Review Article

An update on Oral Manifestations of COVID-19 : a Narrative Review

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Coronavirus disease, since its first case reported in China in 2019, has increased at an exponential rate globally, still growing strong and challenging the Healthcare System Globally. It primarily causes Pneumonia by infiltrating the respiratory tract. However, recent studies detecting SARS-COV RNA in saliva; and affinity of the virus to ACE2 receptors which are abundantly found in epithelial lining of oral mucosa suggest that the oral cavity might probably be the first contact area for the Coronavirus. The aim of this review is to compile and present evidence-based overview of oral manifestations of COVID-19, with a view to presenting a means of early disease detection. The literature shows that the most frequently affected sites in the oral cavity are tongue, lips and palate with varied manifestations like non-specific oral Ulcerations/blisters, Dysgeusia, Xerostomia due to reduced salivary flow, oral candidiasis and Gingivitis. The occurrence of oral lesions in COVID patients could be multifactorial; due to direct or indirect action of SARS-COV-2 on oral mucosa, secondary to the therapeutic drugs used in COVID-19 treatment; lowered general health status following prolonged hospitalisation and co-infections. COVID-19 associated oral manifestations may be underreported due to lack of knowledge among Physicians and Dentists. They should be sensitized to perform a thorough oral examination in COVID affected patients to provide an early diagnosis of the disease and take up measures to limit the progression and spread of disease.

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The outbreak of Novel Coronavirus (COVID-19) has challenged the Healthcare Management Systems worldwide. The fast spread of misinformation about the ongoing Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2) pandemic places the Virus alongside an annoying infodemic and causes unnecessary worldwide panic[1]. World Health Organisation (WHO) report on COVID-19 published on May 28, 2021 states that a total of 168,040,871 cases and 3,494,758 deaths have been recorded Globally with 27,369,09 cases and 315,235 deaths reported in India[2]. Epidemiological data suggest the spread of virus through droplet, direct contact, fomite and airborne transmission[3,4]. Initially, symptomatic patients were assumed to be a major source of disease transmission, however, recent studies suggest that patients in their incubation period and asymptomatic patients could also be a carrier of SARS-COV-2[5,6]. The Epithelial Cells of oral Mucosa are considered to be the best receptor for SARS-COV-2[7]; however, our knowledge on oral manifestations associated with the novel COVID-19 is still limited. The disease is devastating if allowed to progress, hence, this review aims to compile evidence-based overview of oral manifestations of COVID-19, for early detection and diagnosis of the disease.

Editor's Comment :

- Detecting oral lesions of COVID-19 by oral physicians can be useful to perform better preliminary triage in a dental setting. This can provide opportunity for early diagnosis of the disease thereby limiting the severity and spread of the disease.
- The occurrence of oral lesions could be multifactorial such as due to poor oral hygiene, increased susceptibility of COVID patients to viral, fungal, other bacterial co-infections; impaired immunity and pharmacological therapy used.

(1) Saliva as SARS-COV-2 Reservoir :

The Epithelial cells of Salivary glands act as viral receptors, due to significant expression of Angiotensin Converting Enzyme 2 (ACE2), which has been identified as a functional receptor for SARS-COV-2[8]. S-spike protein of SARS-COV-2 attaches to the ACE2 receptors and subsequently undergoes replication and lyses the cells,followed by release of salivary amylase into peripheral blood that facilitates an inflammatory reaction causing destruction of tissues of salivary gland which causes apparent signs and symptoms of discomfort, inflammation and pain in salivary glands[9]. SARS-COV RNA can be found in saliva even before

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lung lesion emerges with a positive rate of 92% or more, which accounts for the spread through contaminated saliva of asymptomatic patients[10]. Due to abundance of disease biomarkers in saliva with relative ease in its sampling procedure being non-invasive and cost-effective, research suggests the use of saliva as a viable diagnostic tool for early detection of COVID-19[11,12].

(2) Oral Manifestations of COVID-19 :

Oral lesions were reported to be symptomatic in 68% of cases with equal prevalence in both males (51%) and females (49%)[13]. Patients with older age and higher severity of disease reported to have more widespread and severe oral lesions. Oral lesions in mild cases, may appear before or at same time as initial respiratory symptoms; and in few critical cases requiring hospitalisation, they appeared 7 to 28 days after onset[14].

2.1 Xerostomia / Dry Mouth :

More than 50% COVID-19 patients reported to have Xerostomia and a significant correlation has been found between Xerostomia and Dysgeusia in these patients[15]. Factors such as aging, comorbidities, use of certain medications and psychological disturbances causing hyposalivation, increases the risk of an individual to COVID-19, as the presence of proteins and antiviral proteins in saliva are reduced[16-20]. A study revealed 38% of total COVID patients, who were severely ill, showed a strong relationship between salivary gland ectasia and high levels of CRP, a marker of systemic inflammation and LDH, a marker of overall Necrosis[21]. Due to significant expression of ACE2 receptors, SARS-COV-2 affects major and minor salivary glands resulting in Acute Sialadenitis with symptoms of discomfort, swelling and pain in salivary glands. Acute phase is followed by repair of salivary glands with fibroblast proliferation and fibrous connective tissue formation, which may lead to ductal stenosis and hyposecretion of saliva; ultimately leading to xerostomia due to Chronic Obstructive Sialadenitis[9].

2.2 Taste Alterations :

Interaction of SARS-COV-2 with ACE2 receptors, which is highly expressed in Epithelial Cells of tongue, may result in gustatory dysfunction. It is reported to be either the first symptom or the only symptom detected of this disease[22-25] with a wide range of prevalence between 5.6% and 92.64%[21,26]. The prevalence seems to be higher in female patients with mild to moderate COVID-19 severity[14]. Taste disorders are of three types: Hypogeusia- a decreased sense of taste; Ageusia- absence of sense of taste; Dysgeusia- a qualitative distortion of taste perception and it was found that 38% of COVID-19 patients showed Dysgeusia; 35% showed Hypogeusia; and 24% showed Ageusia, according to a recent systematic review[27]. Due to neuroinvasive action of SARS-COV-2, xerostomia may also be associated with gustatory dysfunction, eventually leading to Burning mouth syndrome[28]. Although not specific, Chemo Sensitive Disorders might be markers of early infection, Identification of which might help in early case identification and isolation thereby containing the spread of the disease[29-31].

2.3 Lesions Associated :

2.3.1 Oral Ulcerations —

Recurrent oral ulcers can be an inaugural symptom of COVID-19. A report of 3 cases showed occurrence of painful herpetic like oral blisters even before systemic symptoms could be seen in COVID positive patients[32]. Fidan *et al* performed a prospective Observational study on 74 COVID positive patients and reported that frequency of oral lesions in these patients is 78.4%. The most prevalent oral lesion were Aphthous like ulcers (36.5%); erythema (25.7%) and lichen planus (16.2%), commonly affecting sites such as tongue followed by buccal mucosa; gingiva and lastly the palate[33]. Brandao *et al* reported a case series of 8 COVID positive patients presenting two different patterns of Oral Ulcerations- Aphthous like and Superficial Necrosis spread throughout the oral cavity[34]. Reportedly, Aphthous like ulcers were seen in young patients with mild COVID infections and other Widespread Lesions resembling HSV1 Necrotic Ulcers were seen in older, severely infected and immunocompromised individuals.

Gianfranco Favia *et al* studied 123 COVID positive cases and reported that most frequently detected Oral Lesions were painful Ulcerative Lesions (52.8%-65%) presenting as single (40%) or multiple (60%) lesions[35]. Blisters were seen in 15.4% which collapsed into Superficial Erythematous Ulcerative Lesion associated with pain and minor bleeding. Asymptomatic petechiae was seen in 11.4% cases located on hard and soft palate and tongue. Angina bullosa was observed on soft palate, tongue and cheek that appeared as brown-black single multiple bullae. A study correlating the clinical and histopathological features of oral lesions describes that there is partial or complete Thrombotic Vascular Occlusion resulting in Superficial Necrotic areas along with wide inflammatory reaction in deeper tissues[36].

2.3.2 Tongue Lesions —

E Gherlone revealed that 28% patients showed tongue abnormalities limited to hairy white tongue

showing marked Hypertrophy of Filiform Papillae due to excess keratin production or poor oral hygiene[21]. Study describing changes in tongue show that in, early stages, tongue appeared pale/reddish with slimy white tongue fur. In middle stage, tongue appeared red with yellow dry fur. During early severe stage, it appeared crimson with yellow dry fur. In late severe stage, tongue seemed dark purple with thick dry fur. In recovery stage, tongue appears pale, tender, soft and enlarged that later becomes red with thin fur[37].

2.3.3 Necrotising Periodontal Disease —

Asymptomatic patient showed hyperpigmented labial Gingiva due to increased melanogenesis in response to immunoinflammatory processes, that increases the levels of prostaglandins, leukotrienes, cytokines (TNF alpha, IL-1) and inflammatory mediators[38]. Critically ill patients showed signs of Ulcero-necrotic Gingivitis associated with bleeding due to poor oral hygiene. Patel and Woolley hypothesised a rise in incidence of Acute Necrotising Periodontal Disease (ANPD) with increasing COVID cases, due to bacterial co-infections of Prevotella intermedia, alongside Streptococci, Fusobacterium, Veillonella and Treponema species, which have been detected in metagenomic analyses of patients affected by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)[39].

2.3.4 Coinfections —

A few studies including: 5 case reports, one case-series, one cross-sectional study and one open-label trial[14,39-45], have reported cases of Oral Candidiasis in patients with COVID disease. Most cases developed Oral Pseudomembranous Candidiasis as a result of inflammatory processes to viral infection, use of antibiotics, Diabetes Mellitus or secondary to immunosuppression seen due to rapid and generalised Lymhopenia in patients with SARS-COV-2.

(3) Associated Syndromes :

3.1 Kawasaki-like Disease :

An Italian observational study showed 30 times higher monthly incidence of Kawasaki Disease during COVID outbreak; showing either the classic form or the incomplete form of Kawasaki Disease. In Kawasaki disease, mainly diagnosed in children below 5 years of age with peak incidence at 10 months; changes of lips and oral cavity may occur including Erythema, Fissuring, Dryness, Peeling, Crackling, Bleeding of Lips and Strawberry tongue, that may become worse if associated with COVID-19, hence are reported as Kawasaki-like disease[46].

3.2 Multisystem Inflammatory Syndrome in Children (MIS-C) :

A postviral immunologic reaction due to SARS-COV-2 infection, might result in MIS-C. A confirmed case of COVID-19, aged 21 years or less with fever and laboratory evidence of inflammation involving 2 or more organ systems, necessitating hospitalization, is categorized under MIS-C[47], showing oral manifestations such as red or swollen lips, redness in inner cheek, and strawberry tongue.

3.3 Melkerson- Rosenthal Syndrome :

A case report of a 51-year-old female with past history of cured Melkerson-Rosenthal Syndrome, developed COVID-19 disease and complained of malaise, unilateral lip swelling, fissured tongue and right facial paralysis, which was cured after treatment of COVID-19[48].

(4) Newer Complications:

4.1 Mucormycosis/Black Fungus :

Mucormycosis is a rare fungal infection caused by fungi of the order Mucorales, of the class Zygomycetes, that progresses rapidly and may have a fatal outcome[49]. Mucormycosis mainly affects immunocompromised individuals with risk factors like Diabetes Mellitus or on broad spectrum antibiotics/ steroids/monoclonal antibodies or immunomodulatory drug (Tocilizumab) therapy[50]. CAM has affected 18 Countries;however, India was the hardest hit country with over 20,000 cases in first week on June, 2021[51]. Inhalation of sporangiospores seems to be a main route of infection causing pulmonary infection which can spread contagiously into other organs. Diabetics with ketoacidosis provides a favourable environment for rapid proliferation of fungus and its subsequent invasion into orbit, cerebrum, paranasal sinuses, palate and skin of face[52]. Prevention of COVID-associated Mucormycosis focuses on addressing underlying risk factors such as glycemic control in diabetics; appropriate use of Systemic Corticosteroids and avoiding unnecessary use of antibiotics, antifungals and other immunomodulators; proper sterilisation and disinfection of medical equipment; good ventilation in hospitals; and proper line management in hospitals.Oral manifestation of Mucormycosis starts as Palatal Ulceration or Necrosis followed by perforation of palate as the fungi invades into the nasal cavity or paranasal sinuses through vascular channels. Patient usually presents with Facial Cellulitis and Anesthesia, Nasal discharge, Necrotic turbinates, Blackish discoloration over bridge of nose/palate, toothache, loosening of teeth and local pain on cheekbone[49].

Conclusion :

The current knowledge on the occurrence of Oral lesions and its association with COVID-19 disease is still inconclusive. Whether oral ulcerations or blisters are manifestations of COVID-19, needs more clinical studies to be carried out with large number of samples. The occurrence of Oral Lesions could be multifactorial such as due to increased susceptibility of COVID patients to viral, fungal, other bacterial co-infections; due to impaired immunity and Pharmacological Therapy used. It is important to be cautious of spreading information related to oral manifestations of COVID-19, as these acute oral Lesions could be a shared presentation by many conditions. Dentists, as oral physicians, have the opportunity to provide an early diagnosis and make proper referral, thereby limiting the severity and spread of the disease.

References

1 Zhu Z, Lian X, Su X, Wu W, Marraro GA, Zeng Y — From SARS and MERS to COVID-19: a brief summary and comparison of severe acute respiratory infections caused by three highly pathogenic human coronaviruses. *Respir Res* 2020; **21(1):** 1-14.

2 World Health Organization — Available at https://covid19.who.int. (Accessed on 28th May,2021)

3 Centers for Disease Control and Prevention — Interim domestic infection control precautions for aerosol-generating procedures on patients with severe acute respiratory Syndrome (SARS). Available at: www.cdc.gov/ncidod/sars/aerosolinfectioncontrol.htm.

4 Seto WH, Tsang D, Yung RW — Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* 2003; **361:** 1519-20.

5 Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, *et al* — A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020; **395(10223):** 514-23.

6 Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, *et al* — Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med* 2020; **382(10):** 970-971.

7 Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, *et al* — Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Sci China Life Sci* 2020; **63(3):** 457-60.

8 Liu L, Wei Q, Alvarez X, Wang H, Du Y, Zhu H, *et al* — Epithelial cells lining salivary gland ducts are early target cells of severe acute respiratory syndrome coronavirus infection in the upper respiratory tracts of rhesus macaques. *J Virol* 2011; **85(8):** 4025-30.

9 Wang C, Wu H, Ding X, Ji H, Jiao P, Song H, *et al* — Does infection of 2019 novel coronavirus cause acute and/or chronic sialadenitis? *Med Hypotheses* 2020; **24:** 109789.

10 Xu J, Li Y, Gan F, Du Y, Yao Y — Salivary glands: potential reservoirs for COVID-19 asymptomatic infection. *J Dent Res* 2020; **99(8):** 989-9.

11 Santosh TS, Parmar R, Anand H, Srikanth K, Saritha M — A review of salivary diagnostics and its potential implication in detection of COVID-19. *Cureus* 2020; **12(4):** e7708

12 Han P, Ivanovski S — Saliva - friend and foe in the COVID-19 outbreak. *Diagnostics* 2020; **10(5):** 290-300.

13 Iranmanesh B, Khalili M, Amiri R, Zartab H, Aflatoonian M — Oral manifestations of COVID-19 disease: A review article. *Dermatol Ther* 2021; **34(1):** 14578.

14 Amorim dos Santos J, Normando AGC, Carvalho da Silva RL, Acevedo AC, de Luca Canto G, Sugaya N, *et al* — Oral Manifestations in Patients with COVID-19: A Living Systematic Review. *J Dent Res* 2021; **100:** 141-54.

15 Biadsee A, Biadsee A, Kassem F, Dagan O, Masarwa S, Ormianer Z — Olfactory and oral manifestations of COVID-19: sex-related symptoms - a potential pathway to early diagnosis. *Otolaryngol Head Neck Surg* 2020; **163(4):** 722-8.

16 Farshidfar N, Hamedani S — Hyposalivation as a potential risk for SARS CoV 2 infection: inhibitory role of saliva. *Oral Dis* 2021; **27 Suppl 3:** 750-1.

17 Bergdahl M, Bergdahl J — Low unstimulated salivary flow and subjective oral dryness: association with medication, anxiety, depression, and stress. *J Dent Res* 2000; **79(9):**1652-8.

18 Fu L, Wang B, Yuan T, Chen X, Ao Y, Fitzpatrick T, *et al* — Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. *J Infect* 2020; **80(6):** 656-65.

19 Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R — Features, Evaluation, and Treatment of Coronavirus (COVID-19). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.

20 Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al* — Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395(10229): 1**054-62.

21 Gherlone EF, Polizzi E, Tetè G, De Lorenzo R, Magnaghi C, Querini PR, *et al* — Frequent and Persistent Salivary Gland Ectasia and Oral Disease After COVID-19. *J Dent Res* 2021; **100(5):** 464-71.

22 Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, *et al* — Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020; **77(6):** 683-90.

23 Paderno A, Schreiber A, Grammatica A, Raffetti E, Tomasoni M, Gualtieri T, *et al* — Smell and taste alterations in COVID-19: a cross-sectional analysis of different cohorts. *Int Forum Allergy Rhinol* 2020; **10(8):** 955-62.

24 Hjelmesæth J, Skaare D — Loss of smell or taste as the only symptom of COVID-19. *Tidsskr Nor Laegeforen* 2020; 140(7).

25 Jang Y, Son HJ, Lee S, Lee EJ, Kim TH, Park SY — Olfactory and taste disorder: The first and only sign in a patient with SARS-CoV-2 pneumonia. *Infect Control Hosp Epidemiol* 2020; **41(9):** 1103.

26 Lorenzo Villalba N, Maouche Y, Alonso Ortiz MB, Cordoba Sosa Z, Chahbazian JB, *et al* — Anosmia and Dysgeusia in the Absence of Other Respiratory Diseases: Should COVID-19 Infection Be Considered? *Eur J Case Rep Intern Med* 2020; **7(4):** 001641.

27 Bénézit F, Le Turnier P, Declerck C, Paillé C, Revest M, Dubée V, Tattevin P — RAN COVID Study Group. Utility of hyposmia and hypogeusia for the diagnosis of COVID-19. *Lancet Infect Dis* 2020; **20(9):** 1014-5.

28 Freni F, Meduri A, Gazia F, Nicastro V, Galletti C, Aragona P, *et al* — Symptomatology in head and neck district in coronavirus disease (COVID-19): A possible neuroinvasive action of SARS-CoV-2. *Am J Otolaryngol* 2020; **41(5):** 102612.

29 Mariz BALA, Brandão TB, Ribeiro ACP, Lopes MA, Santos-Silva AR — New Insights for the Pathogenesis of COVID-19-Related Dysgeusia. *J Dent Res* 2020; **99(10):** 1206.

30 Kucharski AJ, Klepac P, Conlan AJK, Kissler SM, Tang ML, Fry H, *et al* — CMMID COVID-19 Working Group 2020. Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study. *Lancet Infect Dis* **20(10):** 1151-60.

31 Prather KA, Wang CC, Schooley RT — Reducing transmission of SARS-CoV-2. Science 2020; **368(6498):** 1422-4.

32 Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, Jané-Salas E, Somacarrera Pérez ML — Oral vesiculobullous lesions associated with SARS-CoV-2 infection. *Oral Dis* 2021; **27 Suppl 3:** 710-2.

33 Fidan V, Koyuncu H, Akin O — Oral lesions in Covid 19 positive patients. *Am J Otolaryngol* 2021; **42(3):** 102905.

34 Brandão TB, Gueiros LA, Melo TS, Prado-Ribeiro AC, Nesrallah ACFA, Prado GVB, *et al* — Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ? *Oral Surg Oral Med Oral Pathol Oral Radiol* 2021; **131(2):** e45-e51.

35 Favia G, Tempesta A, Barile G, Brienza N, Capodiferro S, Vestito MC, *et al* — Covid-19 Symptomatic Patients with Oral Lesions: Clinical and Histopathological Study on 123 Cases of the University Hospital Policlinic of Bari with a Purpose of a New Classification. *J Clin Med* 2021; **10(4):** 757.

36 Sabino-Silva R, Jardim AC, Siqueira WL — Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis. *Clin Oral Invest* 2020; 1-3.

37 Abdul MSM, Fatima U, Khanna SS, Bhanot R, Sharma A, Srivastava AP — Oral Manifestations of Covid-19 - Are they the introductory symptoms? J *Adv Med Dent Scie Res* 2020; **8(5):** 41-3.

38 Corchuelo J, Ulloa FC — Oral manifestations in a patient with a history of asymptomatic COVID-19: Case report. *Int J Infect Dis* 2020; **100:** 154-7.

39 Patel J, Woolley J — Necrotizing periodontal disease: Oral manifestation of COVID-19. *Oral Dis* 2021; **27 Suppl 3:** 768-9.

40 Cantini F, Niccoli L, Matarrese D, Nicastri E, Stobbione P, Goletti D — Baricitinib therapy in COVID-19: A pilot study on safety and clinical impact. *J Infect* 2020; **81(2):** 318-56.

41 Baraboutis IG, Gargalianos P, Aggelonidou E, Adraktas A — Initial real-life experience from a designated COVID-19 centre in Athens, Greece: a proposed therapeutic algorithm. *SN Compr Clin Med* 2020; **2(6):** 689-93.

42 Díaz Rodríguez M, Jimenez Romera A, Villarroel M — Oral manifestations associated with COVID-19. *Oral Dis* 2020: 10.1111

43 Dima M, Enatescu I, Craina M, Petre I, Iacob ER, Iacob D — First neonates with severe acute respiratory syndrome coronavirus 2 infection in Romania. Medicine (Baltimore) 2020; **99(33):** e21284.

44 Riad A, Gad A, Hockova B, Klugar M — Oral Candidiasis in Non-Severe COVID-19 Patients: Call for Antibiotic Stewardship. *Oral Surg* 2020; **10:** 1111

45 Salehi M, Ahmadikia K, Mahmoudi S — Oropharyngeal candidiasis in hospitalised COVID-19 patients from Iran: Species identification and antifungal susceptibility pattern. *Mycoses* 2020; **63(8):** 771-8.

46 Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, *et al* — An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: An observational cohort study. *Lancet* 2020; **395(10239):** 1771-8.

47 Halepas S, Lee KC, Myers A, Yoon RK, Chung W, Peters SM — Oral manifestations of COVID-2019-related multisystem inflammatory syndrome in children: a review of 47 pediatric patients. *J Am Dent Assoc* 2021; **152(3):** 202-8.

48 Taþlýdere B, Mehmetaj L, Özcan AB, Gülen B, Taþlýdere N — Melkersson-Rosenthal Syndrome Induced by COVID-19. *Am J Emerg Med* 2021; **41:** 262.e5-262.e7.

49 Doni BR, Peerapur BV, Thotappa LH, Hippargi SB — Sequence of oral manifestations in rhino-maxillary mucormycosis. *Indian J Dent Res* 2011; **22(2):** 331-5.

50 Revannavar SM, Supriya PS, Samaga L, Vineeth KV — COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? *BMJ Case Rep* 2021; **14(4):** e241663.

51 Yasmin F, Najeeb H, Naeem A, Dapke K, Phadke R, Asghar MS, *et al* — COVID-19 Associated Mucormycosis: A Systematic Review from Diagnostic Challenges to Management. *Diseases* 2021; **9(4):** 65.

52 Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, *et al* —Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect Dis* 2019; **19(12):** e405-e421.