# CHALLENGES IN SELECTING ANTIBIOTICS TREATMENT FOR *H. PYLORI* IN VIETNAM

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***Key words***: *H. pylori*, clarithromycin resistance

## BACKGROUND

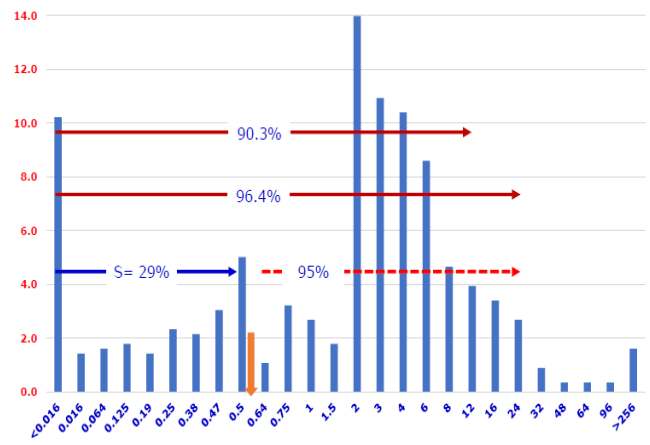
Antibiotics recommended in the eradication therapy for *H. pylori* include: Amoxicillin, Metronidazole, Clarithromycin, Levofloxacin, Tetracycline. However, in Vietnam, these antibiotics have been reported resistant by *H. pylori*, particularly Metronidazole, Clarithromycin and Levofloxacin. Therefore in Vietnam, the antibiotic resistance of *H. pylori* is a major challenge in the use and development of therapeutic regimens for *H. pylori* eradication.

## AIMS

Analyze the results of microbiological and molecular biology tests for *H. pylori* insolates in more than two years from 2015 to 2017 to make the following observations: (1) Percentage of *H. pylori* with virulence via the detection of cagA and vacA genes; (2) Resistance of the *H. pylori* isolates to 5 antibiotics including Amoxicillin, Metronidazole, Clarithromycin, Levofloxacin, Tetracycline; (3) levels of clarithromycin by analyzing the MIC results of this antibiotics on the *H. pylori* isolates; (4) and finally determine the CYP2C19 genotype of the patients to help doctors maximize their antibiotic treatment efficacy by selecting PPIs and appropriate PPI doses.

## MATERIALS – METHODS

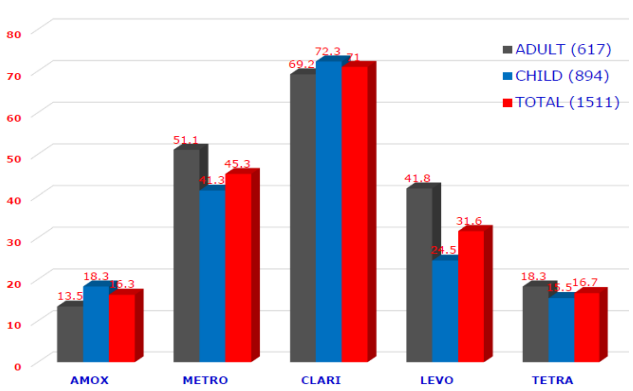
Samples are gastro-duodenal ulcers biopsy obtained through endoscopy. *H. pylori* was isolated on agar plate supplemented with 10% horse blood and with antibiotic and incubate micro-aerobic at 37 ° C for 4 days. Antibiotics susceptibility testing of Amoxicillin, Tetracycline, Metronidazole, Clarithromycin and Levofloxacin were obtained by culture of *H. pylori* isolates on the media plate with and without antibiotic at breakpoint concentrations. For Clarithromycin, the Etest were also used to determine MIC. Real-time PCR techniques were also performed directly on the samples to detect the *cag*A gene and the *vac*A gene of *H. pylori* and to identify the patient's CYP2C19 genotype.



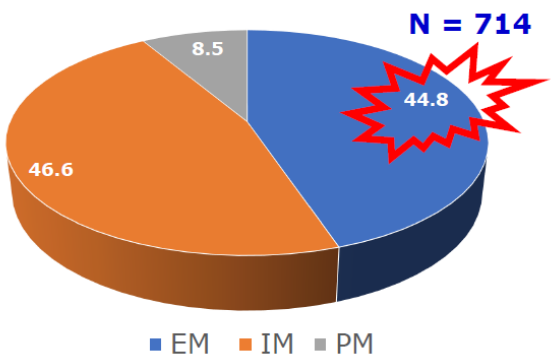

*Graph 2*: The distribution of clarithromycin MIC to H. pylori said that 95% of the resistance strains have MIC of clarithromycin lower than 24µg/ml

## RESULTS - DISCUSSIONS

In 2016 there were 1511 cases of *H. pylori* were isolated in which 894 were from children and 617 were from adults. In terms of antimicrobial resistance, the results showed 71% of the isolates resistant to clarithromycin, 45% metronidazole resistance, 32% levofloxacin resistance, 16% tetracycline resistance, and 17% amoxicillin resistance. The results also showed that $MIC_{90}$ of clarithromycin was 12µg/ml and thus, in terms of pharmacokinetics and pharmacokinetics of the gastric clarithromycin (rapid dissipation in the first 30 minutes in the stomach), *H. pylori* was still sensitive to this kind clarithromycin. Analysis of the distribution the clarithromycin MIC, 96.4% *H. pylori* had the MIC of 24µg/ml or less and clarithromycin was able to reach this concentration. The *H. pylori* multi-drug resistance analysis revealed 1% the isolates resistant to all antibiotics, 3% resistant to four antibiotics, 18% resistant to three antibiotics, 41% resistant to two antibiotics. 26% were resistant to 1 antibiotic, and 11% were completely antibiotic-susceptible. Analysis of the virulent genotype of the *H. pylori* isolates resulted 77% of *H. pylori* isolates from adults or children carrying the cagA gene. In *H. pylori* existing cagA gene, vacA gene in isolates from adults and children was 60.4% and 69.4% s1m1, 39.3% and 30% s1m2, 0.3% and 0.1% s2m1, 0% and 0.4% s2m2. Analysis of the CYP2C19 genotype, results showed that 44.8% were extentive metabolism, 46.6% were moderate metabolism, 8.5% were poor metabolism.




*Graph 1*: The resistance ratio of *H. pylori* to AMOX (amoxicillin), METRO (metronidazole), CLAR (clarithromycin), LEVO (levofloxacin) and TETRA (tetracycline)




*Graph 3*: The CYP2C19 genotype of 714 patients infected by H. pylori showed that 44.8% of patients were EM (extensive metabolizer) for PPI

## CONCLUSION

This is a comprehensive study in Vietnam on microbiology and molecular biology on a large number of *H. pylori* isolated from gastro-duodenal ulcer biopsies. The most notable result of this study is that *H. pylori* in Vietnam has a relatively high resistance to antibiotics, especially clarithromycin and metronidazole. However, the level of clarithromycin resistance is not high because the clarithromycin MICs to *H. pylori* are still lower than the clarithromycin concentration achieved in the stomach if clarithromycin is used for the treatment is the gastric clarithromycin, not pulmonary clarithromycin.

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