American Journal of Internal Medicine
2014; 2(4): 72-78
Published online July 30, 2014 (http://www.sciencepublishinggroup.com/j/ajim)
doi: 10.11648/j.ajim.20140204.14
ISSN: 2330-4316 (Print); ISSN: 2330-4324 (Online)

The frequency and etiology of recurrent apthous stomatitis in helicobacter pylori posıtıve patients

Ayşe Neslin Akkoca[1, *], Zeynep Tuba Özdemir[2], Serdar Yanık[3], Seçil Günher Arıca[4], Hülya Yalçin[5], Gül Soylu Özler[6]

[1]Mustafa Kemal University, Faculty of Medicine, Department of Family Medicine, Hatay, Turkey
[2]Bozok University, Faculty of Medicine, Department of İnternal Medicine, Yozgat, Turkey
[3]İskenderun State Hospital, Department of Pathology, Hatay, Turkey
[4]Istanbul Okmeydanı Research Hospital,Department of Famıly Medicine,Istanbul,Turkey
[5]Mustafa Kemal University, Faculty of Medicine, Department of Nuclear Medicine,Hatay ,Turkey
[6]Mustafa Kemal University, Faculty of Medicine, Department of Otorhinolarıngology, Hatay ,Turkey

Email address:
ayseneslinoguzhan@hotmail.com (A. N. Akkoca)

To cite this article:
Ayşe Neslin Akkoca, Zeynep Tuba Özdemir, Serdar Yanık, Seçil Günher Arıca, Hülya Yalçin,Gül Soylu Özler. The Frequency and Etiology of Recurrent Apthous Stomatitis in Helicobacter Pylori Positive Patients. *American Journal of Internal Medicine.* Vol. 2, No. 4, 2014, pp. 72-78. doi: 10.11648/j.ajim.20140204.14

Abstract: Objective: Recurrent aphthous ulcerations (RAU) is a disease characterized by recurrent painful ulcerations of the oral mucosa. The etiopathogenesis of the disease still unknown, and recently the role of Helicobacter pylori (HP) is overlooked. RAU frequency and etiologic factors of HP positive patients have been investigated in this study. Materials and Methods: 64 patients who attended to Mustafa Kemal University Department of Nuclear Medicine and presented with positive HP were included in the study. A questionnaire about sociodemographic characteristics and etiologies for RAU was administered to the patients. Results: The mean age of 64 patients determined a HP infection with C- 14 urea breath test was 54.1 ± 19.3. 35(54.7%) of 64 patients were females , 29(45.3 %) of 64 patients were males . Smoking prevalence rate were 65.6%. 43.8 % of patients had RAU 1-3 times per year , 35.9 % more than 3 times. 35.9 % of the patients had RAU in tongue, 28.1% of the patients had RAU on lips, tongue and cheek. 42% of the patients had minor, 51.6 % of patients had major, 6.4% of patients had herpetiform ulcers. The average degree of pain (score out of ten) were found 7.39 ± 1.54 . There was correlation between the number of aphthae in the past year and the degree of pain. The degree of pain in herpetiform ulcers were higher. Familial history was found to be 32.8%. 68.7 % of the patients had reflux. 51.6 % of the patients declared hoarseness. Conclusion: High incidence of RAU in HP positive patients and patients with reflux may cause the idea that HP may be suspected to be an etiologic factor of RAU.

Keywords: Helicobacter Pylori, Recurrent Aphthous Ulcers, Aphthae

1. Introduction

RAU is the most common ulcerative disease which affecting 10-25% of population. Some researchers claims that prevalence in certain populations are up to 50% (1). RAU, can be seen at any age from childhood or adolescence and is characterized by recurrent episodes of painful ulcers which can last about 1-4 weeks.

As regards the clinical manifestations, the basic lesion is a recurrent, painful, rounded or oval ulcer with a necrotic base. Three clinical subtypes of RAU have been established according to the magnitude, number and duration of the outbreaks (2):

• Minor RAU: This is the most common presentation of the disease, representing 70-85% of all cases. It manifests as small rounded or oval lesions covered by a grayish-white pseudomembrane and surrounded by an erythematous halo. Each minor RAU episode usually involves the appearance of 1-5 ulcers measuring under 1 cm in diameter. These episodes are self-limiting and resolve within 4-14 days without leaving scars (3-6).

• Major RAU: This is the most severe presentation of the disease, representing 10% of all cases. In this subtype the ulcers measure over 1 cm in size and tend to appear on the

lips, soft palate and pharynx. The lesions persist for over 6 weeks and can leave scars.

• Herpetiform RAU: This subtype accounts for 1-10% of all cases and is characterized by recurrent outbreaks of small, deep and painful ulcers. Up to 100 aphthae can develop simultaneously, measuring 2-3 mm in size, though they tend to merge to form larger ulcerations with an irregular contour. This presentation is more often seen in women and in patients of older age, in contrast to the other two clinical subtypes of the disease (2,3,6.7).

The diagnosis of RAU is based on the patient anamnesis and clinical manifestations. There is no specific diagnostic test, though it is essential to discard possible underlying systemic causes particularly in the case of adults who suffer sudden outbreaks of RAU. It is advisable to request a complete series of laboratory tests. A biopsy of the lesions is only recommended in the case of diagnostic uncertainty, since the findings only indicate a simple nonspecific inflammatory lesion (2,3,7).

RAU is a non-infectious disease beginning at the oral mucosa and usually the first line of immunological and mechanical defense against infectious agents and physical injuries. Characteristic histological features of RAU are vascular dilatation, inflammatory cell infiltration and epithelial ulceration (8,9). Non-vascular infiltration of erythrocytes on the side of ulcers, may indicate that the disorder is in the vessel wall.

The etiopathogenesis of RAU so far remains not fully understood. The potential factors are: genetic predisposition, viral and bacterial infections, food allergies, vitamin and microelement deficiencies, systemic diseases (e.g., celiac disease, Crohn's disease, ulcerative colitis, AIDS), increased oxidative stress, hormonal defects, mechanical injuries and anxiety (10-12,2). Recently, also the atopic background of the condition has been suggested (13). In genetically predisposed patients, the effect of certain factors initiates the cascade of proinflammatory cytokines, directed against selected regions of the oral mucosa. The microscopic observation of the aphtha region reveals a massive leukocytic infiltration, which varies depending on the disease duration and severity. In the initial phase which precedes the ulcer formation, monocytes and lymphocytes (mainly of the T type) together with single mast and plasmatic cells accumulate under the basal cell layer (14).

Among the potential factors some authors mention bacterial (Streptococcus oralis, Helicobacter pylori) and viral (herpes simplex virus, varicella-zoster virus, cytomegalovirus, adenoviruses) antigens. The studies results, however, are ambiguous and conflicting (15,16). The elevated serum level of antibodies against some streptococcal strains in RAS patients reported in the 1960s was not confirmed in latter studies, similarly in the case of antibodies against H. pylori (17,19). Tas et al. (20)proved the beneficial effect of H. pylori eradication in patients with RAS. The underlying mechanism, however, is rather related with the increase in serum vitamin B12 levels after the eradication than with the direct action of the bacteria. The attempts to isolate herpes simplex, cytomegalovirus, varicella-zoster and Epstein-Barr viral DNA from the biologic material collected from aphthae and mononuclear peripheral blood cells were successful only in single case of RAS, which also does not confirm the direct role of viruses in the etiopathogenesis of the condition (15).

Tobacco use is reported to cause an increase in keratinization in the oral mucosa. Although there are controversial results it has been reported that tobacco use causes decrease in the frequency of occurrence of aphthae (21,22).

Helicobacter pylori (HP) is a microaerophilic, gram negative bacteria which has affinity to gastric mucosa. Infection with this organism is serious, transmissible and connected with peptic and duodenal ulcers (23-27). Based on the statistics, 20-30% of adult people in the developed countries and more than 90% of them in the developing countries are probably infected by this bacterium (26). Being infected with this pathogen is basically asymptomatic and the person will be a carrier through his life, till the time when eradication therapy is done (28,29). The exact mechanism by which H. pylori induces tissue injury is not clear. Some immune-mediated mechanisms are suggested.

The way this bacterium is transmitted is not yet quite clear. However, they are mostly found in contaminated foods, feces, saliva and the dental plaque of healthy individuals and also in patients with upper digestive system disease(30). Thus, the infection can be caused via oral-oral, fecal- oral or gastro-oral through gastrointestinal refluxes (23,28,29,31-34). Specialists believe that, dental plaque might be a bed of H. pylori and possibly cause re-infection of gastric mucosa, and that it is transient in the oral cavity or is mixed with normal oral microflora (23,25,28,35-38).

Different studies have revealed that H. pylori can be isolated from the oral cavity, dental plaque (supragingival and subgingival plaque), dorsum of the tongue and salivary secretions(39-42). Wide variations in the prevalence of H. pylori in the oral cavity are partly due to employing different detection methods. For example, in a study by Butt et al, using urease test and cytology, H. pylori was detected in 100% and 88% of dental plaque samples, respectively (42). In another study, H. pylori was detected in the saliva of 54.1% and in dental pockets in 48.3% of examined cases (41) and was considered a resident of the oral cavity. However, Chitsaziet al detected H. pylori in 34.1% of dental plaque samples (43).

Because of similarities in the histological characteristics of gastric ulcers and oral aphthous ulcers which respond to treatment with broad-spectrum antibiotics, it seems logical to assume that H. pylori could play a role in the development of recurrent aphthous ulcers. The data regarding the potential relation between RAS and H. pylori infection are limited and controversial. Accordingly, the aim of the present study was to determine the association between H. pylori and RAS. For these reasons, in our study, the C-14 urea breath test determined HP infection in

patients and we investigated the relationship between HP and RAU frequency, etiology and cigarette.

2. Materials and Methods

2.1. Working Groups and Work Plan

The study population included HP C-14 urea breath test positive 92 patients of Mustafa Kemal University Faculty of Medicine Hospital in the Department of Nuclear Medicine. Those with systemic disease (Ulcerative Colitis, Chrohn, Behçet Disease) and those applied in the previous month dental surgery were excluded from the study. To determine sociodemographic characteristics, the incidence and etiology of RAU in patients a questionnaire was administered. İn questionnaire age, gender, smoking history were asked. 64 patients with RAU was assessed of the incidence of apht, apht settlement, type of apht , subjective complaints, in association with a history of reflux, in association with a history of hoarseness.

2.2. Statistical Analysis

Data was entered in SPSS 15.0 package program. The mean of descriptive data, standard deviation, percentages were calculated. İn the comparison between groups who have normal distribution parametric data Student t test, Pearson's correlation test was used. Comparison of nonparametric data Mann-Whitney U test, Spearman correlation test and Chi-square test was used. p-value less than 0.05 was considered as significant ones.

3. Results

Demographic data: 64 (69.56%) of 92 patients had a history of RAU and mean was 54.1 ± 19.3 . 35 (54.7%) patients were female, 29 (45.3%) were men. 34.4% of were regular smokers, 65% of nonsmoker.

The frequency of RAU: 20.3% of patients once a year, 43.8% of patients 1-3 times per year, 35.9% of patients described RAU more than 3 times per year.

Settlement of RAU: 20.3% of patients had RAU in the lips, 15.6% of the patients in the cheek, 35.9% of patients in the tounge, 28.1% of the patients in lips, cheeks and tongue were found to occur together. None of the patients had aphthae in the tonsils and gums.

Type of RAU: 42% of patients had minor aphthae, 51.6% patients major aphthae, 6.4% patients herpetiformis aphthae.

Complaints caused by RAU: Pain, swallowing difficulty ,eating difficulty was present in 40.6% of patients. In addition, lack of appetite and difficulty in speaking was both present in 46.9% patients. Who described pain in patients, average degree of pain (score out of ten) was found to be 7.39 ± 1.54.

In the past year apht number was found statistically significant with the degree of pain a($p = 0.0001$). it was observed that according to type of apht the degree of pain changes, patients pain degree was higher in herpetiformis aphthae ($p = 0.0001$). Minor and major aphthae when we look at the degree of pain were not statistically different ($p = 0.779$).

20.3% of patients were found to have no changes in sense of taste. Taste changes were in 35.9% of patients at sometimes ,in 28.1% of the patients mostly , in 15.6% of patients were seen at all times.

Relationship with a family history of RAU: RAU family history was positive in 32.8% of patients. 67.2% of perceived any family history.

RAU relationship with reflux: 68.7% of patients were complaining of reflux. Hoarseness or sound bifurcation was in 51.6% of patients.

RAU relationship with smoking: Smoking reduces the formation of aphthae by increasing mucosal keratinization .İt is repoted that of starting smoking again with reduced prevalence of aphthae (6,7). In our study, this result was not significant ($p> 0.05$). Major and herpetiform aphthae of those were smoking amnesty. But it was not statistically significant ($p> 0.05$).

4. Discussion

İmmunodeficiency, hematological problems, microbial factors such reasons known to have a role in the etiology of RAU, but none yet to be fully elucidated (44). İt have been reported that in the etiology of RAU genetic factors may play a role and also suggested that in patients with a positive family history disease becomes earlier with high ratio (45). In the literature there are many studies available about genetic, nevertheless the presence of genetic transmission has not been certainly established (46,47).

1/3 of RAU patients has the family history. In these people, the disease developing at an earlier age and is with more severe symptoms (45). İn our study consistent with the literature, those patients with a family apht history had numerous aphthae in the past year and this was significant ($p <0.05$).

İn some of patients with duodenal ulcer there is HP in saliva and suggested that it comes from the stomach to the mouth with reflux or acid regurgitation. Even if there is HP inside the mouth it is an indicator of HP gastritis. İt is also suggested that HP comes into the mouth from external sources at HP positive or negative person (48,49). Especially gastric colonization and mucosal involvement exposure in individuals HP, recurrent oral aphthous ulcers It is suggested to play a role in the pathogenesis (48).

In our study, relation was found between patients with reflux and the incidence of aphthous stomatitis. There was no difference between the types of aphtae. HP-positive patients with reflux there was significant relationship between the occurrence of hoarseness.

In a study on oral ulcers, H. pylori was detected in six (20.7%) out of 29 cases, and all the positive samples were located in the buccal mucosa (50). In another study on recurrent aphthous ulcers, 71.9% of cases were positive for H. Pylori (48). Fritscher et al, studying 105 children and

adolescents, found that 9.4% of 53 patients with recurrent aphthous stomatitis were positive for H. Pylori, and in the control group only 3.8% were positive. They did not find any statistically significant relationship between the presence of H. Pylori and recurrent aphthous stomatitis (18).

Rubin et al, working on 61 samples from head and neck malignant and premalignant conditions, detected H. pylori positivity in 16.3% of oral cavity samples (51).

H. pylori usually spreads via the fecal-oral route, and possibly by the oral-oral route and the spread of contaminated secretions (52-56). An investigation of H. pylori genotypes in saliva, dental plaques, stools and gastric biopsy samples from 300 patients found that the fecal-oral route was the main method of H. pylori transmission. Furthermore, the oral cavity might serve as a reservoir for H. pylori because the genotypes of H. pylori isolates from saliva, stomach and stool are similar (57-60). Debate continues regarding whether or not the oral cavity is the major reservoir of H. pylori for gastric re-infection (61-69). Although some investigators have reported that the oral cavity is the reservoir for H. Pylori (70-81), insufficient evidence supports the notion that dental treatment can prevent recurrent gastric H. pylori infection (24).

A relationship with H. pylori has been investigated among various oral disorders including periodontal disease (82-85), glossitis, burning mouth syndrome (86), halitosis (87-89), Behçet's syndrome (90), lichen planus (91,92), and taste perception (93). Combining periodontal with systemic therapy might be a promising approach to improving therapeutic effects and decreasing the risk of recurrent gastric infection (94). However, an association between H. pylori and various periodontal disorders has not been established.

H. pylori might comprise part of the normal oral microflora (95). H. pylori in dental plaque might not be associated with brushing frequency and oral health status and one study of 161 patients concluded that H. pylori is not pathogenic in the oral cavity (96-98).But most studies suggest that whether or not H. pylori in the oral cavity plays a pathogenic role remains debatable. Nonetheless, dentists and dental professionals are at increased risk of exposure to H. pylori through contact with the oral cavities of infected patients(99,100).

It can be hypothesized that, if H. pylori has a role in the development of RAS, we can decrease the frequency and the severity of the RAS lesions, by omitting the organism through chlorhexidine mouth rinses or irrigation and developing oral hygiene via mechanical plaque removal parallel to the triple therapy (a therapeutic period by antibiotics for digestive infections), (24) which itself results in patient's comfort and a better quality of life. The idea that, after eradication of H. pylori, the severity and recurrence frequency of RAS is decreased has been supported by Karaca et al. and Farmaki et al(101).

As a result; oral cavity is a gastric reservoir for HP and we think that gastric HP settles through the oral mucosa by reflux due to gastric HP may play a role in the pathogenesis of RAU.

[Note: For I have seen in the research literature; research often built on recurrent aphthous ulcers in patients with Helicobacter pylori detection. But in our study of Helicobacter pylori-positive people with recurrent aphthous ulcers were evaluated.]

References

[1] Rogers RS, Mehregan DA. Disorders of the oral cavity.In: Moschella SL,Hurley HJ, eds. Dermatology, 3th ed. Philadelphia :W.B. Saunders Company,1992:2087-121.

[2] Scully C, Porter S. Oral mucosal disease: recurrent aphthous stomatitis. Br J Oral Maxillofac Surg.2008;46:198–206.

[3] Chavan M, Jain H, Diwan N, Khedkar S, Shete A, Durkar S. Recurrent aphthous stomatitis:a review. J Oral Pathol Med. 2012;41:577–83.

[4] Zhou Y, Chen Q, Meng W, Jiang L, Wang Z, Liu J. Evaluation of penicillin G potassium troches in the treatment of minor recurrent aphthous ulceration in a Chinese cohortOral Surg Oral Med Oral Pathol Oral Radiol Endod.2010;109:561–6.

[5] Meng W, Dong Y, Liu J, Wang Z, Zhong X, Chen R. A clinical evaluation of amlexanox oral adhesive pellicles in the treatment of recurrent aphthous stomatitis and comparison with amlexanox oral tabletsTrials. 2009;10:30.

[6] Liang MW, Neoh CY. Oral aphthosis: management gaps and recent advances. Ann Acad Med Singapore.2012;41:463–70.

[7] Preeti L, Magesh KT, Rajkumar K, Karthik R. Recurrent aphthous stomatitis. J Oral Maxillofac Pathol.2011;15:252–6.

[8] Jurge S, Kuffer R, Scully C, Porter SR. Recurrent aphthous stomatitis. Oral Dis 2006; 12: 1-21.

[9] Shashy RG, Ridley MB. Aphthous ulcers: A difficult clinical entity. Am. J. Otolaryngol 2000; 21: 389-393.

[10] Bilgili SG, Ozkol H, Takci Z, et al. Assessment of the serum paraoxonase activity and oxidant /antioxidant status in patients with recurrent aphthous stomatitis. Int J Dermatol. 2013

[11] Koybasi S, Parlak AH, Serin E, et al. Recurrent aphthous stomatitis: investigation of possible etiologic factors. Am J Otolaryngol. 2006;27:229–232.

[12] McCullough MJ, Abdel-Hafeth S, Scully C. Recurrent aphthous stomatitis revisited; clinical features, associations, and new association with infant feeding practices? J Oral Pathol Med. 2007;36:615–620.

[13] Veller-Fomasa C, Gallina P. Recurrent aphthous stomatitis as an expression of pathergy in atopics. Acta Dermatovenerol Alp Panonica Adriat. 2006;15:144–147.

[14] Poulter LW, Lehner T. Immunohistology of oral lesions from patients with recurrent oral ulcers and Behçet's syndrome. Clin Exp Immunol. 1989;78:189–195.

[15] Natah SS, Konttinen YT, Enattah NS, et al. Recurrent aphthous ulcers today: a review of growing knowledge. Int J Oral Maxillofac Surg. 2004;33:221–234.

[16] Shimoyama T, Horie N, Kato T, et al. Helicobacter pylori in oral ulcerations. J Oral Sci. 2000;42:225–229.

[17] Barile MF, Graykowski EA, Driscoll EJ, et al. L form of bacteria isolated from recurrent aphthous stomatitis lesions. Oral Surg Oral Med Oral Pathol. 1963;16:1395–1402.

[18] Fritscher AM, Cherubini K, Chies J, et al. Association between Helicobacter pylori and recurrent aphthous stomatitis in children and adolescents. J Oral Pathol Med. 2004;33:129–132.

[19] Mansour-Ghanaei F, Asmar M, Bagherzadeh AH, et al. Helicobacter pylori infection in oral lesions of patients with recurrent aphthous stomatitis. Med Sci Monit. 2005;11:CR576–CR579.

[20] Taş DA, Yakar T, Sakalli H, et al. Impact of Helicobacter pylori on the clinical course of recurrent aphthous stomatitis. J Oral Pathol Med. 2013;42:89–94.

[21] RoduB, MattinglyG. Oral mucosal ulcers :diagnosis and managament . J Am Dent Assoc 1992 :123 : 83-6.

[22] Rogers RS.Recurrent aphtous stomatitis: clinical characteristics and associated systemic disorders. Semin Cutan Med Surg 1997,16(4):278-83.

[23] Navabi N, Aramon M, Mirzazadeh A. Does the presence of the Helicobacter pylori in the dental plaque associate with its gastric infection? Dent Res J (Isfahan) 2011;8:178–82.

[24] Albanidou-Farmaki E, Giannoulis L, Markopoulos A, Fotiades S, Aggouridaki X, Farmakis K, et al. Outcome following treatment for Helicobacter pylori in patients with recurrent aphthous stomatitis. Oral Dis. 2005;11:22–6.

[25] Dowsett SA, Kowolik MJ. Oral Helicobacter pylori: Can we stomach it? Crit Rev Oral Biol Med. 2003;14:226–33.

[26] Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, et al.Helicobacter pylori infection and the development of gastric cancer. N Engl J Med. 2001;345:784-9

[27] Solnick JV, Vandamme P. Taxonomy of the Helicobacter Genus. In: Mobley HL, Mendz GL, Hazell SL, editors. Helicobacter pylori: Physiology and Genetics. Washington (DC): ASM Press; 2001. Chapter 5.

[28] Kilmartin CM. Dental implications of Helicobacter pylori. J Can Dent Assoc. 2002;68:489–93

[29] Czesnikiewicz-Guzik M, Bielanski W, Guzik TJ, Loster B, Konturek SJ. Helicobacter pylori in the oral cavity and its implications for gastric infection, periodontal health, immunology and dyspepsia.J Physiol Pharmacol. 2005;56(Suppl 6):77–89

[30] De Giacomo C, Fiocca R, Villani L, Lisato L, Licardi G, Diegoli N, et al. Helicobacter pyloriinfection and chronic gastritis: Clinical, serological, and histologic correlations in children treated with amoxicillin and colloidal bismuth subcitrate. J Pediatr Gastroenterol Nutr. 1990;11:310–6

[31] Dye BA, Kruszon-Moran D, McQuillan G. The relationship between periodontal disease attributes and Helicobacter pylori infection among adults in the United States. Am J Public Health. 2002; 92: 1809–15.

[32] Riggio MP, Lennon A, Wray D. Detection of Helicobacter pylori DNA in recurrent aphthous stomatitis tissue by PCR. J Oral Pathol Med. 2000;29:507–13.

[33] Silva Rossi-Aguiar VP, Navarro-Rodriguez T, Mattar R, de Melo Peres MP Siqueira, Correa Barbuti R, Silva FM, et al. Oral cavity is not a reservoir for Helicobacter pylori in infected patients with functional dyspepsia. Oral Microbiol Immunol. 2009;24:255–9.

[34] Brown LM. Helicobacter pylori: Epidemiology and routes of transmission. Epidemiol Rev. 2000; 22:283–97.

[35] Pedersen A. Are recurrent oral aphthous ulcers of viral etiology? Med Hypotheses.1991;36:206–10.

[36] ilva DG, Tinoco EM, Rocha GA, Rocha AM, Guerra JB, Saraiva IE, et al. Helicobacter pylori transiently in the mouth may participate in the transmission of infection. Mem Inst Oswaldo Cruz. 2010; 105:657–60.

[37] Thomas E, Jiang C, Chi DS, Li C, Ferguson DA., Jr The role of the oral cavity in Helicobacter pylori infection. Am J Gastroenterol. 1997;92:2148–54.

[38] Nguyen AM, el-Zaatari FA, Graham DY. Helicobacter pylori in the oral cavity. A critical review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1995;79:705–9.

[39] 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;19:277–80.

[40] Song Q, Haller B, Schmid RM, Adler G, Bode G. Helicobacter pylori in dental plaque: A comparison of different PCR primer sets. Dig Dis Sci . 1999;44:479–84.

[41] Pytko-Polonczyk J, Konturek SJ, Karczewska E, Bielański W, Kaczmarczyk-Stachowska A. Oral cavity as permanent reservoir of Helicobacter pylori and potential source of reinfection. J Physiol Pharmacol . 1996;47:121–9.

[42] Butt AK, Khan AA, Khan AA, Izhar M, Alam A, Shah SW, Shafqat F. Correlation of Helicobacter pylori in dental plaque and gastric mucosa of dyspeptic patients. J Pak Med Assoc. 2002;52:196–200.

[43] ChitsaziMT ChitsaziMT, Fattahi E, Farahani RM, FattahiS FattahiS. Helicobacter pylori in the dental plaque: Is it of diagnostic value for gastric infection? Med Oral Patol Oral Cir Bucal 2006;11:E325-8.

[44] Braun –Falco O,PlewigG,Wolff HH,Burgdorf WHC. Disease of the Lips and Oral Mucosa .In: Dermatology. 4th ed. Berlin : Springer-Verlag. 1996:1163-94.

[45] PorterSR , ScullyC. Aphthous stomatitis an overview of actiopathogenesis and management. Clin Exp Dermatol 1991:16(4):235-43.

[46] Rennie JS, Reade PC, Hay KD, Scully C. Recurrent aphthous stomatitis. Br Dent J 1985;159(11): 361-367.

[47] Shashy RG, Ridley MB. Aphthous ulcers: a difficult clinical entity. Am J Otolaryngol 2000; 21: 389-393.

[48] Birek C,Grandhi R,Mcneil K,Singer D,Ficarra G,Bowden G.Detection of Helicobacter pylori in oral aphtous ulcers .J Oral Pathol M ED 1999;28(5):197-203

[49] Greenspan JS, Gadol N, Olson JA, Hoover CI, Jacobsen PL, Shillitoe EJ,et al. Lymphocyte function in recurrent aphthous ulceration. J Oral Pathol 1985; 14(8): 592-602

[50] Leimola-Virtanen R, Happonen RP, Syrjänen S. Cytomegalovirus (CMV) and Helicobacter pylori (HP) found in oral mucosal ulcers. J Oral Pathol Med . 1995;24:14–7.

[51] Rubin JS, Benjamin E, Prior A, Lavy J. The prevalence of Helicobacter pylori infection in malignant and premalignant conditions of the head and neck. J LaryngolOtol . 2003;117:118–21.

[52] Marshall B. Helicobacter pylori: 20 years on. Clin Med. 2002;2:147–152.

[53] Piqueres P, Moreno Y, Alonso JL, Ferrús MA. A combination of direct viable count and fluorescent in situ hybridization for estimating Helicobacter pylori cell viability. Res Microbiol. 2006;157:345–349.

[54] Silva DG, Tinoco EM, Rocha GA, Rocha AM, Guerra JB, Saraiva IE, Queiroz DM. Helicobacter pylori transiently in the mouth may participate in the transmission of infection. Mem Inst Oswaldo Cruz. 2010;105:657–660.

[55] Dowsett SA, Archila L, Segreto VA, Gonzalez CR, Silva A, Vastola KA, Bartizek RD, Kowolik MJ. Helicobacter pylori infection in indigenous families of Central America: serostatus and oral and fingernail carriage. J Clin Microbiol. 1999;37:2456–2460.

[56] Allaker RP, Young KA, Hardie JM, Domizio P, Meadows NJ. Prevalence of helicobacter pylori at oral and gastrointestinal sites in children: evidence for possible oral-to-oral transmission. J Med Microbiol. 2002;51:312–317.

[57] Assumpção MB, Martins LC, Melo Barbosa HP, Barile KA, de Almeida SS, Assumpção PP, Corvelo TC. Helicobacter pylori in dental plaque and stomach of patients from Northern Brazil. World J Gastroenterol.2010;16:3033–3039.

[58] Gao J, Li Y, Wang Q, Qi C, Zhu S. Correlation between distribution of Helicobacter pylori in oral cavity and chronic stomach conditions. J Huazhong Univ Sci Technolog Med Sci. 2011;31:409–412.

[59] Namavar F, Roosendaal R, Kuipers EJ, de Groot P, van der Bijl MW, Peña AS, de Graaff J. Presence of Helicobacter pylori in the oral cavity, oesophagus, stomach and faeces of patients with gastritis. Eur J Clin Microbiol Infect Dis. 1995;14:234–237.

[60] Momtaz H, Souod N, Dabiri H, Sarshar M. Study of Helicobacter pylori genotype status in saliva, dental plaques, stool and gastric biopsy samples. World J Gastroenterol. 2012;18:2105–2111

[61] Sahin FI, Tinaz AC, Simşek IS, Menevşe S, Görgül A. Detection of Helicobacter pylori in dental plaque and gastric biopsy samples of Turkish patients by PCR-RFLP. Acta Gastroenterol Belg. 2001;64:150–152.

[62] Doré-Davin C, Heitz M, Yang H, Herranz M, Blum AL, Corthésy-Theulaz I. Helicobacter pylori in the oral cavity reflects handling of contaminants but not gastric infection. Digestion. 1999;60:196–202.

[63] Cheng LH, Webberley M, Evans M, Hanson N, Brown R. Helicobacter pylori in dental plaque and gastric mucosa. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996;81:421–423.

[64] Bürgers R, Schneider-Brachert W, Reischl U, Behr A, Hiller KA, Lehn N, Schmalz G, Ruhl S. Helicobacter pylori in human oral cavity and stomach. Eur J Oral Sci. 2008;116:297–304.

[65] Cześnikiewicz-Guzik M, Karczewska E, Bielański W, Guzik TJ, Kapera P, Targosz A, Konturek SJ, Loster B. Association of the presence of Helicobacter pylori in the oral cavity and in the stomach. J Physiol Pharmacol.2004;55 Suppl 2:105–115.

[66] Cammarota G, Tursi A, Montalto M, Papa A, Veneto G, Bernardi S, Boari A, Colizzi V, Fedeli G, Gasbarrini G. Role of dental plaque in the transmission of Helicobacter pylori infection. J Clin Gastroenterol.1996;22:174–177.

[67] Loster BW, Majewski SW, Cześnikiewicz-Guzik M, Bielanski W, Pierzchalski P, Konturek SJ. The relationship between the presence of Helicobacter pylori in the oral cavity and gastric in the stomach. J Physiol Pharmacol. 2006;57 Suppl 3:91–100.

[68] Oshowo A, Tunio M, Gillam D, Botha AJ, Holton J, Boulos P, Hobsley M. Oral colonization is unlikely to play an important role in Helicobacter pylori infection. Br J Surg. 1998;85:850–852.

[69] Chaudhry S, Iqbal HA, Khan AA, Izhar M, Butt AK, Akhter MW, Izhar F, Mirza KM. Helicobacter pylori in dental plaque and gastric mucosa: correlation revisited. J Pak Med Assoc. 2008;58:331–334.

[70] Berroteran A, Perrone M, Correnti M, Cavazza ME, Tombazzi C, Goncalvez R, Lecuna V. Detection of Helicobacter pylori DNA in the oral cavity and gastroduodenal system of a Venezuelan population. J Med Microbiol. 2002;51:764–770.

[71] Zou QH, Li RQ. Helicobacter pylori in the oral cavity and gastric mucosa: a meta-analysis. J Oral Pathol Med. 2011;40:317–324.

[72] Cellini L, Grande R, Artese L, Marzio L. Detection of Helicobacter pylori in saliva and esophagus. New Microbiol. 2010;33:351–357.

[73] Fernández-Tilapa G, Axinecuilteco-Hilera J, Giono-Cerezo S, Martínez-Carrillo DN, Illades-Aguiar B, Román-Román A. vacA genotypes in oral cavity and Helicobacter pylori seropositivity among adults without dyspepsia. Med Oral Patol Oral Cir Bucal. 2011;16:e175–e180.

[74] Eskandari A, Mahmoudpour A, Abolfazli N, Lafzi A. Detection of Helicobacter pylori using PCR in dental plaque of patients with and without gastritis. Med Oral Patol Oral Cir Bucal. 2010;15:e28–e31.

[75] Karczewska E, Konturek JE, Konturek PC, Cześnikiewicz M, Sito E, Bielański W, Kwiecień N, Obtułowicz W, Ziemniak W, Majka J, et al. Oral cavity as a potential source of gastric reinfection by Helicobacter pylori. Dig Dis Sci. 2002;47:978–986.

[76] Madinier IM, Fosse TM, Monteil RA. Oral carriage of Helicobacter pylori: a review. J Periodontol.1997;68:2–6.

[77] Nguyen AM, Engstrand L, Genta RM, Graham DY, el-Zaatari FA. Detection of Helicobacter pylori in dental plaque by reverse transcription-polymerase chain reaction. J Clin Microbiol. 1993;31:783–787

[78] Silva DG, Stevens RH, Macedo JM, Albano RM, Falabella ME, Veerman EC, Tinoco EM. Detection of cytotoxin genotypes of Helicobacter pylori in stomach, saliva and dental plaque. Arch Oral Biol. 2009;54:684–688.

[79] Rasmussen LT, Labio RW, Gatti LL, Silva LC, Queiroz VF, Smith Mde A, Payão SL. Helicobacter pylori detection in gastric biopsies, saliva and dental plaque of Brazilian dyspeptic patients. Mem Inst Oswaldo Cruz.2010;105:326–330.

[80] Oshowo A, Gillam D, Botha A, Tunio M, Holton J, Boulos P, Hobsley M. Helicobacter pylori: the mouth, stomach, and gut axis. Ann Periodontol. 1998;3:276–280.

[81] Al Asqah M, Al Hamoudi N, Anil S, Al Jebreen A, Al-Hamoudi WK. Is the presence of Helicobacter pylori in dental plaque of patients with chronic periodontitis a risk factor for gastric infection? Can J Gastroenterol.2009;23:177–179.

[82] Silva DG, Stevens RH, Macedo JM, Albano RM, Falabella ME, Fischer RG, Veerman EC, Tinoco EM. Presence of Helicobacter pylori in supragingival dental plaque of individuals with periodontal disease and upper gastric diseases. Arch Oral Biol. 2010;55:896–901.

[83] Hardo PG, Tugnait A, Hassan F, Lynch DA, West AP, Mapstone NP, Quirke P, Chalmers DM, Kowolik MJ, Axon AT. Helicobacter pylori infection and dental care. Gut. 1995;37:44–46

[84] Rajendran R, Rajeev R, Anil S, Alasqah M, Rabi AG. Helicobacter pylori coinfection is a confounder, modulating mucosal inflammation in oral submucous fibrosis. Indian J Dent Res. 2009;20:206–211.

[85] Bago I, Bago J, Plečko V, Aurer A, Majstorović K, Budimir A. The effectiveness of systemic eradication therapy against oral Helicobacter pylori. J Oral Pathol Med. 2011;40:428–432.

[86] 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.

[87] Adler I, Denninghoff VC, Alvarez MI, Avagnina A, Yoshida R, Elsner B. Helicobacter pylori associated with glossitis and halitosis. Helicobacter. 2005;10:312–317

[88] Tangerman A, Winkel EG, de Laat L, van Oijen AH, de Boer WA. Halitosis and Helicobacter pylori infection. J Breath Res. 2012;6:017102.

[89] Suzuki N, Yoneda M, Naito T, Iwamoto T, Masuo Y, Yamada K, Hisama K, Okada I, Hirofuji T. Detection of Helicobacter pylori DNA in the saliva of patients complaining of halitosis. J Med Microbiol.2008;57:1553–1559.

[90] Yildirim B, Oztürk MA, Unal S. The anti-Helicobacter pylori antibiotherapy for the treatment of recurrent oral aphthous ulcers in a patient with Behcet's syndrome. Rheumatol Int. 2009;29:477–478

[91] Attia EA, Abdel Fattah NS, Abdella HM. Upper gastrointestinal findings and detection of Helicobacter pylori in patients with oral lichen planus. Clin Exp Dermatol. 2010;35:355–360

[92] Pourshahidi S, Fakhri F, Ebrahimi H, Fakhraei B, Alipour A, Ghapanchi J, Farjadian S. Lack of association between Helicobacter pylori infection and oral lichen planus. Asian Pac J Cancer Prev. 2012;13:1745–1747

[93] Cecchini MP, Pellegrini C, Bassetto MA, Osculati F, Sbarbati A, Marcolini L, Pegoraro M, Fontana R, De Franceschi L. Might Helicobacter pylori infection be associated with distortion on taste perception? Med Hypotheses. 2013;81:496–499.

[94] Zaric S, Bojic B, Jankovic Lj, Dapcevic B, Popovic B, Cakic S, Milasin J. Periodontal therapy improves gastric Helicobacter pylori eradication. J Dent Res. 2009;88:946–950.

[95] Song Q, Lange T, Spahr A, Adler G, Bode G. Characteristic distribution pattern of Helicobacter pylori in dental plaque and saliva detected with nested PCR. J Med Microbiol. 2000;49:349–353.

[96] Namiot DB, Leszczyńska K, Namiot Z, Chilewicz M, Bucki R, Kemona A. The occurrence of Helicobacter pylori antigens in dental plaque; an association with oral health status and oral hygiene practices. Adv Med Sci.2010;55:167–171.

[97] Chaudhry S, Khan AA, Butt AK, Idrees M, Izhar M, Iqbal HA. Helicobacter pylori in dental plaque; is it related to brushing frequency, plaque load and oral health status? J Coll Physicians Surg Pak. 2011;21:589–592

[98] 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.

[99] Loster BW, Czesnikiewicz-Guzik M, Bielanski W, Karczewska E, Loster JE, Kalukin J, Guzik TJ, Majewski S, Konturek SJ. Prevalence and characterization of Helicobacter pylori (H. pylori) infection and colonization in dentists. J Physiol Pharmacol. 2009;60 Suppl 8:13–18.

[100] Nguyen AM, el-Zaatari FA, Graham DY. Helicobacter pylori in the oral cavity. A critical review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1995;79:705–709.

[101] Karaca S, Seyhan M, Senol M, Harputluoglu MM, Ozcan A. The effect of gastric Helicobacter pylorieradication on recurrent aphthous stomatitis. Int J Dermatol. 2008;47:615–7.