Clinical Relevance of vacA, cagA, and iceA Genotypes of Helicobacter pylori

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Abstract

Introduction: Helicobacter pylori infection is associated with variable clinical outcomes, including gastroduodenal diseases, and genetic factors may be relevant in this process. The aim of this study was to investigate any association between the H. pylori genotypes and the clinical outcome in patients diagnosed with gastrointestinal diseases.

Methods: Antral gastric biopsy specimens were collected from 250 patients with gastritis. Clinical diagnosis was based on histology, and endoscopy. Specimens were tested for H. pylori genotypes by PCR, and the presence of vacA s and m regions, cagA, and iceA genotypes were analyzed for association with the clinical disease.

Results: Significant associations were found between the genotypes vacA s1 with gastritis (P=0.052), atrophy (P=0.001), vacA s2 and vacA m2 with erosion (P=0.004, and < 0.001 respectively), cagA with duodenitis (P=0.005). Several genotypes present in certain diseases were significantly associated with the patients’ gender, while, no association between the genotypes, and the age of the patient was found.

Conclusions: This study reports the genotypes of three virulence genes in H. pylori for the first time in Jordan; it adds new pieces of information in this respect. Overall, the results demonstrated that certain H. pylori genotypes showed significant correlation with the clinical outcome, and their presence might be used to predict the disease outcome.

Introduction

Helicobacter pylori is known to cause gastroduodenal diseases such as chronic atrophic gastritis, [1,2] peptic ulcer, [3-5] and is associated with certain types of gastric cancer [6-8]. Physiological differences resulting from the apparent genomic variation among strains have been suggested to be responsible for the diversity of disease associated with H. pylori infection. Studies have demonstrated the involvement of bacterial virulence factors, host genetics and environmental factors in contributing to the development of disease [9]. Bacterial virulence factors include proteins mediating establishment/colonization, persistence of infection and long-term damage to the host [10].

The cytotoxin associated gene (cagA) is considered a marker for the presence of one pathogenicity island of about 40 Kbp in H. pylori [11]. The presence of cagA was reported to be associated with duodenal ulcer, gastric mucosal atrophy, and gastric cancer [12,13]. The bacterium elicits its pathological activity at least partly through direct contact with the target epithelial cells [14]. Although CagA protein is a H. pylori virulence factor, its presence is not sufficient for the prediction of disease outcome.

Some H. pylori strains produce a vacuolating cytotoxin (VacA), another virulence factor that causes vacuolation in cultured epithelial cells [15]. These strains are isolated more frequently from patients with peptic ulcer than from patients without, and constitute an increased risk for development of gastric cancer [16,17].

Antibodies to this cytotoxin protein were detected in patients infected with toxin producing strains, demonstrating the VacA production in vivo. The corresponding protein is produced by approximately 50% of H. pylori strains, and although, there was heterogeneity in the level of vacA transcription among these strains, the vacA gene encoding the cytotoxin was present in all H. pylori strains tested. The vacA gene contains both conserved regions and regions of diversity, and allelic variations in the gene are found in the signal (s1, s2) and the middle region (m1a, m1b, m2), and the s1 type is associated with ulcer disease [12,17]. Global variation in the distribution of vacA alleles may explain diverse reports linking vacA genotypes to clinical disease from different geographic areas [18].

The iceA gene (induced by contact with the epithelium) exists in allelic variants, including iceA1 and iceA2, and only iceA1 was induced following contact with the gastric epithelium. Adherence to gastric epithelial cells in vitro stimulates the transcription of iceA1 [19]. The IceA1 genotype was significantly associated with peptic ulceration and increased mucosal IL-8 concentrations. Some studies have reported an association of iceA1 strains with the presence of peptic ulcers [20], and a higher prevalence of iceA2 strains among patients with non-ulcer dyspepsia [13]. A study of H. pylori infection in patients subjected to...
an upper gastrointestinal endoscopy in Jordan reported high prevalence [21], and confirmed that its presence was significantly associated with gastritis and peptic ulcer. This study reports the genotypes of three virulence genes in H. pylori for the first time in Jordan; it adds new pieces of information in this respect. It reports on the association of various H. pylori genotypes prevalent among Jordanian patients with the clinical outcome, and the severity of disease in these patients.

Methods

Collection of Samples
Two hundred and fifty antral biopsies were collected by gastroenterologists at King Abdullah and Princess Basma hospitals from patients with gastritis who underwent upper gastrointestinal endoscopy [22]. The symptoms reported by these patients were abdominal pain, epigastria pain, vomiting, or heartburn. The study was approved by the Ethics Committee of the University (IRB). Each patient signed a written informed consent prior to specimen collection, and all clinical specimens were tested undercode.

Patients’ Data
The information recorded for each patient included: Patient's hospital number, age, gender, history, and clinical diagnosis was based on histology, and endoscopy provided in the pathology reports or patients’ files, and previous treatment (e.g., anti-H. pylori, three had proton pump inhibitors or antacids).

Sample testing for H. pylori
Sets of biopsy specimens were used for histology, and PCR. All the 250 biopsies were tested by PCR, and 151 (60.4%) were histologically examined by a pathologist [22].

Detection and genotyping of virulence genes (vacA, cagA, and iceA) by PCR
The biopsy specimens were homogenized, and DNA was extracted using Wizard Genomic DNA purification kit (Promega, Madison, WI, USA). The presence of H. pylori was detected by separate PCRs aimed at the cagA, vacA s and m regions, and iceA genotypes were determined by separate iceA1- and iceA2-specific PCRs [23,24]. Five species-specific primer sets (Alpha DNA, Montreal, Canada) were used to amplify highly conserved regions within the indicated genes.

Statistical Analysis
The association between H. pylori genotypes and the clinical outcome of the studied cases was analyzed using Fisher’s exact and Chi-Square tests (statistical package for social sciences, SPSS Inc. Chicago, Illinois USA). A P value of < 0.05 was considered statistically significant, values of P > 0.05 were not significant. Averages, ranges, and percentages of positive samples were calculated.

Results

Clinical diagnosis
The results of the endoscopy, and clinical diagnosis of the Helicobacter positive cases by PCR in both sexes are presented in Table 1. Out of the 250 patients, 110 (44%) were positive by PCR. The male: female ratio of the patient’s was 58 (52.7%) males: 52 (47.3%) females; (mean age 42.03 ± 15.135 years; range, 17-67 years).

Diagnosis of H. pylori was based on endoscopic findings, histology, and/or PCR method. The presence of duodenal diseases such as duodenal ulcer, duodenitis with or without erosions was based on endoscopic examination. Individuals clinically diagnosed with one disease may have different pathological presentations e.g., gastritis as diagnosed histologically, was classified as mild to severe, three of the gastritis cases were with lymphoid follicles, one with nodular gastritis, one with diffuse gastritis, and one with fibrosis in the antrum. Based on microscopic examination, one of the biopsies showed tiny superficial fragments of unremarkable looking gastric mucosa, and was considered as a gastritis case. Some cases showed overlapping e.g., the same patient having both gastritis and duodenitis.

Helicobacter pylori genotypes
The prevalence of the cagA, iceA2 and allelic variants of vacA genotypes and their presence in different gastroduodenal diseases are presented in Table 2.

iceA genotype
None of the 110 biopsies had the iceA1 genotype, while 81 (73.6%) had the iceA2 genotype.

The cagA and vacAs1 genotypes
The cagA genotype was detected in 8/17 (47.1%) of the vacA s1 genotype, compared to 5/20 (25%) of the vacA s2 genotype.

The association between the vacA, cagA, and iceA2 genotypes with the clinical outcome
The genotypes that were significantly associated with certain clinical outcome were: vacA s1 with gastritis cases (P=0.052), and atrophy cases (P=0.001), vacA s2 and vacA m2 with erosion cases (P= 0.004, and < 0.001 respectively), cagA genotype with duodenitis cases (P= 0.005).

The presence of both cagA and vacA s genotypes in the same patient and their association with the clinical outcome is presented in Table 2.
The vacAs1 cagA genotype was present in 8 (10.1%) cases of gastritis, 2 (14.3%) of PUD, and in one case in each of the duodenitis (8.3%), intestinal metaplasia (16.6%) and atrophy (50%) cases. The vacA s2 cagA was present in 5 cases; 2 (2.5%) of gastritis cases, 1 (8.3%) of duodenitis, and 2 (15.4%) of erosion cases. On the other hand, a negative or insignificant correlation was found between the vacA s1 genotype and the clinical outcome (P > 0.05), and the presence of the vacA s2 (P = 0.513), m2 (P = 0.234) genotypes in the erosion cases among males. The negative correlation means that the case was independent on the genotype. The iceA2 genotype showed the highest prevalence among all genotypes, and was observed in all types of clinical cases with different frequencies (Table 2). Of the 79 gastritis cases; 3 had lymphoid follicles, one diffused, and one had nodular pattern. One patient with erosion was probably drug induced as this patient had non-steroidal anti-inflammatory drugs, as was indicated in the patient’s report. Only one patient with the iceA2 gene showed a history of adenoma.

The combination of iceA, vacA, and cagA genotypes

The presence of more than one genotype and their association with the clinical outcome is presented in Table 3.

The association between genotypes and gender of the patient

Analysis of data showed a significant association between certain genotypes and the gender of the patient. In females, the presence of both vacA s2 (P = 0.007), and vacA m2 (P = 0.008) genotypes in erosion cases, the presence of both vacA s2 (P = 0.04), and vacA m2 (P = 0.006) genotypes in duodenitis cases. While in males, the presence of the cagA genotype in duodenitis cases (P = 0.033), the presence of the iceA2 genotype in erosion cases (P = 0.007), and the presence of the vacA m1 genotype in peptic ulcer disease (P = 0.044) was significantly associated.

The association between genotypes and age

There was no association between the genotypes, and the age of the patient.

Discussions and Conclusion

There have been reports correlating between different H. pylori genotypes and the severity of the disease in adults and children [20,25,26]. This study showed that the most observed genotypes in the 14 PUD cases were the iceA2 being present in 11 (78.5%) (Table 2), followed by the vacA m1 present in 4 (28.6%), and the combined vacA s1 cagA genotype present in 2 (21.4%) of these cases. However, none of these genotypes showed a significant correlation with the disease (P > 0.05). Moreover, PUD cases were independent (P > 0.05) on the presence of either vacA s2, or vacA m2 (each present in one case), which may explain the low prevalence of both genotypes in these cases.

In the 13 erosion cases, the vacA s2 (6 cases) and vacA m2 (7 cases) were the most prevalent genotypes, and were significantly correlated with erosion (P = 0.003, and P < 0.0001 respectively), while the iceA2 was negatively correlated (P = 0.001) with these cases. The cagA genotype was the most prevalent among the 12 duodenitis cases being present in 7 (58.3%), and it was significantly correlated with the disease. The iceA2 9 (75%) genotype did not have a significant correlation with these cases.

The presence of vacA s1 genotype in the gastritis cases was significantly correlated (P = 0.052), but it was not present in any case with normal gastric mucosa.

The iceA2 genotype was the most common genotype observed in 81 (73.6%) of the H. pylori positive cases especially in patients with gastritis and PUD. Our results for the iceA2 genotypes and its presence in PUD were similar to those reported in a Brazilian population [27], where the iceA2 genotype was more prevalent than the iceA1 especially in patients with duodenal ulcer and gastric carcinoma. Also, in Calcutta, India both the iceA1 and iceA2 genotypes were present in the population, but the iceA2 seemed to be disease associated [28]. In Bangladesh, the iceA2 was more reported in H. pylori found in patients with peptic ulcer [29]. Surprisingly, none of the cases in our study had the iceA1 genotype. However, different findings were reported in the United States [13, 19], and Europe [9], where isolates from PUD patients showed a predominance of iceA1 alleles.

The negative association between the iceA genotype and the vacA genotypes was previously reported [30], but neither the presence of iceA nor the combination of the iceA, vacA, and cagA genotypes were helpful in predicting the clinical presentation of H. pylori infection. In Nigeria, the vacAs1, cagA, iceA1 genotypes were more prevalent in patients with duodenal ulcer or non-ulcer dyspepsia, suggesting that the cagA and vacA genotypes may not predict the clinical outcome of infection [31].

In the current study, the presence of the vacAs1 allele was significantly associated (P = 0.001) with the two atrophy cases that were diagnosed. The presence of the cagA and iceA2 genes each in one atrophy case
was not significantly correlated (P = 0.426) (Table 2). The same negative results were found for the vacA s2, m1, and m2 genotypes, which might explain the absence of these genotypes in the atrophy cases. In the six cases of intestinal metaplasia, the presence of iceA2 in 4 (66.6%), the vacA m1 allele in 2 (33.3%), and both vacA s1 and cagA in 1 (16.6%) was not significantly correlated with these cases (P > 0.05). Other studies have reported that vacA s1, m1 alleles, and cagA genotype to be a risk factor for atrophy or intestinal metaplasia [32,33]. A study conducted on Portuguese and Colombian patients infected with H. pylori [33], suggested that vacA s1, vacA m1, cagA positive genotypes were significantly associated with higher H. pylori density, higher degrees of lymphocytic and neutrophilic infiltrates, the type of intestinal metaplasia, atrophy, and the presence of epithelial damage. The iceA1 genotype was only associated with epithelial damage in the Portuguese patients [33].

The association between vacA s1 allele and cagA gene with ulcers or gastric carcinoma cases has been reported [15, 30,34]. In Germany [15], the presence of H. pylori vacA s1 genotype was reported in 96% of the patients with PUD, while the vacA s2 genotype was present in only 4% of these patients, compared to 31% of the patients with non-ulcer dyspepsia. The presence of the cagA positive H. pylori with the vacA s1 genotype was associated with the vacA expression, and cytotoxin activity and increased the risk for peptic ulceration, so the vacA genotype may allow identification of infected subjects at different levels [30]. The presence of the vacA s1 allele in 3/14 (21.4%) compared to vacA s2 allele present in only 1/14 (7.1%) of the PUD cases in our study is in agreement with a previous study [13], which reported the frequent presence of the vacA s1 allele in peptic ulcer patients, a higher prevalence of cagA among these patients than patients with dyspepsia, and a strong association between the presence of cagA with the vacA s1 allele. Our results showed that the presence of certain genotypes was significantly associated with the gender, but not with the age of the patient. Moreover, the combination of certain genotypes was significantly correlated with gender and the clinical outcome as they were present in certain diseases among females or males. The high prevalence of the vacA s2, and vacA m2 genotypes (65%, and 75% respectively) among females has significant correlation with duodenitis and erosions cases. The presence of the cagA gene in duodenitis cases (P = 0.033), and the iceA2 in erosion cases (P = 0.007) was significantly correlated with male gender. On the other hand, no significant correlation was found between the cagA genotype in duodenitis cases and the female gender (P = 0.104), but there was a tendency to be significant in the presence of the iceA2 gene in the erosion cases among females (P = 0.067). No significant correlation was found between any of the vacA s2 (P = 0.513), m2 (P = 0.234) genotypes in the erosion cases among males. The vacA m1 was detected in equal amounts in both genders, and it has a significant correlation with the 4/14 (28.6%) PUD cases present in males (P = 0.044). These findings were in agreement with a previous study suggesting that male gender might be a risk factor for increased duodenal ulcer disease [35]. Although duodenitis cases were low 13/106 (12.3%) in this study, it was diagnosed more in males (75%) than in females (25%), contrary to the erosion cases that were diagnosed more in females (69.2%) than in males (31%). The presence of the vacA s1 genotype in the gastritis (79/106), and in the atrophy (2/106) cases was significantly correlated (P = 0.052, and 0.001 respectively) with females, but not males.

In conclusion, certain genotypes showed significant correlation with the clinical outcome, and their presence might be used to predict the disease outcome.

Acknowledgements

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Authors Contribution(s)

Professor L. F. Nimri: experimental design, execution of PCR assays; data analysis, and writing the paper. Dr. K. E. Bani-Hani: providing antral biopsies collected from patients at King Abdullah with gastritis who underwent upper gastrointestinal endoscopy. Dr. I. Matalka: Histological/pathological diagnosis and classification of gastritis in biopsies. M. Ibrahim: Execution of PCR assays.

References

3. Goodwin CS, Mendall MM, Northfield TC.
### Illustrations

#### Illustration 1

Table 1. The clinical diagnosis of 110 patients positive for H. pylori by PCR in both sexes.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of cases (%)</th>
<th>Gastritis (%)</th>
<th>Normal (%)</th>
<th>PUD* (%)</th>
<th>Erosion (%)</th>
<th>Duodenitis (%)</th>
<th>IM** (%)</th>
<th>Atrophy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>58 (52.7)</td>
<td>45 (57)</td>
<td>7 (35)</td>
<td>10 (71.4)</td>
<td>4 (31)</td>
<td>9 (75)</td>
<td>2 (33.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Female</td>
<td>52 (47.3)</td>
<td>34 (40)</td>
<td>13 (65)</td>
<td>4 (28.5)</td>
<td>9 (69.2)</td>
<td>3 (25)</td>
<td>4 (66.6)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>110</td>
<td>79 (74.5)</td>
<td>20 (18.9)</td>
<td>14 (13.2)</td>
<td>13 (12.3)</td>
<td>12 (11.3)</td>
<td>6 (5.7)</td>
<td>2 (1.9)</td>
</tr>
</tbody>
</table>

* PUD: Peptic ulcer disease, **IM: intestinal metaplasia.
Illustration 2

Table 2. The prevalence of the cagA, iceA2 and allelic variants of vacA genotypes and their presence in different gastroduodenal diseases.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Prevalence (%)</th>
<th>Gastritis (%)</th>
<th>Normal (%)</th>
<th>PUD** (%)</th>
<th>Erosion (%)</th>
<th>Duodenitis (%)</th>
<th>IM** (%)</th>
<th>Atrophy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 110</td>
<td>n = 79</td>
<td>n = 20</td>
<td>n = 14</td>
<td>n = 13</td>
<td>n = 12</td>
<td>n = 6</td>
<td>n = 2</td>
</tr>
<tr>
<td>vacA s1 *</td>
<td>17 (46)</td>
<td>16 (20.6)</td>
<td>0</td>
<td>3 (21.4)</td>
<td>2 (15.4)</td>
<td>2 (16.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (16.6)</td>
<td>2 (100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>vacA s2</td>
<td>20 (54)</td>
<td>13 (16.6)</td>
<td>5 (25)</td>
<td>1 (7.1)</td>
<td>6 (46.2)</td>
<td>3 (25)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vacA m1</td>
<td>20 (48.7)</td>
<td>15 (19)</td>
<td>3 (15)</td>
<td>4 (28.6)</td>
<td>1 (7.7)</td>
<td>2 (16.6)</td>
<td>2 (33.3)</td>
<td>0</td>
</tr>
<tr>
<td>vacA m2</td>
<td>21 (51.2)</td>
<td>17 (21.5)</td>
<td>3 (15)</td>
<td>1 (7.1)</td>
<td>7 (54)</td>
<td>3 (25)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vacA s1m1</td>
<td>12 (46.2)</td>
<td>11 (14)</td>
<td>0</td>
<td>3 (21.4)</td>
<td>1 (7.7)</td>
<td>2 (16.6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vacA s2m2</td>
<td>12 (46.2)</td>
<td>8 (10.1)</td>
<td>2 (10)</td>
<td>0</td>
<td>4 (30.7)</td>
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</tr>
<tr>
<td>vacA s1m2</td>
<td>2 (7.7)</td>
<td>2 (2.5)</td>
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<td>0</td>
<td>1 (7.7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Genotype</td>
<td>IM=</td>
<td>PUD=</td>
<td>IM=</td>
<td>PUD=</td>
<td>IM=</td>
<td>PUD=</td>
<td>IM=</td>
<td>PUD=</td>
</tr>
<tr>
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<td>------</td>
</tr>
<tr>
<td>cagA</td>
<td>29 (26.4)</td>
<td>20 (25.3)</td>
<td>6 (30)</td>
<td>3 (21.4)</td>
<td>3 (23.1)</td>
<td>7 (58.3)</td>
<td>1 (16.6)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>iceA2</td>
<td>81 (73.6)</td>
<td>60 (76)</td>
<td>14 (70)</td>
<td>11 (78.5)</td>
<td>5 (38.5)</td>
<td>9 (75)</td>
<td>4 (66.6)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>vacA s1 cagA*</td>
<td>8 (47.1)</td>
<td>8 (10.1)</td>
<td>0</td>
<td>2 (14.3)</td>
<td>0</td>
<td>1 (8.3)</td>
<td>1 (16.6)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>vacA s2 cagA</td>
<td>5 (25)</td>
<td>2 (2.5)</td>
<td>0</td>
<td>0</td>
<td>2 (15.4)</td>
<td>1 (8.3)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* The vacA s1 and vacA s2 genotypes were calculated from the total 37 cases that had vacA s. The vacA m1 and vacA m2 genotypes were calculated from the total 41 cases that had vacA m. The vacA s1m1, vacA s2m2, and vacA s1m2 were calculated from the total 26 cases that had vacA sm. The total number of clinical outcomes for all genotypes included the combined genotypes. The vacA s1 cagA and vacA s2 cagA percentage were calculated based on the number of cases having the cagA genotype vacA s1 cagA (17), and vacA s2 cagA (20).

** IM= intestinal metaplasia, PUD = Peptic ulcer disease.
Illustration 3

Table 3. The prevalence of combined genotypes and their presence in different gastroduodenal diseases.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Prevalence* (%)</th>
<th>Gastritis (%)</th>
<th>Normal (%)</th>
<th>PUD** (%)</th>
<th>Erosion (%)</th>
<th>Duodenitis (%)</th>
<th>IM** (%)</th>
<th>Atrophy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>n = 79</td>
<td>n = 20</td>
<td>n = 14</td>
<td>n = 13</td>
<td>n = 12</td>
<td>n = 6</td>
<td>n = 2</td>
</tr>
<tr>
<td>cagA iceA2</td>
<td>8 (7.3)</td>
<td>4 (5.1)</td>
<td>3 (15)</td>
<td>1 (7.1)</td>
<td>2 (16.6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vacA s1 iceA2</td>
<td>1 (0.9)</td>
<td>1 (1.3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (50)</td>
</tr>
<tr>
<td>vacA m1 iceA2</td>
<td>4 (3.6)</td>
<td>3 (3.8)</td>
<td>1 (5)</td>
<td>1 (7.1)</td>
<td>0</td>
<td>0</td>
<td>2 (33.3)</td>
<td>0</td>
</tr>
<tr>
<td>vacA s1m1 iceA2</td>
<td>5 (4.5)</td>
<td>5 (6.3)</td>
<td>0</td>
<td>1 (7.1)</td>
<td>1 (8.3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vacA s2 iceA2</td>
<td>3 (2.7)</td>
<td>2 (2.5)</td>
<td>1 (5)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vacA m1 cagA iceA2</td>
<td>2 (1.8)</td>
<td>0</td>
<td>2 (10)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>vacA m2 iceA2</td>
<td>1 (0.9)</td>
<td>1 (1.3)</td>
<td>0</td>
<td>1 (7.1)</td>
<td>0</td>
<td>0</td>
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<td>Prevalence</td>
<td>IM</td>
<td>PUD</td>
<td>IM</td>
<td>PUD</td>
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<td>PUD</td>
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<tr>
<td>vacA s1m1 cagA iceA2</td>
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<td>3 (3.8)</td>
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<tr>
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<td>1 (1.3)</td>
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<td>0</td>
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<tr>
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<td>1 (1.3)</td>
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<td>0</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>vacA m2 cagA iceA2</td>
<td>1 (0.9)</td>
<td>1 (1.3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (8.3)</td>
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</table>

* Some of the patients had more than one disease so the total number of cases for the same genotypes was more than the prevalence.

** IM= Intestinal metaplasia, PUD = Peptic ulcer disease.
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