DOI: https://doi.org/10.53350/pjmhs22169535

ORIGINAL ARTICLE

Histological Type and Tumor Site of Gastric Cancer; Helicobacter Pylori, Vitamin C and E, Sodium Intake and Smoking as a Risk Factor of Gastric Cancer

SHAISTA ALAM[1], FATIMA DAUD[2], MOHIBULLAH KHAN[3], NAYAB SARWAR[4], ASFANDYAR SHAH ROGHANI[5], ADNAN SARWAR[6], KALSOOM TARIQ[7], SAJID ALI[8], SUDHAIR ABBAS BANGASH[9]

[1]*Department of Pathology, Pak International Medical College I, Peshawar.*
[2]*Department of Anatomy, Pak International Medical College, Peshawar*
[3]*Department of Pathology, Pak International Medical College, Peshawar*
[4]*Department of Pathology, Pak International Medical College, Peshawar*
[5]*District Pathologist, Women and children Hospital Rajjar Charsadda*
[6]*Department of Pathology, Pak International Medical College, Peshawar*
[7]*Department of Biochemistry Khyber Girls Medical College, Peshawar*
[8]*Assistant professor medical oncology Ayub Teaching Hospital Abbottabad*
[9]*Faculty of Life Science, Department of Pharmacy, Sarhad University of Science and Information Technology, Peshawar*
Corresponding authors: Fatima Daud, Email: fdkhan39@yahoo.com & Kalsoom Tariq, Email: drkalsoomtariq@yahoo.com)

ABSTRACT

Introduction: Stomach bacteria Helicobacter pylori (H. pylori) & diet are peril variables that are most strongly linked to gastric cancer. Using a case-control research of hospital, this research analyzed whether the H. pylori, vitamin C and E, sodium intake and smoking play any role as a risk factor of gastric cancer.

Methodology: There were 207 cases and 410 controls in this research. Preference of taste of salt was evaluated for all participants, IgG antibodies were used against H. pylori to ascertain infection, and questionnaires consisting of questions about gastric cancer & its potential risk factors were administered to cases & control. Statistical analyses were used to calculate measures of risk.

Results: At intervals of 1.7-7.3 g/l & 7.2 g/l salt taste percentage was significantly greater in cases than controls (2.12- 4.11), Individuals who consume a lot of salt are more likely to get stomach cancer when they have H. pylori infection. The varied salt intake measurements were significantly modified by tumor site & smoking; the highest salt taste was correlated with inflated chance of developing cancer in people who have never smoked or who have non-cardia malignancies.

Conclusion: Salt or sodium intake, smoking, drinking and H. pylori infection is the risk factors for gastric cancer while no evidence of vitamin C intake as a risk factor of gastric cancer was observed.

Keywords: gastric cancer, H. pylori, tumor, risk factor, diet intake

INTRODUCTION

Gastric cancer (GC) development is a multistep, complex process. While the diffuse kind of GC is more frequently linked to genetic defects, the intestinal type is more frequently linked to environmental factors such nutrition, lifestyle, & infection of H. pylori. Stomach cancer carcinogenesis has recently come under the spotlight thanks to developments in molecular medicine, which have also provided innovative methods for its prevention, detection, and treatment. GC Japanese Classification divided the gastric adenocarcinoma histological type into undifferentiated kind (poorly distinguished adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma) and well- or slightly divided tubular carcinoma and papillary adenocarcinoma), each of which has unique risk factor for lymph node metastases in patients with primary GC is histologic type. Individuals with differentiated types typically have better survival outcomes and a decreased risk of lymph node metastases than patients with undifferentiated types. Therefore, differentiated type is regarded as a key sign for Endoscopic submucosal dissection (ESD) treatment, while patients with undifferentiated type are typically advised to have curative gastrectomy with lymphadenectomy. However, the histologic heterogeneity of stomach cancer tissues is typically evident. Surgically removed samples typically contain a mixture of several distinct cancer cell types rather than just one histological type. According to reports, 12.6-25.4% of early GC patient have a mixed histologic type which contains both differentiated components (Tang et al., 2020).

About 50% of people infects with H. pylori worldwide. The chance of developing duodenal and gastric ulcer, in addition to GC, is considerably increased by H. pylori infection, which also results in chronic inflammation. The indestructible risk factor for stomach cancer, the second-leading cause of cancer-related deaths globally, is H. pylori infection. Fact that H. pylori survives after colonizing the stomach environment suggests that the host's immune system is unable to eradicate this bacterium. A Gram-negative bacterial infection called H. pylori preferentially colonizes the stomach epithelium. The spiral-shaped bacterium has 3 to 5 polar flagella that are employed for locomotion and is positive for the enzymes oxidase, urease catalase. Most isolates of H. pylori produce virulence factors designed to interfere with host cellular signaling pathways. By converting urea into ammonia by urease, a disinterested environment created around the microbiomes, H. pylori is able to colonies the highly acidic environment within the stomach, unlike other viruses and bacteria. Indeed, genetic analyses show that H. pylori has been colonizing humans for at least 59,000 years, providing further evidence that H. pylori and humans have coexisted for tens of thousands of years.

GC is intimately linked to modifiable factors, like food, according to ethnic & geographic differences, cancer incidence trend through time, & variations in incidence patterns seen among immigrants. Salt and salty meals were associated as GC risk factor in 2007. Consuming salt is known to produce gastritis in rats in experimental trials, and when supplied together with N-methyl-N-nitro-N-nitrosoguanidine known gastric carcinogens it increases their ability to cause cancer (Kato et al., 2006). An excess of salt content in stomach, ethnic-geographic disparities, trends in cancer incidence through time, and variations in incidence patterns among immigrants all point to a close connection between GC and modifiable factors like food. Salt and meals that are salted or salty were recognized as GC risk factor. In experimental studies on rats, salt consumption cause gastritis, & when combined with recognized carcinogens i.e. N-methyl-N-nitro-N-nitrosoguanidine, their capacity to cause cancer is increased in a stomach that contains a lot of salt (Ge et al., 2012). Hence, the literature suggests that dietary salt intake is positively associated with the risk of gastric cancer.

Stomach cancer related with H. pylori has been increased by smoking showed by numerous studies. According to Japanese men a population-based prospective research of, H. pylori and cigarette smoking both raise the risk of developing stomach cancer, and the two factors together significantly raise that risk,

and a Swedish investigation produced comparable results. In a population-based case-control research conducted in Germany, smoking cigarettes and having H. pylori CagA+ strains of the bacteria were both found to increase the chance of getting stomach cancer H. pylori and cigarette smoking were both found to be independently related with stomach cancer in a case-control research conducted in Japan, but no correlation between the two was found to be statistically significant (Butt et al., 2019). A population-based case-control research did not found any statistical association of stomach cancer risk with smoking. and smokers who have H. pylori infection, despite a tendency toward greater risk among current smokers being noted (Wroblewski et al., 2010). All of the available information suggests an association of the smoking and H. pylori infection with the risk of developing GC. It is also likely that the sum of all environmental factors contributes to the risk of developing GC in people who have H. pylori infection. This research was conducted with the objectives to study the impact of H. pylori, Vitamin C and E, sodium intake and Smoking on the GC.

METHOD AND MATERIALS

An investigation of newly diagnosed stomach admission of cancer patients in surgical wards was done. This study was carried out at Hayatabad Medical Complex from November 2021 to August 2022. 207 cases of histologically proven stomach cancer, among patients aged 40 to 75, were reported. When healthy people went to the hospital for a standard physical examination, 436 controls were recruited. The final component of the sample was 410 controls, who ranged in age from 35 to 77, or 94.03% of the population. Participants with no digestive tract diseases malignant tumors in the controls were eligible for this study. A standardized questionnaire with questions covering demographic, social, behavioral, and medical aspects was administered by trained interviewers to both patients and controls' questionnaire on food frequency that is semi-quantitative (FFQ) with 65 food items that has previously been validated was used to record dietary patterns.

A total of 201 cases were omitted from this study because they claimed to have altered their diet within the previous 12 months of their interview due to gastrointestinal complaints. Participants from both groups were asked to describe the dietary consumption in the previous year, along with any alterations in lifestyle behaviors which had happened in the previous year as a result of any other preexisting condition, although they were not excluded from the research. The serum from a blood sample was frozen at -20 °C. By using ELISA, anti-H. pylori serum IgG titers were measured. According to the manufacturer's instructions, participants were categorized as negative if they had, if their antibody concentration was between 16 and 22 RU ml-1, they were borderline, and the 22 RU ml-1 were considered positive. In our studies, those having borderline IgG titers were categorized as infected. Salt intake was measured in two distinct ways. First, we took into account the daily consumption of food's inherent salt, which was assessed using the FFQ. The sodium or salty food consumption seen in control was utilized as cutoffs to establish exposure groups for study. Second, taste-preference tests were performed for gauging a patient' salt consumption. We applied a number of NaCl solutions to the tongue's tip in order to determine the salty taste threshold, as stated in prior research (Zhang and Zhang, 2011).

Statistical analysis: According to infection of H. pylori, smoking level, cancer site & histological type, analyses of salt intake were carried out. The odds ratios (OR) and associated 95% confidence intervals (CI) for stomach cancer in respect to the relevant exposure were determined using the unconditional logistic regression. Using crude odds ratios and odds ratios that had been corrected for gender, education, age, smoking, and H. pylori infection, the relationship of salt consumption & stomach cancer was measured (ORs). and using unconditional logistic regression, the appropriate 94% confidence intervals (98% CIs) were calculated. By introducing interaction variables in the regression models for infection status (negative or positive) and smoking status, it was possible for H. pylori or smoking to modify an effect (never or ever). Every p-value reported for trend test significance was two-sided. All of the analysis was performed in STATA (version 10.0).

RESULTS

Two groups of dietary intake were identified: 3 times/week and 3 times/week. Nonsmokers were separated from smokers who smoke 10-12 (or more) cigarettes weekly for at least six months. Three categories of salt intake were used: 3g per day, 3-5g per day, and more than 5g per day. Taste of each test for NaCl solution was divided into three categories: 1.6 g/L, 1.5-7.3 g/L, and 7.3 interval. NaCl solution concentration was divided into six grades from 0.45 g per L to 14.6 g per L with 0.9 g per L interval. Additionally, the flavour of NaCl solution was divided into three groups: 1.6 g/L, 1.5-7.3 g/L, and 7.3 interval.

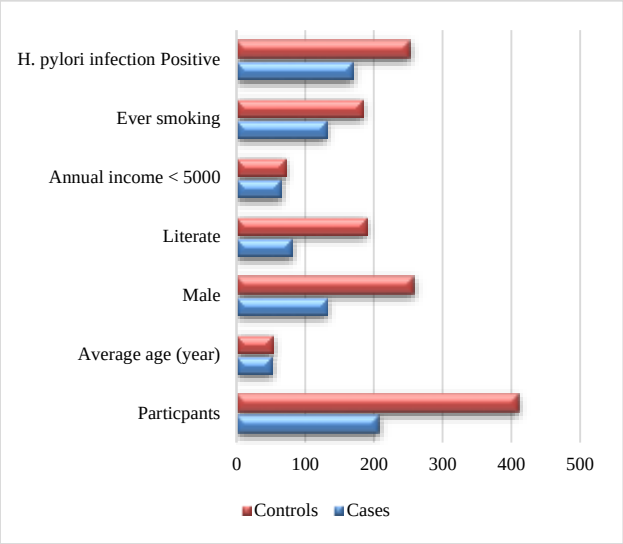

Figure 1: Socio-demographic distribution of the participants

The clinical examination and past record of the participants included in cases showed that intestinal cancers made up the majority of histopathological cancers (n=30; 61.8%). Furthermore, a lot of the tumors were found in the cardia region (n=20; 81.6%). Figure 1 shows the frequency of participants. Regarding gender and age, there were no discernible difference in the cases and controls. Males made up 258 out of 410 (62.9%) of the controls and 132 out of 2017 (63.7%) of the cases (Table 1). The common ages of cases were 16, 20 and 53 while that of controls were 52, 85 and 90. H. pylori infections were more common in cases (n=170/207; 82.1%) than in controls (n=252/410; 61.4%). The percentage of cases (n=131) who had ever smoked was 63.2%, which was greater than the percentage of controls (n=184; 44%). In terms of ever drinking, there were no discernible difference in cases & controls. Table 2 shows the association OR with the 95% CIs for Sodium Intake, Salt Taste Preference and GC.

Table 1: Characteristics of GC patients & matched controls

Variables	No. of cases* (%)	No. of controls** (%)	P value
Average age (year)	52.8±5.90	53±6.20	0.16
Male, n (%)	132(63)	258(62)	0.84
Literate, n (%)	81(39)	189(46)	0.1
Annual income < 5000	65 (31)	71 (17)	<0.001
Ever smoking, n (%)	131(63)	184(44)	<0.001
H. pylori infection Positive, n (%)	170(82)	252(61)	<0.001

*n=207, n=410

Table 2: OR & 95% CIs for Sodium Intake, Salt Taste Preference and GC

	Characteristics	No. of cases* (%)	No. of controls** (%)	Odds ratio
Intake of sodium (g/day)	Median	3.79±0.17	3.05±0.13	-
	<3	46(22.6)	117(28.4)	1.0
	3~5	109(52.6)	215(53.9)	1.87(1.19-2.18)
	>5	53(25.4)	85(21.0)	2.54(1.63-2.75)
Preference of salt taste	<1.8	58(28.8)	134(32.7)	1.0
	1.7-7.3	103(49.8)	193(47.1)	1.56(1.23-3.64)
	>7.2	46(22.2)	83(20.2)	2.03(2.12-4.11)

*n=207, n=410

DISCUSSION

According to Lou et al. (2020), global incidence rates of GC increased with age in both sexes. In the age range of 15–39 years, men had similar rates with women, except the age range of 25–29 years in which men had significantly lower risk than women. These results were almost similar to findings of our research as well as with the results of Dijksterhuis et al. (2021). However, the results of the present study regarding relation of age and gender with the GC are contradictory with the finding by Yao et al. (2020). Both extrinsic and intrinsic factors may have contributed to the sex difference in GC. Sex hormones may play a role in the development of cardia cancer and intestinal type of GC (Yao et al., 2020). Hence, it is suggested that both age and gender must be taken into account when predicting survival from GC, the investigators conclude.

The demographically case-control analysis revealed that dietary salt intake, as evaluated by several ways, was significantly connected to an elevated risk of GC, and that this risk was reduced by infection with H. pylori, smoking, and tumour location. Consuming these highly salty foods may cause gastritis and intensify the carcinogenic effects of stomach carcinogens when combined with N-methyl-Nitro-N-nitrosoguanidine (Takahashi and Hasegawa, 1985). Our study's findings that salt intake increases the incidence of GC support notion that both salt & nitrosated substances play a part in the development of the disease. H. Pylori infection was found frequently in smokers and similar results were found by Shirin et al. (2004), Raei et al. (2016) and Park et al. (2018).

CONCLUSION

Salt or sodium intake, smoking, drinking and H. pylori infection is the risk factors for GC while no evidence of vitamin C intake as a risk factor of GC was observed.

REFERENCES

1. Butt, J., Varga, M. G., Wang, T., Tsugane, S., Shimazu, T., Zheng, W., Abnet, C. C., Yoo, K. Y., Park, S. K., Kim, J., Jee, S. H., Qiao, Y. L., Shu, X. O., Waterboer, T., Pawlita, M., & Epplein, M. (2019). Smoking, Helicobacter Pylori Serology, and Gastric Cancer Risk in Prospective Studies from China, Japan, and Korea. Cancer prevention research (Philadelphia, Pa.), 12(10), 667–674. https://doi.org/10.1158/1940-6207.CAPR-19-0238
2. Dijksterhuis, W. P., Kalff, M. C., Wagner, A. D., Verhoeven, R. H., Lemmens, V. E., van Oijen, M. G., ... & van Laarhoven, H. W. (2021). Gender differences in treatment allocation and survival of advanced gastroesophageal cancer: a population-based study. JNCI: Journal of the National Cancer Institute, 113(11), 1551-1560. https://doi.org/10.1093/jnci/djab075
3. Duynhoven, Y. T. V., & Jonge, R. D. (2001). Transmission of H. pylori : a role for food?. Bulletin of the World Health Organization, 79(5), 455-460.
4. Ge, S., Feng, X., Shen, L., Wei, Z., Zhu, Q., & Sun, J. (2012). Association between Habitual Dietary Salt Intake and Risk of Gastric Cancer: A Systematic Review of Observational Studies. Gastroenterology research and practice, 2012, 808120. https://doi.org/10.1155/2012/808120
5. Kato, H., Takeuchi, O., Sato, S., Yoneyama, M., Yamamoto, M., Matsui, K., ... & Akira, S. (2006). Differential roles of MDA5 and RIG-I helicases in the recognition of RNA viruses. Nature, 441(7089), 101-105.
6. Lee, J. Y., & Kim, N. (2015). Diagnosis of H. pylori by invasive test: histology. Annals of translational medicine, 3(1).
7. Miyamae, M., Komatsu, S., Ichikawa, D., Kosuga, T., Kubota, T., Okamoto, K., ... & Otsuji, E. (2016). Histological mixed-type as an independent risk factor for nodal metastasis in submucosal GC. Tumor Biology, 37(1), 709-714.
8. Park, H., Park, J. J., Park, Y. M., Baik, S. J., Lee, H. J., Jung, D. H., ... & Park, H. (2018). The association between H. pylori infection and the risk of advanced colorectal neoplasia may differ according to age and cigarette smoking. Helicobacter, 23(3), e12477.
9. Raei, N., Behrouz, B., Zahri, S., & Latifi-Navid, S. (2016). H. pylori infection and dietary factors act synergistically to promote GC. Asian Pacific Journal of Cancer Prevention, 17(3), 917-921.
10. Shirin, H., Sadan, O., Shevah, O., Bruck, R., Boaz, M., Moss, S. F., ... & Avni, Y. (2004). Positive serology for H. pylori and vomiting in the pregnancy. Archives of Gynecology and Obstetrics, 270(1), 10-14.
11. Takahashi, M., & Hasegawa, R. (1985, January). Enhancing effects of dietary salt on both initiation and promotion stages of rat gastric carcinogenesis. In Princess Takamatsu Symposia (Vol. 16, pp. 169-182).
12. Takizawa, K., Ono, H., Kakushima, N., Tanaka, M., Hasuike, N., Matsubayashi, H., ... & Nakajima, T. (2013). Risk of lymph node metastases from intramucosal GC in relation to histological types: how to manage the mixed histological type for endoscopic submucosal dissection. GC, 16(4), 531-536.
13. Tang, X., Zhang, M., He, Q., Sun, G., Wang, C., Gao, P., & Qu, H. (2020). Histological Differentiated/Undifferentiated Mixed Type Should Not Be Considered as a Non-Curative Factor of Endoscopic Resection for Patients With Early Gastric Cancer. Frontiers in oncology, 10, 1743. https://doi.org/10.3389/fonc.2020.01743
14. Wabinga, H. R. (2002). Comparison of immunohistochemical and modified Giemsa stains for demonstration of H. pylori infection in an African population. African health sciences, 2(2), 52-55.
15. Walczak, H., Miller, R. E., Ariail, K., Gliniak, B., Griffith, T. S., Kubin, M., ... & Lynch, D. H. (1999). Tumoricidal activity of tumor necrosis factor–related apoptosis–inducing ligand in vivo. Nature medicine, 5(2), 157-163.
16. Wroblewski, L. E., Peek, R. M., Jr, & Wilson, K. T. (2010). Helicobacter pylori and gastric cancer: factors that modulate disease risk. Clinical microbiology reviews, 23(4), 713–739. https://doi.org/10.1128/CMR.00011-10
17. Yao, Q., Qi, X., & Xie, S. H. (2020). Sex difference in the incidence of cardia and non-cardia GC in the United States, 1992–2014. BMC gastroenterology, 20(1), 1-7. https://bmcgastroenterol.biomedcentral.com/articles/10.1186/s12876-020-01551-1
18. Zhang, P., Prakash, J., Zhang, Z., Mills, M. S., Efremidis, N. K., Christodoulides, D. N., & Chen, Z. (2011). Trapping and guiding microparticles with morphing autofocusing Airy beams. Optics letters, 36(15), 2883-2885.Lou, L., Wang, L., Zhang, Y., Chen, G., Lin, L., Jin, X., ... & Chen, J. (2020). Sex difference in incidence of GC: an international comparative study based on the Global Burden of Disease Study 2017. BMJ open, 10(1), e033323. http://dx.doi.org/10.1136/bmjopen-2019-033323