

Fungal osteomyelitis in diabetic patients and COVID-19

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ABSTRACT

Background: COVID-19 pandemic has become a big medical problem worldwide. In this era, COVID-19 patients' along with diabetes mellitus are at an increased risk of developing opportunistic infections. This study demonstrate association of COVID-19 infection in patients having uncontrolled diabetes with the fungal osteomyelitis.

Subjects and methods: This prospective cross-sectional study was done at a Nishter Institute of Dentistry, Multan. Patients diagnosed with fungal osteomyelitis of jaw bones presented during April to December 2021 were included in this study. Data was collected from the patients regarding history of the disease, clinical diagnosis, imaging findings by plain radiographs and CT scans, histopathology. Association of disease process with diabetes and COVID-19 was analyzed in SPSS.

Results: Between the period April 2021 to December 2021, 23 cases presented in Nishter Institute of Dentistry Multan with fungal osteomyelitis were diagnosed clinically and fungal organism was identified by immunohistochemical studies by PAS and GMA stains. 22/23 (95.6%) patients were with uncontrolled diabetes mellitus and 18/23(78.2%) gave the history of Covid 19 infection 2 to 3 months before with moderate to severe symptoms. 11/23 (47.8%) gave the history of treatment with systemic steroid. Age range was 38-72 years of age with mean age 53.26. 12/23(52.1%) were males and 11/23 (47.8%) were females. 17/23 (73.9%) patients presented with pain in jaws with exposed bone and 6/23(23%) complained of pain and loose teeth in arch. In 22/23 (95.6%) involved jaw was maxilla. In one patient associated medical condition was hepatitis C virus infection also with diabetes. 2 patients were cardiac and 3 were hypertensive along with diabetes. One patient was previously treated with radiotherapy of mandible due to alveolar cancer. Only one (0.04%) patient was non diabetic. She was on chemotherapy for renal cancer.

Conclusion: There is increased incidence of fungal osteomyelitis of jaws mostly maxilla in diabetic and COVID-19 infected patients.

Keywords:

Mucormycosis, Diabetics, COVID-19, Fungal osteomyelitis of jaws, Maxillary osteomyelitis

INTRODUCTION

The COVID-19 pandemic has impacted a lot in oral health. Oral post-COVID-19 complications such as abnormal taste and smell have been reported. However, the incidence of fungal infections especially with jaw osteomyelitis.¹ is being increasingly reported in the literature.

Diabetes mellitus is an immunocompromised condition which is the leading causes of morbidity worldwide and is the risk factors for many infectious diseases. The host response to COVID-19 infection and diabetes share similarities that may lead to an increased incidence of such pathologies of the jaw. With so little information in this context, it is difficult to determine the association of COVID-19 and fungal infections. More literature and studies on large samples is needed for better understanding of the

pathophysiology of these opportunistic infections in diabetic patients following COVID-19 infection.²

Periodontal diseases, salivary disorders, neurosensory disturbance such as taste abnormalities and microbial infections such as rhinocerebral mucormycosis, necrotizing cellulites and osteomyelitis of jaws are the chief manifestations of diabetes.²

Rhinocerebralmucormycosis is a fungal disease that is initiated through nose into paranasal sinuses towards orbits and cranial cavity. It occurs mainly in patients with dehydration and acidosis, such as those with poorly controlled diabetes, leukemia and odontogenic infection is associated with this condition.³

Osteomyelitis is an inflammatory condition starting from the medullary cavity, of bones and extends to the periosteum.⁴ The fungal growth and resulting pus within the bone marrow puts pressure on the endothelial lining of periosteal blood vessels, causing vascular insufficiency resulting in ischemia and necrosis. Fungal osteomyelitis is more infiltrative than bacterial osteomyelitis.⁵

Conflict of Interest: The authors declared no conflict of interest exists.

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Fungal osteomyelitis is a fatal condition that occurs mainly in immunocompromised patients such as patients with AIDS, uncontrolled diabetes, on chemotherapy, antibiotics and immunosuppressive agents and recently studies show association with COVID-19 ⁶⁻⁸

Current study determined the incidence of fungal osteomyelitis of jaw in diabetic and COVID-19 infected patients.

PATIENTS AND METHODS

This study was carried out at a tertiary care teaching hospital Nishtar Institute of Dentistry Multan. Patients diagnosed with fungal osteomyelitis of jaw bones presented at Oral & Department Nishtar Institute of Dentistry Multan during period April 2021 to December 2021 were included in this study. Patients presented with pain and exposed bone and loose teeth were included. Exclusion criteria was patients with other bacterial and viral infections (such as AIDS, herpes, cytomegalovirus, odontogenic infection, tuberculosis, toxoplasmosis, etc.) and traumatic processes and other co morbidities.

It was longitudinal prospective study. All patients underwent a thorough clinical and medical assessment on basis of history clinical examination. All suspected of fungal infection so two biopsy samples were taken under local anesthesia and one was sent in normal saline for immunohistochemical stains and other in formalin for histopathology. GMS and PAS stains were used for immunohistochemical studies to diagnose fungal infection. Insulin and intravenous liposomal Amphotericin B 250 mg was started. Intraoral vestibular incisions or envelop flaps were used for debridement of infection.

RESULTS

A total of 22/23 (95.6%) patients were with uncontrolled diabetes mellitus and 18/23 (78.2%) gave the history of COVID-19 infection 2 to 3 months before with moderate to severe symptoms. Among them 11/23 (47.8%) gave the history of treatment with systemic steroid. Age range was 38-72 years of age with mean age 53.26. 12/23 (52.1%) were males and 11/23 (47.8%) were females. 17/23 (73.9%) patients presented with pain in jaws with exposed bone and 6/23 (23%) complained of pain and loose teeth in arch. In 22/23 (95.6%) involved jaw was maxilla. In one patient associated medical condition was hepatitis C virus infection also with diabetes. Two were cardiac patients and 3 were hypertensive along with diabetes. One

patient was previously treated with radiotherapy of mandible due to alveolar cancer. Only 1 (0.04%) patient was non diabetic. She was on chemotherapy for renal cancer.

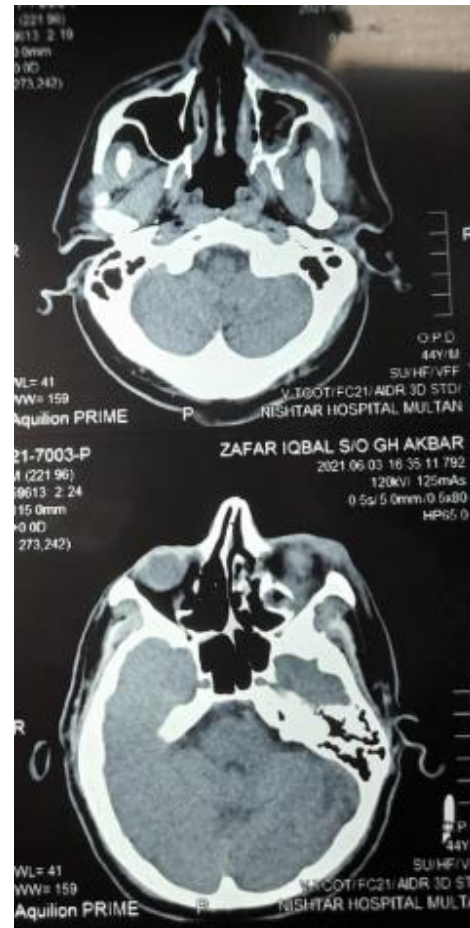


Figure 1: CT scan of patient showing soft tissue mass causing mucosal thickening of the left maxillary antrum and left alveolar ridge with partial destruction and opacification of roof, anterior and lateral wall and floor of left maxillary sinus.



Figure 2: Intra oral fungal infection showing ulceration and exposed maxillary left bone.

DISCUSSION

COVID-19 infection caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) is a global pandemic.^{9,10} COVID-19 patients has suppressed Immune system which is found to be caused by fall in CD4+T and CD8+T cells count³ resulting in a wide range of secondary microbial infections that may co-exist with preexisting morbidity such as diabetes mellitus and other immunocompromised condition.

Zou et al showed in one study that Fungal manifestations were considered the leading cause of death in 25% to 73.7% of post Covid infected patients. However further studies in this context are needed¹⁰

Researchers have shown the association of diabetes with SARS CoV 2 infection as COVID-19 enters the cells through angiotensin converting enzyme receptors (ACE2). Organs with an abundant distribution of ACE2 receptors can become viral host cells along with a large amount of ketone bodies in diabetics help in favorable media for the growth of the organism.^{11,12} So the results of this study shows that 95.6% of patients with fungal osteomyelitis were diabetic.

Another study showed that COVID-19, infected lung epithelial cells produce cytokines that by chemotaxis attracts neutrophils and T cells so lymphopenia was observed in these patients. D-dimer and fibrinogen levels were also found to be high in these patients. Vasodilation, and fibrinolysis, results and aggregation of platelets is reduced. COVID-19 patient's hypercoagulable profiles indicate a significant endothelial injury. Bacterial invasion is facilitated by increased microvascular permeability¹³. Chinese authors have reported a high percentage of secondary bacterial or fungal infections (8–15%) in COVID-19 patients. Chen et al. concluded from the data collected by his study that only 5% of cases developed fungal infection in their study having 99 participants.⁶ This study shows that 78.2% patients gave the history of infection with COVID 19 virus. Further data is needed and further studies are needed in this context.

Uncontrolled Diabetes Mellitus results in an immunocompromised state as it causes damage to the function of neutrophils and antioxidant system.⁷ High glucose levels, abundant ketone bodies, low pH environment and concentrated oxygen provides media for growth of fungal spores. Hyperglycaemia also results in increased glycosylation of transferrin and ferritin causing low iron binding capacity. So increases the serum iron which binds with rhizoferrin which is produced by fungal hyphae to form iron-rhizoferrin complexes which further facilitate the growth,

development, and reproduction of fungal spores.¹⁴ Vegetative forms invade vessels to form thrombus, causing ischemic necrosis cause further tissue death in adjacent areas. So in this study most of the patients (95.6%) presented with fungal osteomyelitis were diabetics. Only one (0.04%) patient was non diabetic. She was on chemotherapy.

Another cause of oral fungal infections in post-COVID-19 patients is steroid treatment which also alters of the oral microbial flora allowing the oral commensals to become pathogenic. Dry mouth because of disease/drugs also aids the fungal growth.¹⁴ In this study, 47.8% of patients of COVID-19 steroids were given.

The epidemiological data, history, clinical evaluation, and immunohistochemical studies by PAS and GMA stains to detect fungal organisms of such patients could help in better understanding of disease process. Simple documentation of isolated case reports or case series of patients with fungal osteomyelitis of jaws in post-COVID-19 patients would help to shed more light on the disease process.

CONCLUSION

There is increased incidence of fungal osteomyelitis of jaws mostly maxilla among diabetic and COVID-19 infected patients.

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