

## INFLUENCE OF *HELICOBACTER PYLORI* INFECTION ON ATHEROSCLEROSIS RISK FACTORS IN OLDER PEOPLE

Zean Zefenkey<sup>a</sup>

<sup>a</sup> Department of Medical Laboratory Science, College of Science, Knowledge University, Erbil 44001, Iraq –  
([zean.feteh@knu.edu.iq](mailto:zean.feteh@knu.edu.iq))

**Received:** 16 Jan., 2022 / **Accepted:** 12 Mar., 2022 / **Published:** 14 Mar., 2022 <https://doi.org/10.25271/sjuoz.2022.10.1.884>

**ABSTRACT:**

Atherosclerosis is a significant cause of mortality from cardiovascular disease. The role of *Helicobacter pylori* (*H. pylori*) infection in atherogenesis is debatable. The current study aimed to assess the association between *H. pylori* infection and some risk factors of atherosclerosis in older people. 180 males and females, apparently healthy, over 60 years old, were examined by Faecal Helicobacter Pylori-Antigen ELISA test for *H. pylori* infection. Blood pressure, high-density lipoprotein-cholesterol (HDL-cholesterol), low-density lipoprotein-cholesterol (LDL-cholesterol), triglyceride (TG), fasting blood glucose, and body mass index (BMI) were measured for all participants.

The faecal *H. pylori* antigen-positive group had a lower HDL-cholesterol level and higher levels of LDL-cholesterol, triglyceride, fasting blood glucose, and BMI than the faecal *H. pylori* antigen-negative group with a statistical difference ( $P < 0.05$ ). The faecal *H. pylori* antigen-positive group had 2.4, 2.2, 2.6, 2.5 fold more likely to have increasing in the LDL-cholesterol, triglyceride, BMI, and decreasing in HDL-cholesterol, respectively. This risk became more considerable after adjustment for gender, age, blood pressure, and fasting blood glucose (adjusted odds ratio (AOR)= 3.1, 3.0, 3.3, 3.3), respectively.

The infection by *H. pylori* in older adults is an independent factor for increasing lipid profile and BMI, which are the key modifying factors for the progress of atherosclerosis.

**KEYWORDS:** Helicobacter pylori, atherosclerosis, older people, cardiovascular diseases, faecal H. pylori antigen test.

**1. INTRODUCTION**

*H. pylori* is a gram-negative, microaerophilic bacteria colonizing the stomach's epithelial cells. This bacterium is a significant reason for chronic active gastritis, as well as a potent risk factor for peptic ulcers and gastric malignancy (Warren, 1983; Robinson, 2021). *H. pylori* infection was detected in roughly half of the world's nation, with the frequency being higher in developing populations (Hooi et al., 2017). Infection with *H. pylori* has been linked to a variety of extra-digestive disorders, including osteoporosis (Fisher et al., 2020) and multiple sclerosis (Kountouras et al., 2020). Furthermore, those who have an infection with *H. pylori* have a threefold increased risk of coronary artery disease (CAD) compared to healthy people (Rogha et al., 2012).

Atherosclerosis has a crucial role in cardiovascular diseases (CVDs), particularly stroke and coronary artery diseases (Bhatt et al., 2006). Diabetes, hyperlipidemia, hypertension, clotting factors changes, obesity, smoking, and lifestyle are well-known modifying factors for the development of atherosclerosis, while age is the main unmodifying factor (Ross, 1993; Lujan-Vega et al., 2021).

*In vitro* studies on serum and vascular tissue specimens have recently revealed evidence for the involvement of infectious (bacterial and viral) genera in the pathology of atherosclerosis (Hemmat et al., 2018; Khoshbayan et al., 2021). In persons with *H. pylori* infection, elevated values of proinflammatory and procoagulant markers such as C-reactive protein, increased white blood count, increased fibrinogen concentration, and changed plasma lipid profile was reported (Sun, 2016; Markus, 1998). On the other hand, there are disagreements over the influence of *H. pylori* infection on main plasma biochemical atherogenesis risk

factors. Some researchers believe that *H. pylori* infection promotes atherosclerosis by altering plasma concentrations of biochemical atherogenesis indices (Shimamoto et al., 2020; Bener et al., 2020). In contrast, others genuinely think that the organism directly contributes to atherogenesis by inducing a chronic inflammatory response in the vascular wall without causing significant changes in biochemical atherosclerotic risk factors (Buzás, 2014; Akbas et al., 2010).

The global population of older persons aged 65 and up is increasing, and CVDs are the primary cause of morbidity and mortality among this group (Sturlaugsdottir et al., 2016; Benjamin et al., 2019), particularly coronary artery disease. (Aronow and Frishman, 2001).

This study aimed to estimate the association between *H. pylori* infection and some risk factors of atherosclerosis among elderly persons, mainly focusing on the influence of *H. pylori* infection on some blood chemicals involved in atherogenesis.

**2. METHODS****2.1. Study Design and Participants**

From March 2019 to April 2021, 180 apparently healthy over 60-year-olds participants were included in this cross-sectional study. We ruled out any confounding medical factors that are known to be linked to the health consequence to prevent confounding bias. The following were the criteria for exclusion: 1) usage of antibacterial, proton pump inhibitors (PPI), or histamine H2-receptor antagonists in the last three months, 2) smoking, 3) acute or chronic disease, and 4) age under 60.

The study was authorized by the Clinical Research Ethics Committee of the ministry of health, Kurdistan Region, Iraq, and performed in line with the guidelines of the Declaration of Helsinki. All participants agreed to participate after they being told about the study's goal and protocol and obtained assurances that all information would be treated in strict confidence, all

participants were asked to come to the lab after fasting for at least 12 hours for blood collection, with a faeces sample taken in a clean, leak-proof container; stool storage period is indicated to be up to 24 hours at 2-8 °C. All of the participants' ages and genders were recorded.

## 2.2. Detection of *H. pylori* Infection

The presence of *H. pylori* antigen was determined using the Faecal *Helicobacter Pylori*-Antigen ELISA - Ibl-international (Tecan, Hamburg) following the manufacturer's manual. Briefly, the test utilizes a highly purified monoclonal *H. pylori* antibody adsorbed to microplate wells. Faecal samples were diluted with Buffer, and after centrifuging, the supernatant was used by adding 100 µl into the designated microwell. After the incubation for 60 minutes (20-25 °C) and proper washing, a 100 µl of Enzyme Conjugate was added and followed by incubation for 30 minutes at (20-25 °C), a second washing was done before adding 100 µl of TMB Substrate. The last incubation was for 20 minutes at (20-25 °C), then 100 µL of ELISA Stop Solution was added. The absorbance was measured at a wavelength of 450 nanometers. Positive Cut-Off was 0.165, and Negative Cut-Off was 0.135

## 2.3. Other Clinical Data Collection

All participants were barefoot and wearing light clothes when measuring their height and weight. BMI was computed by dividing weight (kg) by height square (m<sup>2</sup>).

Blood pressure (BP) was obtained by expert medical staff after resting for a minimum of 15 minutes using a mercury-gravity manometer; the mean of three measurements was calculated and saved for processing.

A fasting blood sample for at least 12 hours was obtained for each participant to measure serum LDL-cholesterol, HDL-cholesterol, triglyceride, and glucose with a Cobas c 111 analyzer (Roche, Germany).

## 2.4. Statistical Analysis

A cross-sectional study was proceeded to assess the significant correlation between *H. pylori* infection and atherosclerosis risk factors. According to Faecal *Helicobacter Pylori*-Antigen test results, all participants were distributed into two groups. The chi-square test assessed categorical variables, which were reported using a percentage (%), and the two-sample t-test was used to evaluate quantitative data recorded as mean ± standard deviation (SD). In order to generate adjusted odds ratios (AORs), a logistic regression analysis model was applied.

The SPSS software (Windows Version 23.0) was utilized for all statistical processing. When the p-value was <0.05, the difference was judged statistically significant. preparing.

## 3. RESULTS

A total of 180 subjects (94 male and 86 female, mean age 66.5 ± 5.5 years) were tested using the Faecal *Helicobacter Pylori*-Antigen ELISA test. Infection with *Helicobacter Pylori* was found in 54.4 %. Following the ELISA test, the study subjects were separated into the faecal *H. pylori* antigen-positive group and the faecal *H. pylori* antigen-negative group. The characteristics of the subjects in each group are presented in Table 1.

The faecal *H. pylori* antigen-positive group had a higher mean LDL-cholesterol, triglyceride, and BMI with statistically significance (P = < 0.05).

Table 1. Characteristics of the study subjects according to Faecal *Helicobacter Pylori*-Antigen ELISA test.

Parameter	Faecal <i>H. pylori</i> antigen-positive group (n= 98)	Faecal <i>H. pylori</i> antigen-negative group (n= 82)	P value
Age, years (mean ± SD)	65.8 ± 5.3	67.6 ± 5.9	0.3
Male, n (%)	53 (54.1%)	41 (50%)	0.5
LDL-cholesterol, mg/dl (mean ± SD)	162.5 ± 17.7	142.5 ± 39.7	0.02
HDL-cholesterol, mg/dl (mean ± SD)	43.3 ± 0.9	47.2 ± 0.9	0.02
Triglyceride, mg/dl (mean ± SD)	134.5 ± 5	114.5 ± 4.7	0.01
Glucose, mg/dl (mean ± SD)	116.9 ± 33.7	128.2 ± 40.2	0.5
SBP, mmHg (mean ± SD)	128.6 ± 9.8	131.1 ± 10.2	0.3
DBP, mmHg (mean ± SD)	83.3 ± 5.1	85.5 ± 5.5	0.2
BMI, kg/m <sup>2</sup> (mean ± SD)	27.5 ± 3.9	25.9 ± 5.5	0.02

On the contrary, HDL-cholesterol was lower in patients with *H. pylori* infection (P = 0.02). There wasn't a statistically significant between faecal *H. pylori* antigen-positive and faecal *H. pylori* antigen-negative groups according to gender, level of fasting blood glucose, and blood pressure.

To explore whether present *Helicobacter pylori* infection is an independent factor for increasing LDL cholesterol, TG, and BMI levels and decreasing HDL cholesterol, we assessed the risk in the faecal *H. pylori* antigen-positive group compared with the faecal *H. pylori* antigen-negative group by computing crude odds ratio (COR). The subjects with *H. pylori* infection were 2.4, 2.2, 2.6, 2.5 fold more likely to increase LDL cholesterol, triglyceride, BMI, and decreasing HDL cholesterol, respectively. After adjusting for a number of other factors that may impact lipid profile and BMI, namely, gender, age, blood pressure, and blood glucose, this risk became more significant, AOR were 3.1, 3.0, 3.3, 3.3 respectively for increasing in the LDL-cholesterol, triglyceride, BMI, and decreasing in HDL-cholesterol. (Fig 1, 2).

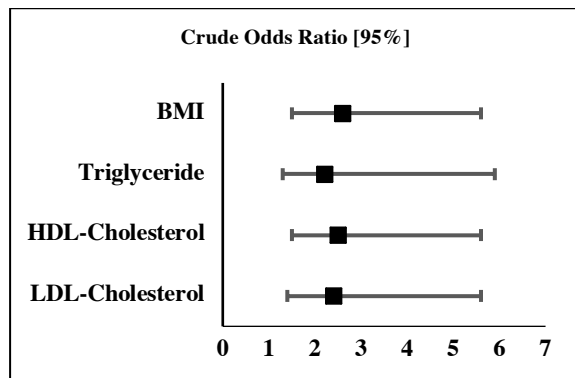


Figure 1. Crude Odds Ratio for LDL-cholesterol, HDL-cholesterol, triglyceride, and BMI, using logistic regression for calculation with 95% confidence intervals.

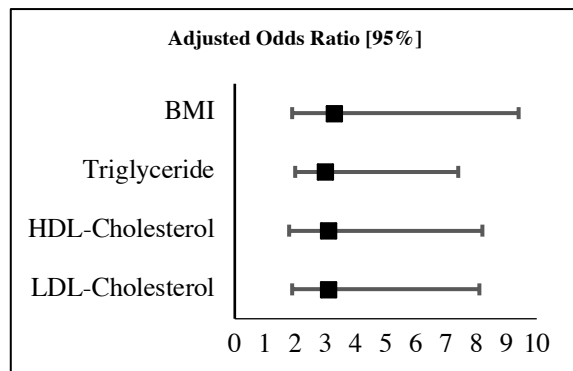


Figure 2. Adjusted Odds Ratio for LDL-cholesterol, HDL-cholesterol, triglyceride, and BMI, using logistic regression for calculation with 95% confidence intervals.

#### 4. DISCUSSION

The current study showed that infection with *H. pylori* is popular among older people in Kurdistan region-Iraq (54.4%), with no difference according to gender, 54.2% for males and 50% for females ( $P=0.5$ ). This result means that half of the older people have *H. pylori* infection and are at risk of complications. This result is consistent with another study that adopted molecular methods for the detection of *H. pylori* infection in the Kurdistan region-Iraq, the prevalence was 50% among people older than 50 years old (Rahman et al., 2020)

The fact that cardiovascular mortality has been rising since 2010 is quite worrying (Pearson-Stuttard et al., 2016). A recent study (Wang et al., 2018) assessed an extensive database that included 208,196 patients showed that the early treatment of *H. pylori* infection led to a lower mortality rate. The relation between *H. pylori* infection and atherosclerosis was consistent across many studies (Zhang et al., 2019; Lee et al., 2018; Haider et al., 2002). The pathophysiology by which *H. pylori* infection induces atherosclerosis is still not evident.

This work studied atherosclerosis's most important risk factors, including cholesterol, triglyceride, fasting blood glucose, blood pressure, and BMI. Participants with *H. pylori* infection had considerably greater LDL-cholesterol and triglyceride levels than those without the infection. In contrast, HDL-cholesterol levels in participants with *H. pylori* infection were remarkably reduced than the other participants without *H. pylori* infection. Some evidence suggests that dysregulated lipid metabolism may worsen atherosclerosis in participants with *H. pylori* infection (Pohjanen et al., 2016; Chen et al., 2016). *Helicobacter pylori*

carry lipopolysaccharides and cause the host to upregulate specific cytokines in gastric mucosa, including tumour necrosis factor- $\alpha$ , that may inhibit lipoprotein lipase, causing lipid mobilization from tissues and low HDL cholesterol levels in the blood (Kountouras et al., 2017; Makoveichuk et al., 2017).

This study also found that the mean BMI was more elevated in faecal *H. pylori* antigen-positive group than in faecal *H. pylori* antigen-negative group. The exact process that underpins this result is unknown. Many elements could be implicated. For instance, both gastrointestinal hormones, ghrelin and leptin, are essential in energy balance and metabolic control. Ghrelin is a hormone generated in the gastrointestinal tract that can increase food intake. Leptin has the reverse effect. It is made chiefly in the body fat (Ahima and Flier, 2000) and generated by P cells in the epithelium of the stomach (Bado et al., 1998). In many studies, *H. pylori*-positive patients had lower serum leptin and Ghrelin levels (Kasai et al., 2016; Francois et al., 2011). Leptin has the ability to inhibit eating, and its insufficiency may play a role in overeating and obesity. At the same time, the reduction in plasma Ghrelin levels reflected a physiological response to the obesity-related positive energy balance (Xu et al., 2019).

There are two types of *H. pylori* diagnostic tests: invasive and noninvasive. Because the serology assay of *Helicobacter pylori* IgG is rapid, affordable, and noninvasive, it has been used in most investigations on the relation between *H. pylori* infection and cardiovascular diseases (Ikeda et al., 2013; Rogha et al., 2012). However, there are conflicting findings when it comes to *H. pylori* seropositivity and CVD. Several researchers have found a strong link between CVD and infection by *H. pylori*. (Tabata, 2016; Park, 2011) and others showing no such association (Ikeda et al., 2013; Rogha et al., 2012). One probable explanation for these conflicting findings is the serologic test's limitations for *H. pylori* infection diagnosis (Chmiela et al., 2015). More critically, serologic antibody testing can't differentiate between a recent and previous infection; in contrast, a positive faecal *H. pylori* antigen test means a current infection (Atkinson and Braden, 2016). The difference between the methodologies used for the detection of *H. pylori* infection can also interpret other conflicts between researches about the relation between *H. pylori* infection and both blood glucose level and blood pressure. For instance, this study did not find a difference in blood glucose between participants with and without *H. pylori* infection, which is compatible with the Upala study. (Upala et al., 2017), but inconsistent with Wan's study (Wan et al., 2018; Wan et al., 2020).

If present *H. pylori* infection is linked to atherosclerosis risk factors, it may be anticipated that eradicating *H. pylori* infection will assist prevent atherosclerosis progression. Our findings may provide insights for further investigation into the impact of *H. pylori* treatment on the prevention of future atherosclerosis development.

To our knowledge, the current study is the first one to use Faecal *H. pylori* Antigen test to link current *H. pylori* infection with some risk factors of atherosclerosis in healthy older people. Anyway, there were some limitations in the present study. We lack Carotid ultrasonography and atherosclerosis detection to confirm subclinical atherosclerosis. In addition, the following of the lipid profile and BMI after *H. pylori* eradication is vital to establish a causal relationship. Lastly, this study is limited to older people. It is undoubtedly desirable to expand it to include the younger cohort.

#### 5. CONCLUSION

The current study revealed that *H. pylori* infection in older people was an independent risk factor for increasing LDL-cholesterol, triglyceride, and BMI levels and decreasing HDL-cholesterol level, which are the main modifying factors for the development of atherosclerosis. This result proposes that eradicating *H. pylori* infection could be beneficial in preventing atherosclerosis and its sequelae.

## REFERENCES

- Ahima, R. S., & Flier, J. S. (2000). Leptin. *Annual review of physiology*, 62, 413–437. <https://doi.org/10.1146/annurev.physiol.62.1.413>
- Akbas, H. S., Basyigit, S., Suleymanlar, I., Kemaloglu, D., Koc, S., Davran, F., Demir, I., & Suleymanlar, G. (2010). The assessment of carotid intima media thickness and serum paraoxonase-1 activity in *Helicobacter pylori* positive subjects. *Lipids in health and disease*, 9, 92. <https://doi.org/10.1186/1476-511X-9-92>
- Aronow W.S., Frishman W.H. (2001) Risk Factors for Atherosclerosis in the Elderly. In: Rosenthal R.A., Zenilman M.E., Katlic M.R. (eds) Principles and Practice of Geriatric Surgery. Springer, New York, NY. doi: 10.1007/978-1-4757-3432-4\_31
- Atkinson, N. S., & Braden, B. (2016). *Helicobacter Pylori* Infection: Diagnostic Strategies in Primary Diagnosis and After Therapy. *Digestive diseases and sciences*, 61(1), 19–24. <https://doi.org/10.1007/s10620-015-3877-4>
- Bado, A., Levasseur, S., Attoub, S., Kermorgant, S., Laigneau, J. P., Bortoluzzi, M. N., Moizo, L., Lehy, T., Guerre-Millo, M., Le Marchand-Brustel, Y., & Lewin, M. J. (1998). The stomach is a source of leptin. *Nature*, 394(6695), 790–793. <https://doi.org/10.1038/29547>
- Bener, A., Ağan, A. F., Al-Hamaq, A., Barisik, C. C., Öztürk, M., & Ömer, A. (2020). Prevalence of *Helicobacter pylori* Infection among Type 2 Diabetes Mellitus. *Advanced biomedical research*, 9, 27. [https://doi.org/10.4103/abr.abr\\_248\\_19](https://doi.org/10.4103/abr.abr_248_19)
- Benjamin, E. J., Muntner, P., Alonso, A., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Chang, A. R., Cheng, S., Das, S. R., Delling, F. N., Djousse, L., Elkind, M., Ferguson, J. F., Fornage, M., Jordan, L. C., Khan, S. S., Kissela, B. M., Knutson, K. L., Kwan, T. W., ... American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee (2019). Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation*, 139(10), e56–e528. <https://doi.org/10.1161/CIR.0000000000000659>
- Bhatt, D. L., Steg, P. G., Ohman, E. M., Hirsch, A. T., Ikeda, Y., Mas, J. L., Goto, S., Liao, C. S., Richard, A. J., Röther, J., Wilson, P. W., & REACH Registry Investigators (2006). International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA*, 295(2), 180–189. <https://doi.org/10.1001/jama.295.2.180>
- Buzás G. M. (2014). Metabolic consequences of *Helicobacter pylori* infection and eradication. *World journal of gastroenterology*, 20(18), 5226–5234. <https://doi.org/10.3748/wjg.v20.i18.5226>
- Chen, L. W., Chien, C. Y., Hsieh, C. W., Chang, L. C., Huang, M. H., Huang, W. Y., Kuo, S. F., Chien, C. H., Lin, C. L., & Chien, R. N. (2016). The Associations Between *Helicobacter pylori* Infection, Serum Vitamin D, and Metabolic Syndrome: A Community-Based Study. *Medicine*, 95(18), e3616. <https://doi.org/10.1097/MD.0000000000003616>
- Chmiela, M., Gajewski, A., & Rudnicka, K. (2015). *Helicobacter pylori* vs coronary heart disease - searching for connections. *World journal of cardiology*, 7(4), 187–203. <https://doi.org/10.4330/wjcv7.i4.187>
- Fisher, L., Fisher, A., & Smith, P. N. (2020). *Helicobacter pylori* Related Diseases and Osteoporotic Fractures (Narrative Review). *Journal of clinical medicine*, 9(10), 3253. <https://doi.org/10.3390/jcm9103253>
- Francois, F., Roper, J., Joseph, N., Pei, Z., Chhada, A., Shak, J. R., de Perez, A. Z., Perez-Perez, G. I., & Blaser, M. J. (2011). The effect of *H. pylori* eradication on meal-associated changes in plasma ghrelin and leptin. *BMC gastroenterology*, 11, 37. <https://doi.org/10.1186/1471-230X-11-37>
- Haider, A. W., Wilson, P. W., Larson, M. G., Evans, J. C., Michelson, E. L., Wolf, P. A., O'Donnell, C. J., & Levy, D. (2002). The association of seropositivity to *Helicobacter pylori*, *Chlamydia pneumoniae*, and cytomegalovirus with risk of cardiovascular disease: a prospective study. *Journal of the American College of Cardiology*, 40(8), 1408–1413. [https://doi.org/10.1016/s0735-1097\(02\)02272-6](https://doi.org/10.1016/s0735-1097(02)02272-6)
- Hemmat, N., Ebadi, A., Badalzadeh, R., Memar, M. Y., & Baghi, H. B. (2018). Viral infection and atherosclerosis. *European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology*, 37(12), 2225–2233. <https://doi.org/10.1007/s10096-018-3370-z>
- Hooi, J., Lai, W. Y., Ng, W. K., Suen, M., Underwood, F. E., Tanyingoh, D., Malfertheiner, P., Graham, D. Y., Wong, V., Wu, J., Chan, F., Sung, J., Kaplan, G. G., & Ng, S. C. (2017). Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis. *Gastroenterology*, 153(2), 420–429. <https://doi.org/10.1053/j.gastro.2017.04.022>
- Ikeda, A., Iso, H., Sasazuki, S., Inoue, M., Tsugane, S., & JPHC Study Group (2013). The combination of *Helicobacter pylori*- and cytotoxin-associated gene-A seropositivity in relation to the risk of myocardial infarction in middle-aged Japanese: The Japan Public Health Center-based study. *Atherosclerosis*, 230(1), 67–72. <https://doi.org/10.1016/j.atherosclerosis.2013.06.013>
- Kasai, C., Sugimoto, K., Moritani, I., Tanaka, J., Oya, Y., Inoue, H., Tameda, M., Shiraki, K., Ito, M., Takei, Y., & Takase, K. (2016). Changes in plasma ghrelin and leptin levels in patients with peptic ulcer and gastritis following eradication of *Helicobacter pylori* infection. *BMC gastroenterology*, 16(1), 119. <https://doi.org/10.1186/s12876-016-0532-2>
- Khoshbayan, A., Taheri, F., Moghadam, M. T., Chegini, Z., & Shariati, A. (2021). The association of *Chlamydia pneumoniae* infection with atherosclerosis: Review and update of in vitro and animal studies. *Microbial pathogenesis*, 154, 104803. <https://doi.org/10.1016/j.micpath.2021.104803>
- Kountouras, J., Papaefthymiou, A., Gavalas, E., Polyzos, S. A., Boziki, M., Kyriakou, P., Katsinelos, P., Zavos, C., Liatsos, C., Tzivras, D., Tzitivridou-Chatzopoulou, M., Dardiotis, E., Deretzi, G., Vardaka, E., & Doulerberis, M. (2020). *Helicobacter pylori* infection as a potential risk factor for multiple sclerosis. *Medical hypotheses*, 143, 110135. <https://doi.org/10.1016/j.mehy.2020.110135>
- Kountouras, J., Polyzos, S. A., Katsinelos, P., Zeglinas, C., Artemaki, F., Tzivras, D., Vardaka, E., Gavalas, E., Romiopoulos, I., Simeonidou, C., Grigoriadis, N., Kountouras, C., Dardiotis, E., & Deretzi, G. (2017). Cardio-cerebrovascular disease and *Helicobacter pylori*-related metabolic syndrome: We consider eradication therapy as a potential cardio-cerebrovascular prevention strategy. *International journal of cardiology*, 229, 17–18. <https://doi.org/10.1016/j.ijcard.2016.11.265>
- Lee, M., Baik, H., Park, J. S., Kim, S., Kyung, C., Baik, S. J., Lee, B. K., Kim, J. H., Ahn, C. W., Kim, K. R., & Kang, S. (2018). Current *Helicobacter pylori* infection is significantly associated with subclinical coronary atherosclerosis in healthy subjects: A cross-sectional study. *PLoS one*, 13(3), e0193646. <https://doi.org/10.1371/journal.pone.0193646>
- Lujan-Vega, C., Keel, M. K., Barker, C. M., & Hawkins, M. G. (2021). Evaluation of Atherosclerotic Lesions and Risk Factors of Atherosclerosis in Raptors in Northern California. *Journal of avian medicine and surgery*, 35(3), 295–304. <https://doi.org/10.1647/20-00078>

- Makoveichuk, E., Vorrjö, E., Olivecrona, T., & Olivecrona, G. (2017). TNF- $\alpha$  decreases lipoprotein lipase activity in 3T3-L1 adipocytes by up-regulation of angiopoietin-like protein 4. *Biochimica et biophysica acta. Molecular and cell biology of lipids*, 1862(5), 533–540. <https://doi.org/10.1016/j.bbalip.2017.02.005>
- Markus, H. S., & Mendall, M. A. (1998). Helicobacter pylori infection: a risk factor for ischaemic cerebrovascular disease and carotid atheroma. *Journal of neurology, neurosurgery, and psychiatry*, 64(1), 104–107. <https://doi.org/10.1136/jnnp.64.1.104>
- Park, M. J., Choi, S. H., Kim, D., Kang, S. J., Chung, S. J., Choi, S. Y., Yoon, D. H., Lim, S. H., Kim, Y. S., Yim, J. Y., Kim, J. S., & Jung, H. C. (2011). Association between Helicobacter pylori Seropositivity and the Coronary Artery Calcium Score in a Screening Population. *Gut and liver*, 5(3), 321–327. <https://doi.org/10.5009/gnl.2011.5.3.321>
- Pearson-Stuttard, J., Guzman-Castillo, M., Penalvo, J. L., Rehm, C. D., Afshin, A., Danaei, G., Kypridimos, C., Gaziano, T., Mozaffarian, D., Capewell, S., & O'Flaherty, M. (2016). Modeling Future Cardiovascular Disease Mortality in the United States: National Trends and Racial and Ethnic Disparities. *Circulation*, 133(10), 967–978. <https://doi.org/10.1161/CIRCULATIONAHA.115.019904>
- Pohjanen, V. M., Koivurova, O. P., Niemelä, S. E., Karttunen, R. A., & Karttunen, T. J. (2016). Role of Helicobacter pylori and interleukin 6 -174 gene polymorphism in dyslipidemia: a case-control study. *BMJ open*, 6(1), e009987. <https://doi.org/10.1136/bmjopen-2015-009987>
- Rahman, L. Q., Rahman, A. Q., Bakir, A. A., Muhamadamin, R. A., & Khudhur, P. K. (2020). DNA detection of Helicobacter pylori in saliva of patients with low salivary pH. *Zanco Journal of Medical Sciences (Zanco J Med Sci)*, 24(2), 283–290.
- Robinson, K., & Atherton, J. C. (2021). The Spectrum of Helicobacter-Mediated Diseases. *Annual review of pathology*, 16, 123–144. <https://doi.org/10.1146/annurev-pathol-032520-024949>
- Rogha, M., Nikvarz, M., Pourmoghaddas, Z., Shirmeshan, K., Dadkhah, D., & Pourmoghaddas, M. (2012). Is helicobacter pylori infection a risk factor for coronary heart disease?. *ARYA atherosclerosis*, 8(1), 5–8.
- Ross R. (1993). The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature*, 362(6423), 801–809. <https://doi.org/10.1038/362801a0>
- Shimamoto, T., Yamamichi, N., Gondo, K., Takahashi, Y., Takeuchi, C., Wada, R., Mitsushima, T., & Koike, K. (2020). The association of Helicobacter pylori infection with serum lipid profiles: An evaluation based on a combination of meta-analysis and a propensity score-based observational approach. *PloS one*, 15(6), e0234433. <https://doi.org/10.1371/journal.pone.0234433>
- Sturlaugsdottir, R., Aspelund, T., Bjornsdottir, G., Sigurdsson, S., Thorsson, B., Eiriksdottir, G., & Gudnason, V. (2016). Prevalence and determinants of carotid plaque in the cross-sectional REFINE-Reykjavik study. *BMJ open*, 6(11), e012457. <https://doi.org/10.1136/bmjopen-2016-012457>
- Sun, Y., Fu, D., Wang, Y. K., Liu, M., & Liu, X. D. (2016). Prevalence of Helicobacter pylori infection and its association with lipid profiles. *Bratislavské lekarske listy*, 117(9), 521–524. [https://doi.org/10.4149/bll\\_2016\\_103](https://doi.org/10.4149/bll_2016_103)
- Tabata, N., Sueta, D., Akasaka, T., Arima, Y., Sakamoto, K., Yamamoto, E., Izumiya, Y., Yamamuro, M., Tsujita, K., Kojima, S., Kaikita, K., Morita, K., Oniki, K., Saruwatari, J., Nakagawa, K., & Hokimoto, S. (2016). Helicobacter pylori Seropositivity in Patients with Interleukin-1 Polymorphisms Is Significantly Associated with ST-Segment Elevation Myocardial Infarction. *PloS one*, 11(11), e0166240. <https://doi.org/10.1371/journal.pone.0166240>
- Upala, S., Sanguankeo, A., Saleem, S. A., & Jaruvongvanich, V. (2017). Effects of Helicobacter pylori eradication on insulin resistance and metabolic parameters: a systematic review and meta-analysis. *European journal of gastroenterology & hepatology*, 29(2), 153–159. <https://doi.org/10.1097/MEG.0000000000000774>
- Wan, Z., Hu, L., Hu, M., Lei, X., Huang, Y., & Lv, Y. (2018). Helicobacter pylori infection and prevalence of high blood pressure among Chinese adults. *Journal of human hypertension*, 32(2), 158–164. <https://doi.org/10.1038/s41371-017-0028-8>
- Wan, Z., Song, L., Hu, L., Hu, M., Lei, X., Huang, Y., & Lv, Y. (2020). Helicobacter pylori infection is associated with diabetes among Chinese adults. *Journal of diabetes investigation*, 11(1), 199–205. <https://doi.org/10.1111/jdi.13102>
- Wang, J. W., Tseng, K. L., Hsu, C. N., Liang, C. M., Tai, W. C., Ku, M. K., Hung, T. H., Yuan, L. T., Nguang, S. H., Yang, S. C., Wu, C. K., Chiu, C. H., Tsai, K. L., Chang, M. W., Huang, C. F., Hsu, P. I., Wu, D. C., & Chuah, S. K. (2018). Association between Helicobacter pylori eradication and the risk of coronary heart diseases. *PloS one*, 13(1), e0190219. <https://doi.org/10.1371/journal.pone.0190219>
- Warren, J. R., & Marshall, B. (1983). Unidentified curved bacilli on gastric epithelium in active chronic gastritis. *Lancet (London, England)*, 1(8336), 1273–1275.
- Xu, X., Li, W., Qin, L., Yang, W., Yu, G., & Wei, Q. (2019). Relationship between Helicobacter pylori infection and obesity in Chinese adults: A systematic review with meta-analysis. *PloS one*, 14(9), e0221076. <https://doi.org/10.1371/journal.pone.0221076>
- Zhang, L., Chen, Z., Xia, X., Chi, J., Li, H., Liu, X., Li, R., Li, Y., Liu, D., Tian, D., Wang, H., Petroski, G. F., Flaker, G. C., Hao, H., Liu, Z., & Xu, C. (2019). Helicobacter pylori infection selectively increases the risk for carotid atherosclerosis in young males. *Atherosclerosis*, 291, 71–77. <https://doi.org/10.1016/j.atherosclerosis.2019.10.005>