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Association between Hepatitis G and Unknown Chronic Hepatitis

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Abstract

Background: Hepatitis G virus (HGV) is a hepatotrope virus with unknown importance. The genome of the virus has been detected in patients with acute or chronic non-A-E hepatitis, cirrhosis, and hepatocellular carcinoma. The aim of this study was to determine the association between hepatitis G and unknown chronic hepatitis.

Methods: This case-control study was performed in Ebne-Sina military hospital in Hamadan, Iran. The cases were 35 military staff with unknown chronic hepatitis. The control group consisted of 59 healthy subjects who had normal levels of serum alanine aminoteransferase (ALT). The data were analyzed by SPSS, version18, using Fisher's exact test, the Student's t-test, and multivariate logistic regression analysis**.**

Results: Only one patient in the case group (2.9%) tested positive for HGV antibodies, and no one was infected in the control group. There was no association between HGV infection and unknown chronic hepatitis in our study (P=0.37). A significant association was found between the male gender and unknown chronic hepatitis (OR=14.9, P=0.01).

Conclusion: No association between HGV infection and unknown chronic hepatitis was found in our study, so it was not necessary to evaluate these patients for HGV infection.

Keywords: hepatitis G, chronic hepatitis

1. Introduction

1.1. Bachground

The asymptomatic elevation of liver enzymes is a common problem, and, if it goes undetected, it can damage the liver over time (1). In a survey of 1959 blood donors in Iran, 5.1% had asymptomatic elevated liver enzymes, and the common diagnoses for half of those affected were nonalcoholic steatohepatitis (NASH) (88%), hepatitis C (7.7%), and alcohol and drug-related liver injury (1.9%) (2). Another study of about 2000 people in Golestan Province in northern Iran found that the prevalence of persistently-elevated liver enzymes was 3.1% with an unknown etiology in about 80%, hepatitis B in 9.3%, hepatitis C in 6.2%, alcoholic liver disease in 4.6%, and fatty liver disease in 2% (3).

1.2. Statement of the problem

HGV is an RNA flavivirus transmitted mainly by the parenteral route. HGV RNA and HGV antibody (anti-E2) seropositivity in blood donors is about 1-4% and 3-14%, respectively (4). The mean prevalence of HGV in blood donors is 4.8% and is different in diverse world regions, e.g., 4.5% in Caucasians, 3.4% in Asians, and 17.2% in Negros (5). It seems that Iran has the least prevalence of HGV, i.e., about 1%, among other countries in the Middle

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East, e.g., Turkey (4.1%), Kuwait (24.6%), Jordan (9.8%), and Saudi Arabia (2%) (7-10). Seventy-five percent of infected patients have normal liver enzymes with no symptoms of hepatic disease; however, it can cause acute and chronic hepatitis (11). In a study of 41 acute and 67 chronic hepatitis patients with unknown etiology in China, HGV RNA was detected in six patients (14.6%) and 12 patients (17.9%), respectively (12). A similar study of 55 acute unknown hepatitis patients indicated that 29.1% had HGV RNA seropositivity and very severe clinical syndrome (13). Multiple studies have expressed doubts about the relationship between HGV infection and hepatic damage (14-16). Thus, our aim was to investigate the association between HGV infection and unknown chronic hepatitis.

1.3. Objective of the research

The aim of this research was to evaluate the association of hepatitis G with unknown chronic hepatitis. The specific objectives of the study were:

1) To determine the frequency of HGV antibodies in the case group and the control group
2) To determine the difference in the HGV seropositivity between the two groups

2. Materials and Methods

2.1. Research design and setting

A case-control study was conducted at the Ebne-Sina Army Hospital in Hamadan, Iran, from September 2011 through October 2012. Patients with unknown chronic hepatitis were evaluated for HGV infection. The cases were 35 military staff with unknown chronic hepatitis, and the controls were 59 patients with normal serum ALT levels who were selected from the orthopedic and gynecologic clinics at the same hospital. Chronic hepatitis was defined as serum ALT≥40 IU/L for more than six months (17).

2.2. Data collection

A checklist containing demographic data, ALT levels, and HGV antibody states was designed to collect the data (Table 1). One hundred and seventy-three subjects with serum ALT ≥ 40 IU/L were evaluated for:

1) Viral hepatitis B and C by the detection of HB antigens and HCV antibodies using the ELISA method with 5-ml samples of serum.
2) Non-alcoholic fatty liver disease (NAFLD) using abdominal sonography by an expert radiologist.
3) History of alcohol or hepatotoxic drug consumption or recent infectious processes, such as cold, fever, sore throat, myalgia, arthralgia, diarrhea, abdominal pain, and vomiting (2, 3, 17).

Any patients who had any of the three conditions described above were excluded from the study. In this way, 115 subjects were selected for the study, and they were followed for 6-9 months without any intervention, and 35 patients with permanent ALT ≥ 40 IU/L were selected as the case group. The control group was comprised of patients with normal serum ALT levels who were referred to the orthopedic and gynecologic clinics at the same hospital. Five-milliliter serum samples were taken from the members of both the case and control groups and sent to a private laboratory to be assessed for HGV infection. The laboratory used the Cortez 4^{th} generation kit (manufactured in the U.S.), and HGV anti-E2 was detected by ELISA with 99.8% sensitivity**.**

2.3. Ethical considerations

This research was approved by the Ethics Committee at the AJA University of Medical Sciences. Participation in the study was voluntary, and the physicians explained the purpose and procedures of the study to the participants and asked each one to sign a consent form. For the sake of confidentiality and privacy, the serum samples were coded and sent anonymously to the laboratory.

2.4. Statistical analysis

SPSS version 18 (SPSS Inc., Chicago, IL, U.S.) was used to analyze the data. Fisher's exact test, the Student's t-test, and multivariate logistic regression were used for data analysis. An alpha level of 0.05 was considered to be significant.

3. Results

The mean ages of the members of the case group and the control group were 34.9±8.5 and 40±12.3 years, respectively. All of patients in the case group were males, and the male-to-female ratio in the control group was 2.28. There was a significant difference between the ages of the patients in the case and control groups, with the former having a significantly lower mean age than the latter based on the Student's t-test (P=0.021) (Table 1).

Among all of the people in the case group and the control group, there was just one person who tested HGV anti-E2 positive in the case group (2.9%); all of the people in the control group tested negative. Thus, Fisher's exact test indicated that there was no significant statistical difference of HGV infection between case group and the control group (P=0.372). In multivariate logistic regression analysis, a significant relationship was found between unknown chronic hepatitis and being male (OR=14.9; 95% CI=1.9-117.6, P=0.010), but there was no such relationship for age (P=0.446) or HGV infection (P=0.269) (Table 2).

Table 1. Reasons for excluding patients with elevated liver transaminases (n = 58)

Reason for exclusion	n	%
Fatty liver syndrome	38	65.5
History of recent infectious processes or symptoms/signs of ongoing infectious processes	17	29.3
HBV infection	2	3.4
Long term methotrexate consumption	1	1.7
Total	58	100

Table 2. Demographic characteristics of the study population (n = 94)

Variables		Cases		Controls		P-Value
		n	%	n	%	
Age group (year)	<30	11	31.4	14	23.7	0.021
	30-39	15	42.8	14	23.7	
	40-49	7	20.0	19	32.2	
	50-59	2	5.7	8	13.6	
	≥60	0	0	4	6.8	
Gender	Male	34	97.1	41	69.5	0.001
	Female	1	2.9	18	30.5	

4. Discussion

In our study, the frequency of HGV antibodies was not different between the patients with unknown chronic hepatitis and the healthy subjects, confirming that the HGV infection did not injure the liver. Our results were in agreement with the results of a similar study conducted in Italy on 50 unknown chronic hepatitis patients and 50 healthy persons (18). Some studies have concluded that it was doubtful that HGV was responsible for chronic hepatitis (19, 20), and several studies have shown the correlation of HGV with hematologic disorders, such as non-Hodgkin's lymphoma (21-23), aplastic anemia (24, 25) and chronic renal failure (26-29). In our study, chronic hepatitis was more frequent in males due to the selection of the cases from active military patients participating in a military health monitoring program.

The main challenges associated with HGV infection are liver injury and chronic hepatitis. It seems that co-infection with other viral forms of hepatitis, such as HBV and HCV, can lead to hepatic damage whereas the HGV infection alone does not. One survey of 64 Japanese children infected with HCV with co-infection with HGV showed no clinical, virological, or pathological differences between those with HCV/HGV co-infection and HCV alone (30). In another study of 130 patients with chronic hepatitis B and 173 patients with chronic hepatitis C, the prevalence of HGV RNA was about 8% and 17%, respectively, and, while HGV co-infection did not worsen the clinical symptoms of disease, it accelerated the progression to chronic hepatitis and increased the risk of hepatocellular carcinoma (31). Regarding the limitation of the study, we did not study patients with unknown chronic hepatitis for auto-immune hepatitis, which might have a role in liver inflammation and chronic hepatitis in these patients.

5. Conclusion

This study showed no association between a history of HGV infection and chronic hepatitis in the patients with unknown chronic hepatitis. Therefore, it seems that screening for HGV antibodies is not recommended. However, we believe that HGV RNA measurement in the patients with unknown chronic hepatitis may help identify any ongoing inflammation. Further studies are recommended to evaluate HGV RNA seropositivity in patients with unknown chronic hepatitis.

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Conflict of Interest:
There is no conflict of interest to be declared.

Authors' contributions:
All of authors contributed to this project and article equally. All authors read and approved the final manuscript.

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