Prevalence and Handedness Correlates of Recurrent Aphthous Stomatitis in the Turkish Population

Yasin Çiçek, DDS, PhD; Varol Çanakçi, DDS, PhD; Mehmet Özgöz, DDS; Ümit Ertas, DDS, PhD; Ebru Çanakçi, MD

Abstract

Objectives: *The present study was designed to determine the relationship between recurrent aphthous stomatitis (RAS) and handedness, and to assess the prevalence of RAS in the Turkish population.* ***Methods:*** *The present study was conducted among 11,360 persons (5,705 males and 5,655 females) with a mean age of 30.4 years. A questionnaire focusing on handedness was administered to these patients. Handedness was assessed according to the Edinburgh Handedness Inventory. The diagnosis of RAS was made on the basis of clinical appearance, location, and the patient's health history. RAS information of patients was collected by means of a data form specifically designed for this study. Subjects were informed about RAS. We took anamneses and filled out the investigation forms. Apart from patients with registration of current aphthae (average point prevalence, APP), patients who had a past two-year history (self-reported two-year prevalence, SRTP) of the lesion were also included in this study. Data were analyzed using the chi-square and logistic regression tests.* ***Results:*** *The prevalence of RAS (APP) was 2.7 percent and that of a history of RAS (SRTP) 22.8 percent. Thus, the total prevalence (APP+ SRTP), including present lesions and a two-year history (SRTP), was 25.5 percent. Adjusted results showed that females, left-handers, 10–30-year-olds, and nonsmokers were 1.53, 1.69, 2.05, and 1.61 times more likely to have RAS (APP+SRTP) than males, right-handers, 31–50-year-olds, and smokers, respectively (*$P<.0001$*).* ***Conclusion:*** *The present study suggests that left-handedness appears to be a predictor factor for RAS. [J Public Health Dent 2004;64(3):151-56]*

Key Words: prevalence, recurrent aphthous ulcer, handedness, etiology.

Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosal pathologic conditions (1,2). During the past decades, many studies focused on prevalence and etiology of RAS (3-6). Because of the different study design and distinct characteristic of samples, the prevalence of RAS for the general population within these studies varied widely from 0.4 percent (3) to 66 percent (4), with a mean of 20 percent.

It has been reported that the age and sex distribution of the subjects and type of population studied can influence the prevalence of RAS (7-10). The condition was found to be slightly more common in females (9,11). RAS may appear at any age, with the greatest frequency in young adults (9,11). The increased prevalence of the disease in certain populations may be at least partially associated with social class, tradition, as well as the genetic background of the population (12,13).

Although many theories of the etiology of RAS exist, no single causative factor appears to exist (14). A number of authors make a distinction between etiology and predisposing factors (15-17). The latter are important in determining the prevalence, severity, and presentation of this disease. Of the predisposing factors, there is now evidence that immune responses may be involved in the pathogenesis of RAS, and other factors may precipitate or modulate the immune responses (14-17). However, researchers have reported an association between left-handedness and immune disorders (e.g., asthma, autoimmune diseases, eczema, and allergic rhinitis) (18-21). To our knowledge, the influence of handedness on RAS has not been reported before in the scientific literature, and the association between RAS and handedness is not clear. Also, we have not found any research about prevalence of RAS in the Turkish population. The present study was designed to determine the relationship between RAS and handedness, and to assess the prevalence of RAS in the Turkish population.

Methods

Over the last 6 months, 21,870 patients have been registered in the Atatürk University Faculty of Dentistry. Of these, 13,278 patients aged 10–50 years old were seeking treatment for various dental conditions.

RAS information of patients was collected by means of a data form specifically designed for this study. In addition to personal information (age, sex, socioeconomic situation, education level, smoking, and alcohol use) about the patient, the form had questions concerning the history, frequency, and distribution of RAS and triggering factors for RAS. Apart from patients with registration of current aphthae (average point prevalence, APP), patients who had a past two-year history (self-reported two-year prevalence, SRTP) of the lesion were also included in the present study. Anamneses of the subjects who were under the age of 15 years were obtained together with the patients' parents. Written informed consent was obtained from patients and, for patients aged <18 years old, the patients'

Send correspondence and reprint requests to Dr. Çiçek, Atatürk University, Faculty of Dentistry, Department of Periodontology, 25240 Erzurum, Turkey. E-mail: ycicek@atauni.edu.tr or yasincicek@tnn.net. Dr. V. Çanakçi, Özgöz, and Ertas are with the Faculty of Dentistry; Dr. E. Çanakçi is with the the Faculty of Medicine, all at Atatürk University, Erzurum. Manuscript received: 9/3/03; returned to authors for revision: 10/7/03; final version accepted for publication: 1/20/04.

parents.

The presence of current ulcers was noted at the time of the oral examination. The diagnosis of APP was made on the basis of clinical appearance, location, and each patient's health history. The subjects included in the study had similar inclusion criteria for APP and/or SRTP, including the following: a history of recurrent minor aphthous ulcers; the presence of current ulcers; one to three minor aphthous ulcers of less than 48 hours' duration in an area of the mouth easily accessible; had not undergone dental surgery within two weeks of study entry or be using orthodontic braces or an orthodontic retainer that could come into contact with the ulcer; >10 years of age; not be pregnant or lactating; not have any concurrent clinical condition that could pose a health risk to the subject by being involved with the study; not have ulcers that are manifestations of a systemic disease process such as ulcerative colitis, Crohn's disease, Behçet's syndrome, or anemia; no history of allergy; systemic corticosteroid and immunomodulatory agents had not been used for at least one month; not taken nonsteroidal anti-inflammatory agents, except occasional use for headaches; not taken oral antihistamines for at least one month; and topical medications and systemic antibiotics were not used in the preceding two weeks.

The factors determining socioeconomic status (SES) included the stage of the life style, occupation, employment status, and household income. Based on these criteria, SES were divided into two categories: upper level and lower level.

A questionnaire focusing on handedness was administered to these patients. Handedness was assessed according to the Edinburgh Handedness Inventory (22). The questions pertained to which hand was used by the subject for writing, drawing, throwing, cutting with scissors, using a toothbrush, using a knife (without fork), using a spoon, holding a shovel, striking a match, and twisting off the lid of a jar. The columns "always right," "usually right," "either hand," "usually left," "always left," were scored as +10, +5, 0, –5, and –10, respectively. Hand preference was divided into two classes for convenience in data analysis: right-handers (Geschwind score (GSc) from 80 to 100) and left-handers (GSc from –80 to –100). This study included the patients who had GSc as described above.

Clinical criteria for present ulcer at clinical examination were: the presence of well-demarcated ulcers on the keratinized or nonkeratinized mucosa, showing a red, inflammatory surrounding zone. The ulcers were painful to touch, and the patient reported a history of recurrence. A history of RAS was recorded when the RAS lesion, as described by words and color prints, was clearly recognized by the patient, and it was established that the lesion had been present at least once during the past two years. These criteria are in rough accordance with described by Ship (23), Stanley (24), and Axell and Henricsson (8).

Frequencies of RAS were assessed as APP and SRTP, while triggering factors and distribution for RAS were evaluated in only patients with registration of current aphthae.

The clinical examinations for APP was performed in full-designed dental chairs in Faculty of Dentistry, and were carried out by four of the authors (YÇ, VÇ, MÖ, ÜE) who participated in the training and calibration exercise for the criteria used to identify RAS. Dental examiners were also blinded as to the handedness of patients.

The reliability of the registrations was assessed by reexamining 317 subjects. The probability that a diagnosis would be registered at both examinations was 0.83 for aphthae present

TABLE 1
Average Point Prevalence, Self-reported 2-year Prevalence, and Total Prevalence among 11,360 Patients, by Sex, Age, Handedness, SES, and Smoking Status

	Average Point Prevalence (APP)			Self-reported 2-year Prevalence (SRTP)			Total Prevalence (APP+SRTP)		
Variables	RAS (Yes) *n* (%)	RAS (No) *n* (%)	*P*-value	RAS (Yes) *n* (%)	RAS (No) *n* (%)	*P*-value	RAS (Yes) *n* (%)	RAS (No) *n* (%)	*P*-value
Sex									
Female	171 (3.0)	5,884 (97.0)	<.01	1,476 (26.1)	4,179 (73.9)	<.0001	1,647 (29.1)	4,008 (70.9)	<.0001
Male	132 (2.3)	5,573 (97.7)		1,113 (19.5)	4,592 (80.5)		1,245 (21.8)	4,460 (78.2)	
Age (years)									<.0001
10–30	191 (3.3)	5,678 (96.7)	<.0001	1,658 (28.3)	4,211 (71.7)	<.0001	1,849 (31.5)	4,020 (68.5)	
31–50	112 (2.0)	5,379 (98.0)		931 (17.0)	4,560 (83.0)		1,043 (19.0)	4,448 (81.0)	
Handedness									
Left	49 (6.4)	712 (93.6)	<.0001	226 (29.7)	535 (70.3)	<.0001	275 (36.1)	486 (63.9)	<.0001
Right	254 (2.4)	10,345 (97.6)		2,363 (22.3)	8,236 (77.7)		2,617 (24.7)	7,982 (75.3)	
SES									
Low	62 (1.1)	5,425 (98.9)	<.0001	1,190 (21.7)	4,297 (78.3)	<.001	1,252 (22.8)	4,235 (77.2)	<.001
High	241 (4.1)	5,632 (95.9)		1,399 (23.8)	4,474 (76.2)		1,640 (27.9)	4,233 (72.1)	
Smoking									
Yes	58 (1.1)	5,377 (98.9)	<.0001	1,146 (21.1)	4,289 (78.9)	<.001	1,204 (22.2)	4,231 (77.8)	<.0001
No	245 (4.1)	5,680 (95.9)		1,443 (22.8)	4,882 (75.6)		1,688 (28.5)	4,237 (71.5)	
Total	303 (2.7)	11,057 (97.3)		2,589 (22.8)	8,771 (77.2)		2,892 (25.5)(	8,468 (74.5)	

*Based on chi-squared test.

TABLE 2
Frequency Distribution and Result of Logistic Regression Modeling of Explanatory Variables on RAS for Total Prevalence (APP+SRTP)

	RAS *n* (%)							
	Yes		No		Unadjusted		Adjusted*	
Variables	*n*	(%)	*n*	(%)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Sex								
Male	1,245	(21.8)	4,460	(78.2)	1		1	
Female	1,647	(29.1)	4,008	(70.9)	1.47 (1.35, 1.60)	.0001	1.53 (1.40, 1.67)	.0001
Age (years)								
31–50	1,043	(19.0)	4,448	(81.0)	1		1	
10–30	1,849	(31.5)	4,020	(68.5)	1.96 (1.79, 2.14)	.0001	2.05 (1.88, 2.24)	.0001
Handedness								
Right	2,617	(24.7)	7,982	(75.3)	1		1	
Left	275	(36.1)	486	(63.9)	1.73 (1.48, 2.01)	.0001	1.69 (1.45, 1.98)	.0001
SES								
Low	1,252	(22.8)	4,235	(77.2)	1		1	
High	1,640	(27.9)	4,233	(72.1)	1.31 (1.21, 1.43)	.001	0.95 (0.79, 1.12)	.514
Smoking								
Yes	1,204	(22.2)	4,231	(77.8)	1		1	
No	1,688	(28.5)	4,237	(71.5)	1.40 (1.29, 1.53)	.0001	1.61 (1.36, 1.92)	.0001

*Adjusted for all other variables shown in table.

TABLE 3
Frequency Distribution and Result of Logistic Regression of Explanatory Variables on RAS for Self-reported 2-year Prevalence (SRTP)

	RAS *n* (%)							
	Yes		No		Unadjusted		Adjusted	
Variables	*n*	(%)	*n*	(%)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Sex								
Male	1,113	(19.5)	4,592	(80.5)	1		1	
Female	1,476	(26.1)	4,179	(73.9)	1.46 (1.33, 1.6)	.0001	1.50 (1.37, 1.64)	.0001
Age (years)								
31–50	931	(17.0)	4,560	(83.0)	1		1	
10–30	1,658	(28.3)	4,211	(71.7)	1.93 (1.76, 2.11)	.0001	1.98 (1.81, 2.17)	.0001
Handedness								
Right	2,363	(22.3)	8,236	(77.7)	1		1	
Left	226	(29.7)	535	(70.3)	1.47 (1.25, 1.73)	.0001	1.45 (1.22, 1.71)	.0001
SES								
Low	1,190	(21.7)	4,297	(78.3)	1		1	
High	1,399	(23.8)	4,474	(76.2)	1.13 (1.03, 1.24)	.004	0.87 (0.73, 1.04)	.121
Smoking								
Yes	1,146	(21.1)	4,289	(78.9)	1		1	
No	1,443	(22.8)	4,882	(75.6)	1.21 (1.10, 1.31)	.002	1.49 (1.24, 1.78)	.0001

(APP) at examination and 0.89 for a history or recurrent aphthae (SRTP). This demonstrated a very high degree of reliability between the two occasions.

Data analysis included descriptive statistics (frequency distribution and cross-tabulation). Statistical significance for the association between the occurrence of RAS and sex, age, handedness, SES, and smoking was carried out by using chi-square and logistic regression tests. Logistic regression was used to identify potential predictors of RAS. First, a simple logistic re-

TABLE 4
Frequency Distribution and Result of Logistic Regression of Explanatory Variables on RAS for Average Point Prevalence (APP)

	RAS *n* (%)							
	Yes		No		Unadjusted		Adjusted	
Variables	*n*	(%)	*n*	(%)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Sex								
Male	132	(2.3)	5,573	(97.7)	1		1	
Female	171	(3.0)	5,884	(97.0)	1.32 (1.05, 1.66)	.011	1.42 (1.13, 1.79)	.030
Age (years)								
31–50	112	(2.0)	5,379	(98.0)	1		1	
10–30	191	(3.3)	5,678	(96.7)	1.61 (1.28, 2.05)	.0001	1.78 (1.39, 2.25)	.0001
Handedness								
Right	254	(2.4)	10,345	(97.6)	1		1	
Left	49	(6.4)	712	(93.6)	2.80 (2.05, 3.84)	.0001	2.68 (1.95, 3.69)	.0001
SES								
Low	62	(1.1)	5,425	(98.9)	1		1	
High	241	(4.1)	5,632	(95.9)	3.74 (2.86, 4.97)	.0001	1.81 (1.12, 2.96)	.013
Smoking								
Yes	58	(1.1)	5,377	(98.9)	1		1	
No	245	(4.1)	5,680	(95.9)	3.99 (2.99, 5.34)	.0001	2.54 (1.55, 4.19)	.0001

gression was carried out for each variable studied. Next, all variables were forced into a multiple logistic regression model to adjust for possible confounding effects and to identify the independent contribution of each explanatory variable. Variables were included independently of statistical significance, if they were conceptually relevant. The level of significance was set at 5 percent.

Results

The mean age of the patients was 30.4 years (standard deviation=11.3). The study included 11,360 subjects; 5,705 (50.2%) of the patients were male and 5,655 (49.8%) were female. Patients were classified according to sex, age, handedness, SES, and smoking status. Preliminary analysis showed no differences in rates of handedness with respect to sex and age. Overall, 6.7 percent of the patients were left-handed.

The prevalence of RAS (APP) was 2.7 percent and that of a history of RAS (SRTP) was 22.8 percent. Thus, the total prevalence (APP+SRTP), including present lesions (APP) and a two-year history (SRTP) was 25.5 percent (Table 1). Females, left-handers, patients of high SES, those aged 10–30 years, and nonsmokers had more RAS than males, right-handers, patients of low SES, those aged 31–50 years, and smokers.

The result of simple logistic regression modeling for APP, SRTP, and total prevalence (APP+SRTP) of RAS showed a highly statistically significant association between RAS and sex ($P<.0001$), age ($P<.0001$), handedness ($P<.0001$), SES ($P<.001$), and smoking ($P<.0001$) (Tables 2–4). The results of multiple logistic regression modeling confirmed the statistically significant associations observed in the simple logistic regression models, but not with SES in SRTP and total (APP+SRTP) of RAS. SES was statistically significant in unadjusted results for APP, SRTP, and APP+SRTP, but did not remain statistically significant after adjusting for the other variables studied except in the multiple regression model for APP.

Adjusted results showed that females were 1.42 (95 percent confidence interval [CI]=1.13, 1.79) times more likely than males to present with a current aphthae (APP). Similarly, females were more likely to have SRTP (OR=1.50; 95% CI=1.37, 1.64) or any history of RAS (OR=1.53; 95% CI=1.13, 1.79). Persons aged 10–30 years were 1.78 times (95% CI=1.39, 2.25) more likely than the 31–50-year-old group to have RAS during examination. Smoking was negatively related to prevalence of RAS. Smokers were 2.54, 1.49, and 1.61 times less likely than nonsmokers to have RAS for APP, SRTP, or APP+SRTP. RAS was more common in left-handers than in right-handed subjects. The adjusted odds ratio for APP in left-handers was 2.68 (95% CI=1.95, 3.69). This condition for SRTP and APP+SRTP was 1.45 (95% CI=1.22, 1.71) and 1.69 (95% CI=1.45, 1.98), respectively.

The most commonly reported frequency of RAS was two to four times a year (49.5% for APP and 49.7% for SRTP), followed by once a year (29% for APP and 27.8% for SRTP), and less than once a year (9.2% for APP and 10.1% for SRTP). A frequency of five to 11 times per year was reported by 7.6 percent of subjects, and 1.3 percent reported constantly having RAS. Triggering factors were not completely explained by many patients (37.3%) with current RAS. However, the most commonly reported factor was catching a cold (14.5%), which was higher in left-handers than in right-handers. Other reported factors were fatigue (7.9%); poor oral hygiene (7.6%); stress (6.9%); stomach problems (6.3%); trauma (5.6%); menstruation (6.0%); changes of season (2.3%); salty appetizers, nu-

tritional deficiency, visiting a dentist (2.0% each); and allergies (1.7%). There were some apparent differences in reported triggering factors by sex, age, or handedness. For example, catching a cold was more frequently reported by left-handers (22.4%) than right-handers (13.0%). Stomach problems were more frequent in the 31–50-year-old group (11.6%) than in the 10–30-year-old group (3.1%) (data not presented).

Discussion

The prevalence of RAS (APP) was 2.7 percent and that of a history of RAS (SRTP) 22.8 percent. Thus, the total prevalence, including present lesions (APP) and a two-year history (SRTP), was 25.5 percent. Different types of prevalence have been used for studies on RAS by different investigators. In view of the natural history and recurrent nature of these lesions, cross-sectional clinical surveys tend to underestimate the true prevalence of RAS, as active lesions may not be present at the time of the examination (10). Large discrepancies exist in reports on the prevalence of RAS. Variation in the prevalence reported in the different studies can partly be attributed to the usage of differing type of prevalence. For example, in Axell's study consisting of 20,333 Swedish persons older than 15 years, the APP of RAS was found to be lower (2%) than the SRTP (17.7%) (8). Such a result would be expected, as the APP of clinically present ulcers represent only a small component of either SRTP or total prevalence, since the chances of capturing aphthous ulcers on a given day are small. Thus, the prevalence of RAS in the present paper was evaluated as APP, SRTP and total prevalence.

The prevalence of RAS in published reports varied from 0.4 percent to 66 percent. The lowest prevalence of 0.4 percent was SRTP+APP and was reported by Taiyeb et al. (3) in elderly (>60 years) Malaysian persons. The highest prevalence of 48.3 percent was SRTP+APP for 234 dental clinic outpatients in a study by Axell et al. (25). The prevalence rate of the present study falls within this range. The prevalence of RAS in the present study is much higher than the prevalence reported by Axell and Henricsson (8) in Swedish county residents older than 15 years of age (SRTP+APP of 19.7%), but lower than that reported in a Thai dental clinic as 48.3 percent (SRTP+APP) (3) among Malaysian glass factory workers (38.9%) or steel mill workers (56.5%) (26). The great variation in reported prevalence may be because of a number different factors such as limited occupational or age groups, type of sample, or geographical and behavioral differences between study locations and countries. For example, in Zain et al.'s study (26), the sample was limited to factory workers. Another study by Zain (27) included male army personnel. However, the prevalence of RAS in the present study was similar to those in some other studies by Axell et al. (25) and Zain and Axell (28) (SRTP+APP of 27.0% and 28.0%, respectively).

Many studies have reported that RAS may appear at any age; the highest frequency of onset of RAS is during the second and third decades (9,11,14). In the present study, RAS was most frequently encountered in the 10–30-year-old groups for two sexes. Our study confirms the findings of numerous studies showing that prevalence of RAS was more frequent in females than males (8,9,11,14).

It has been reported that a negative epidemiologic association was found between smoking and RAS (13,29,30). The present study shows that nonsmokers more frequently have RAS than smokers. This may be explained by the opinions that smokers increase keratinization of the oral mucosa and the keratin layer probably acts as a mechanical and chemical local line of defense against any evoking possible etiologic cause, including trauma or bacterial penetration of the mucosa (13,29,30).

SES in unadjusted results (for APP, SRTP, and APP+SRTP) was statistically significant, but SES did not remain statistically significant after adjusting for the other variables studied, except in models of APP. However, it may be said that the prevalence of RAS was slightly higher in patients with high SES than patients with low SES. The previous studies suggested that a greater prevalence of the disease and severity of expression was associated with increasing social class (12,13). Also, Ship (12) reported that increasing social class results in increasing prevalence of RAS. Our finding is partly consistent with results obtained by the researchers mentioned above.

Most patients were effected by RAS two to four times a year, followed by once a year. The result concerning frequency of episodes is in accordance with previous studies (8,15).

Triggering factors were not completely explained by many patients with current RAS. These factors suggest a disease process that may be induced by a variety of etiologic agents, each of which is capable of producing RAS in certain subgroups of patients. To state it simply, the causation appears to be "different things in different patients." However, catching a cold was the most prevalent factor reported. This finding may be explained by the opinion that the process is probably initiated through decreased body resistance (6,8).

The present study has also provided the first opportunity to estimate prevalence of RAS according to handedness. The influence of handedness on RAS of patients has not been reported before. The present study shows left-handed patients more frequently had RAS than right-handed patients. The reasons that left-handers would be at increased risk for RAS are unclear. Possible theories may be suggested. Biological differences between left-handers and right-handers may play a role in a increased RAS risk among left-handers (18,31). Researchers have reported an association between left-handedness and immune disorders (e.g., asthma, autoimmune diseases, eczema, and allergic rhinitis) (18-21). The Geschwind-Behan hypothesis also suggests that immune disorders are more common among left-handed than among right-handed persons (32).

Although many theories of the etiology of RAS exist, there appears to be no single causative factor. A large number of studies indicate that RAS is an immunopathological disorder. Also, there is now evidence that immune responses may be involved in the pathogenesis of RAS, and other factors may precipitate or modulate the immune responses (14-17). The literature points to an immunologic basis that appears to be a primary cause in some and a secondary cause in others. Analysis of the peripheral T-lymphocytes in patients with aphthae shows a decreased ratio of T-helper (CD+) cells to T-suppressor/cytotoxic (CD8+) cells (1). Several studies have demonstrated a general immunologic abnormality that results in altered im-

munoregulatory balances of the patients as compared with RAS-free controls. Generally, increased CD8+ (T-suppressor/cytotoxic) peripheral blood counts and decreased CD4+ (T-helper that provides help to B-cells for antibody production) counts are obtained during active RAS. Also, current evidence suggest that immunologically mediated cytotoxicity of the oral epithelium is important in the development of ulcers in RAS (1,13,33,34). Interestingly, researchers have reported that an association between left-handedness and immune disorders such as asthma, autoimmune diseases, eczema, and allergic rhinitis (18-21). Orbak et al. (35) reported that CD+ lymphocyte value and CD4/CD8 rates were lower among left-handers than right-handers, and handedness may play an important role in local immune responses. In addition, among triggering factors for patients with current aphthae (APP) in our study, catching a cold was the most prevalent one in left-handers. This finding suggests that it may possibly be mediated thorough the immunologic system, which probably plays an important role in pathogenesis of RAS. The relationship between RAS and handedness with respect to immunologic events may give some plausible reason why this correlation exists. In the present study, the fact that left-handers more frequently had RAS than right-handers may be explained by the above-mentioned studies, data, and theories.

References

1. Neville BW, Damm DD, Allen CM, Bouquat JE. Oral and maxillofacial pathology. Philadelphia: WB Saunders Company, 1995:236-41.
2. Ship JA. Recurrent aphthous stomatitis. An update. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;81:141-7.
3. Taiyeb Ali TB, Razak IA, Raja Latifah RJ, Zain RB. An epidemiologic survey of oral mucosal lesions among elderly Malaysians. Gerodontol 1995;12:37-40.
4. Ship II, Brightman VJ, Laster LL. The patient with recurrent aphthous ulcerations and the patient with recurrent herpes labialis: a study of two population samples. J Am Dent Assoc 1967;74:645-54.
5. Katz J, Chaushu G, Peretz B. Recurrent oral ulcerations associated with recurrent herpes labialis—two distinct entities? Community Dent Oral Epidemiol 2001;29:260-3.
6. Orbak R, Çiçek Y,Tezel A, Dogru Y. Effects of zinc treatment in patients with recurrent aphthous stomatitis. Dent Mater J 2003;22:21-9.
7. Axell T, Henricsson V. Association between recurrent aphthous ulcers and tobacco habits. Scand J Dent Res 1985;93: 239-42.
8. Axell T, Henricsson V. The occurrence of recurrent aphthous ulcers in an adult Swedish population. Acta Odontol Scand 1985;43:121-5.
9. McCarthy PL, Shklar G. Diseases of the oral mucosa. 2nd ed. Philadelphia: Lea and Febiger, 1980:319-33.
10. Zain RB. Classification, epidemiology and aetiology of oral recurrent aphthous ulceration/stomatitis. Ann Dent Univ Malays 1999;6:34-7.
11. Lehner T. Oral ulceration and Behçet's syndrome. Gut 1977;18:491-511.
12. Ship II. Epidemiological aspects of recurrent aphthous ulcerations. Oral Surg Oral Med Oral Pathol 1972;33:400-6.
13. Scully C, Gorsky M, Lozada-Nur F. Aphthous ulcerations. Dermatol Ther 2002;15:185-205.
14. Rennie JS, Reade P C, Scully C. Recurrent aphthous stomatitis. Br Dent J 1985;159: 361-7.
15. Graykowski EA, Barile MF, Lee WB, Stanley HR Jr. Recurrent aphthous stomatitis, clinical therapeutic, histopathology and hypersensitivity aspects. JAMA 1966;196:637-44.
16. Francis TC. Recurrent aphthous stomatitis and Behçet's disease. Oral Surg 1970; 30:476-87.
17. Lennette EH, Pagoffin RL. Virologic and immunologic aspect of major oral ulcerations. JADA 1973;87:1055-73.
18. Geschwind N, Behan P. Left-handedness: association with immune disease, migraine, and developmental learning disorder. Proc Nat Acad Sci USA 1982;79: 5097-100.
19. Searleman A, Fugagli AK. Suspected autoimmune disorders and left-handedness: evidence from individuals with diabetes, Crohn's disease, and ulcerative colitis. Neuropsychologia 1987;25:367-74.
20. Smith J. Left-handedness: its association with allergic disease. Neuropsychologia 1987;25:665-74.
21. Chengappa K, Cochran J, Rabin BS, Ganguli R. Handedness and autoantibodies. Lancet 1991;338:694.
22. Oldfield RC. The assesment and analysis of handedness: the Edinburg Inventory. Neuropsychologia 1971;9:97-113.
23. Ship II. Inheritance of aphthous ulcers of the mouth. J Dent Res 1965;44:837-44.
24. Stanley HR. Aphthous lesions. Oral Surg 1972;33:407-16.
25. Axell T, Zain RB, Siwamogstham P, Tantiniran D, Thampipit J. Prevalence of oral soft tissue lesions in outpatients at two Malaysian and Thai dental schools. Community Dent Oral Epidemiol 1990;18:95-9.
26. Zain RB, Abdullah F, Jalaluddin M. The oral health of glass factory workers: a comparative study. Dent J Malays 1995; 16:44-8.
27. Zain RB. A preliminary report on the prevalence of oral mucosal lesions in army personnel in Johor, Malaysia. Dent J Malays 1995;16:37-9.
28. Zain RB, Axell T. Prevalence of oral mucosal lesions in 999 outpatients at a government dental clinic in Malaysia. Dent J Malays 1995;15:9-11.
29. Shapiro S, Olson D, Chellemi SJ. The association between smoking and aphthous ulcers. Oral Surg Oral Med Oral Pathol 1970;30:624-30.
30. Atkin PA, Xu X, Thornhill MH. Minor recurrent aphthous stomatitis and smoking: an epidemiological study measuring plasma cotinine. Oral Dis 2002;8:173-6.
31. Canakci V, Akgul HM, Akgul N, Canakci CF. Prevalence and handedness correlates of traumatic injuries to the permanent incisors in 13–17-year-old adolescents in Erzurum, Turkey. Dent Traumatol 2003;19:248-54.
32. McKeever WF, Rich DA. Left-handedness and immune disorders. Cortex 1990; 26:33-40.
33. Sistig S, Cekic-Arambasin A, Rabatic S, Vucicevic-Boras V, Kleinheinz J, Piffko J. Natural immunity in recurrent aphthous ulceration. J Oral Pathol Med 2001;30: 275-80.
34. Savage NW, Mahanonda R, Seymour GJ, Bryson GJ, Collins RJ. The proportion of suppressor-inducer T-lymphocytes is reduced in recurrent aphthous stomatitis. J Oral Pathol 1988;17:293-7.
35. Orbak R, Canakci V, Erciyas K, Kaya H. Flow-cytometric analysis of T-lymphocyte subset in sinistral and dextral patients with gingivitis. Int J Neurosci 2003; 113:1-13.