

# Primary and secondary resistance of *Helicobacter pylori* in Slovenia, 2011-2014

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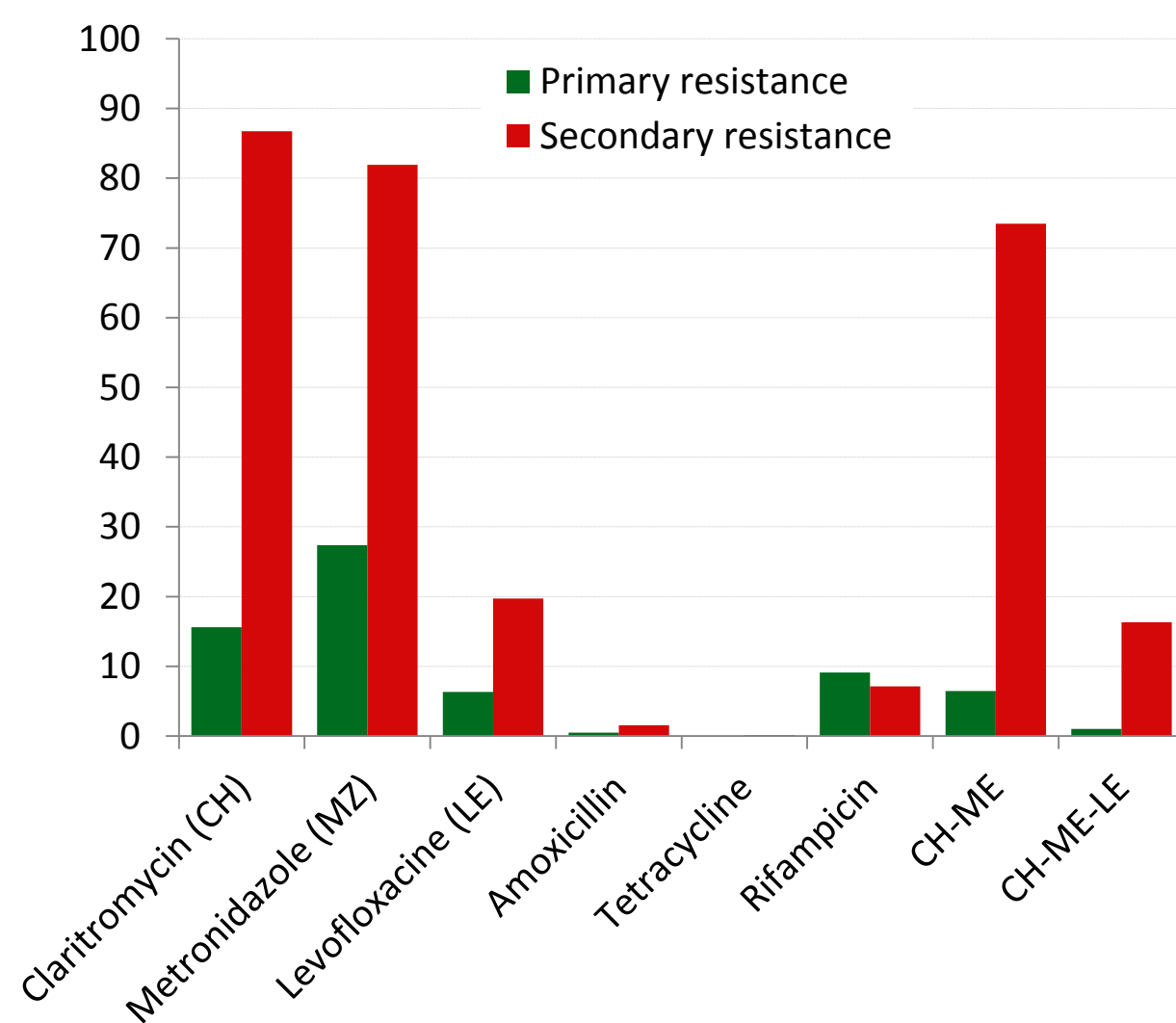
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## OBJECTIVE

Infection with *Helicobacter pylori* is a major public health concern. It is acquired during childhood, persists throughout lifetime and causes chronic active gastritis, which may progress to peptic ulcer, gastric cancer or MALT lymphoma. Schematic (i.e. empiric) antimicrobial therapy is a main strategy for eradication of infection. However, treatment failures are common and may reach >30%, depending on a clinical setting. Antimicrobial susceptibility surveillance of *H. pylori* is crucial for generating treatment recommendations on a local level. Herein, we present primary resistance (treatment naïve patients) and secondary resistance (after treatment failure) of *H. pylori* in Slovenia in the period 2011-2014.

**Figure 1:** Primary and secondary resistance of *H. pylori* in Slovenia (2011-2014).



## METHODS

Consecutive gastric biopsy samples from treatment naïve patients and from patients after eradication failure were analysed for basic demographic, clinical and susceptibility data. Biopsies were collected and transported in Portagerm pylori (bioMerieux) transport medium. After homogenisation in 1 ml of PBS, 0.1 ml aliquots were inoculated for gram stain and culture while approximately 0.5 ml of homogenate was frozen at -80°C. Phenotypic antimicrobial susceptibility was performed with Etests (bioMerieux) and MIC Test Strips (Liofilchem) and results were interpreted using EUCAST V4.0 clinical breakpoints. Salvage molecular susceptibility testing (i.e. in case of negative culture) was performed from frozen biopsies using GenoType HelicoDR (Hein Lifescience).

## RESULTS

A total of 1842 gastric biopsies from 1765 patients aged 3-86 (mean age: 47 years) were analysed. 79.5% (n=1464) of biopsies were positive: 73.9% (n=1362) with culture and 5.5% (n=102) with molecular test. Information about previous eradication treatment was available for 92.8% (n=1358) of positive samples: 31.7% (n=430) were from treatment naïve patients and 68.3% (n=928) were from treatment failures. Primary resistance rates for clarithromycin, metronidazole, levofloxacin, amoxicillin, tetracycline and rifampicin were 15.6%, 27.4%, 6.3%, 0.5%, 0.0%, and 9.1%, respectively. Secondary resistance rates were 86.7%, 81.9%, 19.7%, 1.5%, 0.1% and 7.1%, respectively. Dual resistance (clarithromycin / metronidazole) and triple resistance (clarithromycin / metronidazole / levofloxacin) were detected in 6.5% (n=26) and 1.0% (n=4) among primary isolates; and 73.5% (n=621) and 16.3% (n=138) among secondary isolates, respectively.

## CONCLUSION

Primary resistance of *H. pylori* to antimicrobial agents commonly used for eradication therapy in Slovenia was high. More worryingly, secondary resistance after one or multiple treatment failures was extremely high, with 73.5% of isolates possessing dual resistance to both clarithromycin and metronidazole, and 16.3% also to levofloxacin. Current strategy of schematic eradication treatment and delayed susceptibility testing (i.e. after several treatment failures) effectively produces difficult to treat *H. pylori* infections. Susceptibility testing after several unsuccessful eradication treatments produces predictable results. Culture or molecular based antimicrobial susceptibility testing early in the treatment of *H. pylori* infection (i.e. before or at maximum after first treatment failure) could be warranted in Slovenia.

**Table 1:** Prevalence of antibiotic resistance among *H. pylori* isolates in Slovenia in the period 2011-2014.

Agent	PRIMARY RESISTANCE			
	No. of strains	No. resistant	% resistant	
Clarithromycin	430	67	15.6	
Metronidazole	402	110	27.4	
Levofloxacin	429	27	6.3	
Amoxicillin	403	2	0.5	
Tetracycline	408	0	0.0	
Rifampicin	329	30	9.1	
Agent	SECONDARY RESISTANCE			
	Clarithromycin	928	805	86.8
	Metronidazole	845	692	81.9
	Levofloxacin	923	192	19.7
	Amoxicillin	846	13	1.5
	Tetracycline	845	1	0.1
Rifampicin	732	52	7.1	