H. pylori as a risk factor for IHD in male at Hilla province

Amir .S. Al-Mumin * Osama .F. Al-Jubori **

*MBchB, FICMS, Lecturer College of Medicine , Babylon University
Marjan Teaching specialized Hospital

**MBchB, MSc. Clinical Biochemistry, laboratory departments
Marjan Teaching specialized Hospital

Abstract:

In the present study the aim was to determine whether there is an association between H. pylori infection and IHD or not , which was demonstrated in Hilla province patients, thirty male patients admitted to c.c.u. complaining of acute MI Their Age range (35 – 45) was estimated for anti H. pylori antibodies in their sera with thirty healthy persons as control .

The study revealed that twenty one patients with acute MI shows positive test for anti H. pylori antibodies while only nine of them shows negative test, using a chi square statistical method we found a significant association of H.pylori infection with IHD ($P<0.05$), in relation to control.

The sensitivity of the test in general 70 % while the specificity is 30 % , using percentage and according to the type of MI , ant MI shows the highest percentage (50%) while the lat. MI shows the lowest percentage (3.3%).suspect to idea of possible relation of site of myocardial infarction with H. pylori infection.

الخلاصة

إن الهدف من هذه الدراسة هو تحديد العلاقة بين الاصابة بأحتشاء العضلة القلبية والاصابة بالتهاب بكتيريا الهليكوباكتر بايلوري بالذات ضمن المرضى من سكان مدينة الحلة للفئة العمرية (٣٥ -٤٥ سنة) و بعدد ثلاثون مريضا تم إدخالهم إلى وحدة العناية القلبية من الذين يعانون من احتشاء العضلة القلبية الحاد .تم إخضاعهم جميعا لفحص خاص يحدد مدى اصابتهم ببكتيريا الهيلكوبكتر بايلوري وبالمقارنة مع ثلاثون شخص سليم وضمن نفس الفئة العمرية .

الدراسة اثبتت ان احدى وعشرون مريظا كانت نتيجة فحص بكتيريا الهيلكو باكتر بايلوري ايجابية بينما كانت النتيجة سلبية لتسعة مرضى فقط .

وجد ارتباط مؤثر بين هيلكو باكتر بايلوري واحتشاء العضلة القلبية بقيمة باستخدام التحليل الاحصائي(Chi – square) , احتمالية($p < 0.05$) بالمقارنة مع الاصحاء.

كانت الحساسية للفحص كعلاقة بين هيلكو باكتر بايلوري واحتشاء العضلة القلبية وبصورة عامة ٧٠ % بينما الخصوصية ٣٠ % .

باستخدام النسبة المؤية وحسب نوع الاحتشاء للعضلة القلبيةاظهرت الدراسة بان اعلى نسبة مؤية (٥٠ %) للاصابة بالهيلكوباكتر بايلوري هو للاحتشاء الامامي للعضلة القلبية في حين اوطأ نسبة مؤية (٣,٣ %)للاصابة بالهيلكوباكتر بايلوري هو للاحتشاء الجانبي للعضلة القلبية .

Introduction

Helicobacter pylori infection has bee linked strongly with peptic ulcer disease, atrophic gastritis and gastric cancer [1, 2].

Acute myocardial infarction (AMI) is one of the heading cases of global mortality in countries with established marked economies [3].

(HP) Gram-negative spiral bacilli present in gastric mucosa with sever inflammation was first reported [4]. Measurements of anti-H. pylori antibodies titers in serum samples revealed a high prevalence of H. pylori infection in areas showing high increase of gastric cancer. Thus, H. pylori infection is focused as an etiological factor for gastritis and peptic ulcer disease in addition to gastric cancer [5]. Immunological studies have also been conducted there after by demonstrating that colonization of these bacteria on epithelial cells in the gastric mucosa stimulates cytokine secretion and induces neutrophil infiltration nearby. In particular, vaculating toxin (VT) producing H. pylori has been shown to produce a large amount of IL8 [6]. In recent years, it has been shown that such enhancement of local cytokine production and elevated concentrations of circulating inflammatory cytokines causes vascular endothelial cell injury, suggesting a close relation ship with the path physiology of myocardial infarction [7, 8]. However an association between IHD and infection has been reported not only with H. pylori but also with Chlamydia pneumonia [9, 10, 11, 12, and 13].

Patients & Methods:

A-Samples:

- ***Collection of the samples:*** this Study was performed in Marjan teaching hospital from January 2005- January 2006, a total of 30 patients and 30 controls with a mean age 40 years old that was admitted to coronary care unit complained of acute M.I., all patients were chosen according to specific exclusion and inclusion criteria,
  - Not H.T
  - Not DM
  - No thyroid disease
  - Not hyperlipdemia
  - Not DU
  - Not smokes
  - No Hx of Endoscopies
  - No Hx of Epigastria pain suggested DU
  - Not Hx of IHD

And 30 healthy persons at the same mean age and with the same exclusion criteria, as control were included in this study, a 2 ml. serum was taken from all male to be estimated for anti H. pylori antibodies.

B-Estimation of serum H. pylori:

The **ACON** rapid one step test device for the qualitative detection of the antibodies to Helicobacter pylori (H. pylori) in human serum and plasma was used this is for professional in vitro diagnostic use only.

This test device (serum & plasma) is a rapid chromatographic immunoassay for the qualitative detection of antibodies to H. pylori in serum or plasma.

The principle of this test device is a qualitative membrane based immunoassay for the detection of H. pylori antibodies in serum or plasma, the test procedure is an anti-human IgG is immobilized in the test line region of the test, after specimen is added to the specimen well of the device, it reacts with H. pylori antigen coated particles in the test . this mixture migrates chromatographically along the length of the test and interacts with the immobilized anti-human IgG .

If the specimen contains H. pylori antibodies, a colored line will appear in test line region indicating a positive test result. If the specimen dose not contains H. pylori antibodies, a colored line will not appear in test line region indicating a negative test result.

To serve as a procedural control , a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred .Thus the content of the test device is H . Pylori antigen coated particles and anti-human IgG coated on the membrane.

Results:

30 patients with acute M.I compared with (30 control) responding H. pylori infection and the result was that twenty one patients with acute M.I showed positive test for H. pylori while only nine of them showed negative test as shown in table (1) and fig (1), using percentage and according to the type of acute M.I. acute ant. M.I. show the highest percentage (50%) while lat& inf-lat M.I. show the lowest percentage (3.3%)as shown in the table [2] and fig [2].

Using a chi-square statistical method found that a significant association between H, pylori infection and IHD ($P<0.05$) in relation to control.

The sensitivity of the test in general 70% while the specificity is 30%as shown in fig [4].

Table [1] the number of positive and negative H. pylori test according to the type of M.I.

Type of M.I	No. of pt. +ve test	No. of pt. –ve test
Anterior M.I.	**11**	4
Inferior M.I.	**4**	4
Lateral M.I.	**0**	1
Anterolateral M.I.	**5**	0
Lnferolateral M.I.	1	0

Fig [1] the number of positive and negative H. pylori test according to the type of M.I.

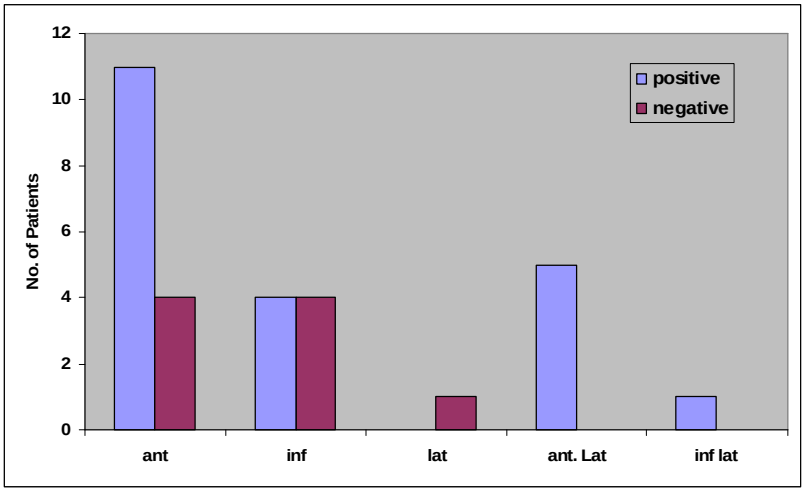


Table [2] the percentage positive and negative of the H. pylori test according to the type of M.I.

Type of M.I	Percentage of +ve test	Percentage –ve test
Anterior M.I	**36.67 %**	13.33%
Inferior M.I.	**13.33%**	13.33%
Lateral M.I.	**0 %**	3.33%
Anterolateral M.I.	**16.67%**	0%
Lnferolateral M.I.	3.33%	0%

Fig [2] the percentages positive and negative of the H. pylori test according to the type of M.I.

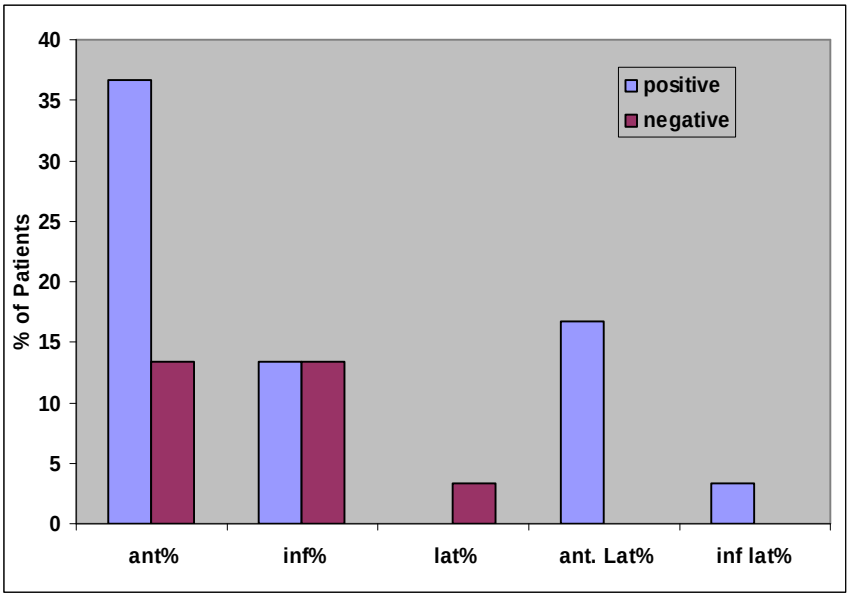


Table [3] the sensitivity and the specificity of the H. pylori test according to the type of M.I.

Type of M.I	sensitivity	specificity
Anterior M.I	**73.33**	26.67
Inferior M.I.	**50**	50
Lateral M.I.	**0**	100
Anterolateral M.I.	**100**	0
Lnferolateral M.I.	100	0

Fig [3] the sensitivity and the specificity of the H. pylori test according to the type of M.I.

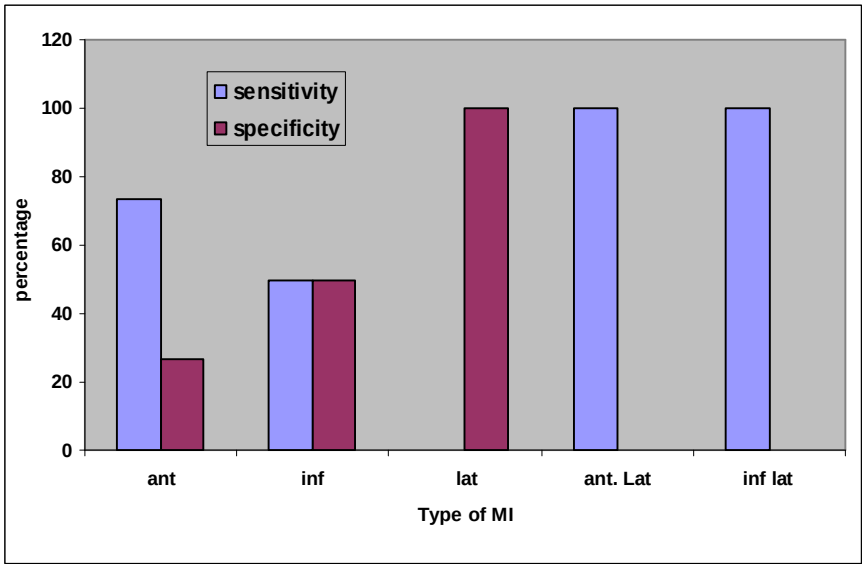
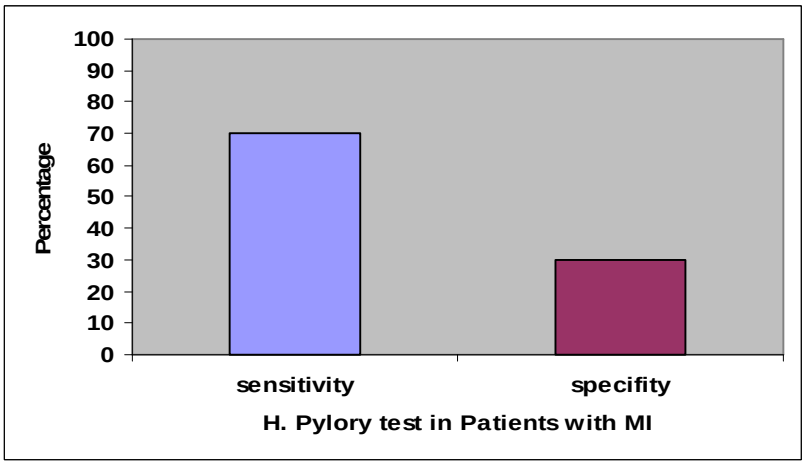


Fig [4] the sensitivity and specificity of H. pylori test in patients with M.I. in general.



Discussion:

The present study showed that there was strong statistical association between IHD and H. pylori inf. [3, 14, 15, 16, 17].

The positive H. pylori tests were found to be increased in patient with acute M.I and mainly with ant. M.I. [18, 19].

H. pylori infection stimulates the production of pro inflammatory cytokines, such as tumor necrosis factor, IL6, IL8 which have been implicated in atherogensis [20, 21].

The association of H. pylori with the elevation of serum C reactive protein and fibrinogen, both of which have been linked to the risk of cardio vascular disease [22, 23].

H. pylori infection was associated with reduction in HDL [24], and elevated serum triglyceride and total cholesterol concentrations ,it has been hypothesized that chronic inflammation could contribute to the risk of vascular disease by increasing some acute phase reactants and inflammation mediators , damaging endothelial cells altering lipid levels and oxidation and changing blood coagulation [24, 25].

H. pylori infection activates neutrophils via induction of many cytokines, particularly IL8, IFN-8 from peripheral lymphocytes and mono cytes, thereby causing vascular injury via production of reactive oxygen species which lead to IHD; this may lead to the development of rupture or erosion of atheromatous plaques [26, 27, and 28].

Study by Elizalde et al. They demonstrated that mice infected with H. pylori had significant increase of circulating platelet aggregates. After damage of mesenteric arteriole endothelium, the embolus also persisted longer among the H. pylori infected mice [29, 30], platelet activation and aggregation is possible via the expression of P. selectin on the platelet surface.

Activated platelet can accumulate and recruit additional platelets expanding the thrombus with a final result of occlusive thrombus formation H. pylori produce a pro inflammatory cytokines which in turn stimulate endothelial cells to express inter cellular adhesion molecular-1 and activate platelets. The sum of these events might trigger a pro-thrombotic status [31].

Conclusion and Recommendation:

- There is positive association between H. pylori infection and IHD.
- It needs farther study to be more supported.
- It needs to give antibiotics to patients with H. pylori infection and follow them to see the progress.

References:

1- Parsonnet J, Friedman GD, Vander steen DP, Chanh Y Vogelman JH, Orentreich N, Sibley RK; Helicobacter pylori infection and gastric carcinoma. NEngl. J Med. 1991; 325; 1127-1131.

2- The EUROGAST study Group: An international association between Helicobacter pylori infection and gastric cancer. Lancet 1993; 341: 1359-1362.

3- Murray CJL, Lope2 AD. Mortality by cause for eight regions of world: Global Burden of Disease study. Lancet 1997; 349: 1269.

4- Nomura A, Semmermann GN, Chyou P, Kato I, Pere2- Pere2 GI, Blasa MJ, Helicobacter pylori infection and gastric carcinoma among Japanese Americanism Hawaii, N Engl J Med. 1991; 325: 1132-6.

5- Correa P, Fox J, Fontham E, Helicobacter pylori and gastric carcinoma, serum antibody. Prevalence in populations with contrasting cancer risks. Cancer 1990, 66: 2569-74.
6- Marchildon PM, Ciota LM, Zamaniyau FZ, Peacak Js, Graham DY. Evaluation of three commercial enzyme immunoassays with the BC areabreath test for detection of Helicobacter pylori infection Jelin Micro biol 1996; 34: 1147-52.
7- Evans DJ; Evans DJ, Graham DY, Klein PD. A sensitive and specific serologic test for detection of campylo buda pyloi infection, Gastroenterology 1989; 96: 1004-8.
8- Marshal BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984; 1: 1311-4.
9- Patel P, Mendall MA, Carring ton D, Strachan DP, Leatham E, Molineanx N, Lvy J., Blakeston C, Seymour CA, Camm AJ, North field TC: Association of Helicobacter pylori and chlanydia pneumonia infections with coronary heart disease and cardiovascular risk factor. BMJ 1995; 311: 711-714.
10- Campbell LA, O'Brien ER, Cappuccio AL, Kuo C, Wang S, Stewart D, Patton DL, Cummings PK, Grayston JT; Detection of Chlamydia pneumonia TWAR in human coronary atherectomy tissues. J infect Dis 1995; 172: 585-588.
11- Danesh J. coronary heart disease, Helicobacter pylori, dental disease, chamydia pneumonia and cytomegalovirus virus: meta-analysis of prospective studies. Am heart J. 1999; 138: S 434-S 437.
12- Strachan DP. Non-gastro intestinal consequences of Helicobacter pylori infection Br Med. Bull 1998; 54: 87-93.
13- Ridker. PM. Are the associations between infection and coronary disease causal are due to confounding? Am. J Med. 1999; 106; 376-7.
14- Hennekens CH. Increasing burden of cardiovascular disease. Current knowledge and future directions for research on risk factors. Circulation 1998; 97: 1095.
15- Shaper AG, Pocock SJ, Walker M, Phillips AN, Whitehead TP, Macfarlane PW. Risk factors for ischemic heart disease: the prospective phase of the British Regional Heart Study. J Epideniol community Health 1985; 39: 197.
16- Mendall MA, Goggin PM, Molineaux N, Levy J, Toosy T, Strachan D, Relation of Helicobacter pylori infection and coronary heart disease. Br Heart J 1994; 71: 437.
17- Martin de argila C, Boixeda D, Canton R, Gisbert JP, Fuertes A. High sero prevalence of Helicobacter pylori infection in coronary heart disease. Lancet 1995; 346: 310.
18- Rathbone B, Martin D, Stephens, J, Thompson JR, Samani NJ. Helicobacter pylori seropositivity in subjects with acute myocardial infarction, Heart 1996; 76: 308.
19- Morgando A, Sanseverino P, Perottoc, Molino F, Gai V, Ponzetto A. Helicobacter pylori

seropositivity in myocardial infarction. Lancet 1995; 345: 1380.

20- Carbtree JE, Shallcross TM, Heatley RV, Wyatt JI. Mucosanl tumour necrosis factor and inter Leukin-6 in patients with Helicobacter pylori associated gastric. Gut 1991: 32: 1473- 1477.

21- Moss SF, Legou S, Devies J, Calam J: Cytokine geue expression in Helicobacter pylori associated autral gastritis. Gut 1994: 35: 1567-1570.

22- Liu220 G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB Maseri A: Prognostic value of C-reaction protein and plasma amyloid A protein in severe un stable angina, N Eugl. J Med. 1994: 331: 417-424.

23- Niemela S, Karttumen T, Korhoneu T, Laara E, Karttuneu R , IKaheimo M, Kesaniemi YA: could Helicobacter pylori infection increase the risk of coronary heart disease by modifying serum lipid concentration? Heart 1996: 75: 573, 575.

24- Fraser AG, ScraggR, Metcalf P, Mc Cullough S, Yeates NJ. Prevalence of Helicobacter pylori infection in different ethnic groups in New Zealand children and adults. Aust NZJ Med 1996; 26: 646-50.

25- Laurila A, Bloigh A, Nayha S, Hassi L, Leinoneu M, Saikku P. Association of Helicobacter pylori infection with elevated serum lipids, Athero sclerosis 1999; 142: 207.

26- Karttunen R, Karttunen T, EKre H-PT, Donald TT. Interferon gamma and interleukin 4-sedreting cells in the gastric ant rum in Helico bacter pylori positive and negative gastrics. Gut 1995; 36: 341-5.

27- Karttunen R, Andersson G, Poikonen K, Helicobacter pylori induces lymphocyte activation in peripheral blood cultures. Clin Exp immunol 1990; 82: 485-8.

28- Pasceri V, Cammarota G, Patti G, et al. Association of virulent Helicobacter pylori strains with isdemic heart disease. Circulation 1998; 97: 1675-9.

29- Elizalde JI, Gomez J, Panes J, Lozano M, Casadevall M, Ramire2 J, Platelet activation in mice and human. Helicobacter pylori infection. J Clin Invest 1997; 100:996.

30- Aguejouf O, Mayo K, Malfatti E, Doutremepuich C, Megrand F. A terial thrombosis and chronic Helicobacter pylori infection in mice. Gut 1998; 43 [Suppl 2]: A 104.

31- Saikku P, Leinonen M, Mattila K, Ekman MR, Nieminen MS, Makela PH, et al. Serological evidence of an association of a novel Chlamydia, TWAR, with chronic coronary heart disease and acute myocardial infarction. Lancet 1988; II: 983.