JMB 2009; 28 (1) DOI: 10.2478/v10011-008-0034-z

UDK 577.1 : 61 **ISSN 1452-8258**

JMB 28: 22–29, 2009

Original paper
Originalni naučni rad

THE INFLUENCE OF CHRONIC *HELICOBACTER PYLORI* INFECTION ON SOME SERUM LIPID PROFILE PARAMETERS, APOLIPOPROTEINS A-I AND B AND Lp(a) LIPOPROTEIN

UTICAJ HRONIČNE *HELICOBACTER PYLORI* INFEKCIJE NA NEKE PARAMETRE LIPIDSKOG STATUSA, APOLIPOPROTEINE A-I I B I Lp(a) LIPOPROTEIN

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Summary: Data on proatherogenic lipid profile alterations due to chronic *Helicobacter pylori (HP)* infection are contradictory. Aim of this study was to examine the differences in some lipid parameters between 55 subjects of both gender with a chronic HP infection (IgG>50 U/mL and IgA <20 U/mL) and 55 gender matched HP seronegative subjects (IgG and IgA <20 U/mL). Total cholesterol (TC) ($p<0.001$), triglycerides (TG) ($p<0.05$), LDL-cholesterol (LDL-C) ($p<0.02$), non-HDL-cholesterol (non-HDL-C), apolipoprotein (apo) B ($p<0.001$), Lp(a) and HDL-cholesterol (HDL-C) serum levels were higher in HP seropositive than in seronegative subjects, while there were almost no differences in apo A-I. In HP seropositive subjects, the frequency of pathological TC ($p<0.001$), TG ($p<0.05$), LDL-C ($p<0.01$), non-HDL-C ($p<0.01$), apo B ($p<0.02$) and Lp(a) serum levels was higher compared to seronegative. Serum HP IgG titers correlated negatively with TC, LDL-C ($p<0.05$), non-HDL-C, apo B and Lp(a) levels, and positively with TG, HDL-C and apo A-I levels. Results are similar for both genders. Our results confirm the hypothesis that a chronic HP infection could modify the lipid profile in a proatherogenic way.

Keywords: atherosclerosis, *Helicobacter pylori*, lipids, atherogenic risk

Kratak sadržaj: Podaci o proaterogenim promenama lipidskog statusa u sklopu hronične *Helicobacter pylori (HP)* infekcije su kontradiktorni. Cilj istraživanja bio je da se ispitaju razlike u nekim lipidskim parametrima između 55 osoba oba pola s hroničnom HP infekcijom (IgG >50 U/mL i IgA <20 U/mL) i 55 HP seronegativnih osoba (IgG i IgA <20 U/mL) oba pola. Serumske koncentracije ukupnog holesterola (TC) ($p<0,001$), triglicerida (TG) ($p<0,05$), LDL-holesterola (LDL-C) ($p<0,02$), non-HDL-holesterola (non-HDL-C), apolipoproteina (apo) B ($p<0,001$), Lp(a) i HDL-holesterola (HDL-C) bile su više kod HP seropozitivnih u odnosu na seronegativne osobe, dok gotovo da nije bilo razlika u nivoima apo A-I. Kod HP seropozitivnih osoba, učestalost patoloških TC ($p<0,001$), TG ($p<0,05$), LDL-C ($p<0,01$), non-HDL-C ($p<0,01$), apo B ($p<0,02$) i Lp(a) vrednosti bila je viša u odnosu na seronegativne. Ustanovljena je negativna korelacija serumskih titara HP IgG antitela s TC, LDL-C ($p<0,05$), non-HDL-C, apo B i Lp(a), a pozitivna s TG, HDL-C i apo A-I nivoima. Rezultati su slični za oba pola. Naši rezultati idu u prilog hipotezi da bi hronična HP infekcija mogla da modifikuje lipidske parametre na proaterogeni način.

Ključne reči: ateroskleroza, *Helicobacter pylori*, lipidi, aterogeni rizik

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List of abbreviations: HP – *Helicobacter pylori*; Cag A – cytotoxin-associated gene A; IgG – immunoglobulin G; IgA – Immunoglobulin A; IL-6 – interleukin-6; TNF-α – tumor necrosis factor alpha; SAA – serum amyloid A; apo – apolipoprotein; apo A-I – apolipoprotein A-I; apo B – apolipoprotein B; apo (a) – apolipoprotein (a); LDL – low-density lipoprotein; HDL – high-density lipoprotein; non-HDL – non-high-density lipoprotein; Lp(a) – lipoprotein (a); TC – total cholesterol; TG – triglycerides; HDL-C – HDL-cholesterol; LDL-C – LDL-cholesterol; non-HDL-C – non-HDL-cholesterol

Introduction

In the past few years, many studies have indicated that atherosclerosis is associated with several infectious pathogens, including *Helicobacter pylori*, *Chlamydia pneumoniae*, cytomegalovirus and herpes simplex virus (1–8). There has been increasing evidence that inflammation and infection could alter some atherogenic vascular factors involved in the development of atherosclerosis and its complications. The number of infectious pathogens to which an individual has been exposed (pathogen burden) has been linked to the development and prognosis of coronary artery disease (7, 9).

Helicobacter pylori (HP) is a gram-negative microaerophilic spiral bacterium which causes one of the most prevalent infections in the world, affecting approximately 50% of the world's population (10). HP occurs naturally and inhabits the mucous layer that covers the gastric epithelial cells. It is considered to be a causative agent of many gastrointestinal (e.g., peptic ulcer, gastric adenocarcinoma, primary gastric lymphoma of the mucosa-associated lymphoid tissue) and extra-gastric (e.g., atherosclerotic processes, peripheral vascular disorders, skin diseases) manifestations.

Recent studies have suggested that chronic HP infection may be associated with an increase of the atherogenic risk (2, 3, 8, 11) and several possible mechanisms of this relationship have been reported. Proposed mechanisms involving HP in the atherogenesis are production of excessive amounts of proinflammatory factors (such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α)) (8) and acute phase reactants (such as fibrinogen and C reactive protein) (12), cross-mimicry between HP and host proteins (13), immunomediated vascular damage and endothelial dysfunction (2), modifying the serum lipid profile (14) and promotion of the oxidation of LDL-cholesterol (15), abnormalities in haemostasis (9), hyperhomocysteinemia, direct bacterial invasion of atherosclerosis plaques, etc. Recently, it has been hypothesized that only certain HP strains, which express the cytotoxin-associated gene A (Cag A) encoding the Cag A protein, may have a link with atherosclerosis (3, 9), but this is still controversial (11).

Although most authors reported about an association between HP infection and a proatherogenic lipid profile (6, 16–19) which was normalized after successful eradication of HP (4, 20), few studies did not confirm these results (1, 2, 5, 10, 21). Therefore, the influence of chronic HP infection on lipid parameter changes and their implication in atherogenic mechanisms of this infection are still unclear.

The aim of this study was to examine the influence of chronic HP infection on some lipid parameters i.e. the lipid parameter differences between subjects with chronic HP infection and HP seronegative ones.

Materials and Methods

Fifty-five subjects (20 male and 35 female) with chronic HP infection (mean age 50.12±13.82 years) and 55 gender matched HP seronegative subjects (mean age 40.02±16.88 years), singled out consecutively in the frame of routine work in the Department of Specialised Laboratory Diagnostics (Center for Laboratory Medicine, Clinical Center of Vojvodina), were evaluated. Immunoglobulin G (IgG) titer for HP higher than 50 U/mL and immunoglobulin A (IgA) titer for HP lower than 20 U/mL were regarded as chronic HP infection, whereas IgG and IgA titers lower than 20 U/mL were regarded as absence of HP infection.

After an overnight fasting period of 12–14 hours, blood samples were taken, serum samples were separated from the cells by centrifugation at 3000 rpm for 10 min, and serum IgG and IgA for HP, total cholesterol (TC), triglycerides (TG), HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C), as well as apolipoprotein (apo) A-I, apo B and Lp(a) lipoprotein (Lp(a)) levels were measured.

IgG and IgA titers for HP were measured by the enzyme-linked immunosorbent assay (ELISA) (Virion/serion, Germany). Concentrations of serum TC (BioMérieux, France), TG (BioMérieux, France) and HDL-C (Randox, United Kingdom) were determined by standard enzymatic methods on an autoanalyzer (Technicon RA-XT System, Technicon Instruments Corporation, USA). Values of LDL-C (Friedewald formula) (22) and non-HDL-C (non-HDL-C = TC – HDL-C) were obtained by calculation. Apo A-I and B (Olympus, Lismeehan, Ireland) and Lp(a) (Sentinel, Milano, Italy) serum levels were measured by immunoturbidimetry on an autoanalyzer (Olympus AU 400, Olympus, Germany). Lipid parameter levels above or below the desirable serum concentrations were regarded as pathological (23).

All the examined parameters were expressed as mean value and standard deviation. Their comparisons and the significance assessment of obtained differences were performed using the Student's *t*-test. The significance assessment of the HP IgG titer and examined lipid parameter relationship were performed using correlation analyses according to the Pearson's correlation test. A p value <0.05 was accepted as significant.

Results were treated using the Microsoft Excel 2000 program for statistical data treatment.

Results

In the examined group, differences with regard to age between HP seropositive and seronegative subjects were found. Considering all subjects (50.12 ±13.82 vs. 40.02±16.88 years; $p<0.001$), as well as females (48.86±13.15 vs. 38.13±16.28 years, $p<0.01$), HP seropositive patients were significantly

Table I Lipid parameter serum levels in HP seropositive and seronegative subjects.

	All subjects		Men		Women	
	HP positive (n = 55)	HP negative (n = 55)	HP positive (n = 20)	HP negative (n = 20)	HP positive (n = 35)	HP negative (n = 35)
mmol/L						
TC	6.01±1.04****	5.18±0.97	6.05±1.02	5.33±1.20	5.98±1.07****	5.10±0.82
TG	1.86±1.16*	1.42±0.78	2.28±1.29*	1.57±0.75	1.62±1.03	1.34±0.80
HDL-C	1.39±0.29	1.31±0.22	1.35±0.41	1.24±0.20	1.40±0.20	1.35±0.22
LDL-C	3.69±1.14**	3.23±0.78	3.52±1.20	3.38±0.96	3.79±1.11***	3.14±0.66
non-HDL-C	4.62±0.98****	3.87±0.97	4.69±0.86	4.09±1.12	4.58±1.06****	3.75±0.86
g/L						
Apo A-I	1.37±0.15	1.37±0.13	1.33±1.13	1.33±0.10	1.40±0.12	1.39±0.14
Apo B	1.10±0.26****	0.90±0.23	1.13±0.22***	0.93±0.23	1.08±0.28***	0.89±0.23
Lp(a)	0.28±0.28	0.21±0.27	0.23±0.23	0.19±0.24	0.31±0.30	0.22±0.29

HP – *Helicobacter pylori*; TC – total cholesterol; TG – triglycerides; HDL-C – HDL-cholesterol; LDL-C – LDL-cholesterol; non-HDL-C – non-HDL-cholesterol; Apo A-I – apolipoprotein A-I; Apo B – apolipoprotein B; Lp(a) – Lp(a) lipoprotein. Values are presented as mean ± standard deviation. Statistical significance with respect to HP seronegative subjects: * p<0.05; ** p<0.02; *** p<0.01; **** p<0.001.

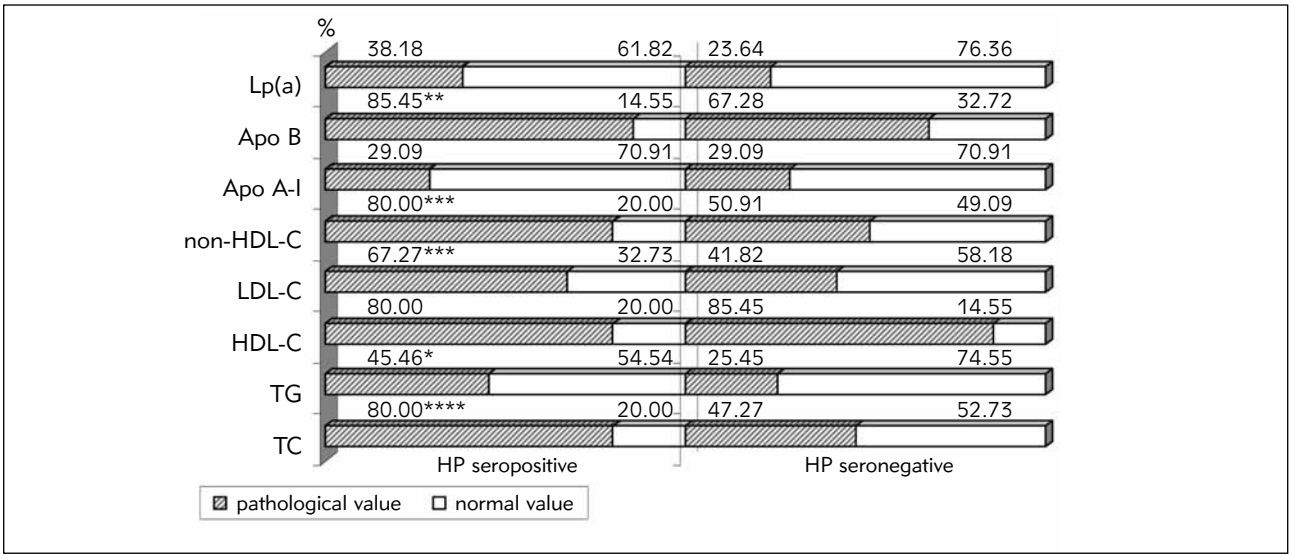

Figure 1 Frequency of pathological lipid parameter levels in HP seropositive and seronegative subjects.

HP – *Helicobacter pylori*; TC – total cholesterol; TG – triglycerides; HDL-C – HDL-cholesterol; LDL-C – LDL-cholesterol; non-HDL-C – non-HDL-cholesterol; Apo A-I – apolipoprotein A-I; Apo B – apolipoprotein B; Lp(a) – Lp(a) lipoprotein. Statistical significance with respect to HP seronegative subjects: * p<0.05; ** p<0.02; *** p<0.01; **** p<0.001.

older than those HP seronegative, while in males this difference did not reach statistical significance (52.88 ±15.27 vs. 43.56 ±17.93 years).

The examined lipid parameter values are shown in *Table I*. Serum TC, TG, LDL-C, HDL-C, non-HDL-C, as well as apo B and Lp(a) levels of HP seropositive subjects were higher than those of HP seronegative ones. In the whole subject group, TC (p<0.001), TG (p<0.05), LDL-C (p<0.02), non-HDL-C (p<0.001) as well as apo B (p<0.001) levels were significantly higher in HP seropositive subjects, while differences in Lp(a) (33.33%) and HDL-C (6.11%) levels were insignificant. Similar results were found with regard to gender. HP seropositive females had significantly higher TC (p<0.001), LDL-C (p<0.01), non-HDL-C (p<0.001) and apo B (p<0.01) levels, while TG (20.90%), Lp(a) (40.91%) and HDL-C (3.70%) levels were higher without significance. In HP seropositive males, only TG (p< 0.05) and apo B (p<0.01) levels were significantly higher than in seronegative male subjects, and differences in TC (13.51%), LDL-C (4.14%), HDL-C (8.87%), non-HDL-C (14.67%) and Lp(a) (21.05%) levels were not significant.

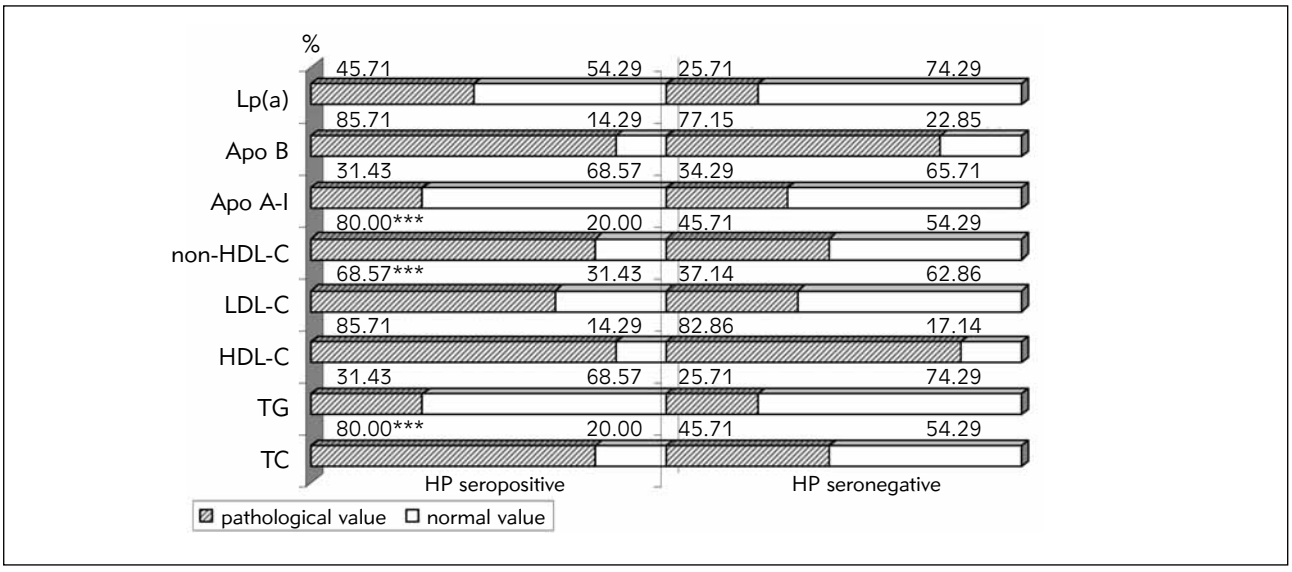

Figure 2 Frequency of pathological lipid parameter levels in HP seropositive and seronegative women.

HP – *Helicobacter pylori*; TC – total cholesterol; TG – triglycerides; HDL-C – HDL-cholesterol; LDL-C – LDL-cholesterol; non-HDL-C – non-HDL-cholesterol; Apo A-I – apolipoprotein A-I; Apo B – apolipoprotein B; Lp(a) – Lp(a) lipoprotein. Statistical significance with respect to HP seronegative subjects: * $p<0.05$; ** $p<0.02$; *** $p<0.01$.

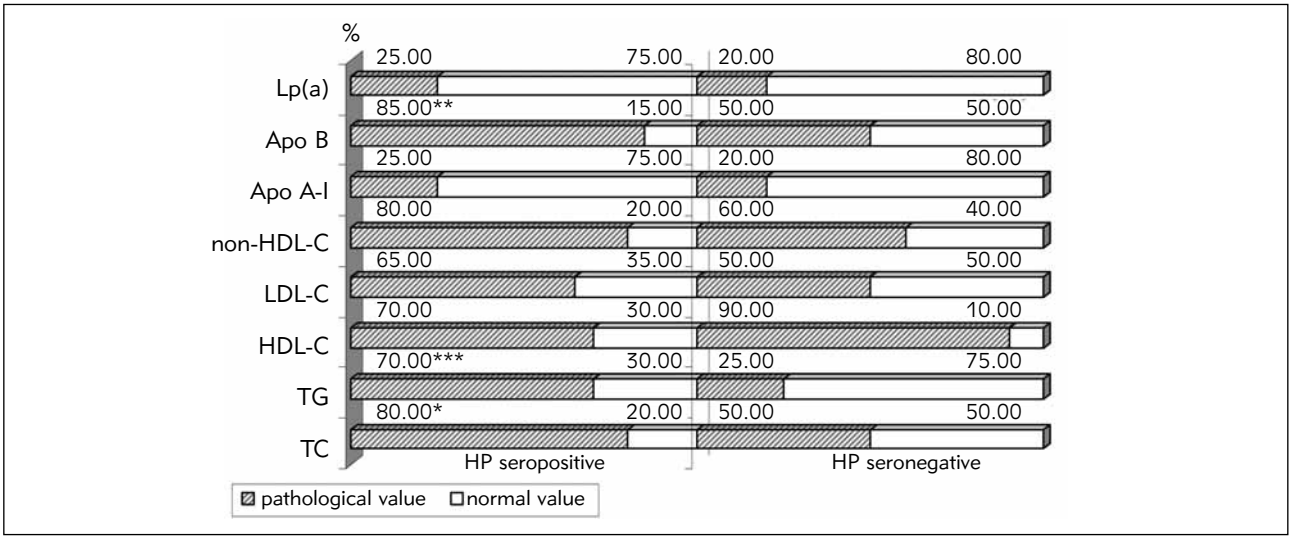

Figure 3 Frequency of pathological lipid parameter levels in HP seropositive and seronegative men.

HP – *Helicobacter pylori*; TC – total cholesterol; TG – triglycerides; HDL-C – HDL-cholesterol; LDL-C – LDL-cholesterol; non-HDL-C – non-HDL-cholesterol; Apo A-I – apolipoprotein A-I; Apo B – apolipoprotein B; Lp(a) – Lp(a) lipoprotein. Statistical significance with respect to HP seronegative subjects: * $p<0.05$; ** $p<0.02$; *** $p<0.01$; **** $p<0.001$.

Analysis of the frequency of pathological levels of examined lipid parameters showed that HP seropositive subjects had pathological TC, TG, LDL-C, non-HDL-C and apo B levels significantly more frequently than HP seronegative subjects, while higher frequency of pathological Lp(a) levels was not statistically significant. Differences in the frequency of pathological HDL-C and apo A-I levels between HP seropositive and seronegative subjects were not statistically significant. In the whole subject group (*Figure 1*), the frequency of pathological TC (80.00 vs. 47.27%; $p<0.001$), TG (45.46 vs. 25.45%; $p<0.05$), LDL-C (67.27 vs. 41.82%; $p<0.01$), non-HDL-C (80.00 vs. 50.91%; $p<0.01$), and apo B (85.45 vs. 67.28%; $p<0.02$) levels were significantly higher, while pathological Lp(a) levels (38.18 vs. 23.64%) were insignificantly more frequent. HP seropositive females (*Figure 2*) had pathological TC (80.00 vs. 45.71%; $p<0.01$), LDL-C (68.57 vs. 37.14%; $p<0.01$) and non-HDL-C (80.00 vs. 45.71%; $p<0.01$) levels significantly more frequently, while higher frequency of pathological TG (31.43 vs. 25.71%), apo B (85.71 vs. 77.15%) and

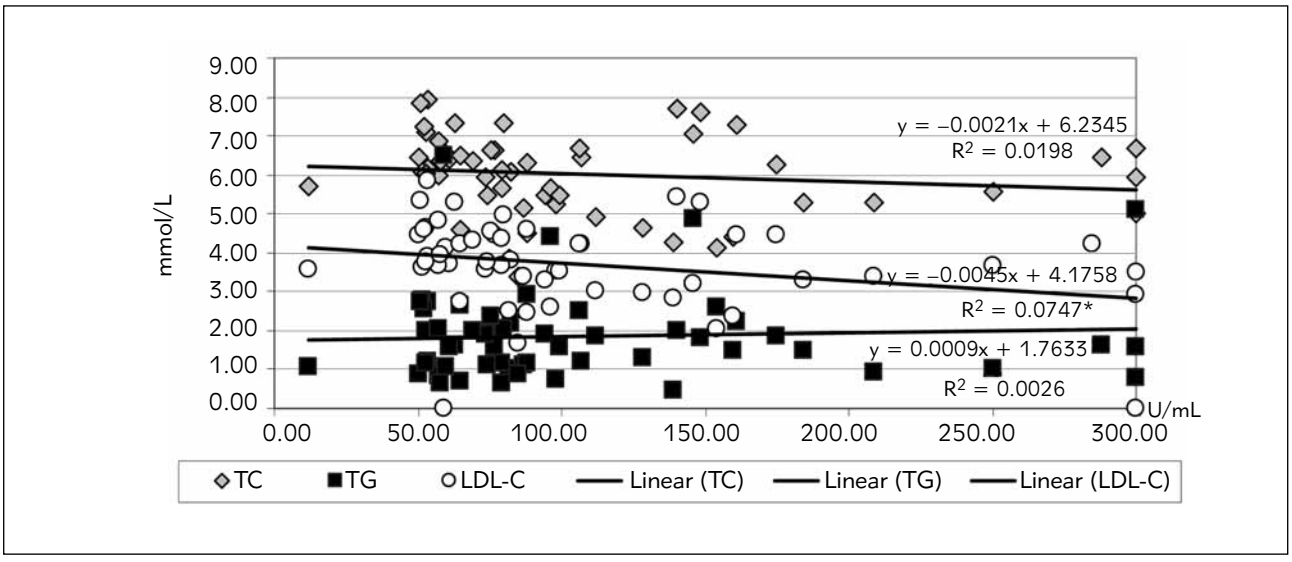

Figure 4 Correlation between serum HP IgG titers and total cholesterol, triglyceride and LDL-cholesterol levels in HP seropositive subjects.

HP – *Helicobacter pylori*; TC – total cholesterol; TG – triglycerides; LDL-C – LDL-cholesterol. Statistical significance of univariate correlation analysis: * $p<0.05$.

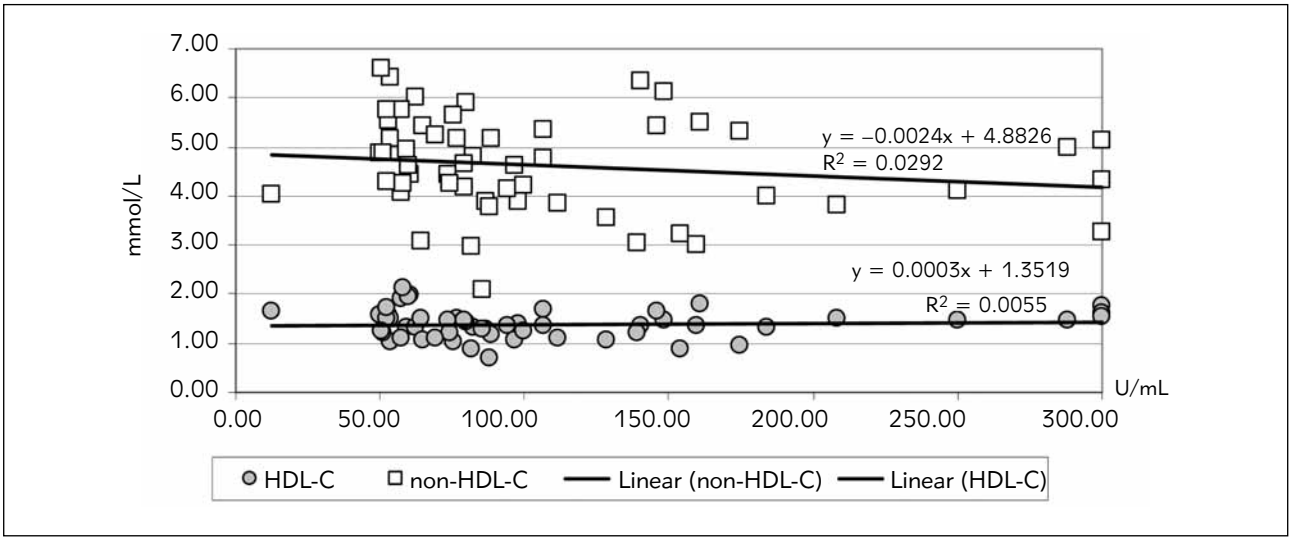

Figure 5 Correlation between serum HP IgG titers and HDL-cholesterol and non-HDL-cholesterol levels in HP seropositive subjects.

HP – *Helicobacter pylori*; HDL-C – HDL-cholesterol; non-HDL-C – non-HDL-holesterol.

Lp(a) (45.71 vs. 25.71%) levels was not significant. In HP seropositive males (*Figure 3*), the frequency of pathological levels was significantly higher for TC (80.00 vs. 50.00%; $p<0.05$), TG (70.00 vs. 25.00%; $p<0.01$) and apo B (85.00 vs. 50.00%; $p<0.02$), but for LDL-C (65.00 vs. 50.00%), non-HDL-C (80.00 vs. 60.00%) and Lp(a) (25.00 vs. 20.00%) higher frequency was not significant.

To evaluate the relationship between atherosclerosis risk factors of lipid origin and chronic HP infection, univariate correlation analyses were performed between the examined lipid parameters and HP IgG titers in seropositive subjects (*Figure 4–6*). Serum HP IgG titers correlated negatively with TC ($r = –0.147$), LDL-C ($r = –0.279$), non-HDL-C ($r = –0.181$), apo B ($r = –0.123$) and Lp(a) ($r = –0.193$) levels, significantly only with LDL-C ($p<0.05$). Positive correlations with TG ($r = 0.042$), as well as with HDL-C ($r = 0.088$) and apo A-I ($r = 0.219$) levels did not reach statistical significance.

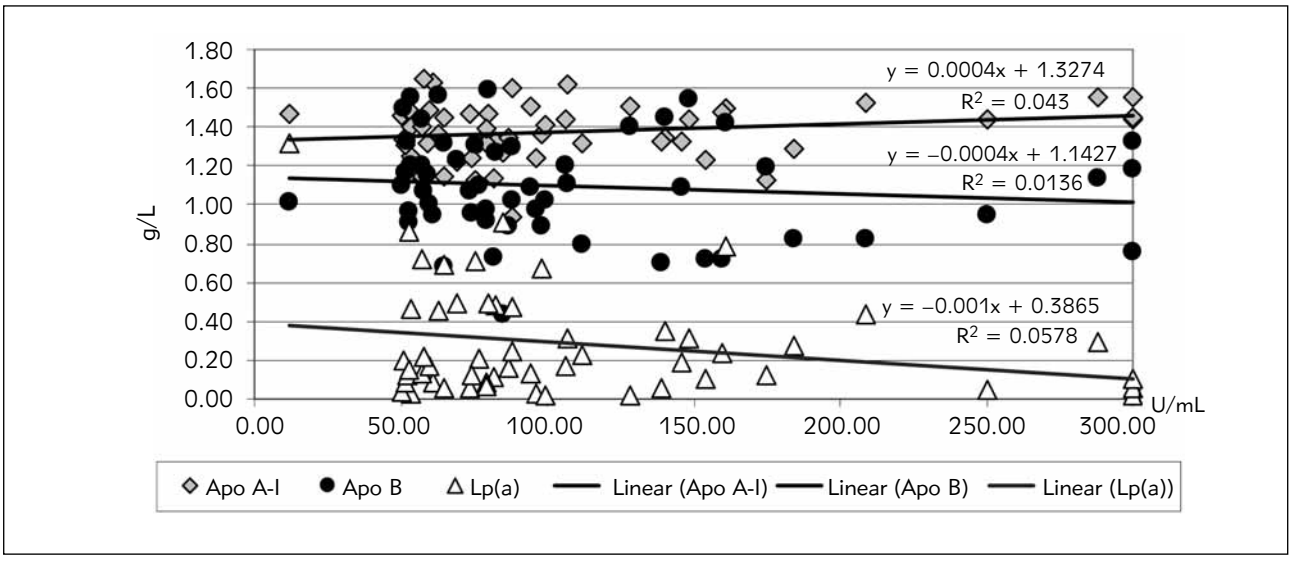

Figure 6 Correlation between serum HP IgG titers and apo A-I, apo B and Lp(a) levels in HP seropositive subjects.

HP – *Helicobacter pylori*; Apo A-I – apolipoprotein A-I; Apo B – apolipoprotein B; Lp(a) – Lp(a) lipoprotein.

Discussion

Analysis of the examined group showed that HP seropositive subjects were older than seronegative ones in the whole subject group ($p<0.001$), as well as in females ($p<0.01$) and males. This is in agreement with the previous reports which indicated higher seropositivity in an older population (3, 11, 16, 24). Sung et al. (16) who analyzed the seropositivity rate in different age groups of Korean adults found the highest seropositivity rate in participants over 50 and the lowest in subjects younger than 30 years, and also that HP seropositive participants were significantly older than those seronegative ($p<0.05$). Chimienti et al. (11) found that HP infected subjects were significantly older than uninfected (50.8±8.3 vs. 43.5± 10.5 years; $p<0.0001$), as well. The reason for this could be a long period of possible exposure to the pathogen, as well as coexistence of other pathological conditions and a weaker defense ability in older persons, which could contribute to higher proneness to infectious agents. However, few studies did not confirm this finding (1, 2, 10, 17, 18).

In our investigated patients, serum TC ($p<0.001$), TG ($p<0.05$), LDL-C ($p<0.02$), non-HDL-C ($p<0.001$) and apo B ($p<0.001$) levels were significantly higher in HP seropositive than in seronegative subjects, while the difference in Lp(a) levels (33.33%) was not significant. There were almost no differences in HDL-C and apo A-I levels. The results were similar in both gender groups.

Most authors observed higher atherogenic lipid parameter levels in HP seropositive subjects in comparison with seronegative ones, which is consistent with our results. Aslan et al. (17) and Sung et al. (16) reported that serum TG, TC and LDL-C levels in HP seropositive subjects were significantly higher than in HP seronegative ones (all $p<0.05$). In a study of Kanbay et al. (20), normalization in lipid parameters after a successful eradication of HP infection was observed. Majka et al. (4) and Kucukazman et al. (18) found that plasma levels of TC and LDL-C were significantly higher in HP seropositive subjects, and after 6 months of successful anti-HP therapy those levels were significantly lowered (4). Hoffmeister et al. (19) reported an atherogenic modified lipid profile associated with HP infection and after multivariable adjustment, association with increased apo B levels persisted and remained significant ($p=0.02$). Significantly higher serum TG concentrations ($p= 0.03$) in HP seropositive subjects were found by Niemela et al. (6). However, some authors (1, 2, 5, 10, 21) reported no difference in TC, TG and LDL-C levels of HP seropositive and seronegative status.

Elevation of TG has been detected especially in infections caused by gram-negative bacteria (14) such as HP. It is thought that HP induced inflammation can be a trigger to the production of high levels of IL-6 and TNF-α. It is known that IL-6 can increase hepatic gluconeogenesis and TG synthesis and TNF-α inhibits lipoprotein lipase activity and stimulates hepatic lipogenesis, leading to lipid mobilisation from tissues and to elevated serum TG and lowered HDL-C concentrations (1, 10, 14). The pathogenic mechanisms underlying the increase in TC and LDL-C levels in HP seropositive subjects are still unclear. A possible suggested mechanism is that the effect of HP might be mediated via certain cytokines that can modulate enzyme activity and receptor expression and induce oxidative stress, affecting cholesterol metabolism (1, 14, 25–28), but this hypothesis needs more explanation.

Reported data concerning HDL-C and apo A-I levels in HP infection are also contradictory. Most studies have reported lower HDL-C and apo A-I levels in HP seropositive subjects compared to seronegative ones (6, 14–17, 19, 24) or their increase after HP eradication treatment (1, 29). It is known that HDL-C, as a negative acute phase reactant (29), has an antiinflammatory activity (30) and low concentrations in various inflammatory diseases in human beings and animals (6, 7, 12, 19, 31) have been reported. The decrease in HDL-C levels can be related to an increase in serum amyloid A (SAA) during chronic inflammation which becomes the major HDL apolipoprotein replacing apo A-I. The SAA-enriched particles become denser and larger, and because of that their clearance is increased. Besides, it has been reported that SAA inhibits lecithin-cholesterol acyltransferase activity, and both mechanisms can reduce the concentrations of HDL-C (1). Our results are in agreement with the studies which have observed no significant difference in HDL-C and apo A-I levels between HP seropositive and seronegative subjects (2, 5, 10, 18).

Explanation for higher Lp(a) levels that we have found could rely on the immunologic response induced in the host. It has been reported that HP infection is able to affect the concentrations of both mucosal and circulating proinflammatory cytokines (especially IL-6 (1)) (32) and later has been shown to have a role in modulating (i.e. stimulating) the apolipoprotein (a) (apo (a)) gene expression (33). De Luis et al. (1) observed a decrease in Lp(a) levels ($p<0.05$) after HP eradication treatment in type 1 diabetic patients, but in the study of Scharnagl et al. (29) changes in Lp(a) levels after eradication treatment were not observed. Sung et al. (16) and Paximadas et al. (21) did not find any significant difference in Lp(a) levels between HP seropositive and seronegative subjects. Inconsistency of these results was explained by Chimienti et al. (11). They found that HP seropositive subjects infected by the CagA(–) strains showed a reduction and by the CagA(+) strains an increase in the Lp(a) levels when compared with the uninfected ones, suggesting that the variations in the Lp(a) levels might derive from an altered balance between Lp(a) stimulatory and inhibitory cytokines, that could be different for the two strains.

Univariate correlation analyses in HP seropositive subjects showed negative correlation of HP IgG titers with serum TC, LDL-C ($p<0.05$), non-HDL-C, apo B and Lp(a), and positive correlation with TG, HDL-C and apo A-I serum levels. Our subject population was relatively small, so there may be a limitation related to the statistical power of obtained results. Negative correlation of TC, LDL-C and apo B levels with serum HP IgG titers might be a consequence of the higher rate of catabolism and/or cholesterol consumption in inflammatory processes which occur in the infectious focus. Besides, although it is known that Lp(a) is a positive, and HDL-C a negative reactant of the acute inflammatory phase, our correlation analyses results are not consistent with these evidence. Opposite to our results, Sung et al. (16) reported a significant positive correlation of HP IgG titers with TC, LDL-C and apo B and a negative correlation with HDL-C and apo A-I levels in apparently healthy Korean adults.

Our results showed that chronic HP infection is associated with higher serum levels of proatherogenic lipid parameters, namely, total cholesterol, triglycerides, LDL-cholesterol, non-HDL-cholesterol, as well as apolipoprotein B and Lp(a) lipoprotein. This supports the hypothesis that chronic HP infection could contribute to atherosclerosis development by modifying lipid metabolism in a proatherogenic way. Further research is needed to clarify the precise role of Helicobacter pylori infection and proper mechanisms of its effects on the development of atherosclerosis.

References

1. De Luis DA, Garcia Avello A, Lasuncion MA, Aller R, Martin De Argila C, Boixeda De Miquel D, De La Calle H. Improvement in lipid and haemostasis patterns after Helicobacter pylori infection eradication in type 1 diabetic patients. Clin Nutr 1999; 18 (4): 227–31.
2. Oshima T, Ozono R, Yano Y, Oishi Y, Teragawa H, Higashi Y, Yoshizumi M, Masayuki Kambe M. Association of Helicobacter pylori Infection With Systemic Inflammation and Endothelial Dysfunction in Healthy Male Subjects. J Am Coll Cardiol 2005; 45: 1219 –22.
3. Sawayama Y, Ariyama I, Hamada M, Otaguro S, Machi T, Taira Y, Hayashi J. Association between chronic *Helicobacter pylori* infection and acute ischemic stroke: Fukuoka Harasanshin Atherosclerosis Trial (FHAT). Atherosclerosis 2005; 178: 303–9.
4. Majka J, Rog T, Konturek PC, Konturek SJ, Bielanski W, Kowalsky M, Szczudlik A. Influence of chronic Helicobacter pylori infection on ischemic cerebral stroke risk factors. Med Sci Monit 2002; 8 (10): CR675–84.
5. Lu YH, Yen HW, Lin TH, Huang CH, Lee KT, Wang WM, Wu DC, Voon WC, Lai WT, Sheu SH. Changes of coronary risk factors after eradication of Helicobacter pylori infection. Kaohsiung J Med Sci 2002; 18 (6): 266–72.
6. Niemela S, Karttunen T, Korhonen T, Läärä E, Karttunen R, Ikäheimo M, Kesäniemi YA. Could Helicobacter pylori infection increase the risk of coronary heart disease by modifying serum lipid concentrations? Heart 1996; 75: 573–5.
7. Georges JL, Rupprecht HJ, Blankenberg S, Poirier O, Bickel C, Hafner G, Nicaud V, Meyer J, Cambien F, Tiret

L. Impact of pathogen burden in patients with coronary artery disease in relation to systemic inflammation and variation in genes encoding cytokines. Am J Cardiol 2003; 92: 515–21.

8. Franceschi F, Leo D, Fini L, Santoliquido A, Flore R, Tondi P, Roccarina D, Nista EC, Cazzato AI, Lupascu A, Pola P, Silveri NG, Gasbarrini G, Gasbarrini A. *Helicobacter pylori* infection and ischaemic heart disease: An overview of the general literature. Dig Liver Dis 2005; 37: 301–8.
9. Grabczewska Z, Nartowicz E, Kubica J, Rošć D. Endothelial function parameters in patients with unstable angina and infection with Helicobacter pylori and Chlamydia pneumoniae. Eur J Intern Med 2006; 17: 339–42.
10. Hamed SA, Amine NF, Galal GM, Helal SR, Tag El Din LM, Shawky OA, Ahmed EA, Abdel Rahman MS. Vascular Risks and Complications in Diabetes Mellitus: The Role of Helicobacter Pylori Infection. J Stroke Cerebrovasc Dis 2008; 17 (2): 86–94.
11. Chimienti G, Russo F, Lamanuzzi BL, Nardulli M, Messa C, Di Leo A, Correale M, Giannuzzi V, Pepe G. *Helicobacter pylori* is associated with modified lipid profile: impact on Lipoprotein(a). Clin Biochem 2003; 36: 359–65.
12. Mostaza JM, Camino N, Gerique JG, Pena R, Baquero M, Lahoz C. C-reactive protein levels and prevalence of chronic infections in subjects with hypoalphalipoproteinemia. Metabolism 2005; 54: 33–7.
13. Lamb DJ, El Sankary W, Ferns GAA. Molecular mimicry in atherosclerosis: a role for heat shock proteins in immunisation. Atherosclerosis 2002; 167: 177–85.
14. Laurila A, Bloigu A, Nayha S, Hassi J, Leinonen M, Saikku P. Association of *Helicobacter pylori* infection with elevated serum lipids. Atherosclerosis 1999; 142: 207–10.
15. Kayo S, Ohsawa M, Ehara S, Naruko T, Ikura Y, Hai E, Yoshimi N, Shirai N, Tsukamoto Y, Itabe H, Higuchi K, Arakawa T, Ueda M. Oxidized low-density lipoprotein levels circulating in plasma and deposited in the tissues: Comparison between Helicobacter pylori-associated gastritis and acute myocardial infarction. Am Heart J 2004; 148: 818–25.
16. Sung KC, Rhee EJ, Ryu SH, Beck SH. Prevalence of Helicobacter pylori infection and its association with cardiovascular risk factors in Korean adults. Int J Cardiol 2005; 102: 411–7.
17. Aslan M, Nazligul Y, Horoz M, Bolukbas C, Bolukbas FF, Gurc M, Celik H, Erel O. Serum paraoxonase-1 activity in Helicobacter pylori infected subjects. Atherosclerosis 2008; 196: 270–4.
18. Kucukazman M, Yavuz B, Sacikara M, Asilturk Z, Ata N, Ertugrul D, Yalcin A, Kizilca G, Yenigun E, Ulger Z, Nazligul Y. Evaluation of lipid levels in patients infected with Helicobacter pylori [abstract]. Atherosclerosis Supp 2008; 9 (1): 83.
19. Hoffmeister A, Rothenbacher D, Bode G, Persson K, Marz W, Nauck MA, Brenner H, Hombach V, Koenig W. Current infection with Helicobacter pylori, but not seropositivity to Chlamydia pneumoniae or cytomegalovirus, is associated with an atherogenic, modified lipid profile. Arterioscler Thromb Vasc Biol 2001; 21: 427–32.
20. Kanbay M, Gur G, Yucel M, Yilmaz U, Boyacioglu S. Does eradication of *Helicobacter pylori* infection help normalize serum lipid and CRP levels? Dig Dis Sci 2005; 50: 1228–31.
21. Paximadas S, Pagoni ST, Kosmidis M, Tsarouchas X, Christou M, Chatziantonakis N, Papachilleos P. The lipid profile in adults with negative or positive antibody Helicobacter pylori [abstract]. Atherosclerosis Supp 2005; 6 (1): 74.
22. Friedewald TW, Levy IR, Fredrickson SD. Estimation of the concentration of LDL cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18: 499–502.
23. The Expert Panel. The Third Report of the National Education Program (NCEP), Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III); Final report. Circulation 2002; 106: 3143–421.
24. Longo-Mbenza B, Nkondi Nsenga J, Vangu Ngoma D. Prevention of the metabolic syndrome insulin resistance and the atherosclerotic diseases in Africans infected by Helicobacter pylori infection and treated by antibiotics. Int J Cardiol 2007; 121: 229–38.
25. Amir Kol A, Libby P. The Mechanisms by Which Infectious Agents May Contribute to Atherosclerosis and Its Clinical Manifestations. Trends Cardiovasc Med 1998; 8: 191–9.
26. Libby P, Ridker PM, Maseri A. Inflammation and Atherosclerosis. Circulation 2002; 105: 1135–43.
27. Hansson GK, Libby P, Uwe Schonbeck U, Yan Z-Q. Innate and Adaptive Immunity in the Pathogenesis of Atherosclerosis. Circ Res 2002; 91: 281–91.
28. Naito Y, Yoshikawa T. Molecular and cellular mechanisms involved in Helicobacter pylori-induced inflammation and oxidative stress. Free Radic Biol Med 2002; 33 (3): 323–36.
29. Scharnagl H, Kist M, Grawitz AB, Koenig W, Wieland H, März W. Effect of Helicobacter Pylori Eradication on High-Density Lipoprotein Cholesterol. Am J Cardiol 2004; 93: 219–20.
30. Hyka N, Dayer JM, Modoux C, Kohno T, Edwards III CK, Roux-Lombard P, Burger D. Apolipoprotein A-I inhibits the production of interleukin-1beta and tumor necrosis factor-alpha by blocking contact-mediated activation of monocytes by T lymphocytes. Blood 2001; 97: 2381–9.
31. Tietge UJ, Maugeais C, Lund-Katz S, Grass D, DeBeer FC, Rader DJ. Human secretory phospholipaseA2 mediates decreased plasma levels of HDL cholesterol and apoA-I in response to inflammation in human apoA-I transgenic mice. Arterioscler Thromb Vasc Biol 2002; 22: 1213–8.
32. Russo F, Jirillo E, Clemente C. Circulating cytokines and gastrin levels in asymptomatic subjects infected by Helicobacter pylori (H. pylori). Immunopharmacol Immunotoxicol 2001; 23: 13–24.
33. Ramharack R, Barkalow D, Spahr M. Dominant negative effect of TGF-beta1 and TNF-alpha on basal and IL-6 induced Lipoprotein(a) and apolipoprotein(a) mRNA expression in primary monkey hepatocyte cultures. Arterioscler Thromb Vasc Biol 1998; 18: 984–90.

Received: September 12, 2008

Accepted: December 12, 2008