Original Article

Tongue Manifestations in SARS-CoV-2 Infection: Is It Treatment-Related or Part of Disease Spectrum?

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Abstract

Background: The classical manifestations of COVID-19 infection such as loss of smell, loss of taste, fever, myalgia, and other flu like symptoms have been extensively studied in the literature. However, oral manifestations have been ignored due to lack of proper examination of the oral cavity for the fear of transmission. Hence, in this study, we tried to explore the possible association of tongue changes, namely, fissured tongue (FT), depapillated tongue, tongue with fissures and depapillation against flu-like symptoms, and antibiotic regimen in patients with mild COVID-19 disease. **Materials and Methods:** This cross-sectional and observational study included 70 PCR-confirmed COVID-19-infected patients. Tongue images obtained from all patients. Each picture was analyzed to label the tongue as follows: (1) Normal tongue, (2) FT, (3) erythematous depapillated tongue, and (4) depapillation with fissures, on the dorsal surface of tongue by two dental experts independently. Inferential statistics like Chi-square test was applied for qualitative variables to find the association. The level of significance is set at 5%. **Results:** The depapillated variety showed a significant association with the classical symptoms of COVID-19 disease (fever, loss of smell, and loss of taste). Cough, antibiotic treatment, and age did not influence the incidence of tongue lesions in these patients. **Conclusion:** Based on our studies, we suggest that depapillated tongue should be included in spectrum of severe acute respiratory syndrome coronavirus 2 infection.

Keywords: COVID-19, Depapillated tongue, Fissured tongue, Severe acute respiratory syndrome coronavirus 2, Oral manifestations, Autoimmune.

Introduction

Human ecology and its delicate balance have been challenged by the COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The etiopathogenesis of the COVID-19 disease spectrum has been found to be variable.[2,3] Fever, dry cough, myalgia, and malaise are the classical symptoms in most people.[4,5] Oral mucosal lesions have recently been reported as important signs.[6] The presence of oral lesions was detected to be the first sign of COVID-19 in few cases reported.[7] Hence, there has been a growing interest to study the variety of oral lesions in SARS-CoV-2 infection.[8]

Chemosensory dysfunctions in relation to smell and taste are considered as a hallmark in suggesting an early screening test, however, these are subjective and can be seen as part of any viral infection.[9,10] However, the oral manifestations in the background of typical symptomatic complex (fever, dry cough, headache, and fatigue) can increase the detection rate of COVID infection in patients with flu-like symptoms.[11,12] Oral manifestations are objective proof and hence increase the clinical diagnostic ability.[13] Tongue (38%) is the most frequent location for oral lesions followed by lips (26%) and palate (22%).[14]

The various morphological changes in the tongue serve as diagnostic markers in a number of diseases.[15,16] Abnormalities in the tongue could be characteristic of a particular disease or may reflect as a sign of general ill health.[17,18] A lot of importance has been given to subjective symptoms in COVID disease and the obvious oral cavity signs occurring in the early stage of the disease are missed due to skipping of thorough oral examination to avoid transmission.[6] The previous studies on oral manifestations of SARS-COV-2 infection have shown a

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lot of heterogeneity. However, in our study, we observed that specific changes of tongue in patients infected with SARS-COV-2 were fissured and depapillated tongue. Hence, in this study, we tried to explore the possible association of these two tongue changes against the symptoms and treatment in patients with mild COVID-19 disease.

Materials and Methods

This is a cross-sectional observational study with a sample of 90 participants. All subjects had confirmed SARS-CoV-2 infection as determined by nasopharyngeal swab RTPCR. Mild symptomatic diseases with loss of taste and smell, fever, and cough without respiratory distress who did not need oxygen support were included in the study. Out of 90 tongue images, 20 were excluded from the study sample due to poor photographic image. Research participants included both sexes, over half of the cases (72.9%) were males and age ranged from 12 years to 72 years. This study was performed at the temporary COVID-19 quarantine facility at the recognized COVID Care Centre.

Tongue pictures were obtained on smartphone without compromising the barrier protocol followed by the COVID care team. Each image was taken without magnification and filters. Obtained tongue pictures were anonymized with the additional description such as SRF ID, age, and gender of the patient provided in the portal. Evaluation of other associated symptoms such as fever, cough, loss of smell, loss of taste, and treatment provided (specifically antibiotic use) was recorded from the documents.

Each picture was analyzed to label the tongue as follows: (1) Normal tongue, (2) fissured tongue (FT) (Figure 1), (3) erythematous depapillated tongue (Figure 2), and (4) depapillation with fissures (Figure 3), on the dorsal surface of tongue by two dental experts independently.

Statistical Package for the Social Sciences version 20 (IBM SPASS statistics [IBM corp. released 2011]) was used to perform the statistical analysis. Data were entered into the Excel spreadsheet. Descriptive statistics of the explanatory and outcome variables were calculated by mean and standard deviation for quantitative variables, frequency, and proportions for qualitative variables. Inferential statistics like Chi-square test was applied for qualitative variables to find the association. The level of significance is set at 5%.

Results

Distribution of the subjects based on age groups: Among 70 patients, who's tongue images were analyzed, 51 were male (72.9%) and 19 were female (27.1%). The average age of the patients was 36.69 ± 12.69 years (range: 12–70 years).

Cross inference of normal, fissured, depapillated tongue, and combined fissures with depapillation of tongue in screened patients**:** We studied the incidence of the four types of tongue in our sample. Thirteen patients (18.6%) had normal tongue, 18 patients (25.7%) had only depapillated tongue, 11 patients (15.7%) had only FT, and 28 patients (40.0%) had combined

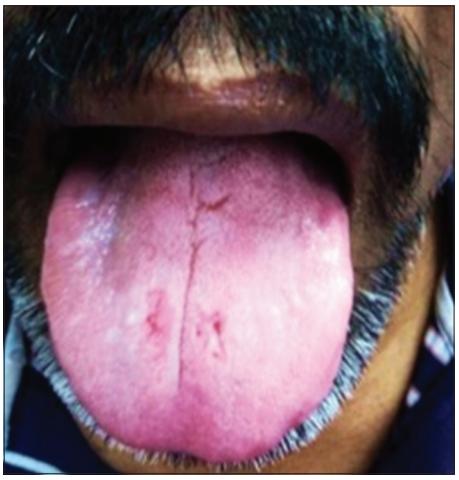

Figure 1: COVID-19 patient presenting fissures on the dorsal surface of tongue

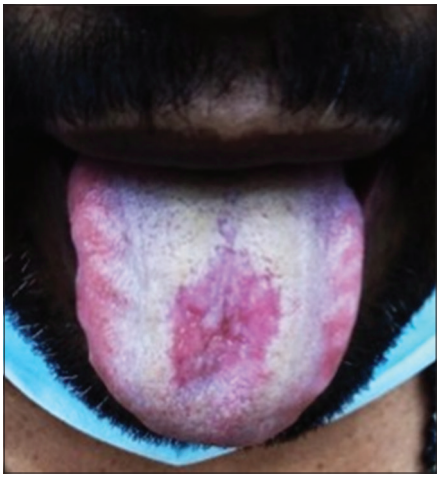

Figure 2: COVID-19 patient presenting with erythematous depapillation of tongue

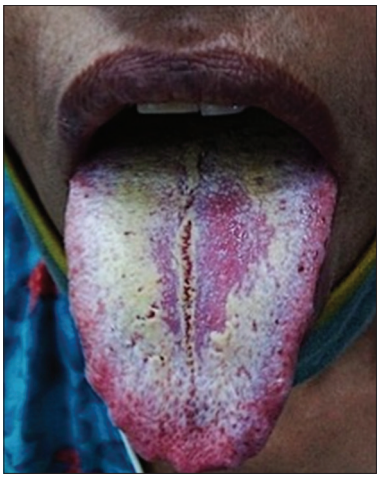

Figure 3: COVID-19 patient presenting depapillation and fissures on the dorsal surface of tongue

depapillation with FT. There were no statistically significant differences, which meant that all the four types of tongues were equally distributed.

Cross inference of loss of taste, smell, fever, cough, azithromycin, and age group in association with FT: 34 (48.6%) patients had loss of taste; 27 (38.6%) had loss of smell; 34 (48.6%) had fever; and 41 (58.6%) presented with cough while none of them had severe disease. In the FT type, none of these symptoms showed statistically significant association. Age group analysis also did not show any statistical significance with FT type.

Cross inference of loss of taste, smell, fever, cough, azithromycin, and age group in association with depapillated tongue: Among 34 patients (48.6%) with loss of taste and 29 (63.0%) of them demonstrated erythematous depapillated tongue which was statistically significant ($P = 0.001$); among 27 patients (38.6%) with loss of smell and 22 (47.8%) of them demonstrated erythematous depapillated tongue which was statistically significant ($P = 0.028$); among 34 patients (48.6%) with fever and 27 (58.7%) of them demonstrated erythematous depapillated tongue which was statistically significant ($P = 0.019$); among 41 patients (58.6%) with dry cough and 30 (65.2%) of them demonstrated erythematous depapillated tongue which was not statistically significant; and among 41 (58.6%) patients who were given an antibiotic (azithromycin) and 30 (65.2%) of them demonstrated erythematous depapillated tongue which was not statistically significant. Age group analysis also did not show any statistical significance with FT type (Table 1).

Table 1: Cross-tabulation of loss of taste, smell, fever, cough, azithromycin, and age group in association with depapillated tongue

Variables	Depapillated tongue		Total	Chi-square value	*P*-value
	No	Yes			
Loss of taste					
No	19	17	36	11.24	0.001*
Yes	5	29	34		
Loss of smell					
No	19	24	43	4.85	0.028*
Yes	5	22	27		
Fever					
No	17	19	36	5.5	0.019*
Yes	7	27	34		
Cough					
No	13	16	29	2.44	0.11
Yes	11	30	41		
Antibiotic use					
No	13	16	29	2.44	0.11
Yes	11	30	41		
Age groups					
>50	4	5	9	1.57	0.81
12–20	3	3	6		
21–30	6	11	17		
31–40	6	14	20		
41–50	5	13	18		

*Significance

Discussion

Mucosal lining of the oral cavity as a whole is prone to be affected by COVID-19, however, dorsal aspect of the tongue is the most common site followed by hard palate, buccal mucosa, gingiva, and lips.[19] The pathophysiology of the tongue involvement could be related to specific receptors. Recent literature suggests that most of the manifestations of COVID-19 disease are related to the distribution of angiotensin-converting enzyme 2 (ACE2) receptors.[20,21]

Expression of ACE2 receptors noted in descending order was found to be highest in type II alveolar cells of lungs, stratified epithelial cells of upper respiratory tract, intestine, myocardial, and kidney cells.[22,23] It is interesting to note that the density of these receptors is highest on the epithelial cells of dorsal surface of the tongue followed by salivary glands, buccal mucosa, and lips.[13,20] All those organs associated with ACE2 receptors pose risk for SARS infection. Hence, it seems logical to assume that oral mucosa is a potential site for entry of the SARS-CoV-2.[24] The host cells so infected with the virus lead to the inflammatory reactions seen in the tongue.[25,26]

In our study sample, all the tongue types (normal tongue, FT, depapillated tongue, and tongue presenting both depapillation and fissures) were equally distributed. This gave us a good diverse sample to compare the effects of disease and treatment with these tongue types, hence, there was no bias. Out of the two pathological types: FT (Figure 1) and depapillated tongue (Figure 2), erythematous depapillated tongue is considered to be an autoimmune phenomenon.[1] With the progression of COVID-19, there occurs disturbance in microcirculation reducing the partial pressure of arterial oxygen circulation and platelet hyperaggregation resulting in erythematous change in tongue.[27,28]

A new term "COVID Tongue" has been coined recently after noticing a close association between geographic tongue (GT) and SARS-CoV-2 infection.[29,30] GT is a chronic autoimmune glossitis characterized by atrophy of the epithelium (filiform papillae in particular).[1] GT and FT have been reported as synchronous lesions in many studies. FT is described as grooves and fissures on the central and lateral glossal surfaces.[31] There is also evidence that GT is associated with higher levels of IL-6, the same inflammatory cytokine that is elevated in severe COVID-19 disease.[1] Psychological factors (stress and anxiety) have been implicated as risk factors for GT and FT which may have a part to play in the high drama of this pandemic too.[32]

Irrespective of symptoms, it was noted that among 70 patients, 39 (55.7%) of COVID-19-positive patients developed FT, 46 (65.7%) of patients developed erythematous depapillated tongue, 28 (40.0%) of patients developed both fissured and erythematous depapillated tongue, and 13 (18.6%) of COVID-19-positive patients had no tongue manifestations.

Interestingly, in our sample, we observed that the erythematous depapillated tongue was significantly common in patients with

fever, anosmia, and ageusia. On the other hand, patients with cough did not show any significant association with tongue manifestations. The antibiotic regimen administered in some of the patients also did not show any significant association with fissured/depapillated tongue which proves that the antibiotic was not the reason for the tongue changes. FT seen in our set of patients did not show significance with the associated typical symptom complex and can be assumed as a sign of stress and general ill health (Table 1).

With the current evidence that is strongly suggesting autoimmune processes to be involved in the various facets of COVID-19 disease, it is not surprising that depapillation (also an autoimmune phenomena) is one of the manifestations of COVID-19 disease.[2,23] We have studied the changes in tongue mucosa of RTPCR confirmed COVID-19 patients in asymptomatic and mildly symptomatic patients. These changes included either fissures or erythematous depapillated areas. Associated yellow membrane coating was seen in few of them, which was also reported in other studies.[24,27] In this regard, we have tried looking for a possible association between the typical symptom complex (ageusia, anosmia, fever, and cough) of COVID-19 disease with the pathological tongue lesions, namely, fissured and erythematous depapillated tongue (Table 1).

Recent studies have proven that tongue manifestations are exclusive to COVID-19 patients when compared to healthy representatives.[17,32] Furthermore, the tongue pictures differed significantly for various presentations of COVID-19 disease.[22] Therefore, we consider adding oral manifestations to the spectrum of COVID-19 symptomatology will improve the detection rates and further help in controlling the transmission. There have been isolated reports of oral manifestations such as ulcers, bullous, and erythematous lesions and acute parotitis in COVID-19 disease.[6,9]

The lack of adequate literature in this area might be due to the limitations of oral examination in these patients for fear of transmission. However, as oral hygiene is an important part of management in these patients, so is the need for a complete oral examination.

Although we assumed that depapillation of tongue is an autoimmune phenomenon, more studies are needed to prove the pathophysiology and the possible role of ACE-2 receptor-mediated direct damage to the mucosal cells.[28,29] Its interesting to note that COVID-19 has been associated with Kawasaki-like disease which is autoimmune vasculitis also affecting tongue (red strawberry tongue).[30,31] COVID-19 has also been reported to present as Melkersson–Rosenthal syndrome (triad of FT, facial nerve palsy, and orofacial edema). These may be additional proof that an autoimmune process is involved in depapillation of tongue.[13,25]

We had several limitations; our sample size was small considering the number of people infected with COVID-19 in the present pandemic, only institutionalized patients were analyzed and not the ones who were under home quarantine and patients in ICU care. This may have led to selection bias. Proportion of male patients was higher than female; hence, the significance in gender association can be biased. The patients included here were in varying phases of COVID infection, hence, the interpretation might not have been uniform and the data were collected only at a single point after their hospitalization, hence, we may have missed tongue findings if they would have appeared later or earlier.

Conclusion

Tongue examination should be a vital part of the assessment of COVID-19 patients. Erythematous depapillated tongue is the most common lesion and was consistently seen in patients with typical symptoms of COVID-19. Hence, it was part of the spectrum of the disease. FT seen in most patients was not directly related to the disease but to stress and poor health. Treatment with antibiotics did not influence either presence or absence of tongue lesions.

Ethical Clearance Number

NO.GDCRI/IEC-ACM(2)/10/2020-21.

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