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ORIGINAL ARTICLE

Factors associated with geographic tongue and fissured tongue

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Abstract

Objectives: The primary objective of this study was to investigate the association of systemic diseases, use of medications, allergies and tobacco habits with geographic tongue (GT) and fissured tongue (FT) lesions. The secondary objectives were to evaluate the clinical characteristics of tongue lesions and to compare the overall results for referred and non-referred patients. *Methodology*: Non-referred patients with GT (GTgp; $n = 130$) and FT (FTgp; $n = 62$) were examined by general practitioners (gp) and compared to a control group without oral mucosal lesions (C; $n = 1029$). Referred patients with GT (GTs; $n = 166$) and FT (FTs; $n = 15$) were examined by oral medicine specialists (s) and compared to GTgp and FTgp. Statistical analyses were performed using unpaired *t*-test or Fisher's exact test. A multiple logistic regression model was developed to control for age and gender as confounders. *Results*: Compared to the C group, GTgp patients used more anti-hypertensive medications and Swedish *snus* ($p < 0.01$). The GTgp group consisted of older males ($p < 0.001$) compared to C. Compared to the GTgp group, the GTs group was younger, more likely to have symptomatic lesions ($p < 0.0001$) and comprised of more females. Among the groups examined, FT patients had the highest mean age. *Conclusion*: This study identified an association between GT and anti-hypertensive medications, as well as the use of Swedish *snus*. It also found differences in the activities and symptoms of the lesions between referred patients and their counterparts who were seen in general dental practice; these parameters influenced the results when these conditions were taken into account.

Keywords: *Benign migratory glossitis*, *oral mucosal lesions*, *tongue lesions*

Introduction

Geographic tongue (GT) is characterized by the loss of filiform papillae, leading to denuded lesions that rapidly undergo change and migrate in a map-like pattern. The lesions typically change over time, with periods of remission [1]. GT is often asymptomatic, although some patients complain of soreness elicited by intake of acidic foods and drinks, increased tongue sensitivity and burning sensations [2–4]. While the etiopathogenesis of GT is unknown, several factors and associated conditions have been proposed. The use of tobacco, hereditary factors, various systemic diseases and fungal infection of the tongue have been suggested to increase susceptibility for the development of GT [5–10]. Stress has also been mentioned as a risk factor for GT [11,12] and the disorder may be accompanied by anxiety and cancer phobia. As stress may be associated with a parafunctional behavior, the latter condition is also potentially associated with GT.

Fissured tongue (FT) is characterized by the presence of grooves or fissures in the dorsal and lateral surfaces of the tongue. As is the case for GT, the etiology of FT remains unclear. Several studies have reported associations between FT and systemic diseases, such as psoriasis, orofacial granulomatosis and diabetes [7,13,14]. That FT is inheritable has also been suggested [6]. In similarity to GT, FT is usually asymptomatic.

The concomitant occurrence of GT and FT has been reported in several studies [15–17]. The concepts that FT follows GT and that FT gradually increases with age have also been put forward [17].

In the present study, we investigated the factors associated with GT and FT and posed the question as to whether referred and non-referred GT or FT

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patients differ with respect to their clinical characteristics, symptoms and demography.

Patients and methodology

Patients

In the present retrospective cross-sectional study, patients with GT or FT were assigned to sub-groups and were compared to each other and to a control group. A survey was conducted of 6448 patients who were seen as part of an annual examination by general dentists between 2004–2006. The patients were examined by one of six general dental practitioners in six private dental clinics in Borås, which is a medium-sized town in the southwest of Sweden, with a total of 66 000 inhabitants. This survey of patients was part of a scientific study, the objectives of which were to calculate the prevalence of oral mucosal lesions in a non-referral adult Swedish population and to estimate the levels of discomfort caused by these lesions [18]. Based on this survey, non-referred patients were examined by general dental practitioners (gp) and presented with GT and/or FT (GTgp, $n = 130$; FTgp, $n = 62$). Patients with missing information from their medical or dental histories or for whom dental images were missing, as well as children aged < 18 years, were excluded from the study. The survey identified 5428 subjects who had presented with a clinically healthy oral mucosa and no oral complaints. From this group, we selected randomly 1029 subjects to serve as the control group (C). Any patient who presented with any kind of oral mucosal lesion was excluded from the control group. The non-referred patient groups (GTgp and FTgp) were compared to the controls to assess factors associated with GT and/or FT.

The patients who had been referred to the clinics of oral medicine and examined by oral medicine specialists (s), presented also with GT and/or FT (GTs, $n = 166$; FTs, $n = 15$). Patients with other oral mucosal lesions were excluded. Referred patients were identified from a clinical database that comprised patients seen by oral medicine specialists, either at the Clinic of Oral Medicine, Public Dental Health, Gothenburg, Sweden between November 1997 and September 2013 or at the Clinic of Oral and Maxillofacial Surgery and Hospital Dental Care, Central Hospital, Karlstad, Sweden between February 1998 and March 2011. Referred patients were compared to non-referred patients to investigate whether there were any differences in clinical characteristics and symptoms between the two groups.

The Central Ethical Review Board in Gothenburg, Sweden approved this study (DNR. 032-12). All patients had to sign an informed consent form prior to the commencement of the study.

Data collection

The general dental practitioners examined the patients in the GTgp, FTgp and C groups, while the oral medicine specialists examined the patients in the GTs and FTs groups. Before the study started, all the general dentists underwent training provided by an oral medicine expert (MJ) regarding calibration in the diagnosis of oral mucosal lesions, data collection and intra-oral photographic techniques. A single electronic form, developed in MedView, was used to collect the clinical information for all the clinical cases and controls. MedView is a computer system for the formalized registration and subsequent analysis of clinical and image-based information related to oral medicine [19]. It operates with an input application focused on the collection and computerized storage of clinical data. During the initial examination, the medical history of each patient was recorded in MedView. The dentists were asked to take clinical images of all the mucosal lesions. All the dentists were equipped with the same type of camera (Sony Handycam 3 CCD). The information was gathered in a single database and exported to MedVisualizer [19]. This application was used for visualization of the information obtained from the database. Finally, data selected for evaluation were transferred to Microsoft® Excel for Mac 2011 software for subsequent statistical analysis.

GT was diagnosed when erythematous depapillated areas surrounded by a red, white or yellow border were observed. A diagnosis of FT was established when multiple grooves or fissures were observed on the dorsal and lateral surfaces of the tongue. The diagnoses made for the GTgp and FTgp groups were confirmed by an oral medicine specialist (MJ) based on the clinical images taken by the general dental practitioners.

Examined variables

In this study, we evaluated systemic diseases, use of medications, self-reported allergies, tobacco use, clinical characteristics and symptomatology for GT and FT patients. Systemic diseases were classified according to the International Classification for Diseases and Health Related Problems, 10th revision (ICD-10; World Health Organization, 2010). The diseases were grouped into categories according to the ICD-10. Medications were classified according to the ATC code (WHO Collaborating Centre for Drug Statistics Methodology, 2011) and the Swedish Medicines Compendium for Physicians (http://www.fass.se)

Allergies were self-reported by patients as 'present' or 'absent'. Use of tobacco products (cigarettes and Swedish *snus*) was registered as 'yes' or 'no'.

Clinical images were used to classify the severity of GT lesions as: 'mild' (single lesion); 'moderate'

(2–5 lesions); or 'severe' (≥6 lesions). Lesions were recorded as 'active' if there were well-demarcated white or red borders or as 'passive' in cases with missing borders, but still having depapillated areas. In fact, we introduced severity and activity parameters to achieve a better understanding of the clinical features of GT. Tongue impressions were registered as 'present' or 'absent'. Simultaneous occurrence of GT and FT was also registered as 'present' or 'absent' (Figures 1–3). Symptoms from the tongue, such as soreness, burning and sensitivity, were registered as 'yes' or 'no' for both GT and FT.

Statistical analysis

The statistical analysis was performed in two stages. First, we compared our variables of interest using an unpaired *t*-test for nominal variables or Fisher's exact test for categorical variables, with a *p*-value <0.05 being considered statistically significant (Tables I–IV). Second, in order to eliminate the confounding effects of age and gender, a multiple logistic regression model (MLR) with *p*-value <0.05 as the threshold for statistical significance was performed for the previously significant pairwise associations identified by Fisher's exact test (Table V). After controlling for age and gender, all findings that were non-significant by multiple logistic regression were discarded. The statistical analysis was performed using the SAS ver. 9.1. software (SAS Institute Inc., Cary, NC).

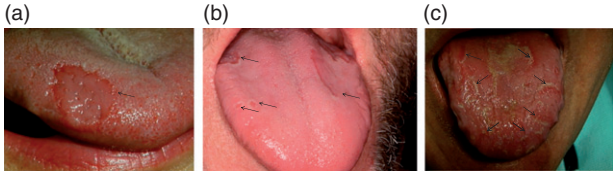

Figure 1. Classification of geographic tongue according to the number of observed lesions. (A) Mild (single lesion); (B) Moderate (2–5 lesions); (C) Severe (≥6 lesions).

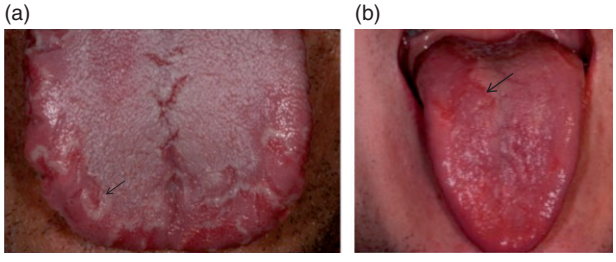

Figure 2. Classification of geographic tongue according to the activity of the lesions. (A) Active lesions have well-demarcated white or red borders. (B) Passive lesions lack distinct whitish borders, but still have depapillated areas.

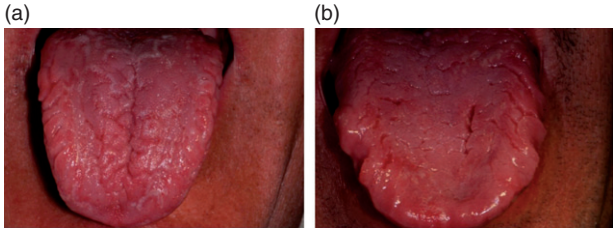

Figure 3. (A) Concomitant geographic tongue (GT) and fissured tongue. (B) Concomitant GT and tongue impressions.

Results

Age and gender distribution

Compared to the control group, the GTgp group had a predominance of males (60.0% vs 40.2%; $p<0.001$) and older age (mean age: 59.9 vs 55.2 years; $p<0.001$) (Table I). The GTs group contained more females than the GTgp group, although this difference did not reach statistical significance (50.6% vs 40.0%; $p=0.07$) and had a lower mean age (48.9 vs 59.9 years; $p<0.0001$).

The two FT groups (FTgp and FTs) had similar gender balances. The patients in the FTgp had a higher mean age than the controls (65.9 vs 55.2 years; $p<0.0001$) and the patients in the GTgp group (65.9 vs 59.9 years; $p<0.01$). The FTs group was also older than the GTs group (mean age = 61.6 vs 48.9 years; $p=0.0089$).

Factors associated with GTgp and FTgp

Compared to the controls, the GTgp patients self-reported more often that they were on anti-hypertensive medications, such as β-blockers and/or calcium-channel blockers (32.3% vs 20.1%, $p<0.01$) (Table II). However, the FTgp patients reportedly use topical corticosteroids for skin diseases more frequently than did the controls ($p<0.01$). Regarding tobacco use, the GTgp group consumed *snus* to a greater extent than the control group (10.1% vs 3.8%, $p<0.01$), whereas cigarette smoking was less common in the GTgp group (5.4% vs 15.4%, $p<0.01$).

A multiple logistic regression model showed that the previously identified statistically significant associations were not confounded by either age or gender (Table V).

Non-referred (GTgp) and referred (GTs) patients with geographic tongue

The frequency of simultaneous GT and FT was higher (albeit not statistically significant) in the GTgp group than in the GTs group (49.2% vs 30.7%) (Table III). In addition, the GTs group had more tongue impressions than the GTgp group (24.7% vs 18.5%), although this difference was not statistically significant. The majority of both the GTgp and GTs patients showed a moderate degree

Table I. Demographics of the patients and controls.

	Non-referred patients		Referred patients		Controls
	GTgp ($n=130$)	FTgp ($n=62$)	GTs ($n=166$)	FTs ($n=15$)	($n=1029$)
Age (years)					
Mean ± SEM	59.9 ± 1.3	65.9 ± 1.7	48.9 ± 1.4	61.6 ± 3.8	55.2 ± 0.5
Median	62	64	49	64	56
No. of females (%)	52 (40.0%)	32 (51.6%)	84 (50.6%)	8 (53.3%)	615 (59.8%)
No. of males (%)	78 (60.0%)	30 (48.4%)	82 (49.4%)	7 (46.7%)	414 (40.2%)

Table II. Factors associated with geographic tongue (GTgp) or fissured tongue (FTgp).

	GTgp	FTgp	Controls
Hypertension	23.85%**	22.6%§	13.3%
CVS[a] drugs	32.3%**	37.1%§	20.1%
Swedish *snus*	10.1%**	4.9%	3.8%
Smoking	5.4%	6.6%	15.4%**

GTgp, FTgp; non-referred patients.
[a]CVS; cardiovascular (anti-hypertensive) drugs, such as β-blockers and/or calcium-channel blockers.
§Hypertension and the use of CVS drugs was significant in the FTgp group compared to controls. However, these associations were found to be confounded by age in the regression model.
**$p<0.01$.

Table III. Clinical characteristics of the non-referred (GTgp) and referred (GTs) patients.

	GTgp	GTs
GT + FT[a]	49.2%	30.7%
GT + TI[b]	18.5%	24.7%
Severity		
Mild	16.9%	22.3%
Moderate	43.1%	48.8%
Severe	40.0%	28.9%
Activity		
Active	38.5%	60.2%***
Passive	61.5%	39.8%
Symptoms[c]	9.2%	47.0%***
Allergy	9.2%*	3.1%

[a]GT + FT; concomitant geographic tongue (GT) and fissured tongue (FT).
[b]GT + TI, concomitant GT and tongue impressions (TI).
[c]Includes soreness and sensations of burning or sensitivity of the tongue.
*$p<0.05$.
***$p<0.001$.

of lesion severity, i.e. 2–5 lesions. Active lesions, assessed based on the appearance of the lesion borders, were more frequent in the GTs group than in the GTgp group (60.2% vs 38.5%; $p<0.001$) (Table III).

The GTs patients reported more symptoms from the tongue, such as soreness and sensation of burning or sensitivity, than the GTgp patients (47.0% vs 9.2%; $p<0.001$) (Table III). Evaluation of symptom-related factors showed that the GTs patients had more symptoms if they had simultaneous GT and FT lesions (51.0% vs 12.5%; $p<0.0001$), co-existing tongue impressions (39.0% vs 12.5%; $p=0.02$) and active lesions (41.0% vs 4.0%; $p<0.0001$) (Table IV), as compared with the GTgp group.

We also found a difference in the frequency of self-reported allergies when the GTgp group was compared to the GTs group (9.2% vs 3.0%; $p<0.05$) (Table III). This result remained valid after controlling for age and gender (as possible confounders) in a regression model with $p=0.04$.

Non-referred (FTgp) and referred (FTs) patients with fissured tongue

Symptoms were more frequent in FTs compared to the FTgp group (73.0% vs 17.7%; $p<0.0001$). This result was also valid after controlling for age and gender in the MLR model ($p<0.001$). A higher frequency of tongue impressions was noted in the FTs group compared to the FTgp group (33.0% vs 17.7%), although this difference did not reach statistical significance.

Discussion

In the present study, we identify anti-hypertensive medications and the use of Swedish *snus* as factors associated with geographic tongue (GT). An inverse association with cigarette smoking is defined. We also show differences between the GT and FT patients seen in an oral medicine clinic (GTs/FTs) as compared to their equivalents seen in a general practice (GTgp/FTgp), with consequent impacts on the results when these conditions are studied.

The presence of hypertension was self-reported by the patients, which is a limitation to the present study in that most patients would not consider themselves as suffering from cardiovascular disease, since their blood pressure had been normalized by medication. Nevertheless, the results are coherent with the reported use of medications for hypertension and a statistically significant association between GTgp and the use of β-blockers or calcium-channel blockers is evident. We also compared the frequencies of hypertension between the GTs and control groups. The control group reported hypertension

Table IV. Factors associated with symptoms experienced by referred (GTs) and non-referred (GTgp) patients.

	GTs		GTgp	
	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic
GT + FT[a]	26***	25	8	56
GT + TI[b]	16*	25	3	21
Active lesions	41***	59	2	48

[a]GT + FT; concomitant geographic tongue (GT) and fissured tongue (FT).
[b]GT + TI, concomitant GT and tongue impressions (TI).
*$p < 0.05$.
***$p < 0.001$.

Table V. Multiple logistic regression (MLR) for factors associated with geographic tongue (GTgp) or fissured tongue (FTgp).

	OR	95% CI	*p*-value
Hypertension	1.7	1.05–2.75	0.029
CVS[a] drugs	1.6	1.01–2.70	0.042
Swedish *snus*	2.1	1.10–4.35	0.025

OR, odds ratio; 95% CI, confidence interval.
[a]CVS, cardiovascular (anti-hypertensive) drugs such as β-blockers and or calcium-channel blockers.

significantly more frequently than the GTs group. However, the regression model eliminated this association, as it was confounded by age, which is reasonable given the difference in mean age between these two groups. This result is in line with the finding that the use of anti-hypertensive medications is not different between the two groups.

Hypertension has previously been reported as one of the most common systemic diseases in Indian and Libyan populations with tongue lesions [20,21]. However, as the tongue lesions were not specified in those studies, it was not possible to conclude an association with GT or FT. In fact, our study is the first to suggest a specific association between GT and hypertension. Thus, it is possible that hypertensive disease or the medications used to treat hypertension in these patients are factors associated with GT.

Our results show that FTgp patients used dermatological preparations of topical corticosteroids significantly more often than the controls. Despite this significant association for the use of topical steroids, we did not find any cutaneous disorders among the FTgp patients. In contrast, Costa et al. [22] reported that FT was significantly associated with cutaneous psoriasis, although no significant associations were reported between topically or systemically administered medications and GT or FT. In the present study, we consider this association as coincidental, with just a few patients ($n = 3$) having used the medication. Thus, based on the results of the present study, it does not appear to have any clinical implications.

Tobacco use has previously been studied in GT and FT patients. We evaluated two different habits: cigarette smoking and the use of Swedish *snus*, which is an orally applied smokeless tobacco. Our results show that both the GTgp and FTgp patients used cigarettes significantly less frequently than the controls, which is in agreement with the previous finding of an inverse association between smoking and GT [5,15,16]. Avcu and Kanli [23] reported the same finding for GT patients, but the opposite finding for FT patients. The putative protective effect of cigarette smoking may be attributable to cytological changes in the oral mucosa, such as increased cellular proliferation and keratinization. Furthermore, nicotine reduces the levels of TNF-α, interleukin (IL)-1 and IL-6, which have anti-inflammatory properties that might prevent the development of GT [15].

In contrast to cigarette smoking, the number of users of Swedish *snus* was significantly higher in the GTgp group than in the control group. Thus, different patterns of tobacco use give different outcomes.

We compared the GTgp and GTs patients in terms of simultaneous FT, tongue impressions, disease severity and activity of lesions based on clinical images of the patients. The concomitant occurrence of GT and FT was seen more often in the GTgp group, which may be explained by the age difference between this group and the GTs group. This finding supports the findings of Yarom et al. [17], who suggested a gradual increase in FT incidence with age.

The GTs group displayed more tongue impressions than the GTgp group. We evaluated tongue impressions as a sign of parafunctional habits, reflecting habitual forcing of the tongue against the teeth. It is possible that tongue impressions are related to patients' stress levels. This hypothesis is supported by the observation of Alikhani et al. [12], who found a positive correlation between GT and anxiety in a group of referral patients.

The majority of the GTgp patients had passive lesions, with fewer tongue impressions and fewer symptoms than the GTs group. The symptoms of the GTs patients increased significantly when they had concomitant FT, tongue impressions and active lesions, as compared to the GTgp patients. Therefore, it seems likely that our activity score reflects the degree of symptoms. Darwazeh et al. [2] reported that 28.0% of GT patients had symptoms, mainly soreness caused by acidic food and drinks, indicating that the tongue mucosa was compromised.

It is reasonable to assume that the active lesions of the tongue observed in our GTs patients represent more vulnerable areas associated with increased discomfort.

By examining the patients' clinical histories, we found that the GTgp group reported significantly more allergies than the GTs group. A significant relationship between GT and allergy and atopic diseases has been reported among Iranians [15]. In contrast, no significant association between GT and allergy or atopy was found in US patients [16]. The reliability of self-reported allergy is questionable, as most patients will not be able to discriminate between general hypersensitivity and true allergy.

FT lesions are often asymptomatic and patients with FT rarely seek referral to oral medicine specialists. This may explain the small size of the FTs group. Nonetheless, our results show that FTs patients are more symptomatic and have more tongue impressions than FTgp patients. Pain may be associated with FT in cases where deep fissures trap food, debris and bacteria, leading to inflammation. Symptoms of idiopathic pain and burning sensation have previously been found to be significantly associated with the presence of fungi on the tongue surface [10].

Our study demonstrates a clear predominance of male GTgp patients, as compared with the controls and GTs patients. A predominance of males has also been reported in Indian and Iranian cohorts [20,24]. In contrast, several studies have shown no significant association between GT and gender [15–17,23]. The predominance of male patients in GTgp, in comparison to previous Swedish studies that showed no predominant gender, may be explained by the observed inverse association between smoking and GT [5,25]. Smoking habits in Sweden have changed over time, with fewer men and more women smokers [26].

The predominance of younger females in our GTs group may be linked to a greater concern among younger women that GT will affect their appearance or that the disorder could be contagious or even precancerous, leading them to seek referrals to specialists. If so, the management of this group should be focused on reassurance and appropriate information about the benign and recurrent nature of the lesion.

Regarding FT, the present study shows no gender predominance among our patients, as observed in previous studies [17,27]. A higher frequency of males with FT has been reported in Jordanian, Swedish, Turkish and Slovenian populations [2,5,23,28], while female predominance has been reported in another Swedish study and in a Hungarian population [25,29]. The median ages of our FTgp and FTs patients were clearly higher than the corresponding values for our GT patients. This is in accordance with several previous studies [2,17,28–30] and our interpretation is that GT is transforming into FT. It seems that GT and FT represent different reaction patterns of the same inflammatory disease of the tongue [31]. The co-existence of GT and FT; together with the fact that FT is present at an older age compared to GT, supports the notion that at least some GT cases become transformed into cases of FT [32].

In conclusion, the present study demonstrates that hypertension or hypertensive medications and the use of *snus* are factors associated with GT. Our results emphasize the differences between non-referred and referred patients. In this study, the referred GT patients were younger women who had more tongue impressions and active and symptomatic lesions. The management of these patients should be focused on reassurance and stress management. Another important implication is that the recruitment of GT/FT patients should be carefully tailored to the purpose of the study, as different populations will have different clinical characteristics.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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