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Association of CagA+ *Helicobacter pylori* infection and gastric carcinoma

Md. Khalilur Rahman, Md. Ismail Patwary and Md. Habibur Rahman

Article Info

Department of Medicine, Sylhet M.A.G. Osmani Medical College, Sylhet, Bangladesh (MKR, MIP); Department of Gastroenterology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh (MHR)

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For Correspondence:
Md. Khalilur Rahman
drkhalilmedicine@gmail.com

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Abstract

The aim of this study was to find out the association of the CagA+ *Helicobacter pylori* infection and gastric carcinoma. This cross sectional comparative study was conducted on 40 patients of gastric carcinoma and 40 healthy volunteers from January 2011 to December 2012. Then, Cag A status was ascertained in both the groups by ELISA method. There was no significant difference between the case and control in relation to Cag A status.

Introduction

Gastric cancer is the second leading cause of cancer-related deaths worldwide. From the data provided by the International Agency for Research on Cancer,[1] malignancy of the stomach is the most common cancer in Asia, nearly two-thirds of which occurs in developing countries.[2] The World Health Organization and International Agency for Research on Cancer consensus group,[3] stated in 1994 that there was sufficient epidemiologic and histologic,[4,5] evidence to classify *Helicobacter pylori* as a definite carcinogen. Our understanding of gastric cancer underwent a discernible shift with the discovery of *H. pylori*. Infection with *H. pylori* probably still plays a leading role in the development of gastric cancer.[6] In a country such as India, where >75% of the population are infected, it has been proved beyond doubt that *H. pylori* infection is high, especially in areas of low socioeconomic status and bad hygiene conditions.[7] The vast majority of *H. pylori* infected people remain asymptomatic throughout their lives with no major clinical events, and only a small proportion present with some form of gastric disorder, such as gastric carcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma.[8] A study by Konturek et al.[9] showed that the risk of gastric cancer in patients with *H. pylori* markedly increased with infection with bacteria that were cytotoxin-associated gene (CagA+) in the age group 40–49 years. Further, a similar study from the Indian sub-continent reported a higher risk of developing gastric cancer in younger patients infected with *H. pylori*.[10] Although some studies have rejected a direct link between *H. pylori* infection and gastric cancer,[10,11] several prospective studies have supported a positive association between these two entities.[12,13] Perhaps the most convincing evidence for the association between *H. pylori* infection and gastric carcinoma was provided by a Japanese study,[14] which showed development of gastric cancer in 2.9% of *H. pylori* infected people, whereas no uninfected subjects developed it. In addition, a number of environmental factors have been shown to be associated with gastric cancer, including high salt diets, N-nitrosamines and low intake of dietary antioxidants typically found in fresh fruit and vegetables.[15,16] A large number of studies have shown increased risk of gastric cancer in people with CagA+ *H. pylori*. However, other data have revealed that the occurrence of gastric malignancy is independent of CagA status.[17] In our country, one small study and several studies from India failed to show higher frequency of CagA+ *H. pylori* infection in patients with gastric cancer than controls. Available evidences did not support difference in *H. pylori* strains as an explanation for this enigma. Despite established etiological role of *H. pylori*, situation is somewhat enigmatic in Asian countries because in countries with higher frequency of infection, there is lower rate of gastric cancer. Host's genetic make-up and dietary and environmental factors might explain this enigma.[18] Several case-control studies, in different countries, have investigated the association between CagA+ *H. pylori* and gastric cancer, and most evidence in literature agrees this association does exist.[19,20] Despite *H. pylori* being an important agent for causing gastric cancer, a randomized controlled trial from high risk region.[21] On the other hand, several studies from India also failed to show higher frequency of *H. pylori* infection in patients with gastric cancer than controls.[18] The conflicting results had not been highlighted firmly as very few studies were carried out till to date. In our country, study had been carried out showing relation of *H. pylori* with gastric malignancy.

But only one study in relation of CagA+ *H. pylori* infection and gastric carcinoma with small number of cases has been done yet. There was no statistically significant difference in CagA status irrespective of cancer and non-cancer population.[22] In SOMCH Gastric carcinoma case is very common in Medicine, Gastroenterology and Surgery wards. Therefore, this study has been planned to show the association of CagA+ H. pylori infection and gastric carcinoma with large number of cases.

Materials and Methods

This comparative study was conducted in the Department of Medicine in collaboration with Department of Gastroenterology and Depart-ment of Surgery, Sylhet MAG Osmani Medical College Hospital, Sylhet from January 2011 to December, 2012. Patients those who were under-going upper GI endoscopy in the Department of Gastroenterology, Sylhet MAG Osmani Medical College Hospital, Sylhet were the study population and among those fulfilled the inclusion and exclusion criteria were the sample population in this study. Inclusion criteria for the case group were endoscopically suspected carcinoma cases confirm-ed on histopathological examination as adenocarci-noma in the stomach, those consented to participate in this study and age 18 years or more. Inclusion criteria for the matched control group were patients submitted to upper GI endoscopy with apparently normal stomach. The exclusion criteria for the cases were those with no histopathological confirmation of diagnosis, mixed type of gastric adenocarcinoma, and gastric lymphoma/MALT. Those with active upper GI hemorrhage, *H. pylori* eradication therapy with antibiotics within last four weeks of endos-copy, history of subtotal gastrectomy and diagnosis of gastric cancer established more than six months ago, were also excluded. The people with refusal to upper GI endoscopy and in pregnancy status were also excluded. The exclusion criteria for control were the patients with active upper GI hemorrhage, *H. pylori* eradication therapy with antibiotics within last four weeks of endoscopy, history of subtotal gastrectomy. pregnancy status and refusal to do upper GI endoscopy were also included in the exclusion criteria.

A total of 40 cases with carcinoma stomach and another 40 patients with apparently normal stomach regarded as control were selected during the study period according to inclusion and exclusion criteria

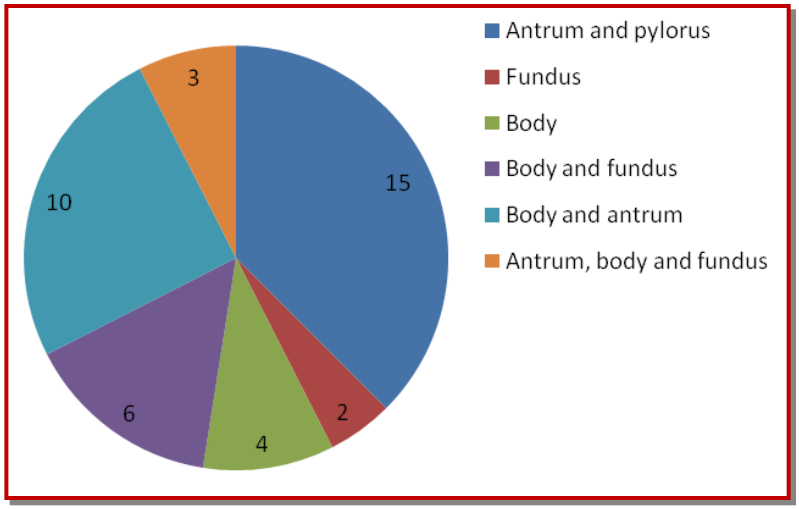

Figure 1: Distribution of site of involvement in gastric carcinoma

Table I

Distribution of participants according to various tests for *H. pylori*

Partici-pant	Rapid urease test or CLO test		Giemsa stain for *H. pylori* (Histology)		ELISA for *H. pylori*	
	Positive	Negative	Positive	Negative	Positive	Negative
Case	23	17	27	13	40	None
Control	19	21	19	21	40	None

Results

Figure 1 shows the distribution of site of involve-ment in gastric carcinoma. Antrum and pylorus were involved in 15 (37.5%) cases; body and antrum were involved in 10 (25.0%) cases; body and fundus were involved in 6 (15.0%) cases; body was invol-ved in 4 (10.0%) cases; fundus was involved in 2 (5.0%) cases; and antrum, body and fundus were involved in 4 (10.0%) cases of the gastric carcinoma.

Table I shows all the study subjects are *H. pylori* positive in serogical test using ELISA.

Table II shows the distribution of patients by CagA status. CagA positive *H. pylori* infection was 1.8 times higher (non-significant) in case group than that of control group [37 (92.5%) vs. 35 (87.5%); OR=1.762 (95% of CI=0.392–7.929); p=0.456].

Discussion

In this study, CagA+ *H. pylori* infection was found 1.8 times higher (non-significant) in case group than that of control group [37 (92.5%) vs 35 (87.5%); OR=1.762 (95% of CI=0.392–7.929); p=0.456]. Ławniczak and Starzyńska,[23] found that gastric cancer patients and controls had the same preva-lence of *H. pylori* CagA antibodies (54.4 vs 52.5%; p = 0.078). The persons with *H. pylori* Cag A (+) and Cag A (-) were at the same risk for developing gastric cancer (OR = 1.08; 95%CI = 0.66-1.49). Shimoyamaetal.[24] found that CagA sero positivity was 60% (49 of 81) in cancer patients and 44% (36 of

Table II

Distribution of patients by CagA status

CagA status	Case (n=40)	Control (n=40)	Odds Ratio (95% of CI)	p value
Positive	37 (92.5)	35 (87.5)	1.762 (0.392–7.929)	*p=0.456
Negative	3 (7.5)	5 (12.5)		

81) in controls. The odds ratio for the risk of cancer if CagA seropositive was 1.93 (95% confidence interval (CI) 1.01 to 3.68; p<0.05).

Azuma et al[25] showed infection with CagA+ *H. pylori* seems to play an essential role in the development of gastric carcinoma, although the bacteria alone cannot be considered a unique factor in the promotion of gastric cancer.

Christian Prinz et al[26] also showed infection with CagA+ strains was not significantly related to risk for non-cardia gastric cancers (OR = 1.4; CI = 0.7-2.8) but was significantly associated with a reduced risk for esophageal/cardia cancers (OR = 0.4; CI = 0.2-0.8).

Maeda et al.[27] and Yamaoka et al[28] stated that since, the majority of *H. pylori* infected individuals in Asian countries harbor CagA+ strains, associations of CagA status and diseases are not observed in Asia. Yusuf et. al.[29] claimed that biologically inactive CagA could be a contributory factor in low prevalence of gastric cancer in a country like India , with high prevalence of *H. pylori* infection. Study carried out in India by Kumar et al.[30] showed that antibodies to CagA protein are not predictive of serious gastroduodenal disease. Ghoshal et al.[31] supported this result that frequency of CagA IgG antibody was similar among the patients with gastric carcinoma and the controls, suggesting that difference in virulence factors of *H. pylori*, at least CagA is unlikely to explain the variation in outcome of *H. pylori* infection. The current study result was also correlated with the study of Hassan et al.[22] that there was no significant association of CagA+ *H. pylori* infection and gastric cancer [35 (87.5%) vs 33 (82.5%); p=1.00].

Conclusion

No significant association of CagA+ *H. pylori* strain and risk of gastric carcinoma was found in the present study. There are several factors other than Cag A positivity in *H. pylori* infection in the causation of gastric carcinoma.

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