Original Research Article

A Study of the Association between Dietary Pattern, and *Helicobacter Pylori* Infection among Gastric Cancer Patients attending Benghazi Medical Centre

Abstract

Stomach cancer is one of the most common cancers in the world and the most common leading cause of death. *H. pylori a*nd dietary factors are associated with the development of stomach cancer. The current study aims to assess the association between dietary patterns, helicobacter pylori infection, and gastric cancer patients in Benghazi Medical Centre. It is a retrospective cohort study. The inclusion criteria are all Libyan, adult Helicobacter pylori patients who are aged eighteen years and older and have confirmed immunity results for the mentioned bacteria, and gastric cancer, body weight records, and food frequency questionnaire. Description and analysis of data were done by SPSS version 22. The prevalence of *H. Pylori* history among 219 subjects of the current research was (57%). Male gender, and frequent intake of fried foods was the variables associated with more prevalence of H. Pylori among gastric cancer patients.

Keywords: *H. Pylori*, Dietary factors, Stomach cancer.

Introduction

Helicobacter pylori (H. Pylori) area Gram-negative bacteria are present in half of the world's nations and persistently colonize the human stomach. Even though most *H. pylori*-infected persons stay asymptomatic, the presence of this organism in the stomach increases the risk of gastric adenocarcinoma. *H. pylori* has been classified as a class I carcinogen. The clinical manifestations of *H. pylori* infection are determined by a variety of variables, including host genetics, environmental factors such as diet, and *H. pylori* strains in an expression of virulence determinants. (1-

3) *Helicobacter pylori* is responsible for some of the most common chronic upper gastrointestinal tract clinical disorders in humans, such as chronic-active gastritis, gastric and duodenal ulcers, low-grade B-cell mucosa-associated lymphoid tissue lymphoma of the stomach, and gastric adenocarcinoma, which is the third leading cause of cancer death worldwide. The mode of infection has not yet been firmly confirmed. Different routes of infection have been suggested. The most commonly accepted hypothesis is that infection takes place through the fecal-oral route. Accordingly, contaminated water and foods might play a significant role in the transmission of the microorganism to humans. (4, 5) Furthermore, several studies have considered *H. pylori* as a foodborne pathogen due to some of its epidemiological microbiological characteristics. *H. pylori* has been detected in seawater, drinking water, vegetables, and foods of animal origin. *H. pylori* survives in complex foodstuffs such as ready-to-eat foods, milk, and vegetables. (6)
Helicobacter pylori invade the stomach and duodenum by several mechanisms. The H. Pylori biochemical products such as ammonia, proteases, and vacuolating cytotoxin A (VacA) are toxic to epithelial cells. These products damage epithelial cells, disrupt tight junctions, and cause apoptosis. *H. pylori* colonization in the stomach can result in chronic gastritis, an inflammation of the stomach lining, at the site of infection. *Helicobacter* cysteine-rich proteins trigger an immune response, causing inflammation. Chronic gastritis usually underlies *H. pylori*-related diseases. (7)
The *H. pylori* colonization location affects the location of the ulcer, depending on the acidity of the stomach. In people producing large amounts of acid, *H. pylori* colonize near the pyloric antrum (exit to the duodenum) to avoid the acid-secreting parietal cells at the fundus (near the entrance to the stomach). In people producing normal or reduced amounts of acid, *H. pylori* can also colonize the rest of the stomach. This also may increase the risk of stomach cancer. (8, 9) Almost 1 million cases of gastric cancer are diagnosed yearly, establishing this disease as the fourth most common cancer worldwide. Stomach cancer is the second leading cause of cancer-related deaths, and approximately 700,000 people

die each year from gastric adenocarcinoma. In some regions of the world, gastric carcinoma is the most common malignancy. Usually, the diagnosis of gastric cancer is delayed by a lack of early specific signs and symptoms, and most patients are diagnosed after cancer has invaded the muscularis propria. Accordingly, the 5-year survival rate for gastric cancer is less than 15%. (10, 11) Histologically, two distinct variants of gastric carcinoma have been identified: diffuse-type gastric cancer, and intestinal-type adenocarcinoma, which progresses through a series of well-defined histological steps. These forms of gastric cancer affect men twice as commonly as women. (12) Two related mechanisms by which *H. pylori* could promote cancer are under investigation. One mechanism involves the production of free radicals and an increased rate of host cell mutation. The second mechanism is called a "perigenetic pathway". It involves alterations in cell proteins, such as adhesion proteins. (14) The interplay between diet, environment, and genetic predisposition is important in many diseases including cancer. Diet is a recognized etiological factor. Nutrition and dietary factors may interact with the process of carcinogenesis in all three stages of initiation, promotion, and progression. Epidemiological studies over the last few decades have highlighted the contribution of dietary and nutritional factors as well as the preventive role of various phytochemicals present in certain foods in different types of cancer. (15-17) The risk of gastric carcinoma is not influenced only by *H. pylori* strain characteristics and host genetic determinants but also by environmental factors. One factor that has uniformly been associated with an increased risk of gastric cancer is high dietary salt intake. This association has been detected in prospective studies, case-control studies, as well as studies that compared urinary salt excretion with gastric morbidity rates. A prospective study of a Japanese population and a case-control study in South Korea each reported that *H. pylori*-infected subjects consuming a high-salt diet had an increased risk of gastric cancer compared to *H. pylori*-infected subjects who consumed lower levels of salt, while another study reported a positive correlation between the prevalence of *H. pylori* infection and levels of dietary salt intake. (14, 15) There has been extensive research

conducted into the protective role of antioxidants found in food against the development of gastric cancer. However, less is known about interactions between *H. pylori* infection and dietary factors in gastric cancer patients. A randomized trial conducted on a population at high risk of developing gastric cancer suggested that eradication of *H. pylori* in conjunction with dietary supplementation with β-carotene and vitamin C increased the regression of preneoplastic lesions at 6 years of follow-up duration. However, following a further 6 years without dietary supplementation, the preventative effects of β-carotene and vitamin C disappeared. (18) A population-based case-control study in Sweden suggested that a high intake of dietary vitamin C and β-carotene may lower the risk of developing gastric cancer in *H. pylori*-infected individuals.(19) Concordant with the study of Ekstrom and others, a case-control study in Hawaii concluded that vegetable intake among individuals infected with *H. pylori* provided some protection against developing gastric cancer. (20) Conversely, a prospective study involving 10 European countries suggested that there was no significant interaction between *H. pylori* infection, plasma vitamin C levels, and the risk of developing gastric cancer. (21) Further studies are needed to determine whether antioxidants are protective against gastric cancer among *H. pylori*-infected patients. (22-25) The current work aims to study the association between dietary patterns, helicobacter pylori infection, and gastric cancer among patients attending Benghazi Medical Centre. Also, it aims to find any risk factor for gastric cancer, the current study will analyze various socioeconomic factors, medical characteristics, including *Helicobacter Pylori* infection, dietary habits, and anthropometric measurements in a retrospective cohort study.

Methodology

This is a retrospective cohort study carried out on dietary patterns of Helicobacter pylori infection and gastric cancer patients in Benghazi Medical Centre and National Cancer Centre. The inclusion criteria for enrolment in the present study are all Libyan, adult Helicobacter pylori-infected patients who are aged eighteen years and older and have

confirmed immunity results for the mentioned bacteria, and confirmed gastric cancer diagnosis, body weight records, and food frequency questionnaire. Based on this criterion a total of 219 patients were assessed between 4th January 2021 to 12th March 2021 (Period of data collection) and were randomly approached to participate in the study. Out of the 241 patients, 12 refused to participate in the study and 10 subjects were excluded from the study because they were unable to answer all the questions required for the study. A total of 219 patients who answered the complete questionnaire were finally enrolled in the study giving a response rate of 90.87 %. The patients were approached at the respective hospital and briefed about the purpose of the study before the questionnaire was interviewer-administered. Informed consent was obtained from all subjects who were also assured of the confidentiality of the collected information. The research was approved by the administration of the Department of Nutrition, Faculty of Public Health, University of Benghazi as well as the concerned hospital. Before the start of the project, the respective hospital administrations were informed in writing about the aim of the study to obtain the maximum possible cooperation to conduct the study. The questionnaire was divided into various sub-sections. It includes socio-economic information, clinical history, gastrointestinal disorders, anthropometric evaluation, physical activity, and dietary history. Height and weight measurements used to calculate Body Mass Index (BMI) were taken in a private area using standard techniques as recommended by the World Health Organisation (WHO). (17) All data were coded before being entered into a computer. Description and analysis of data were done by SPSS version 22. The level of significance was set at *P* value < 0.05. Descriptive Statistics were used to describe the subjects' characteristics. Individual variables were compared using *t* test for continuous variables and *x2 for* categorical data. The contiguous variables distribution was examined for the difference.

RESULT:

Table 1 shows the age distribution. Subjects were predominantly between the ages of 40-59 years old (55%). The remaining half was between 18-39 years (35.3 %) and 60-70 years old (9.7 %). The total means age ± standard deviation (SD) was 50.8 years ± 13.5. All of the subjects (100 %) were of Libyan nationality. A majority of the subjects were married (70 %). Although most of the subjects had some sort of formal education it was mostly at the basic level (36.5%). Those currently employed subjects are 67%. The mean duration of cancer was 13.2 months (± 15.6 S.D) and 60.0 % of the patients were those who had been diagnosed with cancer within the past 12 months (table 3). Most of the subjects were undergoing chemotherapy (74 %) alone while radiotherapy was being followed by 15.5 % of the patients. The remaining (10.5 %) were those who had either undergone radiotherapy in the past and were undergoing chemotherapy now or vice versa as can be seen in table (3). The mean duration of the therapy was 6.9 months (± 10.2) and more than half the subjects (58.5 %) had undergone their respective therapy for less than 6 months. About a quarter (24.5 %) had had the therapy for 6 to less than 12 months while 13.0 % and 4.0 % had undergone it for a longer duration of 12 to less than 24 months and 24 and more months respectively. More than half the subjects (57.0 %) had a history of incidence of Helicobacter Pylori infection in the stomach. Dyspepsia was reported by 48.6 % of the subjects. The history of peptic ulcer within the study group was reported as being a problem by a majority (80.3 %) of the subjects.

Table (1) Subject characteristics

Age (Years) No.(%)	**Male**	**Female**	**Total**
18-39	27(13.3)	45(22)	72(35.3)
40-59	47(21.24)	79(34.51)	126(55)
60-79	11(5.1)	9(4.6)	20(9.7)
Total	87(38.89)	132(61.11)	**219(100)**
Age (Years)Ẍ±	51±3	49±6.2	50±2.9

SD			

Table (2)Socio-economic characteristics of subjects

Characteristics	Subject No.(%)
Marital status	
Unmarried	18(8)
Married	153(70)
Widow/widower	35(16)
Divorcee	13(6)
Educational level	
Illiterate/RW*	19(8.7)
Basic education	80(36.5)
Secondary and its level	72(32.9)
University degree	48(21.9)
Occupation	
Employed	147(67)
Unemployed	54(25)
Retired	18(8)

Table (3) Medical Characteristics

Characteristics	TotalNo.(%)
Cancer duration (months)	
< 6	64(29)
6 < 12	68(31)
12 < 24	53(24)
≥ 24	34(16)
Type of cancer therapy	
CT *	162(74)
RT **	34(15.5)
Both	23(10.5)

Duration of therapy (months)	
< 6	128(58.5)
6 < 12	54(24.5)
12 < 24	28(13)
≥ 24	9(4)
History of Dyspepsia	
Yes	106(48.2)
No	113(51.8)
History of peptic ulcer	
Yes	176(80.3)
No	43(19.7)

A majority of the subjects (70.8 %) were not currently following any special diet as a consequence of the cancer as can be seen in table 4. Among the subjects who were prescribed a special diet as a result of some cancer intervention, all of them did so on the advice of their clinician. Most of the subjects (74.0 %) did not have any food intolerances or allergies. Among those who had any sort of food intolerance or allergy, it was almost equally because of dairy products, meat, and egg or because of any other foods like chocolate, and peanuts. About one-third of the subjects (37.5 %) however complained of some sort of food aversion. Table 4 gives information about the use of nutritional supplements among the study subjects. Only 31.5 % of the subjects reported a current use of any nutritional supplement as opposed to 68.5 % who denied their current use. Almost half the subjects who admitted to currently using any sort of nutritional supplements were taking only vitamins and supplements while only 6.3 % were using a mineral supplement. However, 44.5 % were using supplements that contained both vitamins and minerals. As shown in table (5); more than half of the subjects (67%) prefer eating salty foods such as fried salty foods, salty meat, and meat contain meals, sour milk, salty cheese, and others. Furthermore, (69%) of the subjects mentioned that they prefer pickled foods, especially vegetables. Regarding canning foods, more than half of

the subjects (63%) mentioned that they prefer canning foods. Spicy and fried foods were the top preferred by the subjects; (81%) and (79%) of the subjects preferred these sorts of foods respectively. As per the categorization of the WHO for the BMI range, the study subjects were classified as normal, underweight and overweight, and/or obese. More than half of the subjects (57%) were overweight and/ or obese while 31 % were normal as per the WHO BMI range for the elderly. Only 12 % of the subjects were categorized as underweight as shown in table(6).

Table (4) Dietary Characteristics

Characteristics	TotalNo.(%)
Cancer special diet	
Yes	64(29.2)
No	155(70.8)
Diet prescribed by	
Clinicians	64(100)
Dietician	0
Food intolerance/allergy	
Yes	57(26)
No	162(74)
food intolerance/ allergy	
Dairy, meat, poultry	29(51)
Others	28(49)
Food aversions	
Yes	82(37.5)
No	137(62.5)
Use of	

supplements Yes No	69(31.5) 150(68.5)
Type of supplement Vitamin Mineral Both	 34(49.2) 4(6.3) 31(44.5)

Table (5) Foods Preference characteristics

Diet Characteristics	Total
Salty foods preference **Yes** **No**	 147 (67) 72(33)
Pickled foods Preference **Yes** **No**	 151(69) 68(31)
Canning foods Preference **Yes** **No**	 138(63) 81(37)
Spicy foods Preference Yes No	 177(81) 42(19)
Fried foods Preference Yes No	 173(79) 46(21)

Table (6): BMI categorization

Characteristics	TotalNo.(%)

Underweight	125(57)
Normal	68(31)
Overweight or obese	26(12)

A Chi Square test is carried out to see if there is any statistically significant association between the dietary habits, and H. Pylori infection among gastric cancer patients attending BMC. The researchers also haveassessed various physiological and non physiological factors including select socio-economical factors and their association with dietary habits of this sample of subjects.Male gender, frequency intake of fried foods areassociated at ($P< 0.05$) with more prevalence of H. Pylori among gastric cancer patients.Male gender is associated with more prevalence (67%) of H. Pylori among gastric cancer patients and female gender is associated with less prevalence of H. Pylori among gastric cancer patients. Male as compared to females had a higher percentage of history of H. Pylori infection as shown in (p= 0.026).There was no apparent association between the *H. pylori* infection and other social factors, such as marriage status. Frequency intake of fried foodsis associated ($P=$ 0.031) with more prevalence of H. Pylori among gastric cancer patients. People who consumed frequently fried foods had a higher percentage (71%) of history of H. Pylori infection as shown in (table7).

Table (7)Variables Associated with H. Pylori infection among gastric cancer patients

Characteristics	**History of H. Pylori infection among gastric cancer patients**	
	Yes	**No**
Male **Female**	67 47	33 53
Frequency intake of fried foods **Yes** **No**	71 44	29 56

if possible add graphic representation of obtained data

Discussion

Gastrointestinal malignancies are the most prevalent cancers worldwide and gastric cancer is the leading cause of cancer death with an annual incidence rate of about one million yearly. Moreover, the massive associated mortality rate makes it the second leading cause of cancer-related deaths after lung cancer. (25) In Libya, national reports as well as regional studies have indicated that gastric cancer is responsible for the second highest cancer incidence rate among males after lung cancer, and the second as well in females after breast cancer. (26) Moreover, stomach cancer has been reported as the leading cause of mortality with a far large gap from other cancers, both in Libyan males and females. (27) Helicobacter pylorus colonizes the human stomach and establishes a long-term infection of the gastric mucosa. Strong evidence suggests that this infection has an overwhelming impact on the development of gastric cancers in the presence of some dietary background. (28, 29) In this study; the researchers assess the association between dietary pattern, helicobacter pylori infection, and gastric cancer among patients attending Benghazi Medical Centre. Male gender and frequent intake of fried foods were variables associated with the prevalence of H. pylori among cancer patients. Male gender was a factor that significantly predicted H pylori infection in gastric cancer patients. Epidemiological studies on the general population show a male preponderance in the infection rate by H pylori, although there are controversial reports representing comparable rates. However, the finding of a gender disparity in the rate of infection in the gastric cancer population is a novel finding and may show that males are more vulnerable to developing gastric cancers after getting H pylori infection. One possible explanation is that the level of gastric ghrelin is higher in the stomach mucosa of women than in men. Ghrelin is a peptide hormone that plays an important role in food intake, energy homeostasis, and body-weight regulation. Ghrelin possesses anti-proliferative effects on breast, lung, and thyroid cell lines and exerts protective actions on the gastric mucosa. In the alimentary tract, ghrelin increases acid secretion which is opposite the required condition for H. Pylori. (34, 35) Furthermore, the gastric cancer incidence rate in males is approximately two times that recorded in females. (36) This unique result of the male/female ratio is worldwide consistent, similar in populations with high and low incidence of gastric cancer (37) However, these results remain controversial. Furthermore, hormone replacement therapy for menopausal women reduces gastric cancer risk during the post-menopausal period. (38- 40)

High frequent use of fried foods is significantly associated with increased risk of H. Pylori History among stomach cancer in both males and females in the current study. Deep-oil-fried foods are a common traditional component of Libyan foods and produce human carcinogens at high cooking oil temperatures. (8) Cooking oil fumes contain high concentrations of human carcinogens, such as BaP and DBahA, and heterocyclic aromatic amines, due to high frying temperatures which are also associated with a high prevalence of H. Pylori infection. Benzo(a) pyrene, chrysene, and dibenzathracene have been

detected at significant levels in oil-fried vegetables and fish, meats, and bakeries. A prospective cohort study found that high consumption of deep-fried food increases the risk of stomach cancer among people infected with H. pylori (RR=1.71, 95% CI=0.67–4.34) which was also observed among subjects who consumed fried foods frequently (OR=2.3, 95% CI=1.6–3.2). (41, 42)

Conclusion

Stomach cancer is one of the most common cancers in the world and the most common leading cause of death. *Helicobacter pylori* are bacteria that are present in half of the world's population. H. pylori and several dietary factors are associated with the development of stomach cancers in many nations. The current study aims to assess the association between dietary patterns, helicobacter pylori infection, and gastric cancer among patients attending Benghazi Medical Center. Male gender and frequent intake of fried foods were the variables associated with stomach cancer in subjects infected with H.pylori. All gastrointestinal patients in Benghazi Medical Centre should be routinely screened for H. Pylori due to their health and financial consequences. Early nutritional intervention strategies including nutrition education, involving a multidisciplinary team of clinicians, dieticians, and nursing staff should be implemented with an appropriate follow-up. Multi-faceted and tailor-made strategies to counteract specific malnutrition need to be planned, implemented, monitored, and evaluated among malnourished and at nutritional risk patients. Additional studies need to be carried out among gastric cancer and H. Pylori patients and related dietary factors in different settings as well as other regions of Libya to identify the specific prevalence of diet-related factors associated with it.

Consent

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

Ethical approval

As per international standard and university standard, written approval of Ethics committee has been collected and preserved by the authors.

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