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Letter

Helicobacter pylori cagE is not associated with clinical outcomes in the Kurdistan region of Iraq

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Dear Editor,

We have read with interest the article entitled "cagE as a biomarker of the pathogenicity of *Helicobacter pylori*" by Ramis et al.[1]. In this study, with a sample size of 57, the authors suggested that *cagE* is an important prognostic indicator for developing lesions during *Helicobacter pylori* infection. This suggestion was based on the fact that a statistically significant association was found between *cagE* and gastric erosion, but not between *cagA* and gastric erosion.

With reference to this study, we conducted a study in the Kurdistan region of Iraq to examine relationships between *H. pylori* virulence factors and clinical outcomes. Antral Biopsies were collected from 105 patients visiting the Endoscopy Department at the Azadi Teaching Hospital for diagnostic upper gastric endoscopy. Deoxyribonucleic acid (DNA) was extracted directly from the biopsy samples, and the presence of *H. pylori* was confirmed by polymerase chain reaction (PCR) amplification of the *ureA* gene. We amplified the *cagA*, *cagE*, *vacAs1/m1*, *vacA*, *iceA1*, *iceA2,* and *babA2* genes and found a statistically significant association between *cagA* and gastric and duodenal ulcerations ($p = 0.005$), but no statistically significant association between *cagE* and gastric and duodenal ulcerations ($p = 0.659$). In addition, no association was found between other genes and clinical outcomes.

cagA is a part of a 40-kb DNA insertion cassette designated as the *cag* pathogenicity island (*cag*PAI), which may have a non-*Helicobacter* origin. The *cag*PAI contains 31 putative genes, 6 of which are thought to encode components of a bacterial type IV secretion system. *cagE*, is a homolog of the *virB4* gene from *Agrobacterium tumefaciens*[2] and also is a part of the *cag*PAI region of *Helicobacter pylori* genome . The presence of *cagE* is essential for the formation of type IV secretion system.

Recent studies have indicated that the cagA protein is directly injected into epithelial cells via the type IV secretion system, where it undergoes tyrosine phosphorylation in host cells[3]. The presence of *cagA* has been considered as an important predictor for the severity of the pathogenicity of *H. pylori*, on the other hand the role of *cagE* as a marker of the disease is still to be contemplated, as shown by the data from our study. The contradiction in the results of our study and that of Ramis et al. may be due to differences in the respective study designs and sample sizes. Therefore, a large cross-sectional study involving multi-centers with different populations should be designed to study the association between virulence factors and clinical outcomes. In addition, such a contradiction should not discourage small, national, cross-sectional association studies, because such studies may help suggest new determinants as virulence factors specific for *H. pylori* infections. In addition to the presence of *cagA* and *cagE*, empty-site PCR is also suggested to confirm the presence of *cag*PAI. Finally, we believe that none of the *H. pylori* virulence factors should be considered as predictors for *H. pylori*-related pathogenesis without studying other effects e.g. the host polymorphisms in genes responsible for inflammation and protection against oxidative stress, also genes involved in metabolism of drugs used in eradication of *H. pylori*, and environmental factors[4].

CONFLICT OF INTEREST

The author declare that there is no conflict of interest.

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