LETTER to the EDITOR

Helicobacter Pylori vacA d1 Genotype is associated with Gastric Cancer but not Peptic Ulcers in Kurdistan Region, Northern Iraq

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Dear Editor

We read with interest the paper by Basiri and colleagues studying the prevalence of vacA d1 and d2 genotypes in the *H pylori* isolates from patients with gastric adenocarcinoma, peptic ulcer disease and gastritis in East Azerbaijan region, where the incidence of gastric cancer (GC) is high. They found that 43.4% of the isolate carried the d1 allele and 56.6% carried subtype d2. A significant correlation between vacA d1 and gastric adenocarcinoma or PUD was shown. The study suggested that the *H pylori* vacA d1 genotype helps predict risk for gastric adenocarcinoma and PUD in East Azerbaijan, Iran (Basiri et al., 2014).

Despite the geographical proximity of Iraq and Iran the incidence of gastric cancer differs hugely between these countries; in Iran it ranges from 38-69/10^5 compared to 5/10^5 in Iraq (GLOBOCAN, 2002; Sadjadi et al., 2005; Yavari et al., 2006). Previous studies of *H. pylori* virulence factors were not successful in the explanation of such a difference in cancer rate. We hypothesised that *H pylori* vacA d1 may help understanding this variation in cancer rate in these two neighbouring countries. DNA was extracted from 157 *H. pylori* strains isolated from patients with different clinical outcome (non-ulcer disease (NUD): 81; gastric ulcer (GU): 31; duodenal ulcer (DU):38 and gastric cancer:5). Using the same methodology mentioned in the Basiri et al paper, we typed these strains for vacA d subtypes. Overall, (45/157) 28.6% of our samples typed as vacA d1 and (112/157) 71.4% as vacA d2. It was found that (21/81) 26% of the strains isolated from NUD typed as vacA d1. In addition, vacAd1 genotype was found in (9/38) 23.6% and (10/31) 30.3% of DU and GU samples, respectively. Interestingly, all the isolates obtained from GC patients were vacAd1. No association was found between vacA d genotypes and DU and GU (Chi square test; $p>0.05$). However, a statistical significant relationship was found between vacA d1 and gastric cancer (Exact Fischer test; $p=0.002$).

H. pylori strains possessing cagA are associated with a significantly increased risk for the development of atrophic gastritis, peptic ulcer disease (PUD) and gastric cancer (Atherton, 2006). Previous study comparing *H. pylori* strains from these two countries showed that no difference in prevalence of cagA+ strains between unselected dyspeptic populations from these countries (Hussein et al., 2008). The vacuolating cytotoxin (VacA) is a well-established *H. pylori* virulence factor which has multiple effects including vacuolation of cultured epithelial cells, inducing apoptosis, increasing permability of epithelial monolayers, forming pores in cells and suppressing immune cell function (Atherton, 2006). The vacA gene is polymorphic within its signal, intermediate and mid regions. Also, no significant differences between Iranian and Iraqi populations in other vacA genotypes was found, and in particular in the i region type which has recently been linked with gastric cancer risk in Iran (Rhead et al., 2007). Recently, a fourth disease-related region between the i and m regions has been indentified and named the deletion (d) region. The d region is divided into d1 and d2 with d1 identified a risk factor for GC and PUD in Western strains. Nearly all *H pylori* isolates from East Asia have been found to have a genotype of vacA d1 (Ogiwara et al., 2009). Our results showed that the overall prevalence of vacA d1 genotype is lower than that found in Iran this could contribute to the differences in gastric cancer rates seen between these communities.

In agreement with findings from Basiri et al's paper and results from Western countries, this study showed a significant relationship between vacA d1 and gasric cancer. This study therefore supports the proposal of Basiri et al's conclusion that the *H pylori* vacA d1 genotype might be a new risk marker for gastric cancer and peptic ulcer.

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