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Oral lesions in Covid 19 positive patients



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1. Introduction

Coronavirus disease 2019 (Covid 19) which causes pandemics all over the world, primarily causes pneumonia by infiltrating the respiratory tract [1]. The first stop of viruses that infect the respiratory tract is the oral cavity [2]. Few reports have retailed the oral appearances of COVID-19 [2–5]. Many systemic diseases such as nutritional deficiencies, autoimmune disorders, or human immunodeficiency virus infection can present with oral lesions [6,7].

Prevalent oral lesions contain aphthous lesions, erythema, and lichen planus [8]. Identification and diagnosis need conducting an entire oral investigation. Information of characteristics such as placement, structure and color are useful in confirming the diagnosis [9].

In this study, we tried to identify possible oral lesions for the early diagnosis of Covid-19 which we still have limited information.

2. Methods

Seventy-four Covid 19 patients (age range 19–78 years(mean \pm SD age, 45,6 \pm 12.8)) who presented to our clinic between April 2020 and October 2020 were included in this prospective, observational study. This study was approved by the Local Ethical Committee. Informed consent was obtained from all subjects.

At study entry, all subjects were examined in detail. Also routine blood analyses, real-time reverse transcriptase–polymerase chain reaction (PCR) test of nasopharyngeal swab and chest X-rays were performed in all participants.

All participants who had received hormone therapy and/or steroid therapy in the one month prior to the study or those who were taking any drugs that might affect oral lesion were also excluded from the study. We excluded the subjects whom have oral lesions prior Covid diagnosis.

The PCR trials were accomplished on nasopharyngeal swabs adhering a previously reported procedure [10].

Statistical investigations were accomplished by handling the SPSS software, version 21.0 (SPSS Inc., Chicage, IL, USA) for Windows. Unqualified variables are exhibited as percentages and constant variables are exhibited as mean \pm SD.

Relationships of constant variables in the group were ascertained with Wilcoxon rank-sum tests. Relations between two constant variables were measured with Spearman rank correlation coefficients. Unqualified variables were measured with likelihood ratio χ 2 tests. A value of P < 0.01 was determined as statistically important.

3. Results

In total, seventy four patients who diagnosed Covid 19 were enrolled to the study (mean \pm SD age 49.3 \pm 7.2 years; 49 (66.2%) males, 25 (33.8%) females). Demographic distribution and comparision of Covid 19 patients were shown in Table 1. Table 2 shows the classification of oral lesions and distribution oral lesion areas. Aphthous-like ulcer was the most common oral lesion (n: 27). Respectively, other findings were erythema (n: 19) and lichen planus (n: 12). The most common location of lesions was tongue (n: 23). Respectively, other lesion areas were buccal mucosa (n: 20), gingiva (n: 11) and palate (n: 4).

4. Discussion

Many systemic viral infections such as human immune deficiency virus have oral lesions and progression of systemic viral infections is associated with range of oral manifestations [11]. Oral lesions were found to have diagnostic and prognostic values.

Aphthous-like ulcer is most prevalent oral mucosal lesion. The etiology is frequently multifactorial [12]. Erythema is a T-cell mediated immune condition and it is most prevalently associated with infections in a young to middle aged persons. Erythema is predominantly seen in boys [13].

Lichen planus is an immune mediated T-cell response with an

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Table 1

Demographic distribution and comparision of Covid 19 patients.

Gender	Patients with oral lesions (n/ %)	Patients without oral lesions (n/ %)	Total (n/ %)	р
Male	38/65.5	11/68.8	49/66.2	0.249
Female	20/34.5	5/31.2	25/33.8	
Total	58/100	16/100	74/100	
Age (Mean \pm	$52.8\pm6.9/$	$49.3 \pm 5.8/$	51.4 \pm	0.117
Standard	31-68	28-67	6.3/	
Deviation)/			28-68	
(min-max)				

Table 2

Classification of oral lesions and distribution of lesion areas.

	Aphthous-like ulcer	Erythema	Lichen planus	Total (n/ %)
Tongue	12	8	3	23/39.7
Buccal mucosa	9	7	4	20/34.5
Gingiva	4	3	4	11/18.9
Palate	2	1	1	4/6.9
Total (n/%)	27/46.6	19/32.8	12/20.6	58/100

approximated prevalence of 0.22 to 5% and most frequently affecting middle aged women and typically affecting the buccal mucosa, tongue, lips, gingiva [14].

Oral lesion prevalence in non-Covid subjects varies between 51.4 and 81.3%.^{3,5,10} In our study, the frequency of oral lesions in covid patients is 78.4%.

In the literature, the most prevalent oral lesions in non-Covid subjects were coated tongue (51.4%), leukoplakia (13.8%), traumatic oral lesions in 9.2% [15,16]. In our study, the most prevalent oral lesions in Covid subjects were aphthous-like ulcer (36.5%), erythema (25.7%), lichen planus (16.2%).

In this study we found oral lesions in fifty-eight of seventy-four Covid 19 patients. There is limited reports about oral lesions in patients with Covid 19. There are investigations present that Covid 19 impair to respiratory and other tissues could be associated to the dispersion of angiotensin converting enzyme 2 (ACE2) sensors in body [17]. Hence, cells with ACE2 sensor allocation may enhance entertainer cells for the Covid 19 and additionally cause inflaming responses in associated tissues, such as the oral mucosa [18]. Nearby, accessible affirmation has not constituted an effective drug against COVID-19 up to this time [19,20].

Oral mucosa lesions could be the consequence of many agents, such as stress, insufficiency of oral hygiene or systemic infections [21,22]. Local antiseptics such as hydrogen peroxide based suspensions advised to lessen the viral burden [23].

The oral circumstances confronted by this survey and other published studies fortifies the theory which they are enthusiastically implicative of secondary lesions occurring from the impairment of systemic vigour or appropriate to therapies for Covid-19 [22]. In spite of estimating our analysis of affiliated terms, the otorhinolaryngologist's significance as part of the medical team in evaluating patients with Covid-19, should be foregrounded. Oral investigation should be standard protocol of patients with Covid 19. Additionally surveys with larger groups are required to ascertain whether the Covid 19 is the occasion or the factor that increases probability of oral lesion development.

Declaration of competing interest

The authors whose names are listed immediately below certify that

they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

- Cevik M, Bamford CGG, Ho A. COVID-19 pandemic-a focused review for clinicians. Clin Microbiol Infect 2020 Jul;26(7):842–7. https://doi.org/10.1016/j. cmi.2020.04.023 [Epub 2020 Apr 25].
- [2] Baghizadeh Fini M. Oral saliva and COVID-19. Oral Oncol 2020 Sep;108:104821. https://doi.org/10.1016/j.oraloncology.2020.104821 [Epub 2020 May 27].
- [3] Ding Q, Lu P, Fan Y, et al. The clinical characteristics of pneumonia patients coinfected with 2019 novel coronavirus and influenza virus in Wuhan, China. J Med Virol 2020 Mar 20. https://doi.org/10.1002/jmv.25781 [doi: 10.1002/ jmv.25781].
- [4] Chen Y, Guo Y, Pan Y, et al. Structure analysis of the receptor binding of 2019nCoV. Biochem Biophys Res Commun 2020 Feb 17;525(1):135–40. https://doi. org/10.1016/j.bbrc.2020.02.071.
- [5] Samaranayake LP, Fakhruddin KS, Panduwawala C. Sudden onset, acute loss of taste and smell in coronavirus disease 2019 (COVID-19): a systematic review. Acta Odontol Scand 2020 Aug;78(6):467–73. https://doi.org/10.1080/ 00016357.2020.1787505.
- [6] Carrizales-Sepúlveda EF, Ordaz-Farías A, Vera-Pineda R, et al. Periodontal disease, systemic inflammation and the risk of cardiovascular disease. Heart Lung Circ 2018 Nov;27(11):1327–34. https://doi.org/10.1016/j.hlc.2018.05.102.
- [7] Siu A, Landon K, Ramos DM. Differential diagnosis and management of oral ulcers. Semin Cutan Med Surg 2015 Dec;34(4):171–7. https://doi.org/10.12788/j. sder.2015.0170.
- [8] Fitzpatrick SG, Cohen DM, Clark AN. Ulcerated lesions of the oral mucosa: clinical and histologic review. Head Neck Pathol 2019 Mar;13(1):91–102. https://doi.org/ 10.1007/s12105-018-0981-8.
- [9] Warnakulasuriya S. White, red, and mixed lesions of oral mucosa: a clinicopathologic approach to diagnosis. Periodontol 2000 2019;80(1):89–104. https://doi.org/10.1111/prd.12276. Jun.
- [10] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020. https://doi.org/10.1001/jama.2020.1585. Published online February 7.
- [11] Donoso-Hofer F. Oral lesions associated with human immunodeficiency virus disease in adult patients, a clinical perspective. Rev Chilena Infectol 2016 Oct;33 (Suppl1):27–35. https://doi.org/10.4067/S0716-10182016000700004.
- [12] Shah K, Guarderas J, Krishnaswamy G. Aphthous stomatitis. Ann Allergy Asthma Immunol 2016;117:e341–3.
- [13] Celentano A, Tovaru S, Yap T, Adamo D, et al. Oral erythema multiforme: trends and clinical findings of a large retrospective European case series. Oral Surg Oral Med Oral Pathol Oral Radiol 2015;120:707–16.
- [14] Müller S. Oral manifestations of dermatologic disease: a focus on lichenoid lesions. Head Neck Pathol 2011;5:36–40.
- [15] Kovac-Kavcic M, Skaleric U. The prevalence of oral mucosal lesions in a population in Ljubljana, Slovenia. J Oral Pathol Med 2000;29:331–5.
- [16] Shet R, Shetty SRMK, Kumar MN, Yadav RDSS. A study to evaluate the frequency and association of various muosal conditions among geriatric patients. J Contem Dent Pract 2013;14:904–10.
- [17] Zou L, Ruan F, Huang M, Liang L, et al. SARS CoV-2 viral load in upper Resp specimens of infected patients. N Engl J Med 2020 Mar 19;382(12):1177–9. https://doi.org/10.1056/NEJMc2001737.
- [18] Xu J, Li Y, Gan F, Du Y, et al. Salivary glands: potential reserviors for COVID-19 asymptomatic infection. J Dent Res 2020;99(8):989. Jul.
- [19] Godinho GV, Paz ALLM, de Araújo Gomes EPA, et al. Extensive hard palate hyperpigmentation associated with chloroquine use. Br J Clin Pharmacol 2020 Apr 20;86(11):2325–7. https://doi.org/10.1111/bcp.14313.
- [20] Mehra MR, Desai SS, Kuy S, et al. Cardiovascular disease, drug threapy, and mortality in COVID-19. N Engl J Med 2020 Jun 18;382(25):e102. https://doi.org/ 10.1056/NEJMoa2007621.
- [21] Guo X, Zhu Y, Hong Y. Decreased mortality of COVID-19 with renin-angiotensinaldosterone system inhibitors therapy in patients with hypertension: a metaanalysis. Hypertension. 2020 Aug;76(2):e13–4. https://doi.org/10.1161/ HYPERTENSIONAHA.120.15572.
- [22] Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, et al. Oral vesiculobullous lesions associated with SARS-CoV2 infection. Oral Dis 2020;(May). https://doi.org/10.1111/odi.13382.
- [23] Hasturk H, Nunn M, Warbington M, et al. Efficacy of a fluoridated hydrogen peroxide-based mouthrinse for the treatment of gingivitis: a randomized clinical trial. J Periodontol 2004;75(1):57–65.