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Research Article

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Delta virus predominates and potentially predicts liver cirrhosis among co-infected hepatitis b and hepatitis d virus patients in pakistan

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Abstract

Background: *High prevalence of Hepatitis Delta virus (HDV) has been reported from some pockets in Pakistan. Typically, Hepatitis B (HBV) and HDV co-infection could cause severe hepatitis leading to cirrhosis at an early age. We aim to study the clinical outcomes of HBV/HDV co-infection compared to HBV mono-infection in a Punjabi, Pakistani population.*

Methods: *The retrospective data on all HBV positive patients was extracted from Hepatitis Prevention and Treatment Program (HPTP) of Pakistan Kidney and Liver Institute in Punjab, Pakistan. Majority (32/50) of the HBV/HDV co-infection were identified from Rajanpur clinic of HPTP. Pre-treatment liver tests, HBV-DNA viral load, HDV-RNA viral load; AST to Platelet ratio (APRI) and Fibrosis-4 (Fib-4) were calculated from standard equations. Cirrhosis was based on APRI (≥1.5) or/and Fib4 (≥1.45). HBV-DNA level ≤ 2,000 IU and ≥20,000 IU were categorized as low and high viral load respectively.*

Results: *57 (53%) patients were HBV mono-infected and 50 (47%) were co-infected with HDV. Mean age was 36.2±12.99 in the entire cohort and was not different between the two groups. Older age correlated to a higher APRI and Fib-4 scores in both groups. The two groups were predominantly male, 75% in HBV and 76% HBV/HDV co-infected patients. Sharing of toothbrushes was reported to be significantly higher by HBV mono-infected patients; p 0.005. Other risk factors were equally prevalent. 78% of HBV mono-infected and 79% HBV/HDV co-infected patients had ≤ 20,000 IU/ml HBV-DNA. While 56% and 44% had ≤ 2,000 IU/ml HBV DNA levels respectively.*

APRI and Fib-4 scores were significantly higher in HBV/HDV coinfected; p 0.01. The cirrhosis was diagnosed in 29 patients in HBV/HDV co-infected group, while no patient had cirrhosis in HBV mono-infected group.
Within HBV/HDV co-infected group, mean HDV-viral load was significantly higher compared to HBV viral load; p 0.05. Mean HBV-DNA and HDV RNA levels in non-cirrhotics were 326411 and 35358369; and in cirrhotics 3340429 and 31867418 IU/ml, respectively. 4 patients had undetectable HBV viral load and one of them had cirrhosis. 10 patients were cirrhotics with ≤ 2,000 IU/ml of HBV-DNA. The mean HDV RNA level in these 10 patients was 63, 000000 IU/ml. Mean HDV viral load was one log higher in patients with ≤20,000 IU/ml HBV-DNA compared to those with ≥ 20,000 IU/ml HBV-DNA viral load.

Conclusion: *Overall mode of transmission of HBV and HBV/HDV infections are similar in Punjab. More patients had higher liver fibrosis scores in HDV/HBV co-infected groups. The significantly low level of HBV, in the co-infected population especially cirrhotic patients indicates that liver disease is driven by HDV rather than HBV infection among co-infected Pakistani patients and Peg-interferon alone might be the best treatment option for them.*

Introduction

Hepatitis B virus (HBV) infection is responsible for death of nearly 686,000 people every year. There are 240 million chronic carriers worldwide. HBV infection is a real threat to the health of the people particularly those in the Southeast Asia and Sub-Saharan Africa where the disease has highest prevalence rate [1]. Until now 8 genotypes A-H are identified and the other two I and J have been proposed [2,3].

Hepatitis Delta virus (HDV) require HBV envelope proteins for virion assembly and propagation. As compared to HBV mono-infection, HBV and HDV coinfection is associated more frequently with severe liver disease [4,5]. The estimates suggest that almost 15-20 million people are infected with HDV virus. The declining trend in HDV virus is probably because of the hepatitis B vaccination which results in decrease in HBV carriers [6].

HBV-HDV coinfection is prevalent in specific geographic regions all over the world. The disease is endemic in Turkey and Iran whereas in Mediterranean areas such as southern Italy and southern Greece, the disease infects more than usual number of people [7,8].

Some areas of Pakistan have reported higher frequency of HDV. HBV and HDV co-infection usually cause severe hepatitis and cirrhosis at an early age. Our aim is to study the clinical outcomes of HBV/HDV co-infection compared to HBV mono infection in a Punjabi, Pakistani population.

Methods

A sample of 107 patients included 57 in HBV mono infection and 50 in HBV-HDV coinfection group. The retrospective data on all HBV positive patients was extracted from Hepatitis Prevention and Treatment Program (HPTP) of Pakistan Kidney and Liver Institute in Punjab, Pakistan. Majority (32/50) of the HBV/HDV co-infection were identified from Rajanpur clinic of HPTP.

Pre-treatment liver tests, HBV-DNA viral load, HDV RNA viral load; AST to Platelet ratio (APRI) and Fibrosis-4 (Fib-4) were calculated from standard equations. Cirrhosis was based on APRI (≥1.5) or/and Fib4 (≥1.45). HBV-DNA level ≤ 2,000 IU and ≥20,000 IU were categorized as low and high viral load respectively.

Results

The results showed that 57 (53%) patients were HBV mono-infected and 50 (47%) were co-infected with HDV. Mean age of the entire cohort was 36.2±12.99 years and was not different between the two groups. Older age correlated to a higher APRI and Fib-4 scores in both groups. The two groups were predominantly male, 75.44% in HBV and 76% HBV/HDV co-infected patients (Table 1).

Sharing of tooth brushes was reported to be significantly higher by HBV mono-infected patients (P=0.005). Other risk factors like frequent injectable medications, shave from local barber, and sharing of nail cutters were equally prevalent. 78% of HBV mono-infected and 79% HBV/HDV co-infected patients had ≤ 20,000 IU/ml HBV-DNA; While 56% and 44% had ≤ 2,000 IU/ml HBV DNA levels respectively. APRI and Fib-4 scores were significantly higher in HBV/HDV co-infected (P=0.01). 58% of patients in HBV/HDV co-infected group found to have cirrhosis, while no patient had cirrhosis in HBV monoinfected group.

Within HBV/HDV co-infected group, mean HDV-viral load was significantly higher compared to HBV viral load (P=0.05). Mean HBV-DNA and HDV RNA levels in non-cirrhotics were 326,411 and 35,358,369; and in cirrhotics 3,340,429 and 31,867,418 IU/ml, respectively (Figure 1). 8% of patients had undetectable HBV viral load and one of them had cirrhosis. 20% of patients were cirrhotics with ≤ 2,000 IU/ml of HBV-DNA. The mean HDV RNA level in these patients was 63,000,000 IU/ml. Mean HDV viral load was one log higher in patients with ≤20,000 IU/ml HBV-DNA compared to those with ≥ 20,000 IU/ml HBV-DNA viral load.

Table 1: Cirrhosis in HBV monoinfected group.

		HBV mono infection n=57	HBV/HDV Co-infection n=50	P-vale
Age in years		Mean ± SD=38±13.58 Median=36	Mean ± SD=34±12 Median=35	0.091
Gender	Male	43 (75.44%)	38 (76%)	
	Female	14 (24.56%)	12 (24%)	
Platelets		235 ± 60.91	178.5 ± 72	<0.001
ALT		Mean ± SD=75±162 Median=47	Mean ± SD=121±169 Median=84	1.64
AST		Mean ± SD=53±121 Median=32	Mean ± SD=90.9±70 Median=71	0.069
APRI		Mean ± SD=0.99±1.92 Median = 0.52	Mean ± SD=2.7±3.2 Median=1.37	0.001
Fib4		Mean ± SD=1.04±1.05 Median=0.70	Mean ± SD=2.28±2.3 Median=1.4	0.001

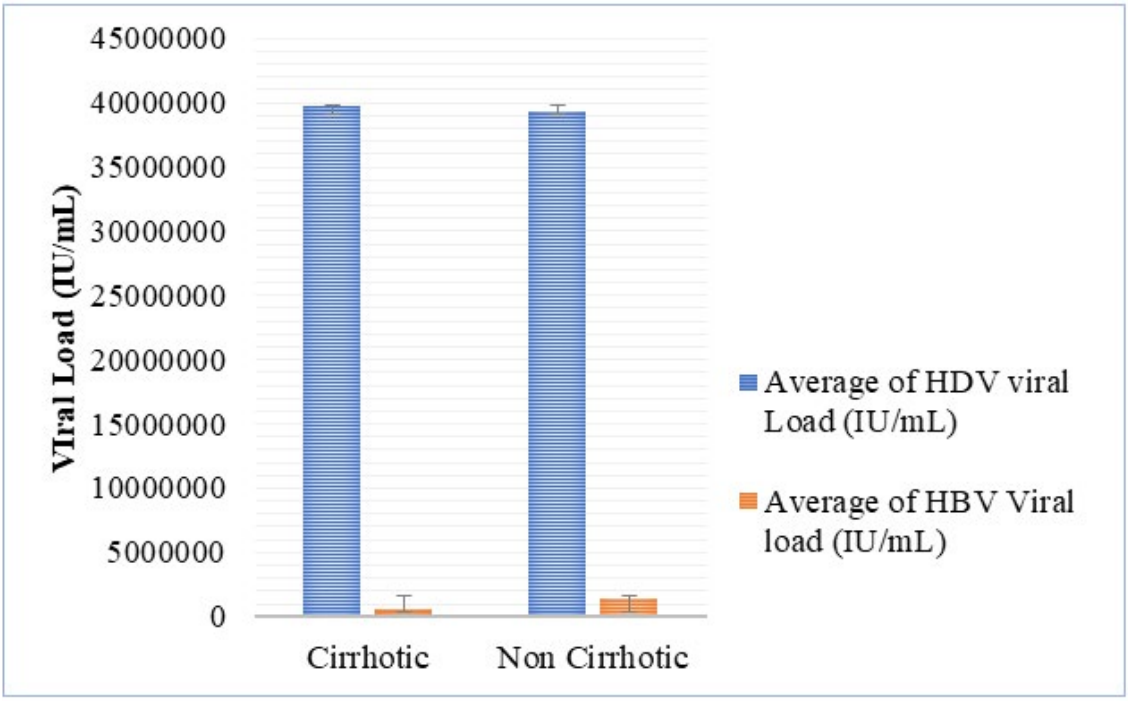

Figure 1: Graph showing the average HBV and HDV viral load in cirrhotic and Non-Cirrhotic Patients.

Discussion

There is high prevalence of HDV infection in some areas of Southern Pakistan that include majority of the rural areas of Sindh and Baluchistan which have the highest prevalence of HDV infection in Pakistan, even urban cities like Karachi and Quetta do not possess low prevalence of HDV [9]. According to an epidemiological survey in Pakistan that included 8721 HBV patients over 14 years of age and tested for anti-HDV antibody from all over the country, the HDV prevalence was 16.6% [10].

The result from our study shows that there is high prevalence of HDV infection in some areas of Southern Pakistan. Our study showed presence of advanced fibrosis & cirrhosis among patients co-infected with HBV & HDV as compared to HBV monoinfection. Our patients were relatively young and predominantly male in both groups. HDV viral load was significantly higher in patients co-infected with HBV & HDV indicating that HDV is the main driver of the disease.

The risk of rapid progression of cirrhosis is more in people having HDV superinfection as compared to individuals suffering from HBV monoinfection. Individuals having HBV-HDV co-infection possess higher risk of fulminant hepatitis and more severe acute disease [11]. It is observed that most of individuals infected with HDV develops the chronic form of the disease and approximately 80% of these individuals, the chronic Hepatitis D progresses to cirrhosis within 5-10 years [12].

Conclusion

Our study showed that HBV and HBV/HDV infections have similar mode of transmission. HDV/HBV co-infected groups showed higher liver fibrosis scores in a significant number of patients. We found significant low level of HBV DNA and high viral load of HDV RNA in our co-infected patients with HBV/HDV particularly in cirrhotics. It suggests that HDV is the main driver of liver disease in our HBV/HDV coinfected patients and Peg-interferon might be the best treatment option for them.

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