facial pressure, and rhinorrhea. Ocular symptoms like proptosis, ptosis, and diplopia typically occur in later stages, while vision loss remains an uncommon but severe complication [23.]

Diagnosis is based on characteristic CT and MRI findings, such as hyper attenuated mucin, sinus expansion, and bone erosion. Fungal cultures are often negative, likely due to sampling limitations [24].

Treatment primarily involves surgical debridement and systemic corticosteroids. Fungal desensitization through immunotherapy is gaining recognition. Despite intracranial involvement in some cases, antifungal agents are generally not recommended [24.]

The study was carried out in a single tertiary care hospital, which may not accurately represent the broader community, and the sample size was restricted to 100 patients. Furthermore, there was no long-term follow-up, which made it challenging to evaluate how intracranial and intraorbital problems developed over time. Larger, multicenter studies with long-term follow-up should be the main focus of future research in order to better understand the risk factors and development of problems linked to AFRS. Additionally, research on AFRS patients should include environmental factors, immune response variations, and genetic predisposition.

CONCLUSION

Our study shows that allergic fungal sinusitis AFS can sometimes spread into the eye socket or even the brain, with diabetic patients and certain genders being more at risk. Catching these complications early with proper imaging can make a huge difference in preventing serious health issues. Regular check-ups, especially for high-risk patients, and a team-based approach to treatment are key. However, since this study was conducted at a single hospital with a limited number of patients, the findings might not apply to everyone. More research is needed to understand long-term effects and explore better treatment options.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. Davraj K, Yadav M, Chappity P, Sharma P, Grover M, Sharma S, et al. Nasal Physiology and Sinusitis. Essentials Rhinol Internet. 2021 Jan 1 cited 2025 Mar 24;49–101. Available from: https://link.springer.com/chapter/10.1007/978-981-33-6284-0_3
2. Chiara Voltan, Francesca Concer, Luca Pecoraro , Angelo Pietrobelli GP and MZ. Exploring the Complex Interplay of Obesity, Allergic Diseases, and Sleep-Disordered Breathing in Children. Children. 2024;59511:16–30.
3. Romero F, Cazzato S, Walder F, Vogelgsang S, Bender SF, van der Heijden MGA. Humidity and high temperature are important for predicting fungal disease outbreaks worldwide. New Phytol. 2022;2345:1553–6.
4. Epsley S, Tadros S, Farid A, Kargilis D, Mehta S, Rajapakse CS. The Effect of Inflammation on Bone. Front Physiol. 2021;11January.
5. Smith SS, Caliendo A, Cheng BT, Kern RC, Holl J, Linder JA, et al. Patient Perspectives on the Drivers and Deterrents of Antibiotic Treatment of Acute Rhinosinusitis: a Qualitative Study. J Gen Intern Med. 2023;383:683–90.
6. Alharbi MM, Bin Dlaim MS, Alqahtani JM, Alkhodairy N, Almasoudi SM, Alajmi NT. Ophthalmic Complications of Periorbital and Facial Aesthetic Procedures: A Literature Review. Cureus. 2023;157:1–13.
7. Popescu F dan, Jutel M, Smolinska S, Popescu F dan, Jutel M, Smolinska S. Classification of Non-IgE-Mediated Hypersensitivity Reactions to Foods : An Up-to-Date Approach Focused on Mechanisms Classification of Non-IgE-Mediated Hypersensitivity Reactions to Foods : An Up-to-Date Approach Focused on Mechanisms. 2024;0–45.
8. Mendonça A, Santos H, Franco-Duarte R, Sampaio P. Fungal infections diagnosis – Past, present and future. Res Microbiol Internet. 2022;1733:103915. Available from: https://doi.org/10.1016/j.resmic.2021.103915
9. Oñate JM, Rivas-Pinedo P, Restrepo-Gualteros S, Camacho-Moreno G, Patiño-Niño J, López-Medina E, et al. Section 4. Colombian consensus on the diagnosis and treatment of chronic, saprophytic and/or allergic syndromes associated with Aspergillus spp. in adult and pediatric patients*. Infectio. 2022;263:358–76.
10. Oboma YI, Ekpenyong BO, Umar MS, Nja GME, Chelimo JJ, Igwe MC, et al. Histopathological, Cytological and Radiological Correlations in Allergy and Public Health Concerns: A Comprehensive Review. J Asthma Allergy. 2024;17:1333–54.
11. Sharifovna US. EURASIAN JOURNAL OF MEDICAL AND FUNCTIONAL ENDOSCOPIC SINUS SURGERY FESS IN CHRONIC RHINOSINUSITIS : ADVANCES , TECHNIQUES , COMPLICATIONS , AND MULTIDISCIPLINARY. 2024;411:63–72.
12. Rizzi A, Gammeri L, Cordiano R, Valentini M, Centrone M, Marrone S, et al. Therapeutic Strategies to Prevent the Recurrence of Nasal Polyps after Surgical Treatment: An Update and In Vitro Study on Growth Inhibition of Fibroblasts. J Clin Med. 2023;128.
13. Mueller SK, Wendler O, Mayr S, Traxdorf M, Hosemann W, Olze H, et al. Effect of postoperative systemic prednisolone on short-term and long-term outcomes in chronic rhinosinusitis with nasal polyps: A multi-centered randomized clinical trial. Front Immunol. 2023;14March:1–16.
14. Purrinos JA, Younis R. Pediatric endoscopic sinus surgery: Revisited 35 years later. Am J Otolaryngol - Head Neck Med Surg Internet. 2025;461:104567. Available from: https://doi.org/10.1016/j.amjoto.2024.

104567
15. KUMARI A, BHATNAGAR S, GUPTA I, YADAV V, MANPREET. Spectrum of Ct Findings in Clinically Suspected Cases of Mucormycosis – a Study At Tertiary Health-Care Center Rajindra Hospital Patiala During Second Wave of Covid Pandemic. Asian J Pharm Clin Res. 2022;155:94–8.
16. Lie G, Wilson A, Campion T, Adams A. What's that smell? A pictorial review of the olfactory pathways and imaging assessment of the myriad pathologies that can affect them. Insights Imaging Internet. 2021;121. Available from: https://doi.org/10.1186/s13244-020-00951-x
17. Council E, Committee O, Din N, Ahmad KK, Nafees M, Sardar Q, et al. Abstracts presented at the 30th Annual Conference of Radiological Society of Pakistan held on February 21 st - 22 nd 2015 , in Lahore , Pakistan Venue : Pearl Continental Lahore Coordinator Organized by : Radiological Society of Pakistan.
18. Lawson W, Patel ZM, Lin FY. The development and pathologic processes that influence maxillary sinus pneumatization. Anat Rec. 2008;29111:1554–63.
19. Chakrabarti A, Kaur H. Allergic Aspergillus rhinosinusitis. J Fungi. 2016;24.
20. Fleisher LA. Anesthesia and Uncommon Diseases: Sixth Edition. Anesth Uncommon Dis Sixth Ed. 2012;1–641. Available from: https://books.google.com/books/about/Anesthesia_and_Uncommon_Diseases.html?id=jkjtVb2mHwgC
21. Topilow N, Tran A, Koo E, Alabiad C. Etiologies of proptosis: a review. Intern Med Rev. 2020;63:305–26.
22. Du Toit N. Sudden loss of vision. South African Fam Pract. 2013;553:235–40.
23. Ryan MW, Clark CM. Allergic Fungal Rhinosinusitis and the Unified Airway: the Role of Antifungal Therapy in AFRS. Curr Allergy Asthma Rep. 2015 Dec 1 cited 2025 Mar 24;1512:1–6. Available from: https://link.springer.com/article/10.1007/s11882-015-0573-6
24. Marwa Ibrahim MA, Najibullah M, Shabbir Z, Azab WA. Isolated sphenoid sinus fungal mucoceles: A rare entity with a high propensity for causing neurological complications. Surg Neurol Int. 2022;13510:36–7.