中文題目: 胃幽門螺旋桿菌抗藥性改變的趨勢 (2013-2019 年): 台灣多中心的報告

英文題目: Trend in changes of antibiotic Resistances for Helicobacter Pylori (2013-2019):

### A multicenter report from Taiwan

作 者:葛振瑜<sup>1</sup>,梁志明<sup>1</sup>,戴維震<sup>1</sup>,許秉毅<sup>2</sup>,吳登強<sup>3</sup>,陳冠仰<sup>4</sup>,蔡成枝<sup>1</sup> 服務單位:<sup>1</sup>高雄長庚紀念醫院 胃腸肝膽系,<sup>2</sup>台南安南醫院 消化內科,<sup>3</sup>高雄醫學大學附設 中和紀念醫院 胃腸內科,<sup>4</sup>台北市立聯合醫院 消化內科

# Background:

The prevalence of antibiotic resistance of *Helicobacter pylori (H. pylori)* varies among countries and may be partly determined by geographical factors. The use of first-line *H. pylori* eradication with standard triple therapy, which consists of a proton pump inhibitor (PPI), clarithromycin and amoxicillin, might lead to a poor outcome (< 80%) due to increase of clarithromycin resistance. However, the eradications rates had been increased to > 90 % by the use of various effect treatment regimens such as high dose dual therapy, hybrid and reverse hybrid therapy, bismuth and non-bismuth quadruple therapies. Clearly, antibiotic resistance determines the success of eradication. This study aimed to determine the trend in the primary, secondary and tertiary antibiotic resistances of *H. pylori* in Taiwan.

# Method:

We analyzed *H. pylori* -infected isolates from patients before first-line eradication therapy (n = 1369), second line eradication therapy (n =196), and third line eradication therapy (n = 184) from January 2013 to December 2019. The *H. pylori* strains were tested for susceptibility to amoxicillin, clarithromycin, levofloxacin, metronidazole and tetracycline using the E-test method. The minimal inhibitory concentration (MIC) was determined by the agar dilution test. MIC values of  $\ge 0.5$ ,  $\ge 1$ ,  $\ge 1$ ,  $\ge 4$  and  $\ge 8$  mg/L were considered to be the resistance breakpoints for amoxicillin, clarithromycin, levofloxacin, tetracycline and metronidazole, respectively.

#### Results:

A progressively higher primary resistance rate was observed for clarithromycin (11.8%-20.4%, p = 0.039 in  $\chi$ 2 test for linear trend), levofloxacin (17.3%-38.8%, *p*< 0.001) and metronidazole (25.6%-42.3%, *p*< 0.001) among patients who receiving first-line eradication therapy. The similar upward resistance trends were found for secondary resistance for levofloxacin (30.5%-64.7%, p = 0.006) and (40.5%-77.4%, p < 0.001), and tertiary resistance for metronidazole and tertiary

resistance for metronidazole (44.4%-88.2%, p = 0.014). The tertiary resistance for levofloxacin increase from 65.9% in year 2013 to 100.0% in year 2019(p = 0.106). The resistance to amoxicillin and tetracycline remained very low in Taiwan. (Amoxicillin: 0.6%-1% for primary resistance, p=0.800; 0% for secondary resistance; 0-5.6% for tertiary resistance, p=0.236; Tetracycline: 0% for primary resistance, p=0.178; 4.3%-7.1% for secondary resistance, p=0.459; 0%-7.7% for tertiary resistance, p=0.087)

#### **Conclusions:**

Primary, secondary and tertiary antibiotics resistance of clarithromycin, levofloxacin and metronidazole for *H pylori* has been increasing in the past 7 years in Taiwan. High clarithromycin resistance (>20%) indicated that more effective treatment options such as high dose dual therapy, hybrid and reverse hybrid therapy, bismuth and non-bismuth quadruple therapies should be prescribed as a first-line *H. pylori* eradication therapy in Taiwan. Levofloxacin-based triple therapy should also be replaced for second line therapy. Third line treatment should be antibiotic susceptibility based.