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Prevalence of hepatitis delta virus infection in various groups with HBV infection in Tehran, Imam Khomeini Hospital (2005-2006)

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Abstract

Background: Hepatitis B virus infection is an important cause of liver morbidity and mortality worldwide. HDV changes the natural course of HBV. The prevalence of HDV infection wasn't determined in the various groups of HBV infection (carriers, acute hepatitis, chronic hepatitis, cirrhosis and HCC) in Iran. We aimed to research the prevalence of hepatitis D virus infection in various groups with HBV infection in Imam Khomeini Hospital, Tehran (2005-2006)

Methods: Serological markers of HBV and HDV infection [HBs Ag, Hbe Ag, Anti Hbe Ab, Anti HDV Ab (IgM, IgG)] were determined by ELISA test in 206 patients with HBV infection who referred to Imam Khomeini Hospital (2005-2006).These patients were categorized to asymptomatic carriers, acute hepatitis, chronic hepatitis, cirrhosis and HCC according to history, physical examination and lab findings.

Result: HDV infection was detected in 12.6% (26/206) of HBV infected patients. It was detected in 1.6%(1/62) of asymptomatic carriers, 20% (1/5) of acute hepatitis, 5.6%(5/88) of chronic hepatitis, 37.2% (16/43) of cirrhosis and 37.5% (3/8) of HCC patients. HDV infection showed a five-fold increase in chronic hepatitis ($P<0.05$) and ~16 fold increase in cirrhosis ($P< 0.001$) compared to HDV infection in asymptomatic carriers. HDV infection was equally distributed between sexes. Mean ages of HDV carriers, acute hepatitis, chronic hepatitis ,cirrhosis and HCC were (28), (33), (39.521), (47.111.5), (58.69,2) year respectively.

Conclusion: The prevalence of HDV infection was 12.6%. The higher prevalence of HDV infection in more severe forms of hepatitis B virus infection suggests that HDV infection increases the severity of chronic hepatitis B. HDV infection remains a major cause of chronic liver disease in Tehran in spite of its decreasing prevalence in countries such as Italy.

Keywords: HBV, HDV, epidemiology.

Introduction

Hepatitis delta virus (HDV) infection is an important cause of liver morbidity and mortality associated with HBV infection. Fulminant hepatitis, chronic hepatitis, liver cirrhosis and hepatocellular carcinoma are the main diseases complicating HDV infection. 350 and 18 millions individuals are infected with HBV and HDV infection world-wide, respectively [1]. In Iran previous studies showed the prevalence of HDV infection to be between 2.5%-6.15% (in different studies),1.8% and 62.5% in asympto-

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	HDV positive		HDV negative	Total
	No (%)	95% CI	No. (%)	No. (%)
Asymptomatic carrier	1(3.9)	1.6 (0-5.6)	61 (33.9)	62 (30.1)
Acute hepatitis	1(3.9)	20 (0-55)	4 (2.2)	5 (2.4)
Chronic hepatitis	5 (19.2)*	5.6 (6-10.6)	83(46.1)	88 (42.7)
Cirrhosis	16 (61.5)**	37.2 (22.8-51)	27 (15)	42 (20.9)
HCC	3 (11.5)	37.5 (4-71)	5 (2.8)	8 (3.9)
Total	26 (100)	12.6 (8-15.2)	180 (100)	206 (100)

*(P< 0.05), **(P< 0.001)

Table 1. Prevalence of HDV infection in different groups of HBsAg positive patients in Tehran (Imam Khomeini hospital)

matic carriers, acute HBV infection and HCC respectively [2,3,4,5].

In this study we aimed to investigate and compare the prevalence, biochemical parameters, virological markers and risk factors in different groups of HDV positive and HDV negative patients, (asymptomatic carriers, acute hepatitis, chronic hepatitis, cirrhosis and HCC), who referred to Imam Khomeini hospital in Tehran (2005-2006).

Methods

According to history, physical examination, lab data (CBC, LFT), abdominal sonography, upper GI endoscopy and liver biopsy, 206 HBsAg positive patients who came to Imam Khomeini hospital (2005-2006) were divided in to five groups:

Asymptomatic carriers 62 (32 males, 30 females); acute hepatitis 5(3 males, 2 females) chronic hepatitis 88 (54 males, 34 females), cirrhosis 43(37 males, 6 females) and HCC 8 patients (8 males). Serum samples of these patients were analyzed for determination of anti-HDV (IgM and IgG) Ab. Levels of serological markers of HBV infection (HBs Ag, Hbe Ag, Anti-Hbe Ab; Anti-HBs IgM and IgG Ab) were measured by ELISA (Diasorine radim 0093, 0042ir, 0086ir Italy).

Anti-HDV levels were then determined by ELISA (Diasorine citi10r2, Italy). The gender distribution, risk factors of transmission, and mean age of patients were determined. LFT and CBC were analyzed in all patients.

In 47 patients in chronic hepatitis and cirrhosis groups liver biopsy was performed for accurate diagnosis and stained by H&E. Grading and staging was determined according to Knodell's -Ishak scoring system. In others, the positive diagnosis was based on physical, laboratory, ultrasonographic and endoscopic findings.

Statistical methods

The differences between HDV prevalence ratios (%) in the five groups were analyzed according to the standard normal distribution Z-test; if the number of patients in each group were less than thirty, we used Kolmogorov-Smirnov Z-test or NPar test. Mean ages of HDV-positive and HDV-negative patients were compared by t-test.

The prevalence of infection in both sexes in the five groups of HDV-positive and HDV-negative patients were compared by chi-square test.

Results

The prevalence of HDV infection in different groups of HBsAg positive patients is presented in Table 1.

Our study detected a prevalence of 12.6% (26/206) of HDV infection in all groups of HBV-infected patients; this means there is a high prevalence (approximately 450000 individuals) of HDV in Iran. HDV infection showed five-fold increases in chronic hepatitis ($p< 0.05$) and ~16 fold increases in cirrhosis ($p< 0.01$) compared to HDV infection in asymptomatic carriers. We also observed an eight-year

		Male	Female	Mean age (yr)
Asymptomatic carrier	HDV+	0 % (0/1)	100 % (1/1)	28
	HDV-	52 % (32/61)	48 % (29/61)	36.6 ± 12.9
Acute hepatitis	HDV+	100 % (1/1)	0 % (0/1)	33
	HDV-	50 % (2/4)	50 % (2/4)	49.7 ± 12.5
Chronic hepatitis	HDV+	60 % (3/5)	40 % (2/5)	39.5 ± 21
	HDV-	61 % (51/83)	39 % (32/83)	35.2 ± 12
Cirrhosis	HDV+	81.3 % (13/16)	18.8 % (3/16)	47.4 ± 11.5
	HDV-	89 % (24/27)*	11 % (3/27)	51.2 ± 14.4
HCC	HDV+	100 % (3/3)	0 % (0/3)	58.6 ± 9.2
	HDV-	100 % (5/5)	0 % (0/5)	57 ± 12.6

*(P< 0.001)

Table 2. Epidemiological characteristics of HDV and HDV infection in Tehran (Imam Khomeini Hospital).

lapse between chronic hepatitis and cirrhosis in HDV-positive patients; this lapse was 16-years in HDV- negative patients. The mean age of cirrhotics in HDV-positive patients was also four-years younger than HDV-negative patients

HDV infection ratios were not significantly different between sexes in different groups (P>0.05). Interestingly however cirrhosis in HDV-negative patients was eight times more frequent in males than females (P<0.01). Serum mean ALT and AST were not significantly different. Serum HBe Ag was positive in 3.9% (1/26) of HDV-positive and in 16 % (30/180) of HDV-negative patients, that was lower in HDV-positive patients significantly (P<0.01).

Serum HBV viral load was significantly lower in the HDV-positive than HDV-negative patients (P<0.001). Anti-HBeAb was positive in 77% (20/26) of the HDV-positive group and 79% (142/180) of the HDV-negative group, without significant difference.

Biochemical and virological findings are presented in Table 3.

We detected risk factors in 78% of patients, all HDV-positive and 75% of HDV-negative patients. Household contact, transfusion, surgery and piercing were more frequent risk factors in both HDV-positive and HDV-negative patients.

Household contact increased the chance of HBV and HDV infections compared to other risk factors, significantly (P<0.001).

Piercing was higher in HDV-positives significantly (P<0.05).

		ALT(IU)	AST(IU)	Hbe Ag+(%)	Hbe Ab+(%)
Asymptomatic carrier	HDV^+	39	25	0% (0/1)	100% (1/1)
	HDV^-	25 ± 8.8	24.5 ± 6.4	9.8% (6/61)	88% (54/61)
Acute hepatitis	HDV^+	478	146	0% (0/1)	100% (1/1)
	HDV^-	636 ± 157	531 ± 148	0% (0/4)	100% (4/4)
Chronic hepatitis	HDV^+	59.8 ± 17	51 ± 14	20% (1/5)	80% (4/5)
	HDV^-	74.1 ± 62	57 ± 41	25.3% (21/83)	69% (57/83)
Cirrhosis	HDV^+	59 ± 37	74 ± 56	0% (0/16)	81.3% (13/16)
	HDV^-	67 ± 38.5	85 ± 23	3.7% (1/27)	92% (24/27)
HCC	HDV^+	99 ± 27	142 ± 31	0 % (0/3)	33% (1/33)
	HDV^-	40 ± 14	109 ± 88	40% (2/5)	40% (2/5)
Total	HDV+	79.8 ± 64.5	79.5 ± 4.1	3.9 % (1/26)	77% (20/26)
	HDV^-	68 ± 41.4	73.6 ± 104	16.6% (30/180)*	79% (142/180)

*(P< 0.001)

Table 3. Biochemical, virological findings of HDV and HDV infection in Tehran (Imam Khomeini Hospital).

	HDV^+ (%)	HDV^- (%)	Total (%)
Household contact	61.5% (16/26)	50% (90/180)	51.5% (106/206)*
Transfusion	15.3% (4/26)	9.5% (17/180)	10% (21/206)
Surgery	7.2% (2/26)	9.5% (17/180)	9.2% (19/206)
Piercing	15.3% (4/26)* *	3.3% (6/180)	4.8% (10/206)
Medical staff	0% (0/26)	1.6% (3/180)	1.4% (3/206)
Hemodialysis	0% (0/26)	0.5% (1/180)	0.4% (1/206)
IVDU	0% (0/26)	0.5% (1/180)	0.4% (1/206)

*(P< 0.001), **(P< 0.05)

Table 4. Risk factors in HDV^+ and HDV^- groups in Tehran (Imam Khomeini Hospital).

Discussion

Five percent of HBV carriers (~ 18 million people) are infected with HDV infection worldwide; areas of high prevalence include: Amazon [6], Colombia, Venezuela [7] and western Asia [8,9]. In Italy HDV infection has greatly declined in the past decade owing to the prevention of HBV infection by means of vaccination, avoidance of paid donor and use of disposable needle and syringes [10].

HDV has three main genotypes. Genotype I predominates in most areas of the world; genotype II was originally discovered in Japan and Taiwan, where an association with less severe disease has been proposed (except for genotype IIbM) [11]. Genotype III predominates with a more severe form of hepatitis [12]. HDV Co-infection leads to a biphasic pattern of rising liver enzymes and leads to chronic liver disease in 7% of patients [13] but HDV super-infection leads to chronic liver disease in 80-90% of patients [14]. HDV related cirrhosis develops one decade earlier than HBV related cirrhosis in endemic areas [1].

The previous studies in Iran estimated the prevalence of HDV to be 1.3% in Tehran, 2% in Hamadan, and 6.15% in Tabriz in asymptomatic carriers; and our study showed 1.6%

A previous study showed HDV in 62.5% of HCC patients in Iran, we found HDV in 37.5% with 95% CI(4-71), so for accurate interpretation, more studies should be performed because in both studies the number of HCC patients were not enough and 95% CI is very wide.

Like others studies, these findings showed that HDV infection accelerates liver damage and the patients suffered from chronic hepatitis and cirrhosis earlier.

The results of HBeAg and HBeAb suggest that the low prevalence of serum HBeAg in HDV positive patients simply reflects the HBeAg/Anti-HBeAb status of the asymptomatic carrier, acute and chronic hepatitis. Also we found lower HBV viral load In HDV positive patients due to the suppressing effect of HDV on HBV especially in chronic hepatitis and cirrhotic patients.

One study in Italy showed IVDU and household contact were the important ways of transmission in 1993. After HBV vaccination, in (1994-2004) IVDU, hospitalization, promiscuous sexual activity and receipt of dental therapy and beauty treatment were important factors.

Our study showed that household contact was an important way of transmission, like Italy in 1993, so HBV vaccination and hygienic living conditions are very important factors in our study.

In conclusion, the higher prevalence in the more severe forms, the shorter interval between chronic hepatitis and cirrhosis and younger age

of cirrhosis in HDV positive patients suggests that HDV infection increases the severity and accelerates the progression of HBV infection to cirrhosis. Household contact is the main way of transmission of HBV (HDV positive and HDV negative) so HBV vaccination in the childhood period, hygienic living conditions and improved socioeconomic and educational status are the cornerstones in the prevention of HBV and HDV infections. Piercing such as tattooing must be prohibited because it increases HDV infection significantly.

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