

## Original Research Article

# Management of invasive fungal rhino sinusitis in a tertiary health care center

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**Received:** 17 August 2018

**Revised:** 15 October 2018

**Accepted:** 17 October 2018

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## ABSTRACT

**Background:** Invasive fungal sinusitis, though considered to be rare entity, is nowadays frequently encountered, mostly in immunocompromised patients like uncontrolled diabetes, haematological malignancy and organ transplants on immunosuppressive drugs. There are only a few landmark studies from the Indian subcontinent on invasive fungal rhino sinusitis. The lack of awareness among clinicians regarding the varying clinical presentations of fungal rhino sinusitis prompted us to undertake this study, as our hospital is referral centre we get to see varying presentations and most terminal stages of disease.

**Methods:** This is a prospective study in which we report 30 cases reported to Gandhi Hospital, Secunderabad, invasive fungal rhino sinusitis. Evaluated in detail the clinical presentation, radiological features, specimens collected were subjected to both microbiology and pathologic examination; data collected and were analysed. Treated medically and surgically.

**Results:** The most common co-morbid condition is uncontrolled diabetes mellitus. Mucoraceae (53%) and Aspergillus (10%) were the main fungi found. Mucosal biopsy confirmed fungal invasion to the nasal mucosa in all cases. Computed tomography and endoscopic findings showed a predominance of unilateral disease, with various stages of nasal involvement. All patients underwent surgical debridement and systemic antifungal therapy immediately after diagnosis.

**Conclusions:** Early medical and surgical treatment is essential to improve the prognosis along with better control of comorbidities.

**Keywords:** Invasive fungal sinusitis, Amphotericin B, Debridement, Mucoraceae, CT para nasal sinuses

## INTRODUCTION

Fungi are ubiquitous organisms in our environment. Invasive fungal rhinosinusitis is characterized by mycotic infiltration of the mucosa of the nasal cavity and paranasal sinuses. Invasive fungal rhinosinusitis is rapidly destructive. IFR (invasive fungal rhinosinusitis) requires urgent diagnosis and treatment; otherwise the

mortality rate could be as high as 50–80%.<sup>1,2</sup> The disease occurs primarily in immunocompromised patients. Most patients with AIFR (acute invasive fungal rhinosinusitis) are already in a state of poor health and are expected to have poorer prognosis because of underlying disease.

Invasive fungal sinusitis has a worldwide distribution. Most cases have been reported in adults, but

immunocompromised children are also at risk; men and women are equally affected.<sup>3-5</sup> Medical advances, such as new chemotherapeutic agents and long-term use of immunosuppressive agents following bone marrow or solid organ transplantation, have resulted in an increase in the population at risk of developing AIFR. Poorly controlled type 1 diabetes mellitus, malnutrition, and excessive storage of iron in haematological diseases can also be predisposing factors for the development of AIFR.<sup>6</sup>

There are very few landmark studies on invasive fungal rhinosinusitis in our country there is insufficient data regarding the causative agents from southern part of the country. Varied presentations and progress of the disease need to be studied in detail.

### Aim

To study the multimodality diagnostic and therapeutic approaches in management of invasive fungal rhinosinusitis.

### Objectives

- To study the underlying risk factor.
- To study the pathogen isolated.
- To study the radiological features of invasive fungal sinusitis.
- To study various treatment modalities.

## METHODS

### Study design, duration of the study, study area, data analysis

This is a prospective study conducted over a period of 3 years from 2015 to 2018 at Department of Otorhinolaryngology, Gandhi Hospital, Secundrabad, Telangana. After taking institutional ethical committee clearance, all cases of invasive fungal rhinosinusitis attending Gandhi Hospital, Secundrabad are included in the study. Patients not willing to participate in the study and patients lost in the follow up are not included in the study. We report 30 cases reported to Gandhi general hospital of invasive fungal rhinosinusitis. Evaluated in detail, the clinical presentation, radiological features, specimens collected were subjected to both microbiology and pathologic examination; data collected and were analysed, Data was analysed using MS Excel. Results are interpreted in terms of percentages.

## RESULTS

Out of 30 cases, 3 cases (10%) were under 20 years age group, 6 cases (20%) were in the 3<sup>rd</sup> decade, 7 cases (23.3%) were in the 4<sup>th</sup> decade, 7 cases (23.3%) were in the 5<sup>th</sup> decade, 7 cases (23.3%) were above 60 years of age group. No particular age preponderance was noted. Incidence of the disease was more in the male population

with 18 cases (69%) whereas the female incidence was 8 cases (31%).

**Table 1: Various age groups.**

S. No	Age of the patient (in years)	Number	Percentage (%)
1	<20	03	10
2	21 to 30	00	0
3	31 to 40	06	20
4	41 to 50	07	23.3
5	51 to 60	07	23.3
6	>60	07	23.3

**Table 2: Presenting complaints of the patient.**

Presenting complaints	Number	Percentage (%)
Nasal discharge	14	46.6
Nasal obstruction	13	43.3
Fever	08	26.6
Eye swelling and eye pain	12	40
Decreased vision	02	6
Altered sensorium	01	3
Facial pain	02	6

In 30 cases the commonest presentation was nasal obstruction in 13 cases (43.3%), nasal discharge in 14 cases (46.6%), eye swelling /eye pain seen in 12 cases (40%), decreased vision in 2 (6%) case, altered sensorium in 1 case (3%), facial pain in 2 cases (6%).

**Table 3: Co-morbid conditions.**

Co morbid conditions	Number	Percentage (%)
Diabetes mellitus	19	63.3
Hypertension	07	23.3
Organ transplants	02	6
Retro viral disease	01	3
Cerebrovascular accident	02	6
Coronary artery disease	01	3
Ca cervix	01	3
Immunocompetent	06	20

Out of 30 cases in our study 19 cases (63.3%) were suffering from diabetes mellitus, hypertension in (23.3%) 7 cases, 2 cases (6%) were patients of organ transplant and on immunosuppressive drugs, 1 patient (3%) was retroviral positive, 2 cases (6%) were suffering from cerebrovascular accident, 1 case (3%) each from coronary artery disease and carcinoma cervix, no comorbidities in 20% of cases

In our clinical findings 28 cases had necrotic tissue in the nasal cavity, purulent discharge in the nose in 11 cases, polypoid in 3 cases, septal erosions in 2 cases, hard

palate erosion in 14 cases, maxilla erosion in 4 cases, so the commonest clinical finding was necrotic tissue in the nasal cavity.



**Figure 1: Various clinical presentations of invasive fungal sinusitis.**

**Table 4: Clinical examination findings.**

S no	Clinical finding	Number	Percentage (%)
1	Necrotic tissue in the nose	28	93.3
2	Purulent nasal discharge	11	36.6
3	Polyposis	03	10
4	Septal erosions	02	6
5	Hard palate erosion	14	46.6
6	Maxilla erosion	04	13.3
7	Proptosis	11	36.6

**Table 5: CT findings.**

Findings	Number	Percentage (%)
<b>Unilateral sinus involvement</b>	Right side: 08	26.6
	Left side: 14	46.6
<b>Bilateral sinus involvement</b>	08	26.6
<b>Hard palate erosion</b>	14	46.6
<b>Lamina papyracea erosion</b>	17	56.6
<b>Maxilla erosion</b>	04	13.3
<b>Intra cranial extension</b>	07	23.3

**Table 6: Pathogen isolated.**

Pathogen	Number	Percentage (%)
<b>Mucor species</b>	16	53.3%
<b>Aspergillus species</b>	03	10%
<b>No fungus isolated</b>	11	36.6%

Study of CT scans of 30 patients revealed unilateral pan sinusitis in (74%) of cases with incidentally more on the left side with 46.6% of cases, bilateral pan sinusitis was seen in 26.6% of cases, with bony erosions of lamina papyracea in 56.6%, hard palate erosion in 46.6%, maxilla erosion was seen in 13.3% of cases and intracranial extension was seen in 23.3% of cases.

On fungal culture of the nasal tissue 53.3% of cases was found to isolate mucor species and 10% of cases isolated to have aspergillous species where as in 36.6% of cases no fungus was grown.

**Table 7: Various complications.**

S no	Complications	Number	Percentage (%)
1	Oroantral fistula	14	46.6
2	Orbital cellulitis	17	56.6
3	Permanent loss of vision	05	16.6
4	CSF leak	01	3
5	Meningitis	06	20
6	Cerebral mucormycosis	02	6
7	Death	06	20

During the course of treatment or disease 14 cases (46.6%) developed oroantral fistula, (56.6%) 17cases developed orbital cellulitis, 05 cases (16.6%) of cases developed permanent loss of vision, 20% of cases developed meningitis and 3% of cases developed CSF leak, 6% of cases developed cerebral mucormycosis, 20% of cases were deceased.

**Table 8: Treatment given.**

S no	Treatment modality	Number	Percentage (%)
1	Endoscopic sinus surgery	26	86.6
2	Injection IV Amphotercin	30	100
	Amphotericin deoxycholate	18	60
	Lipid emulsion	12	40

All cases that were diagnosed as invasive fungal sinusitis either clinically or based on histopathology were treated with IV amphotercin in which 60% of cases were treated with amphotericin deoxycholate and 40% of cases were treated with lipid emulsion amphotericin purely based on the financial status of patient. 87% of cases underwent endoscopic sinus surgery and debridement of fungal debris was done other were excluded as they were not fit for the surgery.

**Table 9: The outcomes in patients with invasive fungal sinusitis.**

<b>Clinical improvement</b>	24	80%
<b>Deaths</b>	06	20%

Out of 30 cases clinical improvement was seen in 24 cases (80%) and 6 cases (20%) were deceased.

## DISCUSSION

In our study the age of the patients were between 5 to 65 years with a mean age group of 47.8 years. According to Pirochchai et al mean age was around 51.7 years and according to Navya et al mean age was around 30 years.<sup>7,8</sup> According to Mehta et al mean age group is 33.19 years.<sup>9</sup> In our study youngest patient was 5 years of age and the eldest was 65 years of age maximum number of patients are between age of 31 years and 65 years probably because increasing incidence of risk factors and occupational exposure to the fungi. In our study the disease was more prevalent in male population with 69% of cases, male: female ratio of 2.25:1, whereas according to Ghazizade et al Male: female was 1.56:1.<sup>12</sup> according to Pirochchai et al Male: female was 1:1.5 whereas according to Mehta et al it was 1.36:1.<sup>7,9</sup>

According to Mehta et al commonest presenting complaint was nasal obstruction and nasal discharge followed by proptosis.<sup>9</sup> According to Iwen et al periorbital swelling (seven patients) and nasal congestion (six patients).<sup>5</sup> Around the nose and facial plane when skin involvement occurred. In our study nasal obstruction (47%) and nasal discharge (43%) was commonest presenting complaint followed by eye pain and eye swelling in (40%) of cases and fever was presenting complaint in only 27% of cases. Orbital symptoms in a case of invasive fungal sinusitis is a late presentation, nasal obstruction and nasal discharge are part of acute rhinitis hence usually neglected and leading to presentation in late stage. Patients presenting with eye symptoms are relatively high with 40% of cases this implies that the patients are presenting in relatively late stage. In our study 19 cases (63.3%) were suffering from diabetes mellitus hypertension in (23%) 7 cases, 2 cases (6%) were patients of organ transplant and on immunosuppressive drugs, 1 patient(3%) was retroviral positive, 2 cases (6%) were suffering from cerebrovascular accident, 1 case (3%) each from coronary artery disease and carcinoma cervix, no comorbidities in 20% of cases.

Other studies show that haematological malignancies are commonest risk factor but our centre is not an oncology institute our study tends to have lesser number of malignancies. Diabetes is the commonest associated risk factor for invasive fungal rhinosinusitis. Is it the diabetes that is making the patients more susceptible to for invasive fungal rhinosinusitis or it is because of the

increased incidence of diabetes, it's a common risk factor, need to be studied.

In our clinical findings 28 cases had necrotic tissue in the nasal cavity, purulent discharge in the nose in 11 cases, polyposis in 3 cases, septal erosions in 2 cases, hard palate erosion in 14 cases, maxilla erosion in 4 cases. So the commonest clinical finding was necrotic tissue in the nasal cavity.

According to Mehta et al lamina erosion was the commonest bony erosion that was observed, followed by roof of maxillary sinus.<sup>9</sup>

Ghazizade et al study showed that palate and nasal floor was involved in 26.8% of cases and skull base erosion in 9.8% of cases where as in our study revealed.<sup>12</sup> Computed tomography of paranasal sinuses revealed unilateral pan sinusitis in (74%) of cases with incidentally more on the left side with 46.6% of cases, bilateral pan sinusitis was seen in 27% of cases, with bony erosions of lamina papyracea in 57%, hard palate erosion in 47%, maxilla erosion was seen in 13% of cases and intracranial extension was seen in 23% of cases.

According to Middlebrooks et al *Aspergillus* sps was isolated in 42.9%, 23.8% of cases *Mucor* species and 19% of cases pathogen was unknown.<sup>14</sup> According to Mehta et al positive fungal growth was seen in 57.7% (*Aspergillus* sps) and negative for fungal growth in 42% of cases.<sup>9</sup> According to Ghazizade et al study showed mucor species was isolated in 80.5% of cases.<sup>12</sup> Our study mucor (53.3%) was the commonest species that was isolated in cases of invasive fungal sinusitis 10% of cases isolated to have *Aspergillous* species where as in 36.6% of cases no fungus was grown, there might be a wrong methodology in sample collection, culture techniques in our study which may have lead to the 36.6% of cases were no fungal species was identified or the representative area must not have been taken for sampling.

Similar modality of treatment was given in all studies where 100% of cases were treated with injection amphotericin and endoscopic debridement of necrotic and fungal debris in most of the cases who are fit for surgery. Few patients were treated with injection amphotericin deoxycholate 69% and few patients 31% of them with lipid emulsion amphotericin B purely based on the financial status of the patients. However clinically significant complications were not noted in the patients who are given amphotericin b deoxycholate.

According to Mehta et al itraconazole has the similar efficacy in treating the cases of invasive fungal sinusitis with fewer side effects compared to amphotericin B.<sup>9</sup>

Payne et al study suggested AIFRS-specific mortality rate was 24.3%.<sup>10</sup>

In study of Kasapoglu et al Evaluation of 26 patients treated, thirteen of their patients died.<sup>13</sup> Nine died due to primary disease or comorbidities, and they had no evidence of residual disease in their sinuses or nasal cavity. Our study revealed clinical improvement in 24 cases (80%) and mortality in 7 cases (20%).

Mortality in all our cases is mostly because of the disseminated invasive fungal sinusitis where intracranial extension proved disastrous to the improvement in our patients. Control of comorbidities in addition to early surgical and medical management is key for improvement in cases of invasive fungal rhinosinusitis.

## CONCLUSION

Invasive fungal rhinosinusitis is a relatively rare disease with high morbidity and mortality. The most common risk factor is uncontrolled diabetes mellitus, is it because of diabetes these people are more prone for the disease or because of the genetic predisposition that lead to the disease in these people. Maintaining a high index of suspicion in at-risk patient populations, followed by prompt evaluation and management, is crucial in suspected AIFRS. Early diagnosis of IFR requires a high level of suspicion because of the non-specific initial symptoms and radiological signs.

All cases on histopathology show submucosal invasion of the fungus. Diagnostic nasal endoscopy and CT paranasal sinuses helps in early detection of bony erosions and necrotic changes and are complementary to microbiology and pathological investigations. IFRS can be successfully treated with a combination of endonasal surgical debridement and systemic antifungal medications. Complete endoscopic excision should be the treatment of choice for highly suspected lesions limited to the nasal cavity. More radical excision including maxillectomy and orbital exenteration, may be necessary in cases of severe necrosis Multimodality treatment in controlling co morbidities is key for prognosis of disease. Early diagnosis and management is the key for the improvement of disease.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Thaduri A, Kamanur SDK, Vishnuvardan DK, Rao AVSH, Reddy KS, Chandrashekar A. Management of invasive fungal rhino sinusitis in a tertiary health care center. *Int J Otorhinolaryngol Head Neck Surg* 2018;4:1468-72.