

Epidemiologic and Clinical Aspects of Delta Hepatitis in the Van Region

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Abstract

Aims: Patients infected with both hepatitis B virus (HBV) and hepatitis B virus (HDV) tend to progress more severe liver injury than those infected with HBV alone. In Eastern Anatolia, HDV infection is one of the the major causes of chronic liver disease. This study was conducted to determine the epidemiology and clinical aspects of delta hepatitis in Van region of Eastern Turkey.

Methods: This study was conducted in the years 2008 and 2009. Serological markers of HBV infection (HBsAg, HbeAg, Anti-HBs) were determined by ELISA test in patients with chronic hepatitis B. Serum HBV- DNA and HDV-RNA were determined by polymerase chain reaction (PCR) method in chronic hepatitis B patients. Thereafter, liver biopsy samples from 24 patients with delta hepatitis were studied.

Results: Chronic HDV infection was more frequent in males ($p<0.001$). Mean age of delta hepatitis patients was $34,3\pm9$ (16-54) years. Delta hepatitis cases had solely greater portal and parenchymal inflammatory changes.

Conclusions: HDV is a novel satellite virus and may increase the degree of hepatic damage in patients with Hepatitis B. Rural clustering of male cases is a striking finding in endemic areas.

Key words: Delta hepatitis, Turkey, Van

Introduction

Delta hepatitis cause considerable public health problem in developing countries. Hepatitis delta virus (HDV) is a small and 1.7 –kb single -strand RNA genome contained virus (1).

It was described by Rizzetto and associates in 1977 as a new virus which was immunologically distinct from the HB surface, core, and e systems hepatitis virus in the hepatocytes of patients infected with HBV (2).

It is important that HDV causes super and coinfections in hepatitis B patients (3). Coexistence of hepatitis D with HBV in the same time is named as coinfection. It may range from

mild to severe fulminant hepatitis. In the superinfection presentation, the preexisting HBV viremia endorses the biological background for the full expression of the virulence of HDV (4). HDV is seen worldwide with wide variations in prevalence.

Worldwide, above 460 million people have HBV and it is estimated that around 20 million also have chronic HDV. Thus, HDV remains a major cause of cirrhosis and liver transplantation (5).

In northern Europe and in the United States, where the prevalence of HDV infection is low, delta hepatitis is mainly seen in intravenous drug users (6).

In hyperendemic areas for hepatitis D virus, as in the Mediterranean basin or Far East, heterosexual activity with multiple partners and common-use of household products are the most important transmission routes for HD (7).

The anti-HDV positivity was 33% in chronic hepatitis B cases in Van (8). We conducted a prospective study to clarify the clinical aspects of HDV infection among HBV-infected patients living in Van city which located near Turkish-Iranian border.

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Table 1. Descriptive statistical analysis for clinical features

	N	Mean	Std. Deviation	Std. Error	Minimum	Maximum
HBV DNA (copy/ml)	21	12790,00	28523,929	6224,432	6	110000
ALT(U/L)	24	101,04	73,967	15,099	28	308
Knodel	24	11,33	3,726	,761	5	18
Fibrosis	24	2,00	1,063	,217	0	4
Globulin(g/dl)	24	3,650	,8460	,1727	2,4	5,9
Albumin(g/dl)	24	4,258	,5912	,1207	2,5	5,2

Table 2. Spearman rank correlation test for clinical features

	Age	HBV DNA(copy/ml)	ALT	Knodel score	Fibrosis	Globulin	Albumin
Age	1						
HBV DNA(copy/ml)	,461*	1					
ALT	-,379	-,233	1				
Knodel score	,208	,101	,240	1			
Fibrosis	,164	,115	,034	,846**	1		
Globulin	-,262	-,244	,255	,287	,321	1	
Albumin	-,436*	-,214	,010	-,433*	-,223	,020	1

*: p<0.05, **:p<0.01

Patients and methods

Between October,2008 and November,2009 we studied 24 chronic coinfecting delta hepatitis patients admitted to Gastroenterology Clinic of Yuzuncuyil University Training and Research Hospital.

There were 21 men and 3 women,aged 16-54 years(mean±SD,34,3±9).All the patients had chronic delta hepatitis. Patients with hepatocellular carcinoma or liver cirrhosis were excluded. Delta hepatitis was defined as HDV-RNA positivity and liver histology showing chronic inflammatory changes.

All patients were of Turkish origin and were born in Turkey. Non were intravenous drug users; non admitted to homosexual activities. 80 percent of patients was living in rural areas of the region.

Standart assays

HBS Antigen, Hepatitis B e Antigen and antibody to HBS were were measured using commercially available enzyme immunoassay (EIA) kits (Abbott Laboratories, North Chicago, IL, USA) HBV DNA was determined by molecular hybridization and PCR. Results obtained as copy/ml. Serum HDV-RNA was detected and measured by nested reverse

transcription polymerase chain reaction (RT-PCR).

Liver biopsy

The liver biopsy was performed for all the patients. Obtained specimens were examined by a pathologist in same center. Knodel scoring system was used for our study.

Statistical analysis

All the data analysis was carried out using the SPSS software Version 10.0 (SPSS, Chicago, IL, USA). A P-value of <0.05 was considered significant. Data was summarized as the means with standard deviations, median with the range and as frequency and percentages. The relationship between values was determined by Spearman rank correlation test where appropriate.

Results

The delta hepatitis were seen in predominantly males (91.2%) and in younger patients (mean±SD,34,3±13). Vast majority of patients was living in rural areas (80%). General features of patients with Delta Hepatitis are shown in Table 1.

Higher Knodel Hepatic Activitiy scores of younger patients with HDV was a striking finding in this study. Furthermore, mean HBV-DNA level

was relatively low. Serum alanine aminotransferase (ALT) level was higher than expected (101 U/L; normal, 1-42 U/L). Mean Knodell score was high (mean±SD,11.3±3.7). Low albumine levels was associated with highest Knodell's scores ($p<0.05$). So, there was minimally hyperglobulinemia (mean±SD,3.7±0.8). Table 2 shows that no significant association was found between various values except HBV-DNA and albumin levels. There was a positive correlation between HBV-DNA levels and older age and was a negative correlation between Knodell Hepatic Activity scores and albumin levels.

Discussion

Hepatitis delta virus (HDV) is a defective RNA virus that requires a endorsement provided by hepatitis B virus (HBV) for replication (9).

The prevalence of HDV infection in Van City is very high. The rate of HDV among the chronic hepatitis B patients in this region have been reported to be 16% (10).

In Turkey the prevalence of HDV in chronic hepatitis B patients and in those with liver cirrhosis diminished, respectively, from 31% to 11% and from 43.3% to 24% in the period 1980–2005 (11).

In the present study, vast majority of our cases was younger male patients (mean age 34 years) similar to earlier studies from other countries and Turkey (12,13,14). Furthermore, we have determined that the highest seroprevalence of HDV infection is found in the rural areas.

As was seen in our study, the majority of patients with delta hepatitis had highest Knodell's Hepatic Activity and fibrosis scores and had elevated tranaminase levels. Because, chronic HDV can cause to cirrhosis frequently and Chronic HBV-HDV infections are associated with severe liver disease. But new epidemiological data from population based large studies in HDV hyperendemic areas have revealed a more fine course in a significant proportion of chronically infected individuals (15). Our study did not support this phenomena and it may be due to significant heterogeneity in the clinical outcome of chronic HBV/HDV infection.

Higher hepatic inflammatory scores in younger patients may indicate to acquire HDV infection early in life, possibly even in early childhood in endemic and asiatic areas (16). Therefore, our findings suggest an association of HDV infection with the development of early cirrhosis in patients those living in Eastern Turkey.

Delta hepatitis remains a devastating health problem in the many asiatic countries where HBV

is endemic. The rate of infection among younger males living in rural areas has been found to be high. The most effective prevention method is vaccination against HBV.

Van Yöresindeki Delta Hepatitli Hastaların Epidemiyolojik ve Klinik Özellikleri

Özet

Amaç: *Hepatit-B Virüsü (HBV) ve Hepatit-Delta Virüsü (HDV) ile infekte olan hastalar yalnız HBV ile infekte olanlara göre daha ağır bir karaciğer hastalığı gelişme riskine sahiptirler. Doğu Anadolu'da Hepatit D enfeksiyonu kronik karaciğer hastalığının en önemli nedenlerinden biridir. Bu çalışma delta hepatininin epidemiyolojik ve klinik özelliklerinin Van ve çevresinde değerlendirilmesi amacı ile yapılmıştır.*

Metod: *Çalışma 2008 ile 2009 yılları arasında yapıldı. HBV enfeksiyonuna ait serolojik belirteçler ELISA testi ile yapıldı. Serum HBV-DNA ve HDV-RNA ölçümleri polimeraz zincir reaksiyonu yöntemi ile yapıldı. Ayrıca 24 hastanın tümüne yapılan karaciğer biyopsi örnekleri incelendi.*

Sonuçlar: *HDV enfeksiyonu erkeklerde daha sıkı ve ortalama yaş 34,3 idi. Delta hepatitli hastalarda portal ve parankimal inflamatuvar değişiklikler baskın özellik göstermekteydi.*

Tartışma: *HDV kronik hepatit B hastalarında karaciğer hasarının ağırlığını artıran yeni bir satelit virüstür. Endemik alanlarda erkek hastalarda daha sık görülmesi çarpıcı bir bulgudur.*

Anahtar kelimeler: *Delta Hepatiti, Türkiye, Van*

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