

**The Extra-gastric Effects of Chronic Helicobacter Pylori Infection on  
Some Metabolic Risk Factors in Dyspeptic patients  
For Coronary Heart Disease**

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**Abstract**

Hyperlipidemia, thrombophilia and hyperhomocysteinemia were all known metabolic risk factors for coronary heart disease. The association between the extra-gastric effects of chronic helicobacter pylori (h.pylori) infection and these risk factors in dyspeptic patients needs to be clarified. Forty subjects were studied for determination of serum total cholesterol, triglycerides, very low density lipoprotein-cholesterol (VLDL-c), low density lipoprotein-cholesterol (LDL-c), high density lipoprotein-cholesterol (HDL-c), plasma clotting factors VII, X, XII activities, fibrinogen concentration, antithrombin III (ATIII) activity as well as plasma total homocysteine. They were 26 males and 14 females. Their age ranged from 31 to 41, with a mean value of  $35.8 \pm 2.6$  years. They were categorized according to the concentration of h.pylori antibodies (IgG) into 15 patients who were seronegative and another 15 patients who were seropositive. These patients were compared with 10 healthy subjects, age and sex matched who served as controls. The results of the present work showed that; serum lipid profile had no significant differences in seronegative and seropositive patients for h.pylori infection compared with the control group ( $p > 0.05$ ). Moreover, plasma clotting factors VII, X, XII had no significant changes while plasma fibrinogen concentration and total homocysteine were significantly higher in seropositive compared with both seronegative patients and the control group ( $p < 0.05$ ). Additionally, seropositivity correlated significantly with plasma fibrinogen concentration ( $r = 0.76$ ;  $p < 0.05$ ).

It could be concluded that, alteration of plasma fibrinogen and total homocysteine might be considered metabolic risk factors for coronary heart disease in dyspeptic patients due to chronic h.pylori infection. However, estimation of these biomarkers are recommended to avoid the future risk of ischemic heart disease.

## Introduction

H.pylori was detected during the 1980s (*Dierkes et al.,2003*). It is a gram-negative microaerophilic bacillus. Its morphology is heterogeneous in that it can take a helicoidal, spiral, or curved shape with 2 to 6 flagellae (*Torres and Gaensly,2002*).

H.pylori infection, usually acquired in childhood (*Torgano et al.,1999*). The bacteria following an oral infection probably reach the stomach covered with salivary mucins containing both sialylated and sulfated components that are known to bind to h.pylori. After ingestion , h.pylori colonizes the human gastric mucus and epithelium by several specific adhesins. However, cell invasion is a rare events (*Dubereuil et al.,2002*).

Although the infection will cause gastric inflammation in virtually all infected subjects, the majority of them will remain asymptomatic, while others develop atrophic gastritis and subsequently gastric ulcer which can further develop to gastric cancer (*Dierkes et al.,2003*).

The persistent inflammation of the stomach induced by h.pylori infection can have consequences on the rest of the body. Many extra-gastric diseases may be associated with h.pylori, e.g vascular diseases, autoimmune diseases, skin diseases, sideropenic anemia, diabetes, Parkinson disease, and bronchiectasis (*Richy and Megraud,2003*).

Moreover, h.pylori infection can cause platelet aggregation and induces a procoagulant activity. It can, also, contribute to atherosclerosis and hence, the acute phase of myocardial infarction (*Pellicano et al.,2000*).

In (1994), *Mendall et al.*, was the first who described a link between h.pylori infection and coronary heart disease. Homocysteine may have an effect on the risk of cardiovascular disease by stimulating

procoagulant factors and/or impair anticoagulant mechanisms or fibrinolysis (*Klerk et al.,2002*)

### **Aim of the work**

The current work aimed to determine whether chronic helicobacter pylori infection in dyspeptic patients is associated with impaired serum levels of lipid profile, plasma procoagulant activity, natural anticoagulant and total homocysteine, as well as their relationship to the future risk of coronary heart disease.

## Subjects and methods

From the period between Mars , 2003 to January 2004 , 30 patients were selected from Gastroenterology Department, Benha University Hospital for the study . Their ages ranged from 32 to 41 years, with a mean value of  $36.2 \pm 2.5$  years. They were 18 males and 12 females . Ten healthy subjects, age and sex matched served as controls . All subjects included in the study were categorized into the followings :

**Control group:** comprised 10 healthy subjects.

**Seronegative group:** comprised 15 patients who were suffering from dyspepsia due to chronic gastritis. The serum level of h.pylori IgG antibodies was less than 8.0 U/ml.

**Seropositive group:** comprised 15 patients who were suffering from dyspepsia due to chronic gastritis. The serum level of h.pylori IgG antibodies was more than 12.0 U/ml.

(N.B. The patients of the study were categorized according to *Gosciniak ,1997*).

All the patients and controls were subjected to the following investigations : history taking , general and local examination, blood pressure monitoring, ultrasonography scanning of the abdomen, endoscopic examination, and body mass index (BMI), was calculated according to *Garrow,(1990)*, where  $BMI = \text{Weight (kg)} / \text{height (m}^2\text{)}$  and laboratory investigations including, serum h.pylori antibodies (IgG), fasting as well as postprandial serum glucose , total cholesterol , triglycerides , very low density lipoprotein-cholesterol (VLDL-c) , low density lipoprotein-cholesterol (LDL-c) , high density lipoprotein-cholesterol (HDL-c) , aspartate aminotransferase (AST) , alanine

aminotransferase (ALT), , plasma clotting factors VII, X, XII activities, fibrinogen concentration, antithrombin III activity, and total homocysteine.

**Exclusion criteria:**

Subjects more than 41 years and less than 32 years, obese, diabetics, smokers or hypertensives as well as those with serum IgG antibodies levels ranged 8-12 U/ml, liver diseases, coronary heart disease or under medications as vitamin K, anti-platelets, contraceptive pills or anticoagulant therapy were excluded from the study.

**Sampling:**

Venous blood sample (9.0 ml) was taken from all subjects in the overnight fasting state . The sample was divided into 3 parts. The first part of the sample (2.0 ml) was taken on dipotassium EDTA, centrifuged and the separated plasma was kept frozen at -80°C for later determination of total homocysteine. The second part (5.0 ml) was left for 15 minutes at room temperature to be clotted and centrifuged . Part of the serum separated was used for determination of the levels of fasting glucose, total cholesterol, triglycerides, VLDL-c LDL-c, HDL-c, and the activities of AST and ALT. The other part of the serum was kept frozen at -80°C for later determination of h.pylori antibodies (IgG). The remaining part of the blood (2.0 ml) was taken on tri-sodium citrate (3.2%) in a ratio of 9 parts : 1 part. These samples were centrifuged as rapid as possible at 3000 r.p.m for 5 min. The plasma separated was kept frozen at -80°C and was assayed within one month for determination of clotting factor VII, X, XII, antithrombin III activities and fibrinogen concentration. Another 2 hours postprandial (after meal) venous blood sample (2.0 ml) was taken and centrifuged.

The serum separated was used for determination of postprandial serum glucose level.

### **Methods:**

-Determination of serum h.pylori IgG antibodies by ELISA (Dynatech instrument, Germany) (*Gosciniak,1997*): The kit was supplied by IBL-Hamburg, Immuno-Biological Laboratories, Germany.

-Determination of serum fasting, postprandial glucose (*Trinder,1969*) , AST (*Reitman and Frankel,1957*), ALT (*Reitman and Frankel,1957*) as well as lipid profile including ; total cholesterol (*Stein,1986*), triglycerides, VLDL-c, HDL-c (*Wahlefeld,1974*) by spectrophotometric method ( Stanbio company, USA) , plasma clotting factor VII (*Moll and Ortel,1997*), X (*Moll and Ortel,1997*) , XII (*Brandt et al.,1991*), ATIII (*Karges and Heimburger,1987*) activities and fibrinogen concentration (*Cooper and Douglas, 1991*) by coagulometric method.

(All the kits used for determination of plasma clotting factors and ATIII activities were supplied by Dade Behring company, Germany. The instrument used for their determination was Behring fibrin timer, model BFII, Germany)

-Determination of serum total homocysteine by ELISA (*Frantzen et al.,1998*) (Dynatech instrument, Germany) : The kit was supplied by IBL-Hamburg, Germany. IBL-cat.-No.:AX51301)

### **Statistical analysis**

The results of the present work were tabulated and statistically analyzed using student (t-test) and correlation coefficient (r). p values <0.05 were considered significant while p values >0.05 were insignificant (*Budneck,1987*).

## Results

Table (1) shows the clinical data of seronegative and seropositive patients for h.pylori infection. The percentage of epigastric pain (13.3% vs 86.7%), discomfort (20% vs 60%), bloating (20% vs 60%), heart burn (26.7% vs 53.3%), eructation (33.3% vs 60%), nausea and vomiting (26.7% vs 46.7%) and loss of weight (6.7% vs 6.7%) in seronegative and seropositive patients, respectively.

Table (2) shows the results of endoscopic examination in seronegative and seropositive patients for h.pylori infection. The percentage of reflux (40% vs 13.3%), hiatus hernia (20% vs 13.3%), congestive gastropathy (13.3% vs 60%), peptic ulcer (26.7% vs 40%) in seronegative and seropositive patients, respectively.

Table (3) shows the mean values  $\pm$ SD of age, BMI, serum fasting , postprandial glucose, AST, and ALT in seronegative and seropositive patients for h.pylori and the control group.

Table (4) shows the mean,  $\pm$ SD and p values of serum IgG antibodies for h.pylori and lipid profile in seronegative and positive patients for chronic h.pylori infection compared with the control group. The mean values of serum IgG ( $5.47 \pm 1.30$  U/ml vs  $4.40 \pm 1.58$  U/ml), total cholesterol ( $176.33 \pm 13.29$  mg/dl vs  $174.00 \pm 14.94$  mg/dl), triglycerides ( $90.27 \pm 7.60$  mg/dl vs  $84.50 \pm 17.38$  mg/dl), VLDL-c ( $18.05 \pm 1.52$  mg/dl vs  $16.90 \pm 3.48$  mg/dl) ,LDL-c ( $121.75 \pm 13.41$  mg/dl vs  $116.80 \pm 16.15$  mg/dl), HDL-c ( $36.53 \pm 3.80$  mg/dl vs  $40.30 \pm 6.82$  mg/dl) showed no significant differences in seronegative patients compared with the control group( $p > 0.05$ ).

Moreover, the mean values of serum IgG ( $22.87 \pm 5.85$  U/ml vs  $4.40 \pm 1.58$  U/ml) was significantly elevated in seropositive patients compared with the control group ( $p < 0.05$ ). Meanwhile, serum total

cholesterol ( $177.60 \pm 14.21$  mg/dl vs  $174.00 \pm 14.94$  mg/dl), triglycerides ( $91.67 \pm 12.71$  mg/dl vs  $84.50 \pm 17.38$  mg/dl), VLDL-c ( $18.33 \pm 2.54$  mg/dl vs  $16.90 \pm 3.48$  mg/dl) LDL-c ( $122.80 \pm 13.85$  mg/dl vs  $116.80 \pm 16.15$  mg/dl) and HDL-c ( $36.47 \pm 2.77$  mg/dl vs  $40.30 \pm 6.82$  mg/dl) showed no significant differences in seropositive patients compared with the control group ( $p > 0.05$ ).

Furthermore, The mean values of serum IgG ( $22.87 \pm 5.85$  U/ml vs  $5.47 \pm 1.30$  U/ml) was significantly elevated in seropositive compared with the seronegative group ( $p < 0.05$ ). Meanwhile, serum total cholesterol ( $177.60 \pm 14.21$  mg/dl vs  $176.33 \pm 13.29$  mg/dl), triglycerides ( $91.67 \pm 12.71$  mg/dl vs  $90.27 \pm 7.60$  mg/dl), VLDL-c ( $18.33 \pm 2.54$  mg/dl vs  $18.05 \pm 1.52$  mg/dl), LDL-c ( $122.80 \pm 13.85$  mg/dl vs  $121.75 \pm 13.41$  mg/dl) and HDL-c ( $36.47 \pm 2.77$  mg/dl vs  $36.53 \pm 3.80$  mg/dl) showed no significant differences in seropositive compared with seronegative patients ( $p > 0.05$ ).

Table (5) shows the mean,  $\pm$ SD and p values of plasma clotting factors VII, X, XII activities, fibrinogen concentration, ATIII activity, and plasma total homocysteine in seronegative and positive patients for chronic h.pylori infection compared with the control group. The mean values of plasma clotting factor VII ( $89.39 \pm 19.01\%$  vs  $77.20 \pm 5.65\%$ ) activity, factor X activity ( $77.62 \pm 6.97\%$  vs  $76.53 \pm 5.45\%$ ), factor XII activity ( $115.29 \pm 22.05\%$  vs  $113.43 \pm 6.22\%$ ), fibrinogen concentration ( $2.96 \pm 0.32$  g/l vs  $2.85 \pm 0.39$  g/l), ATIII activity ( $87.26 \pm 5.91\%$  vs  $93.01 \pm 8.85\%$ ) and plasma total homocysteine ( $14.89 \pm 4.10$   $\mu$ mol/l vs  $12.4 \pm 2.76$   $\mu$ mol/l) showed no significant differences in seronegative patients compared with the control group ( $p > 0.05$ ).

Moreover, the mean values of plasma clotting factor VII activity ( $100.63 \pm 37.68\%$  vs  $77.20 \pm 5.65\%$ ), factor X activity ( $80.59 \pm 13.43\%$  vs  $76.53 \pm 5.45\%$ ), factor XII activity ( $124.31 \pm 25.36\%$  vs  $113.43 \pm 6.22\%$ )



were non significantly elevated while, plasma fibrinogen concentration ( $4.39 \pm 0.54$  g/l vs  $2.85 \pm 0.39$  g/l), plasma total homocysteine ( $30.20 \pm 5.43$   $\mu\text{mol/l}$  vs  $12.40 \pm 2.76$   $\mu\text{mol/l}$ ) were significantly elevated ( $p < 0.05$ ) in seropositive compared with the control group. Meanwhile the mean value of plasma ATIII activity ( $85.38 \pm 9.80\%$  vs  $93.01 \pm 8.85\%$ ) was non significantly lower ( $p > 0.05$ ) in seropositive patients compared with the control group.

Furthermore, the mean values of plasma clotting factor VII activity ( $100.63 \pm 37.68\%$  vs  $89.39 \pm 19.01\%$ ), factor X activity ( $80.59 \pm 13.43\%$  vs  $77.62 \pm 6.97\%$ ), factor XII activity ( $124.31 \pm 25.36\%$  vs  $115.29 \pm 22.05\%$ ) were non significantly elevated while, plasma fibrinogen concentration ( $4.39 \pm 0.54$  g/l vs  $2.96 \pm 0.32$  g/l), plasma total homocysteine ( $30.20 \pm 5.43$   $\mu\text{mol/l}$  vs  $14.89 \pm 4.10$   $\mu\text{mol/l}$ ) were significantly elevated ( $p < 0.05$ ) while, the mean value of plasma ATIII activity ( $85.38 \pm 9.80\%$  vs  $87.26 \pm 5.91\%$ ) was non significantly lower in seropositive compared with seronegative patients ( $p > 0.05$ ).

In table (6) the serum levels of IgG antibodies against h.pylori showed no significant correlation with any of the estimated parameters in the seronegative and seropositive patients for h.pylori except plasma fibrinogen concentration. A significant positive correlation was detected between serum IgG antibodies and plasma fibrinogen in seropositive patients ( $r = 0.76$  ;  $p < 0.05$ ).

**Table (1): clinical data of seronegative and seropositive patients for h.pylori infection.**

<b>Groups</b> <b>Symptomes &amp; Signs</b>	<b>Seronegative h.pylori (n=15)</b>	<b>Seropositive h.pylori (n=15)</b>
Epigastric pain	2(13.3%)	13(86.7%)
Discomfort	3(20%)	9(60%)
Bloating	3(20%)	9(60%)
Heart burn	4(26.7%)	8(53.3%)
Eructation	5(33.3%)	9(60%)
Nausea and vomiting	4(26.7%)	7(46.7%)
Loss of weight	1(6.7%)	1(6.7%)

**Table (2): endoscopic examination of seronegative and seropositive patients for h.pylori infection.**

<b>Groups</b> <b>Endoscopic findings</b>	<b>Seronegative h.pylori (n=15)</b>	<b>Seropositive h.pylori (n=15)</b>
Reflux	6(40%)	2(13.3%)
Hiatus hernia	3(20%)	2(13.3%)
Congestive gastropathy	2(13.3%)	9(60%)
Peptic ulcer	4(26.7%)	6(40%)

**Table (3): mean values  $\pm$ SD of age, BMI, serum fasting and postprandial glucose, AST, and ALT in sero- negative and positive patients for h.pylori and the control group.**

<b>Studied Groups</b> <b>Parameters</b>	<b>Controls (n=10)</b>	<b>Seronegative h.pylori (n=15)</b>	<b>Seropositive h.pylori (n=15)</b>
Age ( Years)	34.50 $\pm$ 3.44	36.93 $\pm$ 2.71	35.47 $\pm$ 2.20
BMI (kg/m <sup>2</sup> )	22.00 $\pm$ 0.82	22.47 $\pm$ 0.74	22.60 $\pm$ 0.63
S. fasting glucose (mg/dl)	90.30 $\pm$ 5.12	90.60 $\pm$ 7.07	90.40 $\pm$ 4.58
S. postprandial glucose (mg/dl)	100.30 $\pm$ 3.65	99.93 $\pm$ 6.51	100.80 $\pm$ 4.80
S.AST (U/l)	24.10 $\pm$ 3.93	26.47 $\pm$ 4.12	26.20 $\pm$ 3.08
S.ALT (U/l)	26.89 $\pm$ 2.03	27.20 $\pm$ 3.63	26.13 $\pm$ 2.80

**Table (4): mean,  $\pm$ SD and p values of serum IgG antibodies for h.pylori, fasting and postprandial total cholesterol, triacylglycerol ,VLDL-c, LDL-c and HDL-c in sero- negative and positive patients for h.pylori compared with the control group.**

<b>Studied Groups</b>  <b>Biochemical Parameter</b>	<b>Controls</b> <b>(n=10)</b>	<b>Seronegative</b> <b>h.pylori</b> <b>(n=15)</b>	<b>Seropositive</b> <b>h.pylori</b> <b>(n=15)</b>
<b>S. IgG antibodies (U/ml)</b> P : P1:	<b>4.40<math>\pm</math>1.58</b>	<b>5.47<math>\pm</math>1.30</b> N.S	<b>22.87<math>\pm</math>5.85</b> <0.05 <0.05
<b>S.total cholesterol (mg/dl)</b> P : P1:	<b>174.00<math>\pm</math>14.94</b>	<b>176.33<math>\pm</math>13.29</b> N.S	<b>177.60<math>\pm</math>14.21</b> N.S N.S
<b>S. triacylglycerol (mg/dl)</b> P : P1:	<b>84.50<math>\pm</math>17.38</b>	<b>90.27<math>\pm</math>7.60</b> N.S	<b>91.67<math>\pm</math>12.71</b> N.S N.S
<b>S.VLDL-c (mg/dl)</b> P : P1:	<b>16.90<math>\pm</math>3.48</b>	<b>18.05<math>\pm</math>1.52</b> N.S	<b>18.33<math>\pm</math>2.54</b> N.S N.S
<b>S. LDL-c (mg/dl)</b> P : P1:	<b>116.8<math>\pm</math>16.15</b>	<b>121.75<math>\pm</math>13.41</b> N.S	<b>122.80<math>\pm</math>13.85</b> N.S N.S
<b>S. HDL-c (mg/dl)</b> P : P1:	<b>40.30<math>\pm</math>6.82</b>	<b>36.53<math>\pm</math>3.80</b> N.S	<b>36.47<math>\pm</math>2.77</b> N.S N.S

**p<0.05 : Significant .**

**P>0.05: No significant (N.S) .**

**P : probability versus control.**

**P1: probability versus seronegative group.**

**Table (5): mean values,  $\pm$ SD and P values of plasma clotting factor VII, X, XII activities , fibrinogen concentration, antithrombin III (ATIII) activity and homocysteine in seronegative and seropositive patients for h.pylori compared with the control group.**

<b>Studied Groups</b> <b>Biochemical</b> <b>Parameter</b>	<b>Controls</b> <b>(n=10)</b>	<b>Seronegative</b> <b>h.pylori</b> <b>(n=15)</b>	<b>Seropositive</b> <b>h.pylori</b> <b>(n=15)</b>
<b>Plasma factor VII activity(%)</b> P : p1:	<b>77.20<math>\pm</math>5.65</b>	<b>89.39 <math>\pm</math>19.01</b> N.S	<b>100.63<math>\pm</math>37.68</b> N.S N.S
<b>Plasma factor X activity (%)</b> P : p1:	<b>76.53<math>\pm</math>5.45</b>	<b>77.62 <math>\pm</math>6.97</b> N.S	<b>80.59<math>\pm</math>13.43</b> N.S N.S
<b>Plasma factor XII activity (%)</b> P : p1:	<b>113.43 <math>\pm</math>6.22</b>	<b>115.29 <math>\pm</math>22.05</b> N.S	<b>124.31<math>\pm</math>25.36</b> N.S N.S
<b>Plasma fibrinogen conc.(gm/l)</b> P : p1:	<b>2.85<math>\pm</math>0.39</b>	<b>2.96<math>\pm</math>0.32</b> N.S	<b>4.39<math>\pm</math>0.54</b> <0.05 <0.05
<b>Plasma antithrombin III (%)</b> P : p1:	<b>93.01<math>\pm</math>8.85</b>	<b>87.26 <math>\pm</math>5.91</b> N.S	<b>85.38<math>\pm</math>9.80</b> N.S N.S
<b>Plasma homocysteine (<math>\mu</math>mol/l)</b> P : p1:	<b>12.40<math>\pm</math>2.76</b>	<b>14.89 <math>\pm</math>4.10</b> N.S	<b>30.20<math>\pm</math>5.43</b> <0.05 <0.05

**p<0.05 : Significant .**

**p>0.05: Non-significant ( N.S ).**

**P : probability versus control.**

**P1: probability versus seronegative group.**

**Table (6): correlation coefficient (r) between serum h.pylori IgG antibodies , lipid profile, clotting factor VII, X, XII activities, fibrinogen concentration, ATIII activity, and total homocysteine in seronegative and seropositive groups.**

Studied Groups Biochemical Parameters	Seronegative h.pylori (n=15)		Seropositive h.pylori (n=15)	
	r	p	r	p
Serum total cholesterol (mg/dl)	0.07	N.S	0.06	N.S
Serum triacylglycerol (mg/dl)	0.13	N.S	0.30	N.S
Serum VLDL-c (mg/dl)	0.13	N.S	0.30	N.S
Serum LDL-c (mg/dl)	0.09	N.S	0.03	N.S
Serum HDL-c (mg/dl)	-0.13	N.S	-0.08	N.S
Plasma factor VII activity(%)	0.36	N.S	0.15	N.S
Plasma factor X activity (%)	0.01	N.S	0.33	N.S
Plasma factor XII activity (%)	0.44	N.S	0.31	N.S
Plasma fibrinogen conc.(gm/l)	0.07	N.S	0.76	P<0.05
Plasma antithrombin III (%)	0.45	N.S	-0.37	N.S
Plasma homocysteine (μmol/l)	0.37	N.S	0.18	N.S

**p<0.05 : Significant .**

**p>0.05: Non-significant ( N.S ).**

## Discussion

H.pylori is known to evoke an inflammatory response in the gastric mucosa by pro-inflammatory cytokines. This involves various bacterial and host dependent toxic substances that are associated with an increased risk of coronary heart disease (*Lee et al., 2004*).

The results of the present work showed that; the mean values of serum lipid profile had no significant differences in seropositive and seronegative patients for h.pylori infection compared to the control group ( $p>0.05$ ). Also, the mean values of serum lipid profile had no significant differences in seropositive compared to seronegative patients for h.pylori infection ( $p1>0.05$ ).

These findings were in agreement with the results of *Elizalde et al.,(2002) and Mach et al.,(2002)* and in disagreement with the results of *Laurila et al.,(1999), and Hoffmeister et al.,(2001)*.

They explained these findings by the fact that h.pylori is known to cause a chronic gastric infection, which may influence lipid metabolism similar to the lipid alterations during any acute infection (*Hoffmeister et al.,2001*).

The cause of this discrepancy may be due the differences in the number of cases, age, gender, race, and physical activity (*Linder et al.,1983* and *green et al.,1985*)

The findings of the present work showed that; the mean values of plasma clotting factor VII, X, XII and ATIII activities had no significant elevation in seropositive and seronegative patients for h.pylori infection compared to the control group ( $p>0.05$ ). Also, the mean values of plasma clotting factor VII, X, XII and ATIII activities had no significant differences in seropositive compared to seronegative patients for h.pylori infection ( $p1>0.05$ ).

There are many studies which reported that; the mean value of plasma clotting factor VII activity had no significant difference in seropositive compared to seronegative patients for h.pylori as *Patel et al.,(1994), Carter et al.,(1996) and Ossei-Gerning et al.,(1997)*.

To date, there is no previous reports about plasma clotting factor X, XII, and ATIII activities in dyspeptic patients with and without chronic h.pylori infection.

The data of the present work showed that; the mean value of plasma fibrinogen had significant elevation in seropositive patients for h.pylori infection compared to the seronegative ( $p < 0.05$ ) and control groups ( $p < 0.05$ ) while the mean value of plasma fibrinogen had no significant elevation in seronegative patients for h.pylori infection compared to the control group ( $p > 0.05$ ).

The persistent inflammation of the stomach induced by h.pylori infection can have consequences on the rest of the body (*Richy and Megraud, 2003*). Plasma fibrinogen is an acute phase protein which may reflect systemic inflammation from other underlying diseases (*Treiber,1999*). It is considered an inflammatory marker and not only a coagulation component (*Luc et al.,2003*).Inflammation plays an etiopathogenic role in atherosclerosis and that some markers of inflammation are associated with a greater risk of coronary cardiopathy or a worse prognosis such as C-reactive protein, white blood cell count, plasma fibrinogen or the presence of heat shock proteins (*Torres and Gaensly,2002*).

Fibrinogen plays a key role as ligand for the platelet glycoprotein IIb/IIIa receptor. Hyperfibrinogenemia was considered to induce platelet aggregation (*Acevedo et al.,2002*). So, it is an important risk factor for ischemic heart disease (IHD) as such elevation has been reported in younger patients infected with h.pylori (*Yusuf and Mishra,2002*).

However, chronic gastritis related to h.pylori may increase platelet embolization after damage to arterioles as well as plasma fibrinogen level through inflammatory mediators like tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6) which are predictors of IHD (*Aguejounf et al.2002*).

These results are comparable to those reported by *Zito et al.,(1999)*, *Yusuf and Mishra,(2002)*, *Aguejounf et al.,(2002)* and contradictory to the results of *Ridker et al.,(2001)*, *Mach et al.,(2002)*, and *Lee et al.,(2004)*.

The results of the current work showed that; the mean value of plasma total homocysteine had significant elevation in seropositive compared to seronegative patients for h.pylori infection ( $p > 0.05$ ) and control groups ( $p < 0.05$ ), while the mean value of plasma total homocysteine had no significant elevation in seronegative patients for h.pylori infection compared to the control group ( $p > 0.05$ ).

The presence of h.pylori on gastric mucosa was reported to reduce serum vitamin B12 level (*Gumurdulu et al.,2003*) which may be due to reduced cobalamin absorption (*Dierkes et al.,2003*) as a results of chronic gastritis associated with h.pylori (*Sanders and Peura,2002*) and impaired secretion of the intrinsic factor. However, deficiency of vitamin B12 raises the serum level of homocysteine (*Sipponen et al.,2003*).

Hyperhomocysteinemia was considered to be a thrombogenic potential for the development of IHD (*Kuch et al.,2001*) via different mechanisms. First, during the autooxidation of homocysteine in plasma, reactive oxygen species are generated. The latter initiate lipid peroxidation in cell membranes (potentially responsible for endothelial dysfunction) and in circulating lipoproteins. Oxidized LDL may trigger platelet activation as well as some of the haemostatic abnormalities. Second, accumulation of S-adenosyl homocysteine in cells inhibits



methyl transferase enzymes, in turn preventing repair of aged or damaged cells (*Coppola et al.,2000*). Third, hyperhomocysteinemia potentiate vascular smooth muscle cells calcification which promote atherosclerosis (*Li et al.,2003*). Fourth, hyperhomocysteinemia might lead to modification of fibrinogen in vivo, thereby causing altered fibrin clot structure. The formed clots are abnormally resistant to fibrinolysis that could directly contribute to the increased risk of thrombosis (*Sauls et al.,2003*).

The hyperhomocysteinemia found in the current work is in agreement with that reported by *Whincup et al., (2000)* and *Tamura et al.,(2002)* and in contradiction with the results of *Yoshino et al.,(2002)* and *Bloemenkamp et al.,(2002)*.

It could be concluded that, alteration of plasma fibrinogen and total homocysteine might be considered metabolic risk factors for coronary heart disease. However, estimation of these biomarkers in dyspeptic patients with chronic h.pylori infection were recommended to avoid the future risk of ischemic heart disease.

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## تأثير الإصابة المزمنة بالبكتيريا الحلزونية خارج المعدة على بعض العوامل الأيضية الخطرة المسببة لأمراض الشرايين التاجية للقلب فى مرضى عسر الهضم

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تلعب البكتيريا الحلزونية دورا هاما فى إلتهابات المعدة والتي تؤدى إلى قرحة المعدة ومن ثم سرطان المعدة قيما بعد. يهدف هذا البحث إلى دراسة تأثير الإصابة المزمنة بالبكتيريا الحلزونية خارج المعدة على مستوى الدهون وعوامل تجلط الدم رقم 10،7،12 والفيبيرينوجين ومضاد تجلط الدم الطبيعي (الأنتى ثرومبين-3) وكذلك مستوى الحامض الأمينى الهوموسيستين فى مرضى عسر الهضم. شملت هذه الدراسة 40 شخصا ممن تتراوح أعمارهم 31-41 عاما. وتم تقسيمهم إلى ثلاث مجموعات: شملت المجموعة الأولى 10 أشخاص أصحاء كمجموعة ضابطة والثانية على 15 مريضا من غير المصابين بالبكتيريا الحلزونية والثالثة على 15 مريضا من المصابين بالبكتيريا الحلزونية. وقد أوضحت نتائج هذا البحث إلى أنه لا توجد فروق ذات دلالة إحصائية بين مستوى الكوليسترول والدهون الثلاثية



والبروتينات المحملة بالدهون ذات الكثافة المنخفضة جدا والبروتينات المحملة بالدهون ذات الكثافة المنخفضة والبروتينات المحملة بالدهون ذات الكثافة العالية بمصل الدم وعوامل تجلط الدم رقم 12،10،7 ومضاد تجلط الدم الطبيعي (الأنثى ثرومين-3) بالبلازما وذلك فى مرضى عسر الهضم المصابين والغير مصابين بالبكتيريا الحلزونية عند مقارنتهما بالمجموعة الضابطة. أما مستوى الفيبرينوجين والهوموسيستين بالبلازما فقد وجد أن هناك زيادة ذات دلالة إحصائية بهما وذلك فى مرضى عسر الهضم المصابين بالبكتيريا الحلزونية عند مقارنتهم بالمجموعة الضابطة.

تخلص هذه الدراسة إلى إعتبار زيادة مستوى الفيبرينوجين والهوموسيستين بالبلازما فى مرضى عسر الهضم نتيجة الإصابة المزمنة بالبكتيريا الحلزونية من العوامل الأيضية الخطرة التى قد تؤثر على الشرايين التاجية للقلب. لذلك توصى هذه الدراسة بقياس مستوى الفيبرينوجين والهوموسيستين بالبلازما فى هؤلاء المرضى لتجنب الإصابة بقصور الدورة الدموية للقلب فى المستقبل.