Journal of Population Therapeutics & Clinical Pharmacology

ORIGINAL RESEARCH ARTICLE
DOI: 10.53555/5h8f8n97

CLINICAL PROFILE OF MUCORMYCOSIS MAXILLOFACIAL REGION

Dr. Tirumalrao [1*], Dr. Bapugouda Mulimani [2], Dr. Jyothi L. [3], Dr. Amarvarma [4], Dr. Shweta Danaraddi [5], Dr. Geeta marishetter [6]

[1*] Associate Professor, Department of Dentistry, Raichur Institute of Medical Sciences, Raichur, Karnataka, India.
[2] Assistant Professor, Department of Dentistry, Raichur Institute of Medical Sciences, Raichur, Karnataka, India.
[3] Professor, Department of Dentistry, Navodaya Dental College, Raichur, Karnataka, India.
[4] Professor, Department of Dentistry, Raichur Institute of Medical Sciences, Raichur, Karnataka, India.
[5] Junior Resident, Department of Dentistry, Raichur Institute of Medical Sciences, Raichur, Karnataka, India.
[6] Junior Resident, Department of Dentistry, Raichur Institute of Medical Sciences, Raichur, Karnataka, India.

***Corresponding Author:** Dr. Tirumalrao
*Associate Professor, Department of Dentistry, Raichur Institute of Medical Sciences, Raichur, Karnataka, India.

ABSTRACT

BACKGROUND: Mucormycosis is a rare, rapidly spreading, fulminant, opportunistic infection that is caused by a group of filamentous molds. The present study was done to know the clinical profile of mucormycosis in the oral cavity, nose and paranasal sinus & to plan early diagnosis & treatment.

METHODS: The present prospective study was conducted at MRD Dept RIMS teaching Hospital, Raichur during the February 2021 to December 2022 among 100 patients diagnosed with mucormycosis were selected on the basis of inclusion and exclusion criteria. Each case's clinical and laboratory data were carefully documented utilizing a systematic proforma.

RESULTS: The mean age of patients was 50.23 years. The number of male patients was 63 and female patients were 37. Out of all the 100 patients 67 had hypertension, 55 had diabetes mellitus. Most structures involved clinically were sinus (34), palatal ulceration (37), mucosal erythema (60), tooth pain (48), mucosal edema (45), bone necrosis (34). Involvement of different structures was seen radiographically like maxillary sinus (91), ethmoid sinus (78), sphenoid sinus (60), frontal sinus (43), orbit (41), optic nerve (4), cranial (3), osteolysis (92), osteosclerosis (8) and soft tissue and spaces (43). The most common treatment used was FESS (97). Mortality was associated with 1 patient.

CONCLUSION: Early indications and oral symptoms of mucormycosis are crucial in promptly diagnosing and treating patients to decrease the risk of death and illness.

KEYWORDS: Fungal, Infection, Morbidity, Mortality, Mucormycosis, Mycosis

INTRODUCTION

Phycomycosis or zygomycosis was initially described by Palatauf in 1885. In 1957, American Pathologist Baker coined the word "mucormycosis" to describe a highly aggressive infection caused by the fungus Rhizopus.The text is enclosed in the tags.[1-3]

Mucormycosis is an infrequent yet deadly fungal illness that typically occurs in individuals with compromised immune systems. Mucormycosis is a pathogenic condition characterized by the invasion of blood vessels by fungi belonging to the genus of mold Rhizopus, order Mucorales, and class Zygomycetes.[4,5]

The early symptoms of the maxillofical region muscormycosis variation encompass discomfort and inflammation in the face, protrusion of the eyeball, and impaired vision. Subsequently, there is necrosis of the mucous membrane in the palate, loss of eyesight, and in advanced stages, the condition may progress to cavernous sinus thrombosis, ultimately resulting in fatality.[6] Additionally, it might present as dental pain and movement of upper jaw teeth, together with the development of abscesses and limited jaw mobility.[7,8] Mucormycosis can have a death rate of up to 50% or more, particularly in cases when patients have widespread and aggressively invasive diseases.[9] The disease's angioinvasive characteristics frequently lead to thrombosis and vasculitis, resulting in necrosis of significant bone and tissue regions. Devitalization of large sections of skin and soft tissues exacerbates the prognosis, as medication absorption is limited in these tissues.[10,11]

Magnetic resonance imaging (MRI) and computed tomography (CT) are the predominant forms of diagnostic imaging employed in complementary and alternative medicine (CAM). MRI has the benefit of being able to assess the extent of fungal invasion, while CT is more effective in identifying bone loss that happens in the advanced stages of infection. Due to its superior resolution, CBCT is typically used to precisely visualize subtle changes in the bone structure and trabecular patterns in the upper jaw and surrounding areas. These changes are often not detectable on the soft tissue algorithms used in CT and MRI scans. Performing microbiological and/or histological investigation on tissues extracted from different lesions can offer a conclusive diagnosis.[12]

Available treatment options for mucormycosis include vigorous removal of contaminated hard and soft tissue and intravenous administration of antifungal medications such as Liposomal Amphotericin B, lipid Amphotericin B, Posaconazole, and itraconazole. Functional endoscopic sinus surgery (FESS) is a minimally invasive surgical procedure that employs an endoscope to remove debris from the paranasal sinuses. It is commonly performed in cases of rhinomaxillary mucormycosis, a fungal infection.[13]

The most often recorded form of mucormycosis in literature is rhinomaxillary mucormycosis. Additionally, there have been several recently published papers and case series that have documented comparable findings.[14,15] Hence the present study was done to know the clinical profile of mucormycosis in the oral cavity, nose and paranasal sinus & to plan early diagnosis & treatment.

MATERIAL AND METHODS

The present prospective study was conducted at MRD Dept RIMS teaching Hospital, Raichur during the February 2021 to December 2022. Ethical clearance was taken from institutional ethics committee before commencement of study. Patients were asked to sign an informed consent form after explaining them the complete procedure.

Through convenience sampling a total of 100 patients diagnosed with mucormycosis were selected on the basis of inclusion and exclusion criteria. The diagnosis of mucormycosis was based on clinical, radiological and/or biopsy samples of the infected tissue collected during the study period.

Inclusion Criteria

- Patients admitted to hospital with severe nasal blockage nasal discharge head ache, pain in maxillary region, multiple teeth mobility of maxillary region, ulcers in gingiva & palate with alveolus.
- Patients who are radiologically diagnosed with mucormycosis by CT scan (plain & contrast), MRI of brain &PNS maxilla, CBCT Of maxilla, nasal and paranasal sinus.

Exclusive Criteria

- Patients with maxillofacial injury trauma
- Patients with maxillofacial cysts &tumors [head & neck]
- Patients with malignancy of head & neck

A comprehensive medical history was acquired from the clinical chart of each participant. As part of the treatment, data from clinical assessments, including examinations of the maxillofacial region, as well as baseline haematological and biochemical studies, were obtained. Each participant had contrast-enhanced magnetic resonance imaging of affected area as well as computed tomography of the paranasal sinuses, in order to assess the extent of the disease and tissue invasion. The findings were recorded and organized.

Each case's clinical and laboratory data were carefully documented utilizing a systematic proforma. The data comprised demographic characteristics, initial clinical symptoms and signs, imaging specifics, surgical interventions, kind and duration of antifungal treatment, follow-up imaging details, and morbidity and death outcomes.The data collected was analysed statically using descriptive analysis. The results are depicted in the form of percentages, bar diagrams, histograms & graphs where ever required.

RESULTS

The mean age of patients was 50.23 years. The number of male patients was 63 and female patients were 37. Out of all the 100 patients 67 had hypertension, 55 had diabetes mellitus, 32 had renal disease and 30 had myocardial infarction as shown in table 1.

Characteristics	**Values**
Mean age (years)	50.23±10.21
Male	63
Female	37
Hypertension	67
Diabetes mellitus	55
Renal disease	32
Myocardial infarction	30

Table 1: Demographic data of patients with risk factors involved

Maxilla was involved in 91 patients and mandible was involved in 9 patients as shown in figure 1.

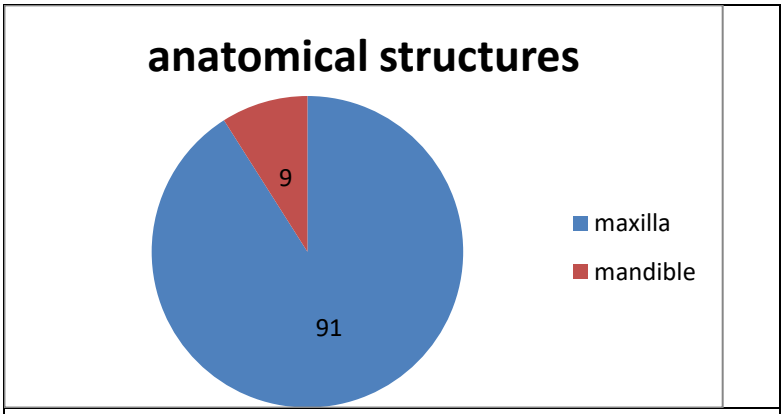

Figure 1: Anatomical structures involved

The clinical presentation is as follows - sinus (34), palatal ulceration (37), mucosal erythema (60), tooth pain (48), mucosal edema (45), bone necrosis (34), facial swelling (66), paraesthesia (90), nasal discharge (24), orbital involvement (43) and cranial involvement (2) as shown in figure 2.

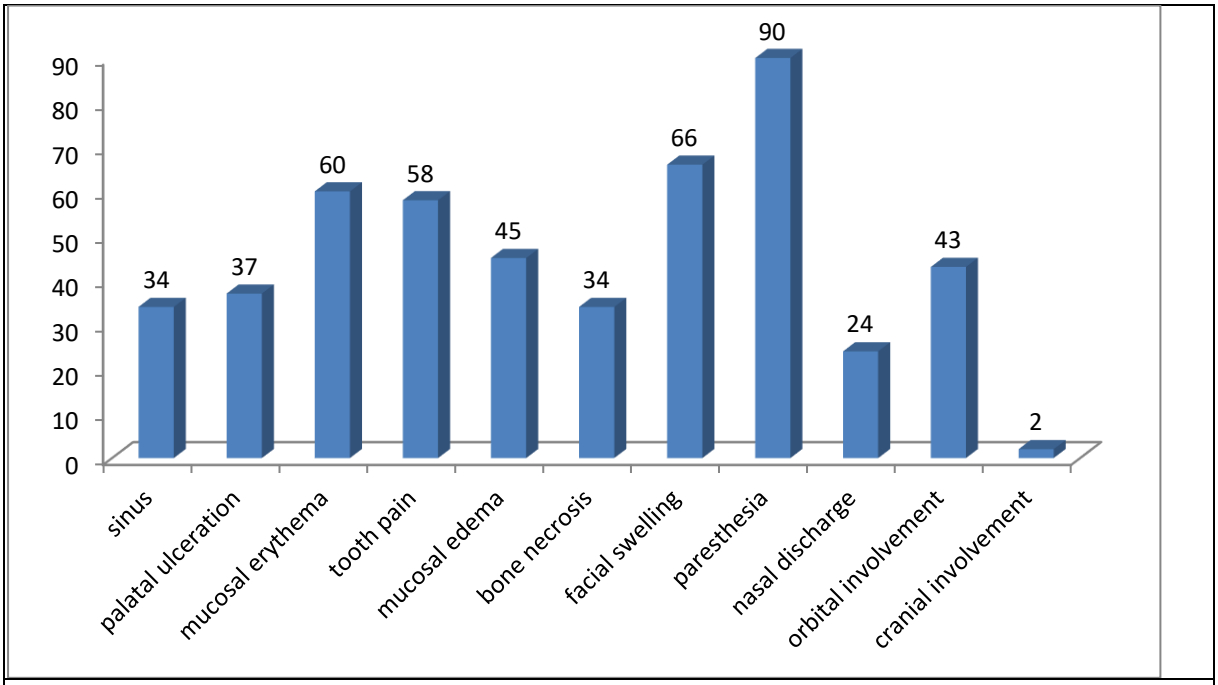

Figure 2: Clinical presentations of patients with mucormycosis

Involvement of different structures was seen radiographically like maxillary sinus (91), ethmoid sinus (78), sphenoid sinus (60), frontal sinus (43), orbit (41), optic nerve (4), cranial (3), osteolysis (92), osteosclerosis (8) and soft tissue and spaces (43) as shown in figure 3.

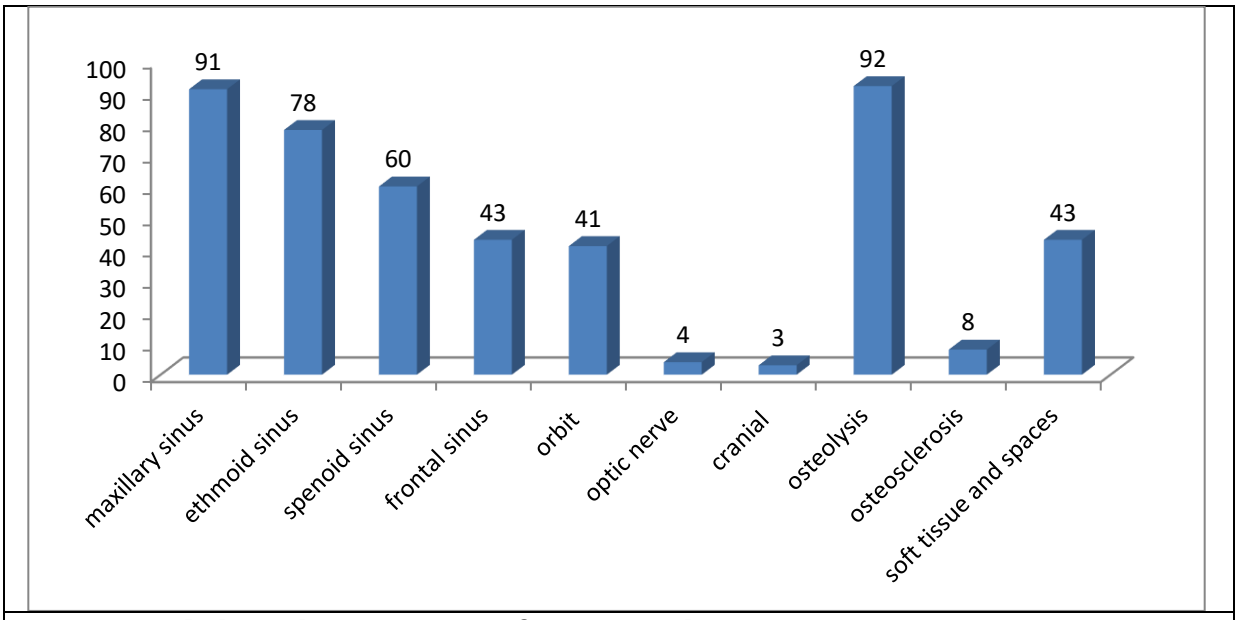

Figure 3: Radiological presentations of patients with mucormycosis

The treatment provided were FESS in 97 patient, micro-debridement of orbit in 5 patient, orbital decompression in 3 patient, partial maxillectomy in 40 patients, alvolectomy in 60 patient, subtotal maxillectomy in 2 patients and debridement in 1 patient. Mortality was associated with 1 patient as shown in table 2.

Parameter		Value
Treatment provided	FESS	97
	Micro-debridement of orbit	5
	Orbital decompression	3
	Partial maxillectomy	40
	Alvolectomy	60
	Subtotal maxillectomy	2
	debridement	1
Mortality associated		1

Table 2: Treatment provided and mortality associated with mucormycosis patient

DISCUSSION

Globally, the occurrence of mucormycosis ranges from 0.005 to 1.7 cases per million people. This fungal infection is more prevalent in India, with a rate approximately 80 times higher (0.14 per 1000) compared to affluent nations.[16] This is an uncommon fungal infection that starts in the paranasal sinuses and often spreads to the orbits and cerebral parenchyma.[17] The Zygomycetes are composed of the orders Mucorales and Entomophthorales. The order Mucorales has six families of fungus, all of which can result in cutaneous and deep infections. These illnesses, known as mucormycosis, primarily affect individuals with weakened immune systems, regardless of whether they reside in poor or industrialised nations.[18] Rhizopus oryzae, also known as Rhizopus arrhizus, is the predominant species of the Mucoraceae family that is commonly found in patients with mucormycosis.[19] Entomophthorales are infrequent etiological agents of subcutaneous and mucocutaneous infections, specifically referred to as entomophthoromycosis. These diseases predominantly occur in immunocompetent individuals residing in underdeveloped nations.[20]

Prior studies and evaluations indicate that the age range for Mucormycosis spans from 10 to 86 years, with a median age of approximately 55 years.[21,22] In our study, we observed that the average age of the participants was 50.23 years. Patel A et al also found that patients had a higher mean age of 56.9 years compared to those with non-CAM who had a mean age of 46.9 years. This age difference could potentially increase their susceptibility to a greater risk of mortality.[23]

In our study, we observed a comparable pattern of gender distribution. Additionally, there has been a greater prevalence of mucormycosis in males within the non-CAM population.[24,25] This could be a plausible explanation for this observation. It could also be due to the fact that males in the Indian population engage in more outside activities than females, which increases their exposure to inhaling fungal spores. One possible explanation for this phenomenon is the presence of hormonal and sexual differences in immune response. Specifically, females tend to exhibit more efficient cell-mediated and humoral pro-inflammatory responses compared to males.[26]

In our study the most associated risk factor with disease were hypertension and diabetes mellitus. A study conducted by Gupta et al in 2021 revealed that a significant proportion of individuals exhibited diabetes.[23] Notably, the vast majority of the documented cases of mucormycosis originated from India. An extensive analysis of 101 instances of mucormycosis reported worldwide in July 2021 unveiled that 80% of patients had diabetes, while 76% of patients had utilised steroids.[1] An extensive nationwide investigation found that diabetes mellitus is the prevailing condition in 79% of individuals with mucormycosis, whereas steroid use is prevalent in 87% of them.[27]

Nearly 90% of the patients exhibited paraesthesia as their first symptom, followed by face swelling, mucosal erythema, tooth discomfort or mobility, mucosal oedema, orbital involvement, bone necrosis, palatal ulceration, sinus or abscess formation, nasal discharge, and cranial involvement. Our study's findings align with those of Motevasseli S. et al. and Sharma S. et al., who similarly found that intra-orbital involvement is frequent whereas intra-cranial involvement is infrequent. In Sen M. et al.'s investigation, it was shown that 16% of rhino-orbital mucormycosis cases had intra-cranial involvement.[12,15,28]

Mucormycosis is radiologically identified by the presence of thickened mucosal lining and cloudiness in the sinuses, as well as brain swelling, inflammation, or tissue death.[8] This study

examined various radiographic criteria, including the maxillary sinus, ethmoidal sinus, sphenoid sinus, frontal sinus, orbital involvement with or without the optic nerve, cranial involvement, osteolysis, and osteosclerosis. The majority of patients in this study exhibited maxillary sinus involvement in addition to osteomyelitic alterations. In contrast to a study conducted by Sharma S et al., it was shown that ethmoidal sinus involvement was present in all instances, followed by maxillary sinus, sphenoid sinus, and frontal sinus.[28] An exhaustive assessment of these factors may aid in comprehending the trajectory of illness transmission.

The majority of patients with sinus involvement underwent functional endoscopic sinus surgery (FESS) while under general anaesthesia. Surgical removal of the jaw bone was performed, taking into account the specific location affected. The masticatory function was lost as a result of bone excision. The observed mortality rate was 1%, potentially attributed to prompt diagnosis and intensive treatment. It is worth noting that the death rate of reported cases from India (36.5%) is lower than the global fatality rate (61.9%). This difference may be attributed to the prevalence of rhinomaxillary mucormycosis, a kind of mucormycosis.[29]

Limitation

As this was a single centre study we could not assess the correct prevalence of mucormycosis.

CONCLUSION

Mucormycosis is linked to a significant likelihood of illness and death. Hypertension, Diabetes mellitus, and renal impairment are linked to an elevated risk of mortality. Timely detection, immediate application of medical treatment, and proper surgical removal of the intrusive portion may enhance the chances of reducing the heightened mortality risks linked to this condition. Further extensive investigations are necessary to gain a more comprehensive understanding of how to effectively manage this potentially life-threatening illness.

REFERENCES

[1] Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr 2021;15:102146.
[2] Paltauf A. Mycosis mucorina. Arch Pathol Anat 1885;102:543-64.
[3] Baker RD. Mucormycosis; a new disease? J Am Med Assoc 1957;163:805-8.
[4] Eucker J, Sezer O, Graf B, Possinger K. Mucormycoses. Mycoses 2001;44:253-60.
[5] Sugar AM. In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 5th edn. New York, USA: Churchill Livingstone 2000.
[6] Rapidis AD. Orbitomaxillary mucormycosis (zygomycosis) and the surgical approach to treatment: perspectives from a maxillofacial surgeon. Clin Microbiol Infection 2009;15(5):98–102.
[7] Patel A, Agarwal R, Rudramurthy SM, Shevkani M, Xess I, Sharma R, et al. Multicenter epidemiologic study of coronavirus disease–associated mucormycosis, India. Emerg Infect Dis 2021;27(9):2349–59.
[8] Rudramurthy SM, Hoenigl M, Meis JF, Cornely OA, Muthu V, Gangneux JP, et al, ISHAM. ECMM/ISHAM recommendations for clinical management of COVID-19 associated mucormycosis in low-and middle-income countries. Mycoses 2021;64(9):1028–37.
[9] Ibrahim AS, Spellberg B, Walsh TJ, Kontoyiannis DP. Pathogenesis of mucormycosis. Clin Infect Dis 2012;54:S16–22.
[10] Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: An update. J Fungi (Basel) 2020;6(4):265.
[11] Farmakiotis D, Kontoyiannis DP. Mucormycoses. Infect Dis Clin North Am 2016;30:143-63.
[12] Motevasseli S, Nazarpour A, Dalili Kajan Z, Yousefi Z, Khosravifard N, Kashi F, et al. Post-COVID mucormycosis osteomyelitis and its imaging manifestations in the North of Iran: case series. Oral Radiology 2024;40(1):69-80.

[13] Rai S, Yadav S, Kumar D, Kumar V, Rattan V. Management of rhinomaxillary mucormycosis with Posaconazole in immunocompetent patients. J Oral Biol Craniofac Res 2016;6(Suppl 1):S5-S8.
[14] Dilek A, Ozaras R, Ozkaya S, Sunbul M, Sen EI, Leblebicioglu H. COVID-19-associated mucormycosis: Case report and systematic review. Travel Med Infect Dis 2021;44:102148.
[15] Sen M, Honavar SG, Bansal R, Sengupta S, Rao R, Kim U, et al. Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India–Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. Indian J Ophthalmol 2021;69(7):1670-92.
[16] Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: Asystematic review of cases reported worldwide and in India. Diabetes Metab Syndr 2021;15:102146.
[17] Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. Cureus 2020;12:e10726.
[18] Dyer O. Covid-19: India sees record deaths as “black fungus” spreads fear. BMJ 2021;373:n1238.
[19] Awal SS, Biswas SS, Awal SK. Rhino-orbital mucormycosis in COVID-19 patients-a new threat? Egypt J Radiol Nucl Med 2021;52:152.
[20] Spellberg B, Edwards J, Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. Clin Microbiol Rev 2005;18:556-69.
[21] Garg D, Muthu V, Sehgal IS, Ramachandran R, Kaur H, Bhalla A, et al. Coronavirus disease (Covid-19) associated mucormycosis (CAM): case report and systematic review of literature. Mycopathologia 2021;186(2):289-8.
[22] John TM, Jacob CN, Kontoyiannis DP. When uncontrolled diabetes mellitus and severe COVID-19 converge: the perfect storm for mucormycosis. J Fungi 2021;7(4):298.
[23] Patel A, Kaur H, Xess I, Michael JS, Savio J, Rudramurthy S, et al. A multicentre observational study on the epidemiology, risk factors, management and outcomes of mucormycosis in India. Clin Microbiol Infection 2020;26(7):944.e9-15.
[24] Hoenigl M, Seidel D, Carvalho A, Rudramurthy SM, Arastehfar A, Gangneux J. The emergence of COVID-19 associated mucormycosis: analysis of cases from 18 countries. Lancet Microbe 2022;3(7):e543–52.
[25] Sattar N. Gender aspects in type 2 diabetes mellitus and cardiometabolic risk. Best Pract Res Clin Endocrinol Metabol 2013;27(4):501–7.
[26] Huebschmann AG, Huxley RR, Kohrt WM, Zeitler P, Regensteiner JG, Reusch JE. Sex differences in the burden of type 2 diabetes and cardiovascular risk across the life course. Diabetologia 2019;62(10):1761–72.
[27] Palanisamy N, Vihari N, Meena DS, Kumar D, Midha N, Tak V, et al. Clinical profile of bloodstream infections in COVID-19 patients: a retrospective cohort study. BMC Infect Dis 2021;21(1):933.
[28] Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. J Laryngol Otol 2021;135(5):442–447.
[29] Muthu V, Rudramurthy SM, Chakrabarti A, Agarwal R. Epidemiology and pathophysiology of COVID-19-associated mucormycosis: India versus the rest of the world. Mycopathologia 2021;186(6):739-54.