TITLE: *cagE* AND *virB11 Helicobacter pylori cag*Pai GENES AS POTENTIAL MARKER FOR SEVERE GASTRIC DISEASE DEVELOPMENT

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ABSTRATC:
Helicobacter pylori infection is a major risk factor for several gastric disorders, such as gastritis, peptic ulceration, and gastric cancer (GC). The outcome is dependent on the bacterial genotype, mainly *vac*A *s1m1* allele and *cag*A, however, just *cag*A cannot explain all the gastric cancers cases and others genes must be involved. The identification of bacterial genotypes associated to the more severe gastric diseases could be a promissory strategy for GC control. Therefore, the aim of this study was to identify *H. pylori* genes in gastric lesions of the different gravity and GC in patients from Ceará and Pará States, Brazil. For that, 354 biopsies from dyspeptic patients histopathologically classified in inactive chronic gastritis (ICG), active chronic gastritis (ACG), and intestinal metaplasia (IM) and also, 150 cases of intestinal gastric cancers obtained from gastrectomy patients were included in this study. *H. pylori* (*ure*C and *vac*A alleles) and *cag*Pai genes (*cag*A, *cag*E and, *vir*B11) were determined by PCR using specific primers previously described. EPI INFO 7.0. and Classification and Regression Trees (CART) were used in statistical analysis. Females were more frequent (62.4%) in dyspeptic disease with a median age of 54 years old, whereas males (70%) with a median age of 65 years old in GC. *H. pylori* was detected in 68.6% ICG, 77% IM, 90.4% AGC and, 90.6% GC. All virulence genes investigated were significantly more frequent in ACG, IM, and GC than ICG, the less inflammatory lesion. Analysis with *cag*Pai genes showed that *H. pylori* strains *cag*E and *vir*B11 positives were statically associated with GC group when compared to AGC (*cag*E p= 0.005; *vir*B11 p= 0.02) and IM (*cag*E p= 0.03; *vir*B11 p= 0.01), and no differences were found for the *cag*A gene. Although, associated genes analysis showed *cag*A and *vir*B11 more frequently in GC than IM (p= 0.03). From CART analysis, *cag*E and *vir*B11 genes highlight as the more important factors for GC development. In this study, the *H. pylori* incidence is high and consistent with epidemiologic data described to regions' sanitary conditions. The *cag*E gene highlight in all analyses as the best predictive factor for gastric diseases outcome, and associated with *vir*B11, can be a potential marker for the development for more severe lesions. These results instigate investigations related to bacterial genotype as marker for gastric disease prognosis.

Keywords: Helicobacter pylori, virulence genes, gastric disease, gastric cancer

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