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Original Article

Seroprevalence of anti-helicobacter pylori antibodies in hepatitis B and C patients with cirrhosis: a case-control study

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Abstract

BACKGROUND: Cirrhosis is terminal stage of many chronic liver diseases like hepatitis C and hepatitis B. In some studies the role of helicobacter pylori has been demonstrated in progress of cirrhosis and its complications, but none of the previous studies has investigated the role of socioeconomic conditions of patients in childhood period in this issue.

METHODS: In a case-control study, we examined 100 cirrhotic patients due to hepatitis (49 hepatitis B and 51 hepatitis C patients) and 101 socioeconomically matched healthy controls presenting to Taleghani Hospital for IgG antibody to helicobacter pylori.

RESULTS: IgG antibody to helicobacter pylori was present in 73% of cirrhotic patients and 52% of control group ($P<0.003$). Odds ratio for the presence of IgG antibody to helicobacter pylori in cirrhotic men comparing with healthy men was 3.2 (95%CI: 1.4-7.4).

CONCLUSIONS: The relative frequency of IgG antibody to helicobacter pylori found to be higher in cirrhotic patients than in controls with regard to socioeconomic condition in childhood.

KEY WORDS: Cirrhosis, hepatitis C, hepatitis B, helicobacter pylori, liver disease.

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Cirrhosis is a disease characterized by nodular liver fibrosis. Cirrhosis is the terminal stage of many hepatic diseases including hepatitis B and C, and has a poor prognosis [1]. Not all HBV and HCV infections lead to cirrhosis [2,3]. Hence, the question remains as what factors cause a patient with HBV or HCV infection to progress towards cirrhosis. A number of factors have so far been studied. Some of these factors are related to the pathogenic agent. For example, genotype Ib hepatitis C is more likely to lead to cirrhosis [4].

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Host-related factors also influence the odds of cirrhosis. For example, it has been suggested that HLA-DR5 has protective effects against cirrhosis [5]. Helicobacter pylori (H. pylori) has been implicated in cirrhosis. The roles of this gram-negative bacterium in peptic ulcer [6] and gastric carcinoma [7] have been demonstrated. H. pylori can induce the release of mediators such as IL1, IL6, TNF-alpha and ICAM-1 [8,9] which can theoretically cause liver damage. Some studies have shown relatively higher levels of anti-H. pylori antibodies in cirrhotic patients [10,11]. The aim of this study was to compare the seroprevalence of anti-H. pylori antibodies in HBV-positive and HCV-positive cirrhotic patients with that in controls.

Methods

This was a case-control study. One hundred patients with chronic hepatitis (49 HBV-positive and 51 HCV-positive patients) were studied. The patients had a mean age of 44 ± 14 years and the male-to-female ratio was 76/24. They were presented to the Gastroenterology and Hepatology Research Center of Taleghani Hospital. The control group consisted of 101 healthy individuals with a mean age of 30.6 ± 7.7 years and male-to-female ratio of 35/66. Cirrhosis was diagnosed by history, physical examination and paraclinical data and/or histology. In cirrhotic group 89 cases had liver biopsy and in 11 patients, the diagnosis was made according to physical examination, sonography and laboratory data. Cirrhosis was defined to be related to hepatitis B when both HBsAg and HBV DNA (PCR method, Cinna Gen Inc, Tehran, Iran) were positive; it was related to hepatitis C when anti HCVAb and HCV RNA (PCR method, Cinna Gen Inc, Tehran, Iran) were positive. HBsAg and HCVAb were done by ELISA based on manufacturer's instructions. Other causes of cirrhosis like alcohol consumption more than 60 gram per day, coinfection of hepatitis B and C and hemochromatosis were excluded. HBsAg and HCVAb were tested in control group, and positive persons were excluded. Both subjects and their parents in case and control groups had similar socioeconomic conditions based on literacy level. Literacy level was divided into three groups of illiterate, till diploma and academic education. Parents educations were recorded based on uppermost level of education. The ELISA method (Enzyme-Linked Immunosorbent Assay) was applied to measure anti-H. pylori IgG in isolated serum specimens, using test kits made by Genesis, UK. The assay sensitivity was 94% and specificity was 87% [12]. All statistical calculations were carried out using SPSS 11 software. To determine whether H. pylori was a significant risk factor of cirrhosis, Mantel-Haenszel X^2 was used. Also for comparing nominal variables, chi-square and for ordinal variables Mann-Whitney tests were used. All P values were two tailed and values less than 0.05 were considered statistically significant.

Results

The case group consisted of 100 patients with cirrhosis (49 HBV-positive and 51 HCV-positive patients, 24 women and 76 men) and the control group included 101 healthy blood donors (66 women and 35 men) ($P<0.01$). The case and control subjects had mean ages of 44 ± 14 and 30.6 ± 7.7 years, respectively ($P<0.01$). Seventy-three patients in the case group and 53 patients in the control group were positive for anti-H. pylori IgG ($P<0.003$). The odds ratio for the presence of anti-H. pylori IgG in cirrhotic patients compared to healthy individuals was 2.44 (95%CI: 1.36-4.4). Of 126 patients positive for anti-H. pylori antibodies, 52 were women and 74 were men. The odds ratio for the presence of anti-H. pylori antibodies in cirrhotic women compared to healthy women was 1.7 (table 1), which was insignificant within a confidence interval of 95% (0.6-4.4). By contrast, the odds ratio for the presence of anti-H. pylori antibodies in cirrhotic men compared to healthy men was 3.2 (table 1), which was significant within a confidence interval of 95% (1.4-7.4). Taking into account of the sex factor when using the Mantel-Haenszel test, the odds ratio for the presence of anti-H. pylori antibodies in cirrhotic patients compared to healthy

individuals was calculated at 2.4, which was statistically significant (95%CI: 1.25-4.52). Of 126 anti-H. pylori-positive subjects, 62 were aged 35 years and below and 64 were above 35. As shown in table 2, the odds ratio for the presence of anti-H. pylori antibodies in cirrhotic patients 35 years and below was 1.2 compared to healthy controls in this age group, which was statistically insignificant (95%CI: 0.9-5.2). The odds ratio for the presence of anti-H. pylori antibodies in cirrhotic patients above 35 was 2.1 compared to healthy individuals in this age group, which was also statistically insignificant (95%CI: 0.7-6.2). Mantel-Haenszel test showed the odds ratio for the presence of anti-H. pylori antibodies in cirrhotic patients of all ages (≤35 and >35) compared to controls to be 2.1, which was statistically significant (95%CI: 1.1-4.2). Difference of literacy levels was not significant among cirrhotic patients and healthy individuals (table 3), and similarly among parents of the two groups (P>0.05).

Table 1. Distribution of HBV- and HCV-positive cirrhotic patients and controls according to sex and H. pylori status

Groups / Anti-H. pylori	Cirrhotic women	Healthy women	Cirrhotic men	Healthy men
Positive	16 (67%)	36 (55%)	57 (75%)	17 (49%)
Negative	8 (33%)	30 (45%)	19 (25%)	18 (51%)
Sum	24 (100%)	66 (100%)	76 (100%)	35 (100%)

Table 2. Age distribution of HBV- and HCV-positive cirrhotic patients and controls according to H. pylori status.

Groups / Anti-H. pylori	Cirrhotic patients under 35 years	Cirrhotic patients above 35 years	Healthy individuals under 35 years	Healthy individuals above 35 years
Positive	20 (69%)	53 (75%)	42 (51%)	11 (58%)
Negative	9 (31%)	18 (25%)	40 (49%)	8 (49%)
Sum	29 (100%)	71 (100%)	82 (100%)	19 (100%)

Table 3. Literacy levels among cirrhotic patients and controls.

Groups / Literacy level	Cirrhotic patients	Healthy individuals	Parents of case	Parents of controls
Illiterate	7 (7%)	9 (9%)	13 (13%)	15 (15%)
Till diploma	72 (72%)	69 (68%)	69 (69%)	66 (65%)
Academic	21 (21%)	23 (23%)	18 (18%)	20 (20%)
Total	100 (100%)	101 (100%)	100 (100%)	101 (100%)

Discussion

The seroprevalence of anti-H. pylori antibodies in cirrhotic patients and controls in this study was 73% and 57.5%, respectively. The odds ratio for the presence of anti-H. pylori antibodies in cirrhotic patients compared to healthy individuals was 2.44, which was significant within the 95% confidence interval. This difference cannot be accounted for by socioeconomic differences between the two groups since they were matched for their level of education, as well as their parents' education. Our results are similar to those reported by Ponzetto and colleagues. Comparing a group of hepatitis C

patients with controls, they found the seroprevalence of anti-H. pylori antibodies to be 73% and 47% in the case and control groups, respectively [13]. Another study found the seroprevalence of anti-H. pylori antibodies to be 86% and 56% in hepatitis B patients and controls, respectively, which demonstrated a statistically significant difference between the two groups [2]. A number of other studies have yielded similar results [10,14-16]. By contrast, some studies such as the one conducted by Wang have not reported any difference between cirrhotic patients and healthy individuals in the community in respect of anti-H. pylori antibodies [15]. The difference between these studies can be explained by the way the two study groups were socioeconomically matched; i.e., most studies matched the case and control groups according to their current socioeconomic status without taking into account of their parents, whose socioeconomic status have influenced the subjects' odds of contracting infections in childhood. The higher seroprevalence of anti-H. pylori antibodies in HCV- or HBV-positive cirrhotic patients is not due to a common route of infection, since H. pylori is not known to be transmissible via the usual routes of HBV and HCV infections (i.e., vertical transmission, sexual transmission and injection). The likelihood of H. pylori playing a role in the development or progression of cirrhosis has been suggested. It has been proposed that H. pylori may cause a moderate form of the systemic inflammatory response syndrome and subsequent liver damage via triggering an autoimmune response [9]. Other helicobacter strains such as Helicobacter hepaticus can theoretically lead to positive anti-H. pylori assays; infection with these strains is also thought to result in liver damage [1,17]. Besides its presumed role in cirrhosis, H. pylori has been implicated in peptic ulcer and its complications such as bleeding [18], hepatic encephalopathy [19,20], and hepatocellular carcinoma [21]. The clinical significance of H. pylori with regard to cirrhosis emanates from the fact that it can be readily detected and eradicated. This study had the limitation of using a single method of detecting H. pylori infection. Serologic method was used in a series of investigations [22-24] and other invasive methods like rapid urease test or UBT were used by others [25,26]. Also, only literacy level was used for determination of socioeconomic condition because we were not able to measure the income in the study population accurately. However, according to our knowledge no similar study has been done in Iran up to now. The odds ratio for the presence of H. pylori antibodies in cirrhotic patients above and below the 35 years were statistically insignificant separately, but the odds ratio regardless of age was statistically significant. Justification for this difference is in inadequacy of study population in age subgroups. We propose simultaneous use of invasive and non-invasive methods for detection of H. pylori in future studies. The role of Cag A and Vac A in causing liver damage is yet to be investigated. In this study, cirrhotic men stood a significantly higher chance of having anti-H. pylori antibodies compared to healthy men, whereas no significant difference was observed between cirrhotic and healthy women. In their study of cirrhotic patients with various etiologies, Calvet and colleagues also established a link between the male sex and peptic ulcers in cirrhotic patients [24]. This finding has yet to be explained; it may be due to unknown exacerbating factors such as smoking that is related to progression of liver fibrosis and is much more prevalent in men [27]. Understanding the role of sex factor and its link to H. pylori infection or related complications warrants further studies.

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