

The Prevalence and Clinical Significance of Hepatitis B and C Coinfection

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Abstract

Background: HBV and HCV coinfection is common, particularly in endemic areas and among high risk groups. In this study we have investigated the prevalence of HBV/HCV coinfection and compared the biochemical and serological characteristics of such patients compare with the patients having hepatitis C infection alone.

Methods: We studied 207 patients diagnosed as having chronic hepatitis C, with HCVAb and HCV-RNA, to detect HBsAg, HBcAb and HBV-DNA. HBsAg and HBcAb were detected by commercially available ELISA kits. HBV-DNA was evaluated using PCR methods and liver enzymes (ALT and AST) were measured by automated instruments.

Results: Twenty three of the 207 patients (11.1%) were positive for HBV-DNA (coinfection). Of these 23 patients, 17 were HBsAg negative. Twenty six of the HCV infected patients were HBcAb positive of whom 21 had coinfection. This finding showed the significant prevalence of coinfection that many of these subjects may not be found by routine serological methods. Biochemical parameters showed no significant differences between the two groups.

Conclusion: Coinfection of HBV and HCV occurs frequently. Detection of this form of infection can significantly affect the management and the treatment of these patients.

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Keywords • HBV • HCV • Coinfection • prevalence • PCR

Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections account for a substantial proportion of liver diseases worldwide.¹ HBV is a DNA virus from Hepadnaviridae family that causes a spectrum of liver disease ranging from acute hepatitis and fulminant hepatic failure to chronic hepatitis, cirrhosis, and hepatocellular carcinoma.¹

It is estimated that over 350 million people are infected with this virus worldwide.² This virus maybe transmitted via direct contact, by blood or other body secretions.² HCV is a RNA virus from Flaviviridae family that can cause chronic hepatitis, cirrhosis, and hepatocellular carcinoma. HCV is the most common cause of hepatitis after blood transfusion.^{1,2}

The two viruses share modes of transmission. And coinfection by the two viruses is common, particularly in areas where the two viruses are endemic and among subjects with

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high risk of parenteral infection.^{3,4} Some studies have indicated that HBV/HCV coinfection has clinical importance because of its poor sensitivity to interferon treatment associated with severe chronic liver disease.⁵ It is also associated with high risk of hepatocellular carcinoma development.⁵

Hallmark of HCV infection is the presence of specific antibodies, Anti-HCV, and viral RNA in the serum. Diagnosis of HBV infection is usually made when circulating hepatitis B surface antigen is revealed.⁶ However many studies have shown that HBV genome may also be present in HBsAg negative patients, particularly in those with HCV related chronic hepatitis.⁶ This form of hepatitis is called occult hepatitis.

The virologic profiles of HBV and HCV and their interplay in coinfection are still undefined. In some patients, HBV replication is suppressed while HCV replication remains active. Some studies showed that HCV core protein is able to suppress the HBV replication.^{6,7} The purpose of this study was to define the prevalence of HBV and HCV coinfection in Iranian patients by polymerase chain reaction (PCR). And to compare the biochemical, serological and probable modes of infection transmission in patients coinfecting with HBV and HCV compare with HCV infection alone.

Patients and Methods

Two hundred and seven patients infected with hepatitis C virus participated in the study. The patients consisted of 173 male and 34 female patients with the age range of 8-79 years who had been referred to the Iranian Blood Transfusion Organization for clinical diagnosis. All of them were positive for HCV-RNA and HCVAb but were not positive for HIV. None of the patients was on treatment. Serum sample of each patient was frozen at -70°C until processing. We also checked liver enzymes, HBsAg, HBcAb, and used PCR assay for detection of HBV-DNA in the serum of all patients.

Serum marker for HBV infection

We used commercially available ELISA kit (Dade, Behring) for evaluating two serological markers of hepatitis B (HBsAg and HBcAb). HBsAg assay was based on two stage methods and HBcAb assay was based on competitive one stage method.

HBV-DNA assay

Serum HBV-DNA was evaluated using PCR method. For DNA extraction commercially available kit was used (Roche Diagnostics, GmbH; UK). Amplification was done by two pairs of the primers to pre-S region of HBV genome.⁵ The

PCR products were separated in 2% agarose gel and ethidium bromide.

Biochemical study

Two important liver enzymes, Alanine amino transferase (ALT) and Aspartate amino transferase (AST) were measured using analytical instrument (Hitachi auto-analyzer; Japan) and Pars Azemun Kit, Iran.

Statistical analysis

We used Student t-test to analyze the data and considered $P < 0.05$ as significant.

Results

Of the 207 patients infected with hepatitis C, 23 patients (11.1%) had coinfection with HBV proved by PCR. Of these coinfecting patients, 17 were negative for HBsAg and 6 patients were positive for HBsAg. Twenty one of the coinfecting patients were positive for HBcAb and two patients were negative for HBcAb. Five patients of all participants were positive for HBcAb but we could not confirm their HBV infection by PCR. These results show that high prevalence of HBV/HCV coinfection may be found by sensitive molecular methods.

The probability modes of contamination based on the history of patients are shown in Table 1. There was no significant differences between the patients coinfecting with HBV and HCV in comparison with patients infected with HCV alone. Transfusion of blood and blood products was the most common mode of contamination. Most of the patients of the two groups had normal or slightly increased liver enzymes levels (ALT and AST) at the time of diagnosis (Table 2).

Table 1: Serological markers and modes of contamination in patients with coinfection of HBV/HCV compare with HCV infection alone.

	HCV+HBV	HCV
Total	23	207
Sex(M/F)	20/3	173/34
HBs-Ag(+)	6	6
HBc Ab	21	26
Modes of contamination		
Transfusion	31.3%	38%
IV-drug	27.4%	26%
Hemophilia	14%	13.6%
Thalassemia	11%	9.8%
Tattoo	9.8%	8.7%
Transfusion IV-drug	6.5%	3.9%

Table 2: Liver enzymes level in patients with coinfection of HBV/HCV compare with HCV infection alone.

	HCV+HBV		HCV	
	ALT(%)	AST(%)	ALT(%)	AST (%)
5-49	70	64.3	46.5	57.8
50-149	17.8	34.5	42.9	33.8
150-249	11.7	1	6.2	4
>250	0.5	0.2	4.4	4.4

Discussion

Because of common transmission mode of hepatitis B and hepatitis C viruses, their coinfection is plausible, particularly in endemic areas and among high risk people.^{3,8} The number of coinfecting patients is higher than what is usually estimated.^{1,8} Many studies have shown that HBV genome may also be present in HBsAg negative patients, particularly in those with HCV related chronic hepatitis. This condition is commonly called "occult HBV infection".⁷

Previous studies suggest that coinfection with HBV and HCV may have considerable clinical importance.⁹ Some other studies have suggested that coinfecting patients suffer from severe disease and have higher relative risk for development of hepatocellular carcinoma.^{5,9} In particular, this condition is generally believed to be a factor favoring the progression of liver fibrosis toward cirrhosis and development of liver cancer.

In spite of its potential clinical impacts, however there is little information about the possible interplay between these two viruses. The results of the present study showed the significant prevalence (11.1%) of coinfection with HBV and HCV, proved by PCR method. The finding is approximately the same as the reports of other countries that are in the intermediate region of contamination with HBV and HCV.^{8,10} We could not detect the HBsAg, in 75% of patients coinfecting with HBV and HCV. These patients might be in the occult form or in the window period of hepatitis B infection.

There were no changes in the level liver enzymes in our patients. This is probably due to similarity of the contamination of the coinfecting patients with those patients who had the infection alone as presumed by previous studies too.^{1,8}

In this study the efficacy of antiviral therapy was not examined, however other studies have shown that the response rate to interferon therapy was very low in patients with dual infection of HBV and HCV as compared with HCV infection alone.^{11,12} It seems that combined therapy with alpha interferon and ribavirin can be more efficient for sustained clearance of HCV replication in a significant proportion of patients with HBV/HCV coinfection.¹² The effect of this treatment on HBV replication is low; however, the danger and significance of reactivation of HBV infection after a decrease in HCV replication needs to be evaluated.¹²

Conclusion

It is important to seek for detection of HBV infection, preferably by sensitive molecular methods, in

patients with HCV infection. It can affect the management and treatment of the disease.

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