Pakistan Journal of Biological Sciences 9 (13): 2538-2540, 2006
ISSN 1028-8880

HBV/HCV Co-infection in Iran: A Seroepidemiological Based Study

[1]Shahryar Semnani, [2]Gholamreza Roshandel, [2]Nafiseh Abdolahi, [2]Sima Besharat,
[2]Abbas-Ali Keshtkar, [2]Hamidreza Joshaqani, [2]Abdolvahab Moradi, [2,3]Khodaberdi Kalavi,
[4]Mohammad Javad Kabir, [4]Seyed Ahmad Hosseini, [2]Danial Roshandel,
[4]Seyed Mehdi Sedaqat and [4]Ahmad Danesh
[1]Gastroenterologist, Golestan University of Medical Sciences,
Golestan Research Center of Gastroenterology and Hepatology (GRCGH)
[2]Golestan Research Center of Gastroenterology and Hepatology (GRCGH),
Golestan University of Medical Sciences (GOUMS)
[3]Faculty of Paramedicine, Golestan University of Medical Sciences (GOUMS)
[4]Department of Health, Golestan University of Medical Sciences (GOUMS)

Abstract: The aim of this study was to determine the seroprevalence of HCV in HBsAg positive subjects. In a population based single stage cluster sampling in Golestan province of Iran, 139 HBsAg positive subjects were detected and enrolled in the study. Serum samples were tested using ELISA method for anti-HCV antibodies. Chi-square and Fisher's exact tests were used to compare the proportions. There were 68(48.9%) male and 71(51.1%) female. The mean age was 41.89±11.30 years (25-64 years). One case was excluded because of inadequate blood sampling. Anti-HCV antibody was positive in 17(12.3%) of 138 remaining subjects. Seropositivity of HCV in female was higher than male (14.1% versus 10.4%, respectively) but the difference was not statistically significant (p = 0.52). No significant relationship was seen between Anti-HCV seroprevalence and demographic factors such as age, place of residence and marital status. The seroprevalence of co-infection with HBV and HCV in our study was higher than such reports from some countries (Italy); but it was in line with worldwide prevalence (>10%). A careful longitudinal evaluation of the viremia levels of both HBV/HCV viruses is essential for making a correct diagnosis and tailoring the appropriate therapeutic schedule in co-infected patients.

Key words: Hepatitis B, hepatitis C, Iran

INTRODUCTION

Hepatitis B and hepatitis C viruses are the most common causes of chronic liver disease (Crockett and Keefe, 2005). Approximately 350 million people are infected with HBV worldwide (Lee, 1997). The prevalence of HBV infection is generally higher in Asia and Africa than other parts of the world (Blum *et al*., 1998). More than 3% of Iranian populations are infected with HBV (Massarat *et al*., 2000). The World Health Organization estimates that approximately 170 million people are infected with HCV. Chronic HBV and/or HCV infection may produce both cirrhosis and complicated by hepatocellular carcinoma (HCC).

As hepatitis B virus (HBV) and hepatitis C virus (HCV) have the same transmission routs, dual infection may occur (Liaw, 2002). In areas of high prevalence of HBV infection such as Asian countries, the phenomenon of HCV super-infection is well described (Liaw, 2002; Liaw *et al*., 2004).

Patients co-infected with both HBV and HCV may have more severe liver disease (Benvegnu *et al*., 1994; Kaklamani *et al*., 1991). Some studies have suggested an increased risk of fulminant hepatitis with HCV and HBV co-infection (Chu *et al*., 1994; Wu *et al*., 1994). Co-infected patients have also higher rates of cirrhosis (Fong *et al*., 1991). Dual infection with HBV and HCV has been shown in many case-control studies to correlate with an increased risk of developing HCC (Kaklamani *et al*., 1991; Mohamed Ael *et al*., 1997). The mortality rate of HCV co-infection in chronic hepatitis B patients may be as high as 10% (Liaw, 2002). Therefore, it is very important to

Corresponding Author: Dr. Gholamreza Roshandel, No. 77, Qabooseieh Passage, Valiasr Street, Gorgan, Gloestan Province, Iran
Tel: 0098-171-2240835 Fax: 0098-171-2269210

identify whether a patient with HBV infection has co-infected with HCV. Present study was conducted to determine the seroprevalence of HCV in HBsAg positive cases.

MATERIALS AND METHODS

A population based cross-sectional study had been conducted in Golestan province of Iran during 2004 to 2005. A total sample size of 1850 subjects had been enrolled using a single stage cluster sampling method. To achieving this sample, 92 clusters had been selected using a systemic random sampling according to last census tract in Golestan province of Iran (2004-2005). In each cluster, 20 subjects had been explored for hepatitis B virus surface antigen using ELISA kit, Diasorin, Italy (Sensitivity: 100%; Specificity: 98.8%). 164 (8.9%) of 1850 subjects had been positive for HBsAg. Unfortunately, the serum samples of 25 HBsAg positive subjects were inadequate or had been lost during the sampling phase. Therefore, 139 of the HBsAg positive subjects were enrolled in our study. Approximately 2 mL blood was drawn from each case. Separation of serum was done under complete aseptic condition and then stored at -70°C until use. The serological tests were performed using commercially available ELISA method according to the instructions provided in the manufacturer's manual. Anti-HCV antibody was detected using ELISA method (DRG, Germany). All data were analyzed by SPSS (Chicago, IL) software, version 12. Proportions were compared by Chi-square and Fisher's exact tests. P values of less than 0.05 were considered significant.

RESULTS

Participants in the study were 68 (48.9%) males and 71 (51.1%) females. The mean age was 41.89±11.30 years (25-64 years). Demographic characteristics of the subjects are summarized in Table 1. One case was excluded because of inadequate blood sampling. Anti-HCV antibody was positive in 17 (12.3%) of 138 remaining subjects. Ten females (14.1%) and 7 males (10.4%) were positive for Anti-HCV antibody; but the difference was not significant (p = 0.51; odds ratio = 1.4, 95%CI: 0.5-3.9). The prevalence of HCV seropositivity in rural population was higher than urban population (15.4% versus 10.5%); but it was not significant statistically. Seroprevalence of hepatitis C virus did not significantly differ between age groups. When recategorizing the age variable into two groups based on median (42 years), the prevalence in younger cases (10%) was lower than older (14.7%), but there was still no significant difference (p = 0.4; odds ratio = 0.64, 95% CI: 0.23-1.8). There were no significant relationship between marital status and HCV seropositivity.

Table 1: Demographic characteristics of HBsAg positive cases in Golestan, Iran

Variables		No. of cases (%)
Sex	Male	68(48.9)
	Female	71(51.1)
Age groups	25-34	44(31.7)
	35-44	32(23.0)
	45-54	40(28.8)
	55-65	23(16.5)
Marital status	Married	119(85.6)
	Single	20(14.4)
Place of residence	Rural area	53(38.10)
	Urban area	86(61.9)

DISCUSSION

We conducted a seroepidemiological survey of co-infection with hepatitis C virus in 139 apparently healthy HBsAg positive individuals living in Golestan province (northeast part) of Iran. 12.3% of participants were anti-HCV antibody positive. This is higher than reports from some other studies. HCV seropositivity among HBsAg positive cases was reported as 2.7% by Barros *et al.* (1994) from Portugal. Gaeta *et al.* (2003) had detected anti-HCV antibody in 7% of HBsAg positive subjects in Italy (2003). Seroprevalence of HCV in the same population from Taiwan was 8% (Chu *et al.*, 1998). In another similar study, anti-HCV was positive in 9.8% of cases (Fattovich *et al.*, 1991). In contrast with these studies, de Miguel *et al.* (1994) from Spain had detected anti-HCV antibody in 16% of HBV infected subjects (higher prevalence rate than ours).

The reported series of seroprevalence of HCV indicate that HCV is found in more than 10% of HBV-infected patients world wide (Liaw, 2002); so they were in conformity with findings of present study. In present study, the seropositivity of HCV in females were higher than males; but Barros *et al.* (1994) inversely had reported a higher prevalence rate in males.

In conclusion, Co-infection with HBV and HCV is common, especially in this area with a relatively high prevalence of hepatitis B. Dual infections present unique management challenges given the complex interaction of HBV and HCV and the propensity for developing more severe liver disease. Caution must be exercised in treating co-infected patients, as flares of the untreated virus may occur. No standard of care has been established for treatment of co-infected patients and larger randomized, controlled trials are needed to clarify the optimal treatment for such patients and the role of newer antiviral agents.

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