



# Evaluation of Clinical and Laboratory Findings at Admission in Diabetic Patients with Acute Invasive Fungal Rhinosinusitis

# Original Investigation

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# Abstract

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**Objective:** Acute invasive fungal rhinosinusitis (AIFR) is a disease with rapid progression, and high mortality and morbidity rates. The objective of this study was to retrospectively study the clinical and surgical findings of diabetic AIFR patients who were recently followed up in our clinic, with a view to determining whether these findings are in accordance with the current literature on the subject.

**Methods:** The study cohort comprised 30 patients with a pathological diagnosis of invasive fungal sinusitis who were evaluated at Hatay Mustafa Kemal University Hospital, Department of Otorhinolaryngology, between 2017 and 2022 and subsequently underwent surgical intervention.

**Results:** A total of 30 patients were included in the study. Of these, 16 were male and 14 were female. All patients were diagnosed with diabetes mellitus. The patients were divided into two groups: those who did not survive (n=12) and those who survived (n=18). Significant differences were observed between the groups in age, presence of diabetic ketoacidosis at presentation, skull base involvement, C-reactive protein (CRP), leukocyte, and neutrophil counts at presentation (p=0.013, p<0.001, p=0.024, p=0.013, p<0.001, p<0.001, p<0.001, respectively).

**Conclusion:** In our study, age, the presence of diabetic ketoacidosis at presentation and CRP values were significantly higher in the non-surviving patient group, and this was consistent with the findings of previous studies. The presence of skull base involvement and significantly higher leukocyte and neutrophil values at presentation in the non-surviving patient group could be a new finding to focus on.

**Keywords:** Rhinosinusitis, mucormycosis, fungal infections, diabetes mellitus, diabetic ketoacidosis, prognosis



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# Introduction

Acute invasive fungal rhinosinusitis (AIFR) is a disease characterized by invasive infiltration of the paranasal sinuses and nasal cavity mucosa with mycotic agents, and high mortality and morbidity rates (1,2). Fungal rhinosinusitis is histopathologically classified as invasive or non-invasive, depending on the extent of tissue invasion (2). Noninvasive fungal rhinosinusitis has two subtypes: allergic fungal rhinosinusitis and mycetoma (3). Invasive fungal rhinosinusitis, on the other hand, is classified into three subgroups: acute, chronic, and granulomatous invasive fungal rhinosinusitis. The occurrence of these subgroups is contingent upon the state of the patient's immune system. It is possible for chronic invasive and non-invasive forms to occur in individuals with normal immune systems; however, AIFR is observed in patients with severe immune system disorders (2,3). It is for these reasons that AIFR is defined as the most aggressive type of fungal rhinosinusitis, with high morbidity and mortality. The cause of immune system impairment in AIFR patients may be uncontrolled diabetes, malignancy, immunosuppressive and chemotherapeutic drugs, acquired immunodeficiency syndrome, solid organ transplantation, severe malnutrition, trauma, severe burns, and the recently described infection caused by the coronavirus disease 2019 (COVID-19) virus (4). In the existing literature, the reported mortality rates vary considerably, from 20% to 80%. However, majority of the studies reported mortality rates above 40% (5-8).

The objective of this study was to retrospectively study, and review in reference to the current literature, the clinical and surgical findings of diabetic AIFR patients who presented to the emergency department and were treated and followed up in our clinic. We hypothesized that there would be significant differences between the clinical and laboratory data of the surviving and non-surviving groups.

## Methods

The study was planned to include all patients who were diagnosed with histopathologically invasive fungal sinusitis and underwent surgical intervention at the Otolaryngology Department of Hatay Mustafa Kemal University Hospital from 2017 to 2022. Thirty patients with a histopathological diagnosis who underwent surgical intervention were retrospectively identified and included in the study. Patients who did not have a histopathological diagnosis of invasive fungal sinusitis, did not undergo surgery, and did not have diabetes were excluded. All patients were provided with strict glycemic control in collaboration with the endocrinology department. The diagnosis of invasive fungal sinusitis was determined by the presence of the appropriate clinical findings, endoscopic and radiological evidence of necrotic tissue, and histopathological confirmation of fungal invasion.

Given the exigencies of the disease, culture confirmation was deemed unnecessary; instead, histopathological detection of invasion was considered sufficient for intervention. Medical treatment was started in a timely manner for all patients with clinical suspicion. Liposomal amphotericin B was administered as a medical agent, intravenously and locally using cotton pads, at a dose of 5-10 mg/kg/day, over a period of 30-60 minutes, for 6-8 weeks. The surgical approach employed for these patients was determined by the extent of the pathology. In cases where the involvement was confined to the paranasal sinuses, endoscopic surgery was employed. Conversely, in cases with palatal, dermal, or orbital involvement, a combined approach was the preferred surgical modality. The objective of the surgical intervention, whether endoscopic or combined, was to thoroughly excise the necrotic tissue up to vital structures, such as the skull base and major vascular structures. The debridement procedure was continued until the perfused tissue became visible, and residual tissue was left only if within vital boundaries. In cases of orbital spread, the procedure was carried out together with the ophthalmology department. Orbital spread was assessed clinically and using magnetic resonance imaging, and the decision to perform exenteration was made together with the ophthalmology department based on parameters such as vision, pupil reflexes, ocular motility, advanced fundus changes, orbital apex involvement, and proptosis associated with orbital involvement. Demographic data, laboratory data, and clinical findings at the time of admission, underlying diseases, pathology results, and outcomes of patients were reviewed. The study was approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (approval no: 21, date: 01.09.2022).

# Statistical Analysis

Statistical analysis was conducted using the IBM SPSS Statistics version 23 package program (IBM Corporation, Armonk, NY, USA). The data were calculated as mean±standard deviation or percentage. In the statistical analysis, the distribution of the groups was studied using the Kolmogorov-Smirnov test. The independent samples t-test was employed for comparisons between two groups for continuous variables that exhibited a normal distribution, whereas the Mann-Whitney U test was utilized for comparisons between two groups for continuous variables that did not conform to a normal distribution. Comparisons between categorical variables were conducted using Pearson's chi-squared test and Fisher's exact test. The level of statistical significance was set at p<0.05.

#### Results

The study cohort comprised 30 patients of whom 16 were male and 14 were female. The age of the patients ranged from 28 to 79 years, with a mean of 59.46±12.54 years. The

demographic data, clinical information and comorbidities of the patients are presented in Table 1. All patients were diagnosed with diabetes mellitus. The second most prevalent comorbidity was hypertension, occurring in 30% of the cases. No patients presented with a hematological or other systemic malignancy. A history of steroid treatment for a previous infection with the COVID-19 virus was present in seven patients (23.3%) within the last six months. A single patient (3.3%) was identified as having an active case of COVID-19 at admission from the emergency department. Following the examination of the biopsy materials, it was determined that mucor from the mucoraceae family was the responsible pathogen in 28 cases (93.3%), while aspergillus was identified in two cases (6.7%). In 10 patients, a purely endoscopic approach was deemed sufficient (33.3%), while in the remaining 20 patients, an endoscopic and open surgical approach was necessary (66.6%).

The clinical findings at the time of initial presentation are given in Table 2. The most prevalent clinical manifestation observed in all patients (100%) was facial pain. The second most prevalent clinical finding was facial fullness, occurring in 86.7% of cases. Other common clinical findings included ophthalmoplegia (66.7%), diplopia (63.3%), visual loss

**Table 1.** Demographic data, associated comorbidities, causative organisms, surgical approach, and outcomes of patients

Variable	Number	Frequency (%)
Total cases	30	100
Age (years) (mean±SD)	59.46±12.54	
Sex		
Male	16	53.3
Female	14	46.7
Comorbidities		
DM	30	100
НТ	9	30
CAD	5	16.7
Asthma	2	6.7
COVID-19 (active)	1	3.3
Post-COVID-19	7	23.3
Organism		
Mucor	28	93.3
Aspergillus	2	6.7
Surgical approach		
Endoscopic	10	33.3
Open+endoscopic	20	66.7
Orbital exenteration	14	46.7
Outcomes		
Did not survive	12	40
Survived	18	60
DM: Diabetes mellitus, HT: Hype	ertension, CAD: Corona	rv artery disease.

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, COVID-19: Coronavirus disease 2019, SD: Standard deviation

**Table 2.** Clinical and examination findings at the time of admission

Variable	Number	Frequency (%)
Fever	4	13.3
Facial pain	30	100
Nasal discharge	9	30
Ophthalmoplegia	20	66.7
Proptosis	17	56.7
Diplopia	19	63.3
Visual loss	18	60
Altered mental state	10	33.3
Palatal necrosis	12	40
Facial paralysis	13	43.3
Septal perforation	9	30
Diabetic ketoacidosis	13	43.3

(60%) (Figure 1) and proptosis (56.7%). Ketoacidosis was observed in 13 patients at the time of presentation (43.3%). Thirteen patients exhibited facial paralysis (43.3%), and 12 demonstrated palatal necrosis (40%) (Figures 1 and 2). Four patients exhibited fever at the time of initial presentation, while no fever was observed in the remaining patients.

Review of the laboratory findings of the patients at the time of admission, revealed that all patients exhibited hemoglobin A1c values above the normal range, with a mean of 10.26±2.2%. In addition, the laboratory findings of the patients at the time of admission included evaluations of other parameters, including C-reactive protein (CRP), haemoglobin, platelet, lymphocyte, leukocyte, and neutrophil counts. The data related to these parameters are presented in Table 3.

The degree of involvement of the nasal and paranasal sinuses was evaluated both radiologically and intraoperatively. The radiological data demonstrated a range of findings, from mucosal thickening to the presence of osteomyelitis in the affected area. In intraoperative debridement, the most crucial factor was the presence or absence of a blood supply in the affected region. The data indicated that the most frequently affected sites were the lateral nasal wall (100%), the maxillary sinus (100%), and the ethmoid sinus (96.7%). Twenty patients exhibited orbital involvement, representing a prevalence of 66.7%. A detailed account of the clinical dissemination of the patients is provided in Table 4.

Review of the patient outcomes in terms of mortality showed that 60% (18 patients) had recovered, whereas 40% (12 patients) succumbed to their conditions. The patients were divided into two groups, namely, those who did not survive (n=12) and those who survived (n=18), and a statistical comparison was conducted. Further details of this evaluation can be found in Table 5. Statistically significant differences were observed between the two groups in terms of age, the



Figure 1.a) Postoperative follow-up image of a patient with facial paralysis among the admission findings, b) preoperative examination image of a patient with eye involvement



Figure 2. a) Preoperative view of a patient with palate involvement, b) postoperative view of another patient with palate involvement

presence of diabetic ketoacidosis (DKA) at presentation, skull base involvement, CRP levels, white blood cell (leucocyte) counts, and neutrophil counts at presentation (p=0.013, p<0.001, p=0.024, p=0.013, p<0.001, p<0.001, p<0.001, respectively).

The results of the receiver operating characteristic (ROC) analysis indicated that the optimal cut-off value for CRP in predicting invasive fungal sinusitis was 93.45 mg/L, with sensitivity and specificity of 75% and 72.2%, respectively [area under the curve (AUC): 0.782; 95% confidence interval (CI): 0.61-0.96]. The optimal cut-off value was determined to be  $93.45 \times 10^3 / \mu L$  for neutrophil count and  $15.55 \times 10^3 / \mu L$ 

for leukocyte count, with sensitivity and specificity values of 100%-92% and 100%-94%, respectively (AUC: 1; 95% CI: 1-1, AUC: 0.995; 95% CI: 0.98-1, respectively) (Table 6).

## Discussion

Initial symptoms in patients with AIFR are not distinctive. Patients frequently present with non-specific initial symptoms of acute-chronic rhinosinusitis. In literature, the most commonly reported presenting symptoms are fever, facial swelling, nasal congestion, and facial pain, with varying rates of occurrence (1-3,5). In a systematic review of 52 studies and 807 patients conducted by Turner et al.

<b>Table 3.</b> Laboratory findings at the time of admission			
Variable	Number (mean±SD)		
HbA1c	10.26±2.2 %		
CRP	111.75±70.34 mg/L		
Нь	11.38±1.93 g/dL		
Platelet	332.17±126.65 10³/μL		
Lymphocyte	1.82±0.87 10³/μL		
Leukocyte	$14.48\pm6.16\ 10^3/\mu L$		
Neutrophil	11.43±5.75 10³/μL		
ODD 0			

CRP: C-reactive protein, HbA1c: Hemoglobin A1c, Hb: Hemoglobin, SD: Standard deviation

Table 4. Clinical extension	n of patients	
Variable	Number	Frequency (%)
Nasal		
Maxillary	30	100
Ethmoid	29	96.7
Sphenoid	23	76.7
Frontal	21	70
Lateral nasal wall	30	100
Septum	9	30
Orbital involvement	20	66.7
Intracranial involvement	5	16.7
Skull base involvement	12	40
Palate	12	40
Skin	5	16.6

(6), the most common presenting symptoms were identified as facial swelling, fever, and nasal congestion, respectively. Depending on the progression of the disease at the time of presentation, early symptoms may include facial pain, nasal congestion, and nasal discharge. Symptoms such as visual loss, proptosis, diplopia, blurred vision, facial swelling, and facial paralysis may also be observed in patients presenting in the advanced stage. When the patients in our study were examined clinically, radiologically, and surgically, it was found that most of them presented in the advanced stage. The most commonly observed symptom in our patient cohort was facial pain, which was present in 100% of the cases. Other common symptoms included facial fullness, ophthalmoplegia, diplopia, visual loss, and proptosis. In contrast to the findings of previous studies, the prevalence of the first five most common symptoms was higher in our sample. It is postulated that this may be attributable to the fact that majority of the patients admitted to the facility exhibited advanced dissemination.

As the symptoms of AIFR disease are non-specific, the examination findings are of greater significance. In literature, the earliest examination finding is reported to be a change in the appearance of the nasal mucosa (1,3,5,9,10). In the initial stages, the presence of white discoloration is indicative of ischemia, whereas in the later stages, black discoloration suggests the onset of necrosis. Mucosal discoloration may be observed in the entirety of the nasal mucosa. In numerous references in literature, the most prevalent site of this alteration is the middle turbinate (1,3,5,8-10). Subsequently,

Variable	Survived (n=18)	Not-survived (n=12)	p-value	95% CI
Age (years) (mean±SD)*	54.94±10.74	66.25±12.36	0.013	2.6-20
Sex				
M	44.4%	66.7%	0.232	
F	56.6%	33.3%		
Fever	1	3	0.274	
Diabetic ketoacidosis*	1	12	<0.001	
Orbital involvement	11	9	0.694	
Intracranial involvement	1	4	0.128	
Skull base involvement*	4	8	0.024	
Facial paralysis	9	5	0.654	
COVID-19	5	3	1.000	
HbA1c (mean±SD)	10.41±2.29%	10.03±2.12%	0.652	-2.08-1.32
CRP*	86.43±63.82 mg/L	$149.74 \pm 64.24 \text{ mg/L}$	0.013	14.47-112.16
Hb	11.48±2.09 g/dL	$11.23\pm1.74~\mathrm{g/dL}$	0.744	-1.74-1.25
Platelet	$370.33\pm131.18\ 10^3/\mu L$	$299.92 {\pm} 80.80 \ 10^{3} / \mu L$	0.109	-157.5-16.7
Lymphocyte	$2.09\pm0.96\ 10^3/\mu L$	$1.60 \pm 0.37 \ 10^3 / \mu L$	0.060	-1.01-0.02
Leukocyte*	$10.11\pm2.89\ 10^3/\mu L$	$21.02\pm3.03\ 10^3/\mu L$	<0.001	8.66-13.16
Neutrophil*	7.28±2.54 10³/μL	17.66±2.62 10 <sup>3</sup> /μL	<0.001	8.41-12.34

the nasal septum, nasal floor and inferior turbinate are examined. Furthermore, the absence of pain during endoscopic examination suggests mucosal anesthesia and is indicative of fungal invasion. Table 4 shows the clinical manifestations observed in the patients included in this study. Accordingly, the most common site of involvement in our patients was the maxillary sinus and the lateral nasal wall, affecting 100% of the cases. The second most common site of involvement was the ethmoid sinuses, with a prevalence of 96.7%. In accordance with the findings in the existing literature, we proceeded to obtain full-thickness biopsies from the nasal cavity areas exhibiting suspicious characteristics, with a particular focus on the middle turbinate.

In literature, the most common computed tomography finding in cases of AIFR is reported to be intranasal or sinus mucosal thickening (3,5,9,11). In their study, Silverman and Mancuso (12) proposed that periantral adipose tissue infiltration could be the earliest radiological finding, and that bone erosion and destruction are indicative of the disease's advanced stages. Magnetic resonance imaging is a more effective method for demonstrating the extent of disease spread to the surrounding soft tissues, differentiating mucus edema, and identifying instances of extra-sinus involvement (3,5). In our study, radiological imaging proved an effective tool in the process of clinical suspicion, determination of the margins of invasion and prediction of the surgical margins to be applied (Figures 3 and 4).

Even when the patient's clinic, endoscopic examination, laboratory data, and imaging findings are consistent with AIFR, a definitive diagnosis can only be reached through a histopathological examination of the biopsy tissue. During endoscopic examination, both suspicious foci should be identified, and biopsies should be taken from these suspicious areas. Given that the middle turbinate is the most commonly reported site of fungal invasion in literature, it would be an appropriate decision to select this site for biopsy (1,3,5,8-10). The presence of fungal elements in the mucosal biopsy may be considered indicative of invasive fungal rhinosinusitis until proven otherwise (13). Süslü et al. (1) argued that mucosal biopsies had limited utility due to the potential for false-positive and false-negative results, bleeding complications, and the risk of creating mucosal damage susceptible to subsequent Aspergillus invasion. In contrast, the authors propose that a deep biopsy, encompassing the mucosa, submucosa, and potentially even the cartilage tissue, should be conducted under operating theater conditions with the use of electrocautery. It is of the utmost importance to perform early debridement to effectively manage the disease. In the early stages of the disease, an endoscopic approach may be sufficient; however, in advanced disease, additional procedures such as orbital exenteration, fascial resection, or maxillectomy may be necessary. In the presented study, endoscopic approach was sufficient in 10 patients, while endoscopic and open approaches were required in 20 patients.

Table 6. ROC analysis of patients' admission values					
Variable	AUC (95% CI)	Cut-off	p-value	Sensitivity (%)	Specificity (%)
CRP	0.782 (0.61-0.96)	93.45	0.01	75	72.2
Neutrophil	1 (1-1)	12.93	<0.001	100	100
Leukocyte	0.995 (0.98-1)	15.55	<0.001	92	94

AUC: Area under curve, CI: Confidence interval, ROC: Receiver operating characteristic, CRP: C-reactive protein

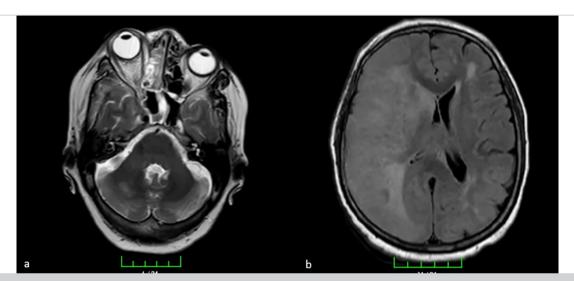
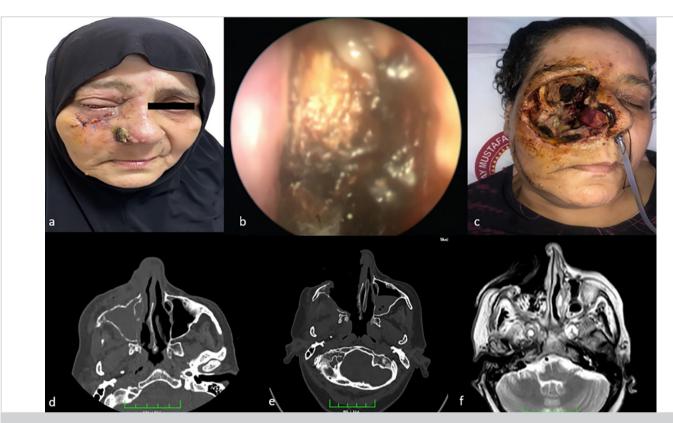


Figure 3. Patient with intracranial involvement a) eye extension and conspicuous proptosis, b) intracranial involvement



**Figure 4. a)** Image of an AIFR patient with skin involvement at presentation, **b)** endoscopic view of the same patient at admission, **c)** view of the operation site after surgical debridement, **d)** preoperative CT image of the patient. Periantral and premaxillary adipose tissue involvement and bone erosion and decalcification are worth noting, **e)** postoperative CT imaging **f)** postoperative MR imaging MR: Magnetic resonance, CT: Computed tomography, AIFR: Acute invasive fungal rhinosinusitis

A total of 14 patients underwent orbital exenteration. In cases where the pathology to be debrided was limited to areas accessible via endoscopy, an endoscopic approach was the preferred method.

In some studies, parameters such as diabetes, delayed diagnosis, orbital and intracranial involvement, advanced age, and neutropenia were identified as negative prognostic factors (6,14-17). In their systematic review conducted to identify the prognostic factors and survival outcomes, Turner et al. (6) identified impaired mental status, intracranial invasion, renal/liver failure, diabetes, and advanced age as the factors predictive of decreased survival, and surgical intervention, endoscopic surgical intervention, and the use of liposomal amphotericin-B in medical treatment as positive prognostic factors. Mahomva et al. (18) posited that an elevated body temperature of unknown origin, low platelet levels and low neutrophil levels would indicate increased risk. The parameters used in the comparison of surviving and nonsurviving groups are provided in Table 5. The comparison of the two groups based on these parameters yielded significant results regarding age, the presence of diabetic ketoacidosis (DKA) at presentation, involvement of the skull base, CRP value, and high leukocyte and neutrophil values. Advanced age and the presence of DKA at the time of presentation were identified as negative prognostic factors in numerous studies

in literature. In a study of 11 patients, Butugan et al. (19) determined a mortality rate of 27.3%. The authors observed that all three patients who succumbed to their illness had DKA at the time of their initial presentation, which was identified as a negative prognostic factor. The findings of our study align with those of previous studies in that advanced age and the presence of DKA at the time of presentation yielded significant results. The relationship between CRP value and AIFR has been the subject of numerous published studies. As reported by Cho et al. (20), elevated CRP was identified as an independent prognostic factor in patients with AIFR. In our study, a significant difference was observed between the surviving and non-surviving groups in terms of high CRP value, and this is consistent with the literature (p=0.013). The results of the ROC analysis indicated that the optimal cut-off value for CRP in predicting invasive fungal sinusitis was 93.45 mg/L, with sensitivity and specificity of 75% and 72.2%, respectively (AUC: 0.782; 95% CI: 0.61-0.96).

Skull base involvement is a common occurrence in patients with AIFR. In a study conducted by Monroe et al. (15), 10 out of the 29 patients observed exhibited skull base involvement. No significant findings were noted when comparing the surviving and non-surviving patients in this regard. In our study, 12 patients had skull base involvement, which was significantly more prevalent in the non-surviving

group (p=0.024). Although skull base involvement is not typically considered a prognostic factor in the literature, and recent meta-analyses have not identified it as a significant predictor, we believe that our findings are nevertheless noteworthy. According to the available literature, orbital and intracranial involvement are generally considered as poor prognostic factors (5). In their study, Turner et al. (6) stated that patients with intracranial involvement had the lowest survival rate. Moreover, the involvement of the orbit has been identified as a risk factor for overall survival in numerous studies (6,21,22). The presented study revealed no statistically significant differences between the surviving and non-surviving groups in terms of intracranial or orbital involvement. The patients' presentation to the emergency department at a late stage, the timing of surgical treatment, non-diabetes-related comorbidities, and medical treatment may have functioned as confounders in this regard.

The results of our study showed that neutrophil and leukocyte counts at admission were significantly higher in non-surviving patients compared to survivors. In the ROC analysis, the optimal cut-off values for predicting invasive fungal sinusitis were  $93.45\times10^3/\mu L$  for neutrophils and  $15.55\times10^3/\mu L$  for leukocytes. These thresholds yielded sensitivities of 100% and 100% and specificities of 92% and 94%, respectively (AUC 1.00; 95% CI: 1.00-1.00 and AUC 0.995; 95% CI: 0.98-1.00).

In the literature, neutrophil recovery has been identified as a positive prognostic factor, particularly in patients with hematological malignancies (23). Gardner et al. (24) reported that 94% of their 21 patients had hematological malignancy and an absolute neutrophil count ≤1×10³/µL at diagnosis. Similarly, Gode et al. (25) showed that leukocyte and neutrophil counts, along with CRP levels, significantly influenced survival. Navuluri et al. (26) also observed that patients with hematological malignancies typically presented with low neutrophil counts and elevated CRP values. Overall, most studies evaluating neutrophil counts have focused on patients with hematological malignancies, whereas data on diabetic patients remain scarce.

Our findings indicate a statistically significant elevation in neutrophil and leukocyte counts at admission in a patient cohort composed exclusively of diabetic individuals without underlying malignancy. This represents a novel and clinically relevant observation that diverges from prior literature and may suggest a different host response profile in this population.

## **Study Limitations**

The limitations of our study include the retrospective design, the small number of patients and the experience of a single tertiary healthcare institution. It is our belief that future studies with larger numbers of patients, and comparative studies will prove beneficial. The homogeneity of our patient cohort, consisting exclusively of individuals with diabetes, represents a key strength of our study, in contrast to the heterogeneous patient groups observed in other studies, including those involving patients with hematological malignancies or mixed patient populations.

### Conclusion

In diabetic patients with AIFR, it should be considered that the possible pathogen may be mucor from the mucoraceae family. In our study, age, presence of DKA at presentation and CRP levels were significantly higher in the non-surviving group. In the surviving group, skull base involvement, leukocyte and neutrophil levels at presentation were statistically significantly higher, which may be a new finding to focus on.

#### **Ethics**

Ethics Approval: The study was approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (approval no: 21, date: 01.09.2022).

**Informed Consent:** Retrospective study.

#### **Footnotes**

#### **Authorship Contributions**

Surgical and Medical Practices: M.İ.G., E.A., M.Ç., D.G., Ş.O., Concept: M.İ.G., E.A., Ş.O., Design: M.İ.G., E.A., Ş.O., Data Collection and/or Processing: M.İ.G., F.K., Analysis or Interpretation: M.İ.G., F.K., Ş.O., Literature Search: M.İ.G., F.K., Writing: M.İ.G.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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#### **Main Points**

- Acute invasive fungal rhinosinusitis (AIFR) is a disease characterized by invasive infiltration of the paranasal sinuses and nasal cavity mucosa with mycotic agents, with high mortality and morbidity rates.
- Initial symptoms in patients with AIFR are not distinctive, patients often present with non-specific initial symptoms of acute-chronic rhinosinusitis.
- A definitive diagnosis can only be reached through a histopathological examination of the biopsy tissue.
- In our study, age, presence of diabetic ketoacidosis at presentation and C-reactive protein levels were significantly higher in the non-surviving group.
- In the non-surviving group, skull base involvement, leukocyte and neutrophil levels at presentation were statistically significantly higher, which may be a new finding to focus on.

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