

# A seven-year retrospective analysis of the clinicopathological and mycological manifestations of fungal rhinosinusitis in a single-centre tropical climate hospital

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## Abstract

**Objective:** To evaluate the clinicopathological and mycological manifestations of fungal rhinosinusitis occurring in the Tengku Ampuan Rahmah Hospital, in Klang, Malaysia, which has a tropical climate.

**Methods:** Records of patients treated from 2009 to 2016 were analysed retrospectively. Data from the records were indexed based on age, gender, clinical presentations, symptom duration, clinical signs and mycological growth.

**Results:** Of 80 samples, 27 (33.75 per cent) had fungal growth. Sixteen patients were classified as having non-invasive fungal rhinosinusitis and 11 as having invasive fungal rhinosinusitis. The commonest clinical presentation was nasal polyposis in non-invasive fungal rhinosinusitis patients ( $p < 0.05$ ) and ocular symptoms in invasive fungal rhinosinusitis patients ( $p < 0.05$ ). The commonest organism was *aspergillus* sp. ( $p < 0.05$ ) in non-invasive fungal rhinosinusitis and mucorales in invasive fungal rhinosinusitis.

**Conclusion:** There is an almost equal distribution of both invasive and non-invasive fungal rhinosinusitis, as seen in some Asian countries. Invasive fungal rhinosinusitis, while slightly uncommon when compared to non-invasive fungal rhinosinusitis, is potentially life threatening, and may require early and extensive surgical debridement. The clinical presentation of nasal polyposis was often associated with non-invasive fungal rhinosinusitis, whereas ocular symptoms were more likely to be associated with invasive fungal rhinosinusitis.

**Key words:** Sinusitis; Rhinitis; Tropical Climate; Fungus Disease; Mycology; Mycoses; Microbiology; Cross-Sectional Studies

## Introduction

Fungal rhinosinusitis is an often-overlooked diagnosis when managing a patient with chronic rhinosinusitis. It is usually diagnosed after reviewing classical signs in a computed tomography scan or through the biopsy of fungal isolates within the sinuses. Clinical signs are often subtle and may be masqueraded by other diseases. In fungal rhinosinusitis, extranasal symptoms such as ocular or intracranial signs may present as early manifestations.

Fungal rhinosinusitis was classified by Bent and Kuhn as non-invasive and invasive.<sup>1</sup> Non-invasive fungal rhinosinusitis is further sub-classified into two subdivisions: allergic fungal rhinosinusitis and mycetoma. Invasive fungal rhinosinusitis is sub-classified into three entities: acute fulminant fungal sinusitis, chronic fungal rhinosinusitis and chronic granulomatous fungal rhinosinusitis.<sup>1</sup>

Both varieties often require surgical intervention as part of the treatment. In acute fulminant fungal rhinosinusitis, patients often present with symptoms of less than one month in duration, with an associated history of immunosuppression. In such cases, surgical intervention may be lifesaving.

In this study, we evaluated the clinicopathological and mycological manifestations of fungal rhinosinusitis in a tropical setting.

## Materials and methods

This study was conducted at Tengku Ampuan Rahmah Hospital. This is an 864-bed tertiary hospital located in the south of Klang, Malaysia, which has a tropical climate, with significant rainfall throughout the year.

Following a review by the Malaysian Research Ethical Committee (National Medical Research

Register number: 16-1692-32476), the records of patients who presented from July 2009 to July 2016, who were clinically diagnosed with fungal sinusitis, with fungal growth and histopathological evidence, were compiled and analysed retrospectively. Information obtained from records was indexed based on age, gender, clinical presentations, symptom duration, clinical signs and mycological growth.

## Results

### Patient overview

Eighty samples obtained from the sinuses of patients who presented from July 2009 to July 2016 were analysed. Twenty-seven of the 80 samples (33.75 per cent) were positive for fungal growth and were included in the study. Fifty-six per cent were from non-invasive fungal rhinosinusitis cases and 44 per cent were from invasive fungal rhinosinusitis cases.

Eighty-eight per cent of all patients had undergone surgery as part of the fungal rhinosinusitis treatment, and 12 per cent had opted for conservative medical treatment. Of those individuals who were operated on, 16.7 per cent required repeated surgery. The mean age of presentation was 49.8 years, with a range of 33 to 67 years. The male-to-female ratio was 1:1.25. Patients had presented with a myriad of symptoms, but the commonest was nasal blockage (22 per cent; Table I). The underlying risk factors in all fungal rhinosinusitis patients are listed in Table II.

### Non-invasive rhinosinusitis

The average duration of symptoms prior to presentation was 154 weeks (3 years). The majority of patients with non-invasive fungal rhinosinusitis had diabetes (37.5 per cent); 31.1 per cent of patients had no previous medical disease (Table III). The commonest fungal growth obtained was aspergillus sp. (62.5 per cent), followed by non-sporulating moulds (18.8 per cent) (Table IV). Significantly more non-invasive than invasive fungal rhinosinusitis patients had nasal polyposis on presentation ( $p < 0.05$ ). In contrast, significantly more invasive than non-invasive fungal rhinosinusitis

TABLE I  
RELATION OF FUNGAL RHINOSINUSITIS TO INITIAL PRESENTING SYMPTOMS

Initial presenting symptom	Non-invasive fungal rhinosinusitis*	Invasive fungal rhinosinusitis <sup>†</sup>	<i>p</i>
Nasal blockage	10 (62.5)	6 (54.5)	0.679 <sup>‡</sup>
Nasal discharge	8 (50.0)	7 (63.6)	0.484 <sup>‡</sup>
Nasal itchiness	1 (6.3)	0 (0)	>0.995**
Facial pain	8 (50.0)	6 (54.5)	0.679 <sup>‡</sup>
Epistaxis	1 (6.3)	1 (9.0)	0.549**
Hyposmia	0 (0)	1 (9.0)	0.407**
Vertigo	1 (6.3)	0 (0)	>0.995**
Ocular symptoms	0 (0)	6 (54.5)	0.009**

Data represent numbers (and percentages) of patients, unless indicated otherwise. \* $n = 16$ ; <sup>†</sup> $n = 11$ . <sup>‡</sup>Chi-square test; \*\*Fisher's exact test

TABLE II  
RELATION OF UNDERLYING RISK FACTORS TO FUNGAL RHINOSINUSITIS AS A WHOLE

Risk factor	Patients with fungal rhinosinusitis ( <i>n</i> (%))*
Diabetes	13 (32.5)
Hypertension	10 (25)
No known medical illness	10 (25)
Cerebrovascular accident	2 (5)
Solid tumours	2 (5)
Implant	1 (2.5)
Gastritis	1 (2.5)
Immunosuppressive drugs	1 (2.5)

\*Total  $n = 27$

TABLE III  
RELATION OF FUNGAL RHINOSINUSITIS TO VARIOUS UNDERLYING MEDICAL DISORDERS

Underlying issue or disease	Non-invasive fungal rhinosinusitis*	Invasive fungal rhinosinusitis <sup>†</sup>	<i>p</i>
Diabetes	6 (37.5)	8 (72.7)	0.072 <sup>‡</sup>
Gastritis	1 (6.25)	0 (0)	>0.950**
Hypertension	3 (18.8)	7 (63.6)	0.018 <sup>‡</sup>
Implants	0 (0)	1 (9.1)	0.407**
Chronic kidney disease	0 (0)	1 (9.1)	0.407**
Malignant solid tumour	1 (6.3)	1 (9.1)	>0.950**
Nasal polyposis	8 (50.0)	1 (9.1)	0.027 <sup>‡</sup>
No previous medical disorder	5 (31.3)	1 (9.1)	0.350**
Immunosuppressive therapy	0 (0)	1 (9.1)	0.407**

Data represent numbers (and percentages) of patients, unless indicated otherwise. \* $n = 16$ ; <sup>†</sup> $n = 11$ . <sup>‡</sup>Chi-square test; \*\*Fisher's exact test

TABLE IV  
RELATION OF FUNGAL RHINOSINUSITIS TO VARIOUS ISOLATED ORGANISMS

Fungal growth	Non-invasive fungal rhinosinusitis*	Invasive fungal rhinosinusitis <sup>†</sup>	<i>p</i> <sup>‡</sup>
Aspergillus sp.	10 (62.5)	1 (9.0)	0.006
Candida	1 (6.3)	1 (9.0)	>0.995
Curvularia sp.	0 (0)	1 (9.0)	0.407
Fusarium sp.	1 (6.3)	0 (0)	>0.995
Penicillium sp.	0 (0)	1 (9.0)	0.407
Perenniporia	1 (6.3)	0 (0)	>0.995
Rhizomucor sp.	0 (0)	1 (9.0)	0.407
<i>Rhizopus oryzae</i>	0 (0)	3 (27.3)	0.056
<i>Scedosporium apiospermum</i>	0 (0)	2 (18.2)	0.157
Non-sporulating mould	3 (18.8)	1 (9.0)	0.624

Data represent numbers (and percentages) of patients, unless indicated otherwise. \* $n = 16$ ; <sup>†</sup> $n = 11$ . <sup>‡</sup>Fisher's exact test

patients had ocular symptoms ( $p < 0.05$ ). All patients with non-invasive fungal rhinosinusitis had survived and are under long-term follow up.

#### *Invasive rhinosinusitis*

The average duration of symptoms prior to presentation at the clinic was one month. The commonest medical disorder associated with invasive fungal rhinosinusitis was diabetes (73 per cent); one patient had a history of chronic steroid intake for nephrotic syndrome and one had sinonasal malignancy (Table III). The commonest symptoms in acute invasive fungal rhinosinusitis cases were ocular symptoms (e.g. eye swelling, blurring of vision) (54.5 per cent). The commonest fungal pathogen isolated was that of mucorales sp. (36.4 per cent) (Table IV), followed by *Scedosporium apiospermum* (18 per cent). The mortality associated with acute invasive fungal rhinosinusitis was 67 per cent. Compared to non-invasive fungal rhinosinusitis, invasive fungal rhinosinusitis was significantly associated with hypertension ( $p < 0.05$ ) (Table III).

#### Discussion

Fungal rhinosinusitis is a well-defined disease of the sinuses. It is linked to the pathogenesis of chronic rhinosinusitis, especially in resistant cases.<sup>2</sup> The incidence of fungal sinusitis has been reported to be increasing, especially in immunocompromised individuals.<sup>3</sup> This trend is also seen in patients on long-term broad-spectrum antibiotics.<sup>4</sup> More than 50 fungal pathogens have been isolated as agents of fungal rhinosinusitis, including aspergillus, rhizopus, alternaria, bipolaris and curvularia.<sup>5</sup> Warm and humid climates tend to foster fungal proliferation, particularly of dematiaceous fungus. These organisms are ubiquitous in nature, and can occur in soil, wood and decomposing plants.<sup>6</sup>

Fungal rhinosinusitis can be classified broadly into two categories: invasive and non-invasive. Invasive fungal rhinosinusitis, in its acute form, can present as a fulminant and highly destructive clinical entity, which is potentially fatal and difficult to treat. These cases typically present with an underlying immunocompromised state and require aggressive debridement to ensure full eradication of the offending fungal agent.<sup>7</sup> Despite aggressive treatment, the prognosis of acute invasive fungal rhinosinusitis patients remains poor, with mortality rates ranging from 50 to 80 per cent.<sup>8</sup> In our series, the mortality rate of acute invasive fungal rhinosinusitis patients was 66 per cent, which is comparable to data reported in mainstream journals.

The pathological spectrum differs from one area to another, suggesting that different climates and environmental factors play a role in fungal growth propensity. A study by Granville *et al.* reported an incidence of non-invasive fungal sinusitis of over 90 per cent compared to invasive fungal sinusitis.<sup>9</sup> A study by Das *et al.* from India reported a 60 per cent incidence of non-invasive fungal sinusitis in comparison to invasive fungal sinusitis.<sup>10</sup> Similarly, Soontrapa *et al.* observed

a 60 per cent incidence of non-invasive fungal sinusitis in Thailand.<sup>11</sup> Our study demonstrates a pattern of clinical presentation similar to that observed in Thailand and India, whereby 56 per cent of patients with fungal growth in the sinuses were diagnosed as non-invasive versus 44 per cent as invasive. These findings suggest an almost equal distribution of non-invasive and invasive fungal rhinosinusitis in Malaysia.

- **There was an almost equal distribution of invasive and non-invasive fungal rhinosinusitis, as in some other tropical countries**
- **Invasive fungal rhinosinusitis, slightly more uncommon than the non-invasive form, is potentially life threatening**
- **Early and extensive surgical debridement is required for invasive fungal rhinosinusitis treatment**
- **Invasive and non-invasive fungal rhinosinusitis were associated with nasal polyposis and ocular symptoms, respectively**
- **Fungal rhinosinusitis is challenging for otorhinolaryngologists in terms of diagnosis and optimal treatment**

Fungal isolates were more predictable in non-invasive fungal rhinosinusitis. Aspergillus was consistently found in fungal isolates of non-invasive fungal rhinosinusitis cases, whereas unconventional and rarer forms of fungal growth were found in invasive fungal rhinosinusitis cases. This pattern has been observed consistently in other studies conducted worldwide.<sup>12</sup> *Aspergillus fumigatus* and *Aspergillus flavus* were the commonest subtypes of aspergillus isolated in the form of fungal balls in the sinus. This finding shows a similar worldwide distribution, despite the variation in geographical locations.<sup>13–15</sup>

In our experience, surgical debridement was the cornerstone of treatment for both forms of fungal rhinosinusitis. Surgical debridement led to the resolution or improvement of symptoms in fungal rhinosinusitis patients, as only 16.7 per cent of patients under our care required repeated surgical intervention. This suggests that the inflammatory reaction of the fungal material is related to symptom severity, as suggested by some authors previously.<sup>16,17</sup> Most patients in our series who had undergone multiple surgical debridement of the sinuses suffered from acute invasive fungal rhinosinusitis, and the treatment was mainly aimed at preventing further extension of fungal growth. Treatment of acute invasive fungal rhinosinusitis was often complemented with antifungals such as amphotericin B, posaconazole and voriconazole as adjunctive therapy, but this was eventually futile.

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