

The Association between dietary total antioxidant capacity with the risk of helicobacter pylori infection among adult: a case–control study

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Abstract

Background Dietary total antioxidant capacity (DTAC) has been assumed as a useful tool to assess the relationship between the cumulative antioxidant food capacity and several chronic disorders. The aim of this study was to evaluate the association between DTAC and risk of *Helicobacter pylori* in a case-control study.

Methods This case-control study was carried out among 150 patients with *Helicobacter pylori* and 302 healthy subjects aged 18–55 years. Dietary data were collected using a validated 168-items quantitative food frequency questionnaire. DTAC was calculated based on the ferric reducing-antioxidant power (FRAP) values that reported by US Department of Agriculture.

Results The mean age and BMI of the study participants were 38.70 years and 25.86, respectively. Compared with control subjects, participants with *H pylori* significantly were older and had higher BMI and smoking use. Patients with *H pylori* compared with control individuals had also lower intake of total fiber, vitamin E, vitamin C, vitamin D, total dairy, whole grain and vegetables. Compared with participants in the lowest tertile of DTAC, those in the highest tertile had a significantly lower OR for *H pylori* after further adjustment for potential confounders (Model 2: OR, 0.20; 95% CI, 0.10 – 0.40; P for trend, < 0.001).

Conclusions Our findings showed that a high DTAC was associated with a reduced risk of *Helicobacter pylori* in adult, which reflects the increased intake of natural dietary antioxidants to prevent the progression of *Helicobacter pylori*. However, further studies are needed to investigate the relation between DTAC and risk of *Helicobacter pylori*.

Background

Helicobacter pylori (*H pylori*), which it has been estimated that its worldwide prevalence is approximately 4.4 billion individuals(1), is a gram-negative micro-aerophilic pathogen replicating on the surface of the gastric epithelium that can cause gastritis, gastric cancer(2). Moreover, the recent document showed that the *H pylori* infection is associated with an increased risk of pancreatic disease(3), lymphoma (4) and atherosclerosis(5). Based on evidence, *H pylori* infection is affected by genetic and environmental factors (6) such as host diet and nutrition status(7).

On other hand, Studies suggest that antioxidants (eg, vitamins and N-acetylcysteine) play a role in reducing active oxygen species and gastric inflammation caused by *H. pylori*, which also exacerbates the disease and prevents the growth of bacteria and eliminates biofilm formation(8). So far, numerous studies have shown that vitamin C and E levels are lower in people with *Helicobacter pylori* than in those without *H. pylori*(8). Thus, impaired antioxidant and anti-inflammatory defenses may cause or exacerbate a chronic condition of pyloric *H* infection. On other hand, various aspects of the effect of natural antioxidants found different in foods on the modulation of oxidative stress and disorders in the antioxidant system have been studied.(9, 10) However, the evaluation of an antioxidant compound alone cannot reflect the total antioxidant potency of the diet and reflect the synergistic and potential effects of

dietary antioxidant interactions. Thus, the term total antioxidant capacity for diet (DTAC) has been developed and is used as a suitable tool to evaluate the effects of dietary antioxidants that is a strong correlation with serum total antioxidant capacity (11) And it is closely related to the quality of the diet to determine the risk of chronic diseases (12).

Several evidences have suggested the potential link between DTAC and reduce the risk of chronic diseases such as diabetes(13), metabolic and oxidative stress markers(14), ulcerative colitis(15), blood pressure(16), and cardiovascular disease(17), which share common metabolic parameters with *H pylori*. However, to our knowledge, the association between DTAC and risk of development *H pylori* have not yet been investigated. Only, a number of studies in vivo and animal studies have shown the ability of nutrients rich in antioxidant to reduced oxidative stress and subsequently reduced risk of *H pylori* including garlic, ginger, quercetin, green tea and Cranberry (18–21). However, the synergistic effects of different antioxidant nutrients, which also found in DTAC and other chemical ingredients utilized in the growing or preparation of food have not been discussed.(22).

Considering the lack of convincing evidence regarding the association of DTAC with liver function, in this study we aimed to investigate the association between DTAC and risk of *H pylori* in Iranian population in order to improve and reduce the burden of diseases.

Methods

Participants

This case-control study was performed on 153 patients with *H pylori* and 306 healthy subjects who had been referred to the Hazrat Rasoul Hospital, Tehran, Iran during the recent years. In this study, patients with *H pylori* infection were confirmed by one of the diagnostic methods of blood antibody, fecal antigen, UBT respiratory test, endoscopy and gastric biopsy and performed Rapid Urease Test or pathological and microscopic examination. If they meet the inclusion criteria, are selected as case group after obtaining written informed consent. The control group was twice as likely as the case group and among other patients referred to other parts of the hospital such as ophthalmology, orthopedics, maxillofacial surgery, ear, nose, and throat who were not diagnosed *H pylori* infection with the diagnostic methods and also not having a history of alcohol or alcohol consumption less than 10 mg / day in women and less than 20 mg / day in men. Case and control were matched regarding age and gender. After entering into the study, information about demographic variables and Hematological parameters were obtained by completing the General Information Questionnaire. Also, the Hematological parameters checked after they came to the hospital, again. Then, for completing data on dietary intake and other information we called the patients to invite them to the research center in a special date. Participants with a history of certain diseases (Gastrointestinal malignant diseases, psychiatric psychosis, diseases that result in lack of reminder like Alzheimer's) were excluded. Also, pregnant and lactating women and subjects with an arbitrary special diet were excluded. In this study, nutritionists were used as interviewers in order to reduce information bias as well as to answer completely to the survey questions. Furthermore, written informed

consent was completed for each participant. Also, in order to assess physical activity levels of participants, we used the General Practice Physical Activity Questionnaire (GPPAQ), a simple questionnaire reflecting an individual's current physical activity (23). This study was approved by the research council and ethics committee Iran University of Medical Sciences, Tehran, Iran (ethics code: IR.IUMS.REC.1398.667).

Anthropometric assessment

Anthropometric measurements were conducted by a trained dietician. Weight was measured using a standard digital seca scale (made in Germany), while participants wore minimum clothes and without shoes and recorded to the nearest 100 g. Height was measured using a mounted tape in a standing relaxed shoulder position with no shoes to the nearest 0.5 cm. Body mass index (BMI) was calculated as weight (kg) divided by height in square meters (m²).

Measurement of Hematological parameters

All stool samples were collected in plastic containers and sent to the laboratory within 2 h. About 5 mL of venous blood were collected from each subject (cases and controls) and divided equally (2.5 mL) in one tube containing K3-ethylenediaminetetraacetic acid (K3-EDTA) to perform a complete blood count (CBC) using a Cell Dyne 1800 electronic counter (Sequoia-Turner Corporation, California, USA) and in a serum tube to determine serum iron using the DiaSys reagent kit. The serum vitamin B12 concentration was determined quantitatively using a solid phase, competitive chemiluminescent enzyme immunoassay (Immulite/Immulite 1000).

Dietary assessment and DTAC calculation

Nutritional status of individuals was assessed by a 168- items FFQ. The questionnaire has a standard size for each food item designed according to the Willett method (24). Study participants were asked to indicate their frequency of consumption of each food item according to their consumption in the past year. Depending on the type of food consumed, the frequency of consumption per day, week or month was questioned. Previous studies using this questionnaire have provided acceptable results and validity of the questionnaire indicates that the questionnaire has acceptable validity. The values listed for each food item were converted to grams daily using the Home Scale Handbook. Then, the amount of nutrients obtained by each individual was obtained using Nutritionist IV software. The total antioxidant capacity of the diet was obtained from previous articles based on the ferric reducing-antioxidant power (FRAP). The FRAP is defined as the ability of dietary antioxidants to reduce ferric to ferrous ions. The FRAP was expressed in milligrams per 100 grams of food(25). For similar foods in Iranian culture (for example, different types of bread), the average total values will be calculated. Finally, the frequency of consumption of each food item is multiplied by the amount of iron-reducing antioxidant power associated with it, and then the diet is collected for each participant to obtain the total antioxidant capacity

Statistical analysis.

All statistical analyses were using SPSS software (version 19.0; SPSS Inc, Chicago IL). The normality of variables was evaluated by Kolmogorov-Smirnov and histogram tests. For the variables that do not have a normal distribution, logarithmic equivalent (Ln transformation) of that variable was used in the analysis. Also, independent sample T test was used for comparing the mean of DTAC as well as the general characteristics and hematological parameters among case and control group. For assessing the relation between DTAC index and *H pylori* in an adjusted model, multiple logistic regressions were used. The data were presented as mean \pm standard deviation and odds ratio with 95% confidence interval, and in all results, the significance level was determined as $P < 0.05$.

Results

The mean \pm SD for the age and BMI of the study population (59.5% women) were 38.70 ± 10.65 years and 25.86 ± 4.84 Kg.m², respectively.

Table 1 shows the distribution of cases and controls according to socio-demographic characteristics, smoking habits, alcohol drinking, body mass composition and hematological parameters. Compared with control subjects, participants with *H pylori* significantly were older and had higher BMI and smoking use. The mean levels of hemoglobin, RBC, WBC, hematocrit, and mean corpuscular hemoglobin concentration (MCHC) were significantly lower among cases compared to controls individuals. Furthermore, no significant differences were found for mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) cases and controls subjects. On comparing cases with controls, the mean levels of serum vitamin B12 and iron were significantly lower in the patients.

Table 2 illustrates the dietary intake of *H pylori* patients compared to controls. Patients with *H pylori* compared with control individuals had also higher intake of energy, protein, carbohydrate, saturated fatty acids, fructose, iron, whole and refine grain, and red and processed meat and lower intake of total fiber, vitamin E, vitamin C, vitamin D, total dairy, Whole grain and vegetables. There were no significant differences in all other characteristics and dietary intake among case and control subjects.

The ORs and 95% CIs for *H pylori* in the tertiles of DTAC are shown in Table 3. Compared with participants in the lowest tertile of DTAC, those in the highest tertile had a significantly lower OR for *H pylori* (crude model: OR, 0.29; 95% CI, 0.14 – 0.6; P for trend, 0.001), which remained significant after further adjustment for BMI, waist circumference, physical activity, smoking, dietary intake of energy and fat. (Model 2: OR, 0.20; 95% CI, 0.10 – 0.40; P for trend, < 0.001).

Discussion

The study investigated the association between DTAC and *H pylori* in a case–control study. We found that DTAC had an inverse association with risk of *H pylori* infection. Participants with higher DTAC score

had a significantly lower OR for H pylori infection compared with low DTAC score, after adjustment for potential factors. Our study suggests that DTAC may potentially reduce the risk of NAFLD.

According to our information, this is the first time that the inverse relationship between DTAC and risk of H pylori infection has been proven. H pylori infection has been documented. In the previous evidences, dietary TAC has been inversely associated with several chronic diseases such as cardiovascular diseases(17), cancer (26)diabetes (13), and metabolic disorders(14), which share common metabolic parameters with H pylori infection.

Overall, an inverse associations between intake of antioxidant micronutrients and antioxidant-rich foods with risk of H pylori infection was registered. For example, The DASH diet (Dietary Approaches to Stop Hypertension), dietary patterns with antioxidant-rich component based on fruit and vegetables, low-fat dairy products, and whole grains, has been shown to eradicate *Helicobacter pylori* and its gastric cancer(27), as well as an inverse association in chronic diseases associated with H pylori infection (28). Furthermore, coffee has been investigated as an antioxidant-rich nutrient as a risk reduction for coffee. So that, Coffee showed a strong antibacterial action against *Helicobacter pylori* (*H. pylori*)(29). This action against *H. pylori* suggests that coffee may have action as a useful natural inhibitor of gastritis and gastric ulcers. Also, the ability of other antioxidant-rich nutrient to increase plasma TAC and finally reduced risk of H pylori infection through several mechanism, garlic, ginger, quercetin, green tea and Cranberry (19–22) was well revealed. The findings were confirmed even in complementary interventions with antioxidants. Besides, the beneficial effects of the combination of antioxidant compounds were also reported, as demonstrated the synergistic effect of Simultaneous administration and combination of one or more antioxidant supplements reducing risk of H pylori infection(19).

The mechanism of action of dietary antioxidant compounds on *H. pylori* is not clear. However, the intake of antioxidant-rich nutrients in animals with *Helicobacter pylori* has been shown to reduce both the number of bacteria in the gastric mucosa and the inflammatory process(8, 20). On the other hand, it is possible that these cultivations, by destroying the Iklova factor, have direct antiseptic properties and prevent NF- κ B nuclear transfer, thereby reducing genetic expression and producing mediators associated with relevant inflammation such as TNF- α , IL-1 β , IL-6 and IL-8. It is possible that antioxidant-rich nutrient, by controlling some of the toxins that cause enough bacteria to grow by creating special anionic channels in the plasma membrane associated with the release of bicarbonate and organic anions in gastric cells, they have a beneficial effect(30). On the other hand, it is possible that these compounds reduce the action of urease on *H. pylori*, because it has been shown that several polyphenolic compounds can alter the activity of this enzyme, which is responsible for the survival of bacteria in acid.(31) In addition, fiber, as part of a healthy diet in many high-antioxidant plant foods, may have health benefits through protection against oxidative damage, as well as improving glucose metabolism and serum lipids (32). Also, some prior studies have declared that dietary fibers can alter abundances of specific gut microbes and change the profile of human gut microbiota (33–36). Fiber fermentation is dependent on microbiota (37) and it has been seen that fiber may increase gram-positive bacteria (38), by decreasing the gut transit time and pH (39, 40). Moreover, we know that *H. pylori* is the gram-negative bacteria so it

may be negatively affected by fiber. Also, a high fiber diet in rich of vegetables, fruits, whole grains and beans (41) can exert a protective effect against *H pylori* infection (42, 43). This may be due to their prebiotic properties which is confirmed in a meta-analysis (44). Besides, fresh vegetables are the source of vitamin C which has been mentioned as a chemopreventive factor against digestive disorders caused by *H pylori* infection (42). As far as we know, vitamin C can lessen stomach cancer risk and exert an effect on the cycle of *H pylori* infection (45). Vitamin C is highly concentrated in stomach mucosa and gastric juice. it has a positive effect on the production and function of immune cells and immunoglobulin (46). In our study, dietary vitamin c consumption was significantly lesser in case group. Also, Dietary antioxidants may reduce the risk of developing this disease by reducing the body's obesity and visceral fat, which are known to be one of the risk factors for Helicobacter pylori infection(47, 48).

This is the first study to assess the relationships between DTAC with risk of H pylori Our sample size was sufficient and we tried to eliminate the effect of confounders as far as possible, by adjusting wide range of variables and a validated questionnaire has been used. As for most case-control studies, the causal relationship can be determined but it cannot be quite definite. Furthermore, some conditions of foods such as the growing condition, cultivation method, storage, processing and cooking condition, and assay method might affect the antioxidants content of the foods (25) Also, information collecting in these kinds of studies are based on individual's reports and memory which is not totally reliable. We have tried to minimize information bias by administrating a questionnaire by trained interviewers.

Conclusion

Our findings showed that a high DTAC was associated with a reduced risk of *H pylori* infection in adult, which reflects the increased intake of natural dietary antioxidants to prevent the progression of. However, further observational studies and clinical trials are needed to investigate the exact relation between DTAC and risk of *H pylori* infection.

Declarations

- ***Abbreviations***

Not applicable.

- ***Ethics approval and consent to participate***

Not applicable.

- ***Consent for publication***

All authors of this manuscript declared their consent for publication.

- ***Competing interests***

The authors declare that they have no competing interests.

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We express our appreciation to the participants of this study.

- ***Authors' contributions***

S.F, and Mh.S contributed in conception, design, and statistical analysis. S.F, and N.H contributed in data collection and manuscript drafting. N. H and Mh.S supervised the study. All authors approved the final version of the manuscript.

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- ***Availability of data and materials***

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1: Baseline characteristics and Hematological parameters of the study participants

	case (n=150)	control (n=302)	P-value
Demographic variables			
Age (years)	42.0 (13.5)	37.0 (8.4)	<0.001
Female, N (%)	48 (32.0)	135 (44.7)	0.01
Body mass index (kg/m ²)	28.0 (6.5)	24.7 (3.2)	<0.001
Physical activity, N (%)			
Low	114 (76.0)	220 (72.8)	0.484
Moderate	29 (19.3)	59 (19.5)	0.465
High	7 (4.7)	23 (7.6)	0.362
Current smokers, N (%)	11 (7.3)	8 (2.6)	0.019
Alcohol drinking, N (%)	16 (10.7)	21 (7.0)	0.175
Hemoglobin (g/dL)	11.2 (3.2)	13.6 (2.9)	0.001
Hematocrit (%)	4.1 (1.2)	4.6 (1.2)	<0.001
Mean corpuscular volume (fL)	6.8 (2.3)	7.3 (2.5)	0.049
Mean corpuscular hemoglobin (pg)	37.8 (6.9)	43.0 (6.7)	<0.001
Mean corpuscular hemoglobin concentration (g/dL)	85.2 (12.3)	84.8 (7.9)	0.589
Serum ferritin (pg)	30.1 (3.5)	30.0 (2.6)	0.651
Serum transferrin (g/dL)	33.4 (2.5)	34.0 (1.3)	0.005
Serum vitamin B12 (pg/mL)	223.4 (98.7)	365.3 (130.6)	0.001
Serum folate (ng/dL)	63.9 (19.8)	74.2 (16.3)	0.001

WBC: white blood cell count; RBC: red blood cell count; Hb: hemoglobin; Hct: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration.

*P < 0.05: significant.

Data are expressed as means ± standard deviation (SD) of 150 subjects.

P values are resulted from chi square and student t-test.

Table 2. Dietary intake among the Case and Control Groups

	case (n=150)	control (n=302)	P-value
Energy Intake			
Energy (Kcal/d)	2629.1 (779.9)	2282.9 (638.6)	<0.001
Hydrate (gr/d)	393.2 (122.3)	325.1 (103.2)	<0.001
Protein (gr/d)	94.5 (32.2)	76.4 (24.2)	<0.001
Fiber (g/d)	83.8 (30.2)	81.3 (29.2)	0.398
Total fatty acids (gr/d)	27.5 (10.6)	24.3 (9.2)	0.001
Saturated fatty acids	27.2 (9.5)	28.0 (10.6)	0.447
Unsaturated fatty acid	16.8 (7.9)	18.2 (7.5)	0.063
Cholesterol (mg/d)	36.1 (19.0)	60.7 (28.2)	<0.001
Sodium (g/d)	20.5 (8.2)	16.8 (9.8)	<0.001
Iron (mg/d)	145.6 (116.4)	126.2 (107.0)	0.079
Zinc (mg/d)	49.3 (29.5)	25.7 (14.0)	<0.001
Vitamin C (mg/d)	127.0 (80.3)	154.0 (70.4)	0.001
Vitamin E (mg/d)	11.6 (5.7)	12.9 (4.9)	0.019
Vitamin B12 (g/d)	3.8 (3.4)	4.1 (2.4)	0.303
Vitamin D (g/d)	1.5 (1.1)	2.0 (1.7)	<0.001
Food Groups			
Dairy (g/d)	315.9 (191.6)	424.9 (246.0)	<0.001
Grain (g/d)	102.2 (118.4)	163.7 (168.2)	<0.001
Whole grain (g/d)	428.7 (246.5)	328.6 (170.3)	<0.001
Red processed meat (g/d)	0.8 (0.7)	0.4 (0.4)	<0.001
Alcohol (g/d)	342.1 (172.0)	333.9 (257.5)	0.687
Legumes (g/d)	232.9 (109.4)	287.0 (170.1)	<0.001

Values are resulted from student t-test

Figure 3 The association between Tertiles of dietary total antioxidant capacity (DTAC) and risk of Hypertension among the participants of study.

	<i>Tertiles of dietary total antioxidant capacity</i>			<i>P for trend</i>
	T1	T2	T3	
Total	20 / 120	46 / 147	84 / 185	
de	1.00 (Ref)	0.93 (0.48 - 1.77)	0.29 (0.14 - 0.61)	0.001
el 1*	1.00 (Ref)	0.76(0.52 - 1.12)	0.37 (0.24 - 0.58)	< 0.001
el 2†	1.00 (Ref)	0.74 (0.42 - 1.28)	0.20 (0.10 - 0.40)	< 0.001

el 1: adjusted for age, sex.

el 2: adjusted for model 1 and BMI, waist circumference, physical activity, smoking, dietary energy and fat.