ORIGINAL ARTICLE

# IgG ANTIBODIES AGAINST *HELICOBACTER PYLORI* IN PATIENTS OF MYOCARDIAL INFARCTION

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**ABSTRACT:** Fifty-six patients of confirmed myocardial infarction were inducted into the study. Healthy attendants of patients donating blood to their relatives were-taken as control. Weight, height, smoking habits and diabetic status were recorded. Base line laboratory investigations, lipid profiles, creatine kinase total and MB, Troponin T and IgG antibodies against *Helicobacter pylori* (HPAb) were done. Mean age ±SD of the patients was 45.6 ± 6.5 years. There were 47 males and 9 females. HPAb were detected in 41 (73.21%) patients. No significant difference in age, BMI, Cholesterol and Triglyceride was observed patients tested positive or negative to HPAb. HDL levels were significantly low in patients who tested positive to HPAb. (95% CI -6.3 to -1.09, p=0.006). Control group comprised 23 subjects with mean age 37.9 +5.7 years. HPAb were positive in 11 (47.82%) of the subjects in control group. Frequency of HPAb was significantly more in patients of myocardial infarction compared to control (p=0.039).

**KEY WORDS:** *Helicobacter pylori* Myocardial Infarction Ischemic Heart Disease Troponin-T

## INTRODUCTION

Since its discovery in 1893 by Bizzero in dogs, *Helicobacter pylori* (HP) remained a controversial organism[1]. In 1906 Krientz discovered these spiral organisms in humans but his findings were viewed with incredulity as most of the spiral organisms were obtained post mortem and thus contamination could not be ruled out[1]. It was not until the work of Marshall in 1983 and Warren in 1984 that the connection between the infection and gastric disease was taken seriously[2]. Now the role of HP in chronic active gastritis (type B) and peptic ulcer is well established[3-6]. Many methods are in vogue to diagnose HP infection, these include both endoscopic and nonendoscopic methods. The endoscopic methods include Rapid Urease Test, Brush Cytology, Histopathology and Culture. Histopathology is the only method that can show both the extent of HP infection and the degree of mucosal damage[7]. Polymerase Chain Reaction can also be used to detect HP in gastric biopsy specimens. Three non-endoscopic methods for diagnosis of *Helicobacter pylori* include $^{13}C$ or $^{14}C$-Urea Breath Test and *Helicobacter pylori* antibodies (HPAb). Breath test are useful for determining whether a treated patient has been cured[9,10]. Serological tests have also been validated for diagnosis and monitoring eradication after antimicrobial treatment. Decrease in IgG titers to less than 50% of the pretreatment sample six months after then end of treatment, shows eradication[11,12]. Helicobacter pylori, apart from gastritis and peptic ulcer are also implicated in other diseases. The organism has been linked to gastric malignancy[13]. Currently the role of HP is under debate for its association with ischaemic heart disease. Many cross sectional studies have reported a positive association of *Helicobacter pylori* with coronary heart disease[14]. Prevalence of HP depends upon the population studied, and the results may be confounded by other risk factors for cardiac disease and HP infection[15]. The present case control, cross sectional study was conducted to investigate the association of HP with myocardial infarction (MI) by comparing a group of with confirmed myocardial infarction patients with a group of controls of a similar age and gender distribution.

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## PATIENTS AND METHODS

Patients presenting with first attack of myocardial infarction at Cardiology or Medicine Wards of Chandka Medical College Larkana during the period of August 1996 and December 1997 were selected for the study. The diagnosis of myocardial infarction was made on the following basis:

- Typical chest pain
- ST-segment elevation
- Total creatine kinase activity within 24 hours after admission more than twice the upper limit of normal along with elevated creatine kinase MB.
- Positive Troponin T test.

A control group of matched age and gender was selected from the healthy attendants of the patients donating blood to their relatives. Informed consent was obtained from all the selected patients. Clinical examination of the patients was carried out and the findings were recorded. Height, weight and body mass index (BMI) of the patients was calculated by dividing the weight in kg by square of the height in meters[16]. Smoking habits with duration and the number of cigarettes per day was also noted. Inquiry was also made about the diabetic history. Patients with known history of acid peptic disease were excluded form the study. Selected patients underwent the investigations such as Complete Blood Counts, Urine DR, Blood Sugar Fasting and Random, Blood Urea,

Lipid profile and IgG Antibodies against *Helicobacter pylori*. The patients' serums for HP antibodies were stored at -10°C till the tests were done. Complete Blood Counts were done on Sysmex K-4500 automated cell counter, IgG antibodies to HP were done by ELISA (HEL- pTEST™ II, Amrad Biotech Australia). For qualitative estimation of serum troponin T, whole-blood rapid-essay device (Boehringer Mannheim, Mannheim, Germany) was used[17]. Positive test was indicated by a colour line appearing within 20 minutes showing the presence of troponin T in the sample above the discriminator value of 0.18 ng/ml[18]. The rest of the tests were done on standard photometer using Boehringer Mannheim reagents. Statistical analysis was done using Student's 't' test, 95% confidence interval (CI) were estimated. P value of less than 0.05 was taken as significant. Statistical Analysis was done on SPSS ver 7.0.

# Results

Fifty-six patients of confirmed myocardial infarction with mean age±SD as 45.6±6.5 years were selected. This included 47 (83.92%) males and 9 (16.1%) females. The control group (CON) group consisted of 23 subjects including 21 (91.3%) males and 2 (8.7%) females with mean age±SD as 37.9±5.7years. The mean values ±SD in MI Group of Total Cholesterol was 201.0±39.2 mg/dl, HDL-Cholesterol was 35.46±4.64 mg/dl and Triglyceride was 167.3±27.2 mg/dl. Out of 56 patients 32 (57.14%) were smokers and 19 (33.92%) were diabetic. IgG antibodies against HP were detected in 41 (73.21%) patients. HDL was significantly lower in the patients positive to HP antibodies (34.46±4.16 mg/dl) compared to those in whom it was negative (38.2±4.9 mg/dl) [95% CI -6.3 to -1.09, p=0.006]. MI group statistics for patients who tested positive to HPAb and those who tested negative are tabulated in Table I and independent sample test in Table II. Breakup of diabetic status, sex and smoking habits of MI Group according to HPAb status is given in Table III. Mean values of total cholesterol, HDL- cholesterol and triglycerides in CON Group were 147.1±121.2 mg/dl, 43.6±7.5 mg/dl and 101.5±11.2 mg/dl respectively. In CON Group HPAb were positive in 11 (47.82%) of the subjects. Frequency of HPAb in two groups was significantly different with p=0.039.

**TABLE I** **MI group statistics for HPAb status**

| | HPAb | Mean | Std. Deviation | Std. Error mean |
|---|---|---|---|---|
| Age | Positive | 46.317 | 6.908 | 1.079 |
| | Negative | 43.800 | 5.158 | 1.332 |
| BMI | Positive | 26.817 | 6.165 | 0.963 |
| | Negative | 24.993 | 4.504 | 1.163 |
| CHO | Positive | 205.634 | 39.678 | 6.197 |
| | Negative | 188.200 | 36.186 | 9.343 |
| HDL | Positive | 34.463 | 4.159 | 0.649 |
| | Negative | 388.200 | 4.901 | 1.265 |
| TG | Positive | 1711.098 | 26.437 | 4.129 |
| | Negative | 156.800 | 27.224 | 7.029 |

**TABLE II** **Independent sample test in MI group for HPAb status on different variables**

| | T-test for equality of means | | | | | 95% confidence interval of the mean | |
|---|---|---|---|---|---|---|---|
| | t | df | Sig. (2-tailed) | Mean Difference | Std. Error Difference | Lower | Upper |
| Age | 1.283 | 54 | 0.205 | 2.517 | 1.961 | -1.415 | 6.449 |
| BMI | 1.046 | 54 | 0.300 | 1.824 | 1.744 | -1.673 | 5.321 |
| CHO | 1.489 | 54 | 0.142 | 17.434 | 11.709 | -6.041 | 40.909 |
| HDL | -2.837 | 54 | 0.006 | -3.736 | 1.317 | -6.377 | -1.096 |
| TG | 1.778 | 54 | 0.081 | 14.298 | 8.040 | -1.821 | 30.416 |

**TABLE III** **Breakup of diabetes, sex and smoking habits according to HPAb in MI**

| HPAb | Diabetic | | Sex | | Smoking habits | |
|---|---|---|---|---|---|---|
| | Non diabetic Count | Diabetic Count | Female Count | Male Count | Non smokers Count | Smokers Count |
| Negative | 12 | 3 | 1 | 14 | 6 | 9 |
| Positive | 25 | 16 | 8 | 33 | 18 | 23 |

# Discussion

The role of *Helicobacter pylori* is currently under debate in patients of ischaemic heart disease. Many articles are appearing in international scientific journals highlighting its role and different mechanisms by which it is mediated, while some articles do not show any such association. In this series we studied the status of IgG antibodies against *Helicobacter pylori* in patients presenting with first attack of myocardial infarction and to compare its frequency with a matched control group.

In the present series, we detected IgG HPAb in 73.21% of patients presenting with myocardial infarction and in the control group the frequency was 47.82%. The difference in the frequency was statistically significant (p=0.039). Another very significant finding was that, HDL was found to be significantly reduced in patients who tested positive to HPAb as compared to those who did not. Some researchers are of view that HP has an independent causative role in coronary heart disease[20] others favour an indirect role[14]. Many mechanisms are described by which *Helicobacter pylori* could inflict the cardiac injury. It is postulated that HP increases the risk factors due to a low-grade chronic inflammatory response. It has been shown that the HP infection could alter the serum lipids and predispose to the coronary heart disease[21]. In another study it was found that the patients with HP infection had lower levels of HDL as compared to those who did not[21]. We had similar results in our series and the HDL levels in HP positive and negative patients were 34.46 mg/dl and 38.2 mg/dl respectively (95% CI -6.3 to -1.09, p=0.006). As HDL levels are protective their decrease could predispose to coronary heart disease. HP also increases the C-reactive proteins, which increases the risk of coronary heart disease[22]. By virtue of causing the chronic gastritis[5,6] HP could lead to the deficiency of vitamins and folate[23]. This in turn could lead to failure of methylation by 5 methyl tetrahydrofolic acid resulting in accumulation of homocystine, which is toxic to endothelial cells and causes coronary heart disease[23]. It has also been shown that the infection with HP in early childhood increases the risk of cardiac disease in adult life[24].

These findings have very important clinical implications. The association needs confirmation in large-scale studies. If HP itself is responsible for the association, then this is of great clinical importance as the infection is easily treatable[25-30] and a

risk factor could be easily abated. HP and MI may have shared risk factors, because low socioeconomic status in childhood may predispose to both conditions[24]. HP may have little impact as an independent risk factor for cardiac disease and a longitudinal study with treatment intervention is needed to examine this association.

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## REFERENCES

1. Axon ATR, Quina M. Ten-year milestones. Curr Opin Gasterol 1994; 10(Suppl 1): 1-5.
2. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984; 1: 1311-5.
3. Hunt RH, Mohammed AH. The current role of *Helicobacter pylori* eradication in clinical practice. Scand J Gastroenterol Suppl 1995; 208: 47-52.
4. Shaikh WM, Sheikh SM, Shah S, Jatoi N. Prevalence of *Helicobacter pylori* infection in acid peptic disorders in Northern Sindh Pakistan. Pakistan J Gastroenterol 1996; 10: 3-6.
5. Konturek PCh, Konturek SJ. Role of *Helicobacter.pylori* infection in gastroduodenal secretion and in pathogenesis of peptic ulcer and gastritis. J Pharmacol Physiol 1994; 45: 333-50.
6. Humama-Tul-Bushrn, Umar M, Khan NY, Latif Z. *Helicobacter pylori* and chronic gastritis. Pakistan J Gastroenterol 1995; 9: 18-22.
7. Price AB. The histological recognition of Helicobacter pylori. In: Lee A, Megraud F, editors. *Helicobacter pylori*: Techniques for Clinical Diagnosis and Basic Research. London: WB Saunders; 1995; pp 33-49.
8. Monteiro L, Birac C, Megraud F. Detection of *Helicobacter pylori* in gastric biopsy by polymerase chain reaction. In: Lee A, Megraud F, editors. *Helicobacter pylori*: Techniques for Clinical Diagnosis and Basic Research. London: WB Saunders; 1995. p. 12-19.
9. Graham DY, Klein PD, Evans DJ, Evans DG, Alper LC, Operkun AR, et al. Campylobacter pyloris detected noninvasively by the 13C-urea breath test. Lancet 1987; 1774-7.
10. Logan RPH, Dill S, Bauer FE, Walker MM, Hirschi AM, Gummett PA, et al. The European 13C-urea breath test for the detection of *Helicobacter pylori*. Eur J Gastroenterol Hepatol 1991, 3: 915-2.
11. Hirschil AM, Brandstatter G, Dragosics B, Hentschel E, Kundi M, Rotter ML, et al. Kinetics of specific IgG antibodies for monitoring the effect of *anti-Helicobacter pylori* chemotherapy. J Infect Dis 1993; 168: 763-6.
12. Kosunen TU, Seppala K, Sarna S, Sipponen P. Diagnostic value of decreasing IgG, IgA and IgM antibody titres after eradication of *Helicobacter pylori*. Lancet 1992; 339: 893-5.
13. Parsonnet J, Friedman GD, Orentreich N, Vogelman H. Risk of gastric cancer in people with CagA positive or CagA negative *Helicobacter pylori* infection. Gut 1997; 40: 297-301.
14. Patel P, Mendall MA, Carrington D, Strachan DP, Leatham E, Molineaux N, et al. Association of *Helicobacter pylori* and Chlamydia pneumoniae infections with coronary heart disease and cardiovascular risk factors [see comments] [published erratum appears in BMJ 11995 Oct 14; 311 (7011): 985]. Br Med J 1995; 311: 711-4.
15. Meggraud F. Epidemiology of *Helicobacter pylori* infection. Gastroenterol Clin North Am 1993; 22: 73-88.
16. Munro J, Edward C, editors. Macleod's clinical examination. 9th ed Edinburgh: ELBS, 1995.
17. Katus HA, Looser S, Hallermayer K, Remppis A, Scheffold T, Brogya A, et al. Development and in vitro chracterization of a new immunoassay of cardiac troponin T. Clin Chem 1992; 38: 386-93.
18. Muller-Bardorff M, Freitag H, Scheffold T, Remppis A, Kubler W, Katus HA. Development and characterization of a rapid assay for bedside determinations of cardiac troponin T. Circulation 1995; 92: 2869-75.
19. Martin B. An introduction to Medical Statistics. Oxford. ELBS Edition 1989.
20. Murray LJ, Bamford KB, O'Reilly DP, McCrum EE, Evans AK. *Helicobacter pylori* infection: relation with cardiovascular risk factors, ischaemic heart disease, and social class. Br Heart J 1995; 74: 497-501.
21. Niemela S, Karttunen T, Korhonen T, Laara E, Karttunen R, Ikaheimo M, Kesaniemi YA. Could *Helicobacter pylori* infection increase the risk of coronary heart disease by modifying serum lipid concentrations? Heart 1996; 75: 573-5.
22. Mendall MA, Patel P, Ballam L, Strachan D, Northfield TC. C reactive protein and its relation to cardiovascular risk factors: a population based cross sectional study [see comments]. Br Med J 1996; 312: 1061-5.
23. Sung JJ; Sanderson JE. Hyperhomocysteinaemia, *Helicobacter pylori* and coronary heart disease. Heart 1996; 76: 305-7.
24. Mendall MA, Goggin PM, Molineaux N, Levy J, Toosy T, Strachan D, et al. Relation of *Helicobacter pylori* infection and coronary heart disease. Br Heart J 1994; 71: 437-9.
25. Freston JW. Emerging strategies for managing peptic ulcer disease. Scand Gastroenterol Suppl 1994; 201: 49-54.
26. Kohli Y, Kato T, Azuma T, Ito S, Hirai M. Lansoprazole treatment of *Helicobacter pylori-positive* peptic ulcers. J Clin Gastroenterol 1995; 20 Suppl 1: S48-51
27. Yousfi MM, el Zimaity HM, al Assi MT, Cole RN, Genta RM, Graharn DY. Metronidazole, omeprazole and clarithromycin: an effective combination therapy for *Helicobacter pylori* infection. Ailment Pharmacol Ther 1995; 9: 209-12.
28. Zuberi BF, Sheikh R, Muzaffar L, Sheikh GM. Nizatidine and clarithromycin: an effective combination therapy in treatment of *Helicobacter pylori* associated peptic ulcer. J Coll Phy Surg Pakistan 1996; 6: 196-8.
29. Al Assi MT, Genta RM, Karttunen TJ Graham DY. Clarithromycin-amoxycilline therapy for *Helicobacter pylori* infection. Aliment Pharmacol Ther 1994; 8: 453-6.
30. Zuberi BF, Lal S, Shaikh MR. Low dose, short term, triple therapy for *Helicobacter pylori* associated peptic ulcer. J Pakistan Med Assoc 1997; 47: 228-30.