T2182C Mutation in 23S rRNA Is Associated with Clarithromycin Resistance in Helicobacter pylori Isolates Obtained in Bangladesh

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Twelve clarithromycin-resistant (MIC, ≥1 µg/ml) Helicobacter pylori isolates were analyzed for point mutations in the 23S rRNA gene. Sequence analysis of all of the resistant isolates revealed a T-to-C transition mutation at position 2182. Transformation experiments confirmed that a single T-to-C transition mutation at position 2182 is associated with clarithromycin resistance.

Eradication of Helicobacter pylori infection by treatment with two antimicrobials (clarithromycin and amoxicillin or metronidazole) and a proton pump inhibitor is recommended by various consensus groups (5, 13). The prevalence of antimicrobial susceptibility of H. pylori varies with geographical regions, and clarithromycin resistance is the major cause of treatment failure (3, 5, 20). Alteration in either one or both copies of the H. pylori 23S rRNA gene is associated with resistance to clarithromycin, and the mechanism is a point mutation (an adenine-to-guanine transition at position 2142 or 2143) or an adenine-to-cytosine transversion at position 2142 (2, 8, 15, 18, 19, 23). However, a T2182C mutation has been proposed to be associated with clarithromycin resistance (2, 8, 15, 18, 19, 23). This mutation at position 2182 is associated with clarithromycin resistance.

The MIC for 25% (3 of 12) of the Cla− isolates was 1 µg/ml, and the mechanism is a point mutation (an adenine-to-guanine transition at position 2182). Transformation experiments confirmed that a single T-to-C transition mutation at position 2182 is associated with clarithromycin resistance.

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for 33.3% (4 of 12) it was 2 g/ml, and for 41.7% (5 of 12) it was 4 g/ml (Table 1) (7, 16). The nucleotide sequences of all CRHP and CSHP isolates and transformants were compared with known sequences of the 23S rRNA (GenBank accession numbers U27270, AE000641, and AE001553). None of the CRHP or CSHP isolates had the expected mutation at positions 2142 and 2143 (4, 6, 24). Rather, all of our CRHP isolates and Clar transformant DM26B R had a single mutation, the T-to-C transition at position 2182 (Fig. 1 and Table 1). However, one to three or no base substitutions at positions 1821, 1826, and 1830 were also observed in some isolates compared to the \textit{H. pylori} 23S rRNA sequence (GenBank accession number U27270), as shown in Table 1. The MIC for the transformants was equal to that for donor CRHP strain Gj50.

Early studies have demonstrated that clarithromycin resistance is attributed to point mutations mainly at positions 2142 and 2143 (cognate \textit{Escherichia coli} positions, 2058 and 2059) within the peptidyltransferase-encoding region in domain V of the 23S rRNA, and these mutations confer resistance by altering the macrolide binding target (19, 23). The prevalence of mutations among the CRHP strains varies in different parts of the world (1, 9, 10, 17, 22, 23). In our study, all 12 of the Clar strains, for which the MICs ranged from 1 to 4 g/ml, showed no mutation at position 2142 or 2143; however, a mutation similar to that in the present study has been identified in a study by Kim et al. in which 33.3% of the isolates with high levels of clarithromycin resistance (MIC range, 16 to 64 g/ml) had the T2182C mutation (10). Recently, it was reported that a T-to-C mutation at position 2142 or 2143 was absent in all of the CRHP isolates, (iii) the resistance phenotype can be transformed by natural transformation of resistance determinants to CSHP isolates, and (iv) the clarithromycin MIC was the same for the transformants and isolates with the resistance phenotype, and they had the same T2182C mutation. Further studies are essential to understand the molecular mechanism of macrolide-resistant \textit{H. pylori}.

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**REFERENCES**


