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High level of resistance to metronidazole and clarithromycin among *Helicobacter pylori* clinical isolates in Qazvin province, Iran

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ABSTRACT

The treatment of patients with *Helicobacter pylori* infection has many limitations, especially because of antibiotic resistance. We aimed to investigate the prevalence and mechanism of antibiotic resistance to metronidazole and clarithromycin in *H. pylori* isolates collected from patients with gastrointestinal symptoms in Qazvin, Iran. In this cross-sectional study, antibiotic susceptibility testing to clarithromycin and metronidazole was performed among 80 clinical strains isolated from *H. pylori*-positive dyspeptic patients referred to Qazvin hospital from July 2018 to November 2018. Polymerase chain reaction (PCR) and sequencing tests were performed to determine the type of mutations in the *rdxA* gene in metronidazole-resistant isolates, and the 23SrRNA gene in clarithromycin-resistant isolates. Thirteen (40.6%) and Twenty-one (65.6%) isolates were resistant to clarithromycin and metronidazole, respectively. 37.5% and 59.4% of clarithromycin and metronidazole resistant isolates had MIC>256. In clarithromycin-resistant isolates, mutations in the 23SrRNA gene was seen at A2143G (15.6%), A2142G (9.4%), C2195T (6.3%), C2244T (3.1%), and G2212A (3.1%) locations. In one isolate, three simultaneous mutations were recorded in locations A2143G, G2110A, and C2121T. Mutations in the *rdxA* gene in metronidazole-resistant isolates, were missense. High resistance to metronidazole and clarithromycin antibiotics were seen in *H. pylori* isolates in Qazvin province. This is the first report of new mutation sites G2212A, G2110A, and C2121T on the 23SrRNA gene in clarithromycin-resistant isolates. It is necessary to evaluate the current situation in terms of resistance and identify the mechanisms involved in its occurrence for the successful treatment of infections caused by this organism.

1. Introduction

Helicobacter pylori (*H. pylori*) is a curved, Gram-negative bacillus that is motile and causes important gastrointestinal diseases such as peptic ulcer, mucosa-associated lymphoid tissue (MALT) lymphoma, gastric cancer, and some systemic diseases, while more than 50% of the world's population is infected with this organism (Ansari and Yamaoka, 2018; Kageyama et al., 2019; Rasheed et al., 2014). Eradication of *H. pylori* infection is an effective strategy in the treatment of gastric ulcers and MALT lymphoma (Chey et al., 2017). The three-drug treatment consists of proton pump inhibitors (PPIs) regimen with two antibiotics (metronidazole and amoxicillin or clarithromycin), and is considered as the first-line treatment for *H. pylori* infection (Thung et al., 2016; Chey et al., 2017). But with increasing drug resistance, it seems that it can be replaced by quadruple and sequential treatment methods (Zhang et al., 2020). Despite the specific treatment pattern of *H. pylori*, its success rate in the world has reached less than 80%, and in 2017, the World Health Organization (WHO) included this organism in the list of drug-resistant bacteria (Savoldi et al., 2018; Arslan et al., 2017). Drug resistance is the most important mechanism involved in the unsuccessful treatment of

Abbreviations: PCR, polymerase chain reaction; *H. pylori*, *Helicobacter pylori*; MIC, minimal inhibitory concentration; MALT, mucosa-associated lymphoid tissue; S, sensitive; R, resistant.

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