Aneurysm and *Helicobacter pylori* relationship: the seropositivity of CagA, VacA and other antigens of *Helicobacter pylori* in abdominal and ascending aortic aneurysms

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SUMMARY

Helicobacter pylori is thought to be related to atherosclerosis and aneurysm development. We aimed to detect virulance factors of *H. pylori* and examine the potential etiopathogenetic relationship between aortic aneurysm and *H. pylori*, 58 abdominal aortic aneurysm (AAA) and 38 ascending aortic aneurysm (AsAA) cases and 57 Healty control group (HCG) were included. We investigated *H.pylori* IgG by ELISA and virulance factors by Western-Blot (WB) method. No difference was found between AAA (67.24%), AsAA (73.68%) and HCG (57.89%) for *H. pylori* IgG ($p>0.05$). A significant difference was found between AsAA (78.95%) and HCG (57.89%) for *H.pylori* IgG ($p<0.05$) by ELISA and a significant difference was found only between AsAA (100%) and HCG (37.5%) for *H. pylori* IgG in the 45-55 age group by WB. A statistically significant difference was found between AAA and AsAA for VacA and CagA+VacA and CagA+VacA+ UreA antigens and also a significant difference was found between AsAA and HCG for CagA+ UreA antigens ($p<0.05$). Finally, we suggest that *H.pylori* VacA has a more important role than CagA in the development of two aneurysms especially in ruptured AAA. New extended studies detecting *H. pylori* DNA are needed to detect the aetiopathogenesis between aneurysm types and *H.pylori*.

KEY WORDS: Aneurysm, *Helicobacter pylori*, CagA

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INTRODUCTION

Helicobacter pylori are spiral, gram-negative, micro-aerophilic bacteria that are important pathogens causing infections in human gastrointestinal system. The bacterium spreads through oral-oral and oral-fecal ways, and virulence factors, such as Cag A, Vac A and Ice A genes related to pathogenicity, as well as host factors were defined.(Dunn *et al.,* 1997; Gatti *et al.,* 2005).
Inflammatory response observed on AAA, AsAA is considered significant in the pathogenesis of the disease and it is also suggested that generally microorganisms are the trigger factors for the initiation of inflammatory process in the host. The most frequently discussed of these microorganisms was initially *Chlamydophila pneumoniae*, but a number of the studies investigating whether Cag A positive *H. pylori* origins increase the risk of atherosclerosis and coronary heart disease has

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increased in recent years with large-series epidemiologic studies detecting *Helicobacter pylori* especially in carotid atherosclerotic plaques (Ameriso *et al.,* 2001; Singh *et al.,* 2002; Mayr *et al.,* 2003; Karlsson *et al.,* 2000).

This study aims to determine the distribution of *H. pylori* Cag A, Vac A, Ice A and other virulence factors in cases diagnosed with abdominal and ascending aortic aneurysm and in healthy control group cases matched for age, gender and smoking habits, and to examine the potential etiopathogenetic relationship between aortic aneurysm and *H. pylori*, using clinical findings and radiodiagnostic data.

MATERIAL AND METHODS

I. Patient and control groups

The study was conducted between April 2008 and January 2009 as a cross-sectional, case control study with 96 cases in total diagnosed with AAA and AsAA according to clinical findings and radiodiagnostic data, who referred to IU Cerrahpasa Faculty of Medicine (CFM), Department of Cardiovascular Surgery and Radiodiagnostics; IU Istanbul Faculty of Medicine, Department of Cardiovascular Surgery and Radiodiagnostics; TR Ministry of Health, Dr. Siyami Ersek Department of Cardiovascular Surgery; Florence Nightingale Hospital, Cardiovascular Surgery Unit; Medical Park Hospital, Cardiovascular Surgery Unit; Memorial Hospital, Cardiovascular Surgery Unit; and theGerman Hospital, Cardiovascular Surgery Unit. The data and results obtained from both groups, such as age, gender, education status, occupation, smoking habits (smokers among the study groups were considered smokers), hypertension, diabetes, cardiovascular disease in family history, total cholesterol, triglyceride, HDL and LDL values, diameter of aneurism, whether it is ruptured and potential stomach complaints were collected and recorded.

Laboratory studies of the research were completed in IU CFM Microbiology and Clinical Microbiology USA ELISA laboratories. Two studies with AAA and AsAA and three groups consisting of 57 healthy control group cases selected by matching the cases were included in the study approved by IU CFM Ethics Committee.

A) ABDOMINAL AORTIC ANEURYSM (AAA) GROUP; (Abdominal Aortic Aneurysm)

58 patients diagnosed with AAA with abdominal aortic diameters of larger than 3 cm as determined with radiodiagnostic methods were included in the study. 13 (22.4%) of the 58 cases had ruptured abdominal aortic aneurysm, whereas 33 (56.9%) had non-ruptured, while both groups had an aneurysm diameter of 5 cm; and other 12 (20.7%) had an aneurysm diameter smaller than 5 cm. All of the cases with AAA included in the study had a past surgical procedure or had undergone endovascular intervention.

B) ASCENDING AORTIC ANEURYSM (AsAA) GROUP; (Ascending Aortic Aneurysm)

38 patients diagnosed with AsAA with ascending aortic diameters larger than 3 cm were registered in the study (Karlsson *et al.,* 2000; Lindholt and Shi, 2006). 2 (5.3%) of 38 cases had ruptured ascending aortic aneurysm, whereas 25 had non-ruptured with minimum 5 cm aneurysm diameters; and number of cases with maximum 5 cm aneurysm diameters were 11 (28.9%). All patients included in AsAA group had undergone a surgical procedure in the past.

C) HEALTHY CONTROL GROUP (HCG)

Healthy control groups was gathered by selecting 57 individuals among the people referring to Computed Tomography (CT) laboratory of IU CFM Department of Radiodiagnostics due to a particular complaint, but having no abdominal or cardiovascular complaints while resembling the AAA and AsAA cases in terms of age, gender and smoking habits (the ones smoking during the study were considered smokers). Abdominal and ascending aortic diameters of 57 individuals included in the study were within normal limits (<3 cm).

II. Blood sampling and test methods

10 ml of venous blood was collected from each of the patient and control group cases included in the study. The blood samples were centrifuged at 3000 rpm for 5 minutes and the preserved serums were stored at -70°C until laboratory studies. *H. pylori* IgG response was determined using ELISA method, and the determination of antibodies against *H. pylori* Cag A, VacA and other antigens was made using Western-blot method on the serums.

1) *H. pylori* ELISA IgG test: *H. pylori* IgG response was determined from the serums prepared by diluting 1/10 l, using *H. pylori* ELISA IgG (Euroimmun, Lübeck-Germany) kit. Fresh lysate obtained from *H. pylori* origin no ATCC 43504 was used in the kit. In the evaluation, <0.8 was considered as negative, 0.8-1.1 as intermediate value, and >1.1 as positive absorbance value.
2) *H. pylori* Western-Blot IgG test: IgG antibodies developed against all antigens of *H. pylori* (CagA, VacA, p75, p67, UreaB, Hsp analog p57, flagellin antigen p54, p53, p33, omp(p30), Urea A, p26, omp(p19) were studied in the patient serum primarily diluted by 1/5l using Western-blot kit (Euroimmun, Lübeck Germany). Specificity of the antigens was assessed in 3 categories according to WB test operation kit:
   - category 1: antigens cross-reacting 41, 50, 54, 57, 67 and 75 kdal;
   - category 2: 66 kdal (UreaseB);
   - category 3: according to highly specific antigens of 17, 19, 26, 30, 33, 95, 120 kdal:
     - negative: No bands or a weaker band of categories 1 and 2 or 3, Positive: Minimum two specific antigen bands from Category 3;
     - intermediate value: A specific band from Category 3 or two weak bands of the same band were evaluated.
3) Statistical analysis

Assessment of the data obtained from the study was performed using SPSS 17.0 statistical program. Chi-square, Fisher, T test and variance analysis were used in the assessment; p<0.05 was found to be significant.

RESULTS

96 patient group cases, of which 58 had AAA, and 38 AsAA, and 57 healthy control group (HCG) patients were included in our study by being matched in terms of age, gender and smoking habits (Table 1). Examining the *H. pylori* IgG responses using ELISA and Western-Blot (WB) methods, WB/ *H. pylori* IgG responses were found to be significant only among the cases of AsAA group and HCG cases.

No significant difference was found in other comparisons (p>0.05) (Table 2). Distribution of patient and HCG *H. pylori* antigens were observed to be 66.6% in cases with Cag A total aneurysm, and 52.6% in HCG (p>0.05), whereas a significant difference in Cag A positivity was found only between AsAA cases and HCG cases (p<0.05). Vac A was assessed in 21.8% in cases with total aneurysm, 15.5% in the AAA group, and 31.5% in the AsAA cases, whereas no Vac A positivity was found in HCG (p<0.05). In total aneurysm and HCG groups, Urea A distribution was assessed in 59.3% and 49.1% respectively, and a significant difference in Urea A positivity was observed only between AsAA and HCG groups (Tables 3 and 4).

Examining the data on gender, age groups and smoking habits obtained in our study, a significant difference in WB and *H. pylori* IgG positivity by gender was found only between male cases of AsAA (82.7%) and HCG (57.7%) groups (OR: 3.5, %95 CI (1-11), X2: 5, p<0.05); a significant difference in WB and *H. pylori* IgG positivity between age groups with total aneurysm (86.6%) and AsAA (100%) and the HCG cases of

TABLE 1 - *Demographic details of Patient and Healthy Control Group cases.*

Studying Groups	*N.*	*Age*[1]	*Gender*[2]		*Smoking*[3]	
			Female	*Male*	*Smoker*	*No-nosmoker*
Total Aneurysm (TA)	**96**	62,94 (45-80)	20	76	31	65
AAA	58	63,56 (45-80)	9	47	20	38
AsAA	38	62 (45-77)	11	29	11	27
HCG	57	63,21 (45-78)	12	45	18	39

AAA: Abdominal Aortic Aneurysm; AsAA: Ascendant Aortic Aneurysm; TA: Total aneurysm; HCG: Healthy Control Group.
[1]TA x HCG p>0.05; [2]TA x HCG p>0.05; [3]TA x HCG p>0.05.

TABLE 2 - *Distribution of ELISA and WB IgG results in Patient group and HCG cases.*

Studying Groups	*n*	*ELISA/H.pylori IgG*				*WB/H.pylori IgG*			
		(+)		*(-)*		*(+)*		*(-)*	
		n	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Total aneurysm	96	67	69,79	29	70,21	69	71,88	27	28,12
ruptured	15	11	73,33	4	26,67	11	73,33	4	26,67
non-ruptured	81	56	69,14	25	30,86	58	71,60	23	28,40
AAA	58	39	67,24	19	32,75	39	7,24	19	32,75
ruptured	13	10	76,92	3	23,07	10	76,92	3	23,07
non-ruptured	45	29	64,44	16	35,55	29	64,44	16	35,55
AsAA	38	28	73,68	10	26,31	30	78,95	8	21,05
ruptured	2	1	50	1	50	1	50	1	50
non-ruptured	36	27	75	9	25	29	80,55	7	19,44
HCG	57	33	57,89	24	42,11	33	57,89	24	42,11

AAA: Abdominal Aortic Aneurysm; AsAA: Ascendant Aortic Aneurysm; TA: Total aneurysm; HCG: Healthy Control Group.

TA x HCG p>0,05	TA x HCG p>0,05
AAA x HCG p>0,05	AAA x HCG p>0,05
AsAA x HCG p>0,05	AsAA x HCG OR: 2.72, %95 CI (1.06-6.98) X2: 4.52, p<0.05

the same age group (37.5%, 45-55) (OR:11.7, 95% CI (1-148), X2: 4.3, p<0.05, OR:10.8, %95 CI (1-85), X2: 5.9, p<0.05). In terms of smoking habits, a significant difference in WB and *H. pylori* IgG positivity between the cases with total aneurysm (ELISA: 77.1%, WB: 80.6%) and smoker HCG cases (ELISA: 38.8%, WB: 40%) (ELISA; OR: 5.3, 95% CI (2-19), X2: 7.2, p<0.05, WB; OR: 5.2, 95% CI (1-19), X2: 6.7, p<0.05). No significant difference was found between non-smoker cases of the groups.

DISCUSSION

Different types of aneurysm characterized by the increase in the outer diameter of the aorta wall due to longitudinal and axial expansion is sug-

TABLE 3 - *Distribution of antigens determined in cases with aneurysm and HCG cases using WB test.*

	N	*Cag A*		*Vac A*		*p33*		*p30*		*Ure A (p29)*		*p26*		*p19*		*p17*	
		n	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Total Aneurysm	96	64	66,66	21	21,88	20	20,83	22	22,92	57	59,38	49	51,04	45	46,88	29	30,21
ruptured	15	11	73,33	6	40	4	26,67	4	26,67	7	46,67	8	53,33	7	46,67	4	26,67
non-ruptered	81	54	66,67	15	18,52	16	19,75	18	22,22	50	61,73	39	48,15	38	46,91	25	30,86
AAA	58	34	58,62	9	15,52	11	18,97	14	24,14	29	50	28	48,28	26	44,83	19	32,76
ruptured	13	10	76,92	5	38,46	3	20,08	3	23,08	6	46,15	7	53,85	6	46,15	4	30,77
non-ruptured	45	24	53,33	4	8,88	8	17,77	11	17,77	23	51,11	21	46,66	20	44,44	15	33,33
AsAA	38	30	78,95	12	31,58	9	23,68	8	21,05	28	73,68	21	55,26	19	50	10	26,32
ruptered	2	1	50	1	350	1	50	1	50	1	50	1	50	1	50	0	0
non-ruptured	36	29	80,55	11	30,55	8	22,22	7	19,44	27	75	20	55,55	18	50	10	27,77
HCG	57	30	52,63	1	1,75	10	17,54	12	21,05	28	49,12	27	47,37	25	43,86	15	26,32

AAA: Abdominal Aortic Aneurysm; AsAA: Ascendant Aortic Aneurysm; TA: Total aneurysm; HCG: Healthy Control Group.

TABLE 4 - *Comparison of Patient group and HCG cases by CagA, VacA, UreaA (p29) positivity determined using WB test.*

Studying Groups	*n*	*CagA (+)*		*VacA (+)*		*UreA (+)*	
		n	*%*	*n*	*%*	*n*	*%*
Total Aneuryms	96	64	66,67	21	21,88	57	59,38
ruptured	15	11	73,33	6	40	7	46,67
non-ruptured	81	53	65,43	15	18,52	50	61,73
AAA	58	34	58,62	9	15,52	29	50
ruptured	13	10	76,92	5	38,46	6	46,15
non-ruptured	45	24	53,33	4	8,88	23	51,11
AsAA	38	30	78,95	12	31,58	28	73,68
ruptured	2	1	50	1	50	1	50
non-ruptured	36	29	80,55	11	30,55	27	75
HCG	57	30	52,63	0	0	28	49,12

AAA: Abdominal Aortic Aneurysm; AsAA: Ascendant Aortic Aneurysm; TA: Total aneurysm; HCG: Healthy Control Group.

TA x HCG p>0,05 TA x HCG: OR; 15,6 %95 CI (2-120), X^2:11,7, p<0,001 TA x HCG p>0,05
AAAX HCG: p>0.05 AAA x HCG: OR; 10,2% 95 CI (1-84), X^2: 6,9, p<0,01 AAAX HCG: p>0.05
AsAAX HCG: OR: 3.3% 95 CI (1.3-8.8) X2: 6.7, p<0.05 AsAAxHCG: OR; 15,6% 95 CI(3-209), X^2:17,2, p<0,001
AsAAX HCG: OR: 2.9, % 95 CI (1.9-7), X2: 5.6; p<0.05

gested to be based on primary risk factors, it cannot be explained clearly and the number of studies conducted on the subject are gradually increasing (Lindholt and Shi, 2006). Atherosclerosis is the mostly emphasized factor among the factors suggested to be related to the pathogenesis in both types of aneurysm.

Unlike the risk factors, such as gender, age, weight, smoking habits, hyperlipidemia known to be involved in atherosclerotic plaque development, it is claimed that the trigger factor may be the inflammatory response of microorganisms in vessel tissue (Mehta *et al.,* 1998; Ross, 1993, Alexander, 1994).

It is also known that mycotic aneurysms may develop due to bacteria such as *Staphylococcus aureus, Staphylococcus epidermidis, Salmonella spp.* and S*treptococcus spp*. reproducing on atherosclerotic plaques. It was reported that culture positivity rates of AAA tissue or thrombi in relevance with such bacteria vary between 5-36%, and then Gram negative aerobic and anaerobic bacteria are added to these bacteria (Steed *et al.,* 1993; Brown *et al.,* 1984).

In 1997, Saikku (1988) reported studies particularly on the role of *Chlamydophila pneumoniae*, suggesting that this bacterium may be the trigger factor in the development of atherosclerosis and arterial diseases.

When respiratory tract monocytes/macrophages are infected by the *C. pneumoniae*, *C. pneumoniae* enters the blood circulation. It multiplies in the vessel lumen and infects new mononuclear cells and endothelial smooth muscle cells. Then, *C. pneumoniae* stimulates the immune responses with lipopolysaccharides and causes TNF-alpha, IL1-beta, IL-6, growth factors, matrix mettaloproteinase expression, as well as disrupting the lipid mechanism in monocytes.

The disturbed lipid mechanism in monocytes causes lipid-rich foamy cells with intensive Hsp 60 proteins. These cells cover vascular endothelial cells causing atherosclerotic plaques. Following this, vasoconstriction develops by NO inhibition. It has been suggested that continuing chronic infection in media smooth muscle cells results in chronic inflammation and eventually atherosclerotic lesions and aortic aneurysms (Gurfinkel *et al.,* 1998; Kalayoglu *et al.,* 1998; Kol *et al.,* 1998; Muhlestein *et al.,* 1998).

The study by Benagiano *et al.,* 2003 (T helper type 1 lymphocytes drive inflammation in human ath-

erosclerotic lesions) reported that in vivo activated T lymphocytes that infiltrate atherosclerotic plaques of *Helicobacter pylori*-infected patients with or without anti-*Chlamydia pneumoniae* antibodies. They found that in all atherosclerotic lesions, T helper type 1 (Th1) cells were predominant. They also reported that *C. pneumoniae*-specific T cells were detected only in the plaques of anti-*C. pneumoniae* seropositive patients, whereas *H. pylori*-specific T cells were found in the gastric mucosa but not in the plaques of the same patients.

They concluded that plaque-derived Th1 cells expressed cytotoxicity, proapoptotic activity, and help for monocyte tissue factor production. They suggested that although multifactorial, atherosclerosis can be regarded as a Th1-driven immunopathological condition.

There are remarkable studies conducted in recent years on *H. pylori* suggested to induce aneurysms and to trigger atherosclerosis due to the constant and mild inflammatory response it creates on the host by seriously increasing acute phase reactants including CRP and fibrinogen, T cell response synthesizing interferon-gamma and proinflammatory cytokine levels in the host, as well as virulence factors such as CagA, VacA, which are known, after *C. pneumoniae*, to be the primary pathogen of gastrointestinal area, particularly gastric tissue (Mendall *et al.,* 1994; Pasceri *et al.,* 1998; Murray *et al.,* 1995; Mendall *et al.,* 1996; Whincup *et al.,* 1996).

The fact that *H. pylori* was associated with coronary heart disease due to atherosclerosis on a seroepidemiological basis in previous studies was reported by Nyberg *et al.* (Nyberg *et al.,* 2008) in 2008 in their study claiming for the first time until our study that a similar pathogenesis may develop aneurysms in AAA.

The relationship between AsAA and *H. pylori* was reported by Koullias (2004) in 2003 and this is the only report on the topic until our study. Apart from these two studies, Falkensammer (2007) published a study on the relationship between AAA and *H. pylori* based on PCR in 2007. Examining the international literature, our study was the first after these two different studies to be designed and conducted to determine both seropositivity and the distribution of virulence factors (CagA, VacA, UreaA etc.) in two groups.

The study found no significant difference between AAA and HCG groups in terms of IgG positivity determined using ELISA and Western-Blot (WB) methods ($p>0.05$), whereas a significant difference was observed only between AsAA and its subgroup rAsAA and HCG in terms of WB IgG positivity.

In their study reported from Sweden in 2008, Nyberg *et al.* (Nyberg *et al.,* 2008) could not determine a significant difference between 119 cases and the control group with similar features in terms of ELISA IgG seropositivity. In another study reported from the USA in 2003 (Koullias *et al.,* 2004), *H. pylori* could not be determined in aneurysm tissues of AsAA cases using immunohistochemical staining. Our conclusion on *H. pylori* seropositivity in AAA cases was consistent with the studies conducted by Nyberg (2008), whereas it differed from the study by Koullias (2004) based on the use of different laboratory methods.

Studying the distribution of virulence factors of *H. pylori* in AAA and AsAA groups and their subgroups of cases with ruptured and non-ruptured aneurysm, the most frequently observed factor was CagA, which is the most frequent found factor also in HCG groups. A significant difference was found between total AsAA group and its subgroup of cases with non-ruptured AsAA and HCG ($p<0,05$). In a case report published in 2008 and conducted with 119 cases with AAA, no significant difference was observed between AAA and ruptured AAA cases and HCG cases in terms of *H. pylori* CagA seropositivity.

It was concluded that there was no significant relationship between CagA positive *H. pylori* and ruptured AAA (Nyberg *et al.,* 2008). This conclusion was in line with our conclusion on the cases with AAA, and similar positivity was determined in AAA and HCG in terms of Cag A. Nonetheless, though conducted with different study groups with Cag A *H. pylori*, Sing (2002) and Mayr *et al.* (Mayr *et al.,* 2003) suggested in their two different studies reported on carotid atherosclerosis and coronary heart disease that Cag A increased the risk of disease.

Results obtained by these researchers were similar to our results: in our study, the result was OR:3.37 for Cag A, whereas it was OR:3.8 and similar to our results in the studies conducted by these researchers. It was claimed that AAA patho-

genesis developed because strains expressing Cag A protein of 140 kD encoded by Cag A gene present in 50-70% origin of *H. pylori* reform the vascular wall matrix of matrix metalloproteinases 3 (MM3) and 9 (MM9).
They then decompose the aortic matrix through inflammatory infiltration containing monocytes, macrophages, Th2 lymphocytes and plasma cells, as a result of chronic infection of in the periphery of aortic outer wall due to its highly strong immunogenic properties. causing an increase in inflammatory cytokines.
Autoimmune mechanisms also play a role in this process (Lindholt and Shi, 2006; Kusters *et al.,* 2006; Fan *et al.,* 1998; Annambhatla *et al.,* 2008).
VacA, which is the most emphasized factor along with Cag A, was found in 9 cases of one of our study group consisting of 58 cases with AAA (15.5%), 5 of which were ruptured and 4 non-ruptured. VacA was also observed in 12 of 38 cases with AsAA (31.58%), 1 of which was ruptured and other 11 non-ruptured.
However, no Vac A was found in HCG cases ($p<0.05$). Although no studies exist in the literature on *H.pylori* VacA for either atherosclerosis, carotid and coronary heart disease or abdominal or ascending aortic aneurysm, it was found interesting and significant with respect to the etiopathogenesis that VacA was observed to be significantly higher than CagA in ruptured and non-ruptured subgroups of AAA and AsAA and that it was not detected in healthy individuals. We concluded that of VacA protein encoded by VacA gene, which can be active only on half of *H. pylori* strains, though it is present in all strains, may trigger the development of aortic aneurysms potentially associated with atherosclerosis in persistent and chronic infections observed in certain cases due its particularities.
These include forming vacuoles in host cell membrane and inducing apoptosis and applying immunosuppression while inducing proinflammatory cytokines, and inducing the activation of Cag A due to its own activation. The fact that CagA is found in both in patient groups and HCG group in a similar amount, whereas VacA was not observed in HCG cases, while found only in cases of patient groups strengthens our opinion (Lindholt and Shi, 2006; Kusters *et al.,* 2006; Fan *et al.,* 1998; Annambhatla *et al.*, 2008, Curci and Thompson, 2004).
UreaA (p29) was detected 50% positive in AAA and 73% positive in AsAA, whereas it was found to be 49.1% in HCG. Among the study groups, a significant difference was found only between AsAA and its subgroup non-ruptured AsAA and HCG ($p<0.05$).
We could not find any studies in the literature conducted on aneurysms with urease enzyme contributing to chronic and persistent inflammatory process caused by the bacteria. However, by taking part in self-protection of *H. pylori* from the acidic environment within the gastric lumen and in the colonization of mucin layer covering the gastric mucosa, Urea A may play a role in the first step of the inflammatory process caused by *H. pylori* in the host.
This is deemed the colonization step as *H. pylori* is implicated as a triggering factor in aneurysm pathology with potential atherosclerotic grounds developed in aorta wall (Kusters *et al.,* 2006; Fan *et al.,* 1998; Montecucco *et al.,* 2003).
In our study, antigens of *H. pylori*, such as p33, p26, p19 and p17, were found in similar rates in the patient group and HCG cases, and no statistically significant difference was found between the groups ($p>0.05$). These results made us believe that more new studies are required on the pathogeneses in clinical settings developed by *H. pylori* primarily in the gastroduodenal area and extra-gastric areas, and about the virulence of such antigens.
Assessing *H. pylori* IgG positivity in patient and HCG group cases in terms of gender, a significant difference in WB IgG seropositivity was found only between male cases with AsAA and male HCG cases ($p<0.05$). Even though we could not find any other study like ours in the literature, another study dated 2001 conducted with study groups and appropriate tools and methods different from our patient groups (Ross, 1993) reported a significant relationship between male cases with carotid atherosclerosis and *H. pylori* presence.
It was also reported by Epsinola-Klein (2002) in 2002 that IgG seropositivity was significantly correlated with male cases based on the relationship between 572 cases with atherosclerosis and *H. pylori*.
Another study conducted by Mayr *et al.* (2003) in 2003 reported that *H. pylori* IgG seropositivity was hiugher in female cases than in male cases

among a study group of 684 cases with atherosclerosis.

Examining the results of the study on gender and the literature, although it was reported that male cases present a significant risk group for atherosclerosis and associated heart diseases, no such finding was obtained in our study cases with AAA.

A significant difference in *H. pylori* seropositivity between the cases with AsAA and AAA+AsAA in the 45-55 age group and the HCG cases in the same age group ($p < 0.05$), *H. pylori* seropositivity rates found in three different age groups with AAA presented no significant difference compared to HCG cases ($p > 0.05$).

Only two publications found in the literature review for the relationship between aortic aneurysm and *H. pylori* seropositivity suggested that *H. pylori* IgG seropositivity was significantly high in cases under 65-55 of age included in the case-control study conducted for the relationship between atherosclerosis-associated coronary vascular disease and *H. pylori*.

These papers also reported that such seropositivity posed a risk of myocardial infarction 1.8 times larger for patients under 65, and 2.25 times larger for patients under 55 (Lindholt and Shi, 2006), even though no comparison was made between patient and HCG groups in terms of *H. pylori* IgG seropositivity based on age groups. Mendall *et al.* (1994) also reported that *H. pylori* IgG seropositivity was significantly higher among male patients 45-65 of age.

Comparing the AAA and AsAA groups with HCG cases in terms of *H. pylori* IgG seropositivity based on smoker and non-smoker groups, a significant difference in *H. pylori* IgG seropositivity was found between the smoker cases of both groups and HCG cases ($p < 0,05$), whereas non-smokers presented no difference ($p > 0,05$).

Though we could not find a detailed study like ours in the literature review, a study conducted by Nyberg *et al.* (2008) with HCG groups divided into as smoker or non-smoker groups with AAA, found no significant difference in *H. pylori* IgG positivity between AAA and HCG groups. Koenig *et al.* (1999) reported in their study evaluating 312 cases with coronary cardiac disease and 479 control group cases that *H. pylori* IgG seropositivity was significantly higher among the smoker patient group.

The significant difference in *H. pylori* IgG seropositivity found between smoker patient groups and smoker HCG groups of our study suggests that chronic *H. pylori* infection accompanied by smoking habits may contribute to the development of atherosclerosis-associated abdominal and ascending aneurysms.

In conclusion, even though we found a significant difference in *H. pylori* seropositivity between AAA and HCG groups of our study conducted as the second seroepidemiology-based study after the Swedish study (Nyberg *et al.,* 2008) of 2008 investigating aortic aneurysms, primarily abdominal aortic aneurysm etiopathogenesis caused by *H. pylori* associated with these diseases and studied partially seroepidemiologically, but predominantly with molecular methods on the relationship between carotid atherosclerosis and coronary heart diseases, a difference was found between AsAA and HCG groups, and the statistically significant difference between Vac A ratios of cases with AAA and AsAA, which are claimed to be caused by multi-factorial reasons, and that of HCG cases suggests that VacA rather than CagA plays a important role in development of these two aneurysms, particularly ruptured and non-ruptured aneurysms potentially associated with atherosclerosis.

However, it is concluded that prospective, large-series new studies should be conducted to detect *H. pylori* DNA specifically using molecular methods to be applied on aneurysm tissue, in order to make a clearer description of the etiopathogenetic relationship between the two types of aneurysms and *H. pylori.*

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