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Study the role of oxidative stress in *helicobacter pylori* induced gastro-intestinal diseases

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***Abstract*---**Background: *Helicobacter pylori* (*H. pylori*) is a multi-flagellated, spiral-shaped, Gram-negative, microaerophilic, slow-growing bacteria and extremely mobile which colonizes the stomach mucosa of a human where it causes a long-lasting infection which consistent with either acute or chronic stomach inflammation. Current study was aimed to evaluate total antioxidant capacity (TAC) and selenium (Se) levels in the serum of *H. pylori* infected individuals and to elucidate the relationship between the two biomarkers. Methods: Two study groups were enrolled in a current case control study; first group was included fifty five subjects with *H. pylori* infection which considered as *H. pylori*-associated patients (HPP), and the second group included thirty five apparently healthy subjects as healthy control (HC). Subjects were selected during the period between November 2021 and June 2022 after stringent application of the eligibility criteria. The HPP group subjects were underwent endoscopy and stool antigen test (SAT) and then both study groups subjects were evaluated for their serum anti-*H. pylori* antibodies (Abs), TAC and Se. Results: The findings revealed a significantly lower serum TAC and Se in HPP group in comparison with HC group. Serum immunoglobulin gamma (IgG) anti-*H. pylori* Abs was positively correlated with serum TAC in both study groups and negatively correlated with serum Se in HPP group. Serum TAC and Se levels were inversely correlated in both study groups. Conclusions: Oxidative stress (OS) was correlated with *H. pylori* infection with considerably reduced serum TAC and Se levels in HPP compared with HC, thereof these biomarkers may play particular roles in the pathophysiology,

development, and flow up of the diseases which may be uses as supplements to improve the OS status of patients.

Keywords*---H. pylori*, oxidative stress, selenium, antioxidant.

Introduction

Helicobacter pylori bacterium is spiral-shaped, slow-growing, Gram negative, microaerophilic, multiflagellated, and actively motile [1] that colonizes in the human stomach's mucosa, where it causes a long-lasting infection accompanied by acute or chronic gastric inflammation that could lead to a peptic ulcer diseases (PUD) and an atrophic gastritis (AG) accompanied by gastric cancer (GC) or intestinal metaplasia [2, 3]. *Helicobacter pylori* infection is diagnosed using both invasive and non-invasive techniques. Histology, urease testing, and culture are invasive diagnostic techniques. The non-invasive techniques include; SAT, urea breath assay and serological tests [4]. Inflammation triggers due to *H. pylori* colonization, and its elimination reduces inflammation, which histologically appears as multinuclear and mononuclear cells aggregation, infiltration, and disappearance, destroying and regenerating the microstructure of the gastric mucosa. Endoscopy may be used to detect *H. pylori* infection because increasingly sophisticated endoscopic methods have made it feasible to see tiny mucosal structures such the patterns of gastric pits and microvascular branching [5].

Stool antigen (Ag) test are non-invasive and affordable method to diagnose *H. pylori* infections that are active. There are two variations of this test: immunoassay for enzymes (EIA) and additionally immunochromatography. *Helicobacter pylori* infection eradication is assessed by SAT. So, both before and after *H. pylori* treatment, this test is helpful [4].

Helicobacter pylori infection causes a strong immunological response that leads to high titers of anti-*H. pylori* Abs and this response is insufficient to eradicate the pathogen, and infection will persist for the rest of life if it is not treated with antibiotics [6]. Tests for the detection of serum anti-*H. pylori* Abs are widely used because they are relatively straightforward, convenient and economical [7].

There are growing evidences that microbial pathogens stimulate OS production in the infected host's cells, and this may be a key mechanism causing epithelial cells damage during *H. pylori* infection. Other cell systems have shown that numerous routes can be used OS to regulate cell cycle events, with the end results including abnormal proliferation, cytotoxicity, and cell death. The altered epithelial cells proliferation, increased apoptosis could all be caused by OS and deoxyribonucleic acid (DNA) damage linked with *H. pylori* related diseases [8]. Hence, in the current reserach TAC was used to evaluate the role of OS in the *H. pylori* infection.

Selenium is an important trace element in many of the redox reactions, as well as the human immune system. In the form of selenocysteine, it is found in the structure of various selenoproteins such as glutathione peroxidase. Selenium deficiency may result in various complications such as OS impairment, immune response disorders, susceptibility to infection, malignancies and etc. [9]. Given

the importance of the assessment and maintenance of the normal levels of the micronutrients, Se is an essential micronutrient that is required by most organ systems in the body [9]. A few previous studies with conflicting findings that looked on the relationship between Se serum level and *H. pylori* infection. Lower plasma Se level were found in high-risk populations for GC compared to low risk one, according to Camargo *et al.*, research's [10]. Subjects with and without *H. pylori* colonization had similar serum Se level, according to Öztürk *et al.*, [11]. Contrarily, it is proposed that Se builds up in stomach tissue during *H. pylori* infection due to increased reactive oxygen species (ROS) synthesis [12]. We aimed to evaluate TAC and Se levels in the serum of *H. pylori*-infected individuals compared with control group and to elucidate the relationship between the two biomarkers to determine the final outcome of *H. pylori* infection and to hypothesis to use them as supplement therapy.

Materials and Methods

- **Study design and subjects**: A case control study with two study groups, the first group included fifty five subjects with *H. pylori* infection (27 males and 28 females) with an age range from 13 years to 75 years which considered as HPP, and the second group included thirty five apparently healthy subjects (16 men and 19 women) having an age range from 11 years to 70 years as HC. The patients were chosen from those attending the Endoscopic Unit at Imam Al-Hussein Teaching Hospital, Al-Nasiriyah Teaching Hospital and Al-Rifia Hospital at Thi-Qar Province (Iraq) during the period between November 2021 and June 2022 after stringent application of the eligibility criteria that mentioned below. A written consent was obtained from each patient participating in this study to fulfill the international research ethical criteria and current study was accepted by ethical consideration committee at Ministry of Health, Thi-Qar Health Department. The tests procedure for endoscopy was performed at above mentioned medical centers, serum anti-*H. pylori* Abs, serum TAC and SAT were executed in Imam Al-Hussein Teaching Hospital/Health Department of Thi-Qar, whereas the laboratory test procedure for serum Se have been done at Al-Shatra Technical Institute, Southern Technical University.

- **Eligibility criteria:** For HPP group, the patients were excluded from the current study based on the following criteria; under antibiotic therapy for the last 2 weeks, using non-steriodal anti-inflammatory drugs for the last 7 days, taking corticosteroid therapy for the last 4 weeks, under biological agents therapy currently or previously, had recent blood transfusion (during the last 6 months), had recent surgery (during the last 6 month), presence of any autoimmune or chronic disease and taking any biological agent, whereas the patient with the following criteria were included in the current study and considered as HPP; clinical manifestations were consistent with *H. pylori* infection, endoscopic findings were consistent with *H. pylori* associated diseases, *H. pylori* SAT positive by *H. pylori* Ag cassette, serologically *H. pylori* positive by *H. pylori* Abs cassette assay, serologically *H. pylori* positive by *H. pylori* IgG enzyme linked immune-sorbent assay (ELISA) and not had any of the above mentioned exclusion standards.

For HC group subjects, the same exclusion standards of the HPP group were followed for this group, and as well, subjects with even mild infection were also disregarded. All subjects of this group have no gastrointestinal illness of any type.

- **Endoscopy and samples collection:** Endoscopic examination was conducted at Endoscopic Unit of the above mentioned medical centers. Patients were fasted for at least 8 hours (hrs) before endoscopic examination. All HPP group were subjected to diagnostic oesophago-gastro-duodenoscopy for primary endoscopic findings. Endoscopic examination was performed by physician with using Olympus Endoscopy (Japan) under local pharyngeal anesthesia.

  A fresh stool sample about 2 gram (g) (for solid or semi-solid stool) and 2 milliliter (ml) (for liquid stool) was collected in sterile screw-cap vial form each subjects of HPP group which used immediately for SAT.

  By using disposable syringes five ml of venous blood were drowning from redial vein of each subject. The blood was placed in a gel tube and allowed to clot at room temperature. They were centrifuged (*Hettich, Germany*) at 3000 round per minute for 10 minutes for serum production. Each serum sample was divided into several aliquots in eppendrof tubes and stored at -20 Celsius degree until needed for serological investigations.

- **Stool antigen test:** This test was performed with using *H. pylori* Ag cassette kit (*Linear, Spain, Ref: 4245122*) which is a lateral flow chromatographic immunoassay for the qualitative detection of *H. pylori* Ag in human fecal specimen.

- **Anti-*H. pylori* Abs (cassette assay):** *Helicobacter pylori* Abs was qualitatively detected in serum with using *H. pylori* Abs cassette kit (*Linear, Spain, Ref: 4260240*).

- ***Anti-H. pylori* Abs (IgG) detection and titration (serum):** This assay was performed with using *H. pylori* IgG ELISA kit (*Demeditec, Germany, Ref: DEHEL01*) which was based on the principle of the EIA. The results of this biomarker was expressed in Unit (U)/ml and was considered positive at concentration of >12 U/ml.

- **Determination of TAC concentration (serum):** Human TAC level was detected and titrated with using human TAC-ELISA Kit (*Shanghai YL Biont, China, Catalog No: YLA1926HU*) which based on the biotin double Abs sandwich technology in U/ml.

- **Determination of serum Se concentration (serum):** The sera samples were digested by adding 2 ml of concentrated nitric acid (*BDH, England*) and 1 ml of concentrated perchloric acid (*BDH, England*) to 0.5 ml of subject's serum in Pyrex tube. The mixture was heated for 1 hrs at 160 °C using paraffin oil (*BDH, England*) bath, then samples were cooled, and the volume was completed to10 ml by 0.3 N of hydrochloric acid (*BDH, England*). Then the digested sera were used to measure the serum Se level by the atomic

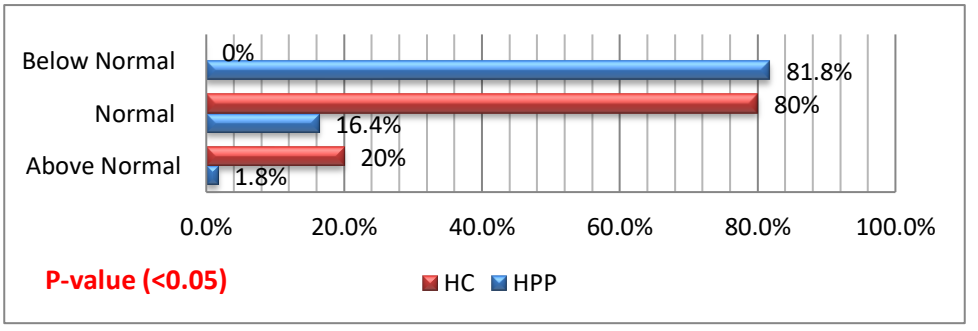
absorption spectrophotometer technique with using Flame Atomic Absorption Device (*Buck Scientific Model 210 VGP, England*). In this technique, light from the hollow cathode lamp was in a lean air-acetylene flame and absorbed by ground state atoms. The mount absorbance of light was directly related to the atoms concentration in the condition of gas in the light path and thus, to the Se concentration in the solution.

- **Statistical analysis:** All statistical analysis was performed by using a statistical package for social sciences (Version 26) and Microsoft Office Excel 2010 for Windows. Data were expressed as frequency and mean±standard deviations. Normally distributed continuous variables were compared with using the method of variance (ANOVA) and independent T-test (two-tailed), whereas the Mann Whitney *U* test and Kruskal-Wallis test was used for those variables that were not normally distributed, also used Pearson's correlation coefficients and simple liner regression when calculated the correlations. *P*. value <0.05 was reported as statistically significant.

Results

A total of ninety (90) subjects were enrolled in the current study after application the exclusion and inclusion criteria that mentioned in our materials and methods. Out of ninety subjects, fifty five (55) subjects were suffering from clinical manifestations of gastrointestinal diseases with *H. pylori* infection (27 males and 28 females) with an age range from 13 years to 75 years which considered as HPP, and thirty five (35) apparently healthy subjects (16 males and 19 females) with an age range from 11 years to 70 years as HC.

In Figure (1) depicts the TAC outcomes in all study groups, the frequency percent of TAC below normal level was significantly (*p<0.05*) higher among HPP group (81.8%) in comparison with the HC group (0%). The mean titer of TAC was exhibited a decreased level among HPP group subjects (7.23 U/ml) compared with an elevated level among the subjects of HC group (18 U/ml). The difference in mean titers between HPP group and HC group was significant (*P<0.05*).



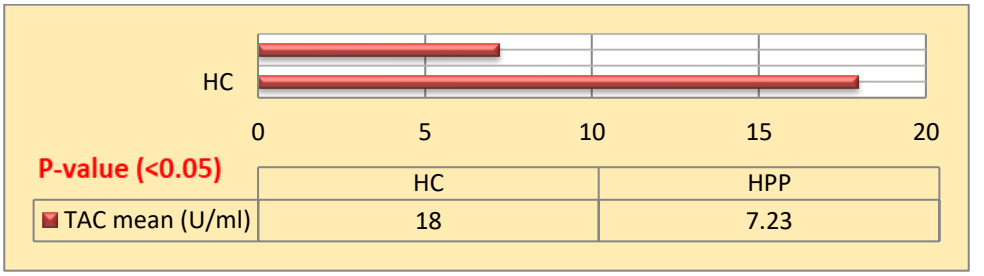


Figure (1): The results of frequency (%) and mean titer of total antioxidant capacity in both study groups (**TAC**: total antioxidant capacity, **U/ml**: units per milliliter, **HC**: healthy control, **HPP**: *Helicobacter pylori* associated patients, **Below normal**: <10 U/ml, **Normal**: 10-20 U/ml and **Above normal**: >20 U/ml).

The results of Se in both study groups were demonstrated in Figure (2). The frequency percent of Se below normal level was higher in HPP group (23.6%) compared with HC group (5.7%) with a significant differences (*P<0.05*). For mean titer, HPP group had exhibited the low mean titer (91.3 nanogram (ng)/ml) in comparison with HC group (111 ng/ml) with a significant differences (*P<0.05*).

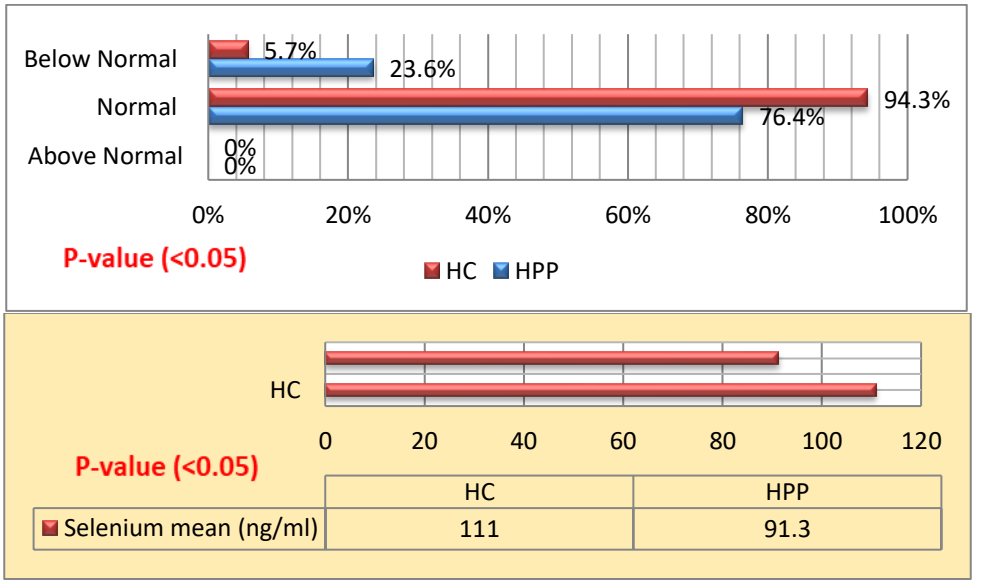


Figure (2): The results of frequency (%) and mean titer of selenium in both study groups (**ng/ml**: nanogram per milliliter, **HC**: Healthy control and **HPP**: *Helicobacter pylori*-associated patients, **Below normal**: <70 ng/ml, **Normal**: 70-150 ng/ml and **Above normal**: >150 ng/ml).

Table (1) showed the relationship between IgG anti-*H. pylori* Abs and TAC in all study groups. For HPP group, the frequency percent of below normal serum TAC level was low 42/52(80.8%) within HPP with high positive IgG level compared

with subjects with low positive IgG anti-*H. pylori* 3/3 (100%) and the different was statistically significant ($p<0.05$). For mean titer, the results revealed that the mean titer of serum TAC was highest among HPP with high positive IgG level (7.4 U/ml) with a significant differences ($p<0.05$) in comparison with low positive IgG level (4.2 U/ml) within the same study group.

The regression analysis in Figure (3) revealed a significant positive correlation ($p<0.05$) between serum TAC and serum anti-*H. pylori* IgG levels in both study groups (HPP and HC).

Table (1): Correlation between IgG anti-*Helicobacter pylori* and total antioxidant capacity in all study groups

Biomarkers			Total Antioxidant Capacity (U/ml)								p. value
			Below N (<10)		Normal (10-20)		Above N (>20)		Total		
			FR(%)	Mean	FR(%)	Mean	FR(%)	Mean	FR(%)	Mean	
Anti-*Hp* IgG (U/ml)	HPP (n=55)	L Positive (n=3)	3(100)	4.2	0(0)	0	(0)		3(100)	4.2	<0.05
		H Positive (n=52)	42(80.8)	5.5	(17.3)	13.2	(1.9)	2.5	52(100)	7.4	
		Total (n=55)	45(81.8)	5.4	9(16.4)	13.2	(1.8)	32.5	55(100)	7.2	
	HC (n=35)	Negative (n=35)	0(0)	0	28(80)	16.9	7(20)	22.2	35(100)	18	------
		Total (n=35)	0(0)	0	28(80)	16.9	7(20)	22.2	35(100)	18	-

HPP: *Helicobacter pylori-associated* patients, **HC:** healthy control, **IgG:** immunoglobulin gamma, **FR:** frequency, **%:** percent, **n:** number, **U/ml:** units per milliliter, **N:** normal, **L:** low (13-33 U/ml) and **H:** high (>33 U/ml).

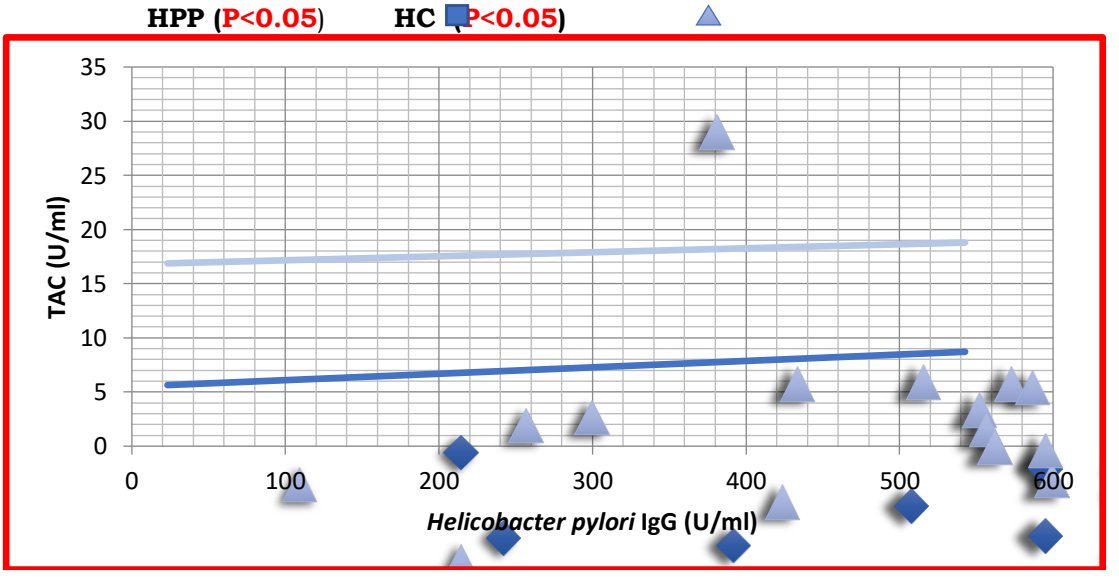


Figure (3): Regression analysis of *Helicobacter pylori* IgG antibody and total antioxidant capacity in all study groups (HPP: *Helicobacter*

pylori-associated patients, **HC:** healthy control, **TAC:** total antioxidant capacity, **IgG:** immunoglobulin gamma and **U/ml**: units per milliliter).

The results of the correlation between IgG anti-*H. pylori* and Se in both study groups was demonstrated in Table (2). The frequency percent of normal serum Se level was low 39/52(75%) in HPP with high positive IgG anti-*H. pylori* level as compared with subjects with low positive IgG anti-*H. pylori* 3/3 (100%) with statistical significant differences (*p<0.05*). For mean titer, the results revealed that the mean titer of Se was significantly (*p<0.05*) lower among HPP with high IgG anti-*H. pylori* level (90.7 ng/ml) by comparison with HPP with low positive IgG anti-*H. pylori* level (100.7 ng/ml).

The regression analysis (Figure 4) showed that there was an inverse non-significant (*p>0.05*) relationship between serum anti-*H. pylori* IgG level and serum Se level in HPP group, whereas the HC group revealed a positive non-significant *(p>0.05*) relationship.

Table (2): Correlation between IgG anti-*Helicobacter pylori* and selenium in all study groups

Biomarkers			Selenium (ng/ml)								p. value
			Below N (<70)		N (70-150)		Above N (>150)		Total		
			FR(%)	Mean	FR(%)	Mean	FR(%)	Mean	FR(%)	Mean	
Anti-Hp IgG (U/ml)	HPP (n=55)	L Positive (n=3)	0(0)	0	**3(100)**	100.7	0(0)		3(100)	**100.7**	**<0.05**
		H Positive (n=52)	13(25)	63.7	**39(75)**	99.7	0(0)		52(100)	**90.7**	
		Total (n=55)	13(23.6)	63.7	42(76.4)	99.8	0(0)		55(100)	91.3	
	HC (n=35)	Negative (n=35)	2(5.7)	60.0	33(94.3)	114.6	0(0)	0	35(100)	111	------
		Total (n=35)	2(5.7)	60.0	33(94.3)	114.6	0(0)	0	35(100)	111	

HPP: *Helicobacter pylori-associated* patients, **HC:** healthy control, **IgG:** immunoglobulin gamma, **FR:** frequency, **%:** percent, **n:** number, **U/ml:** units per milliliter, **ng/ml:** nanogram per milliliter, **N:** normal, **L:** low (13-33 U/ml) and **H:** high (>33 U/ml).

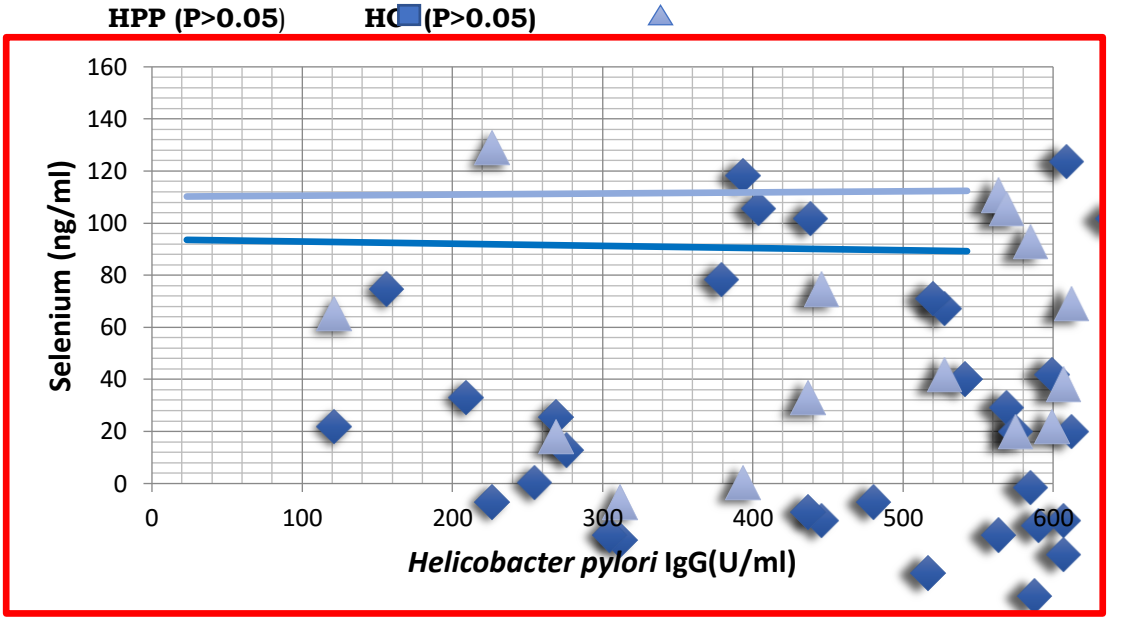


Figure (4): Regression analysis of *Helicobacter pylori* IgG antibody and selenium in all study groups (HPP: *Helicobacter pylori-associated* patients, **HC:** healthy control, **IgG:** immunoglobulin gamma, **U/ml**: units per milliliter **and ng/ml:** nanogram per milliliter).

Table (3) showed the relationship between serum TAC and serum Se in both study groups. The frequency percent of below normal serum Se level was low 10/45(22.2%) in HPP patients with below normal TAC level and the different was statistically significant ($p<0.05$) in comparison with peoples with normal TAC level 3/9 (33.3%). For mean titer, the results revealed that the mean titer of Se was high among patients with below normal TAC level (92.9 ng/ml) when compared with patients with normal TAC level (84.7 ng/ml) with a significant difference ($p<0.05$). For HC group, the frequency % of normal Se level was higher with a significant differences ($p<0.05$) in the subjects with normal TAC level 27/28 (96.4%) comparatively with low frequency percent among subjects with above normal TAC level 6/7 (85.7%). A higher mean titer of Se level (114 ng/ml) was among subjects with normal TAC level with a significant differences ($p<0.05$) in comparison with subjects with above normal TAC level (101.1 ng/ml).

The findings of the current paper (Figures 5) identified a significantly negative relationship ($p<0.05$) among serum TAC and serum Se levels in both study groups.

Table (3): Correlation between total antioxidant capacity and selenium in all study groups

Biomarkers			Selenium (ng/ml)								p. value
			Below N (<70)		Normal (70-150)		Above N (>150)		Total		
			FR(%)	Mean	FR(%)	Mean	FR(%)	Mean	FR(%)	Mean	
TAC (U/ml)	HPP (n=55)	Below N (n=45)	10(22.2)	63.5	35(77.8)	101.3	0(0)		45(100)	92.9	<0.05
		Normal (n=9)	3(33.3)	64.6	6(66.7)	94.8	0(0)		9(100)	84.7	
		Above N (n=1)	0(0)	0	1(100)	78.0	0(0)		1(100)	78.0	
		Total (n=55)	13(23.6)	63.7	42(76.4)	99.8	0(0)		55(100)	91.3	
	HC (n=35)	Normal (n=28)	1(3.6)	55.0	27(96.4)	115.8	0(0)	0	28(100)	114	<0.05
		Above N (n=7)	1(14.3)	55.0	6(85.7)	108.8	0(0)	0	7(100)	101.1	
		Total (n=35)	2(5.7)	50.0	33(94.3)	114.6	0(0)	0	35(100)	111	

HPP: *Helicobacter pylori-associated* patients, **HC:** healthy control, **TAC:** total antioxidant capacity, **FR:** frequency, **%:** percent, **n:** number, **U/ml:** units per milliliter, **ng/ml:** nanogram per milliliter, **N:** normal, **Below normal:** (<10 U/ml), **Normal:** (10-20 U/ml) and **Above normal:** (>20 U/ml).

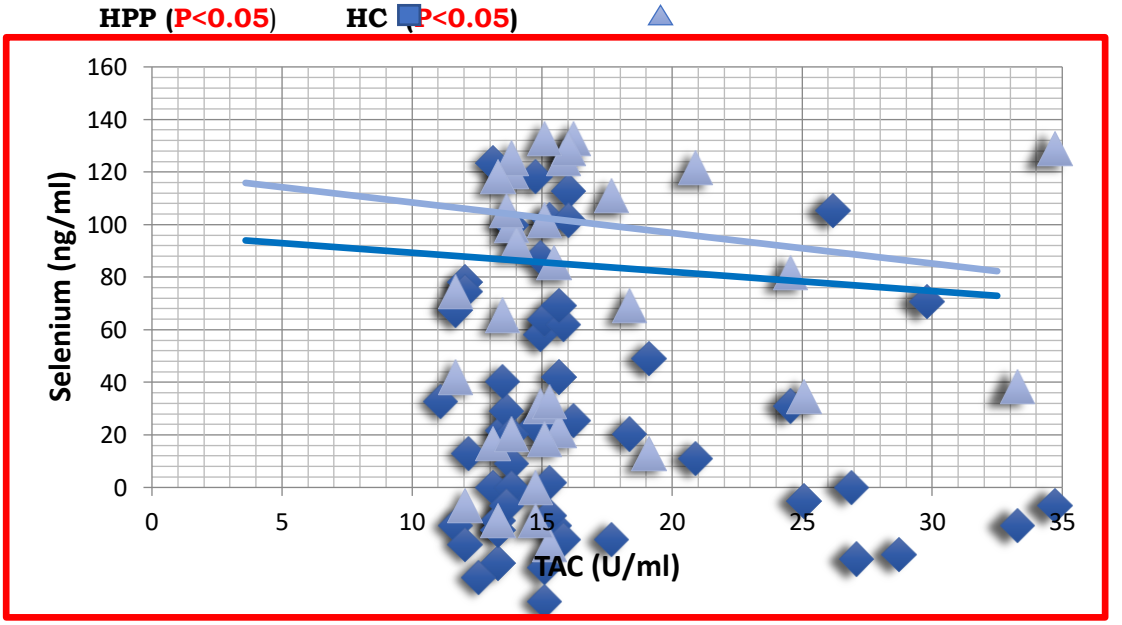


Figure (5): Regression analysis of total antioxidant capacity and selenium in all study groups (HPP: *Helicobacter pylori-associated* patients, **HC:** healthy control, **TAC:** total antioxidant capacity, **U/ml**: units per milliliter **and ng/ml:** nanogram per milliliter).

Discussion

Infection with *H. pylori* is probably one among the major prevalent chronic global bacterial disease, which is related with gastrointestinal complications, including ulceration, dyspepsia, adenocarcinoma, and gastroesophageal reflux disease [13]. Increased ROS production has been linked to *H. pylori* infection, which increase OS in the gastric mucosa. Increased OS is crucial factor in the pathophysiology of the gastroduodenal mucosal inflammation that is seen when *H. pylori* infection is present [9]. In line with these findings, our results (Figure 1) revealed a higher depletion in TAC concentration in HPP group compared to HC group. Oxidative stress is one of the main problems that related to *H. pylori* colonization [14], and therefore, intensifies injury to the host cells, these bacteria encourage OS and inflammation in gastric epithelial cells that are already injured. Superoxide radicals are produced as a result of the recall and recruitment of neutrophils by *H. pylori* infection to site of gastric epithelial cells damage [15]. Overall, current study findings (Figure 1) were consistent with other previous study [16] had showed the generation of OS and impaired mucosal antioxidant balance during *H. pylori* infection [17]. An important source of antioxidants is dietary supplementation [18]. The inability to absorb important vitamins, trace minerals, and antioxidants is caused by potential factors such starvation or malabsorption. The disparity between ROS and TAC causes OS elevation and mucosal damage.

Selenium deficiency may result in a various complications such as OS disturbance, immune response disorders, susceptibility to infection, malignancies and etc. [9]. Our study results (Figure 2) expressed a significant depletion in Se level among HPP group in comparison to elevated level among HC group. Consistent with current study findings, another previous study [19] was reported low Se concentration among *H. pylori* infected patients compared to healthy subjects. *Helicobacter pylori* infections are able to impaired trace element nutritional absorption in infected subject, it is recommended that any trace element discrepancy in these patients should be considered as an important outcome [20]. By contrast to current study findings, a previous study [20], revealed a higher but non-significant Se level, was observed among patients with *H. pylori* gastritis. Wu *et al.*, [21], reported no significant differences between serum level of Se in *H. pylori* infected individuals compared with control subjects. A reasonable justification may be related to absorption impairment that caused by changes in inflammation status in *H. pylori* infected patients.

By minimizing the production of peroxynitrite from superoxide, *H. pylori* are capable to make a way for antioxidant defenses. *Helicobacter pylori* can deplete arginine in phagocytes by secreting arginase and stimulating the synthesis of arginase II by macrophages. Inducible nitric oxide synthase is enzyme responsible for nitric oxide synthesis that requires arginine for proper translation. As nitric oxide and superoxide combine to create the extremely poisonous reactive nitrogen species peroxynitrite, blockade of nitric oxide synthesis prevents the production of this harmful oxidant [22]. Former findings was in accordance with current study findings (Table 1 and Figure 3) that verified an elevated level of TAC among HPP with an elevated IgG anti-*H. pylori* Abs and the two biomarkers were positively correlated. Along the same lines of the current study findings, Khanzode *et al.*, [23] found that patients with *H. pylori* infection have considerably greater blood

levels of superoxide dismutase, and this was explained by elevation OS during the course of *H. pylori* disease, as superoxide dismutase is primarily an intracellular antioxidant enzyme with a low extracellular activity. As well Noguchi *et. al.*, [24] speculated that superoxide dismutase is a crucial antioxidant defense for the *H. pylori*-infected gastric mucosa because it protects against ROS. Hazell *et. al.*, [25] observed a considerably elevated catalase production by *H. pylori* bacteria compared to other similar bacteria, which may help the organism survive in *vivo*, whereas Mori *et. al.*, [26] reported that the generated amount of *H. pylori* catalase and superoxide dismutase enzymes would not be enough to remove extracellular ROS. Variation in OS biomarkers during *H. pylori* infection may be influenced by the number of patients studied, the location, the length, and the degree of severity of the *H. pylori* infection.

A previous study reported that the detection of IgG anti-*H. pylori* in the serum of gastrointestinal track (GIT) patients is helpful in the avoidance of more invasive diagnostic tests as endoscopy and biopsy in the diagnosis of *H. pylori* infection and the titer of Abs was positively correlated with AG [27]. Nevertheless Se concentration is markedly depleted in the antral mucosa of subjects with AG [28]. In line with former two studies findings, the present study recorded a significantly low Se level in HPP with high IgG anti-*H. pylori* Abs (Table 2) and the two markers were negatively correlated (Figure 4). Franceschi *et al.*, demonstrated that vitamins B_{12}, C, and E, beta-carotene, folic acid, zinc, Se and other supplements were less effectively absorbed as a result of *H. pylori* infection [28] this may explain the negative correlation between IgG anti-*H. pylori* Abs and Se in our study findings.

In many previous studies there is a significant correlation between *H. pylori* infection and increased OS biomarkers [20]. Endogenous antioxidants are the first line of protection against OS, such as protective selenoenzymes, with antioxidant function, such as glutathione peroxidases. In this issue, Se induce it's crucial involvement in blocking the destruction that occur due to increase in ROS concentration [29] and Se high dose supplementation may improve inflammatory markers and OS [30]. For these reasons, a normal level of Se in the blood is needed to produce its activity against the OS [29]. In agreement with these findings, our results revealed a negative relationship between serum Se level and serum TAC level (Se level was positively correlated with OS) in both study group (HPP and HC) (Table 3 and Figure 5). This increase in serum Se level may be explained as compensatory response as a result of increased OS level and depleted TAC in our cohort. The peculiar redox properties of selenocysteine, its involvement in antioxidant enzymes like thioredoxin reductase, and Se role as a component of several important antioxidants. Membrane integrity is supported by glutathione peroxidases that involved in the elimination of reactive oxygen metabolites [31].

The limitations of the current study were; the small number of the participants as a results of exclusion and inclusions criteria of the present study, the sensitivity and specificity of detection kits that used for biomarkers detection which may affect the final results, some of our study cohort may be taken certain drugs (not written in patient's record or patient's claims) before samples collection and this may be effect on the biomarkers levels in their sera, finally, further studies are

needed to correlated the OS biomarkers with degree and severity of histopathological findings and with present of PUD or GC.

Conclusions

According to our findings, we can conclude that in HPP, TAC and Se levels might change, and these biomarkers may have particular involvement in pathophysiology, development and follow up of the diseases and may be uses as supplements to improve the OS status of patients. The result suggested that there was a significant positive correlation between anti-*H. pylori* IgG positivity titer and TAC level which led to speculation that the *H. pylori* was able to decrease OS in some situation to improve it's survival. In addition, anti-*H. pylori* IgG seropositivity titer was negatively correlated with Se level, which suggested that high density of *H. pylori* infection may induce trace element (Se) nutritional absorption impairment. The high level of Se was inversely correlated with TAC level which indicated the compensatory role of this trace element to control the OS, thereof it is recommended that discrepancy in Se level in the related subjects should be considered as an important outcome. For the future studies, evaluation and comparison of serum and tissue TAC, Se and the other micronutrients is suggested for better understanding the exact correlation of them with *H. pylori* final outcomes.

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List of Abbreviates:

Abs: antibodies, **Ag:** antigen, **AG:** atrophic gastritis, **DNA:** deoxyribonucleic acid, **EIA:** enzyme immunoassay, **ELISA:** enzyme linked immunosorbent assay, **GC:** gastric cancer, ***H. pylori*:** *Helicobacter pylori*, **HC:** healthy control, **HPP:** *H. pylori*-associated patients, **IgG:** Immunoglobulin gamma, **ml:** milliliter, **ng:** nanogram, **OS:** oxidative stress, **PUD:** peptic ulcer disease**s**, **ROS:** reactive oxygen species, **SAT**: stool antigen test, **Se:** selenium, **TAC:** total antioxidant capacity and **U:** Unit.

Tables Legend:

- **Table (1):** Correlation between IgG anti-*Helicobacter pylori* and total antioxidant capacity in all study groups.

- **Table (2):** Correlation between IgG anti-*Helicobacter pylori* and selenium in all study groups.

- **Table (3):** Correlation between total antioxidant capacity and selenium in all study groups.

Figures Legend:

- **Figure (1):** The results of frequency (%) and mean titer of total antioxidant capacity in both study groups.

- **Figure (2):** The results of frequency (%) and mean titer of selenium in both study groups.

- **Figure (3):** Regression analysis of *Helicobacter pylori* IgG antibody and total antioxidant capacity in all study groups.

- **Figure (4):** Regression analysis of *Helicobacter pylori* IgG antibody and selenium in all study groups.

Figure (5): Regression analysis of total antioxidant capacity and selenium in all study groups.

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