dupA$_1$ Is Associated with Duodenal Ulcer and High Interleukin-8 Secretion from the Gastric Mucosa

We read with interest the recent article by Jung et al. addressing the relationship of the *dupA* gene cluster with clinical outcomes and gastric mucosal interleukin 8 (IL-8) secretion (4). It was found that *Helicobacter pylori* infection with strains possessing a complete *dupA* cluster increased duodenal ulcer risk compared to that with *H. pylori* infection with strains with an incomplete *dupA* cluster or without the *dupA* gene. Findings were independent of the *cag* pathogenicity island (PAI) status. It was also found that gastric mucosal IL-8 levels were significantly higher in the complete *dupA* cluster group than in the incomplete *dupA* cluster group or the group without the *dupA* gene (4).

Using the same methodology described in Jung et al., we studied the relationship between *dupA* cluster genes, clinical outcomes, and gastric mucosal IL-8 levels in 68 (22 duodenal ulcer [DU], 5 gastric ulcer [GU], 41 nonulcer dyspepsia [NUD]) Iraqi samples. The prevalence of *dupA* was 48.4% (33/68), and those of other *vir* gene homologues were 76.5% for *virB8* (52/68), 57.4% for *virB9* (39/68), 67.6% for *virB10* (46/68), 77.9% for *virB11* (53/68), 52.9% for *virD4* (36/68), and 73.5% for *virD2* (50/68) (Table 1). In contrast with Jung et al.'s report, none of the *H. pylori* strains possessed all 6 *vir* gene homologues. We did not observe associations between the presence of the *dupA* gene and clinical outcomes; this result is consistent with results from other countries, such as Brazil and Iran (1, 3). As *dupA* was previously classified into *dupA*$_1$ (functional) and *dupA*$_2$ (nonfunctional, including the original form described in which the open reading frame was broken by a stop codon) (2), we sequenced *dupA* genes from a collection of *H. pylori* strains isolated in Iraq as described previously (2). A total of 33% (11/33; 8 DU, 0 GU, 3 NUD) of *dupA*-positive Iraqi strains typed as *dupA*$_1$. A significant association was observed between *dupA*$_1$ and DU ($P < 0.01$). This result may indicate that *dupA*$_1$ is important in DU development. Therefore, *dupA* polymorphisms may explain the contradictory association between *dupA* and clinical outcomes, and this may be more important than an intact *dupA* gene cluster.

TABLE 1 The prevalence of *dupA* and *vir* genes in 68 Iraqi strains[a]

Gene	No. of strains (%) in each group containing the indicated gene			
	All	DU	GU	NUD
virB8	52 (76.5)	19 (86.4)	5 (100.0)	28 (68.3)
virB9	39 (57.4)	13 (59.1)	3 (60.0)	23 (56.1)
virB10	46 (67.6)	15 (68.2)	1 (20.0)	30 (73.2)
virB11	53 (77.9)	15 (68.2)	5 (100.0)	33 (80.5)
virD4	36 (52.9)	14 (63.6)	2 (40.0)	20 (48.8)
virD2	50 (73.5)	13 (59.1)	1 (20.0)	36 (87.8)
dupA	33 (48.5)	12 (54.5)	2 (40.0)	19 (46.3)

[a] The 68 strains were composed of 22 DU, 5 GU, and 41 NUD.

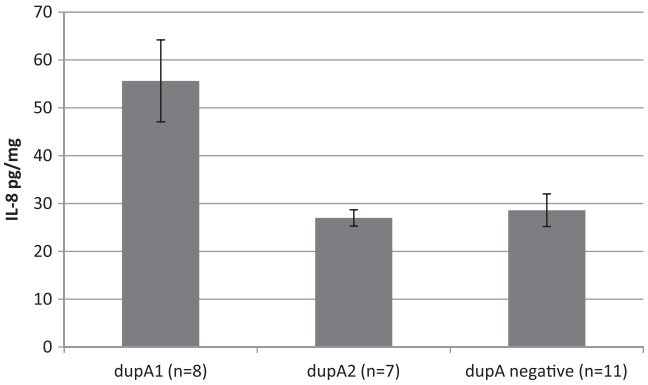

FIG 1 IL-8 secretion from the gastric mucosas of patients infected with *H. pylori*. Error bars indicate the standard deviation. Gastric mucosal IL-8 levels were significantly higher in patients carrying *dupA*$_1$ than in other groups.

Additionally, we studied gastric mucosal levels of IL-8. We classified our patients into 3 groups according to *dupA* status: patients carrying *dupA*$_1$ strains, those with *dupA*$_2$ strains, and those with *dupA*-negative strains. Gastric mucosal IL-8 levels were significantly higher in patients carrying *dupA*$_1$ strains than in the other groups (*dupA*$_1$, 55.6 ± 8.6 pg/mg; *dupA*$_2$, 27 ± 1.7 pg/mg; *dupA* negative, 28.6 ± 3.4 pg/mg; $P < 0.05$) (Fig. 1). These findings suggest that *dupA*$_1$ is important in IL-8 production in the gastric mucosa.

In conclusion, classification of *dupA* into *dupA*$_1$ (functional) and *dupA*$_2$ (nonfunctional), rather than either *dupA* status or the presence of an intact *dupA* gene cluster, correlates with clinical outcome and gastric IL-8 levels in Iraqi *H. pylori* infection. Further research is needed to investigate the role of *dupA* in *H. pylori*-associated disease development.

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