

Nutritional risk factors in the gastric cancer patients attending in Imam Ali Hospital, Zahedan, Iran

Mansour Karajibani, Farzaneh Montazerifar, Alireza Dashipour, Abdollah Ozhabrیمانesh

Zahedan Health Promotion Research Center, Pregnancy Health Research Center and Nutrition and Food Science Department, School of Medicine, University of Medical Sciences, Zahedan, Iran

Objective: To assess the dietary factors of Gastric Cancer (GC) in Zahedan, Iran.

Methodology: 46 case GC and 46 healthy subjects participated in this case-control study. Food frequency questionnaire (FFQ) was used to determine the intake of different food groups. Besides food habits, cooking process and preparation of foods were recorded. The data were analyzed using Chi-square and student's t-test.

Results: A significant relationship was observed between GC and smoking cigarette, hookah, and

opium and consumption of salty meat. But this correlation was not significant with paan consumption.

Conclusion: There was a significant difference between GC patients and controls regarding food preparation methods. Therefore, it is suggested to modify the food habits and cooking methods and adopt a healthy lifestyle to prevent GC. (Rawal Med J 2014;39:19-24).

Keywords: Gastric cancer, food habits, food preparation.

INTRODUCTION

Carcinoma of stomach is still the second major cause of cancer death worldwide.¹ The highest incidence rate of gastric cancer (GC) is reported in East Asia, Eastern Europe and south America.² Rate of esophageal cancer and GC is much higher in East Asia than other parts of the world.^{3,4} The case – fatality rate of GC is higher than common malignancies such as colon, breast and prostate Cancers.⁵ According to reports by the Ministry of Health and Medical Education, GC is the third major cause of death in Iran after coronary heart disease and accidents.⁶ GC has multi-factorial etiology the most important of which has been H. Pylori infection.^{2,5} Besides, diet, lifestyle, genetic, socioeconomic status and other factors are worth mentioning.⁵ In addition to specific components of the diet, certain cooking processes such as broiling meat, roasting, grilling, baking, and deep frying in open furnaces, sun drying, salting, curing, and pickling, all of which increase the formation of N-nitroso compounds (NNC) are associated with increased risk of GC.⁷ Polycyclic aromatic hydrocarbons such as benzo[a]pyrene formed in smoked food have been incriminated in high GC rates in many areas of the world.^{7,8}

A negative relationship between refrigerator use, fruit intake and GC mortality and also a positive relationship between salt intake and GC have been

observed.⁹ It has been shown that high intake of salted fish, soy sauce, pickle, cured meat and other salted-preserved foods increase H. pylori colonization and the risk of GC resulting in gastritis.^{2,5,10,11} Environmental factors or human genetic diversity are more frequent in populations with high incidence of the disease, but determination and favoritism of these factors is challenging.¹² People living in the Ardabil province of North-West Iran suffer from a high risk of GC.¹³ Selenium deficiency, H. Pylori infection, dietary and bacterial factors attribute to the high risk of GC among the population in Ardabil.¹⁴

Cancer in digestive system and related secretory organs more readily shows to have some relation to food.¹⁵ Avoiding cancer risk factors including smoking, overweight and not getting enough exercise, or eating a healthy diet may help prevent certain cancers. Some studies have shown that the consumption of whole-grain cereal, antioxidants, carotenoids, green tea, and garlic may reduce the risk of GC.¹⁶ It was also observed that increase of nitrate in the drinking water had positive correlation with esophagus cancer but not with GC.¹⁷ Therefore, the present study was aimed at determining the relationship between nutritional risk factors and dietary habits with GC in the patients attending in Imam Ali Hospital in Zahedan, Iran.

METHODOLOGY

Subjects: In a case-control study, 50 GC patients (33 men and 17 women) aged 60 ± 14.5 years were enrolled from Imam Ali Hospital, Zahedan, the center of Sistan and Baluchistan Province, located in Southeast of Iran. Usually, 3- 4 GC patients are referred to hospital every month. Diagnosed GC patients were selected between December 2011 and October 2012. The criteria for diagnosis of GC in patients were determined according to pathological or cytology findings. A total number of 46 healthy subjects (30 men and 16 women) aged 59 ± 14.1 years old were also selected as control group. The patients were matched with healthy subjects based on age, sex, job and economic status and chronic diseases such as diabetes and cardiovascular disease.

Cytology findings: The International Agency for Research on Cancer (World Health Organization) IARC /WHO guideline and the Pekka Lauren's system were used to classify tumors and the histological method was defined for the diagnosis of GC.^{18,19}

General Measurements: Demographic characteristics of the two groups including age, sex, occupation, and education levels were recorded. Other pieces information including smoking cigarette or hookah, drug abuse, paan and alcohol consumption were completed by subjects and their relatives. Weight was measured with seca platform scale with 0.5 Kg of accuracy. Height was measured using a measuring tape (non-stretch) with 0.5 centimeter accuracy. Body mass index (BMI) was calculated and a BMI at less than 18.5 kg/m^2 was classified as underweight, between 25 and 29.9 kg/m^2 as overweight, and greater than 30 as obese. A healthy BMI for adults was considered between 18.5 and 24.9 kg/m^2 .

Dietary questionnaire: Food frequency questionnaire (FFQ) was designed to determine intake of different foods. The FFQ is a retrospective review of food intake as often, sometimes, seldom and never per day, per week, or per month. We completed FFQ for the period immediately before hospitalization and before illness to obtain a complete and accurate history.²⁰ We also studied the eating habits of patients and enquired about process and preparation of food and consumption of red

meat, frying foods, fatty meat, salty meat, garlic, and alcohol.

Statistical analysis: Data are expressed as mean \pm SD. Statistical analysis was performed using SPSS version 11.5. For comparison of the quantitative data t-test and for

comparison of the qualitative data, Chi-square test was used. $P < 0.05$ was considered statistically significant.

RESULTS

Of the 50 GC patients, 4 patients (3 men and 1 woman) were excluded. The rest completed the study. Demographic characteristics are presented in Table 1. There was a significant difference between the two groups in accordance with the body weight and BMI ($P = 0.0001$).

Table 1. Demographic characteristics of study groups.

Groups	GC patients		Control group		P- value
Parameter	n= 46	Min-Max	n= 46	Min-Max	
Age (yr)	60 ± 14.5	(24 – 90)	59 ± 14.1	(24- 88)	0.8
Weight (Kg)	52 ± 9.1	(35 – 75)	66 ± 14.5	(40 – 104)	0.0001
Height (Cm)	164 ± 8	(147 – 90)	162 ± 8	(157 – 188)	0.5
BMI (Kg/m ²)	19 ± 4	(12 – 24.6)	24 ± 4.1	(18– 36)	0.0001

Most GC patients and controls were office staff (both groups 21.7%). Regarding the education level, 54.3% of GC patients and 47.8% of controls were illiterate. There was a significant difference between GC patients and controls regarding number of cigarettes a day ($P = 0.02$) and frequency of Paan consumption ($P = 0.01$). But there was no significant difference in the two groups considering the frequency of smoking hookah ($P > 0.05$) (Table 2).

Table 2. Comparison of cigarette smoking or hookah, Paan consumption in the study groups.

Groups	GC patients		Control group		P- value
Parameter	n= 46	Min-Max	n= 46	Min-max	
Number of cigarettes a day	14 ± 7	(2 – 20)	9 ± 7.9	(3 – 24.6)	0.02
Frequency of Paan					
Consumption	6 ± 2	(3 – 10)	2 ± 1.3	(1 – 3)	0.01
Frequency of hookah	3 ± 1.6	(1 – 6)	2 ± 1.1	(1 – 3)	0.4

Most of GC patients and controls seldom consumed

salty meats, and also they had less consumption of frying and fatty meats (Table 3). A significant difference was seen between the two groups in frequency consumption of fatty meat ($P=0.0001$) and frying meat ($P=0.04$) (Table 4).

Table 3. Daily consumption of salty meat in the study group.

	Often	Less	Seldom	Total
GC patients <i>n</i> (%)	3 (6.5%)	11 (23.9%)	32 (69.6%)	46 (100%)
Control group <i>n</i> (%)	0 (0%)	7 (15.2%)	39 (84.8%)	46 (100%)
$X^2 = 4.57$, $P = 0.1$				

There was a significant relationship between cancer in the patients and smoking ($X^2 = 4.8$, $P = 0.02$), hookah ($X^2 = 5.39$, $P = 0.02$), opium ($X^2 = 9.6$, $P = 0.002$) and consumption of salty meat ($X^2 = 3.8$, $P = 0.04$), respectively. But this correlation was not significant with paan consumption ($P > 0.05$).

Table 4. Comparison of consumption of frying and fatty meat in the study group.

Groups Consumption of meat (daily)	Often	Sometimes	Less	Never	Total	P- value
Frying meat $X^2 = 8.2$ 0.04	GC patients <i>n</i> (%)	9 (19.6%)	11 (23.9%) (100%)	24 (52.2%)	2 (4.3%)	46
	Control group <i>n</i> (%)	4 (8.7%)	6 (13 %) (100%)	41 (47.4 %)	5 (10.9%)	46
Fatty meat $X^2 = 23$ 0.0001	GC patients <i>n</i> (%)	14 (30.4%)	14 (30.4%)	16 (34.8%)	2 (4.3%)	46 (100%)
	Control group <i>n</i> (%)	3 (6.5%)	4 (8.7%)	25 (54.3%)	14 (30.4%)	46 (100%)

DISCUSSION

This study revealed that consumption of some foods and food preparation was associated with increased risk of GC. A significant relationship was found between fatty meat consumption and prevalence of GC. In addition, a significant difference in the consumption of fatty meat and frying meat between GC patients and controls was observed. In previous studies, increased risk of GC was associated with saturated fat intake.^{10,21,22}

Dietary fat may modulate carcinogenesis by modifying the responsiveness of hormone receptors of the tumor cells or by accelerating formation of arachidonic acid and then of prostaglandins, which may help tumor growth.²² A study by Kim et

al²³ showed that there was an association between diet and GC. So, foods rich in nitrate, or nitrite, a high salt diet, smoked meat or fish and a high carbohydrate diet increase the risk of GC, whereas high consumption of fresh vegetables, fruits and dairy products reduce the risk of GC. Never the less, the findings are not always constant.

In the present study, GC patients and controls used pipeline water almost equally (87% vs. 80.4%) and few of the participants used water purifier in either group (13% vs. 19.6%). Besides, there was not significant association between kind of drinking water and GC. The nitrate content of fertilizers, soil, and water contribute to dietary nitrate. There are nitrates naturally in foods or added during preservation. However, nitrite, nitrate and nitrosating agents can be synthesized by reaction of bacteria or activated macrophages.²⁴ Nitrate contamination of drinking water can increase cancer risk. Nitrate reduces to nitrite and nitrosation reactions increases N-nitro compounds which are carcinogenic and can act regularly.²⁵ In this study, nitrate level in drinking water was not determined.

According to local food habits, the studied patients tended to consume fried foods or barbeque. It was found significant relationship between fried meat and GC in our study. Jagerstad et al²⁶ reported an association between frying as the main cooking technique and GC. Frying at high temperature probably more than boiling can produce toxicants and potential mutagens (e.g., heterocyclic amines and acrylamide).²⁶

The results showed that 32.6% of GC patients consumed salty meat compared to 15.2% of controls. It has been reported that high consumption of salted fish, cured meat and salted- preserved foods increase *H. pylori* and risk of GC by damaging gastric mucosa.⁵ Salt induces hypergastrinemia and mutations, promoting epithelial cell proliferation which leads to parietal cell loss and GC progression.⁵ Salt is not a directly acting carcinogen, but a high salt intake can lead to atrophic gastritis through direct damage to the gastric mucosa which results in gastritis, increased DNA synthesis and cell proliferation.²⁴

Consumption of red meat is quite high in this area. Sincere meat contains significant amount of fat, it

can be considered as an important risk factor of cancer. In several studies, a positive correlation between consumption of red meat and GC risk has been shown, whereas high plasma vitamin C, some carotenoids, retinol, and alpha-tocopherol, high intake of cereal fiber, and the Mediterranean diet exhibited inverse association with GC.²⁷ It seems that in addition to physical characteristics of population and daily food intake, dietary habits can also be considered as a risk factor of the cancer.¹⁵ It has been reported that red meat consumption is associated with higher rate of intestinal metaplasia.²⁵ Of all, 26.1% and 23.9% of GC patients and 8.7% and 6.5% of healthy subjects smoked cigarette and hookah, respectively (data not shown). A correlation between cancer with cigarette smoking and opium was observed. Although, Paan is known as a carcinogen,²⁸ and its consumption is high in this area, no correlation was found between paan consumption and GC. It may be due to the limitation for evaluation of real consumption of paan in the studied population, which might not have been recorded correctly. GC patients used more opium compared to control group (23.9% vs. 2.2%). However, nobody in either group used alcohol. In a population-based prospective cohort study, a direct correlation was observed between consumption of alcohol and tobacco and risk of GC.²⁹

According to frequency of smoking hookah, there was a significant difference between GC patients and control group (23.9% vs. 6.5%). A significant association was observed between the intensity and duration of cigarette smoking with GC. Smoking is known to decrease prostaglandins that maintain gastric mucosal integrity. Significant dose-response relationships were observed with age at which smoking was initiated and with lifetime exposure to smoking.

Stomach cancer incidence is known to increase with age with the peak incidence occurring at 60-80 years.⁵ In a study in Japan, cigarette smoking was a noticeable factor not only in lung cancer, but also in GC.¹⁵ Tobacco smoke has been reported to induce the development of precursor gastric lesions such as gastritis, ulceration, and intestinal metaplasia. Smokers tend to have a higher incidence of *H. pylori* infection and gastroduodenal inflammation than

non-smokers.⁵

Sistan and Baluchistan people enjoy eating roasted nuts, seeds and pickles which have favorite taste for them. These food habits along with other factors (e.g. genetic, socioeconomic status, physical characteristics, daily food intakes, smoking, tobacco, *H. pylori* infection, etc) can be considered in causing cancer.^{5,15} Pickles are a risk factor for GC due to containing high amount of salt and N-nitroso compounds.¹⁰ Different methods of food preparation and cooking process such as boiling meats, roasting, grilling, baking, and deep frying in open furnaces, sun drying, salting and pickling, all of which increase the formation of N-nitroso compounds (NNC) are associated with increased risk of GC.⁵

It has also been reported that high consumption of garlic is associated with reduction of intestinal metaplasia and dysplasia.³⁰ It has protective effects in progression of precancerous gastric lesions. Anti-carcinogenic effect of garlic is attributed to natural components such as allicin and methyl linoleate. These phytochemicals induce enzymatic detoxification systems, including mixed function oxidase and glutathione-S-transferase.²³ However, consumption of raw garlic in both GC patients and controls was low and significant difference was not found between patients and controls.

South-East part of Sistan and Baluchistan province is located on the beach; and people often eat salted or smoked fish that can be considered as a risk factor for cancer. Moreover, according to ecological condition of this area there is limitation in consumption of fresh fruits and vegetables. Unfortunately, there was not enough information regarding consumption of them in this study.

CONCLUSION

There was a significant difference between GC patients and control regarding food preparation. However, GC may be affected by other factors. It is suggested, to modify the food habits, dietary practice, and adapting a healthy life style to prevent GC. Further studies are needed to clarify the effect of dietary factors and food habits on GC and also more carefully investigate its etiology.

Author contributions:

Conception and design: Mansour Karajibani
Collection and assembly of data: Farzaneh Montazerifar, Abdollah Hozhabrmanesh

Analysis and interpretation of the data: Alireza Dashipour

Drafting of the article: Mansour Karajibani

Critical revision of the article for important intellectual content: Mansour Karajibani, Farzaneh Montazerifar

Statistical expertise: Alireza Dashipour

Final approval and guarantor of the article: Mansour Karajibani, Farzaneh Montazerifar

Acknowledgments: We would like to thank Dr. Arbabi and staff of Cancer Clinic of Imam Ali hospital, Zahedan, Iran for their collaboration. We also sincerely thank the patients who kindly participated in this study.

Funding sources: This research has been approved and supported by Deputy of Research of

Corresponding author email: mkarajibani@yahoo.com

Conflict of interest: None declared

Rec. Date: Aug 05, 2013 Accept Date: Nov 05, 2013

REFERENCES

1. Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *Lancet* 2005;366:1784-93.
2. Pereira L, Zamudio R, Soares-Souza G, Herrera P, Cabrera L, Hooper CC, et al. Socioeconomic and Nutritional Factors Account for the Association of Gastric Cancer with Amerindian Ancestry in a Latin American Admixed Population. *PLoS One* 2012;7:2-8.
3. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL. Harrison's principles of internal medicine. McGraw-Hill, New York. 2005:523-33.
4. Feldman M, Friedman LS, Sleisenger MH, Sleisenger and Fordtran's gastrointestinal and liver disease. Saunders, Philadelphia. 2006: 949-78, 1139-1170, 2759-2810
5. Siddavaram N. Carcinoma of the stomach: A review of epidemiology, pathogenesis, molecular genetics and chemoprevention. *World J Gastrointest Oncol* 2012;15:156-69.
6. Kolahdoozan S, Radmard R, Khademi H. Five common cancers in Iran. *Arch Iran Med* 2010;13:143-6.
7. Jedrychowski W. Contribution of epidemiology in Poland for better understanding of the natural history of diseases in gastrointestinal tract. *J Physiol Pharmacol* 2003;54 Suppl 3:245-61.
8. Wogan GN, Hecht SS, Felton JS, Conney AH, Loeb LA. Environmental and chemical carcinogenesis. *Semin Cancer Biol* 2004;14:473-86.
9. Park B, Shin A, Park SK, Ko KP, Ma SH, Lee EH, et al. Ecological study for refrigerator use, salt, vegetable, and fruit intakes, and gastric cancer. *Cancer Causes Control* 2011;22:1497-1502.
10. Pakseresht M, Forman D, Malekzadeh R, Yazdanbod A, West RM, Greenwood DC, et al. Dietary habits and gastric cancer risk in north-west Iran. *Cancer Causes Control* 2011;22:725-36.
11. Navarro Silvera SA, Mayne ST, Risch HA, Gammon MD, Vaughan T. Principal component analysis of dietary and lifestyle patterns in relation to risk of subtypes of esophageal and gastric cancer. *Ann Epidemiol* 2011;21:543-50.
12. Sharma A, Radhakrishnan V. Gastric cancer in India. *Indian J Med Paediatr Oncol* 2011;32:12-16.
13. Babaei M, Jaafarzadeh H, Sadjadi AR, Samadi F, Yazdanbod A, Fallah M, et al. Cancer Incidence and Mortality in Ardabil: Report of an Ongoing Population-Based Cancer Registry in Iran, 2004-2006. *Iran J Public Health* 2009;38:35-45.
14. Pourfarzi F, Whelan A, Kaldor J, Malekzadeh R. The role of diet and other environmental factors in the causation of gastric cancer in Iran-A population based study. *Int J Cancer* 2009;12:1953-60.
15. Oiso T. Incidence of stomach cancer and its relation to dietary habits and nutrition in Japan between 1900 and 1975. *Cancer Res* 1975;35:3254-58.
16. Kushi LH, Tim Byers T, Colleen Doyle C, Bandera EV, McCullough M, Gansler T, et al. American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention: Reducing the Risk of Cancer with Healthy Food Choices and Physical. *Cancer J Clin* 2006;56:5:254-81.
17. Semnani SH, Arabali A, Keshtkar AA, Behnampoor N, Besharat S, Roshandel GH. Nitrate and nitrite level of drinking water and the risk of upper gastro intestinal cancers in urban areas of Golestan Province, Northeast of Iran. *JKMS* 2009;16:281-90. [In Persian]
18. Hamilton SR, Aaltonen LA. World Health Organization (WHO). Organization Classification of Tumors, Pathology and genetics of tumors of the digestive system: tumors of the oesophagogastric junction. LARS Press, Lyon 2000.
19. Laurén P. The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma: an attempt at a histo-clinical classification. *Acta Pathol Microbiol Scand.* 1965;64:31-49.
20. Mahan LK, Escott-Stamp S, Raymond JL. Krause's food and nutrition care process. Part 1. Nutritional assessment. 13th edit. Elsevier, USA. 2012:138-140, 163-167.
21. Decarli A, Amadori D, Avellini C, Bianchi S, Bonaguri C, Cipriani F, Cocco P, Giacosa A, et al. A case-control study of gastric cancer and diet in Italy: II. Association with nutrients. *Int J Cancer* 1990;45:896-901.
22. Karmali RA. Prostaglandins and cancer. *Prostaglandins Med* 1980;5(1):11-28.
23. Kim HJ, woong KI, Chang WK, Kim MK, Lee SS, Choi BY. Dietary factors and gastric cancer in Korea: A case-control study. *Int J Cancer* 2002;97:531-5.
24. Suzuki H, Iijima K, Scobie G, Fyfe V, McColl KE.

- Nitrate and nitrosative chemistry within Barrett's oesophagus during acid reflux. *Gut* 2005;54:1527-35.
25. Weyer, PJ, Cerhan JR, Kross BC, Hallberg GR, Kantamnei, Breuer G, et al. Municipal drinking water nitrate level and cancer risk in older women: The Iowa women's health study. *Epidemiol* 2001;12:327-38.
 26. Skoog K. Genotoxocity of heat-processed foods. *Mutat Res* 2005;574:156-72.
 27. Buckland G, Agudo A, Luján L, Jakszyn P, Bueno-de-Mesquita HB, et al. Adherence to a Mediterranean diet and risk of gastric adenocarcinoma within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study. *Am J Clin Nutr* 2010;91:381-90.
 28. Merchant A, Husain SS, Hosain M, Fikree FF, Pitiphat W, Siddiqui AR, Hayder SJ, et al. Paan without tobacco: an independent risk factor for oral cancer. *Int J Cancer* 2000;86:128-31.
 29. Nakamura T, Yao T, Niho Y, Tsuneyoshi M. A clinicopathological study in young patients with gastric carcinoma. *J Surg Oncol* 1999;71:214-9.
 30. You WC, Zhang L, Gail MH, Ma JL, Chang YS, Blot WJ, et al. *Helicobacter pylori* infection, garlic intake and precancerous lesions in a Chinese population at low risk of gastric cancer. *Int J Epidemiol* 1998;27:941-4.