RESEARCH COMMUNICATION

Helicobacter Pylori Infection Reduces the Risk of Esophageal Squamous Cell Carcinoma: A Case-Control Study in Iran

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Abstract

Background: Some studies have indicated a protective role of *H.pylori* against risk of esophageal squamous cell carcinoma (ESCC). The purpose of this study was to explore this possible relationship in a case-control study. Methods: One hundred consecutive patients diagnosed with ESCC and 100 healthy people were entered with informed consent. All were asked to provide a blood sample and serum immunoglobulin G (IgG) antibodies against HP-CSAs were measured with an enzyme-linked immunosorbent assay (ELISA). Results: There was significant reverse association between *H. pylori* positivity and tumour development (OR=0.28, 95% CI: 0.15-0.54), but not with a Cag A positive status. Conclusion: Our findings provide further evidence that *H. pylori* infection decreases the risk of ESCC but that this is not linked to a Cag A positive status.

Keywords: Esophageal squamous cell carcinoma - H pylori - Cag A status - case-control study - Iran

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Introduction

Esophageal cancer is the 8th most common incident cancer in the world (Kamangar et al., 2006). Squamous cell carcinoma (ESCC) constitutes the large majority of all esophageal cancer cases in the world (Kamangar et al., 2006; Corley and Baffler., 2001). Esophageal squamous cell carcinoma (ESCC) is disturbing because of its violent clinical path and high mortality rate. However, the prognosis has been improving recently (Isono et al., 1991; Inoue, 1997; Ando et al., 2000; Takeshita et al., 1997). The prevalence rate varies according to geographical situation. In the high prevalent regions such as China, Northeastern of Caspian Littoral in Iran and Transkei in south Africa, the prevalence of ESCC is raised to 100/100,000 persons (Yamada et al., 1999).

It is straightforward that infection of *Helicobacter pylori* (*H. pylori*) causes non-cardiac gastric carcinoma (Watanabe et al., 1998; Parsonnet et al., 2006), although there is still debate regarding to the association between *H pylori* and gastric cardia adenocarcinoma. Some studies (Kikuchi et al., 1995; Komoto et al., 1998; Limburg et al., 2001) indicated an increased risk of cardia cancer in *H. pylori*-infected subjects, in contrast there are those which reported a protective role (Chow et al., 1998; Wu et al., 2003; Ye et al., 2004). Among recent studies, the relationship between *H. pylori* infection and esophageal squamous cell carcinoma (SCC) is inconclusive (Ye et al., 2004; Kamangar et al., 2007; Siman et al., 2007). The purpose of the present case-control study was to explore the relationship of *H. pylori* infection with ESCC.

Materials and Methods

One hundred consecutive patients who diagnosed with esophageal squamous cell carcinoma (referred from Imam Reza hospital and Sina hospital in Tabriz, Iran) (Khoshbaten et al., 2010) and one hundred healthy people as controls (from same hospitals and matched by age and sex) entered to this study. Those control subjects with any clinical evidence of gastrointestinal symptoms which had related to *H.pylori* or esophageal reflux disease were excluded from the analysis. Written informed consent was obtained from all patients and controls before their examinations. Subjects were asked to provide a blood sample, which was drawn from case patients during the initial hospital stay and from control subjects. After centrifugation, all serum samples serum immunoglobulin G (IgG) antibodies against HP-CSAs were measured with an enzyme-linked immunosorbent assay (ELISA, PatanTeb, Iran).

Results

The total of 100 patients (64 men, 36 women) and 100 health controls (66 men, 34 women) included in this study. The mean±SD of age for patients was 63.9±9.89 year and for controls was 61.3±11.7. There was no statistically difference between case and control's age (P=0.1) and sex (P=0.76).

The mean titre of HP IgG in ESCC patients was 41.2±36.95 and in controls was 56.2±29.5 and there was a statisticaly difference between case and control (P=0.002).

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Table 1. HP IgG and Cag A Levels in Patients with ESCC and Control Subjects

	Cases		Controls		P-Value
	Men	Women	Men	Women	
Age	64.5±9.74	63.7±10.2	61.1±11.7	61.3±11.7	0.100
HP IgG	43.3±37.5	37.3±36.0	50.2±31.3	56.2±29.5	0.002
Cag A	22.6±31.1	23.3±29.9	25.9±35.5	41.3±38.2	0.092

Table 2. The Number of HP Positive and Cag A Positive Cases and Controls

	Case		Control		OR	95% CI	P-Value
	Pos	Neg	Pos	Neg			
HP	58	42	83	17	0.28	0.15-0.54	<0.001
Cag A	28	72	36	64	0.69	0.38-1.25	0.22

The results of mean levels for HP IgG and Cag A according to sex group was appeared in Table 1 and for HP positive and Cag A positive in Table 2, indicating a reverse association between HP infection and risk of ESCC (OR=0.28) but not a Cag A positive status.

Discussion

In this study, HP infection was strongly associated with a reduced risk of ESCC. Our study is in contrast to a study by Ye et al (2004) who found an inverse association between *H.pylori* infection and the risk of esophageal adenocarcinoma and indicating that patients with Cag A serum antibodies had a statistically significantly increased risk of esophageal squamous-cell carcinoma.

The association of *H.pylori* and ESCC is still in debate, some studies showed the increased risk of Hp infection on ESCC (Ye et al., 2004; Wang et al., 2006), whereas others did not find a significant association (Kamangar et al., 2007; Siman et al., 2007) and a meta analysis showed an inverse statistically significant relationship of *H.pylori* infection with both esophageal adenocarcinoma and Barrett's esophagus, but no statistically significant relationship with squamous cell carcinoma (Rokkas et al., 2007).

A hypothesis postulates that the apparent protection associated with *H. pylori* infection is mediated via gastric atrophy and a reduced load of esophageal acid (Richter et al., 1998) and this hypothesis supported by some cross-sectional studies (Raghunath et al., 2003). Besides, a recent study provides indirect evidence of the inverse association between *Hp* infection and ESCC risk, which is possibly due to *Hp*-induced apoptosis in ESCC cells (Wu et al., 2009).

Our findings suggested that *H. Pylori* infection decreases the risk of ESCC but no statistically association between Cag A positive and risk of ESCC was found. Further study with higher sample size is necessary to confirm the rule of *H.pylori* in reducing the risk of ESCC.

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