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Full Length Research Paper

Serologic evaluation of hepatitis B and D in patients with cirrhosis

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Hepatitis D is the important complication in cirrhotic patients. Diagnosis of hepatitis D is based on detection of HBSAg and HDV Ab titer determination. The present research was performed on a number of cirrhotic patients with the aim to assess the prevalence of hepatitis D and B. In present study all the cirrhotic patients who were referred to Gastroenterology and Endoscopy ward of Imam Khomeini hospital during a period of 18 months were included. The level of anti HDV Ab, anti HBS Ab and HBS Ag were determined by method of ELISA (Pishtaz Teb). In this study 60 cirrhotic patients were evaluated. 16 patients were HBS Ag positive with mean age of 51.9 years, and from this group, 13 patients were anti HBC positive with mean age of 53.23 years and from this group, 8 patients were HDV Ab positive with mean age of 49 years. Hepatitis D remains as one of the problems in developing countries. By timely screening of cirrhotic patients for HDV, patients could undergo additional treatments.

Key words: Liver cirrhosis, hepatitis D, hepatitis B, HBS Ag, HBC Ab, HDV Ab.

INTRODUCTION

400 million patients in the worldwide are affected by chronic hepatitis B, especially in developing countries. Unfortunately patients with chronic hepatitis B might be asymptomatic while carrying the hepatitis virus (HBS Ag positive) (Tsatsralt-Od et al., 2005; Mandell et al., 2000). 15 million people in the world have chronic hepatitis D. Hepatitis D or Delta virus is a small round RNA virus which is dependent on hepatitis B virus. This virus cannot live or replicate unless with the envelop of hepatitis B virus and Similar to healthy carriers of hepatitis B , healthy carriers of hepatitis D exist too.(Farci et al., 2004; Mandell et al., 20004). Diagnosis of hepatitis D is based on detection of HBS Ag and HDV Ab titer in serum. Hazardous complications of chronic hepatitis are liver cirrhosis, liver failure, hepatocellular carcinoma and spontaneous rupture of the liver tissue which could result in death.

The present study is implemented on a number of cirrhotic patients with the aim to assess the prevalence of hepatitis D and B in this group.

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MATERIALS AND METHODS

This study included all the cirrhotic patients who were referred to Gastroenterology and Endoscopy ward of Imam Khomeini hospital during a period of 18 months. They were admitted and blood samples were collected. Cirrhosis was confirmed in these patients. A diagnosis of cirrhosis was made on the basis of clinical findings, abdominal sonogram; endoscopic features were done by fellowship in gasteroenterology. Laboratory parameters and/or liver biopsy were applied. At the time of inclusion a questionnaire was completed and patient serum was obtained and stored at -20°C until analyzed. Thereafter the level of total anti HDV Ab, anti HBS Ab and HBS Ag were determined. The method for measuring Ab levels was ELISA and the kits were manufactured by Pishtaz Teb Company in Iran. The specificity and sensitivity of these kits were above 98%.

Results of the experiments and data from the questionnaires were gathered and analyzed by SPSS software, t test, X2 and regression.

RESULTS

In the present study 60 cirrhotic patients who were

admitted in Gastroenterology and Endoscopy ward of Imam Khomeini hospital were evaluated. Patients included 38 male patients with mean age of 45.39 years (SD = 18.36) and 22 female patients with mean age of 48.59 years (SD = 16). 16 patients were HBS Ag positive with mean age of 51.9 years (SD = 14.16). There was no significant difference in age parameter between HBS Ag positive and HBS Ag negative patients (P = 0.721). In group of 16 HBS Ag positive patients, 13 patients were anti HBC positive with mean age of 53.23 years (SD = 14.39). There was no significant difference in age parameter between HBC Ab positive and HBC Ab negative patients (P = 0.189). In a group of 13 HBC Ab positive patients, 8 patients were HDV Ab positive with mean age of 49 years (SD = 13.2). There was no significant difference in age parameter among HDV Ab positive and HDV Ab negative patients (P value = 0.371). There was no significant correlation between age and HBS Ag positive in cirrhotic patients (P value = 0.936). There was no significant correlation between sex and HBC Am positive in cirrhotic patients (P value = 0.254). There was no significant correlation between sex and HDV Ab positive cases among cirrhotic patients (P value = 1). In total cirrhotic patients, 16 (26.7%) were positive for HBs Ag and in total HBs Ag positive cases, 13 (81.3%) were positive for HBC Ab and 8 (50%) were positive for HDV Ab. These estimations are summarized in Table 1.

The number of HDV Ab and HBC Ab positive cases in cirrhotic patients and its correlation with sex is indicated in Table 2. Significant correlation between these two factors were found (P value = 1). Comparative prevalence of HBs Ag, HBC Ab and ADV Ab in different age groups of studied cirrhotic patients was indicated on Figure 1.

Table 1. Results of the univariate analysis.

Features		Total
Sex	Male	38
	Female	22
Age	≤ 20	6
	20 to 29	7
	30 to 39	6
	40 to 49	10
	50 to 59	14
	60 to 69	14
	≥ 70	5
HBs Ag positive		16
HBC Ab positive		13
HDV Ab positive		8

DISCUSSION

Three hundred million people are HBS Ag carriers worldwide and in these carriers approximately 5% are HDV positive. According to the survey 69 cirrhotic patients in India, among 28 (40.6%) were HBS Ag positive and in HBS Ag positive patients, 7 (25%) were anti HBC Ab positive and 5 (17.9%) were anti HDV Ab positive (Tsatsralt-Od et al., 2005). HDV or Delta Ag is a defective RNA virus which depends on hepatitis B virus for replication. Infections caused by HBV and HDV are more severe than infections caused by HBV alone. Patients who are infected by both HBV and HDV have worse prognosis and less hope for recovery compared to those cirrhotic patients who are only infected by HBV (Farci et al., 2004; Chakraborty et al., 2005). There are several surveys published about incidence and prevalence of HDV in Cirrhotic. According to a study on Mongols in Japan, among 41 cirrhotic patients, 26.6% were infected by HBV and HDV which 14.4% of them had hepatocellular carcinoma (Mandell et al., 2000). Therefore, mortality among cirrhotic patients who are HDV positive is much higher than those who are HDV negative (60 versus 4.4%). It is only by long term treatment of these patients with Interferon alpha and Adefovir that their life expectancy could be increased to some extent (Simekova and Viechova, 2005; Zuberi et al., 2006). Thus the mortality rate among these patients have a significant difference (P<0.001). On the other hand, complications such as Hepatic Encephalopathy and Fulminant Hepatitis had higher incidence in cirrhotic patients who were both HBV and HDV positive than those who were HBV positive alone (Grattagliano et al., 2006).

A number of studies have been carried out on infectivity and mortality rate in cirrhotic patients who are both HBV and HDV positive. The study carried out by Fattovich et al. (2000) on 200 HBS Ag positive cirrhotic patients, indicated 20% co infection with HDV. The majority of these patients were in younger ages than other cirrhotic patients. In addition, in anti HDV Ab positive patients cirrhosis occur 15 years earlier than patients who are just anti HBV positive (Anis et al., 2008). Today, RT-PCR and RNA hybridization easily enable detection of hepatitis D viruses in liver cells (Degertekin et al., 2008; Ching-Jung et al., 2007). Similar survay in Tajikistan showed that 41.1% HBV positive in total of 124 hepatitis. Furthermore, concurrent infection with HBV and HDV was seen in 41.1% of the patients. In this study mortality cases caused by Hepatitis B was seen in younger ages than mortality cases caused by hepatitis C (Pourkarim et al., 2008). In addition, a number of cases of spontaneous rupture of liver was seen in concurrent infection with HBV and HDV (Roshandel et al., 2007).

Prevalence of hepatitis D, among chronic hepatitis B

Table 2. Correlation between HBC Ab and HDV Ab positivity and Sex in cirrhotic patients.

HDVAb / Genes HBC Ab		Positive		Negative		Total	
		Number	Percent	Number	Percent	Number	Percent
Male	Positive	5	55.6	4	44.4	9	23.7
	Negative	-	-	29	100	29	76.3
	Total	5	13.2	33	86.8	38	100
Female	Positive	3	75	1	25	4	18.2
	Negative	-	-	18	100	18	81.8
	Total	3	13.6	19	86.4	22	100
Total	Positive	8	13.3	5	8.4	13	21.7
	Negative	-	-	47	78.3	47	78.3
	Total	8	13.3	52	86.7	60	100

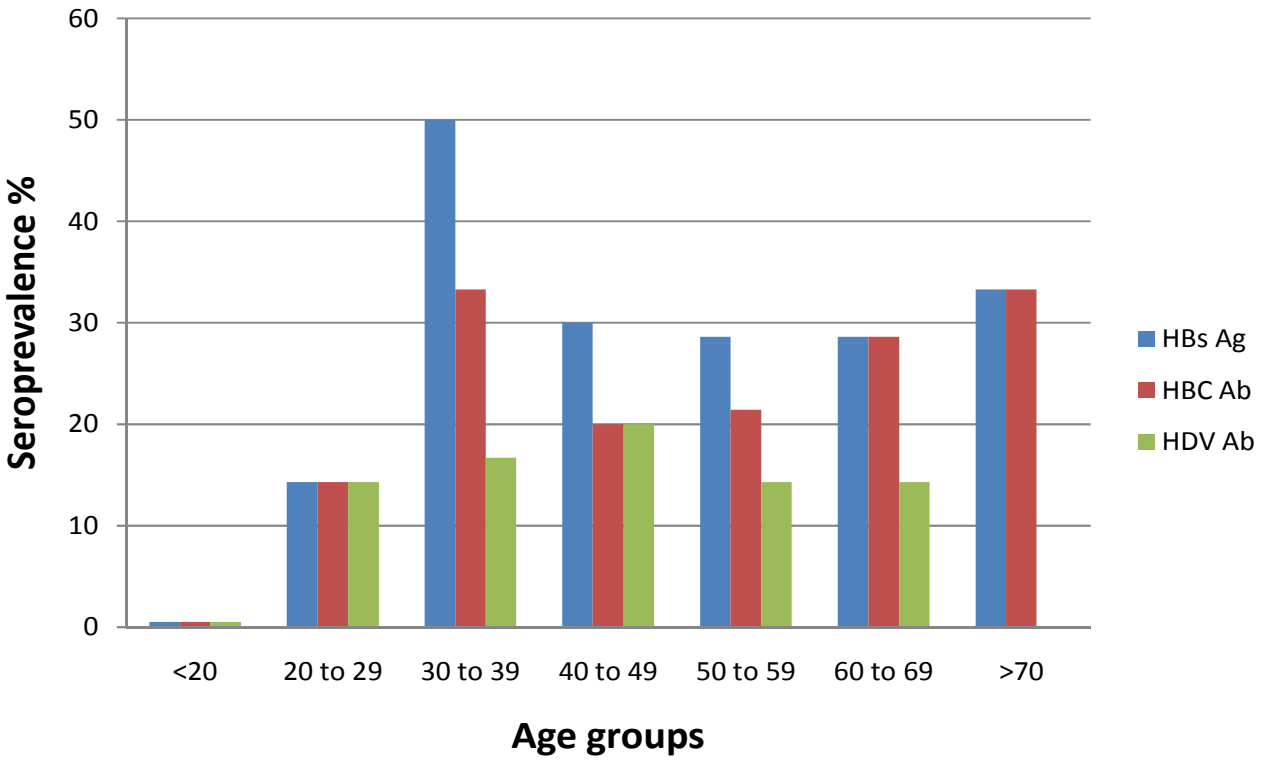

Figure 1. Comparative prevalence of HBs Ag, HBC Ab and HDV Ab in different age groups of studied cirrhotic patients.

and cirrhotic patients has decreased in Turkey (endemic region) from 29% in 1995 to 12% in 2007. However, hepatitis D remains as one of the problems in developing countries such as Iran (Fattovich et al., 2000). In south east of Iran the prevalence of hepatitis B and its later complications is higher, due to immigration of Afghans. Studies show that most Afghans who were HBS Ag and anti HBC Ab positive were in the age range of 51 to 60 years and only a few numbers were in age range of 28 to 35 years (Shao-Ping et al., 2003). In Iran, few studies have been conducted on prevalence of hepatitis D. One is the study by Gh. Roshandel in the province of

Golestan. His study was about the prevalence of hepatitis D in blood donors. The results showed that of 1850 blood samples, 139 (5.8%) were both HBS Ag and anti HDV Ab positive. This reveals a high prevalence of hepatitis D in this region of Iran (Gupta et al., 2005). No paper has been published in Iran about prevalence of hepatitis D in cirrhotic patients. However; there are reports of Hepatitis D prevalence in hemophilic patients and blood donors. In this study, all cirrhotic patients admitted in gastroenterology and endoscopy ward of Imam Hospital during a period of 18 months were studied. Blood samples were collected and examined for HBS Ag, anti HBV Ab and anti HDV Ab. No significant correlation was found between sex of the patients and hepatitis B and hepatitis D infection. Therefore, an equal number of male and female cirrhotic patients were infected with hepatitis B and D. Moreover, no significant correlation was seen between the age of the patients and infection with hepatitis B and D.

In total patients, 16 were HBS Ag positive while 13 patients were anti HBV positive indicating acute hepatitis B. Of total cirrhotic patients with active hepatitis B, 8 (50%) were anti HDV Ab positive indicating concurrent infection with HBV and HDV in these cirrhotic patients. In general, among the 60 cirrhotic patients in this study, 8 (13.3%) were infected with hepatitis D which is lower in comparison to the reports from other countries such as India and Japan but almost similar statistics were obtained in Turkey, so the prevalence of hepatitis D in cirrhotic patients are similar in region countries. In spite of that and considering the worse complications in cirrhotic patients infected by both HBV and HDV and higher mortality risk in these patients compared to other cirrhotic patients, more concern is essential because patients with hepatitis D earlier to patients with hepatitis B can progress to liver cirrhosis. In addition, by timely screening of cirrhotic patients for HDV, patients could undergo additional treatments.

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