

ORIGINAL

Antimicrobial resistance of *Helicobacter pylori* isolated from dental plaque specimens

Resistencia antimicrobiana de Helicobacter pylori aislado de muestras de placa dental

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Abstract

Background: *Helicobacter pylori* strains isolated from dental plaque samples may harbor severe antimicrobial resistance. The present research was performed to assess the antimicrobial resistance pattern of *H. pylori* strains isolated from dental plaque samples of individuals referred to dental clinics.

Methods: Forty-two *H. pylori* strains were isolated from dental plaque samples. Isolation was performed using routine instructions in a microaerophilic condition. Isolates were subjected to disk diffusion to assess their antimicrobial resistance.

Results: *H. pylori* strains harbored the uppermost resistance rate toward ampicillin (88.09%), clarithromycin (83.33%), amoxicillin (76.19%), metronidazole (71.42%), and tetracycline (69.04%) antimicrobials. *H. pylori* isolates harbored the lowermost resistance rate toward spiramycin (23.80%), furazolidone (26.19%), and rifampin (28.57%) antimicrobials. All isolates (100%) harbored simultaneous resistance toward at least 3 different antimicrobial agents, while simultaneous prevalence of resistance toward more than 7 antimicrobial agents was 35.71%.

Conclusion: Authorized spiramycin, furazolidone, and rifampin antimicrobial agents prescription can be a suitable choice for oral *H. pylori*.

Keywords: *Helicobacter pylori*, antimicrobial resistance, dental plaque.

Resumen

Antecedentes: Las cepas de *Helicobacter pylori* aisladas de muestras de placa dental pueden albergar una grave resistencia a los antimicrobianos. La presente investigación se realizó para evaluar el patrón de resistencia a los antimicrobianos de las cepas de *H. pylori* aisladas de muestras de placa dental de individuos remitidos a clínicas dentales.

Métodos: Se aislaron 42 cepas de *H. pylori* de muestras de placa dental. El aislamiento se realizó siguiendo las instrucciones de rutina en condiciones de microaerofilia. Los aislados se sometieron a difusión en disco para evaluar su resistencia antimicrobiana.

Resultados: Las cepas de *H. pylori* presentaron la mayor tasa de resistencia a los antimicrobianos ampicilina (88,09%), claritromicina (83,33%), amoxicilina (76,19%), metronidazol (71,42%) y tetraciclina (69,04%). Los aislados de *H. pylori* presentaron la menor tasa de resistencia a los antimicrobianos espiramicina (23,80%), furazolidona (26,19%) y rifampicina (28,57%). Todos los aislados (100%) presentaban resistencia simultánea a al menos 3 agentes antimicrobianos diferentes, mientras que la prevalencia simultánea de resistencia a más de 7 agentes antimicrobianos era del 35,71%.

Conclusiones: La prescripción autorizada de agentes antimicrobianos espiramicina, furazolidona y rifampicina puede ser una opción adecuada para *H. pylori* oral.

Palabras clave: *Helicobacter pylori*, resistencia antimicrobiana, placa dental.

Introduction

Dental plaque is a classic example of host-associated biofilm occurred mainly due to the microbial accumulation with particular load of bacteria. Subgingival and supragingival plaque provide an optimal microaerophilic and aerophilic conditions for the growth and survival of bacteria. About 6 billion microorganisms representing 400 species in the oral cavity¹.

The microbial composition of the dental plaques varies at distinct sites on a tooth (approximal surfaces, fissures, and gingival crevice) and reflects the inherent differences in their anatomy and biology². Previously, *Helicobacter pylori* (*H. pylori*) has been isolated from the dental plaque samples of patients with peptic ulcer diseases and also healthy one³. *H. pylori* is a microaerophilic and Gram-negative spiral coccoid bacterium known as a causative agent for gastric adenocarcinoma, peptic ulcer disease, duodenal ulcer, type B gastritis, and B-cell lymphoma^{5,6}. The area around the dental plaque has a low oxidation potential promoting the growth of facultative anaerobes and even provide microaerophilic conditions⁷. Additionally, these areas contained adequate nutritional components suitable for bacterial growth and survival⁸.

Several antimicrobial choices are available for *H. pylori* infections, particularly in the oral cavity^{9,10}. However, *H. pylori* isolates harbored severe resistance toward commonly used antimicrobial agents, particularly clarithromycin, amoxicillin, metronidazole and ampicillin^{10,11}. Thus, studying the profile and pattern of antibiotic resistance amongst *H. pylori* isolates of dental plaques as novel reservoirs of bacteria seems essential.

According to the high importance of bacteria and the absence of epidemiological surveys in this field, the present research was performed to assess the antimicrobial resistance of *H. pylori* strains isolated from dental plaque specimens collected from individuals referred to Armenian dental clinics.

Materials and methods

Ethics

All personal information of individuals included in the study were kept secret. Written informed consent was taken from all individuals. The study protocol was ethically approved by the University of Traditional Medicine of Armenia.

Bacteria

A total of 42 *H. pylori* strains were included in this survey. Strains were isolated from dental plaque specimens of patients referred to the Armenia dental clinics for routine check-ups. *H. pylori* isolation was performed using the protocol presented previously by Ghorbani et al. (2016)⁵.

Briefly, microaerophilic conditions (5% oxygen, 85% nitrogen, and 10% CO₂) were performed for bacterial growth. All culture media were supplemented with 5% of horse serum (Sigma, St. Louis, MO, USA), vancomycin (10 mg/L), nalidixic acid (30 mg/L), trimethoprim (30 mg/L), and cycloheximide (100 mg/L) (Sigma, St. Louis, MO, USA). Suspected colonies were then identified using Gram stain, motility, colony morphology, and biochemical tests such as urease, oxidase, and catalase tests⁴.

Antimicrobial resistance profile of isolates

Mueller-Hinton agar (Merck, Germany) was applied to assess antibiotic resistance patterns using the simple disk diffusion technique. Antibiotic resistance profile of *H. pylori* bacteria was researched toward different antibiotics against (Oxoid, UK) using the guidelines of previous research¹² and also those of Performance Standards for Antimicrobial Susceptibility Testing-Clinical and Laboratory Standards Institute - NCCLS, 2007¹³. Bacterial suspensions were adjusted to the 0.5 McFarland standard (equivalent to 1–2 × 10⁸ CFU/mL) and were used to inoculate Muller Hinton agar plates (Merck, Germany). The resistance of bacteria was experienced toward levofloxacin (5 µg), ampicillin (10 µg), clarithromycin (2 µg), metronidazole (5 µg), streptomycin (10 µg), amoxicillin (10 µg), cefsulodin (30 µg), tetracycline (30 µg), erythromycin (5 µg), furazolidone (1 µg), trimethoprim (25 µg), rifampin (30 µg), and spiramycin (100 µg) (Oxoid, UK). Positive controls (NCTC 13206 (CCUG 38770) and NCTC 13207 (CCUG 38772)) were accompanied in this experiment. Antibiotic disks were placed on media containing the bacteria, and the plates were incubated under microaerophilic conditions at 35°C for 16–18 h. The zones of growth inhibition produced by each antibiotic were measured and interpreted by standard procedure^{14–18}.

Data analysis

Data were subjected to Microsoft Office Excel (version 15; Microsoft Corp., Redmond, WA, USA). The statistical analysis was performed employing the SPSS 21.0 software (SPSS Inc., Chicago, IL, USA). Chi-square test and Fisher's exact two-tailed test were applied to measure any significant relationship. *P*-value <0.05 was considered as a significant numerical level^{19–26}.

Results

Disk diffusion pattern

Figure 1 shows the patterns of antimicrobial resistance of *H. pylori* isolates of dental plaque samples.

Antimicrobial resistance

Table I shows the disk diffusion antimicrobial pattern of *H. pylori* strains isolated from dental plaque samples. According to obtained data, *H. pylori* strains harbored the uppermost resistance rate toward ampicillin

(88.09%), clarithromycin (83.33%), amoxicillin (76.19%), metronidazole (71.42%), and tetracycline (69.04%) antimicrobials. Reversely, *H. pylori* isolates harbored the lowermost resistance rate toward spiramycin (23.80%), furazolidone (26.19%), and rifampin (28.57%) antimicrobials. Statistically significant differences were obtained for the resistance rates between different antimicrobial agents ($P < 0.05$).

Multidrug resistance pattern

Figure 2 shows the prevalence of multidrug resistance amongst examined *H. pylori* isolates. Data showed that all *H. pylori* isolates (100%) harbored simultaneous resistance toward at least 3 different antimicrobial agents. Results showed that only 35.71% of *H. pylori* isolates harbored simultaneous resistance toward more than 7 antimicrobial agents.

Figure 1: Disk diffusion pattern of isolated *H. pylori* strains of dental plaque samples.

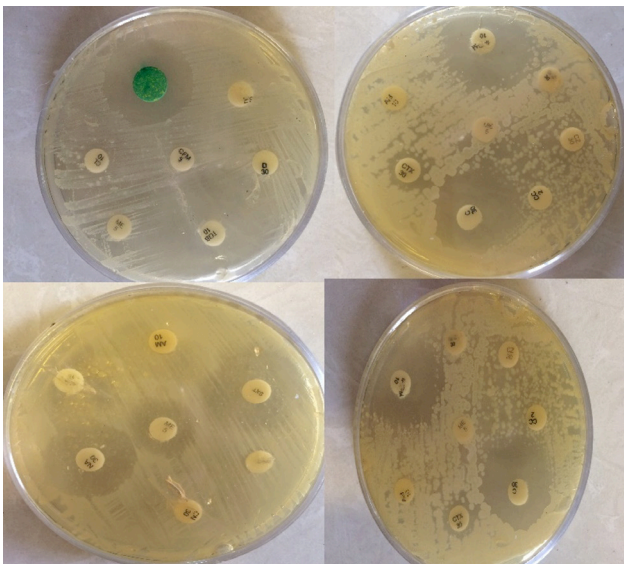


Figure 2: Prevalence of multidrug resistance amongst examined *H. pylori* isolates.

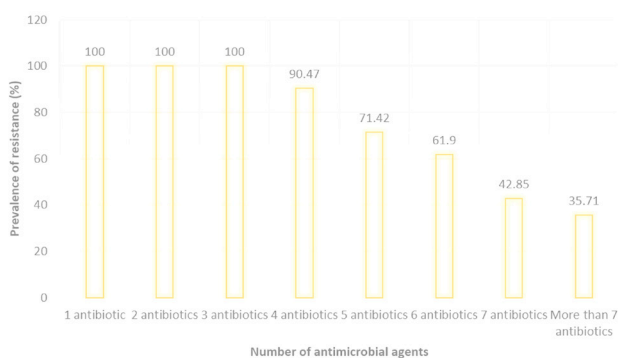


Table I: Disk diffusion antimicrobial pattern of *H. pylori* strains isolated from dental plaque samples.

Types	N. isolates harbored resistance toward each antibiotic disk (%)												
	Specimens (N. positive)	Clr*	Amx	Met	Amp	S10	Frz	Lev	Tet	Rif	Ert	Trp	Spr
Dental plaques (42)	35 (83.33)	32 (76.19)	30 (71.42)	37 (88.09)	25 (59.52)	11 (26.19)	20 (47.61)	29 (69.04)	12 (28.57)	24 (57.14)	23 (54.76)	10 (23.80)	20 (47.61)

*Clr: clarithromycin (2 µg), Amx: amoxicillin (10 µg), Met: metronidazole (5 µg), Amp: ampicillin (10 µg), S10: streptomycin (10 µg), Frz: furazolidone (1 µg), Lev: levofloxacin (5 µg), Tet: tetracycline (30 µg), Rif: rifampin (30 µg), Ert: erythromycin (5 µg), Trp: trimethoprim (25 µg), Spr: spiramycin (100 µg), Cfs: cefsulodin (30 µg).

Discussion

Despite the huge developments occurred in medicine, diverse complicated infectious diseases faced with the human²⁷⁻³². For example, *H. pylori* have become a developed public health issue in the last century³³.

To date, *H. pylori* has been detected in samples of dental plaque, saliva, and dental pulp^{34,35}. Some researches have reported an association between *H. pylori* infection and its presence in the oral cavity. Okuda et al. (2000)³⁶ stated that 22% of *H. pylori*-infected subjects harbored *H. pylori* in their dental plaque. Likewise, Bagot et al. (2011)³⁷ showed that 21% of *H. pylori*-infected subjects possessed the bacterium in their saliva. Therefore, the *H. pylori* presence in the oral cavity appears to be indicative of *H. pylori* infection.

The present investigation revealed that *H. pylori* strains isolated from dental plaque samples harbored the high prevalence of resistance toward commonly used antimicrobial agents, particularly amoxicillin, ampicillin, metronidazole, and clarythromixin. High and illegal antibiotic prescription in veterinary and medicine caused a significant increase in antibiotic resistance. Additionally, excessive use of disinfectants and self-treatment by antibiotics are other reasons. High *H. pylori* resistance toward amoxicillin, ampicillin, metronidazole, and clarythromixin antimicrobials was reported from Russia³⁸, Mexico³⁹, Iran⁴⁰, United States⁴¹, Brazil⁴², Malaysia⁴³, and Greece⁴⁴. Thus, it seems that amoxicillin, ampicillin, metronidazole, and clarythromixin prescriptions are not effective against human *H. pylori*. Reversely, High efficacy of spiramycin, furazolidone, and rifampin antimicrobials against *H. pylori* strains has been reported from Korea⁴⁵, Italy⁴⁶, and Iran⁴⁷.

Some tested strains harbored simultaneous resistance against diverse kinds of antimicrobials. Comprehensive surveys conducted on Taiwan, India, Saudi Arabia, Senegal, China, Thailand, Nigeria, Brazil, Egypt, Colombia, and Argentina presented the high resistance of *H. pylori* toward amoxicillin, ampicillin, tetracycline, trimethoprim, erythromycin, and clarithromycin antibiotic agents⁴⁸, which was similar to our report. Similar reports indicated that the mean prevalence of resistance of *H. pylori* strains toward spiramycin, furazolidone, trimethoprim, levofloxacin, tetracycline, amoxicillin, clarithromycin, erythromycin, and metronidazole antibiotic agents ranged

between 9.00-16.00%, 9.00-29.00%, 34.00-63.00%, 36.00-58.00%, 63.00-90.00%, 72.00-94.00%, 53.00-80.00%, and 27.00-89.00%, respectively^{9, 49-50}.

The present research was limited to the lack of the study of the nutritional resistance pattern of patients without dental plaques and absence of genotypic distribution of antibiotic resistance amongst the *H. pylori* isolates. Lack of demographical characters of the targeted population is another important limitation.

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Conclusion

Considering the low prevalence of resistance of *H. pylori* strains against spiramycin, furazolidone, and rifampin antimicrobial agents, their proper and authorized prescription can diminish the risk of *H. pylori* in dental plaque samples as a reservoir for extra oral infections.

Interests conflict

The researchers declare that they have no conflict of interest.

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