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ORIGINAL ARTICLE

H. Pylori Gastritis and Gastric Carcinoma: Uncovering Histological Links and Risk Factors

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ABSTRACT

Objective: Aim was to determine the risk of gastric carcinoma among patients of Helicobacter pylori gastritics and its risk factors.

Study Design: Retrospective study

Place and Duration: Department of gastroenterology, DHQ Teaching Hospital and Ghazi Khan Medical College DG Khan, Punjab in the duration from November, 2022 to April, 2023.

Methods: Total 131 patients who had gastric carcinoma were included. Stored serum samples collected, were tested for IgG antibodies to H. pylori by enzyme-linked immunosorbent assay. Data on cigarette use, blood group, ulcer disease, and gastric surgery were obtained from questionnaires administered at enrollment. Tissue sections and pathology reports were reviewed to confirm the histologic results. SPSS 23.0 was used to analyze data.

Results: In our study, male patients were higher in numbers 86 (65.6%) as compared to females 45 (34.4%). The patients mean age was 51.17±6.20 years and had mean BMI 24.16 ±7.46 kg/m^2. 73 (55.7%) patients had smoking history. 97 (74.04%) patients had gastric ulcer. Average time from serum collection to stomach gastric carcinoma was 12.7±3.26 years. Among all, 74 (56.5%) patients had adenocarcinoma, gastroesophageal junction was found in 20 (15.3) cases, gastric lymphoma in 11 (8.4%) cases and 26 (19.4%) cases had undetermined or other cancers. We found that 83 (63.4%) patients had history of H.pylori infection. There was a significant negative association between a history of peptic ulcer disease and eventual gastric carcinoma (P = 0.003) and an independent association between a history of gastric surgery and the development of cancer (p = 0.004).

Conclusion: The results of this research led us to the conclusion that an infection with H. pylori is linked to an elevated risk of gastric adenocarcinoma and may play a role as a cofactor in the process that leads to the development of this malignant condition.

Keywords: H.pylori infection, Gastric Carcinoma, Risk Factors

INTRODUCTION

Cancer remains the third greatest cause of death across the globe, behind only cardiovascular disease and infectious diseases.More than 900,000 people were diagnosed with stomach cancer in 2002[1]; roughly two-thirds of these instances occurred in poor countries[2]. However, there is no clear pattern to the regional distribution of stomach cancer. In fact, some of the greatest risk regions (like Asia) have low rate countries (like India). Also, even in low-risk communities, there are subgroups with a higher risk (such as Koreans in the United States)[3,4].

Across all populations, men have roughly twice the risk that women do at the same age. Furthermore, the incidence rate for women is always equal to the rate for men 10 years younger[3]. In most parts of the world, just one out of every five patients with stomach cancer is still alive after 5 years[5,6]. In Japan, however, mass screening programmes have increased the 5-year survival rate to roughly 60%.

The Lauren staging system is the gold standard for describing gastric cancer. Morphology, genetics, clinical parameters, progression pattern, and epidemiology are used to distinguish between intestinal and diffuse GC [7]. Diffuse GC is characterised by a lack of gland development and a proliferation of loosely organised, solitary cells. Differentiated glandular or tubular components make up intestinal-type GC [8]. Signet ring cell GC has been on the rise while overall GC rates have been falling. Lauren's classification [8] previously placed GC with a signet ring cell in the "diffuse type" category. Now, tumour cells in signet-ring cell carcinoma are characterised by abundant cytoplasmic mucin and an eccentrically positioned, crescent-shaped nucleus [9]. Despite the name, not all cases of "undifferentiated" or "diffuse" stomach cancer involve signet ring cells.

Infection with Helicobacter pylori (H. pylori) is one of many risk factors for developing gastric cancer; however, it is not the only one. The chance of getting GC is increased by around a factor of six due to H. pylori infection [10]. Because of this, the WHO labelled H. pylori a class I carcinogen in 1994. In 1982, Australian researchers discovered the bacteria H. pylori, also known as Campylobacter pylori [11], in the human mucous membrane of the digestive system. The Latin name for this pathogen, which derives from the word for "helix" (which means "spiral"), alludes to its distinctive shape, which likely aids in its ability to infiltrate the mucous membrane lining the digestive tract. Because the bacteria are found mostly in the distal region of the stomach, the pylorus, the second component of the name H. pylori originates from pylorus. H. pylori was shown to be unharmed by gastric acid, and in fact, it appeared to thrive in the acidic environment. H. pylori was later shown to infect other organs outside the stomach, such as the liver and the eye [12].

Researchers observed that having H. pylori in the stomach or duodenum increased the risk of developing an ulcer in those areas. On the other hand, peptic ulcer disease is not always caused by a bacterial infection. Few people infected with the virus will develop stomach cancer. The prevalence of H. pylori infection has been documented to lie between 60% and 84%, with the highest prevalence being observed in individuals with stomach cancer. Differences in mortality rates between groups of people, such as those defined by race or gender, suggest the presence of additional, crucial cofactors determining risk. Genetic variations, the age at which H. pylori infection sets up, variations in gastric acidity, and environmental factors including nutrition (particularly salt consumption and smoking) are also potential contributors. H. pylori infects over 80% of adults and about 30% of children in Poland [12]. The prevalence of H. pylori infection is higher in developing nations. Meanwhile, 5-10% of adults get stomach or duodenal peptic ulcer disease. This means that only about one in ten people infected with H. pylori will develop peptic ulcer disease.

Furthermore, H. pylori is not detected in some patients with peptic ulcer disease. Therefore, H. pylori cannot explain the aetiology of gastric cancer by itself [13], and it cannot be the sole cause of gastric and duodenal ulcers.

Many researchers throughout the world have worked to develop serologic assays for H. pylori, and these tests have proven to be invaluable for shedding light on the epidemiology of this bacterium. When comparing ELISAs to endoscopy, which uses a positive culture or histologic stain to define infection, ELISAs have been shown to be more sensitive and specific for the identification of active disease. Antibodies specific to Campylobacter jejuni, Escherichia coli, or Campylobacter foetus are not detected by these tests. There is no evidence to suggest that positive titers indicate anything other than ongoing disease; people with positive serologic results, including unnoticed control subjects, have been confirmed to have active infections when gastric biopsy was performed at the same time. Given the reliability of serologic testing in detecting persistent infection, some have proposed replacing biopsy with serologic analysis as the gold standard for diagnosis.In order to assess the correlation between various forms of gastric cancer and prior H. pylori infection as measured by ELISA, we conducted a nested case-control research [14,15].

MATERIALS AND METHODS

This retrospective study was conducted at Department of gastroenterology, DHQ Teaching Hospital and Ghazi Khan Medical College DG Khan, Punjab in the duration from November, 2022 to April, 2023 and comprised of 131 patients. The serum samples were then sent to, where they are currently being classified and stored. Participants' hospitalization rates and tumor registry data were tracked regularly, and cancer outcomes were reported and typically verified through record review.

Each patient was paired with a subject from the same multiphasic health checkup who did not have gastric carcinoma based on age at serum donation (12 months), sex, race, date of serum donation (6 months), and location. Questionnaires filled out at the time of enrolment in the multi-stage health checkup revealed information about smoking history, ulcer illness, and gastric surgery performed prior to serum donation. On the survey, both stomach and duodenal ulcers were lumped into a single category labeled "ulcer disease." Smoking-related ulcer questionnaire results have been verified. Records produced for the multi-stage health checkup also included information on blood groups.

H. pylori IgG levels were determined in serum samples using an ELISA. The ELISA antigen was the high-molecular-weight cell-associated proteins from three different H. pylori strains that were purified using an agarose A-5m column. In each test, 1 L of serum diluted 1:200 and 1:1,000 dilutions of peroxidase conjugate antihuman IgG were utilized. The histologic characteristics of the patients' tissue samples and biopsy reports were examined. Tumors were classified according to whether they were located in the stomach's cardia (the upper part of the stomach), body (the fundus), or antrum (the lower part of the stomach). Adenocarcinomas of the gastroesophageal junction were classified individually due to their relationship with Barrett's esophagus. Each piece of information was analyzed using SPSS 23.0.

RESULTS

In our study, male patients were higher in numbers 86 (65.6%) as compared to females 45 (34.4%).(figure-1)

The patients mean age was 51.17±6.20 years and had mean BMI 24.16 ±7.46 kg/m^2. 73 (55.7%) patients had smoking history. 97 (74.04%) patients had gastric ulcer. Average time from serum collection to stomach gastric carcinoma was 12.7±3.26 years.(table 1)

Among all, 74 (56.5%) patients had adenocarcinoma, gastroesophageal junction was found in 20 (15.3%) cases, gastric lymphoma in 11 (8.4%) cases and 26 (19.4%) cases had undetermined or other cancers.(table 2)

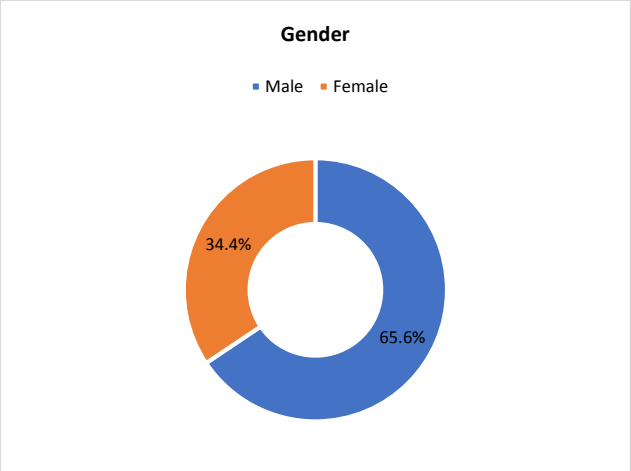

Figure-1: Gender of the enrolled cases

Table-1: Demographics of the enrolled cases

Variables	Frequency	Percentage
Mean age (years)	51.17±6.20	
Mean BMI (kg/m^2)	24.16 ±7.46	
Smoking History		
Yes	73	55.7
No	58	44.3
Gastric Ulcer		
Yes	97	74.04
No	34	25.96
Mean time of serum to Gastric cancer (years)	12.7±3.26	

Table-2: Diagnosis of cases by histology

Variables	Frequency (131)	Percentage
Histological Results		
adenocarcinoma	74	56.4
gastroesophageal junction	20	15.3
gastric lymphoma	11	8.4
Undetermined/other	26	19.6

We found that 83 (63.4%) patients had history of H.pylori infection in which 69 cases were had adenocarcinoma.(table 3)

Table-3: Relation of H.pylori infection and Gastric Carcinoma

Variables	Frequency	Percentage
H.Pylori		
adenocarcinoma	69	52.7
Others	14	10.7
Total	83	63.4

There was a significant negative association between a history of peptic ulcer disease and eventual gastric carcinoma (P = 0.003) and an independent association between a history of gastric surgery and the development of cancer (p = 0.004).(table 4)

Table-4: Relation of a peptic ulcer and gastric surgery with cancer (n=74)

Variables	Peptic ulcer disease	Gastric surgery
Gastric Carcinoma		
Yes	0	60 (81.1%)
No	12 (16.2%)	2 (2.7%)

DISCUSSION

Infection or chronic inflammation can cause cancer. Vesicular schistosomiasis, squamous-cell carcinoma, and ulcerative colitis are examples. Our study found a strong link between stomach adenocarcinoma and H. pylori infection, which always induces gastric inflammation. H. pylori-positive individuals were three times more likely to develop gastric adenocarcinoma in the next 1 to 24 years than age- and race-matched controls.

Previous research[16,17] and the recognised epidemiologic aspects of gastric adenocarcinoma[18,19] led us to hypothesise that H. pylori was associated with intestinal-type cancer but not diffuse disease. This was not the case, however, as H. pylori was found to raise the chance of developing any type of adenocarcinoma in the stomach, including those in the body, the antrum, or both. The possibility of misclassification of the tumour type that led to this observation cannot be ruled out, although the epidemiological features of the patients with these two histologic forms of cancer were consistent with those previously described. Although H. pylori infection has been associated to Barrett's oesophagus, it has not been linked to tumours of the gastroesophageal junction, which develop from the aberrant mucosa in Barrett's oesophagus. Since H. pylori infection is linked to an elevated risk of all gastric adenocarcinomas occurring distal to the cardia, we draw that conclusion.

In current study 131 patients of gastric carcinoma were included. Male patients were higher in numbers 86 (65.6%) as compared to females 45 (34.4%). The patients mean age was 51.17±6.20 years and had mean BMI 24.16 ±7.46 kg/m^2. 73 (55.7%) patients had smoking history. 97 (74.04%) patients had gastric ulcer. Average time from serum collection to stomach gastric carcinoma was 12.7±3.26 years. These results were comparable to the studies conducted in past.[20,21] Recent research has also suggested that gastrin may play a role in the control of autophagy, suggesting that targeting autophagy in conjunction with standard cytostatic medicines may be an effective strategy for the treatment of GC (Rao et al., 2017). Statins have been shown to improve the efficacy of antibiotics in eradicating H. pylori and to decrease H. pylori-mediated inflammation by increasing autophagy (Liao et al., 2016), albeit the mechanisms behind these effects are not well understood.[22,23]

It is possible that an unidentified factor increases susceptibility both to H. pylori infection and to gastric carcinoma and that H. pylori might just be a marker for an increased risk of cancer. H. pylori, however, is a plausible pathophysiologic cofactor for cancer. Several potential mechanisms can be postulated: metabolic products of the organisms directly transform the mucosa; rapid turnover of cells resulting from infection-related injury increases the risk of DNA damage, predisposing the mucosa to transformation by ingested or endogenous mutagens; and endogenous byproducts of inflammation, such as Superoxide and hydroxyl ions, cause oxidative damage, mutation, and malignant transformation.**[24]** These mechanisms are not mutually exclusive, and a combination of mechanisms is likely.

It is clear, however, that infection with H. pylori alone cannot explain the pathogenesis of gastric carcinoma. H. pylori infection is extraordinarily common, affecting approximately 50 percent of North American adults who are older than 50 years, and in some developing nations it affects almost all adults.[25]Only a very small percentage of infected persons will ever have gastric carcinoma. There must be other critical cofactors affecting risk, cofactors that may also explain the difference in risk between blacks and whites and between men and women. Possible cofactors are age at the onset of infection, diet, and differences in gastric acidity.

As has been previously reported,**[26]** gastric surgery was an independent risk factor for cancer. The negative association with peptic ulcer disease, however, was unanticipated. In the light of the close association of H. pylori infection with both ulcer disease and gastric carcinoma, one would expect ulcer disease and gastric carcinoma to be directly, rather than inversely, related. It is possible that cofactors in the pathogenesis of H. pylori—related ulcer disease protect against the subsequent development of gastric carcinoma. For example, acid might be necessary for peptic ulcer disease to occur but might inhibit gastric carcinogenesis. Similarly, ulcer disease might reflect the occurrence of an acute infection in adulthood and the absence of a chronic infection in childhood. Alternatively, treatment of ulcer disease may impart protection against gastric carcinoma. If the inverse relation between ulcer disease and cancer is corroborated, important clues to the pathogenesis of carcinoma may be uncovered.

Gastric carcinoma remains a major killer worldwide. Crude etiologic-fraction calculations of data from this study suggest that 60 percent of gastric adenocarcinomas are attributable to infection with H. pylori; this implies that 60 percent of the cases of cancer would disappear if H. pylori did not exist. H. pylori infection is both readily diagnosed and curable. Whether eradication of gastric infection would actually decrease the risk of cancer, however, remains to be seen. Even if elimination of the organism is found to affect the risk of cancer, indiscriminate treatment of all infected persons is unlikely to be a practical, cost-effective approach to reducing the incidence of this uncommon cancer. Populations considered to be at particularly high risk, however, might benefit from screening for H. pylori infection, treatment, palliation (e.g., with antioxidant vitamins), or preventive measures. To define high-risk populations further, epidemiologic and laboratory studies are needed to explore interactions of H. pylori infection with potential cofactors for cancer.[27,28]

CONCLUSION

The results of this research led us to the conclusion that an infection with H. pylori is linked to an elevated risk of gastric adenocarcinoma and may play a role as a cofactor in the process that leads to the development of this malignant condition.

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