sciendo
10.2478/bjdm-2020-0013

BALKAN JOURNAL OF DENTAL MEDICINE

BaSS

ISSN 2335-0245

The Role of *Helicobacter Pylori* in Development of Lesion in Oral Cavity

Mirjana Popovska[1], Žana Osmani Jusuf[2], Vera Radojkova-Nikolovska[1], Biljana Evrosimovska[3], Kristina Mitić[1], Bruno Nikolovski [4], Ana Spasovska[5], Biljana Rusevska[3]

[1]Faculty of dentistry, University "Ss. Cyril and Methodius", Skopje, North Macedonia
[2]PHO Dendia esttetica, Gostivar, North Macedonia
[3]University dental clinic "St. Pantelejmon", Skopje, North Macedonia
[4]Center for dental health - ETERNAdent, Skopje, North Macedonia
[5]TD Ilinden 96, Skopje, North Macedonia

SUMMARY

Background/Aim: *to examine the connection of H. Pylori in saliva and biopsy material with oral lesions.* ***Material and Methods:*** *Sixty patients with dyspeptic complaints were followed up at the Clinic for Gastroenterology at University Medical Clinical Centre in Skopje, divided into two groups: first group consisted of 30 patients without presence of H. pylori, and the second group with 30 subjects and presence of H. pylori. The presence or absence of H. pylori has been ascertained after endoscopic examination-gastroscopy, and implemented urease test (CLO-test). All patients were clinically followed in order to determinate mouth burning, recurrent aphthous stomatitis (RAS), acid taste and lingual papillary hyperplasia according to Cohen and Proctor. The presence of H. pylori in saliva has been ascertained before endoscopic examination, after chewing Orbit gum without sugar for 1 min using by Pronto dry test. Determination of H. pylori in biopsy material has been ascertained by rapid urease test (RUT).* ***Results:*** *At 30 patients with dyspeptic complaints and presence of Helicobacter pylori, 16 patients (53,33%) had lingual papillary hyperplasia, acid taste, burning mouth and recurrent aphthous stomatitis (RAS). At 4 patients (13,33%) was confirmed acid taste, and also at 4 patients (13,33%) burning mouth. At 2 patients (6,67%) was confirmed lingual papillary hyperplasia, burning mouth, and recurrent aphthous stomatitis (RAS). At the same time, at 2 patients (6,67%) was confirmed burning mouth, and recurrent aphthous stomatitis (RAS), until at 1 patient (3,33%) lingual papillary hyperplasia, as at 1 patient (3,33%) lingual papillary hyperplasia and acid taste. At patients without presence of Helicobacter pylori but with dyspeptic complaints, was confirmed burning mouth in 14 patients (46,67%), lingual papillary hyperplasia, burning mouth, and acid taste in 7 patients (23,33%); in 3 patients (10,00) lingual papillary hyperplasia, burning mouth, and in 2 patients (6,67%) was confirmed recurrent aphthous stomatitis (RAS). Acid taste was registered in 2 patients (6,67%), and also lingual papillary hyperplasia in 2 patients (6,67%). There was a significant differences in clinical aspect between the patients with and without presence of H. pylori, for p< 0,01(p= 0,002); Pearson Chi-square= 20,10 u and p<0,05(p= 0,01).* ***Conclusions:*** *H. pylori in saliva and biopsy material detected with CLO test are reason for oral lesions at patients with dyspeptic complaints who have the presence of H. pylori.*

Key words: CLO-test, H. pylori, Oral Lesions, Halitosis, Recurrent Aphthous Stomatitis

ORIGINAL PAPER (OP)
Balk J Dent Med, 2020;77-83

Introduction

It is believed that oral cavity may be a key factor for the survival and transmission of *H. pylori* into and from the stomach. Its presence in the oral media is indisputable, there are various data, some suggest up to 100% [1-4] presence in different oral media, and in others it is questionable[5,6]. According to Wang[5] and Anand[6], *H. pylori* in the oral cavity survives very briefly, only for a few hours so no live specimens of this bacterium have been identified.

In recent years, however, significant progress has been made in the detection of *H. pylori* in the oral cavity, using various methods to confirm that oral cavity is a secondary location for colonization of this bacterium[7]. There is evidence that *H. pylori* is present in the oral cavity, isolated from the root canals of the teeth[8] and identified in the dental plaque, which confirms a strong association with chronic periodontitis (CP)[9]. Hence the infected endodontium may be *H. pylori's* survival reservoir, and the presence of this bacterium may be a potential risk factor for CP[8,10,11]. The prevalence of *H. pylori* has been associated with the progression of chronic periodontitis, while oral hygiene and treatment of periodontal disease are believed to stopped the progression of periodontal disease[11]. The manner in which it act is likely to co-aggregate with *Campylobacter spp*. and *Fusobacterium spp*. which facilitate the colonization of *H. pylori*[12].

The mechanism of cell invasion is complex[13], but it has been shown that *H. pylori* inhibits the proliferation of human periodontal ligament fibroblasts (hPDLFs) causing an invasive effect through the Cdc25C/CDK1/ cyclin B1 signaling cascade. The authors conclude that its inhibitory effect on proliferation is stronger in group with high-concentration of *H. pylori*[14].

However, many articles have shown a strong association between oral and gastric infection with *H. pylori*[15]. In addition to the association and possible affection on periodontal disease, it is detected in recurrent aphthous stomatitis[16,17] and is mentioned in leukoplakia and lichen planus[18]. Therefore, *H. pylori* is blamed for causing oral and/or periodontal lesions, so the treatment of the affected periodontium increases the success rate of eradication of the bacterium and reduces the recurrence of gastric infection[19].

Relying on the literature data we set out to examine the association of *H. pylori* in saliva and biopsy material with oral lesions by applying the CLO-test.

Material and Methods

Sixty patients with dyspeptic symptoms and indication for endoscopic intervention- gastroscopy were followed. Experimental group (selected patients) fullfills additional criteria for inclusion and exclusion from the study:

Inclusion criteria:

Patients in the last two months can not receive drugs which belongs to the group of proton pump inhibitors; not receive systemic antimicrobial agents, not receiving non-steroidal and other anti-inflammatory drugs.

Exclusion criteria:

All patients who have less than 20 teeth in the mouth. In conducting the study, all patients gave written consent for inclusion in the survey. Following the anamnesis and clinical procedure in all patients from the experimental group were diagnosed dyspeptic complaints. The selection of patients is conducted at the Clinic for Gastroenterology at University Medical Clinical Center in Skopje.

The experimental group was divided into two groups:

- First group has 30 patients with dyspeptic complaints, in which is not registered the presence of *H. pylori*.
- The second group also comprised of 30 subjects with dyspeptic complaints in which the presence of *H. pylori* is confirmed.

All participants signed a standard informed consent form approved by the ethical committee.

The presence or absence of *H. pylori* has been ascertained after endoscopic examination-gastroscopy, when biopsy material was taken and implemented urease test (CLO-test). At all patients in experimental group was made a clinical test to observe mouth burning, aphtae, acid taste and lingual papillary hyperplasia according to Cohen Proctor.

A. Determination of *H. pylori* in samples of saliva

Determination of *H. pylori* in samples of saliva was performed at the Clinic of oral pathology and periodontology. Saliva samples were taken before endoscopic examination of each patient after application of gum Orbit sugar-free. Chewing time was 1 minute. After collecting the saliva Pronto dry test was applied. Through direct outpouring of saliva from the mouth of the patient in the next minutes, the samples were applied to patented membrane point inserted between the reading point and detection ring, containing urease and phenol red indicator. Reading of the results was performed after 1 hour.

B. Determination of *H. pylori* in biopsy material

Determination of *H. pylori* in biopsy material was performed at the Clinic for Gastroenterology in endoscopy room. Endoscopy was done without anesthesia. During endoscopic examination several biopsy samples were taken, one of which is used for rapid urease test (RUT). The examination which is performed during gastroscopy used Pronto Dry tests. Mucosal biopsy is taken from the antrum ventriculi 2 cm. from the pylorus, from macroscopic healthy mucosa. The material was put into patented membrane point inserted between the point of read out and detection ring, which contains urea and phenol red indicator. Urease produced by *H. pylori* hydrolyzes urea to ammonia, which changes the pH of the medium, which reflects the change of the color from yellow (negative) in the red (positive). Positive or negative results are read after 60 min.

According to the assessment of therapists, there were no indication biopsy samples from any patient to be processed at the Clinic for Radiology and Oncology, in order confirmation doubt for malignancy. Oral examination was conducted at University Dental Clinical Center at Faculty of dentistry in Skopje.

The data analysis was conducted in the statistical program Statistics For Windows 7.1 and SPSS Statistics 7.0. The significance is determined for p <0,05. Data are presented in tables and Figures.

Results

The results from clinical examination at patients with dyspeptic complaints and *H. pylori* are presented at Table 1. At 30 patients, 16 patients (53,33%) had lingual papillary hyperplasia, acid taste, burning mouth and recurrent aphthous stomatitis (RAS) which are the most important symptoms, at 1 patient (3,33%) lingual papillary hyperplasia, at 1 patient (3,33%) lingual papillary hyperplasia and acid taste (Figure 1, Table 1).

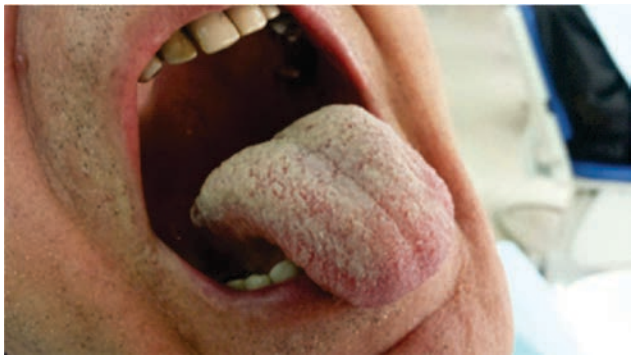

Figure1. Long lasting lingual papillary hyperplasia at patients with positive CLO test

Table1. Oral clinical signs and symptoms at patients with dyspeptic complaints and H. pylori infection

Clinical findings	No	Cumulative No	%	Cumulative %
Acid taste	4	4	13,33	13,33
Burning mouth	4	8	13,33	26,67
Lingual papillary hyperplasia	1	9	3,33	30,00
Lingual papillary hyperplasia, burning mouth, acid taste, aphtae	16	25	53,33	83,33
Lingual papillary hyperplasia, burning mouth, aphtae	2	27	6,67	90,00
Burning mouth, aphtae	2	29	6,67	96,67
Lingual papillary hyperplasia, acid taste	1	30	3,33	100,00
Missing	0	30	0,00	100,00

Cumulative No- cumulative frequency of absolute values
Cumulative percent- cumulative percent of absolute values

At patients without *Helicobacter pylori* but with dyspeptic complaints, the important symptoms were confirmed burning mouth in 14 patients (46,67%). In 2 patients (6,67%) was confirmed recurrent aphthous stomatitis (RAS), acid taste was registered in 2 patients (6,67%), and also lingual papillary hyperplasia in 2 patients (6,67%), (Table 2)

Table 2. Oral clinical signs and symptoms at patients with dyspeptic complaints without H. pylori infection.

Clinical findings	No	Cumulative No	%	Cumulative %
Aphtae	2	2	6,67	6,67
Acid taste	2	4	6,67	13,33
Burning mouth	14	18	46,67	60,00
Lingual papillary hyperplasia	2	20	6,67	66,67
Lingual papillary hyperplasia, burning mouth	3	23	10,00	76,67
Lingual papillary hyperplasia, burning mouth, Aphtae, acid taste	7	30	23,33	100,00
Missing	0	30	0,00	100,00

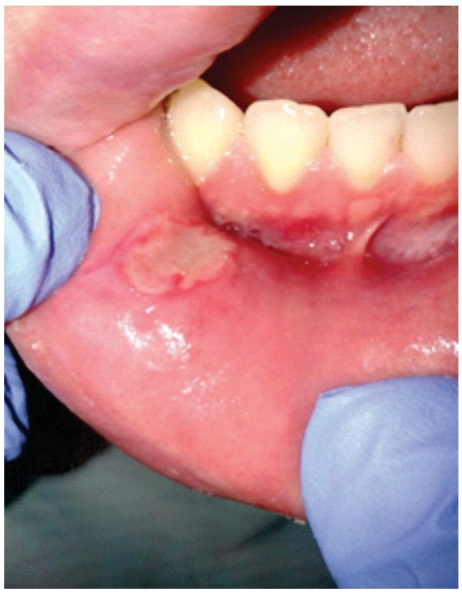

Figure 2. Positive CLO-test, aphtae

The results of the crosstabulation from findings of gastric biopsy and clinical findings, are shown in Table 3.

Table 3. Crosstabulation from findings of gastric biopsy and clinical findings

		Clinical findings	Biopsy		Total
			without *H.pylori*	with *H.pylori*	
1	No	Aphtae	2	0	2
	%		3,33%	0,00%	3,33%
2	No	Acid taste	2	4	6
	%		3,33%	6,67%	10,00%
3	No	Burning mouth	14	4	18
	%		23,33%	6,67%	30,00%
4	No	Lingual papillary hyperplasia	2	1	3
	%		3,33%	1,67%	5,00%
5	No	Lingual papillary hyperplasia, Burning mouth	3	0	3
	%		5,00%	0,00%	5,00%
6	No	Lingual papillary hyperplasia, burning mouth, aphtae, acid taste	7	16	23
	%		11,67%	26,67%	38,33%
7	No	Lingual papillary hyperplasia, burning mouth, aphtae	0	2	2
	%		0,00%	3,33%	3,33%
8	No	Burning mouth, aphtae	0	2	2
	%		0,00%	3,33%	3,33%
9	No	Lingual papillary hyperplasia, acid taste	0	1	1
	%		0,00%	1,67%	1,67%
	No	Total	30	30	60
	%		50,00%	50,00%	

From 30 patients with dyspeptic complaints with proven presence of *H. pylori*, in 16 (26,67%) were proven lingual papillary hyperplasia, burning mouth and acid taste. At 4 patients (6,67%) it was proven acid taste, 4 patients (6,67%) with burning mouth and acid taste, 2 patients (3,33%) lingual papillary hyperplasia, burning mouth and aphtae. From all examined patients, at 2 patients (3,33%) was proven burning mouth and aphtae. One of them (1,67%), had lingual papillary hyperplasia and the others (1,67%), had lingual papillary hyperplasia and acid taste (Table 3). From 30 patients with dyspeptic complaints without proven presence of *H. pylori*, in 14 (23,33%) burning mouth, at 7 patients (11,67%) it was proven lingual papillary hyperplasia,acid taste, burning mouth, at 3 patients (5,00%) lingual papillary hyperplasia, and burning mouth. Aphtae were proven at 2 patients (3,33%), at 2 patients (3,33%) acid taste and 2 patients (3,33%) with lingual papillary hyperplasia (Figure 3). For $p<0,01$($p=0,002$), there is a significant differences between the patients with dyspeptic complaints and *Helicobacter pylori* and patients with dyspeptic complaints but without *Helicobacter pylori.* Pearson Chi-square= 20,10 and $p<0,05$($p= 0,01$).

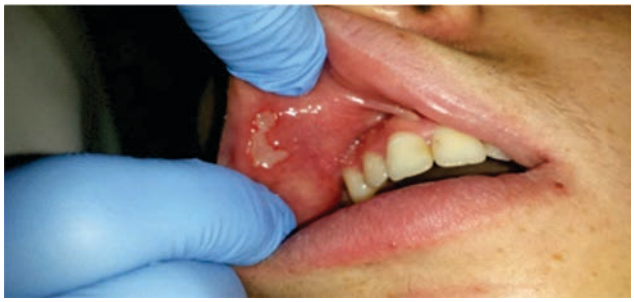

Figure 3. Aphtae in patient with positive CLO-test in saliva and positive Helicobacter pylori

Discussion

According to our results, we can notice that there is a significant difference in clinical findings between patients with dyspeptic complaints with and without *H. pylori*. At most of the patients with and without *H. pylori,* there is lingual papillary hyperplasia and burning mouth, but acid taste and aphtae are present a much more in patients without *H. pylori.*

Because of similarities in the characteristics of peptic ulcers and oral aphthous ulcers, it seems reasonable to hypothesize that *H. pylori* could play a role in the development of RAS. The obtained results from Rajendra et al. claim that there is no connection between *H. pylori* infection and recurrent aphtous stomatitis (RAS)[20]. Contrary to these findings, it has been demonstrated that *H. pylori* plays a role in the development of RAS, and the eradication of *H. pylori* may result in a reduced possibility of RAS occurrence[16].

According to Gomes[21], although the eradication of the infection may affect the clinical course of oral lesions whose mechanisms are still unclear, painful ulcers are not associated with the presence of bacteria in the oral cavity. Gaal-Troselj *et al.*[22] revealed that mucosal changes and atrophic glossitis present in oral mucosa, might be caused by *H. pylori*, compared with normal mucosa, and this mechanism may play a role in its oro-oral transmission. The conclusion was made after examination, which was performed to detect the presence of *H. pylori* on tongue and oral mucosa. *H. pylori* was found in 43 samples (16%). Bacteria were significantly less present in tongue mucosa affected with benign migratory glossitis compared with atrophic glossitis.

Mravak-Stipetić *et al*.[23] revealed that *H. pylori* is not pathogenic in the oral cavity, nor is it associated with common oral pathologic processes. Nested PCR was used for the detection of *H. pylori* DNA in specimens collected from seven different topographic sites in the oral cavity.

It has long been known that *H. pylori* can cause gastric diseases such as gastritis, gastric ulcer and gastric cancer. Who is the medium this bacterium is transmitted through, is debatable and has yet to be determined[24]. Recent findings from Jordanian populations indicate a significant increase in *H. pylori* in dental plaque. The authors suggest that studying the genotype of *H. pylori* in the dental plaque on the one hand can be an essential tool for infection prevention and on the other hand to predict the severity and prognosis of gastric infection caused by *H. pylori*[25].

Clearly, the prevalence of *H. pylori* will vary among different population groups and this may account partly for the conflicting data presented in the literature about the presence of this organism in the oral cavity[25, 26]. The main question that arise from presence of *H. pylori* in oral cavity, are if they represent a bacterium residua, or part of biofilm, or they have another origin with pathogenic role. Some examiners suggest that *H. pylori* could be the key factor in etiology of recurrent aphtous stomatitis and oral cancer[21, 22, 27].

According to results from Czesnikiewicz-Guzik[28] study, there is no evidence for connection between periodontitis, gingivitis and *H. pylori*. These findings are in agreement with the results of Okuda *et al*.[29] that *H. pylori* was present in the oral cavity only as a transient organism. Fritscher *et al*.[30] have studied patients with recurrent aphtous stomatitis. The results revealed that there is no difference between the patients with recurrent aphtous stomatitis and control group.

Despite of detection of *H. pylori* in a few samples, the authors suggests that they were only isolated cases. They concluded that *H. pylori* is not the reason for mucosal changes, but also they can make the oral environment more acceptable for *H. pylori* colonization compared with normal mucosa[22,29].

The *H. pylori* role in periodontitis and gastritis is still unclear. Some authors have confirmed the detection of bacterium on and under the gingiva[31, 32], but the others could not confirmed this relationship[33, 34]. Okuda *et al*.[29] show that periopathogens like *Porphyromonas gingivalis* and *Fusobacterium nucleatum* are able to connect to *H. pylori*. Various oral bacterial species inhibited the growth of oral endogenous bacteria and *H. pylori* strains in stab cultures. *Streptococcus mutans* and *Prevotella intermedia* are present in oral biofilm and they could produce bacteriocin (inhibitory protein) that could inhibit the growth of *H. pylori*. This statement supports the idea that *H. pylori* was present in the oral cavity only as a transient organism. Its short time of presence is due to elimination by plaque bacteria[29].

The results of the crosstabulation from CLO-test of saliva and clinical findings, are with significant differences, because out of 30 patients with positive *H. pylori* infection, 16 patients had lingual papillary hyperplasia, burning mouth, acid taste and aphtae at the same time, and positive CLO-test, although the others had burning mouth, aphtae and negative CLO-test.

The second group of patients without *H. pylori* infection, 14 (46,67%) of 30 patients examined, had burning mouth, 11 of them had negative saliva CLO-test, and 3 (10,00%) positive CLO-test, 7 (23,33%) patients had lingual papillary hyperplasia, burning mouth, aphtae, acid taste, and they all have positive saliva CLO-test. Aphtae were presented in 2 (6,67%) and negative CLO-test of saliva. Acid taste was registered in 2 (6,67%), 1 of 2 (3,33%) had positive and 1 negative CLO-test of saliva. 2 patients (6,67%) had lingual papillary hyperplasia and negative CLO-test of saliva.

Our results agreed in part with Gall-Troselj *et al*.[22] and Mravak-Stipetic[23], although Mravak-Stipetic[23] have been examining *H. pylori* in oral lesion, independently of positive CLO-test in biopsy material. In this study, subjective parameters (acid taste, burning mouth) and

objective parameters (lingual hyperplasia, aphtae) are much more presented in group with confirmed *H. pylori* in biopsy material than the other examined group.

We believe that positive CLO-test in biopsy material and saliva could be the reason for oral lesions which were frequently present in examined patients, with confirmed *H. pylori.* Patients with negative CLO-test in biopsy material had more poor clinical findings in saliva that correspond with clinical findings.

Conclusions

H. pylori in saliva and biopsy material detected with CLO test are reason for oral lesions at patients with dyspeptic complaints who have the presence of *H. pylori*. We explained the symptoms that however were part of the clinical findings with additional factors that may cause the initiation of the findings in the oral cavity. In this case maybe the insignificant presence of *H. pylori* can only add to and give the final shape of the clinical symptomatology.

References

1. Mapstone NP, Lynch DA, Lewis FA, Axon AT, Tompkins DS, Dixon MF et al. Identification of Helicobacter pylori DNA in the mouths and stomachs of patients with gastritis using PCR. J Clin Pathol, 1993;46:540-543.
2. Hardo PG, Tugnait A, Hassan F, Lynch DA, West AP, Mapstone NP et al. Helicobacter pylori infection and dental care. Gut, 1995;37:44-46.
3. Fritscher AM, Cherubini K, Chies J, Dias AC. Association between Helicobacter pylori and recurrent aphthous stomatitis in children and adolescents. J Oral Pathol Med, 2004;33:129-132.
4. Parsonnet J, Friedman GD, Vandersteen DP, Chang Y, Vogelman JH, Orentreich N et al. Helicobacter pylori infection and the risk of gastric carcinoma. N Engl J Med, 1991;325:1127-1131.
5. Wang XM, Yee KC, Hazeki-Taylor N, Li J, Fu HY, Huang ML. Oral Helicobacter pylori, its relationship to successful eradication of gastric H. pylori and saliva culture confirmation. J Physiol Pharmacol, 2014;65:559-566.
6. Anand PS, Kamath KP, Anil S. Role of dental plaque, saliva and periodontal disease in Helicobacter pylori infection. World J Gastroenterol, 2014;20:5639-5653.
7. Yee JK. *Helicobacter pylori* colonization of the oral cavity: a milestone discovery. World J Gastroenterol, 2016;22:641-648.
8. Ogaya Y, Nomura R, Watanabe Y, Nakano K. Detection of Helicobacter pylori DNA in inflamed dental pulp specimens from Japanese children and adolescents. J Med Microbiol, 2015;64:117-123.
9. Nisha KJ, Nandakumar K, Shenoy KT, Janam P. Periodontal disease and Helicobacter pylori infection: a community-based study using serology and rapid urease test. J Investing Clin Dent, 2016;7:37-45.
10. Wei X, Zhao HQ, Ma C, Zhang AB, Feng H, Zhang D et al. The association between chronic periodontitis and oral Helicobacter pylori: A meta-analysis. PLoS One, 2019;14:e0225247.
11. Flores-Treviño CE, Urrutia-Baca VH, Gómez-Flores R, De La Garza-Ramos MA, Sánchez-Chaparro MM, Garza-Elizondo MA. Molecular detection of Helicobacter pylori based on the presence of cagA and vacA virulence genes in dental plaque from patients with periodontitis. J Dent Sci, 2019;14:163-170.
12. Hu Z, Zhang Y, Li Z, Yu Y, Kang W, Han Y et al. Effect of *Helicobacter pylori* infection on chronic periodontitis by the change of microecology and inflammation. Oncotarget, 2016;7:66700-66712.
13. Huang Y, Wang QL, Cheng DD, Xu WT, Lu NH. Adhesion and invasion of gastric mucosa epithelial cells by Helicobacter pylori. Front Cell Infect Microbiol, 2016;6:159.
14. Li H, Liang D, Hu N, Dai X, He J, Zhuang H, Zhao W. Helicobacter pylori inhibited cell proliferation in human periodontal ligament fibroblasts through the Cdc25C/CDK1/cyclinB1 signaling cascade. J Periodontal Implant Sci, 2019;49:138-147.
15. Ren Q, Yan X, Zhou Y, Li WX. Periodontal therapy as adjunctive treatment for gastric Helicobacter pylori infection. Cochrane Database Syst Rev, 2016;2:CD009477.
16. Gülseren D, Karaduman A, Kutsal D, Nohutcu RM. The relationship between recurrent aphthous stomatitis, and periodontal disease and Helicobacter Pylori infection. Clin Oral Investig, 2016;20:2055-2060.
17. Gomes CC, Gomez RS, Zina LG, Amaral FR. Recurrent aphthous stomatitis and Helicobacter pylori. Med Oral Patol Oral Cir Bucal, 2016;21:e187-191.
18. Kazanowska-Dygdała M, Duś I, Radwan-Oczko M. The presence of Helicobacter pylori in oral cavities of patients with leukoplakia and oral lichen planus. J Appl Oral Sci, 2016;24:18-23.
19. Amiri N, Abiri R, Eyvazi M, Zolfaghari MR, Alvandi A. The frequency of Helicobacter pylori in dental plaque is possibly underestimated. Arch Oral Biol, 2015;60:782-788.
20. Rajendra K, Purnachandra SM, Patel PC, Cota J, Singh VR, Vatsal A. A Clinical and Microbiological Evaluation of Helicobacter pylori in Recurrent Aphthous Stomatitis. J Contemp Dent Pract, 2017;18:1194-1197
21. Gomes CC, Gomez RS, Zina LG, Amaral FR. Recurrent aphthous stomatitis and Helicobacter pylori. Med Oral Patol Oral Cir Bucal, 2016;21:e187-191.
22. Gall-Troselj K, Mravak-Stipetić M, Jurak I, Ragland WL, Pavelić J. Helicobacter pylori colonization of tongue mucosa--increased incidence in atrophic glossitis and burning mouth syndrome (BMS). J Oral Pathol Med, 2001;30:560-563.
23. Mravak-Stipetić M, Gall-Troselj K, Lukac J, Kusić Z, Pavelić K, Pavelić J. Detection of Helicobacter pylori in various oral lesions by nested polymerase chain reaction (PCR). J Oral Pathol Med, 1998;27:1-3
24. Payão SL, Rasmussen LT. *Helicobacter pylori* and its reservoirs: a correlation with the gastric infection. World J Gastrointest Pharmacol Ther, 2016;7:126-132.

25. Abu-Lubad M, Alzoubi H, Jarajreh D, Sawalqa AA, Bruggemann H, Albataineh E. Analysis of Helicobacter pylori Genotypes Amongst Jordanians' Dental Plaque Samples. Gastroenterol Res,2018;11:46-51.
26. Mendoza-Cantú A, Urrutia-Baca VH, Urbina-Ríos CS, De la Garza-Ramos MA, García-Martínez ME, Torre-Martínez HHH. Prevalence of Helicobacter pylori vacA Genotypes and cagA Gene in Dental Plaque of Asymptomatic Mexican Children. Biomed Res Int, 2017;2017:4923640.
27. Murata M. Inflammation and cancer. Environ Health Prev Med, 2018;23:50.
28. Czesnikiewicz-Guzik E, Karczewska WB, Guzik TG, Kapera P, Targosz A, Konturek SJ et al. Association of the presence of Helicobacter pylori in the oral cavity and in the stomach. J Physiol Pharmacol, 2004;55:105-115.
29. Okuda K, Ishihara K, Miura T, Katakura A, Noma H, Ebihara Y. Helicobacter pylori may have only a transient presence in the oral cavity and on the surface of oral cancer. Microbiol Immunol, 2000;44:385-388.
30. Fritscher AM, Cherubini K, Chies J, Dias AC. Association between Helicobacter pylori and recurrent aphthous stomatitis in children and adolescents. J Oral Pathol Med, 2004;33:129-132.
31. Young KA, Allaker RP, Hardie JM. Morphological analysis of Helicobacter pylori from gastric biopsies and dental plaque by scanning electron microscopy. Oral Microbiol Immunol, 2001;16:178-181.
32. Gebara EC, Pannuti C, Faria CM, Chehter L, Mayer MP, Lima LA. Prevalence of Helicobacter pylori detected by polymerase chain reaction in the oral cavity of periodontitis patients. Oral Microbiol Immunol, 2004;19:277-280.
33. Hu W, Cao C, Meng H. Helicobacter pylori in dental plaque of periodontitis and gastric disease patients. Zhonghua Kou Qiang Yi Xue Za Zhi, 1999;34:49-51.
34. Kignel S, de Almeida Pina F, Andre EA, Alves Mayer MP, Birman EG. Occurrence of Helicobacter pylori in dental plaque and saliva of dyspeptic patients. Oral Dis, 2005;11:17-22.

Conflict of Interests: Nothing to declare.
Financial Disclosure Statement: Nothing to declare.
Human Rights Statement: All the procedures on humans were conducted in accordance with the Helsinki Declaration of 1975, as revised 2000. Consent was obtained from the patient/s and approved for the current study by national ethical committee.
Animal Rights Statement: None required.

Received on November 19, 2019.
Revised on December 8, 2019.
Accepted on December 20, 2019.

Correspondence:

Bruno Nikolovski
Center for dental health – ETERNAdent
Skopje, North Macedonia
e-mail: bnikolovski@eternadent.com.mk