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Helicobacter pylori vacA as Marker for Gastric Cancer and Gastroduodenal Diseases: One but Not the Only Factor

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We read with interest the recent article by Memon et al. (1). In this study involving the Belgian population, the *Helicobacter pylori* vacuolating cytotoxin (*vacA*) genotype was shown to be a strong marker for gastric cancer and duodenal ulcer disease. The finding that certain *H. pylori vacA*-positive strains are associated with key clinical outcomes is important, but available data are unfortunately contradictory.

Closer to Europe, a study from Sweden did not show any significant association between 146 *vacA* isolates with gastroduodenal diseases (2). Yamaoka et al. studied *H. pylori* isolates from four different countries (107 strains from Bogota, Colombia; 70 strains from Houston, TX; 135 strains from Seoul, South Korea; and 112 strains from Kyoto, Japan) but likewise did not find any significant association between *vacA* status and clinical outcomes (3).

Our unpublished recent data from the Iranian population in Tehran did not observe any significant association between gastric cancer and the presence of *vac-s1* (odds ratio, 0.61; 95% confidence interval [CI], 0.51 to 3.14), *vac-m1* (odds ratio, 0.55; 95% CI, 0.22 to 5.5), and *vacA-i* (odds ratio, 0.22; 95% CI, 0.16 to 2.25) in 55 isolates. However, a significant association was seen between duodenal ulcer disease and *vacA* (odds ratio, 1.70; 95% CI, 1.18 to 5.74) in 64 isolates. Previous published data from another group in Tehran, Iran, also did not find an association between *vacA* and gastric cancer or peptic ulcer disease (4).

The above observations suggest that geography and ethnicity are important factors that account for the observed variations in the distribution of certain virulent *H. pylori* strains (5, 6). The study by Memon et al. did not specify the ethnic and geographic distributions of the Belgian population, and this information may potentially have an impact on the clinical outcomes studied. The results could also be affected by the small number of cases of gastric cancer. Furthermore, patients with nonulcer dyspepsia in that study were not controlled for environmental and lifestyle factors that are frequently associated with gastric cancer, including smoking, high salt intake, and obesity (7). In determining clinical outcomes, besides *cagA* and *vacA*, there are a few other genotypes, including *oipA* and *dupA*, whose significance and interactions are still unclear (8, 9).

To conclude, the contradictory data suggest that the causes of gastric cancer and gastroduodenal diseases are multifactorial in nature and that they are not due to certain *H. pylori* strains; however, at-risk populations may be more susceptible to specific genotypes, although verification of this requires more compelling population-based studies.

ACKNOWLEDGMENT

We have no conflicts of interest to declare.

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Editor: G. V. Doern

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For the author reply, see doi:10.1128/JCM.02667-14.

doi:10.1128/JCM.02640-14