GASTRIC ADENOCARCINOMA AND HELICOBACTER PYLORI INFECTION

Adhikari R C¹, Pokharel B M¹, Shrestha H G¹

ABSTRACT

Gastric adenocarcinoma is of major importance worldwide as a cause of death from malignant disease. It is the commonest malignant tumor in T.U. Teaching Hospital. Helicobacter pylori infection is an important risk factor for the development of gastric cancer. This prospective study was carried out to correlate H. pylori infection with gastric adenocarcinoma. This study was done from January 1999 to January 2000; included 38 cases of gastric adenocarcinomas of which 28 (73.69%) cases were tubular type; 6 (15.79%) cases were signet-ring cell type; 2 (5.26%) cases were papillary type and 2 (5.26%) cases were mucinous type. Gastric adenocarcinomas were more common in male (73.68%) and after the age of 50 years. Giemsa staining revealed H. pylori in 30 cases (78.95%) of adenocarcinomas; whereas H. pylori seropositivity (IgG) was found in 29 (76.31%) cases. H. pylori were histologically detected in 88.3% cases of resected specimens and in 71.4% cases of endoscopic gastric biopsies. Both histological method and serological test showed positivity for H. pylori in 65.78% cases. Thus, H. pylori infection is associated with gastric carcinognesis.

Key Words: Gastric adenocarcinoma, Helicobacter pylori, Giemsa stain.

INTRODUCTION

Malignant tumors of stomach are very common forms of malignant neoplasms. Among these, gastric carcinoma is the most common. Gastric cancer is sixth most common fatal malignancy in UK¹ and accounts for 10% of all deaths from malignant diseases. In France it holds 5th place.² Carcinoma of the stomach is one of the 'captains of the men of death'. It is more common in male and after the age of 50 years³ and more frequent in populations with blood group A.⁴

1. TU Teaching Hospital, Maharajgunj, Kathmandu, Nepal.

Address for correspondence : Dr. Ram Chandra Adhikari Lecturer, Department of Pathology Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu Email: rcadhikari@hotmail.com

JNMA, October - December, 2002, 41

Adhikari et al. Gastric Adenocarcinoma and Helicobacter Pylori Infection

The exact etiology of gastric carcinoma is not known, however some of the factors are blamed to be associated with its development. One of these is H. pylori infection. Others are Epstein-Barr virus infection,^{5,11} presence of carcinogens in food, cigarette smoking,⁶ alcohol consumption, atrophic gastritis, gastric ulcer, hereditary factors etc.

Gastric adenocarcinomas, grossly, may take the form of polypoid, fungating, ulcerated, diffusely infiltrating (linitis plastica) types or may show combination of these.⁷ The WHO subdivides gastric adenocarcinomas into tubular, papillary, mucinous and signet-ring cell types; while Lauren divided into intestinal and diffuse types. Early gastric carcinoma is limited to the mucosa or the mucosa & submucosa only. Immunohistochemically, the gastric adenocarcinoma cells express for keratin, EMA and CEA. The 5 year survival rate in early gastric carcinoma and advanced gastric carcinoma is in order of 90% and 20-30% respectively.

Helicobacter pylori is gram negative, spirally shaped, unipolar multiflagellate bacteria, discovered by Warren & Marshall. H. pylori is one of the commonest chronic bacterial infections of humans worldwide and causes chronic gastritis and peptic ulceration.^{8,9,10} It is known that H. pylori colonizes gastric antral epithelium and a Working Group of the International Agency for Research on Cancer would have concluded that H. pylori is carcinogenic to humans.

H. pylori produces toxins (vacuolating toxin - 87kd; cytotoxin - 120kd), urease, alcohol dehydrogenase and mucolytic factors. These agents may be responsible for carcinogenesis. H. pylori infection is also found to be associated with some extragastric diseases^{12,13} like atherosclerosis, myocardial infraction,^{14,15} Raynaud phenomenon, Sjogren's syndrone, chronic idiopathic urticaria, sideropenic anaemia etc. H. pylori infection can be diagnosed by histological method (on gastric tissue), serological method (detection of antibody against H. pylori), biopsy urease method, urea breath test and culture.

This prospective study was designed to correlate gastric adenocarcinoma & H. pylori infection.

MATERIALS AND METHODS

This study included 38 cases of gastric adenocarcinomas during the period of January 1999 to January 2000. The specimens consisted of 17 gastrectomies & 21 endoscopic gastric biopsies.

The specimens were fixed in 10% neutral buffer formalin and processed by the usual graded alcohol dehydration in the automated histokinette using an overnight schedule of 16-18 hours. Then, tissues were embedded in paraffin wax and microtome sectioning was done with a thickness of 3-4 micrometer. Hematoxylin & Eosin and standard Giemsa stain were done in all cases. Special stains like Alcian blue and Periodic acid schiff (PAS) were done when required.

The presence of curved or spiral form bacilli in Giemsa stained tissue sections was taken as positive histological test to diagnose the H. pylori. The presence of antibodies (IgG) to H. pylori was estimated by the use of Helicobacter pylori IgG Enzyme Immunoassay method (ELISA).

RESULTS

Primary gastric adenocarcinomas were found more common in male (73.68%) and after the age of 50 years. Mean age of patients was 56.9 years with a range of 26-87 years. Table I shows age & sex distribution.

458



Table II shows morphological variants of gastric adenocarcinomas. Tubular type (fig.1) was found to be the commonest one.

Table No. II : Morphological variants of
gastric adenocarcinomas

Table III shows H. pylori positivity in tissue sections. H. pylori (fig.5) were detected histologically in 30 (78.95%) cases. H. pylori were histologically detected in 88.3% cases of resected specimens and in 71.4% cases of endoscopic gastric biopsies. H. pylori seropositivity (table no. IV) was seen in 29(76.31%) cases. H. pylori were detected by both (histological & serological) techniques in 25(65.78%) cases. H. pylori positivity was found in all cases of signet-ring cell carcinomas by both techniques. Serological & histological methods were compared in table no. 5. Sensitivity, specificity, positive predictive value and negative predictive value of serological method taking histological method as the gold standard in detecting H. pylori are 83.33% ; 50% ; 86.2% and 44.4%. The likelihood ratio for positive value is 1.66.

Table No. V : Comparision ofserological & Histological method

460 Adhikari et al. Gastric Adenocarcinoma and Helicobacter Pylori Infection		
Fig. 1	Fig. 4	
Fig. 1: Showing tubular adenocarcinoma.	Fig. 4: Showing mucinous adenocarcinoma.	
Fig. 2	Fig. 5	
Fig. 2: Showing Signet-ring cell carcinoma.	Fig. 5: Showing Helicobacter pylori in tissue section.	
	DISCUSSION	
Fig. 3	Gastric cancer is the one of the common malignant tumors and commonest malignant tumor in Nepal. ¹⁶ It is one of the 'captains of the men of death'.	
Fig. 3: Showing papillary adenocarcinoma.	Gastric cancer is considered to be a disease, primarily affecting the middle aged and the elderly; indeed its peak incidence occurs in patients older than 50 years. ¹⁷ In this study, age of patients with gastric carcinoma ranged from 26 to 87 years with mean age of 56.9 years. Patients with above 50 years of age were 84.2% & below 50 years were of	

age were 15.8%. Scott A Hundahl et al.¹⁸ found mean age of 68.3 years in gastric cancer patients during the year 1992-93; while Charles P Theuer et al.¹⁹ found mean age of 67 years. Manohar et al.²⁰ found that gastric cancer patients below the age of 50 years were 39.14% and above the age of 50 years were 61.6%.

Gastric carcinoma is more common in male with a M:F ratio of 2:1 in 60-70 years of age.²¹ In this study ,73.7% patients were male and 26.3% were female. In a study of Scott A Hundahl et al.¹⁸ during the year 1992-93, male patients of gastric carcinoma constituted 61.4% & female 38.6%.

Helicobacter pylori has been documented to be associated with gastric cancer. In this study, H. pylori seropositivity (IgG) was found in 76.31% cases of gastric adenocarcinomas. Wu MS et al.22 found H. pylori seropositivity (IgG) in 65.6% cases of gastric carcinoma. In a study of Komoto et al.,²³ H. pylori seroprevalence was prevalent in 93% patients with gastric carcinoma and it was more prevalent in non-cardia tumors. In the city of Malmo, Sweden, the overall seropositivity prevalence in gastric cancer cases was 82%.²⁴ In this study, H. pylori histologically detected in 78.95% cases of gastric adenocarcinomas. Massimo R et al.²⁵ detected H. pylori histologically in 70.5% cases of gastric carcinomas. In resected specimens H. pylori was detected only in 27.5% cases with adenocarcinoma using hematoxylin-eosin stain in a study of Hung et al.²⁶ In this study, H. pylori were histologically detected in 88.3% cases of resected specimens (with Giemsa stain) and in 71.4% cases of endoscopic gastric biopsies. Thus, H. pylori is strongly associated with gastric carcinogenesis.

CONCLUSION

Gastric adenocarcinoma is common malignant condition. These tumors are more common in male

and after the age of 50 years. Among adenocarcinomas, tubular type predominates; followed by signet-ring cell type. Helicobacter pylori is detected in most of the cases of gastric carcinomas. So it is concluded that H. pylori infection is strongly associated with development of gastric carcinoma and detection of H. pylori in tissue section by Giemsa Staining is more sensitive,feasible and economic method to diagnose H. pylori infection in our context.

REFERENCES

- Clark ML, Talbot I C & William CB. Tumors of the gastrointestinal tract. I n: Weatherall DA. Oxford textbook of medicine, 3^{ed} edition, Oxford Medical Publications.1996;2: 1982-1985.
- Faivre J, Benhamiche A M. Epidemiology and etiology of malignant gastric tumors. Rev. Prat.1997;47(8):833-6.
- Dupont JB Jr, Lee JR, Burton GR, Cohn I Jr. A denocarcinoma of the stomach. Review of 1,497 cases. Cancer 1978;41:941-947.
- Glenn R D. Neoplasms of the stomach. In: Sleisenger MH & Fordtran JS. Gastrointestinal disease. 5th Edition. W.B.Saunders Company. 1993;769.
- Y anai H, Takada K, Shimizu N, Mizugaki Y, Tada M, Okita K. Eptein-Barr virus infection in noncarcinomatous gastric epithelium. J. Pathol. 1997;183(3):293-8.
- 6. Neugut A I , Hayek M, Howe G. Epidemiology of Gastric cancer. Semin. Oncol. 1996;23(3):281-91.
- Campbell F, Bogomoletz WV, Williams GT. Tumors of the esophagus and stomach. In: Christopher DMF. Diagnostic histopathology of tumors. Churchill Livingstone. 1995;1:211-234.
- Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. L ancet 1994;1:1311-15.
- 9. Goodwin CS, Armstrong JA, Marshall BJ. Campylobacter pyloridis, gastritic and peptic

462	Adhikari et al. Gastric Adenocarcino	ma and	Helicobacter Pylori Infection
\bigcap	ulceration. J. Clin. Pathol. 1986;39:353-65.		carcinoma. Cancer 1997;80:2333-41.
10.	Baldini L, Pretolani S, Bonvicini F, Miglio F, Epifanio G, Gentiloni SN. Effect of helicobacter pylori infection, age and epithelial cell turnover in a general population at high risk for gastric cancer	19.	Charles P Theur, Tom K, Thomas HT, Hoda A. U nique features of gastric carcinoma in the young . Cancer 1998;83:25-33.
	Panminerva. Med. 1999;41(3):187-92.	20.	$\label{eq:masses} \begin{array}{l} \mbox{Manohar}\ P, A \mbox{ dhikari}\ R \ C, \ J \ oshi A \ , \ Sigdel \ B \ , B \ asnet \\ R \ B \ , A \ matya \ VJ \ et \ al . \ Present \ cancer \ status \ in \ T \ . U \ . \end{array}$
11.	Levine PH, Stemmermann G, Lennette ET, Hildesheim A, Shibata D, Nomura A. Elevated antibody titers to Epstein-Barr virus prior to the diagnosis of Epstein-Barr-virus associated gastric adenocarcinoma. Int. J. Cancer 1995;60(5):642-4.	21.	Jass JR. Tumors of the stomach. In: James O'D McGee, Peter GI, Nicholas AW. Oxford textbook of pathology, Oxford University Press.1992;2a:1165-73.
12.	Giuseppe R, Maria PD, Laura F. Extradigestive manifestations of Helicobater pylori infection. Digestive diseases and sciences.1999;44:229-236.	22.	Wu MS, Hung HW, Wang JT, Tseng CC, Shun CT, Wang HP et al. Helicobacter pylori-seronegative gastric carcinoma: a subset of gastric carcinoma
13.	Gasbarrini A, Franceschi F, Armuzzi A, Ojetti V, Candelli M, Sanz Torre E et al. Extradigestive manifestations of Helicobacter pylori gastric		with distinct clinicopathologic features. Hepatogastroenterol. 1998;45(4):2432-6.
14.	Pellicano R, Parravicini PP, Bigi R, La Rovere MT, Baduini G, Gandolfo N et al. Patients with acute myocardial infartion in northen I taly are often infected by Helicobacter pylori. Panminerva	23.	Komoto K, Haruma K, Kamada T, Tanaka S, Yoshihara M, Sumii K et al. Helicobacter pylori infection and gastric neoplasia: correlations with histological gastritis and tumor histology. Am. J. Gastroenterol. 1998;93(8):1271-6.
15.	Med.1999;41(4):279-82. Danesh J, Y oungman L, Clark S, Parish S, Peto R, Collins R. Helicobacter pylori infection and early onset myocardial infarction: case control and sibling pairs study. BMJ.1999;319(7218):1157-62.	24.	Siman J.H., Forsgren A., Berglund G., Floren C.H. A ssociation between Helicobacter pylori and gastric carcinoma in the city of Malmo,Sweden. A prospective study. Scand. J. G astroenterol.1997;32(12):1215-21.
16.	Shrestha HG, Dali S, Sayami G, Osti B, A matya VJ & Basnet RB. Present cancer scenario and its changing pattern at T.U. Teaching Hospital, Nepal. JNMA, Souvenir 1997;35:45-51.	25.	Massimo R, Graziella B, Mauro C, Y ih-Horng S, Valentina R, Gioacchino L. et al. Patients younger than 40 years with gastric carcinoma. Cancer1999;85:2506-11.
17.	Maehara Y, Sakaguchi Y, Moriguchi S, Orita H, Korenaga D, Kohnoe S et al. Signet-ring cell carcinoma of stomach. Cancer 1992;69:1645-50.	26.	Hung Y B, Wang CS, Hsueh S, Hwang TL, Chen MF. Helicobacter pylori in surgical specimens from patients with respectable gastric adenocarcinoma. Chang. Keng. I. Hsueh. Tsa. Chih.1998;21(2):179-83.
18.	Scott A H, Herman R M, Edward G M, David PW. The national cancer database report on gastric		E E E E E

JNMA, October - December, 2002, 41