Investigation of Relationship between Hepatitis B Virus and Gastric Adenocarcinoma

Dear Editor,

Gastric cancer is the second leading cause of cancer-related deaths worldwide¹⁻³ while some genetic and environmental factors such as infectious agents were shown to be linked to carcinogenesis.² Infectious agents notably viruses were shown to induce 20-25% of all cancers around the globe.^{4,5} *Helicobacter pylori* (*H. pylori*) is one of those infectious agents to be related to gastric carcinogenesis.^{1,2} *Epstein bar virus* was inconstantly demonstrated to be associated with gastric cancer that may be due to the presence of the cofactor of *H. pylori* that can immortalize abnormal epithelial cells.⁶

Hepadnaviridae, the most powerful infectious related cause of hepatoma has been reported with other malignancies such as renal cell carcinoma, gastric and oral cancers. One study showed an association between anti-hepatitis C virus (HCV) antibody in 10.6% of sera of patients and gastric cancer. Gastric cancer is assumed to be more prevalent in cirrhotic patients. Expression of hepatitis B virus (HBV) antigens in H. pylori bearing gastric mucosa was shown by immunostaining methods. Here we evaluated the association between HBV infection and gastric carcinoma in north of Iran.

We collected one hundred formalin-fixed paraffin embedded blocks of biopsies confirmed as gastric cancer in pathology department of our university belonging to patients who underwent gastrectomy during 2005-2010. Besides, 100 blocks of normal gastric mucosa tissues were provided as control group. Polymerase chain reaction for HBV DNA detection was performed.

Sixty nine percent of gastric cancer patients were male (Male/female ratio: 69/31) with a mean age of 67.14±10.98 years. The most common histological type of adenocarcinoma was intestinal type (68%) followed by diffuse (26%) and mixed (7%) types while the location was respectively proximal (57%), distal (22%) and diffuse (6%). The majority patients were diagnosed at advanced stage III (68%) followed by stage 2 (19%), stage 4 (9%) and stage 1 (4%). The most common grade was grade 2 (52%), grade 1 (41%) and grade 3 (7%).

HBV genome was undetectable in all cases and control subjects using PCR (Figure 1).

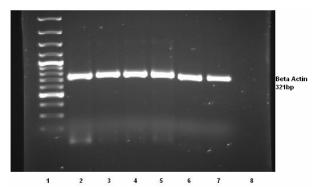


Fig. 1: Agarose gel electrophoresis illustrated a positive control for patients DNA (Beta actin as house keeping gene) compared to negative gastric cancer cases. 1: DNA ladder (50 bp-1000bp),

2, 3, 4, 5, 6, 7: Beta actin (321 bp), 8: Negative control.

Previous studies confirmed the role of HBV in the pathogenesis of hepatocellular carcinoma. 4.5 Besides, limited studies have revealed association between HBV antigens and/or antibodies with other malignancies such as renal carcinoma, oral cancer, and gastric carcinoma. 7-10 Zullo *et al.* showed 2.6 folds increases in prevalence of gastric cancer in cirrhotic patients compared to non-cirrhotic individuals using endoscopic and histological examinations. 9

Chen *et al.* showed the expression of HBV antigens in *H. pylori* infected gastric mucosa of patients with chronic liver disease using immunostaining. Our findings showed that HBV genome was undetectable in gastric cancers. We demonstrated that HBV was not correlated with gastric carcinoma in north of Iran.

Keywords: HBV; Gastric cancer; Adenocarcinoma

Conflict of interest: None declared.

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References

- Dicken BJ, Bigam DL, Cass C, Mackey JR, Joy AA, Hamilton SM. Gastric adenocarcinoma: review and considerations for future directions. *Ann Surg* 2005;**241**:27-39. [15 621988]
- Werner M, Becker KF, Keller G, Höfler H. Gastric adenocarcinoma: pathomorphology and molecular pathology. J Cancer Res Clin Oncol 2001;127:207-16. [11315254] [doi. org/10.1007/s004320000195]
- 3 Mojiri A, Behzad-Behbahani A, Saberifirozi M, Ardabili M, Beheshti M, Rahsaz M, Banihashemi M, Azarpira N, Geramizadeh B, Khadang B, Moaddeb A, Ghaedi M, Heidari T, Torab A, Salah A, Amirzadeh S, Jowkar Z, Mehrabani D, Amini-Bavil-Olyaee S, Dehyadegari MA. Hepatitis B virus genotypes in southwest Iran: molecular, serological and clinical outcomes. World J Gastroenterol 2008;14:1510. [18330 939] [doi:http://dx.doi.org/10.3748/wjg.14.1510]
- 4 Pagano JS, Blaser M, Buendia MA, Damania B, Khalili K, Raab-Traub N, Roizman B. Infectious agents and cancer: criteria for a causal relation. Semin Cancer Biol 2004; 14:453-71. [15489139] [doi.org/10. 1016/j.semcancer.2004.06.009]
- 5 Damania B. DNA tumor viruses and human cancer. *Trends Microbiol* 2007;**15**:38-44. [17113775] [doi.org/ 10.1016/i tim 2006.11.002]
- 10.1016/j.tim.2006.11.002]
 6 Wang Q, Tsao SW, Ooka T, Nicholls JM, Cheung HW, Fu S, Wong YC, Wang X. Antiapoptatic role of BARF-1 in gastric cancer cells. Cancer Lett 2006;238:90-103. [16054293] [doi.org/10.1016/j.canlet. 2005.06.023]
- 7 Gordon SC, Moonka D, Brown KA, Rogers C, Huang MA, Bhatt N, Lamerato L. Risk for renal cell carcinoma in chronic hepatitis C infection. Cancer Epidemiol Biomarkers Prev 2010;19:1066-73. [20332260] [doi.org/10.1158/1055-9965.EPI-09-1275]

- 8 Nagao Y, Sata M, Tanikawa K, Itoh K, Kameyama T. High prevalence of hepatitis C virus antibody and RNA in patients with oral cancer. J Oral Pathol Med 1995;24:354-60. [7500 291] [doi.org/10.1111/j.1600-0714. 1995.tb01199.x]
- 9 Nelson R. Hepatitis C infection doubles risk for kidney cancer. Cancer Epidemiol Biomarkers and Prevention 2010;16:1066.
- 2ullo A, Romiti A, Tomao S, Hassan C, Rinaldi V, Giustini M, Morini S, Taggi F. Gastric cancer prevalence in patients with liver cirrhosis. Eur J Cancer Prev 2003;12:179-82. [1277 1554] [doi.org/10.1097/00008469-200306000-00002]
- 11 Chen NL, Bai L, Deng T, Zhang C, Kong QY, Chen H. Expression of hepatitis B virus antigen and Helicobacter pylori infection in gastric mucosa of patients with chronic liver disease. Hepatobiliary Pancreat Dis Int 2004;3:223-5. [15138114]