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Distribution of *Helicobacter pylori cagA*, *cagE*, *oipA* and *vacA* in different major ethnic groups in Tehran, Iran

Hossein Dabiri[*,†], **Parviz Maleknejad**[*], **Yoshio Yamaoka**[‡], **Mohammad M Feizabadi**[*], **Fereshteh Jafari**[†], **Maryam Rezadehbashi**[†], **Farrokh A Nakhjavani**[*], **Akbar Mirsalehian**[*], and **Mohammad R Zali**[†]

[*] Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

[†] Research Center for Gastroenterology and Liver Diseases in Shaheed Beheshti University, MC, Tehran, Iran

[‡] Department of Medicine-Gastroenterology, Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, Texas, USA

Abstract

Background and Aim—There are geographical variations in *Helicobacter pylori* virulence genes; *cagA*, *cagE*, *vacA* and *oipA*. The present study compared the distribution of these genotypes in major ethnic groups residing in Tehran, Iran and their association with clinical outcomes.

Methods—A total of 124 *H. pylori*-positive patients living in Tehran were enrolled in this study. The ethnic distribution was 74 Persians, 33 Turks and 17 other ethnics including Kurds, Lurs, Afghanis and Arabs. The presence of the *cagA*, *cagE* and *oipA* genes and *vacA* alleles (signal [s] and middle [m] region) were determined by polymerase chain reaction (PCR) from *H. pylori* DNA.

Results—The *cagA*-positive status was predominant in all three ethnic groups (e.g. 65% in Persians and 73% in Turks). In contrast, the *cagE*-positive status was less than half in Persians (47%) and Turks (30%), whereas it was 77% in other ethnicities ($P = 0.008$). The predominant *vacA* genotypes were s1 and m1 in all three ethnic groups (e.g. 68% in Persians and 70% in Turks were s1). There was no significant association between *cagA* and *cagE* status or *vacA* genotypes and clinical outcomes. The *oipA*-positive strains were more common in non-ulcer dyspepsia (NUD) (63%) than in peptic ulcer patients (15%) ($P = 0.001$) in Persians, but the association was not observed in other ethnic groups.

Conclusion—There are some differences in the *H. pylori* genotypes among the ethnic groups in Iran. However, none of these markers seemed to be clinically helpful in predicting the clinical presentation of a *H. pylori* infection in Iran.

Keywords

clinical outcome; ethnic; *Helicobacter pylori* genotype; Iran; virulence factor

Correspondence: Dr. Akbar Mirsalehian, Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, 100 Poursina St, Keshavarz Blvd, Tehran, Iran. mirsalehiana@yahoo.com.

Introduction

Helicobacter pylori is a major human pathogen. In developing countries, *H. pylori* infects the majority of the population and more than 90% of the Iranian population are reported to be infected with *H. pylori.*[1] *H. pylori* infection causes chronic gastritis, peptic ulcer disease (PUD), gastric carcinoma (GC) and mucosa associated lymphoid tissue (MALT) lymphoma.[2,3] Several *H. pylori* virulent genes have been identified to contribute to the risk and severity of these diseases. These include the *cag* pathogenicity island (PAI) that encodes a type IV secretion apparatus.[4,5] The presence of the *cagA* gene and/or *cagA* special type (e.g. East Asian type or type 1a) is associated with more severe clinical outcomes than the absence of the gene.[6–9] The *cag* PAI contains a gene known as *cagE* that encodes a secretory protein that is required for the induction of interleukin (IL)-8[10] and for translocation and phosphorylation of the CagA protein.[11] The presence of the *cagE* gene has been associated with a severe clinical outcome, especially in developed countries.[12]

Another important virulence factor of *H. pylori* is a vacuolating cytotoxin (VacA), which is associated with injury to epithelial cells. The *vacA* gene is virtually present in all *H. pylori* and has at least two variable parts, the signal or s-region (s1a, s1b and s1c, s2) and the middle or m-region (m1a, m1b and m1c, m2).[13–15] The mosaic combination of s- and m-region allelic types determines the production of the cytotoxin and is, thereby, associated with pathogenicity of the bacterium.[13] *vacA* s1a strains appear to be more pathogenic than s1b or s2 strains and are found more frequently in patients with ulcer diseases,[16,17] although this is not consistent.[18,19] *vacA* m1 strains are associated with greater gastric epithelial damage than m2 strains.[13] There is geographical variation in the *vacA* genotypes.[14,15,19] For example, studies have consistently shown that *vacA* s1a strains predominate in northern Europe, s1b in Central and South America, Spain and Portugal, s1a and s1b in the USA and s1c in East Asia.[14] These variations may contribute to the varying prevalence of gastric diseases in these areas.

The expression of the outer inflammatory protein A (OipA), one of the large outer membrane protein families, has been reported to correlate with IL-8 induction[20] and to be associated with severe clinical outcomes.[21,22]

In Iran, in addition to Persian and Azeri Turks (Turks) as the major ethnic groups, three distinct ethnic groups predominate: Kurds, Lurs and Arabs. Turks and Persians are the predominant ethnics of Tehran, the capital of Iran. In addition, the Afghanis have migrated to Iran for nearly the past two generations. There are several recent studies examining the relationship between *H. pylori* virulence factors and clinical outcomes in Iran;[18,23,24] however, no previous studies took account of the relationship between *H. pylori* virulence factors and ethnic groups. We therefore compared the distribution of *vacA* alleles, *cagA*, *cagE* and *oipA* status in these ethnic groups residing in Tehran, Iran, and their association with clinical outcomes.

Methods

Population studied

A total of 124 patients from six different ethnicities (Persians, Turks, Kurds, Lurs, Arabs and Afghanis) who had upper endoscopy in Taleghani Governmental Hospital during February 2007 to May 2008, and living in Tehran, Iran were enrolled in this study. All eligible patients meeting inclusion criteria were entered.

Inclusion criteria included patients with *H. pylori* infection proven by the culture of *H. pylori*, patients with an absence of non-gastrointestinal chronic medical conditions and the

absence of contraindications to upper gastrointestinal endoscopy, patients providing informed consent, and patients with a willingness to complete a standardized data-collection form. Exclusions included patients with upper gastrointestinal bleeding, patients who had received non-steroidal anti-inflammatory drugs, steroids or proton pump inhibitors at least 3 months prior to endoscopy, patients who had received any antibiotics at least 1 month prior to endoscopy, and patients who had received previous treatment for *H. pylori* infection.

All of the patients studied, except Afghanis, were born in Tehran and had lived in Tehran for at least two generations. Distribution of different ethnicities in the current study was not representative of the normal ethnic distribution in the Tehran population (i.e. ethnically, Turks are more predominant than Persians in Tehran). The Afghanis were born in Afghanistan and were living in Tehran for more than 10 years. According to patients' self-reports, none of the selected patients had a mixed ethnic background. Demographic features such as gender, age, education, income, smoking and occupation were also taken into account. Informed consent was obtained from all patients, and the protocol was approved by the ethical committee of Research Center for Gastroenterology and Liver Diseases in Shaheed Beheshti University of Medical Science.

Isolation and identification

Three biopsy specimens were taken from the greater curve of the antrum; two were used for histological examination and one for *H. pylori* culture. Gastric biopsy specimens for culture were kept in transport medium and brought to the laboratory on the day of endoscopy. In each case, the gastric biopsy specimens were cultured and the organisms were identified as *H. pylori* as previously described.[23,25] The identified *H. pylori* was then subcultured to single colonies for DNA extraction

Preparation of genomic DNA and polymerase chain reaction

DNA from each *H. pylori* isolate was extracted using a commercially available kit (Qiagen, Hilden, Germany). The genotypes of *vacA* s-region (s1 or s2) and m-region (m1 or m2), and the presence of the *cagA*, *cagE*, *oipA* and *glmM(ureC)* genes were determined by PCR as previously described.[13,15,19,26,27] The *cagA* genotypes (East Asian type [type 1a] or Western type [type 2a]) were also determined by polymerase chain reaction (PCR) as previously described.[28,29] The *glmM(ureC)* gene was used as a control for detecting *H. pylori* DNA. All PCR was done as described before.[23,25] Mixed infection of different genotypes and *vacA*-negative samples were excluded from the analyses.

Data analysis

Chi squared and Fisher's exact tests were used for analysis of categorical data and ANOVA was used for continuing data. The effects of the *H. pylori* genotypes on the risk of developing GC and PUD in patients were expressed as odds ratios (OR) with 95% confidence intervals (CI) with reference to NUD adjusted by age, sex and ethnic groups. Analyses were done using Sigma Stat for Windows V2.03 (SPSS, Chicago, IL, USA). A *P* value less than 0.05 was accepted as statistically significant. In addition, all figures including percentages in tables and text were rounded down if they were <0.5, and were presented as whole numbers if they were ≥0.5.

Results

A total of 124 *H. pylori* cultures were obtained from the following ethnic groups: 74 strains from Persians (36 men and 38 women, mean age 46 ± 17 years), 33 from Turks (15 men and 18 women, mean age 49 ± 17 years) and 17 strains from other ethnicities (eight men and nine women, mean age 37 ± 18 years) including seven from Kurds, five from Lurs, three

from immigrant Afghanis and two from Arabs (Table 1). Overall, there were 59 men and 65 women. The mean age was 46 ± 17 years (range 18–81 years). Twenty-two (18%) patients had PUD (six gastric ulcers and 16 duodenal ulcers), 91 (73%) had non-ulcer dyspepsia (NUD), and 11 (9%) had gastric carcinoma (GC). GC was the most common in Turks (21%) compared with Persians (5%) or other ethnicities (0%) ($P = 0.03$) (Table 1). Demographic factors such as gender, education, income, smoking and occupation, but not mean age, did not show any statistical differences in PUD, NUD and GC groups (Table 2). As expected, the mean age in GC patients were significantly higher than other groups ($P = 0.02$) (Table 2).

cagA genotypes

Overall, 84 patients (68%) were infected with *cagA*-positive strains (Table 3). The *cagA* gene was present in 65%, 73% and 71% of isolates from Persians, Turks and other ethnicities, respectively. All *cagA* genes detected were Western type *cagA* gene (type 2a) irrespective of the ethnicities.

The *cagA* gene was present in 73%, 55% and 55% of *H. pylori* strains isolated from patients with NUD, PUD and GC, respectively (Table 4). There were also no statistical differences between the *cagA* status and clinical outcomes irrespective of the ethnic groups (Table 4). OR adjusted by age, sex and ethnic groups also showed that the presence of the *cagA* gene was independent of the risk for PUD and GC (Table 5).

cagE status

Fifty five patients (44%) were infected with *cagE*-positive strains (Table 3). The *cagE*-positive isolates were present in 47% and 30% of isolates from Persians and Turks, respectively, whereas 77% of those from other ethnicities were infected with *cagE*-positive strains. This difference was statistically significant ($P = 0.008$ among the three groups).

Overall, 48% of patients with PUD and 47% of those with NUD were infected with *cagE*-positive isolates (Table 4). In Turkish patients, *cagE*-positive strains were isolated more frequently in patients with PUD (60%) than in those with NUD (32%); however, the association was not statistically significant ($P = 0.23$ among three diseases). There were also no statistical differences between the *cagE* status and clinical outcomes in Persians and other ethnicities (Table 4). OR adjusted by age, sex and ethnic groups also showed that the presence of the *cagE* gene was independent of the risk for PUD and GC (Table 5).

vacA subtypes

The most common *vacA* s-region genotype was s1 (69%): 68% of isolates from Persians, 70% from Turks and 76% from other ethnicities (Table 3). For the *vacA* m-region, 86 patients (69%) were infected with m2 strains. The m2 genotype was the most common in strains isolated from Persians (70%), Turks (67%) and other ethnicities (71%). In the combination of s- and m-region genotypes, s1m2 was the most common in strains isolated from Persians, Turks and other ethnicities. When we examined each minor ethnic group separately, two of three (67%) Afghani strains were s1m1 type (Table 3).

There were also no statistical differences between the *vacA* genotypes and clinical outcomes both by univariate analyses (Table 4) and adjusted by age, sex and ethnic groups (Table 5). Regardless of ethnicities and clinical outcomes, the s1a subtype was present in approximately 40% of s1 strains and the m1a subtype was present in approximately 55% of m1 strains (data not shown).

oipA status

Sixty-one (49%) patients were infected with *oipA*-positive strains (Table 3). The *oipA*-positive isolates were present in 51% of Persians and in 71% of other isolates. In contrast, only 33% of Turkish patients were infected with *oipA*-positive *H. pylori* ($P = 0.04$ among three groups).

Overall, 10% of GC patients, 41% of PUD patients and 56% of NUD patients were infected with *oipA*-positive strains ($P = 0.009$ among three diseases) (Table 4). OR adjusted by age and sex also showed that the presence of the *oipA* gene prevented the risk for GC (OR: 0.10, 95% CI: 0.01–0.84) (Table 5). However, when the analyses were carried out in each ethnic group, the differences were not statistically significant. The *oipA*-positive strains were significantly more common in NUD patients (63%) than in PUD patients (15%) or in GC patients (0%) in Persians ($P = 0.001$ among three diseases) (Table 4). In contrast, the *oipA*-positive strains were more common in PUD patients (60%) than in NUD patients (33%) or in GC patients (17%) among Turks, although the differences were not statistically significant ($P = 0.25$) (Table 4).

Discussion

Ethnicities versus genotypes

The present study investigated the *cagA*, *cagE*, *vacA* and *oipA* status of *H. pylori* isolated from patients of diverse geographical origins living in Tehran. Because the strains were obtained from symptomatic patients, the results reflect the findings in these groups of patients rather than in entire populations. The current study confirms the distinctive difference in *H. pylori* genotypes in Iranian ethnic groups residing within the same city. This is consistent with other studies from the USA, Malaysia and Kuwait.[19,30,31] The difference in *H. pylori* strains among different ethnic groups living in the same area suggests that they were brought in by immigrants and have remained in that population for many generations.[19]

The *cagA* positivity in Iranian isolates has been reported to vary from 44% to 91% in different reports.[23,32] In the present study, 68% of the patients were infected with *cagA*-positive strains, similar to another Iranian report (67%).[33] However, this is different from studies in East to South Asian countries where more than 90% of the strains carry the *cagA* gene regardless of clinical outcomes.[15,19,34–36] Our result is consistent with studies in Europe and the USA where the prevalence of *cagA*-positive strains are between 60 and 70%.[14,37] In fact, we found that all *cagA* genes detected in this study are Western type *cagA* gene (type 2a). The high prevalence of *cagA*-positive strains in Lurs and the low prevalence in Afghans might be due to the small number of patients; however, the data are in agreement with previous studies showing that the prevalence of the *cagA*-positive strains was 90% in strains isolated from Lurs from Iran[32] and that the low prevalence of *cagA*-positive strains has been reported from a neighbor of Afghanistan: Pakistan (15%).[38]

The presence of the *cagE* gene was also reported to be different in various geographical regions and/or ethnic groups (e.g. 64% in the USA, 71.2% in the UK, 70% in Malaysia, 88.4% in Thailand and 77.5% [NUD] to 92.5% [PUD] in India).[19,26,35,39,40] Similarly, in the present study, the prevalence of the *cagE* gene was different in different ethnic groups in Iran (e.g. 47% in Persians and 77% in other ethnicities). The prevalence of the *cagE* gene was less common in Iranian Turkish patients (30%) (Table 2), which was similar to that in Turks living in Turkey (28%).[41]

H. pylori vacA s1 was the predominant genotype in all studied ethnic groups in Iran. The *vacA* s1m2 genotype was predominant in Turks and Persian strains similar to reports from

Western countries.[16] The s1m1 genotype was predominant in Afghani strains similar to reports from India.[15,42] In the case of two Arab patients, s1m2 and s2m2 genotypes were observed which might be an indication of a close relationship of these Iranian Arabs with other Arabs in the Middle East where s1 and s2 are distributed equally,[31,43,44] rather than with Arabs in Africa where s2 is predominant.[31] However, the number of patients was too small, and further studies will be necessary to confirm the hypothesis.

OipA expression was reported to be linked to severe inflammation and the induction of IL-8 secretion.[45] The *oipA* gene was detected in different ranges according to ethnic groups. In previous studies, the *oipA* gene was present in most strains and the status was regulated by strip strand repairing based on the number of CT nucleotide repeats in the signal sequences.[20] In contrast, there were many *oipA*-negative cases in the present study. We used the same PCR primers as used in previous studies, which worked well both in Asian and Western strains.[27] Therefore, there should be two possibilities: one is that the nucleotide sequences of PCR primer regions are considerably different in Iranian strains from other countries and another possibility is that there are *oipA*-negative strains in Iran. Further studies will be necessary as to which possibilities will be applied to Iranian strains.

Clinical outcome versus genotypes

The present study did not reveal any associations between the *vacA* and *cagA* status and clinical outcomes. This finding is in agreement with other reports from Iran,[24,32] but was different from that in many studies in Western countries where *vacA* s1 and *cagA*-positive strains are more often isolated from patients with PUD than with NUD.[46] One possibility for the difference in the *cagA* status might be due to large genomic variations in the *H. pylori* genomes (e.g. a PCR primer set that amplified the *cagA* gene from *H. pylori* isolated in one country is reported to have failed to detect the gene in isolates from another country[47,48]). There may be several distinct forms of the *cagA* gene with an uneven geographical distribution, that differences in *cagA* genotypes may provide a marker for differences in virulence among *cagA*-positive *H. pylori* strains and that only some forms of the *cagA* gene are associated with severe gastroduodenal diseases.[49] Our data showed that the presence of the *cagE* gene could be a better marker for severity of *H. pylori* infection in Turks (60% in PUD *vs* 32% in NUD); however, the differences were not statistically significant. This finding is similar to reports from Turkey.[41,50]

Surprisingly, the *oipA*-positive strains were significantly more common in NUD patients (63%) than in PUD patients (15%) in Persian patients ($P = 0.004$). In addition, OR adjusted by age and sex showed that the presence of the *oipA* gene prevents the development of GC (Table 5). These data were different from previous studies in which the *oipA*-positive status was significantly associated with the presence of DU and GC.[20–22] However, in the present study, the prevalence of the *oipA*-positive strains was more common in patients with severe clinical outcomes in Turks (60% PUD *vs* 33% NUD), although the differences were not statistically significant. Therefore, the presence of the *oipA* gene and clinical outcomes are still unclear. In previous studies, the *oipA* gene was present in most strains and the *oipA* status was evaluated by functional status (i.e. ‘on’ or ‘off’ status), but not by the presence/absence of the gene. As the numbers of patients in the current study is relatively small, further studies with larger numbers are necessary to clarify the roles of *oipA* in clinical outcomes.

In conclusion, the present study clarified differences between ethnic groups living for a long time in the same region. However, we could not reveal clear associations of the *cagA*, *cagE* and *oipA* status and *vacA* genotypes with clinical outcomes in any of the studied ethnicities.

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Table 1

Demographic characterization of 124 patients based on ethnic groups and clinical outcome

Ethnicity	Number	Sex		Mean age ± SD	GC	PUD	NUD
		Male	Female				
Persians	74	36	38	46 ± 17	4 (5%)	13 (18%)	57 (77%)
Turks	33	15	18	49 ± 17	7 (21%)	5 (15%)	21 (64%)
Others							
Kurds	7	4	3	33 ± 20	0	1 (14%)	6 (86%)
Lurs	5	1	4	44 ± 22	0	2 (40%)	3 (60%)
Afghanis	3	3	0	28 ± 8	0	1 (33%)	2 (67%)
Arabs	2	0	2	49 ± 6	0	0 (0%)	2 (100%)
Subtotal	17	8	9	37 ± 18	0	4 (24%)	13 (76%)
Total	124	59	65	46 ± 17	11 (9%)	22 (18%)	91 (73%)
P value		0.82		0.05	0.03	0.76	0.33

Subtotal, total of minor groups (other ethnicities); Total, all groups.

P value is calculated by comparing Persians, Turks and Subtotal groups with respect to sex, age, GC, PUD and NUD.

GC, gastric carcinoma; NUD, non-ulcer dyspepsia; PUD, peptic ulcer disease.

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Table 2

Demographic characterization of 124 patients in three clinical outcome groups based on social status and habits

Demographic	NUD *n* = 91	PUD *n* = 22	GC *n* = 11	Total *n* = 124	*P* value
Age (mean ± SD	44 ± 16	47 ± 17	59 ± 20	46 ± 17	0.02
Sex					
Male	41 (45%)	11 (50%)	7 (64%)	59 (48%)	0.49
Female	50 (55%)	11 (50%)	4 (36%)	65 (52%)	
Education					
High school diploma or below	76 (84%)	18 (82%)	10 (91%)	104 (84%)	0.78
College or higher	15 (16%)	4 (18%)	1 (9%)	20 (16%)	
Income (Rial)					
<5 000 000	36 (40%)	11 (50%)	4 (36%)	51 (41%)	0.85
5 000 000–10 000 000	51 (56%)	10 (46%)	6 (55%)	67 (54%)	
10 000 000<	4 (4%)	1 (4%)	1 (9%)	6 (5%)	
Smoking+	8 (9%)	3 (13%)	1 (9%)	12 (10%)	0.79
Occupation					
Other	15 (16%)	7 (32%)	3 (27%)	25 (20%)	0.53
Home duties	35 (39%)	7 (32%)	3 (27%)	45 (36%)	
Service and business	41 (45%)	8 (36%)	5 (46%)	54 (44%)	

P value is calculated by comparing Age, Sex, Education, Income, Smoking and Occupation in three clinical groups (NUD, PUD and GC).

GC, gastric carcinoma; NUD, non-ulcer dyspepsia; PUD, peptic ulcer disease.

Table 3

Distribution of virulence markers of *H. pylori* among 124 patients with different ethnic groups

Ethnicity		Number of *H. pylori* positive for										
		cag PAI		*vacA*								*oipA*
	No. patients	*cagA*	*cagE*	s1	s2	m1	m2	s1m1	s1m2	s2m1	s2m2	
Persians	74	48 (65%)	32 (47%)	50 (68%)	24 (32%)	22 (30%)	52 (70%)	15 (20%)	35 (47%)	7 (9.5%)	17 (23%)	38 (51%)
Turks	33	24 (73%)	10 (30%)	23 (70%)	10 (30%)	11 (33%)	22 (67%)	6 (18%)	17 (51.5%)	5 (15%)	5 (15%)	11 (33%)
Others												
Kurds	7	4 (57%)	7 (100%)	6 (86%)	1 (14%)	3 (43%)	4 (57%)	2 (29%)	4 (57%)	1 (14%)	0 (0)	4 (57%)
Lurs	5	5 (100%)	4 (80%)	4 (80%)	1 (20%)	0 (0)	5 (100%)	0 (0)	4 (80%)	0 (0)	1 (20%)	4 (80%)
Afghanis	3	1 (33%)	1 (33%)	2 (67%)	1 (33%)	2 (67%)	1 (33%)	2 (67%)	0 (0)	0 (0)	1 (33%)	2 (67%)
Arabs	2	2 (100%)	1 (50%)	1 (50%)	1 (50%)	0 (0)	2 (100%)	0 (0)	1 (50%)	0 (0)	1 (50%)	2 (100%)
Subtotal	17	12 (71%)	13 (77%)	13 (76%)	4 (24%)	5 (29%)	12 (71%)	4 (23%)	9 (53%)	1 (6%)	3 (18%)	12 (71%)
Total	124	84 (68%)	55 (44%)	86 (69%)	38 (31%)	38 (31%)	86 (69%)	25 (20%)	61 (49%)	13 (11%)	25 (20%)	61 (49%)
P value		0.9	0.008	0.9		0.9			0.9			0.04

Subtotal, total of minor groups (other ethnics); Total, all groups.

P value is calculated by comparing Persians, Turks and Subtotal with respect to *cagA*, *cagE*, *vacA* and *oipA* status.

GC, gastric carcinoma; NUD, non-ulcer dyspepsia; PUD, peptic ulcer disease.

Table 4

Distribution of virulence markers of *H. pylori* among 124 patients with different ethnic groups and diseases

Patient group	Disease	Number of *H. pylori* isolates positive for										
		cag PAI				*vacA*						*oipA*
		cagA	*cagE*	s1	s2	m1	m2	s1m1	s1m2	s2m1	s2m2	
Persians	NUD (*n* = 57)	41 (72%)	27 (52%)	38 (67%)	19 (33%)	15 (26%)	42 (74%)	12 (21%)	26 (46%)	3 (5%)	16 (28%)	36 (63%)
n = 74	PUD (*n* = 13)	6 (46%)	4 (33%)	8 (62%)	5 (38%)	6 (46%)	7 (54%)	2 (15%)	6 (46%)	4 (31%)	1 (8%)	2 (15%)
	GC (*n* = 4)	1 (25%)	1 (25%)	4 (100%)	0 (0)	1 (25%)	3 (75%)	1 (25%)	3 (75%)	0 (0)	0 (0)	0 (0)
P value*		0.13	0.41	0.34		0.36			0.07			0.001
Turks	NUD (*n* = 21)	16 (76%)	6 (32%)	16 (76%)	5 (24%)	7 (33%)	14 (67%)	4 (19%)	12 (57%)	3 (14%)	2 (10%)	7 (33%)
n = 33	PUD (*n* = 5)	3 (60%)	3 (60%)	2 (40%)	3 (60%)	0 (0)	5 (100%)	0 (0)	2 (40%)	0 (0)	3 (60%)	3 (60%)
	GC (*n* = 7)	5 (71%)	1 (17%)	5 (71%)	2 (29%)	4 (57%)	3 (43%)	2 (29%)	3 (43%)	2 (29%)	0 (0)	1 (17%)
P value*		0.76	0.23	0.28		0.11			0.08			0.25
Others	NUD (*n* = 13)	9 (69%)	10 (77%)	10 (77%)	3 (23%)	5 (38%)	8 (62%)	4 (31%)	6 (46%)	1 (8%)	2 (15%)	8 (61%)
n = 17	PUD (*n* = 4)	3 (75%)	3 (75%)	3 (75%)	1 (25%)	0 (0)	4 (100%)	0 (0)	3 (75%)	0 (0)	1 (25%)	4 (100%)
	GC (*n* = 0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
P value*		1.0	1.0	1.0		0.26			0.54			0.51
Total	NUD (*n* = 91)	66 (73%)	43 (47%)	64 (70%)	27 (30%)	27 (30%)	64 (70%)	20 (22%)	44 (48%)	7 (8%)	20 (22%)	51 (56%)
	PUD (*n* = 22)	12 (55%)	10 (48%)	13 (59%)	9 (41%)	6 (27%)	16 (73%)	2 (9%)	11 (50%)	4 (18%)	5 (23%)	9 (41%)
	GC (*n* = 11)	6 (55%)	2 (20%)	9 (82%)	2 (18%)	5 (45%)	6 (55%)	3 (27%)	6 (55%)	2 (18%)	0 (0)	1 (10%)
P value**		0.17	0.19	0.38		0.52			0.71			0.009

* *P* value is calculated by comparing clinical outcome (NUD, PUD and GC) in each ethnic group with respect to *H. pylori* genotype;

** *P* value is calculated by comparing *H. pylori* genotype in three clinical outcomes (NUD, PUD and GC) irrespective to ethnic groups.

GC, gastric carcinoma; NUD, non-ulcer dyspepsia; PUD, peptic ulcer disease.

Table 5

Age, sex and ethnic adjusted risks for PUD and GC in relation to *H. pylori* genotypes

	PUD (*n* = 22) *vs* NUD (*n* = 91)			**GC (*n* = 11) *vs* NUD (*n* = 91)**		
	OR	**95% CI**	***P* value**	**OR**	**95% CI**	***P* value**
cagA+ *vscagA*−	0.42	0.16–1.11	0.08	0.30	0.07–1.24	0.10
cagE+ *vscagE*−	0.85	0.31–2.30	0.74	0.27	0.05–1.43	0.12
vacA s1 *vs* s2	1.86	0.69–5.01	0.22	0.55	0.10–2.96	0.49
vacA m1 *vs* m2	1.12	0.40–3.20	0.83	0.58	0.15–2.22	0.42
oipA+ *vsoipA*−	0.53	0.20–1.41	0.20	0.10	0.01–0.84	0.03

When calculating the risk for GC *vs* NUD, ethnic information was not included, as there are no GC cases in other ethnic groups.

cagA+, *cagA*–positive; *cagA*−, *cagA*–negative; *cagE*+, *cagE*–positive; *cagE*−, *cagE*–negative; *oipA*+, *oipA*–positive; *oipA*−, *oipA*–negative.

CI, confidence interval; GC, gastric carcinoma; NUD, non-ulcer dyspepsia; OR, odds ratio adjusted by age and sex; PUD, peptic ulcer disease.