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## Biochemical Changes Associated with *Helicobacter pylori* Infection

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### Abstract

This study was performed to investigate the biochemical alteration of Biochemical effects of *Helicobacter pylori* infection on iron metabolism and its related components in human. Ninety Patients (male & female) were divided according to ages into four groups; the group (I) contained 20 healthy individuals aged (10 – 65) years used as control for all groups. Group (II): consisted from 30 infected patients with *Helicobacter pylori* aged (10 – 25) years. Group (III): consisted from 30 infected patients with *Helicobacter pylori* aged (25 – 40) years. Group (IV): consisted from 30 infected patients with *Helicobacter pylori* aged (40- 65) years. The blood samples were collected and the obtained results revealed that, Significant increases in serum gastrin, amylase, ammonia, total iron binding capacity (TIBC), transferrin, total cholesterol, triacylglycerols (Tg), low density lipoprotein-cholesterol (LDL), very low density lipoprotein-cholesterol (VLDL), high density lipoprotein-cholesterol (HDL) Furthermore, significant decreases were in plasma serum iron, Ferritin, haptoglobin, Vitamin B<sub>12</sub>, leptin and HDL in compared to control group. From the obtained results it could be concluded that, we must take care from *Helicobacter pylori*.

**Key Words:** *Helicobacter pylori*, ammonia, haptoglobin, Vitamin B<sub>12</sub> and leptin.

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### Introduction

At the end of the last century *H. pylori* was appeared with reports from several investigators who observed helicobacter in the human and mammalian stomach (Abdel-Shafeik, 2015). Acute infection with *H. pylori* during childhood can be accompanied by diarrhea and slowing of weight gain (Konno et al., 2005). *Helicobacter pylori*, is a Gram a negative curved S shaped rod colonizes in the stomach with a worldwide spreading. More than 50% of the world's populations are infected with higher prevalence in developing countries (Brown, 2000). The possibility that some *H. pylori* strains have a specific ability to interfere with iron metabolism seems unlikely as neither virulence factors nor mutations in the bacterial genes involved in iron uptake have been demonstrated to be associated with it Choe et al., ( 2010). Recent study provides increase in prevalence of it among infected persons such as Berg et al., (2010) suggesting that *H. pylori* produces anemia by altering iron metabolism. Overall, the study suggests that *H. pylori* may cause micro bleeding and /or affect iron uptake and thus deplete iron stores in persons with IDA, independently of ulcer

disease (Victor 2006). Population-based studies demonstrated a strong relationship between serum ferritin levels and presence of IgG anti *H. pylori* (Berg 2001). The aim of the present study is to show the biochemical alterations of serum iron , Ferritin , Haptoglobin ; Amylase ; Ammonia ; Leptin ; Gastrin ; Vitamin B<sub>12</sub> and Lipid Profile (Cholesterol, T.G, HDL, LDL, and VLDL) in patients with *Helicobacter pylori* infection .

### Study Design

The study taken out on: A- 20 healthy person as control group; B- 90 patients infected with *H.pylori*, with age range between 25 and over 65 years, patients was selected from Gamal Abdel - Naser General Hospital in medicine and endemic medicine departments for treatment from continuous (pyloric burning) heart burning and upon analysis them blood samples for the presence of *H.pylori* antibodies they are positive. In the present study, the four groups classified according to age into four equal groups as follow:  
Group I: Control healthy individuals consist of 20- persons with ages ranged from 10 to over 65 year.

Group II: Consisted from 30-diseased patients with age ranged from 10 to 25 years.

Group III: Consisted from 30-diseased patients with age ranged from 25-40 years.

Group IV: Consisted from 30-diseased patients with age ranged from 40 to 65 years.

#### **Blood sampling:**

Blood samples were collected from every patient whole blood was obtained in the sterile tubes for complete agglutination to obtaining serum. Then the blood samples were centrifuged at 3000 rpm for 10 minutes. The clear specimens were aspirated carefully by Pasteur pipettes and transferred into dry, clean and sterile labeled tubes.

Then, the following biochemical parameters were analysis was performed for the following parameters:-

#### **Biochemical parameters are:**

- Plasma Ammonia ( Neeley and Philipson 1988).
- Serum Amylase (Garaway et al.,1959).
- Lipid profile Total cholesterol (Fossati and principle 1982), HDL-C ( Allain et al.,1974), LDL-C (Fahlolt et al., 1973),VLDL-C (Friedewald 1973) and Triacylglycerol (Bucolo and David, 1973).
- Serum Gastrin (Goetze and Rehfeld 2003).
- Serum leptin (Titez 1995).
- Serum iron (Henry 1974), Ferritin (Valberg 1980), total Iron Binding Capacity (TIBC) (Nissen, 1972), Transferrin (Fairbanks and Klee 1987) and serum Haptoglobin (Johnson et al.,1999).
- Serum Vitamin B<sub>12</sub> (Sadasivam and Balasubraminan, 1987).
- *H.pylori* antibodies determined by one step (Marshall et al, 1985).

#### **Statistical analysis:**

Statistical analysis of the result was carried out using student's T-test.Data were expressed as mean  $\pm$  S.E. and were statistically analyzed according to Steel and Torrie (1980).

#### **Results**

The present data revealed that *H. pylori* infection associated with low iron stores and anemia gave a reason for these unexplained cases of iron deficiency anemia (IDA), its infection, with or without gastric cells atrophy, should always be considered a possible cause of IDA (David 2005), A correct diagnosis is relevant for the management of the patient as this is the only GI cause of IDA potentially curable with a medical treatment (Dickey 2002). The study of (Ashorn 2004), provides increase in prevalence of IDA among *H. pylori* infected persons due to it produces an altering in iron metabolism. Overall, the study suggests that *H. pylori* may cause micro bleeding and/or affect iron uptake and thus deplete iron stores in persons with IDA, independently of ulcer

disease. Recent population-based studies demonstrated a strong relationship between serum ferritin levels and presence of IgG anti *H. pylori* (Victor et al., 2006).

#### **1. Biochemical parameters Table (1):**

The result revealed that significant increase in Ammonia in group III and group IV, and significant increase in Amylase in group IV as compared with the control group, while the Vitamin B<sub>12</sub> was significantly decrease in group III and highly significant decrease in group IV as compared to control group.

#### **2. Hormonal parameters Table (2):**

Showed significant increase in serum gastrin in group II and highly significant increase in groupIII and groupVI as compared to the control group.On the other hand there was significant decrease in serum Leptin in group III and groupIV on comparison to the control group.

#### **3. Lipid profile parameter Table (3):**

Showed significant increase in T.C in group III, IV in addition LDL-C level in group III showed highly significant increase in LDL-C level in group IV and non significant increase in VLDL-C level. While it significantly decreased in HDL-C in group IV when compared to the control group.

#### **4. Iron status parameters Table (4)**

There was significant decrease in serum iron level in group IV and in ferritin level in group II, III .while there was highly significant decrease in ferritin in group IV as compared to the control group. On the other hand, there was significant increase in transferrin in group III, IV and TIBC in group II and there was highly significant increase in TIBC in group III and IV on comparison with the healthy group.

#### **Discussion**

The obtained data in tables indicated that the recorded increase in plasma ammonia in *H. Pylori* infection can be generated by the urease activity of *H. pylori* in the gastric mucosa, which accounts for more than 6% of overall bacterial proteins Le Veen et al., (2004). Also, Queiroz et al., (2006) found that *H. pylori* infection is associated with elevated blood ammonia and the eradication of *H. pylori* may reduce the blood ammonia levels in cirrhotic patients.

The notices significant increase in serum amylase activities came in agreement with the recorded data of Jaworek et al., (2000), who found that, Gastric infection with *H. pylori* caused gastric

pathologies, also it able to determine systemic effects and diseases with increasing evidence that *H. pylori* infection affected the pancreas so increases amylase activities

The significant increases in serum cholesterol, T.G, LDL, VLDL in group II, group III and group IV as compared with group I (Control); and decreased HDL in group II, group III and group IV are due to the positive correlation between *H. pylori* infection and the risk of cardiovascular disease Franceschi et al(2009), Gen et al., (2010), whereas others have not confirmed such findings Khairy et al., (2013).

The significant increase in serum gastrin level when comparing each of the infected groups with the control one, and also when comparing its level in group II with that in group III; and also when comparing its level in group III with that in group IV, are because of the age at which this bacterium is acquired seems to influence the possible pathologic outcome of the infection - people infected at an early age are likely to develop more intense inflammation that may be followed by atrophic gastritis with a higher risk of gastric ulcer, gastric cancer or both. Acquisition at an older age brings different gastric changes that are more likely to result in duodenal ulcer. Individuals infected with *H. pylori* have a 10 to 20% lifetime risk of developing peptic ulcers and a 1 to 2% risk of acquiring stomach cancer (Kusters et al., 2006).

The Significant decrease in serum Leptin in group II, group III and group IV as compared with group I (Control) which is an adipocyte-derived hormone that causes reduced food intake and BMI, has also been shown to be present in the gastric mucosa, where the decreased gastric leptin level with gastric epithelial injuries caused by *H. pylori* infection, as stated by (Gholamreza et al. 2013) who showed that, *H. pylori* infection may influence leptin production. Advanced age might expose the individual to *H. pylori* infection and consequently influence the leptin level. The study we could not find an association between *H. pylori* infection and high serum leptin levels. It might be assumed that *H.pylori* infection may alter gastric leptin levels through inducing injuries on gastric mucosa and consequently leptin producing cells, leading to decline of circulating leptin level.

The Significant decrease in serum iron in group II, group III and group IV as compared with group I (Control) is an essential micronutrient for both animals and microorganisms and is a cofactor for enzymes involved in oxygen transport, DNA synthesis and electron transport (Conrad and Umbreit, 2010).

Whereas Janjetic et al., (2010) study revealed that *H pylori* infection was not associated with iron deficiency, anemia, or zinc concentrations; however, a positive relation with copper status was found after adjusting for confounding factors.

The Significant increase in TIBC in group II, group III and group IV as compared with Control group

agreed with Park et al., (2010) stated that, *H. pylori* infection decreases RBC indices and serum iron and increases TIBC in children. These changes become prominent as age increases. This age effect may be related to the duration of *H. pylori* infection. The significant increase in serum transferrin in group II, group III and group IV as compared with group I (Control) which is a blood-derived component. In gastrointestinal bleeding diseases, it may be leaked into gastrointestinal tract and then discharged with the stool. Transferrin is stable in faeces and a good marker to detect gastrointestinal bleeding. This immunochrom - atographic assay detects simultaneously *H. pylori* and human transferrin in stool samples, obtaining more accurate testing results regarding the *H. pylori* infection (Abdel- Shafeik 2015).

Our results showed that an increase in Transferrin which agree with Choe et al., (2009) and Keramati et al., (2007), who revealed that, Since the prevalence of both *H. pylori* infection and iron deficiency are high. Our results in Table (1) show significant decrease in serum Vitamin B<sub>12</sub> in group II, group III and group IV as compared with group I (Control) this decrease is agree with the data of Khedmat et al., (2013) who suggested a correlation between vitamin B<sub>12</sub> deficiency in CKD patients and the HP infection status. Due to *H. pylori* gastritis leads to the impairment of the production of pepsinogen and acid which are essential to cobalamin absorption Brusa et al., (2004).

The significant decrease in serum Haptoglobin in group II, group III and group IV as compared with group I (Control) indicate that this protein in humans is encoded by the HP gene as proved by ( Wassell 2010).

In contrast, Saremi et al., (2012) stated that Haptoglobin levels that are decreased but do not accompany signs of anemia may indicate liver damage, as the liver is not producing enough haptoglobin to begin with. Test protocol Haptoglobin is ordered whenever a patient exhibits symptoms of anemia.

## Conclusion

*H.pylori* infection associated with increased ammonia, amylase and Gastrin level which are associated with precipitate hepatic encephalopathy, pancreatic disease and gastric cancer. Also, this infection change serum lipid concentration, increasing the risk of atherosclerosis and ischemic heart disease *H. pylori* is probably responsible of IDA (iron deficiency anemia) and pernicious anemia through several mechanisms and affect regulation of appetite.

**Table 1. Effect of *Helicobacter pylori* infection on plasma ammonia, serum amylase, Vitamin B<sub>12</sub> and haptoglobin.**

Parameter groups	Ammonia (Umol/L)	Amylase (U/L)	Vitamine B12 (Pg/mL)	Haptoglobin (g/L)
G I	45.80 ± 2.11	88.50 ± 1.79	194.51 ± 4.53	137.181 ± 4.11
G II	51.80 ± 1.91	76.5 ± 1.87	115.00 ± 2.97	110.81 ± 3.12
G III	63.19 ± 2.21*	96.0 ± 2.81	101.11 ± 3.12*	97.61 ± 3.11
G IV	86.89 ± 2.75*	126.0 ± 4.11*	91.78 ± 3.11**	91.8 ± 2.71 * *

Mean ± 5.6, \*P < 0.05 means significant, \*\*P < 0.01 means highly significant

**Table (2): Effect of *Helicobacter pylori* infection on serum Gastrin and plasma leptin.**

Parameter groups	Gastrin (ng/L)	Leptin (ng/L)
G I	71.00 ± 1.91	6.51 ± 0.93
G II	120.11 ± 3.96*	4.91 ± 0.77
G III	125.0 ± 4.75**	4.02 ± 0.87*
G IV	133.65 ± 4.15**	3.81 ± 0.88*

\*P < 0.05 means significant, \*\*P < 0.01 means highly significant

**Table (3): Effect of *Helicobacter pylori* infection on serum lipid profile parameters.**

Parameter groups	T-C (mg/dl)	Tg (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
G I	148.00 ± 3.11	101.51 ± 1.91	41.60 ± 1.81	86.10 ± 2.58	20.30 ± 0.82
G II	168.15 ± 4.12	128.50 ± 3.81	35.33 ± 0.97	107.12 ± 2.59	25.70 ± 0.76
G III	189.85 ± 3.35*	143.51 ± 4.25	30.77 ± 2.75	130.38 ± 2.93 *	28.70 ± 0.85
Group IV	218.41 ± 4.50*	149.18 ± 3.87	30.10 ± 2.75*	158.50 ± 3.51**	29.84 ± 0.78

\*P < 0.05 means significant, \*\*P < 0.01 means highly significant

**Table (4): Effect of *Helicobacter pylori* infection on iron status parameters.**

Parameter groups	Iron (Ug/dl)	Ferritin (ng/dL)	TIBC (Ug/dL)	Transferrin (%)
G I	145.8 ± 3.75	211.81 ± 6.51	255.8 ± 6.11	2.93 ± 0.08
G II	102.75 ± 3.01	121.91 ± 3.33*	286.8 ± 5.81*	3.16 ± 0.12
G III	95.89 ± 3.11	118.81 ± 2.8*	311.00 ± 6.80**	3.69 ± 0.23*
G IV	90.81 ± 2.80*	93.8 ± 1.86**	336.70 ± 7.81**	4.18 ± 0.52 *

\*P < 0.05 means significant, \*\*P < 0.01 means highly significant

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