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- The Oral Manifestation Impact of Moebius Syndrome towards Oral Health-related Quality of Life: A Case Report
- An Early and An Advanced Oral Mucormycosis Lesions: Case Series
- Oral Findings of *Candida Albicans* and Cryptococcus Laurentii in Elderly with Intracerebral Hemorrhagic Stroke in Intensive Care Unit: A Case Report

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"We are like dwarfs sitting on the shoulders of giants. We see more, and things that are more distant, than they did, not because our sight is superior or because we are taller than they, but because they raise us up, and by their great stature add to ours." John of Salisbury

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CASE REPORT

The Oral Manifestation Impact of Moebius Syndrome towards Oral Health-related Quality of Life: A Case Report

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ABSTRACT

Background Moebius syndrome is a rare disease characterized by unilateral or bilateral congenital facial palsy and limited ocular abduction. It may also involve other cranial nerve palsy. Moebius syndrome has many orofacial anomalies, such as cleft palate, micrognathia, gothic palate, tongue weakness, tongue atrophy, microstomia, and open bite. **Objective** This case report highlights the rare presentation of Moebius syndrome and denture stomatitis and its management considerations. **Case Report** A 22-year-old female patient came to the oral medicine clinic of Dental Hospital Universitas Indonesia, referred by a prosthodontist with a working diagnosis of denture stomatitis. On examination we found microstomia, tongue defect with movement limitations, and a gothic palate with an erythematous patch on the denture-bearing area. The patient denied any relevant medical history. However, she admitted that she was not satisfied with her oral condition. We performed a further examination based on the signs presented and found impaired ocular abduction. Furthermore, we gave her an Oral Health Impact Profile (OHIP)-14 questionnaire to assess her oral health-related quality of life. These examinations resulted in the diagnosis of Moebius syndrome with denture stomatitis and poor oral health-related quality of life. We planned a full mouth rehabilitation consisting of denture stomatitis healing, improvement of oral hygiene, root canal therapy, and renewing the denture. **Conclusion** This case underscores the importance of interdisciplinary collaboration and individualized care in managing complex conditions like Moebius syndrome, ensuring comprehensive care that addresses both functional and aesthetic concerns.

Keywords: Moebius syndrome, oral health-related quality of life, OHIP-14

INTRODUCTION

Moebius syndrome is a rare congenital disorder characterized by underdeveloped facial (VII) and abducens (VI) nerves. It was first described in the 1880s by Moebius and von Graefe.[1] This disorder is not progressive and may also be associated with other cranial nerve palsies, orofacial anomalies, and limb defects.[2] Paralysis of the facial nerve is responsible for the absence of mimicry and facial expression, as well as the suction ability.[1] Ocular involvement includes defect abduction and adduction ocular movement, crossed fixation, exotropia, or vertical eye misalignment.[1]

Oral findings in Moebius syndrome patients vary greatly, but almost all have gothic (high-arched) palates.[3] Structural anomalies of Moebius syndrome in the oral cavity can be described as hypoplastic upper lip, microstomia, mouth angle drooping, cleft palate, tongue weakness, fissured tongue, tongue atrophy, and open bite.[3] Besides structural anomalies, functional limitations are also found in Moebius syndrome patients, i.e., the inability to perform mandibular lateral movements and protrusion.[3] These oral findings result in chewing, swallowing, and speech difficulties and subsequently affect the oral health-related quality of life (OHrQoL).[4]

Despite the significant oral and functional challenges faced by patients with Moebius syndrome, the condition has not been widely studied, with most available information derived from individual case reports. To our knowledge, there has not been a comprehensive case report that explores the impact of Moebius syndrome on oral health-related quality of life (OHrQoL). This case report aims to fill this gap by discussing a patient with Moebius syndrome, assessing their OHrQoL score, and detailing the necessary treatment modifications for their oral condition.

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CASE REPORT

A 22-year-old female patient visited the Oral Medicine Clinic, Dental Hospital, Universitas Indonesia. She was referred from the Prosthodontics Clinic with a working diagnosis of chronic atrophic candidiasis on the palate under the upper removable denture. She came to the prosthodontist to have new removable upper and lower dentures made because the old dentures had been worn out.

She had already worn the removable denture, made by a dental technician, for seven years. She did not take off the dentures at night, but as suggested by the prosthodontist, in the last past week, she took them off at night and wore them the next morning. The patient did not feel any pain or burning sensation on the palate. She did not notice that there was an erythematous lesion on her palate because of the dentures.

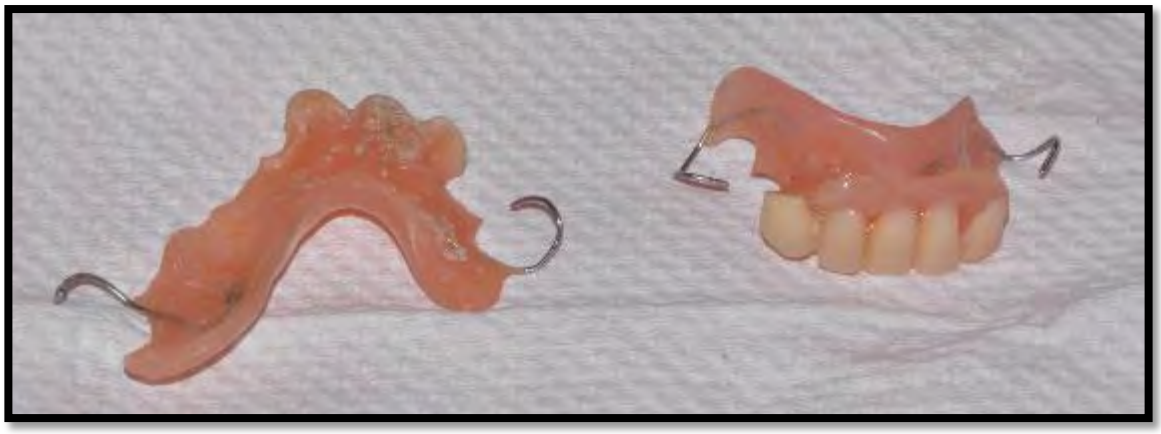

Figure 1. Intaglio surfaces of the removable dentures

Subjective examination of medical history revealed that the patient was born prematurely in the 8th month with a birth weight of 1,200 grams. Unfortunately, detailed records of her growth and development milestones are not unavailable. The patient complained that she has swallowing and speech difficulties. Neither the patient nor her parents were aware of the specific condition affecting her.

Figure 2. Erythema on the denture-bearing area of the palate (*left*) and tongue defect (*right*) at the first visit.

Extraoral examination showed the patient's inability to ocular abduct, frown, lift the eyebrows, and pucker the lips. Intraoral examination showed a tongue defect with movement limitations, a gothic palate, and a relatively small oral cavity. There was also erythema and hyperplasia on the denture-bearing area of the palate. We also took a panoramic radiograph and found several retained dental roots

that needed to be extracted. Based on the examination, the patient was diagnosed with Moebius syndrome and denture stomatitis.

Figure 3. Panoramic radiograph showed multiple remained dental roots in the upper and lower jaw and radiolucency around the apex which all need extractions.

We also gave her the Oral Health Impact Profile-14 (OHIP-14) questionnaire to assess the OHrQoL of this patient related to the Moebius syndrome. The OHIP-14 questionnaire revealed that the patient consistently reported severe functional limitations, physical pain, psychological discomfort, and social challenges, indicating a significant impact on her OHrQoL due to Moebius syndrome.

Based on the examinations, we decided to give her an antifungal to be swished throughout the oral cavity and then swallowed four times daily. The patient was also instructed on proper denture cleaning and taking them off at night. The follow-up visit was two weeks after the first visit.

At the 1st follow-up visit, the erythema of the palate was not significantly improved. We evaluated the treatment and found that swishing the antifungal was ineffective because of the tongue movement limitation. Therefore, we decided to modify the treatment by instructing the patient to apply the antifungal to the denture and put on the denture during the day. We also scheduled her for scaling, extraction, root canal therapy for the remaining teeth, and fabrication of new removable upper and lower dentures.

Figure 4. The erythema area on the palate at the 2nd visit still notable related to the denture bearing area of upper jaw.

On the 2nd, 3rd, and 4th follow-up, the erythema was slightly improved but not fully subsided. On the 4th visit, we also checked the patient's unstimulated salivary flow rate. The unstimulated salivary flow rate was 0.2 ml/min with high viscosity and foamy. On the 5th follow-up, approximately two months after the 1st visit, the erythema of the palate disappeared.

Figure 5. Unstimulated whole saliva was collected and measured. In the measure tube it showed foaminess and only a little amount of saliva.

Meanwhile, the patient had already underwent dental treatment which were dental scaling and extracted six teeth. At the time manuscript was written, the patient was still having root canal therapy with the endodontist and had already made an appointment with the prosthodontist.

Figure 6. Gingiva and palate condition at the 5th follow-up

DISCUSSION

Moebius syndrome was first encountered by Paul Julius Moebius in 1888.[5] The key characteristics of Moebius syndrome are unilateral or bilateral palsy of Abducens (VI) and Facial (VII) Cranial Nerves.[5,6] Paralysis in the Abducens Nerve causes impairments of ocular abduction and paralysis of the facial nerve. These abnormalities cause a lack of facial mimicking, poor or absent sucking, fixed gaze, incomplete eyelid closure during sleep and ptosis.[2] In addition to the involvement of the 6th and 7th cranial nerves, many patients with Moebius syndrome also present with palsies of other cranial nerves, including the hypoglossal (XII), vagus (X), glossopharyngeal (IX), oculomotor (III), vestibulocochlear (VIII), trigeminal (V), trochlear (IV), and accessory (XI) nerves, in descending order of frequency.[1,2,4]

Moebius syndrome lacks established diagnostic criteria, but the presence of abducens and facial nerve paralysis is usually used as the marker of this syndrome. Besides those cranial nerves involvement

previously described, individuals with Moebius syndrome might present with abnormalities of the lower extremity (i.e., talipes equinovarus, syndactyly, ankylosis, absent phalanges), upper extremity (i.e., digital hypoplasia or failure of differentiation, ectrodactyly), facial structure anomalies (i.e., cleft palate, micrognathia, microtia, microphthalmia), or thorax manifestations (i.e., scoliosis, pectoral hypoplasia or breast anomaly, chest wall deformity, breast or pectoral aplasia).[2]

In our case, the patient exhibited an inability to move the eyeballs laterally, frown, pucker the lips, and lift the eyebrows. She also has difficulties with speech and swallowing. Based on these clinical signs, patient's abnormalities consistent with Moebius syndrome diagnosis. The paralysis of the abducens and facial nerves was sufficient for this diagnosis.[2,7] Other manifestations of this syndrome in this patient were glossopharyngeal nerve paralysis, which causes speech and swallowing difficulties, and tongue movement limitation. However, no abnormalities were noted in the upper or lower extremities.

The oral anomalies observed in this patient, including macroglossia, microstomia, tongue defect, and a gothic palate, were among the most common oral manifestations of Moebius.[7] The patient also presented with multiple missing teeth and poor oral hygiene, likely resulting from facial nerve impairment, which can lead to ineffective self-cleansing due to impaired chewing movements.[4,8] While some studies have reported decreased unstimulated salivary flow rates in Moebius syndrome patients, our patient's was below the normal range but not low enough to be classified as hyposalivation. The saliva had high viscosity, which may indicate changes in salivary composition.[4] This needs to be further evaluated. These oral anomalies lead to poor oral hygiene and multiple missing teeth that need to be restored with prostheses.

Our patient also presented with erythema of the denture-bearing area and was diagnosed with denture stomatitis. According to Samaranayake's oral candidiasis classification modified by Axell in 1997, denture stomatitis is one of the candida-associated lesions.[9,10] The first line treatment for local oral candidiasis, such as denture stomatitis, involves the use of nystatin oral suspension.[9,11] The drug is used four times a day to be swished throughout the oral cavity.[9,11] At the first visit, we instructed the patient to swish the nystatin oral suspension for four times a day. Still, at the follow-up visit, we found it ineffective because of the limitation of tongue movement. Therefore, nystatin was applied to the denture four times daily to optimize the contact between the antifungal drug and the palate. At the next follow-up, the treatment was successful, marked by the disappearance of erythema in the denture-bearing area.[9]

Oral health is inseparable from general health and quality of life.[12,13] Therefore, we assessed the patient's oral health-related quality of life to capture her quality of life-related to the oral limitations she experiences. The oral health related quality of life was measured by using the Oral Health Impact Profile-14 (OHIP-14) questionnaire, which has been previously validated in Indonesia.[13,14]

In response to the OHIP-14 questionnaire, the patient reported persistent difficulties with pronunciation, taste disturbances, discomfort while eating, and a range of psychological and social limitations, all of which are consistent with the challenges associated with Moebius syndrome. These findings align with previous reports, such as in Bogart and Matsumoto (2010), which highlighted lower social competence in Moebius syndrome patients compared to control groups, though no significant relationship between the syndrome and overall life satisfaction was observed.[15,16]

Based on the OHIP-14 results, we concluded that our patient was not satisfied with her oral conditions, affecting her oral health-related quality of life. Chewing, swallowing, and speech difficulties, along with the presence of multiple missing and carious teeth, adversely affected her overall well-being. Therefore, we aimed to restore the oral function and improve the oral health-related quality of life through oral hygiene, restoration and root canal therapy for the remaining teeth, and renewal of upper and lower prosthesis.[3,5,17]

CONCLUSION

Dentists, particularly oral medicine specialists, must be aware of patients' oral conditions and their association with overall health. Moebius syndrome, being a rare and challenging condition to diagnose, requires a comprehensive examination to achieve an accurate diagnosis. Treatment in patients with this condition should be individualized, with modifications made as necessary to suit each patient's

unique needs. With proper management, successful treatment outcomes can be achieved, leading to an improved quality of life for the patient.

CONFLICT OF INTERESTS

The authors report no financial, consultant and/or other conflicts of interest and declare that no funding and/or grants have been received to assist in completing this case report.

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CASE REPORT

An Early and Advanced Oral Mucormycosis Lesions: Case Series

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ABSTRACT

Introduction: Mucormycosis is a deep fungal infection caused by *Mucorales*. It is commonly found in immunocompromised patients and is considered the third most common fungal infection after candidiasis and aspergillosis. **Case report**: This paper reports 2 cases of mucormycosis, which involve the oral cavity, lung, maxillary sinus, orbital and cerebral. The first case had haematology disorder with long-term corticosteroid therapy. The brownish oral pseudomembrane was unresponsive to nystatin and mycafungin therapy. The second case had type 2 diabetes mellitus with perforated hard palate, rhinosinusitis, orbital infection and cerebral abscess. Direct mycology from oral specimens showed coenocytic hypha consistent with the *Mucorales* in both cases. Both cases showed responsiveness to Amphotericin B therapy. **Discussion**: Mucormycosis can be invasive to adjacent sites or angioinvasive to distant sites. Thus, an interdisciplinary team approach must be taken. Early diagnosis and prompt treatment are essential in mucormycosis to prevent the further spreading of infection and tissue destruction. A diagnostic procedure using an oral specimen is an option. **Conclusion**: Management of mucormycosis cases requires interdisciplinary teamwork. Early recognition of oral lesions of mucormycosis and diagnosis of mucormycosis is very important to prevent further damage and even death. Identifying *Mucorales* from oral lesions is beneficial since it is more accessible and non-invasive.

Keywords: mucormycosis; deep fungal infection, oral lesion, oral mycology smear

INTRODUCTION

Mucormycosis, formerly known as zygomycosis, caused by *Mucorales*, is an important fungal infection due to its high ability to destroy tissue.[1–3] Compared to other oral deep fungal mycosis, such as Aspergillosis, which is more common than mucormycosis, most cases of mucormycosis are lethal, and the prevalence increases with the increase in cases of diabetes and immunosuppressive therapy.[2,3] The definite prevalence of mucormycosis is unknown but is estimated to be low.[2–5] The estimated worldwide incidence of mucormycosis in 2005 was about 430 to 1700 cases per million people per year, while Chakrabarti et al. showed a rising trend of up to 50 cases per year in a single centre in India.[2,3] The mortality rate of mucormycosis was around 30% to 90%, depending on the underlying condition and site of infection, making it a very lethal disease.[2,4] One of the factors that contribute to the high mortality rate is the delay in diagnosis and Mucorale's resistance to the most available antifungal

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therapy.[6] There has been a rising trend of mucormycosis due to an increase in cases of diabetes mellitus, increasing use of immunomodulating agents in cancer, organ transplant and autoimmune patients, increased awareness among health professionals, and better diagnostic methods.[7]

Members of the order Mucorales are abundant in the human environment, and some are utilized in making cheese and soy products.[1,2,13] The spores can easily fly and be inhaled.[1,2] Mucorales can be cultured from the nose and oral cavity without clinical signs and symptoms in immunocompetent individuals.[1] Three main routes of mucormycosis infection: (1) respiratory system, (2) direct inoculation, and (3) oral.[2] The characteristics of *Mucorales* are the ability to cause thrombosis and tissue necrosis through an angioinvasion mechanism.[1]

Based on location and distribution, there are six types of mucormycosis: rhino-orbital/cerebral/rhinomaxillary, pulmonary, cutaneous, gastrointestinal, and disseminated.[1] Symptoms of mucormycosis include malaise, headache, black eschar, fever, swelling, and facial pain.[1] *Mucorales* spores are very easy to fly and are inhaled, causing Mucorales to infect the nasal or palatal mucosa and then spread to the surrounding sinus cavities and orbital.[1] Orbital involvement can cause proptosis, ptosis, pupillary dilatation, orbital cellulitis, and blindness due to damage to cranial nerves III, IV, and V caused by hyphae penetration.[1]

In this case report, the authors will report two cases of mucormycosis in inpatient ward X Hospital, Jakarta, Indonesia, with early and advanced features of oral lesions.

CASE REPORTS

Case 1

A 62-year-old woman who was referred from a private hospital in Jakarta to Dr. Cipto Mangunkusumo General Hospital Hospital with aplastic anaemia and had received therapy with methylprednisolone 44 mg/day for two weeks and continued with regular dose reduction while hospitalized in the hospital. The patient admitted to the hospital complained of coughing up brown sputum mixed with blood. The complete blood count showed haemoglobin levels ranging from 9 to 11 g/dl, platelet <500,000/uL, and neutrophils ranging from 16% to 36%. The intraoral examination found yellowish-white pseudomembranous lesions with a brownish-black area at the centre of the lesion (Figure 1).

Figure 1. Yellowish white pseudomembrane with the brownish black central area before administration of Amphotericin B on the first patient

The patient was already on nystatin oral suspension 4x1 ml for three days and continued with micafungin 2x50 mg intravenously for one week, all given by the Internist, but there was no improvement. Subsequently, a specimen was taken by scraping off pseudomembranous lesions for fungal examination. Direct examination revealed coenocytic hyphae (ribbon-like hyphae) consistent with mucormycosis and large numbers of yeast cells (Figure 2). The patient was then treated with

amphotericin B. The oral lesion was improved, and the yellowish-white pseudomembranous lesions with a brownish-black area at the centre of the lesion subsided, leaving a shallow reddish ulceration (Figure 3).

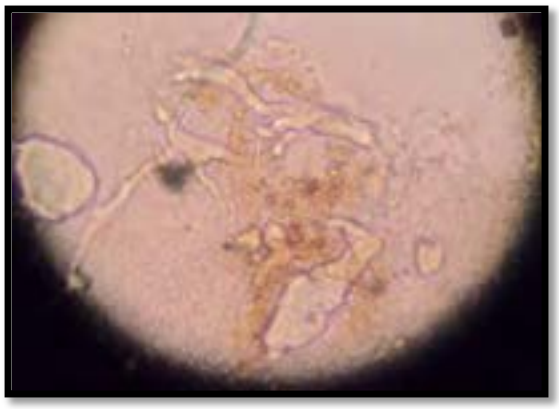

Figure 2. Orthogonal, non-septate, coenocytic hyphae from the oral specimen of the first patient (courtesy of Mycology Laboratory, Department of Parasitology, Faculty of Medicine Universitas Indonesia) Figure 3. Shallow reddish ulcers, three days after administration of Amphotericin B on first patient.

Case 2

A 44-year-old man was referred from a private hospital in Tangerang to Dr. Cipto Mangunkusumo General Hospital in Jakarta with a complaint of redness, swelling, numbness in the neck and left face, soreness on the left palate and visual disturbance in the left eye. The patient was known to have had diabetes mellitus for two years and was on Metformin 500 mg twice daily. Cerebral MRI with Gadodiamide contrast showed abscess and oedema in the left temporal lobe, pansinusitis extending to the infratemporal to intracranial fossa in the left paracella, anterior temporal base and left frontal lobe, and causing left bulbar ptosis (Figure 4). The sagittal view of the cerebral MRI showed defects in the nasal septum, medial wall of the left maxillary sinus, left anterior ethmoid sinus, nasal concha and left ostiomeatal complex (Figure 5).

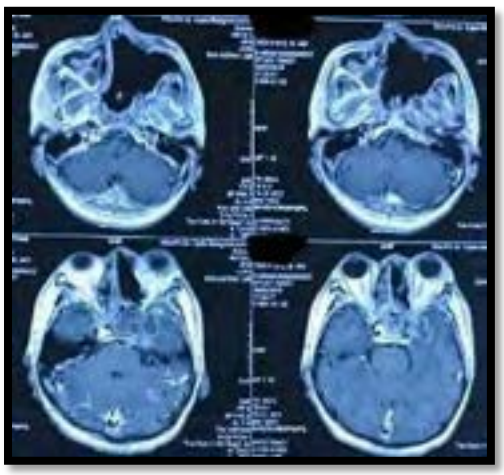

Figure 4. Axial view of cerebral MRI with the contrast of the second patient. Figure 5. The sagittal view of cerebral MRI with the contrast of the second patient

CT scan of the paranasal sinuses showed the lesion extending to the infratemporal fossa to the intracranial, extending to the left orbital cavity, causing left bulbar ptosis, extending to the left para pharynx, destroying the inferomedial orbital wall, left sphenoid wing, anterior-posterior-lateral-medial wall of the left maxillary sinus, wall of the left maxillary sinus, left ethmoid sinus and left cranial base. On intraoral examination, a perforation of the left palate was noticed with black eschar around it and an exposed palatal bone (Figure 6). Specimens were taken by scrapping off necrotic tissue to the border of

the non-necrotic area for fungal examination. Direct fungal examination showed coenocytic hyphae consistent with Mucorales hyphae (Figure 7). The patient received Amphotericin B and necrotic tissue debridement. After debridement, palatal perforation was seen with exposed palatal bone and healthy tissue margin (Figure 8). Perforation of the left orbital nasal was also found (Figure 9).

Figure 6. Necrotic tissue with black eschar and palate perforation before administration of Amphotericin B on the second patient Figure 7. Orthogonal, non-septate, coenocytic hyphae from the oral specimen of the second patient (courtesy of Mycology Laboratory, Department of Parasitology, Faculty of Medicine Universitas Indonesia)

Figure 8. Perforated palate with healthy surrounding tissue without black eschar after administration of Amphotericin B on the second patient. Figure 9. A perforation of the left lateral orbito-nasal wall of the second patient.

DISCUSSION

Mucormycosis, formerly known as Zygomycosis or Phycomycosis, was first introduced by Paultauf in 1885 with the term "mycosis mucorina."[3] Globally, some species are most isolated from the order of *Mucorales* of Mucoraceae, i.e. *Rhizopus sp, Mucor sp*, and Lichtheimia sp.[3] *Rhizopus sp* is responsible for more than 70% of all cases of mucormycosis, specifically *Rhizopus arrhizus* (formerly *Rhizopus oryzae*).[7]

The most important predisposing factors for mucormycosis are diabetes mellitus (with or without ketoacidosis), haematological malignancy and other malignancies, transplantation, neutropenia, corticosteroid, trauma, malnutrition, iron overload, and trauma.[3,7] In stem cell transplant recipients, mucormycosis is the third most common fungal infection after candidiasis and aspergillosis.[7] There is a demographic difference in the epidemiology of mucormycosis between developed and developing countries.[6] This difference is thought to be related to socioeconomic status and malnutrition.[2] There is only limited data available regarding mucormycosis in Indonesia, which roughly estimated 530 cases annually in immunocompromised, trauma burn and diabetic patients group in a single diagnostics facility.[15] Reflecting India as a developing country, even before the COVID-19

pandemic, the number of cases of mucormycosis was predicted to be more than 200,000 per year, accounting for 24% of global invasive fungal infections.[7]

In the first case, the predisposing factor for mucormycosis was a haematological disorder with long-term corticosteroid therapy, while in the second case, diabetes mellitus. Corticosteroids affect the work of neutrophils and decrease their activity against fungal infections, as neutrophils have an important role in inhibiting the proliferation of fungal spores.[2,8] Hyperglycemia is favourable for fungal proliferation in diabetes mellitus. It also impairs the host's chemotaxis and phagocytic activity, which allows the fungi to survive in the acid-rich environment.[9] Hyphae from *Mucorales* produce rhizoferrin, a specific siderophore with a high affinity for iron. Mucorales use the iron-rhizoferrin complex for their survival and also for its virulence properties.[1,10,14] In diabetic ketoacidosis (DKA), increased levels of ferric iron, low pH, and hyperglycemia play an important role in the growth of *Mucorales*.[1,10] In DKA, the availability of keton bodies increases the risk of mucormycosis. This is because *Rhizopus oryzae* produces enzyme ketoreductase, which can use the patient's ketone bodies as nutrients.[1,9,10]

Mucorales are abundant in the environment (food, fruit, and plants), and the spores can fly very easily and are inhaled.[1,2] As a commensal, *Mucorales* can be cultured from the nose and oral cavity without clinical signs and symptoms in immunocompetent individuals.[1] There are three main routes of mucormycosis infection: (1) respiratory system, (2) direct inoculation, and (3) oral.[2] The characteristics of *Mucorales* are the ability to cause thrombosis and tissue necrosis through an angioinvasion mechanism.[1] Necrotic blood vessels will inhibit leukocytes' migration to the area of infection.[8] Angioinvasion plays a vital role in the ability of *Mucorales* to disseminate hematogenously to reach other target organs.[8]

Based on location and distribution, there are six types of mucormycosis: rhino-orbital/cerebral/rhinomaxillary, pulmonary, cutaneous, gastrointestinal, and disseminated.[1] Symptoms of mucormycosis include malaise, headache, black eschar, fever, swelling, and facial pain.[1] *Mucorales* spores in the air infect nasal or palatal mucosa and disseminate to the sinus and orbit.[1] Orbital involvement can cause proptosis, ptosis, pupillary dilatation, orbital cellulitis, and blindness due to damage to cranial nerves III, IV, and V caused by hyphae penetration.[1]

In the first case, the clinical picture was a diffuse yellowish-white pseudomembranous lesion on the oral mucosa with a brownish-black centre. There was no black eschar, swelling or facial pain, a characteristic of mucormycosis. Scraping off the pseudomembrane left reddish superficial ulcers without any evidence of tissue necrosis nor palatal perforation. The patient also had impaired lung function, but due to the patient's condition, it was not possible to perform broncho-alveolar-lavage (BAL) or lung tissue biopsy to confirm the diagnosis of lung mucormycosis.

In the second case, the patient had uncontrolled type 2 diabetes mellitus and developed palatal-rhino-orbita-cerebral mucormycosis. Among uncontrolled diabetic patients, the most prevalent form of mucormycosis is rhino-cerebral (rhino-maxillary).[9] Rhinocerebral mucormycosis starts from the palate or nasal mucosa, which extends to paranasal sinuses and spreads through angular, lacrimal, and ethmoidal vessels.[9] The clinical findings in the second patient were palatal perforation with black eschar, left sinonasal necrosis, ptosis and loss of left eye vision, left facial paralysis, and cerebral abscess. A cerebral biopsy was prepared to determine the organism causing extensive damage involving palatal-rhino-orbita-cerebral.

Ideally, diagnosis is made by biopsy of necrotic and non-necrotic tissue. Hematoxylin & Eosin (H&E) or Periodic Acid Schiff (PAS) staining are performed, as well as KOH wet slide investigations and culture using Sabouraud dextrose agar (SDA) medium for 48-72 hours. Histopathologically, *Mucorales* can be seen in the walls of the necrotic blood vessels.[1,7] Structurally, *Mucorales* have a broader hyphal structure (6-16 μm), coenocytic and orthogonal hyphae compared with Aspergillus, which has a narrow hyphae structure (2-3 μm), septated and branched hyphae.[2,3,11] However, in cases where a biopsy is not possible, direct examination and culture of any specimen could be performed, for example, from sputum.[3,12] The discovery of the hyphae on direct examination is very important because this result can be obtained relatively quickly and strongly supports the diagnosis of mucormycosis.[3,12] Thus, health professionals need to recognise oral lesions of mucormycosis and perform sample collection from oral lesions, particularly when the biopsy of other organs involved cannot be done. Scraping of oral lesions is more accessible and non-invasive.

Direct fungal examinations were performed from oral lesions in both cases by scraping off necrotic tissue. The scraping material was placed into a sterile tube containing 1-2 drops of 0.9% sodium

chloride solution, and KOH direct fungal examination and culture were carried out in the parasitology laboratory immediately. Direct examination found the presence of broad, coenocytic, and orthogonal hyphae consistent with the description of *Mucorales* hyphae. In both cases, Amphotericin B therapy was given as the drug of choice for mucormycosis immediately after the presence of Mucorales hyphae was proved. Amphotericin B works on *Mucorales* by targeting ergosterol and functions by binding and sequestering the ergosterol, resulting in cell membrane instability and pore formation.[13] The response of this regime to both cases was positive.

Early diagnosis, accompanied by radical debridement of necrotic tissue, appropriate systemic antifungal administration, and management of risk factors, determines the success of mucormycosis management.[10,11] An oral medicine specialist has an essential role in establishing an accurate diagnosis of mucormycosis as early as possible, accelerating the diagnosis, and subsequently administering appropriate antifungal therapy to prevent fast deterioration of the patient or even death. A thorough clinical examination is needed to distinguish the initial lesion of mucormycosis, a yellowish-white pseudo membrane with brownish-black areas, from the oral pseudomembranous candidiasis. The absence of response to nystatin and micafungin reinforces the suspicion that the lesion might be mucormycosis.

In both cases where systemic conditions did not support immediate biopsy, a quick decision was needed to take a specimen from a yellowish-white pseudomembranous lesion with a brownish-black area in the centre in the first case and scrape off necrotic tissue on the hard palate in the second case. The successful identification of *Mucorales* hyphae from oral scraping dramatically helps speed up the diagnosis, avoids or replaces more invasive diagnostic procedures (BAL in the first case and cerebral biopsy in the second case), and accelerates the administration of appropriate antifungals for mucormycosis. Tissue necrosis and perforation of the palate in the first case and death from cerebral abscess in the second case could be prevented by the active role of an oral medicine specialist in the interdisciplinary team.

CONCLUSION

Management of mucormycosis requires interdisciplinary teamwork because of the predisposing factors and the extent of infection, which can involve multiple organs. Early recognition and diagnosis of oral lesions of mucormycosis are very important to prevent further damage and even death. Oral mycological smear of oral lesions and direct pathologic examination that follow are non-invasive methods to identify the etiologic agent and establish a diagnosis. They could be beneficial steps in the immediate management of this fungal infection.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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CASE REPORT

Oral Findings of *Candida albicans* and *Cryptococcus laurentii* in Elderly with Intracerebral Hemorrhagic Stroke in Intensive Care Unit: A Case Report

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ABSTRACT

Introduction: Intracerebral haemorrhage patients are susceptible to developing an oral infection due to hospitalised intervention. The systemic disease and degree of consciousness also supported the development of oral infection, especially fungal. **Case:** This case presented an elderly female with an intracerebral haemorrhage stroke. The oral lesion was developed as a pseudo membrane during the five days of endotracheal tube intubation. The direct examination showed the presence of Candida colonies and *Cryptococcus laurentii*. **Conclusion**: Oral hygiene maintenance, including topical antiseptic and anti-fungal, can improve oral health and prevent Candidemia and other fungal sepsis.

Keywords: oral health care; fungal infection, elderly, sepsis

INTRODUCTION

Stroke is a neurological disorder caused by obstructing blood flow to the brain, leading to bleeding or blockage of blood vessels. The signs and symptoms vary based on the location of the affected brain and can result in complete or partial recovery with a disability or even death. Hemorrhagic and non-hemorrhagic strokes are the primary classification of stroke based on pathology and clinical symptoms. [1]

Intracerebral haemorrhage is a type of hemorrhagic stroke commonly observed in the 40-70-year-old age group, with several identified risk factors, including hypertension, advanced ages, anticoagulant use, hematologic abnormalities, and another chronic disease.[1]

Stroke is the leading cause of disability, and patients are susceptible to oral health problems such as decreased salivary flow rate and the growth of microorganisms in the oral cavity.[2,3] These conditions increase the risk of secondary infections, including fungal infections, the incidence of oral ulcers due to device pressure and seizure, periodontitis, and bleeding.[3] In this case report, we discuss oral health management in elderly patients admitted to the intensive care unit diagnosed with intracerebral hemorrhagic stroke to reduce the risk of secondary infection, including candidemia.

CASE REPORT

A 70-year-old female patient with a primary diagnosis of intracerebral haemorrhagic in the cortical hemisphere was referred to the oral medicine clinic by a neurologist to examine the oral cavity condition. The patient has been hospitalized for 47 days with complaints of decreased

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consciousness for five days, preceded by vomiting. During that time, the patient's Glasgow Coma Scale score was 11 (somnolence), and they presented with a nasal cannula. The patient had hypertension, diabetes mellitus and hypercholesterolemia.

Intra-oral examination showed that the oral mucosa was dry, and saliva crusting on the tongue, buccal mucosa, hard palate and desquamation of the lips were found **(Figure 1A-B**). The objective examination of dry mouth was carried out using the Challacombe Scale, and the severity of dry mouth was measured with a nine-point score **(Table 1).**

Table 1. Challacombe Scale of Clinical Oral Dryness of the Patient.

Item	Score
Mirror sticks to buccal mucosa	1
Mirror sticks to the tongue	1
Saliva Frothy	0
No saliva pooling in floor of the mouth	1
Tongue shows generalized shortened papillae (mild depapillation)	1
Altered gingival architecture (ie. smooth)	1
Glassy appearance of oral mucosa (esp. palate)	1
Tongue lobulated or fissured	1
Cervical caries (more than two teeth)	1
Debris on palate or sticking to teeth	1
Total	**9 -(severe dryness)**

Debridement was performed using normal saline to remove saliva crusting and followed by 0.2 % chlorhexidine digluconate to asepsis and the lips was moistened with borax glycerin.

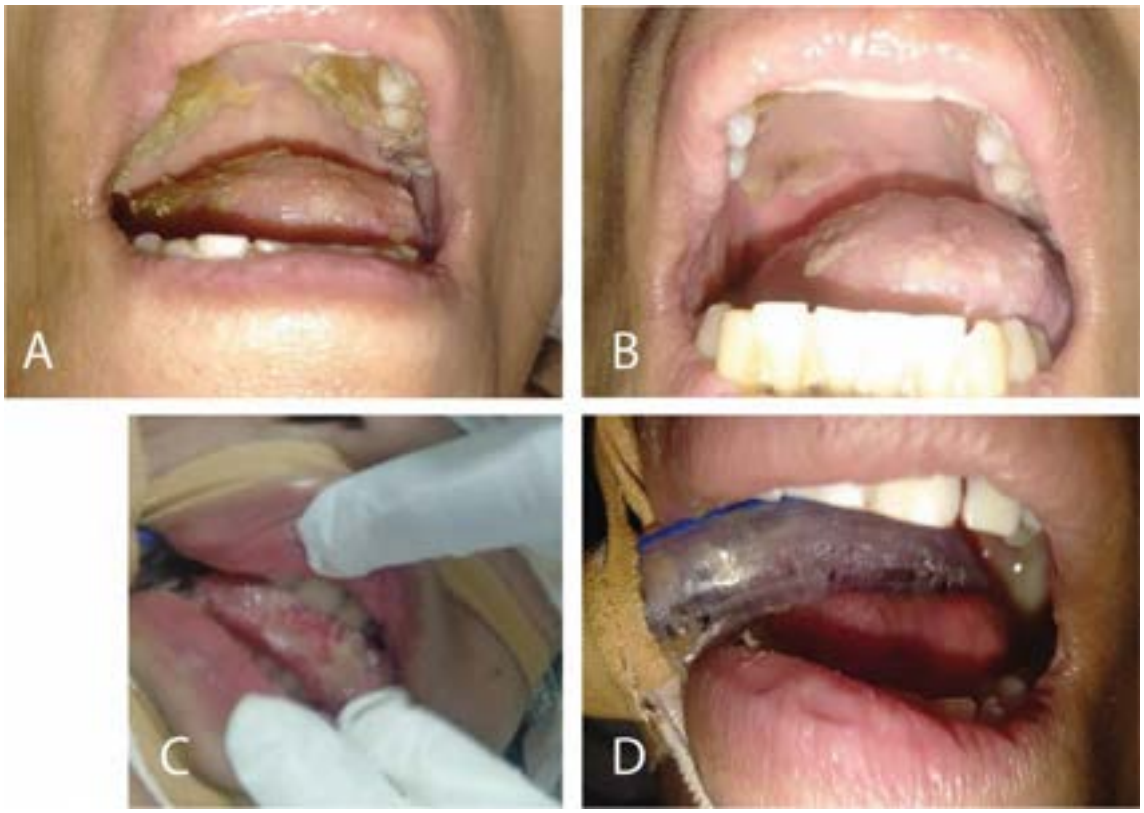

Figure 1. The oral mucosa in the patient with pseudomembrane of palatum and dorsum of the tongue before endotracheal intubation (A-B). The intraoral development after endotracheal intubation (C) and the intraoral after debridement, asepsis, and nystatin application (D).

In the next five days, the patient's consciousness decreased, with 6 of GCS (stupor) and endotracheal intubation connected to a ventilator was installed. Intra-oral examination showed a white-yellowish pseudomembrane on the dorsum of the tongue **(Figure 1C).** The pseudomembrane was scrapped and subjected to microbial examination. The debridement of the pseudomembrane was done using normal saline, followed by 0.2% chlorhexidine, and the lip lesion was applied with borax glycerine.

The haematology studies showed decreased haemoglobin, hematocrit, lymphocytes, and platelets, while leukocytes and neutrophils were increased. The microbial examination of the tongue swab specimen using Vitex® 2 Compact showed Candida albicans and Cryptococcus laurentii. Nystatin 100.000 IU/ml was topically applied to the tongue's surface at 1 ml four times daily for five days. The final condition, the intra-oral, improved, and the pseudomembrane disappeared (**Figure 1D)**.

DISCUSSION

This patient had a stroke with intracerebral hemorrhagic type, resulting in total paralysis and a decrease in consciousness. Consequently, the patient also lost the ability to swallow and close the mouth, which causes xerostomia and the development of saliva crusting. This patient had been hospitalized for 47 days with a decreased general condition. Her immunodeficiency had also trigger susceptibility to secondary infection, with the growth of microorganisms in the oral cavity.[4]

This intraoral problem became worse when the patient was admitted to the ICU. Patients with low consciousness and limitation of movement, especially intraoral, reduce saliva secretion and cause dryness in the mouth. Subsequently, crusts on the oral mucosal surface develop to harbour microbial colonization.[5] As such, hospitalised patient, especially in the ICU, would easily develop fungal infections due to their disability, hospitalised procedures, and unstable vital and medical signs that create retention to fungal growth. [3,4]

Oral candidiasis is a fungal infection that occurs in the oral cavity. The oral cavity is suitable for yeast colonisation because of the moist environment and nutrient availability. *Candida albicans*, the most dominant yeast in the oral cavity and most pathogenic Candida spp are pleomorphic microorganisms with different growth forms: rod-shaped, yeast (blastopore), hyphae or pseudohyphae and chlamydospores. Candida is a commensal oral flora. However, various factors, such as immune system disorders, antibiotics, and corticosteroids, would change the oral microorganism balances and turn the normal flora into pathogenic.[7]

Cryptococcus infection can be found in hospitalized and immunocompromised patients. The immunocompromised and diabetic,[16] chronic lymphocytic leukaemia,[11] HIV,[12]as well as non-HIV are also prone to this infection.[6] In elderly patients with corticosteroid-inhaled, there is a higher incidence of *cryptococcus.*[15] *Cryptococcus Laurentii* is a very rare human pathogen. Initially, this fungus was considered saprophytic and non-pathogenic to humans. However, *Cryptococcus Laurentii* in skin infections have been reported.[7] In this case, *Cryptococcus laurentii* did not manifest clinically and was identified during the culture examination.

One of the antifungal agents used during oral debridement was Chlorhexidine digluconate. It is a broad-spectrum antimicrobial belonging to the bisbiguanide family and is commonly used in its gluconate form. Chlorhexidine attacks gram-positive and negative bacteria, yeast bacteria, and fungi. Antifungals work by damaging the permeability of cell wall membranes and extracellular proteins of fungi, such as *Candida albicans*, protozoa, algae, and viruses.[9,10]

The chlorhexidine formula is considered the gold standard, composed of N1 and N5, a biguanide substitution bonded to hexamethylene and two chlorophenol rings at both ends. Chlorhexidine at low doses will interfere with cellular transport so that the formation of pores in the cellular membrane damages fungal cells. Chlorhexidine digluconate 0.2% is an antiseptic active against bacteria and fungi. Chlorhexidine digluconate 0.2% has been shown to reduce the growth of microorganisms significantly and has a very strong inhibition zone against several fungal species, especially Candida albicans.[9,10]

CONCLUSION

Appropriate oral lesion management is needed to prevent the increased risk of candidemia as a secondary infection, especially in hospitalised patients and the elderly. Oral hygiene procedures are also important to prevent the spread of Candida and Cryptococcus. Antiseptics like 0.2% chlorhexidine digluconate can be used to debride the oral lesion, and topical Nystatin can control the colonisation of *Candida albicans* and Cryptococcus.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

INFORMED CONSENT

Informed consent was obtained before the preparation of the case report, and the authors endeavoured all efforts to ensure anonymity.

ETHICAL STATEMENT

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ORIGINAL ARTICLE

Teledentistry in Oral Medicine Practice: Knowledge Among Dental Students and Dentists in Jakarta, Indonesia

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ABSTRACT

Background: The utilisation of teledentistry in oral medicine practice can solve the problem of the limited number of oral medicine specialists and general practitioners in rural communities, specifically with geographic and economic barriers. **Objectives**: to investigate the knowledge level of dental students and dentists regarding teledentistry by assessing their knowledge in oral medicine practice. **Methods**: Using a self-administered structured questionnaire, a descriptive cross-sectional study consisting of 8 items was conducted at the Faculty of Dentistry X University for dental students and dentists in the Province of Jakarta. **Results**: Three hundred two respondents (210 dental students and 92 dentists) responded to the questionnaire. The present study found that 30.4% of dental students and 64.1% of dentists had a good knowledge of oral medicine. All dentists without postgraduate qualifications had less than 5 years of work experience (68.5%). **Conclusion**: The dental students had low knowledge of teledentistry in oral medicine, and most dentists had a good knowledge of teledentistry in oral medicine.

Keywords: dental students, dentists, knowledge, oral medicine, teledentistry

INTRODUCTION

Teledentistry is a developing area in dentistry which links dental providers, institutions, and health administration to their patients using electronic information and telecommunication technologies.[1-3] Teledentistry has been applied in several countries to advance access, time, cost, manage and provide screenings and referrals for vulnerable and underserved communities in regions such as school and kindergarten conditions, nursing homes and rural facilities.[4,5] It is also used to exchange information and knowledge between patients, general practitioners, and specialists for more precise treatment planning, results, and continuing education for health professionals.[2,4,5] Eventually, teledentistry can enhance patient compliance, comfort, prognosis, and satisfaction by comparing pre- and post-treatment images.[2,3]

Teledentistry has been applied by general practitioners in every specialist branch and practice, especially in Oral Medicine. Teledentistry was performed before the COVID-19 pandemic and should be more common since the new clinical practice era.[2] Although telemedicine has some benefits, face-to-face consultation and examination are still preferred during the Covid-19 pandemic.[6] General practitioners often require opinions from oral medicine specialists when treating complicated orofacial lesions, including oral malignant and recalcitrant lesions, particularly in rural communities.[2,6,7]

To overcome the gap between oral care services and the population and counter the pandemic of Covid-19, teledentistry can be applied to support dental services, particularly in oral medicine [3] and helps general practitioners in rural communities with geographic and economic barriers to managing patients at a distance or over remote distances.[3,5,7,8]

Several studies about the role of teledentistry in oral medicine practice were conducted among dentists in Indonesia. Still, none of these studies included the knowledge level of dentists and dental students to the best of our knowledge. To generate knowledge of teledentistry in oral medicine practice for the future generation of dentists, it is also crucial to assess the knowledge of the present dental students. Hence, the present study was conducted among dental professionals (including dental students) to know the knowledge levels regarding teledentistry in oral medicine practice.

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METHODS

This cross-sectional study, utilizing questionnaires, was conducted on undergraduate dental students of the Faculty of Dentistry, Moestopo University from first to fourth years (academic students) and five to sixth years (dental professional students)[9] and dentists in the Jakarta, Bogor, Depok, Kota Bekasi (Jabodetabek) region from July until October 2021. The participants were explained the study's objectives and methods, and informed consent was obtained. It was explicitly stated that their participation would be voluntary. Respondents were asked to fill out the questionnaires using Google Forms.

The scientific and ethical approval for conducting the research was granted by the Faculty of Dentistry Ethical Committee of Universitas Prof Dr Moestopo (Beragama) (Protocol No:040/KIP/FKGUPDMB/V/2021) on 5th July 2021 and all searches were completed on 24th October 2021. All the participants also signed an informed consent form.

A structured and close-ended questionnaire with only one answer was used to assess the respondents' knowledge level. Respondents must answer all questions before the questionnaire can be submitted. Questionnaires were distributed to 1000 undergraduate students and 200 dentists. Each questionnaire's validity and reliability were tested on 30 respondents by online administration. After the questionnaire validation test, a few questions were modified based on participants' feedback, and afterwards, the survey was distributed electronically via Google Forms. The questionnaire included questions regarding age, gender, and study year, and for dentists, it included length of clinical experience and frequent cases being treated. Eight questions were posed to assess knowledge related to common oral medicine practice. The respondents had to choose only one of the options, 'Agree' or 'Disagree'. The questions were so designed that 'Agree' happened to be the correct answer for all the items and scored 1 point, while the wrong answer had no score. The participants' knowledge was calculated by adding the scores of all items, dividing by 8, and expressing them in percentages. The knowledge of the respondents was graded as 'good' (>75%), 'fair' (56-75%), and 'poor' (<56%) based previous published study.[9]

Data analysis

The data were being input into a programmed statistical analysis. Descriptive statistics (frequencies, percentages, and mean) were used to summarise the data. The chi-square test was used to determine the significant difference in proportions. All the tests were performed after checking all the assumptions at 5% significance levels with a 95% confidence interval. A probability level of less than 0.05 was statistically significant.

RESULTS

A total of 302 questionnaires were completely answered and considered for statistical analysis. This comprised questionnaires answered by 110 first to fourth-year undergraduate students (academic student), 100 fifth-year undergraduates (dental professional programme student),[10] and 92 dentists. These division was convenience based on the Dental School Educational Years. Table 1 shows the demographic details of the respondents. The study's mean age of first to fourth undergraduate students was 20.26±1.36 years, fifth and sixth undergraduates were 23.5±1.24 years, and dentists were 26.25$\pm$11.9 years. Out of 210 dental students, 31 were males and 169 were females, whereas 9 were males and 83 were females for the dentists. The response rate was 21% for dental students and 46% for dentists. All dentists without postgraduate qualifications had less than 5 years of work experience (68.5%) and had never treated oral medicine patients.

Table 2 shows the distribution of dental students' and dentists' questionnaire responses. More than 50% of general dentists and 5th-6th grade dental students agreed on items 1,3 and 4. The percentage of correct answers was more than 50% of the respondents acknowledged the statements for items 2,6,7,8. Half the dentists and almost 50% of dental students provided wrong answers and displayed poor knowledge of item 5.

Table 1. Demographic characteristics of participants

Characteristics							
				Dental Students			
				Year of Study			
Age (in years)		1st	2nd	3rd	4th	5th	6th
Mean±SD				20.26±1.36			23.5±1.24
Gender							
Males		4	4	2	4	6	11
Females		22	23	23	28	51	32
				General Dentists			
Age (in years)			20-30	30-40		41-50	51-60
Mean±SD:26.25±11.9			76	6		6	4
Gender	Males				9		
	Females				83		
Experience (year)			< 1	1 – 2		3 – 5	> 5
N			26	26		22	18
Frequent cases		Conservative	Prosthodontic	Paediatric	Oral Surgery	Periodontic	Orthodontic
N		60	3	5	6	17	1

Table 2. Distribution of responses among dental students and dentists based on items questionnaire.

No	**Questions**	**Choices**	**Dental Students Grade**				**General Dentists**	
			1st – 4th		5th-6th			
			n (% total) % gender		n (% total) % gender		n (% total) % gender	
			Male	Female	Male	Female	Male	Female
1	Teledentistry in oral medicine is the practice of dentistry using computers, the Internet, and intraoral camera technology to provide remote consultations.	Agree	6 (5.45) 42.85	33 (30) 34.38	16 (16) 94.1	77 (77) 92.77	7 (7.61) 77.8	80 (86.95) 96.38
		Disagree	8 (7.27) 57.15	63 (57.27) 65.62	1 (1) 5.9	6 (6) 7.23	2 (2.17) 22.2	3 (3.26) 3.62
2	Teledentistry reduces isolation and helps increase the accessibility of general dentists and oral medicine specialists to rural and underserved communities for oral health care	Agree	10 (9.09) 71.43	64 (58.18) 66.67	12 (12) 70.59	66 (66) 79.52	9 (9.78) 100	82 (89.13) 98.8
		Disagree	4 (3.63) 28.57	32 (29.09) 33.33	5 (5) 29.41	17 (17) 20.48	- 	1 (1.08) 1.2
3	Teledentistry helps in the initial consultation of oral soft tissue disease with an oral medicine specialist after examination with a camera/photo.	Agree	5 (4.54) 35.7	47 (42.72) 52.2	10 (10) 58.82	69 (69) 83.13	7 (7.6) 77.8	78 (84.78) 93.97
		Disagree	9 (8.18) 64.3	49 (44.55) 47.8	7 (7) 41.18	14 (14) 16.87	2 (2.2) 22.2	5 (5.43) 6.03
4	Teledentistry helps make informed decisions about oral disease management and referral to an oral medicine specialist.	Agree	6 (5.45) 42.86	26 (23.63) 27.1	12 (12) 70.59	62 (62) 74.7	7 (7.6) 77.8	67 (72.83) 80.7
		Disagree	8 (7.27) 57.14	70 (63.63) 72.9	5 (5) 29.41	21 (21) 25.3	2 (2.2) 22.2	16 (17.39) 19.3
5	Teledentistry helps general dentists conduct laboratory examinations of patients according to the direction of an oral medicine specialist	Agree	4 (3.63) 28.57	53 (48.18) 55.2	6 (6) 64.7	50 (50) 60.24	4 (4.35) 44.4	42 (45.65) 50.6
		Disagree	10 (9.09)	43 (39.09)	11 (11)	33 (33)	5 (5.43)	41 (44.57)

			71.43	44.8	35.3	39.76	55.6	49.4
6	Teledentistry helps general dentists in diagnosing oral soft tissue disease.	Agree	9 (8.18)	70 (63.63)	12 (12)	56 (56)	8 (8.69)	70 (76.09)
			64.28	72.9	70.59	67.47	88.89	84.3
		Disagree	5 (4.54)	26 (23.63)	5 (5)	27 (27)	1 (1.08)	13 (14.13)
			35.72	27.1	29.41	32.53	11.11	15.7
7	Teledentistry helps general dentists provide drugs prescriptions and instructions for treatment of oral soft tissue disease with the direction of oral medicine specialist	Agree	11 (10)	89 (80.9)	14 (14)	73 (73)	7 (7.6)	53 (57.6)
			78.57	92.7	82.35	87.95	77.8	63.86
		Disagree	3 (2.72)	7 (6.36)	3 (3)	10 (10)	2 (2.2)	30 (32.6)
			21.43	7.3	17.65	12.05	22.2	36.14
8	Teledentistry supports observation of the patient's condition according to the direction and opinion of an oral medicine specialist.	Agree	8 (7.27)	69 (62.72)	15 (15)	70 (70)	9 (9.78)	81 (88.04)
			57.14	71.875	88.23	84.34	100	97.6
		Disagree	6 (5.45)	27 (24.54)	2 (2)	13 (13)	-	2 (2.17)
			42.86	28.125	11.77	15.66		2.4

Table 3 shows the distribution of qualification, gender, and level of knowledge of participants; 5th -6th years dental students showed a better level of knowledge than the 1st to 4th years dental students. The difference was statistically significant (p=0.000), as indicated by the Chi-square test. The mean score of male students for all the questions was 62.9, male participants, including dental students and dentists, were 66.87, while female participants were 72.95. Male and female dental students from 5th-6th years displayed a good level of knowledge better than in 1st-4th grade. The difference between the level of knowledge and the gender of dental students shown was not statistically significant (p=0.115) as indicated by the Chi-square test. The difference between the level of knowledge and the gender of all participants was not statistically significant (p=0.07), as indicated by the Chi-square test. There was a statistically significant difference between the qualification of participants with a level of knowledge (p = 0.000, Chi-square test).

Table 3. Gender study Participants' distribution (n) by Good, Fair and Poor Category of knowledge.

Qualifications	**Gender**	**Level of Knowledge**		
		Good (%)	Fair (%)	Poor (%)
Dental Students (1st – 4th grade)	Male	0 (0)	5(4.5)	9(8.2)
	Female	6(5.5)	52(47.2)	38 (34.6)
Dental Students (5th-6th grade)	Male	7(7)	6(6)	4(4)
	Female	51(51)	21(21)	11(11)
Total of Dental Students	Male	7 (3.3)	11(5.2)	13(6.2)
	Female	57 (27.1)	73 (34.8)	49 (23.4)
Dentists	Male	6(6.5)	2(2.2)	1(1.1)
	Female	53(57.6)	25(27.2)	5(5.4)
Total of Dental Students & Dentists	Male	13(4.3)	13(4.3)	14(4.6)
	Female	110(36.4)	98(32.5)	54(17.9)

DISCUSSION

Teledentistry in oral medicine can support oral lesions and medication management, including exchanging clinical information, past and recent history, relevant imaging, determining remote diagnosis, procedures and oral health services.[3,6,11] Oral medicine specialists have also used teledentistry recently and can diagnose and treat oral lesions [6,12] and prevent transmission of SARS-CoV-2.[6] To the best of our knowledge, this is the first study which determines the level of knowledge about teledentistry in oral medicine in Indonesia. The present cross-sectional study has uncovered an interesting and new point concerning advanced dentistry technologies among dentists and dental students in Jakarta City, Indonesia.

The 62.8 % of dental students and 94.6% of dentists in this study agreed that teledentistry in oral medicine is the practice of dentistry using computers, the internet, and intraoral camera technology to provide remote consultations. Teledentistry, with its application in oral medicine, has been evaluated in developed countries.[13,14] A Study conducted in India showed that the majority (88.6%) of dentists

believed that teledentistry is the practice of using computers, the internet, and intraoral camera technologies for diagnosis and to provide advice about treatment over a distance. Teledentistry increases the rate of document exchange and interaction among dental health providers by utilising oral health documents, advanced technology of telecommunications and teleconferences, digital imaging, and the Internet. Jian Hu et al. stated that most dental health professionals were implementing computers in daily practice.[12,15,16] Dentists can anticipate revolutionary transformation as a result of digital advances.[15] In developing countries, the utilization of smartphone cameras has increased, and they are used to take images of oral lesions in remote settings and diagnose lesions made in distant locations. This was demonstrated in a previous study that showed intraoral camera as a reliable tool for screening for oral lesions.[17,18,19] Dentists' lower perceptions of teledentistry utilization were related to diagnostic precision and the time required to take clinical images which would require additional session to take the photos. [20] The use of an intra-oral camera with a qualified program can shorten the time from taking pictures to transferring and storing the images into a medical record application.[21]

One of the benefits of teledentistry for patients is that it facilitates and accommodates consultations with specialists.[22] It was about 72.38% of dental students and 98.9% of dentists in this study showed good knowledge that teledentistry reduces isolation and helps increase the accessibility of general dentists and oral medicine specialists to rural and underserved communities for oral health care.[12] The majority of oral medicine specialists work in academic settings in urban areas, making it challenging for patients living in rural areas to easily access oral medicine services, for example, in dental schools or academic medical centres.[12] The total number of oral medicine specialists in Indonesia is 230 persons and increasing, but mostly located in Java and Sumatera islands, and this condition is similar to other developing countries.[6]

Most dental students (62%) and dentists (92%) in this study agreed that teledentistry helps in the initial consultation of oral soft tissue disease with an oral medicine specialist after examination with a camera/photo, and 70% of dental students and 85% of dentists for teledentistry helps increase the accessibility of general dentists and oral medicine specialist to rural and underserved communities for oral health care.[13] According to the study conducted by Raja et al., 60% of dentists admitted to the capability of teledentistry to help patients.[23] Moreover, 70% of the dentists also showed agreement with its usefulness among patients in rural and remote areas.[15,23]

In oral medicine practice nowadays, online video consultations (WhatsApp, Zoom, Teams, Skype videoconferencing software), qualified photos or videos of suspected malignant oral lesions can be performed, clinical notes, health records and oral medicine specialists can establish a provisional diagnosis, advice or urgent referral.[3,15,24] Follow-up of patients after initiation of treatment, such as in chronic therapies based on systemic corticosteroids or immunosuppressive (dosage adjustment and adverse event), can be done via telemonitoring, and the specialist can assess the patient and determine the next course of management.[17]

Half of the dental students and 79% of the dentists in this study agreed that teledentistry helps make informed decisions about oral disease management and referral to an oral medicine specialist. Teledentistry can minimize unnecessary referrals to specialists. Carrard et al. reported the potential of teledentistry service in determining the diagnosis of oral medicine and reducing the referral of cases considered simple and that could be treated in the primary care system.[25,26] Teledentistry improves the quality of management remotely, detects the risk or possibility and assesses the suspected premalignant and malignant lesions.[27] Villa et al. Confirmed that most of the physicians in US studies referred patients with oral lesions to an oral medicine specialist.[28] On the contrary, the study by Friesen et al. [29] and Schleyer et al. [30] showed more than 50% of oral medicine patients were referred by the dentist.

A total of 54.3% of dentists in the present study agreed that Teledentistry helps general dentists order laboratory examinations and investigations of patients according to the direction of an oral medicine specialist. In teledentistry, the patient does not need to be present during the consultation. The dentist can receive radiographs, graphical representations of oro-facial tissues, laboratory results, tests, remarks, photographs, and other information transported through multiple providers.[15,23] Study conducted by Alsafwani et al. reported that laboratory studies were ordered in three (2%) patients on their first tele(oral)medicine visit.[13]

Teledentistry helps general dentists in diagnosing oral soft tissue disease, and 79.3% of dentists agreed with this statement. Since 2005, dentists and doctors have practised teledentistry to refer patients to the Regional Oral Medicine Consultant in Northern Ireland. Oral medicine specialists can triage and

treat patients with oral mucosal lesions without tactile examination.[17] The outcomes of several studies explained teledentistry can aid dentists in detecting and making remote diagnoses of oral lesions.[25,31,32] Photographs and videos of oral lesions are the principal diagnostic value in oral medicine and one of the fundamental aspects to determine the provisional diagnosis, following advice or crucial referral.[24,33] Tele(oral)medicine has been proven to be an effective tool to assess oral mucosal disorders promptly and address orofacial pain conditions or postoperative complications that may not necessarily require a face-to-face consultation, thus reducing the risk of potential exposure to COVID-19.[13] Most of the general practitioners have difficulties in discovering, identifying, diagnosing and treat of suspected oral lesions..[22] Deferred diagnosis oral cancer and suspended oral medicine treatment due to COVID-19 may lead to alteration clinical result, treatment and prognosis.[24] Early detection of oral cancer using teledentistry has been shown in several studies.[15,34] Teledentistry had excellent sensitivity (93.8%) and specificity (94.2%) for diagnosing dental pathologies among elderly nursing home residents.[27]

Almost all of the dentists in this study (91.3%) accepted that teledentistry is a useful tool for general dentists to provide drug prescriptions and instructions for treating oral soft tissue disease with the direction of an oral medicine specialist. The study in England recommends teleconsultation for prescribing long-term therapies to patients using systemic corticosteroids or immunosuppressive drugs (dosage adjustment, untoward events).[24] Teledentistry supports the interaction between the dentist and the patient in a follow-up to evaluate the healing progress and medication therapeutic drug administration.[35]

Only 4.3% of dentists did not agree with one of the benefits of teledentistry in supporting observation of the patient's condition according to the direction and opinion of an oral medicine specialist. Teledentistry can be a useful tool for dentists in remote observation, investigation, and evaluation of patients, especially during the COVID-19 pandemic.[35,36] Follow-up using teledentistry for patients with oral pain significantly reduced oral pain, according to 65% of self-reported improvement in oral symptoms.[13]

Most of the knowledge about teledentistry in oral medicine of study participants was fair, and this could relatively be described by impediments such as the demand to expand additional knowledge and skills in digital systems for the implementation of teledentistry.[37] More than half of the dentists in this study had good knowledge about teledentistry in oral medicine, although their experience was less than 5 years. Fresh graduate dentists with less work experience might be more literate with new technology.[15] On the contrary, dental specialists with more than a decade of experience were significantly more capable of implementing teledentistry than general dental practitioners and those with under 10 years of experience.[37-39]

Dentists with more than a decade of work experience had lower levels of knowledge about teledentistry than those with less than 5 and 5-10 years of work experience. Technology literacy could influence the acquisition and implementation of the recommended information and communications technology system. The dental students were adaptive and enthusiastic with a new adaptation of computer-based information systems into the dental curricula, dental health records and management of clinics.[16] Lack of knowledge among dentists in the earlier study was due to the absence of teledentistry in dental curricula and no dental continuing education programs on teledentistry,[23,40,41] and this finding will most probably be the matter in many developing countries.[17] Similar to previous studies, dental students and dentists nowadays use technology in daily life and practice, for example, online class teaching and exams, webinars, dental health records, paperless laboratory and radiography results, and teledentistry.[23]

In the recent study, most dentists had a good knowledge of teledentistry in oral medicine, although restorative and endodontic treatments were the most frequently performed treatments, followed by periodontic, extraction, pedodontics, prosthodontic and orthodontic. Corroborating with the earlier studies reported, most of the participants were endodontists and orthodontists, and these professionals were more adhered to teledentistry.[33] The limitation of this study is there is no data obtained for age/years and experience differences and information and technology mastery capabilities; limited sample size and the possibility of not knowing which participants have positive or negative tendencies towards the study objectives can result in response bias.

CONCLUSION

Finally, these findings revealed that dental students had low knowledge of teledentistry in oral medicine, while most dentists had good knowledge. The lack of knowledge among participants could be overcome by introducing teledentistry into the dental curricula and continuing education programs.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this research report.

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ORIGINAL ARTICLE

The Correlation between Subjective Complaint of Dry Mouth, Unstimulated Salivary Flow Rate, and Oral Mucosal Dryness in Patients with Sjogren's Syndrome

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ABSTRACT

Background: Sjogren's syndrome is an autoimmune disease characterized by the classic symptoms of dry mouth, dry eyes, and arthritis. The most common symptoms are called sicca symptoms, which consist of keratoconjunctivitis sicca, hyposalivation, and xerostomia. Many papers use the term xerostomia and hyposalivation interchangeably. However, these two terms define different conditions. Xerostomia describes the subjective complaint of dry mouth, whereas hyposalivation is objectively measured. **Objective:** To examine the correlation between xerostomia, unstimulated salivary flow rate, and oral mucosal dryness in patients with Sjogren's syndrome. **Results:** The Summated Xerostomia Inventory Indonesian version (SXI-ID) and Clinical Oral Dryness Score (CODS) correlate negatively with unstimulated salivary flow rate. Whereas SXI-ID is positively correlated with CODS. **Conclusion:** Xerostomia assessed using SXI-ID is not always followed by hyposalivation. Hyposalivation affects the wettability of oral mucosa, as it negatively correlates with dryness. Further study is needed to investigate the factors involved in the correlation between xerostomia and hyposalivation.

Keywords xerostomia, hyposalivation, Sjogren's syndrome, SXI-Id, CODS

INTRODUCTION

Sjogren's syndrome (SS) is an autoimmune disease characterized by the classic symptoms of dry mouth, dry eyes, and arthritis.[1,2] Sjogren's syndrome has a wide variety of signs and symptoms. It can be divided into primary Sjogren's syndrome (pSS) and secondary Sjogren's syndrome (sSS).[1] Primary Sjogren's syndrome occurs alone, while secondary Sjogren's syndrome occurs in conjunction with other autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and systemic sclerosis.[1]

The most common symptom of Sjogren's syndrome is Sicca Syndrome, which consists of keratoconjunctivitis sicca, with a complaint about a foreign-body sensation in the eyes, increased sensitivity to light, marked hyposalivation, and xerostomia, with difficulties chewing and swallowing foods.[1] Salivary gland damage becomes one of the hallmarks of pSS. However, this process progresses slowly over the years and is frequently overlooked, resulting in an average delay of diagnosis of pSS for seven years.[3]

Two terms are commonly used in dry mouth: xerostomia and salivary gland hypofunction (hyposalivation). Many papers use these two terms interchangeably when, in fact, each term defines a different condition. Xerostomia is the term used to describe the sensation of dry mouth, a subjective complaint of patients.[4] Since xerostomia is subjective, it can only be diagnosed by directly questioning the individual using the Summated Xerostomia Inventory (SXI); to Indonesians, it's the SXI-Id version.[5,6] While objectively, hyposalivation is a condition of reduced salivary flow rate and can be measured by sialometry. Additionally, the clinical dryness of the oral cavity was objectively measured by the Clinical Oral Dryness Score (CODS).[7]

Xerostomia is not always necessarily experienced in hyposalivation; it can be found in patients with normal salivation.[4] To the extent of our knowledge, no study correlates the subjective complaint of dry

mouth measured by SXI-ID, hyposalivation measured by sialometry and the objective dry mouth measured by CODS in Sjogren's syndrome patients. Thus, this study aims to correlate the subjective complaint of dry mouth (SXI-ID) and the objective finding of dry mouth (sialometry and CODS) in Sjogren's syndrome patients.

MATERIALS AND METHODS

This retrospective cross-sectional study includes Sjogren's syndrome patients presented to Oral Medicine Clinic of Dr. Cipto Mangunkusumo General Hospital from January 2021 to January 2023. The SXI-Id, unstimulated salivary flow rate (USSFR), and CODS examination were conducted as routine examinations in Sjogren's syndrome patients. Data will be presented as mean, standard deviation, or median and minimum maximum. Correlation between SXI-Id and USSFR, SXI-Id and CODS, and SXI-Id and USSFR will be analyzed using the Pearson's or Spearman Correlation Coefficient. The analysis is done using SPSS for Mac version 24. This study was approved by The Ethics Committee of the Faculty of Medicine, Universitas Indonesia-Cipto Mangunkusumo Hospital No. KET-1027/UN2.F1/ETIK/PPM.00.02/2023.

RESULTS

Four hundred thirty patients were included in this study. They were all consulted in the oral medicine clinic with suspected Sjogren's syndrome from January 2021 to January 2023. The age range of the patients was 17 to 80. Most patients were female, 386 (90%) vs 43 (10%) male. The demographic data is shown in Table 1.

Table 1. Demographic data of subjects

Subject Characteristics	Mean (±SD)	N (%)
Gender		
Male		43 (10)
Female		386 (90)
Age	43.3 (±14.1)	

The SXI-ID's median score was 12, within the range of 5 to 25. Among all subjects examined, 38.4% had a lower unstimulated salivary flow rate but had not yet fallen into hyposalivation criteria, and 49.3% had hyposalivation. Only a few subjects had normal or even above-normal unstimulated salivary flow rates. The median score for CODS was 3, which is considered mild oral mucosal dryness, and only a few had severe oral mucosal dryness, as shown in Table 2.

Table 2. The Characteristics of Oral Condition

Oral conditions	Median (min-max)	N (%)
SXI-Id	12 (5 - 25)	
USSFR (ml/min)	0.12 (0 – 1.08)	
Above Normal (>0.4 ml/min)		15 (3.5)
Normal (0.3 - 0.4 ml/min)		38 (8.8)
Below Normal (<0.3 - >0.1 ml/min)		165 (38.4)
Hyposalivation (≤0.1 ml/min)		212 (49.3)
CODS	3 (0 – 8)	
Not Dry (0)		26 (6)
Mild (1-3)		252 (58.6)
Moderate (4-6)		134 (31.2)
Severe (7-10)		18 (4.2)

Study participants' responses to SXI-Id were recorded in five Likert Scale as shown in Table 3.

Table 3. Responses in the score of SXI-Id

SXI-ID	Responses				
	Never	Hardly Ever	Occasionally	Frequently	Always
SXI 1	147	14	19	70	180
SXI 2	328	11	10	19	62
SXI 3	320	13	12	32	53
SXI 4	296	13	21	32	68
SXI 5	132	28	30	58	182

The distribution of the SXI, USSFR, and CODS data was not normal, according to the normality test. Thus, we continue to analyze the correlation using Spearman's correlation.

The SXI-Id version is negatively correlated with USSFR with a correlation coefficient of –0.185 ($p<0.05$) and positively correlated with CODS with a correlation coefficient of 0.112 ($p<0.05$). The correlation between SXI-Id and USSFR, as well as SXI-Id and CODS, are shown in Table 4.

Table 4. The correlation between SXI-Id and USSFR, SXI-Id and CODS

Variable	Correlation (r)	p-value
USSFR	- 0.186	0.000
CODS	0.113	0.000

Unstimulated salivary flow rate negatively correlates with CODS with a correlation coefficient of – 0.480 ($p<0.05$). The correlation between USSFR and CODS is shown in Table 5.

Table 5. The correlation between USSFR and CODS

Variable	Correlation (r)	p-value
CODS	- 0.480	0.000

DISCUSSION

Sjogren's syndrome is a systemic autoimmune disease which characterized by the inflammation and dysfunction of exocrine glands, with dry eyes and dry mouth as a hallmark called Sicca syndrome.[8,9] SS predominantly affects women, with a 9:1 ratio to men, and our study was in accordance with previous data, with a women to men ratio of also 9:1.[9] This high female-to-male ratio of SS was said to be common in Asia compared to other continents or races.[9] SS is commonly diagnosed in the fifth decade of life, but somehow, the mean age of SS patients in this study was younger (43 years old) compared to other documented studies, which range from 51 to 62 years old.[9]

The salivary gland damage, as one of the hallmarks of pSS, progresses slowly over the years and is frequently overlooked, resulting in an average delay of diagnosis of pSS for seven years.[3] The salivary gland dysfunction, which leads to hyposalivation, may hinder the eating and swallowing process, speaking, and taste perception and increase the risk of oral infection, eventually decreasing the patient's quality of life.[10]

There are two terms commonly used in dry mouth: xerostomia and salivary gland hypofunction (hyposalivation). Many papers use these two terms interchangeably when in fact, each term defines a different condition. Xerostomia is the term used to describe the sensation of dry mouth, a subjective complaint of dry mouth by patients.[4] Since xerostomia is subjective, diagnosis of xerostomia can only be made by directly questioning the individual, using the Summated Xerostomia Inventory (SXI) to the Indonesian SXI-Id version.[5,6] Hyposalivation is a condition of reduced salivary flow rate and can be measured by sialometry. The clinical dryness of the oral cavity was objectively measured using the clinical oral dryness score (CODS).[7]

SXI-ID was used to diagnose the presence of the perceived dry mouth, although it does not have a cut-off score to state the degree of the perceived dry mouth. The minimum score of the SXI-ID was

five, which is considered as no perceived dry mouth, and the maximum score was 25, which is considered the most severe perceived dry mouth. The median score of SXI-ID in this study was 12, which can be considered medium-perceived dry mouth. Among 430 subjects, 65.8% complained of dry mouth, and 69.3% had dry lips in the past month. Despite having a dry mouth, we found that most subjects had no eating and/or swallowing difficulties (74.42% and 68.84%, respectively). It is possible that the disease has not yet affected the stimulated salivary flow rate, but unfortunately, this study did not measure the stimulated salivary flow rate; thus, we do not have any evidence to prove this hypothesis.

Xerostomia does not always necessarily arise in hyposalivation; it can be found in patients with normal salivation.[4] This study found only a few subjects with normal (8.8%) and above-normal (3.5%) unstimulated salivary flow rates. Almost half of the subjects (49.3%) suffered from hyposalivation, 38.4% of subjects had below normal unstimulated salivary flow rate, and the median unstimulated salivary flow rate of all subjects was 0.12 ml/minute, which is considered below normal. Although perceived dry mouth or xerostomia does not always arise in hyposalivation, subjects in this study mostly had xerostomia and hyposalivation. This is supported by the correlation analysis between SXI-Id and USSFR, as SXI negatively correlates with USSFR. However, this correlation is considered to be weak with a correlation coefficient of –0.185 ($p<0.05$).

Hyposalivation logically will be followed by the dryness of oral mucosa. Thus, we analyze the correlation between unstimulated salivary flow rate and clinical oral dryness score. This study found that unstimulated salivary flow rate had a moderate negative correlation with CODS, with a correlation coefficient of –0.480 ($p<0.05$). Although the majority of saliva is water (99%), it also contains protein called salivary pellicle.[11] This salivary protein adheres to oral mucosal surfaces and maintains an adsorbed salivary film.[11] Hyposalivation patients may suffer from the loss of saliva pellicle, resulting in poor surface hydration, reduced wettability and higher hydrophobicity of oral mucosal surfaces.[11]

On the other hand, xerostomia (the perception of dry mouth) is not always associated with reductions in unstimulated salivary flow rate.[12,13] One of the factors that influence xerostomia is thought to be the changes in salivary composition. The protein composition in the minor salivary gland is much higher than that of whole saliva, while the sialometry was performed by measuring the whole unstimulated saliva. Thus, unstimulated salivary flow rate alone does not explain xerostomia.[13]

The retrospective nature of this study constituted a drawback. Additionally, we cannot assess the inter-examiner reliability, and we did not examine the stimulated salivary flow rate or further analyze the salivary composition.

CONCLUSION

The hallmarks of Sjogren's symptoms are Sicca symptoms, which are dry eyes and dry mouth. Dry mouth can be subjective (xerostomia) and objective (hyposalivation); these terms are sometimes used interchangeably. Xerostomia is assessed using SXI-ID, which is not always followed by hyposalivation. The hyposalivation affects the wettability of oral mucosa, as it negatively correlates with oral mucosa dryness. Further study is needed to investigate the detailed correlation between xerostomia and hyposalivation and the factors affecting them.

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