Journal of Metabolic Syndrome
ISSN: 2167-0943

Hwang LC, et al., J Metabolic Synd 2017, 6:4
DOI: 10.4172/2167-0943.1000234

Research Article Open Access

The Association between *Helicobacter Pylori* Infection and Metabolic Syndrome in a Taiwanese Adult Population

Yu-Chen Chang[1], **Chun-Yuan Huang**[2], **Lee-Ching Hwang**[1,3*] **and Chia-Chen Chang**[1]

[1]*The Department of Family Medicine, MacKay Memorial Hospital, Taiwan*

[2]*The Department of Family Medicine, China Medical University Hospital Taipei Branch, Taipei, Taiwan*

[3]*The Department of Medicine, Mackay Medical College, New Taipei City, Taiwan*

[*]**Corresponding author:** Dr. Lee-Ching Hwang, The Department of Family Medicine, MacKay Memorial Hospital, No.92, Sec. 2, Zhongshan N. Rd., Zhongshan Dist., Taipei City 104, Taiwan (R.O.C.), Tel: +886-2-25433535; E-mail: hlc@mmh.org.tw

Received date: November 16, 2017**; Accepted date:** November 21, 2017; **Published date:** December 07, 2017

Abstract

Objectives: The global prevalence of *Helicobacter pylori* (*H. pylori*) infection remains high. Recent studies demonstrated the potential relationship among *H. pylori*-induced chronic inflammation, insulin resistance and metabolic disorders. The aim of this study was to investigate the association between *H. pylori* infection and metabolic syndrome (MetS).

Methods: This cross-sectional study enrolled 4,232 health examination participants aged from 30 to 65-year-old in the northern Taiwan in 10 years. The general information and blood tests of all subjects were collected from the health examination center. *H. pylori* infection was diagnosed via ^{13}C-urea breath test. The log-transformed (log) serum high sensitivity C-reactive protein (hs-CRP) was used as the inflammatory parameter. MetS was defined according to the revised National Cholesterol Educational Program Adult Treatment Panel III (Revised NCEP ATP III) criteria. Subjects were divided into two groups based on their *H. pylori* infectious status. The association between *H. pylori* infection and metabolic parameters was assessed with multivariate logistic regression analysis.

Results: A total of 4,232 subjects (2,641 males and 1,591 females, aged 47.0 years ± 8.2 years) were enrolled for the analysis. *H. pylori* infection presented in 44.8% of all subjects. MetS presented in 27.6% of all subjects. Participants with *H. pylori* infection showed higher proportion of MetS, higher body mass index(BMI) and higher serum cholesterol(T-CHO) levels with statistical significance ($p<0.001$). There was no significant difference in the log serum hs-CRP between subjects with and without *H. pylori* infection. *H. pylori* infection increased the risk of large waist circumference component [OR=1.26 (1.10-1.43)] and high fasting plasma glucose component [OR=1.18 (1.04-1.34)], and contributed significantly to the presence of MetS with adjusted OR 1.23 (1.03-1.46).

Conclusions: Adults with *H. pylori* infection was associated with higher prevalence of MetS, higher BMI and higher mean serum T-CHO levels. Furthermore, *H. pylori* infection was identified as a risk factor for MetS.

Keywords ^{13}C-urea breath test; Helicobacter pylori; High sensitivity C-reactive protein; Metabolic syndrome

Introduction

The prevalence of *Helicobacter pylori* (*H. pylori*) infection remains high throughout global population [1,2]. Aside from causing gastrointestinal diseases, including chronic gastritis, peptic ulcers and gastric mucosa-associated lymphoid tissue lymphoma [3], recent studies also implied the potential relationship among the *H. pylori* infection, cardiovascular diseases and atherosclerosis [4,5]. Liu et al. in a meta-analysis demonstrated that *H. pylori* infection was associated with an increased risk of myocardial infarction regardless of age, race or socioeconomic status [6]. Another study conducted by Kowalski proposed a significant link between coronary artery disease and *H. pylori* infection. Patients infected with CagA-positive strains of *H. pylori* showed greater coronary artery lumen loss [7].

Metabolic syndrome (MetS) comprises multiple components of metabolic abnormalities tightly related to insulin resistance. Polyzos et al. in a systemic review indicated a trend toward a positive association between *H. pylori* infection and homeostatic model of assessment insulin resistance (HOMA-IR), which brought up a potential mechanism linking *H. pylori* infection and MetS [8]. Chronic inflammation induced by *H. pylori* infection may increase the release of multiple inflammatory cytokines and the development of insulin resistance, which act as risk factors for MetS [8-10]. However, the causal relationship between *H. pylori* infection and MetS remains unclear and the controversial results also exist [8,11].

A community-based cohort study revealed that H. pylori infection may increase insulin resistance and served as a predictor of MetS in a Taiwanese population [12]. The serostatus of anti-*H. pylori* IgG was used as diagnostic tool for *H. pylori* infection. However, previous studies have reported that serum anti-*H. pylori* IgG existed even after several years of *H. pylori* eradication, which couldn't accurately reflect the active infection [13,14]. Another cross-sectional study with a larger sample size using ^{13}C-urea breath test as diagnostic tool also demonstrated that *H. pylori* infection was positively associated with MetS, especially in females [15]. The average age of participants was younger (35.2 years) and the prevalence of *H. pylori* infection was also

lower (20.2%) when compared to previous epidemiologic studies. Considering the nature of chronic *H. pylori* infection and increasing disease burden of MetS among middle-aged Asian population, we conducted this study to investigate the relationship between *H. pylori* infection and MetS in a large adult population of northern Taiwan.

Methods

Study population

This cross-sectional study enrolled 4,232 subjects aged from 30 years to 65 years who participated in their annual health examination in a health examination center in the northern Taiwan during the past 10 years, and was approved by the Institutional Review Board of MacKay Memorial Hospital prior to recruitment. Individuals with history of cancer or those who received *H. pylori* eradication therapy, proton pump inhibitors, bismuth or histamine type 2(H_2) receptor antagonists 1 month prior to enrollment were excluded. All the subjects were then divided into two groups according to their results of ^{13}C-urea breath test for subsequent analysis.

Data collection

The information of medical history, personal history, physical examination and blood tests of all subjects were collected from the health examination center. The written informed consents were obtained from the participants prior to data collection. Subjects with systemic disease, such as diabetes mellitus or hypertension were also registered.

Waist circumference (WC) was measured at the midline between the lowest border of the subcostal rib and the superior border of the iliac crest. Body mass index (BMI) was measured as weight divided by height squared (kg/m^2).

Alcohol consumption was defined as regular daily alcohol intake. Current smoking was defined as regular daily smoking. Exercise was defined as having daily exercise habits. The presence of *H. pylori* infection was based on the results of ^{13}C-urea breath test. The log-transformed (log) serum high sensitivity C-reactive protein (hs-CRP) value was used as the parameter of chronic inflammation. Blood samples of all subjects were collected after overnight fasting and were immediately analyzed for biochemistry tests.

MetS was defined according to the revised National Cholesterol Educational Program Adult Treatment Panel III (revised NCEP ATP III) criteria. (Presence of at least three of the following five traits: 1) Abdominal obesity, defined as a WC in men and women of ≧ 90 cm and ≧ 80 cm, respectively; 2) serum triglycerides (TG) ≧ 150 mg/dL or drug treatment for elevated TG; 3) serum high-density lipoprotein cholesterol (HDL-C) <40 mg/dL in men and <50 mg/dL in women or drug treatment for low HDL-C; 4) blood pressure (BP) ≧ 130/85 mmHg or drug treatment for elevated BP; or 5) fasting plasma glucose (FPG) ≧ 100 mg/dL or drug treatment for elevated blood glucose [16].

Statistical Analysis

Data were presented as mean ± SD or as percentages. Statistical analysis was performed using SPSS version 24.0 (SPSS Inc., Chicago, IL). Categorical data were analyzed with the chi-squared test, and continuous data were analyzed with the independent samples t-test. Six models were proposed to assess the association between *H. pylori* infection and metabolic parameters by multivariate logistic regression analysis. Model 1 showed the association between *H. pylori* infection and MetS adjusted for age, gender, BMI, presence of hypertension and diabetes mellitus. Model 2 to model 6 showed the relationship between *H. pylori* infection and each component of MetS adjusted for age and gender. The odds ratios (OR) and 95% confidence intervals (CI) were calculated. A two-tailed p-value <0.05 was considered statistically significant.

Results

A total of 4,232 subjects (2,641 males and 1,591 females, aged 47.0 ± 8.2 years) were enrolled for the analysis. ^{13}C-urea breath test showed positive in 44.8% of all subjects. MetS was present in 27.6% of all subjects. Diabetes mellitus and hypertension were present respectively in 6.6% and 18.5% of all cases. Subjects were categorized into two groups according to their *H. pylori* infectious status. The characteristics of demographic data are shown in Table 1.

Characteristics	All subjects (N=4,232)
Age (years)	47.0 ± 8.2
Gender (male, %)	2,641 (62.4)
BMI (kg/m2)	24.8 ± 3.2
Systolic blood pressure (mmHg)	114.9 ± 14.8
Diastolic blood pressure (mmHg)	74.1 ± 10.3
Diabetes (%)	280 (6.6)
Hypertension (%)	782 (18.5)
Current smoking(%)(N=1,899)	145 (7.6)
Alcohol drinking(%)(N=2,070)	53 (2.6)
Exercise(%)(N=3,570)	1045 (29.3)
Waist circumference (cm)	82.7 ± 10.1
Fasting plasma glucose (mg/dL)	101.9 ± 18.7
Total cholesterol(mg/dL)	199.1 ± 34.9
Triglyceride (mg/dL)	125.0 ± 88.3
HDL-C (mg/dL)	58.6 ± 15.7
Metabolic syndrome (%)	1,166 (27.6)
hsCRP (mg/L)	1.7 ± 4.2
Positive ^{13}C-urea breath test (%)	1,897 (44.8)

The continuous variable was shown as mean ± SD; the categorical variables were shown as percentage; BMI: body mass index, HDL-C: High-density lipoprotein cholesterol, hsCRP: high sensitivity C-reactive protein

Table 1: Characteristics of study subjects.

Subjects with *H. pylori* infection exhibited significant higher prevalence of MetS compared to those without *H. pylori* infection (30.3% versus 25.4%, p<0.001). Multiple components of MetS including large WC, high BP and high FPG were significantly higher in those with *H. pylori* infection (p<0.05). In addition, in participants with *H. pylori* infection, higher BMI and mean serum total cholesterol (T-CHO) were also observed with statistically significant differences

(p<0.05). The log serum hsCRP values did not reach significant difference between subjects with and without *H. pylori* infection (p=0.697). The demographic data is shown in Table 2.

	H. pylori (+)	*H. pylori* (-)	p
	N=1,897(44.8)	N=2,335(55.2)	
Age (years)	47.6 ± 8.2	46.4 ± 8.2	<0.001
Gender (women/men) (men%)	734/1163 (61.3)	857/1478 (63.3)	0.184
BMI (kg/m^2)	24.0 ± 3.3	23.7 ± 3.4	<0.001
Diabetes (%)	140 (7.4)	140 (6.0)	0.072
Hypertension (%)	375 (19.8)	407 (17.4)	0.051
Total cholesterol (mg/dL)	201.9 ± 36.3	196.9 ± 33.6	<0.001
Metabolic syndrome (%)	574 (30.3)	592(25.4)	<0.001
Components			
Large WC (%)	676 (35.6)	701 (30.0)	<0.001
Hypertriglycemia (%)	505 (26.6)	594 (25.4)	0.383
Low HDL-C (%)	618 (32.6)	740 (31.7)	0.539
High blood pressure (%)	498 (26.3)	542 (23.2)	0.022
High FPG (%)	939 (49.5)	1049 (44.9)	0.003
Log serum hs-CRP	-0.1 ± 0.5	-0.1 ± 0.5	0.697

BMI: body mass index; WC: waist circumference; HDL-C: High-density lipoprotein cholesterol; FPG: fasting plasma glucose; Log serum hs-CRP: log-transformed serum high sensitivity C-reactive protein; Large WC: ≥ 90 cm (male), ≥ 80 cm (female); Hypertriglycemia: ≥ 150 mg/dL; Low HDL-C: < 40 mg/dL in males, < 50 mg/dL in females; High blood pressure: systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg, or treatment of previously diagnosed hypertension; High FPG: ≥100 mg/dL, or previously diagnosed type 2 diabetes

Table 2: Demographic data among participants with or without *H. pylori* infection.

Table 3 shows the predictive risk of *H. pylori* infection on metabolic syndrome and its five components by using multivariate logistic regression analysis. In model 1, *H. pylori* infection contributed significantly to the presence of MetS after adjusting for age, gender, BMI, presence of hypertension and diabetes mellitus (OR 1.23; 95% CI, 1.03-1.46, p=0.023). Regarding each component of MetS, *H. pylori* infection also increased the risk of large WC (OR, 1.26; 95% CI, 1.10-1.43, p=0.001) and high FPG (OR, 1.18; 95% CI, 1.04-1.34, p=0.013) after adjusting for age and gender.

	OR (95% CI)	p
Model 1(Metabolic syndrome)	1.23 (1.03-1.46)	0.023
Model 2(Large WC)	1.26 (1.10-1.43)	0.001
Model 3(Hypertriglycemia)	1.09 (0.94-1.25)	0.257
Model 4(Low HDL-C)	1.08 (0.94-1.33)	0.275
Model 5(High blood pressure)	1.15 (0.99-1.33)	0.07
Model 6(High FPG)	1.18 (1.04-1.34)	0.013

OR: odds ratio, 95% CI: 95% confidence interval. WC: waist circumference; HDL-C: High-density lipoprotein cholesterol; FPG: fasting plasma glucose; Large WC: ≥ 90 cm (male), ≥ 80 cm (female); Hypertriglycemia: ≥ 150 mg/dL; Low HDL-C: < 40 mg/dL in males, <50 mg/dL in females; High blood pressure: systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg, or treatment of previously diagnosed hypertension; High FPG: ≥100 mg/dL, or previously diagnosed type 2 diabetes.
Model 1: adjusted for gender, age, BMI, hypertension, diabetes
Model 2~Model 6: adjusted for gender, age

Table 3: Odds ratio of *H. pylori* infection for metabolic syndrome and its components.

Discussion

The aim of this study is to investigate the association between the *H. pylori* infection and MetS, furthermore, its predictive role. To our knowledge, this is also the first study applying ^{13}C-urea breath test as the diagnostic assay to explore the inflammatory process linking *H. pylori* infection and MetS. We defined *H. pylori* infection based on the results of ^{13}C-urea breath test, which has proven to be a more accurate diagnostic assay for active infection compared to traditional serology used in most epidemiologic studies [17]. It was found that subjects with *H. pylori* infection presented higher prevalence of MetS, higher BMI and higher mean serum T-CHO. Regarding each component of MetS, the proportion of large WC, high BP and high FPG were also higher in those with *H. pylori* infection. In addition, multivariate logistic regression analysis demonstrated that *H. pylori* infection

contributed significantly to the presence of MetS and two of its five components (large WC and high FPG) after adjusting potential confounders.

There is growing evidence indicating a close relationship among chronic infection, cardiovascular diseases and MetS. Chronic pathogen exposure could contribute to the development of atherosclerosis and insulin resistance by numerous mechanisms, including promotion of endothelial dysfunction and induction of a systemic inflammatory state. The major organisms that have been suggested include Chlamydia pneumoniae, cytomegalovirus and *H. pylori*. Besides, coxsackie viral infection, hepatitis A virus, and herpes simplex virus type 1 and type 2 have also been proposed [18,19].

According to previous reports, over 50% of the world's population was infected by *H. pylori*, with higher rate in the developing countries [1,2,5]. Some epidemiologic studies also indicate most infections could be acquired since childhood [1,20]. In a Taiwanese research, a total of 54.4% of participants presented with *H. pylori* infection, with similar prevalence between both genders [21]. Our result showed slightly lower prevalence compared to previous results. Potential risk factors of acquiring *H. pylori* infection include socially deprived environment and lower social economic status [22,23]. Participants recruited in this study comprised those with relatively higher social economical class. Thus, their professional background may have an influence on the prevalence of *H. pylori* infection. In addition, diagnosis in the former report was based on serologic tests, which may cause a higher false-positive rate than the ^{13}C-urea breath test used in our study.

The development of MetS is mediated by multiple factors. The visceral obesity and the insulin resistance are considered to play the core roles [24,25]. Meanwhile, the visceral obesity also disturbs the balance of pro-inflammatory cytokines. Increased release of these cytokines contributes to a chronic inflammatory state, which affects metabolic risk factors, including blood pressure, lipid profile and glucose intolerance [18,26-28]. Indeed, recent studies also include inflammatory state as a component of MetS, which implies the tight correlation between chronic inflammation and MetS [29,30]. In our results, *H. pylori* infection increased the risk of large WC and high FPG, which may reflect its impact on the visceral obesity and the insulin resistance.

Although the definite pathogenetic association between *H. pylori* infection and MetS has not been well established, some potential mechanisms have been proposed in previous studies. Chronic bacterial infection may trigger the secretion of pro-inflammatory cytokines such as hsCRP, tumor necrosis factor-α (TNF-α), interleukins and interferon-γ, which are involved with atherosclerosis, insulin resistance and lipid metabolism [8,9,12]. In a study performed by Takeoka et al., *H pylori*-associated gastritis was also identified as a risk factor for MetS, which further strengthened the link between *H pylori*-related inflammation and metabolic disorders [31]. Besides, gastric *H. pylori* colonization alters the balance of certain gastrointestinal hormones, including ghrelin and leptin, which could impair insulin homeostasis and lead to weight gain and fat accumulation [32]. Furthermore, *H. pylori* infection also affects the composition of the gut microbiota, mediating the development of obesity, systemic inflammation, and insulin resistance [33,34]. In our results, *H. pylori* infection increased the risk of large WC and high FPG components, which correspond to previous hypothesis and may reflect its impact on the visceral obesity and the insulin resistance.

In our study, we also investigated the potential relationship between *H. pylori*-associated inflammation with MetS by using log serum hsCRP as the inflammatory parameter. Subjects presented no significant difference in the log serum hsCRP values between two groups, which was similar to previous results. In the study carried out by Chen et al. subjects with positive anti-H.pylori IgG exhibited higher level of TNF-α than those without *H. pylori* antibodies. But there was no significant difference among other inflammatory cytokines including hsCRP [12]. In our study, we used log serum hsCRP as the inflammatory parameter. Subjects presented no significant difference in the log serum hsCRP values between two groups, which was similar to previous results. Considering that most individuals acquire *H. pylori* infections since childhood, the impact on inflammatory process and MetS may vary among different age groups and hinder the interpretation of our results. Further research was required to explore the detailed involvement of different cytokines mediated between *H. pylori* infection and metabolic disorders.

A systemic review conducted by Upala S et al. concluded that the *H. pylori* infection was positively associated with MetS, higher TG, FPG, BMI, HOMA-IR, systolic blood pressure and lower HDL-C, most of which were compatible to the results in our study [35]. However, previous reports showed some inconsistencies regarding different components of MetS affected by *H. pylori* infection. In our study, two of five components of MetS(Large WC and high FPG) reached significant difference between subjects with and without *H. pylori* infection. After adjusting for covariates, logistic regression models indicated that *H. pylori* infection increased the risk of two components of MetS. This discrepancy may result from the different virulent strains of *H. pylori* or the diverse host genetic factors [15]. For example, CagA-positive strains of *H. pylori* have been found to associate with a higher average glycated hemoglobin level in adults [32]. In addition, different criteria adopted for MetS and various diagnostic tests used for *H. pylori* infection in different studies also affect the interpretation of results.

Aside from various metabolic parameters influenced by *H. pylori* infection proposed in previous studies, several reports also raised the concern of decreasing metabolic risk factors by *H. pylori* eradication. In a large prospective cohort study conducted by Nam et al., improved lipid profile was observed in patients with *H. pylori* infection 1~3 years after eradication therapy [36]. In another study carried out by Gen R et al., the HOMA-IR, lipid profile and CRP levels in individuals after successful eradication significantly improved from the pretreatment status, which provided favorable perspective for reducing the incidence of MetS and its associated morbidity [37]. However, significant discrepancy and heterogeneous results impede the consistency among different studies. Further large-scale prospective researches with more stringent standards are indicated to determine the actual effects of eradication therapy on metabolic disorders in real-world.

In our study, *H. pylori* infection was identified as a risk factor for MetS. Furthermore, *H. pylori* infection also increased the risk of large WC and high FPG, which were considered as core factors of development of MetS. However, the concrete mechanism regarding the potential role of treating and preventing MetS by *H. pylori* eradication still needs to be clarified.

There were several limitations in this study. First, this was a single-center retrospective study. Thus, the composition of participants may pose unmeasured confounding factors or selection bias for this study. The self-reported collection system of medical history could also mislead the interpretation of our results. Second, although ^{13}C-urea

breath test remained a reliable diagnostic test for *H. pylori* infection, false negative results still existed. Other complementary tests should also be applied to enhance the diagnostic accuracy. Third, we solely used hsCRP as the inflammation parameter. More pro-inflammatory indicators associated with the development of MetS such as TNF-α, adiponectin, ghrelin and leptin should also be assessed in future investigations.

Conclusion

In this study, adult subjects with *H. pylori* infection exhibited higher prevalence of MetS with two main components reaching significant difference (large WC and high FPG). Higher BMI and mean serum T-CHO were also observed in those with *H. pylori* infection. *H. pylori* infection was an independently predictive risk factor for MetS, as well as its two components (large WC and high FPG), which may reflect its negative impact on obesity and insulin resistance. The adjusted OR of MetS with *H. pylori* infection was 1.23 (95% CI, 1.03-1.46, p=0.023). The detailed mechanism and pathophysiology regarding various degrees of different metabolic components influenced by *H. pylori* infection remain to be investigated. In addition, further study was required to establish the comprehensive causative link between *H. pylori* infection and MetS. Finally, aside from preventing some digestive disorders and certain neoplasms, *H. pylori* eradication treatment may also have the therapeutic potential on MetS and its associated comorbidity, including obesity, dyslipidemia, insulin resistance and hypertension.

References

1. Cheng CC (2008) Helicobacter pylori seroepidemiology in five areas of Taiwan and real-time PCR assay for detection of Helicobacter pylori in water. College of Medicine Graduate Institue of Clinical Medicine. National Taiwan University: Taipei.
2. Lin JT, Wang JT, Wang TH, Wu MS, Lee TK, et al. (1993) Helicobacter pylori infection in a randomly selected population, healthy volunteers, and patients with gastric ulcer and gastric adenocarcinoma. A seroprevalence study in Taiwan. Scand J Gastroenterol 12: 1067-1072.
3. Yang W, Xuan C (2016) Influence of Helicobacter pylori Infection on Metabolic Syndrome in Old Chinese People. Gastroenterology research and practice 2016.
4. Franceschi F, Leo D, Fini L, Santoliquido A, Flore R, et al. (2005) Helicobacter pylori infection and ischaemic heart disease: an overview of the general literature. Dig Liver Dis 37: 301-308.
5. Sung KC, Rhee EJ, Ryu SH, Beck SH (2005) Prevalence of Helicobacter pylori infection and its association with cardiovascular risk factors in Korean adults. Int J Cardiol 102: 411-417.
6. Liu J, Wang F, Shi S (2015) Helicobacter pylori infection increase the risk of myocardial infarction: a meta-analysis of 26 studies involving more than 20,000 participants. Helicobacter 20: 176-183.
7. Kowalski M (2001) Helicobacter pylori (H. pylori) infection in coronary artery disease: Influence of H. pylori eradication on coronary artery lumen after percutaneous transluminal coronary angioplasty. The detection H. pylori specific DNA in human coronary atero9sclerotic plaque. J Physiol Pharmacol 52: 3-31.
8. Polyzos SA, Kountouras J, Zavos C, Deretzi G (2011) The association between Helicobacter pylori infection and insulin resistance: a systematic review. Helicobacter 16: 79-88.
9. Albaker WI (2011) Helicobacter pylori infection and its relationship to metabolic syndrome: is it a myth or fact? Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association 17: 165-169.
10. Gunji T, Matsuhashi N, Sato H, Fujibayashi K, Okumura M, et al. (2009) Helicobacter pylori infection significantly increases insulin resistance in the asymptomatic Japanese population. Helicobacter 14: 144-150.
11. Naja F, Nasreddine L, Hwalla N, Moghames P, Shoaib H, et al. (2012) Association of H. pylori infection with insulin resistance and metabolic syndrome among Lebanese adults. Helicobacter 17: 444-451.
12. Chen LW, Chien CY, Yang KJ, Kuo SF, Chen CH, et al. (2015) Helicobacter pylori Infection Increases Insulin Resistance and Metabolic Syndrome in Residents Younger than 50 Years Old: A Community-Based Study. PLoS One 10.
13. Cutler AF, Prasad VM, Santogade P (1998) Four-year trends in Helicobacter pylori IgG serology following successful eradication. Am J Med 105: 18-20.
14. Miernyk KM, Bruden DL, Bruce MG, McMahon BJ, Hennessy TW, et al. (2007) Dynamics of Helicobacter pylori-specific immunoglobulin G for 2 years after successful eradication of Helicobacter pylori infection in an American Indian and Alaska Native population. Clin Vaccine Immunol 14: 85-86.
15. Chen TP, Hung HF, Chen MK, Lai HH, Hsu WF, et al. (2015) Helicobacter Pylori Infection is Positively Associated with Metabolic Syndrome in Taiwanese Adults: a Cross-Sectional Study. Helicobacter 20: 184-191.
16. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (2001) JAMA 285: 2486-2497.
17. Megraud F, Bessede E, Lehours P (2014) Diagnosis of Helicobacter pylori infection. Helicobacter 19 Suppl 1: 6-10.
18. Gunji T, Matsuhashi N, Sato H, Fujibayashi K, Okumura M, et al. (2008) Helicobacter pylori infection is significantly associated with metabolic syndrome in the Japanese population. Am J Gastroenterol 103: 3005-3010.
19. Nabipour I, Vahdat K, Jafari SM, Pazoki R, Sanjdideh Z (2006) The association of metabolic syndrome and Chlamydia pneumoniae, Helicobacter pylori, cytomegalovirus, and herpes simplex virus type 1: the Persian Gulf Healthy Heart Study. Cardiovasc Diabetol 5: 25.
20. Parsonnet J (1995) The incidence of Helicobacter pylori infection. Aliment Pharmacol Ther 9 Suppl 2: 45-51.
21. Kivi M, Johansson AL, Reilly M, Indberg Y (2005) Helicobacter pylori status in family members as risk factors for infection in children. Epidemiol Infect 133: 645-652.
22. Murray LJ, McCrum EE, Evans AE, Bamford KB (1997) Epidemiology of Helicobacter pylori infection among 4742 randomly selected subjects from Northern Ireland. Int J Epidemiol 26 :880-887.
23. Woodward M, Morrison C, McColl K (2000) An investigation into factors associated with Helicobacter pylori infection. J Clin Epidemiol 53: 175-181.
24. Alberti KG, Zimmet P, Shaw J (2005) The metabolic syndrome--a new worldwide definition. Lancet 366: 1059-1062.
25. Eckel RH, Grundy SM, Zimmet PZ (2005) The metabolic syndrome. Lancet 365: 1415-1428.
26. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, et al. (2004) Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med 351: 2599-2610.
27. Ross R (1999) Atherosclerosis--an inflammatory disease. N Engl J Med 340: 115-126.
28. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, et al. (2004) Obesity and the metabolic syndrome in children and adolescents. N Engl J Med 350: 2362-2374.
29. Grundy SM, Brewer HB, Jr., Cleeman JI, Smith SC Jr, Lenfant C, et al. (2004) Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 109: 433-438.
30. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, et al. (2006) Diagnosis and management of the metabolic syndrome: an American

Heart Association/National Heart, Lung, and Blood Institute scientific statement. Curr Opin Cardiol 21: 1-6.

31. Takeoka A, Tayama J, Yamasaki H, Kobayashi M, Ogawa S, et al. (2016). Impact of Helicobacter pylori Immunoglobulin G Levels and Atrophic Gastritis Status on Risk of Metabolic Syndrome. PloS one, 11.
32. Popescu D, Andronescu D, Babeș Petru A (2017) Association Between Helicobacter Pylori Infection and Insulin Resistance: A Systematic Review. Romanian Journal of Diabetes Nutrition and Metabolic Diseases 149.
33. Caricilli AM, Saad MJ (2014) Gut microbiota composition and its effects on obesity and insulin resistance. Curr Opin Clin Nutr Metab Care 17: 312-318.
34. Lopetuso LR, Scaldaferri F, Franceschi F, Gasbarrini A (2014) The gastrointestinal microbiome -functional interference between stomach and intestine. Best Pract Res Clin Gastroenterol 28: 995-1002.
35. Upala S, Jaruvongvanich V, Riangwiwat T, Jaruvongvanich S, Sanguankeo A (2016) Association between Helicobacter pylori infection and metabolic syndrome: a systematic review and meta-analysis. J Dig Dis 17: 433-440.
36. Nam SY, Ryu KH, Park BJ, Park S (2015) Effects of Helicobacter pylori infection and its eradication on lipid profiles and cardiovascular diseases. Helicobacter 20: 125-132.
37. Gen R, Demir M, Ataseven H (2010) Effect of Helicobacter pylori eradication on insulin resistance, serum lipids and low-grade inflammation. South Med J 103: 190-196.