

Original Article

The association of recurrent aphthous stomatitis with general health and oral health related quality of life among dental students

Samaneh Ziaei¹, Hadi Raeisi Shahraki², Sara Dadvand Dehkordi³

¹Department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Shahrekord University of Medical Sciences, Shahrekord, Iran; ²Department of Epidemiology and Biostatistics, Faculty of Health, Shahrekord University of Medical Sciences, Shahrekord, Iran; ³Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran

Received April 26, 2022; Accepted June 29, 2022; Epub August 15, 2022; Published August 30, 2022

Abstract: Background: Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosa diseases. This study aimed to investigate the association of RAS with general health and oral health-related quality of life among dental students of Shahrekord University of Medical Sciences in 2020. Methods: In this cross-sectional study, a researcher-made checklist about the type, size, location, number, and recurrence rate of ulcers, oral health-related quality of life questionnaire (OHIP-14), and a 28-item general health questionnaire (GHQ-28) were completed by 100 dental students. Results: The proportion of RAS was significantly higher among females than males (61.1 versus 38.9, $P=0.03$) and was associated with family involvement history ($P<0.001$) and a Tendency to eat spicy foods ($P=0.02$). Moreover, the oral health-related quality of life was significantly lower among students with a history of RAS (8.17 ± 8.33 versus 4.22 ± 4.10 , $P=0.003$). The results showed that GHQ-positive status was significantly associated with ulcer size ($P=0.01$). The general health status was positively correlated with RAS prevalence ($p=0.04$). Also, an investigation of the OHIP questionnaire showed that there was a significant correlation between physical status ($r=0.31$, $P<0.001$), insomnia, and mental status ($r=0.33$, $P<0.001$) with OHIP total score. Conclusion: The results of this study confirmed a significant association between aphthous stomatitis and general health and oral health-related quality of life. So possibly improving general health and oral health-related quality of life may be effective in preventing aphthous stomatitis.

Keywords: General health, quality of life, recurrent aphthous stomatitis

Introduction

Aphthous Stomatitis or Aphthous Ulcers (AU) is one of the most prevalent mucosal diseases in the oral cavity [1]. It is characterized by inflammatory disorder of oral movable mucosa with the recurrent onset of single or multiple painful ulcers with well-defined erythematous margin and yellowish-gray pseudomembranous center and non-specific histological presentation that can affect several parts of the oral mucosa [2, 3].

RAS prevalence is 5 to 66% by 20% in the mean [4, 5]. Three months recurrence is also high as 50% [6]. The population can influence the prevalence of AU studied diagnostic criteria and environmental factors [7]. Studies showed this

disease is more prevalent among females, non-smokers, white people, and people with low socioeconomic status [2, 3, 8, 9]. In children, the prevalence of RAS is as high as 39% and 90% of them have RAS-positive parents [10, 11].

Signs and symptoms of RAS are variable; the first symptom is a burning sensation that lasts 2 to 48 hours before appearing ulcer. The clinical features of Aphthous stomatitis are dependent on their depth, number in one episode, location, and duration. According to these features, Aphthous Ulcers are in three main categories; Minor, Major, and Herpetiform recurrent aphthous stomatitis ulcers [12]. Significant ulcers are deep usually single and larger than 1 cm in diameter (1 to 3 cm) lesions that mainly

Recurrent aphthous stomatitis and general health

affects soft palate and tonsillar faucets, healing occurs 2 to 6 weeks with scarring, whereas minor ulcers are shallow painful lesions usually smaller than 1 cm in diameter (between 3 to 10 mm) with yellow fibrinopurulent pseudomembrane on it, these type of lesions mainly affect non-keratinized mucosa and affects buccal and labial mucosa frequently, the number of lesions do not exceed than 10 per flare-up, the healing process occurs after 7 to 14 days without scarring, Herpetiform aphthous lesions are most prevalent aphthous lesions with highest incidence rate which appears as multiple, shallow and small (1 to 3 mm in diameter) that some of them will coalesce into extensive irregular lesions erosions that clinically resemble herpetic ulcers the differential diagnosis is made through this fact that RAS always occur in non-keratinized mucosa but HSV lesions mainly affects keratinized mucosa, the healing time is between 2 to 6 days. An erythematous halo surrounds these three forms on an edematous background [1, 3]. Recurrent stomatitis is not relevant to any systemic condition [13].

Severe intraoral pain is one of the critical signs in patients with Oral Aphthous lesions. The psychological impact of long-term chronic pain is inevitable [14]. Depression, Anxiety, Aggressive Behavior as psychological consequences of ulcers' pain are prevalent in patients with RAS [15]. So, the role of supportive psychological therapy is inevitable, especially in patients with a history of psychological disorders and suicide [16]. In order to effectively control these manifestations, it is necessary to, in the first place, gain adequate knowledge toward psychological manifestations of RAS using the well-validated tool. The results of previous studies toward psychological manifestations of RAS are controversial, limited to low samples and different measuring tools [15, 17, 18]. So, the present study aims to investigate the correlation between mental health and RAS in Dental Students.

Methods and material

Study design

In this cross-sectional study, 100 dental students of Shahrekord University of Medical science participated in this study by census method from January to December 2020.

Sample size calculation and patient's criteria

The sample size was calculated as 100 students according to Laxmi et al. [19] and considering type 1 error of 0.05 and a type two error of 0.2. Participants should have no history of psychiatric medications, neurological disorders, and other ulcer-related illnesses such as Reiter's syndrome, Behcet's syndrome, Crohn's disease, or gastrointestinal illness, and have at least a one-year history of ulcer recurrence. Before distributing the questionnaires to ensure the accuracy of students' answers, explanations about the types of aphthous and its differential diagnoses, pictures of different types of aphthous and written explanations about the importance of research were provided and in order to remove ambiguity about the researcher's research questions. In cases where the wounds were created at the site of trauma due to a sharp edge of the tooth, broken repair, orthodontic appliances or partial prostheses, the patient was excluded from the study. Only those who answered the questions were included in the study.

Mental health assessments

The self-administrated checklist was prepared with demographic and clinical information, including age, gender, menstrual condition, type, size, location, number and recurrence rate of ulcers, smoking, triggering agents, clinical duration, and mental health of participants. The mental health of participants was investigated using General Health Questionnaire (GHQ-28).

General health questionnaire

Goldberg and Hillier developed the 28-item form of the General Health Questionnaire in 1979 [19]. The questions were extracted based on factor analysis based on the initial 60-item form, which includes four scales physical symptoms, anxiety, insomnia, social dysfunction, and depression. In Iran, different studies have been conducted on the validity and reliability of this questionnaire. In Taghavi's (2002) study, to assess validity, 75 college students were asked to answer Middlesex Hospital Questionnaire, and for reliability, 95 college students participated. The reliability coefficient is determined by three methods: test-retest, split half, and

Recurrent aphthous stomatitis and general health

Cronbach alpha that achieve 70, 93, and 90, respectively, and its total subscale correlations are calculated between 72 to 87 [20]. Goldberg and Hiller, in 1979 designed a 28-item questionnaire arranged into four subgroups: Somatic symptoms, anxiety and insomnia, social dysfunction, and severe depression [21, 22]. The questionnaire consists of 28 questions that are divided into four-part with seven questions in each one. For answering, A-D options can be chosen that scored with zero, one, two, and three, respectively, and at last entire score is calculated between 0 to 84 and for each subgroup determined in the range of 0 to 21. Score of 22 is considered a cut-off point if the total questionnaire score is higher than 22 shows patients' psychiatric disorders. Pahang and Yaghoubi measured the reliability of this study at 91% and 88%, respectively, and calculated Cronbach's alpha values for each subgroup; 84% for somatic symptoms, 79% for the social function, 81% for depression, and 91% for mental health status [23, 24].

Oral health-related quality of life

The Oral Health-related Quality of life (OHIP-14) questionnaire contains 14 5-item questions. How to score is as follows: never =1, rarely =2, sometimes =3, almost most of the time =4, and in most cases =5, covers mental disability, social disability, and disability. In this questionnaire, all questions have a negative impression; therefore, the score of all questions is inversely proportional to good oral conditions. The minimum score of the questionnaire is 14, and the maximum is 70, and the higher score indicates a higher quality of life dependent on oral health. In the study of Nazeri et al., the validity and reliability of the OHIP-14 questionnaire with Cronbach's alpha of 0.8 were confirmed [25].

Statistical analysis

Descriptive statistics for quantitative variables were expressed as mean \pm standard deviation and number (%) for qualitative variables. Independent t-test, Pearson correlation test, Chi-square, or Fisher's exact test were used in SPSS 21.0 (IBM, Chicago), and the significance level of the tests was considered 0.05.

Results

Study population

The mean age of participants was 22.2 ± 2.4 years, and RAS experience has been reported

in 54 (54%) students. The proportion of RAS was significantly higher among females than males (61.1 versus 38.9, $P=0.03$) and was associated with family involvement history ($P<0.001$) and Tendency to eat spicy foods ($P=0.02$). Moreover, the score of OHIP was significantly lower among students with a history of RAS (8.17 ± 8.33 versus 4.22 ± 4.10 , $P=0.003$, **Table 1**).

General health status and clinical and demographic data

The association between general health status with clinical and demographic data is illustrated in **Table 2**. The results showed that GHQ-positive level was significantly associated with ulcer size ($P=0.01$). In **Table 3**, the GHQ-28 items were investigated according to their role in RAS concurrence. The general health status was positively correlated with RAS prevalence ($P=0.04$).

Physical and mental status

In addition, an investigation of the OHIP questionnaire showed that there was a significant correlation between physical status ($r=0.31$, $P<0.001$), insomnia, and mental status ($r=0.33$, $P<0.001$) with OHIP total score (**Table 4**).

Discussion

In the present study, 54% of participants were positive for RAS, which was higher than the prevalence reported in previous studies by Shirazi et al. (18%) [26], Dovatchi et al. (25.2%) [27], Al-Johan et al. (39%) [28]. The difference in findings would be related to study design, population, and sample size. The high prevalence in the present study could be related to measuring prevalence both with clinical examination and questionnaire, which resulted in mistakes in other lesions with RAS, so it is suggested for future studies to use clinical evaluation besides questionnaires to measure RAS prevalence.

In the present study, male sex was related to RAS occurrence, not constant with previous studies [26]. Other studies reported that RAS was more prevalent in women [29, 30]. Also, older age was related to higher RAS occurrence, which was inconstancy with previous studies [26, 29, 30]. The controversy could be related to the difference in studies' population ethnicity and measurement tool.

Recurrent aphthous stomatitis and general health

Table 1. Comparison of demographic and clinical findings of patients with and without RAS

Parameter	Subgroup	Aphthous Stomatitis		p-value
		No (46)	Yes (54)	
Gender	Male (49)	28 (60.9)	21 (38.9)	0.03 ^a
	Female (51)	33 (39.1)	18 (61.1)	
Marital Status	Single (93)	43 (93.5)	50 (92.6)	0.99 ^a
	Married (7)	3 (6.5)	4 (7.4)	
Mean Annual Recurrence Rate	4-14 (50)	--	50 (92.6)	--
	>30 (4)	--	4 (7.4)	
Ulcers Frequency	1-5 (51)	--	51 (94.4)	--
	5-10 (3)	--	3 (5.6)	
Ulcer size	<10 mm (41)	--	41 (41)	--
	>10 mm (8)	--	8 (8)	
Ulcer Type	1-2 mm (5)	--	5 (5)	--
	Minor (35)	--	35 (35)	
	Major (14)	--	14 (14)	
Mean Ulcer Healing Duration	Herpetiform (5)	--	5 (5)	--
	4-14 (53)	--	53 (98.1)	
Family Involvement History	>30 (1)	--	1 (1.9)	<0.001 ^a
	Yes (53)	15 (32.6)	38 (70.4)	
Tendency to eat spicy foods	No (47)	31 (67.4)	16 (29.6)	0.02 ^a
	Yes (60)	22 (47.8)	38 (70.4)	
Smoking	No (40)	24 (52.2)	16 (29.6)	0.29 ^a
	Yes (15)	5 (10.9)	10 (18.5)	
menstruation	No (85)	41 (89.1)	44 (81.5)	0.001 ^a
	Yes (7)	0 (0)	7 (33.3)	
Location	No (42)	28 (100)	14 (66.7)	--
	Lip, Cheek, Mouth floor (35)	--	35 (64.8)	
	Lip, Cheek, Palate, Pharynx (14)	--	14 (25.9)	
Age	Lip, Cheek, Palate, Pharynx, Gingiva, Mouth floor (5)	--	5 (9.3)	0.04 ^b
	21.17 ± 1.7	22.7 ± 2.8		
Age during diagnosis	--	12.4 ± 4.6	--	
OHIP	4.22 ± 4.10	8.17 ± 8.33	0.003	

^aChi-square test, ^bIndependent t-test.

The participants with a history of RAS were significantly older than other patients, which was inconsistency with the findings of *Shirzaei et al.* [26] and *Rajmane et al.* [31]. The difference in results could be related to the difference in ethnic characteristics. Also, there was no significant correlation between RAS prevalence and marital status.

In the present study, menstruation was significantly related to RAS, following previous studies [26, 31, 32]. These phenomena would be explained by the fact that serum and salivary estrogen during menstruation and pregnancy transmits RAS into the active phase [31]. Also, in the present study, positive familial history

was correlated with RAS occurrence, following *Miller et al.*'s findings on monozygotic twins [33] and other studies [26, 30, 32]. The explanation for such result could be related to the role of genetics on host immune response and common familial habits.

In the present study, smoking did not have a significant role in RAS occurrence, following previous studies [26]. In a study by *Koybasi et al.*, smoking has an important preventive role on RAS occurrence, related to the smoking role in mucosal keratinization [32].

The present study showed a significant positive correlation between RAS prevalence, GHQ-28

Recurrent aphthous stomatitis and general health

Table 2. Comparison of demographic and clinical findings of patients in different category of GHQ

Parameter	Subgroup	GHQ Status		p-value
		negative (54)	positive (46)	
Gender	Male (49)	27 (50)	22 (47.8)	0.83 ^a
	Female (51)	27 (50)	24 (52.2)	
Marital Status	Unmarried (93)	50 (92.6)	43 (93.5)	0.99 ^a
	Married (7)	4 (7.4)	3 (6.5)	
Mean Annual Recurrence Rate	4-14 (50)	32 (95.8)	27 (90)	0.62 ^a
	>30 (4)	1 (4/2)	3 (10)	
Ulcers Frequency	1-5 (51)	24 (100)	27 (90)	0.25 ^a
	5-10 (3)	0 (0)	3 (10)	
Ulcer size	<10 mm (41)	22 (91.7)	19 (63.3)	0.01
	>10 mm (8)	0 (0)	8 (26.7)	
Ulcer Type	1-2 mm (5)	2 (8.3)	3 (10)	0.4
	Minor (35)	17 (70.8)	18 (60)	
	Major (14)	4 (16.7)	10 (33.3)	
Mean Ulcer Healing Duration	Herpetiform (5)	3 (12.5)	2 (6.7)	0.44 ^a
	4-14 (53)	33 (95.8)	30 (100)	
	>30 (1)	1 (4.2)	0 (0)	
Family Involvement History	Yes (53)	24 (44.4)	29 (63)	0.06 ^a
	No (47)	30 (55.6)	17 (37)	
Tendency to eat spicy foods	Yes (60)	30 (55.6)	30 (65.2)	0.33 ^a
	No (40)	24 (44.4)	16 (34.8)	
Smoking	Yes (15)	6 (11.1)	9 (19.6)	0.29 ^a
	No (85)	48 (88.9)	37 (80.4)	
menstruation	Yes (7)	1 (3.7)	6 (27.3)	0.24 ^a
	No (42)	26 (96.3)	16 (72.7)	
Location	Lip, Cheek, Mouth floor (35)	17 (70.8)	18 (60)	0.4 ^a
	Lip, Cheek, Palate, Pharynx (14)	4 (16.7)	10 (33.3)	
	Lip, Cheek, Palate, Pharynx, Gingiva, Mouth floor (5)	3 (12.5)	2 (6.7)	
Age		22.4 ± 2.4	22.0 ± 2.3	0.38 ^b
Age during diagnosis		13.5 ± 4.4	10.9 ± 4.7	0.18 ^b

^aChi-square test, ^bIndependent t-test.

scores (total and physical status), and OHIP scores. In a survey conducted by Al-zwir et al., using the Hospital Anxiety and Depression Scale (HADS), OHIP, and Oral Health-Related Quality-Of-Life in the UK (OHQoL-UK), they reported that RAS decrease oral health and, consequently the quality of life. Still, anxiety does not affect patients' quality of life [34], which was in line with our findings. In another study, Picek et al., with similar tools, reported that depression and anxiety do not significantly differ in patients with and without RAS [35]. However, in another study, depression and anxiety were significantly more in patients with RAS [15, 36-38]. This difference could be relat-

ed to the difference in racial properties and measurement tools in different studies.

The shortcomings of this study included a limited study population and performing this study in a single health center. Furthermore, this study was conducted on dental students, and this could be assumed as a limitation in our study. We recommend that multicentric studies on larger populations, especially the general population, be conducted.

Conclusion

The results of this study confirmed a significant association between aphthous stomatitis and

Recurrent aphthous stomatitis and general health

Table 3. Comparison of GHQ-28 questionnaire parameters according to RAS prevalence

Parameter	Subgroup	Aphthous Stomatitis		p-value
		No (46)	Yes (54)	
Physical signs and symptoms	Negative (68)	36 (78.3)	32 (59.3)	0.05 ^a
	Positive (32)	10 (21.7)	22 (40.7)	
Insomnia and mental signs	Negative (60)	30 (65.2)	30 (55.6)	0.41 ^a
	Positive (40)	16 (34.8)	24 (44.4)	
Social function Disorder	Negative (21)	10 (21.7)	11 (20.4)	0.99 ^a
	Positive (79)	36 (78.3)	43 (79.6)	
Depression	Negative (80)	40 (87)	40 (74.1)	0.14 ^a
	Positive (20)	6 (13)	14 (25.9)	
Total GHQ score	Negative (54)	30 (65.2)	24 (44.4)	0.04 ^a
	Positive (46)	16 (34.8)	30 (55.6)	

^aChi-square test.

Table 4. Mean score of GHQ and OHIP questionnaire and their correlation

Parameter	Mean ± Standard deviation	Total GHQ score	Physical signs and symptoms	Insomnia and mental signs	Social function Disorder	Depression
Total GHQ score	22.5 ± 9.3	1	-	-	-	
Physical signs and symptoms	5.3 ± 2.3	0.77*	1	-	-	
Insomnia and mental signs	5.4 ± 0.4	0.85*	0.64*	1	-	
Social function Disorder	8.4 ± 2.9	0.19	-0.04	-0.06	1	
Depression	3.4 ± 4.4	0.74*	0.42*	0.51*	-0.19	1
OHIP	6.4 ± 0.7	0.31	0.31*	0.33*	-0.04	0.18

*Significant at 0.01.

general health and oral health-related quality of life. So possibly improving general health and oral health-related quality of life may be effective in preventing aphthous stomatitis.

Acknowledgements

This project was financially supported (grant number 3516) by the Research and Technology Deputy of the Shahrekord University of Medical Sciences, Shahrekord, Iran.

Disclosure of conflict of interest

None.

Address correspondence to: Sara Dadvand Dehkordi, Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran. Tel: +983833335653; Fax: +983833334678; E-mail: sara.dadvand1394@gmail.com

References

[1] Luke AM, Mathew S, Altawash MM and Madan BM. Lasers: a review with their applications in oral medicine. *Lasers Med Sci* 2019; 10: 324.

- [2] Tarakji B, Gazal G, Al-Maweri SA, Azzeghaiby SN and Alaizari N. Guideline for the diagnosis and treatment of recurrent aphthous stomatitis for dental practitioners. *J Int Oral Health* 2015; 7: 74-80.
- [3] Ujević A, Lugović-Mihić L, Situm M, Ljubesić L, Mihić J and Troškot N. Aphthous ulcers as a multifactorial problem. *Acta Clin Croat* 2013; 52: 213-221.
- [4] Peacock ZS. Controversies in oral and maxillofacial pathology. *Oral Maxillofac Surg Clin North Am* 2017; 29: 475-86.
- [5] Edgar NR, Saleh D and Miller RA. Recurrent aphthous stomatitis: a review. *J Clin Aesthet Dermatol* 2017; 10: 26.
- [6] Sánchez-Bernal J, Conejero C and Conejero R. Recurrent aphthous stomatitis. *Actas Dermosifiliogr (Engl Ed)* 2020; 111: 471-480.
- [7] Pakfetrat A, Falaki F, Delavarian Z, Dalirsani Z, Sanatkhani M and Zabihi Marani M. Oral manifestations of human immunodeficiency virus-infected patients. *Iran J Otorhinolaryngol* 2015; 27: 43-54.
- [8] Cui RZ, Bruce AJ and Rogers RS 3rd. Recurrent aphthous stomatitis. *Clin Dermatol* 2016; 34: 475-81.
- [9] Belenguer-Guallar I, Jiménez-Soriano Y and Claramunt-Lozano A. Treatment of recurrent

Recurrent aphthous stomatitis and general health

- aphthous stomatitis. A literature review. *J Clin Exp Dent* 2014; 6: e168-174.
- [10] Rivera C. Essentials of recurrent aphthous stomatitis. *Biomed Rep* 2019; 11: 47-50.
- [11] Abdullah MJ. Prevalence of recurrent aphthous ulceration experience in patients attending Piramird dental speciality in Sulaimani City. *J Clin Exp Dent* 2013; 5: e89-94.
- [12] Chiang CP, Chang JY, Wang YP, Wu YH, Wu YC and Sun A. Recurrent aphthous stomatitis-etiology, serum autoantibodies, anemia, hematinic deficiencies, and management. *J Formos Med Assoc* 2019; 118: 1279-89.
- [13] Wu D, Xin J, Liu J and Zhou P. The association between interleukin polymorphism and recurrent aphthous stomatitis: a meta-analysis. *Arch Oral Biol* 2018; 93: 3-11.
- [14] Najafi S, Mohammadzadeh M, Zahedi A, Heidari M and Rezaei N. Association of serotonin transporter gene polymorphism with recurrent aphthous stomatitis. *Avicenna J Med Biotechnol* 2018; 10: 56.
- [15] Zadeh AR, Eghbal AF, Mirghazanfari SM, Ghasemzadeh MR, Nassireslami E and Donyavi V. Nigella sativa extract in the treatment of depression and serum Brain-Derived Neurotrophic Factor (BDNF) levels. *J Res Med Sci* 2022; 27: 28.
- [16] Talarico R, Elefante E, Parma A, Taponeco F, Simoncini T and Mosca M. Sexual dysfunction in Behçet's syndrome. *Rheumatol Int* 2020; 40: 9-15.
- [17] Alrashdan MS and Alkhader M. Psychological factors in oral mucosal and orofacial pain conditions. *Eur J Dent* 2017; 11: 548-52.
- [18] Hariyani N, Bramantoro T, Nair R, Singh A and Sengupta K. Depression symptoms and recurrent aphthous stomatitis-evidence from a population-based study in Indonesia. *Oral Dis* 2020; 26: 948-54.
- [19] Gnambs T and Staufenbiel T. The structure of the General Health Questionnaire (GHQ-12): two meta-analytic factor analyses. *Health Psychol Rev* 2018; 12: 179-94.
- [20] Namjoo S, Shaghghi A, Sarbaksh P, Allahverdipour H and Pakpour AH. Psychometric properties of the General Health Questionnaire (GHQ-12) to be applied for the Iranian elder population. *Aging Ment Health* 2017; 21: 1047-51.
- [21] Wu M, Xu W, Yao Y, Zhang L, Guo L, Fan J and Chen J. Mental health status of students' parents during COVID-19 pandemic and its influence factors. *Gen Psychiatr* 2020; 33: e100250.
- [22] Silverberg JI, Gelfand JM, Margolis DJ, Boguniewicz M, Fonacier L, Grayson MH, Simpson EL, Ong PY and Fuxench ZC. Patient burden and quality of life in atopic dermatitis in US adults: a population-based cross-sectional study. *Ann Allergy Asthma Immunol* 2018; 121: 340-7.
- [23] AlHadi AN, AlAteeq DA, Al-Sharif E, Bawazeer HM, Alanazi H, AlShomrani AT, Shuqdar RM and AlOwaybil R. An arabic translation, reliability, and validation of Patient Health Questionnaire in a Saudi sample. *Ann Gen Psychiatry* 2017; 16: 1-9.
- [24] Shayan Z, Pourmovahed Z, Najafipour F, Abdoli AM, Mohebpour F and Najafipour S. Factor structure of the General Health Questionnaire-28 (GHQ-28) from infertile women attending the Yazd Research and Clinical Center for Infertility. *Int J Reprod Biomed* 2015; 13: 801.
- [25] Arrieta J, Aguerrebere M, Raviola G, Flores H, Elliott P, Espinosa A, Reyes A, Ortiz-Panozo E, Rodriguez-Gutierrez EG, Mukherjee J and Palazuelos D. Validity and utility of the Patient Health Questionnaire (PHQ)-2 and PHQ-9 for screening and diagnosis of depression in rural Chiapas, Mexico: a cross-sectional study. *J Clin Psychol* 2017; 73: 1076-90.
- [26] Hara Y, Shiratuchi H, Kaneko T and Sakagami H. Search for drugs used in hospitals to treat stomatitis. *Medicines (Basel)* 2019; 6: 19.
- [27] Darjani A, Joukar F, Naghipour M, Asgharnezhad M and Mansour-Ghanaei F. Lifetime prevalence of recurrent aphthous stomatitis and its related factors in Northern Iranian population: the PERSIAN Guilan Cohort Study. *Clin Oral Investig* 2021; 25: 711-8.
- [28] Al-Johani K. Prevalence of recurrent aphthous stomatitis among dental students: a cross sectional study. *J Contemp Dent Pract* 2019; 20: 893-895.
- [29] Souza PR, Duquia RP, Breunig JD and Almeida HL. Recurrent aphthous stomatitis in 18-year-old adolescents-prevalence and associated factors: a population-based study. *An Bras Dermatol* 2017; 92: 626-9.
- [30] Tohidinik HR, Rodríguez A, Regueira-Méndez C and Takkouche B. Sleep quality and risk of recurrent aphthous ulcers: a Spanish cohort study. *Oral Dis* 2021; [Epub ahead of print].
- [31] Rajmane YR, Ashwinirani S, Suragimath G, Nayak A, Rajmane VS and Lohana M. Prevalence of recurrent aphthous stomatitis in western population of Maharashtra, India. *J Oral Res Rev* 2017; 9: 25.
- [32] Queiroz SI, Silva MV, Medeiros AM, Oliveira PT, Gurgel BC and Silveira ÉJ. Recurrent aphthous ulceration: an epidemiological study of etiological factors, treatment and differential diagnosis. *An Bras Dermatol* 2018; 93: 341-6.
- [33] Miller MF, Garfunkel AA, Ram CA and Ship II. The inheritance of recurrent aphthous stomatitis. Observations on susceptibility. *Oral Surg Oral Med Oral Pathol* 1980; 49: 409-412.

Recurrent aphthous stomatitis and general health

- [34] Zwiri A. Anxiety, depression and quality of life among patients with recurrent aphthous ulcers. *J Contemp Dent Pract* 2015; 16: 112-117.
- [35] Rodríguez ML and Casariego ZJ. Psychoneuro-immunoendocrine syndrome with impact on the stomatognathic system. *N A J Adv Res Rev* 2020; 7: 155-65.
- [36] Cardoso JA, dos Santos Junior AA, Nunes ML, de Figueiredo MA, Cherubini K and Salum FG. Salivary alpha-amylase enzyme, psychological disorders, and life quality in patients with recurrent aphthous stomatitis. *Int J Dent* 2017; 2017: 5269856.
- [37] Gavic L, Cigic L, Biocina Lukenda D, Gruden V and Gruden Pokupec JS. The role of anxiety, depression, and psychological stress on the clinical status of recurrent aphthous stomatitis and oral lichen planus. *J Oral Pathol Med* 2014; 43: 410-417.
- [38] Dhopte A, Naidu G, Singh-Makkad R, Nagi R, Bagde H and Jain S. Psychometric analysis of stress, anxiety and depression in patients with recurrent aphthous Stomatitis-A cross-sectional survey based study. *J Clin Exp Dent* 2018; 10: e1109.