ORIGINAL ARTICLE

Hepatitis Delta Virus in Intravenous Drug Users in Kuala Lumpur

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Summary

The hepatitis delta virus (HDV) is an RNA containing virus that requires hepatitis B virus (HBV) to supply the envelope proteins. HDV only infect man in the presence of HBV, either as a coinfection or as superinfection in HBV carriers. In the presence of hepatitis B infection, the HDV may cause more severe liver damage than that caused by the hepatitis B virus alone. HDV infection was studied in 44 HBsAg positive serum samples collected from male intravenous drug users sent for screening to the Blood Services Centre (BSC), Hospital Kuala Lumpur (HKL) between 1990 and 1992. The majority (39) were in the 20 to 39 age group. The youngest was 19 years old and the oldest was 61 years old. There were 25 Malays, 13 Chinese, five Indians and one Albanian.

Anti hepatitis delta antibody (Anti-HDV) was detected in 15 out of 44 (34%) of the drug addicts. These results shows an increased in delta infection in HBsAg positive intravenous drug addicts compared to the surveillance results in 1985 when no delta antibodies were detected, and the 1986 and 1989 surveillance which showed 17.8% and 20% delta antibody positivity respectively.

Key Words: Hepatitis D, Intravenous drug users, HIV

Introduction

HDV is a defective RNA viral agent[1] which requires HBV to supply the envelope protein. It only infects man in the presence of HBV[2]. Infection with HDV may occur simultaneously with HBV infection (co-infection) or it may occur in hepatitis B carriers (superinfection). With coinfection, the clinical course is usually self limiting because HDV cannot outlive the transient HBV infection, but with a superinfection the attack can be very severe. However, studies in the UK[3] and USA[4] have suggested that simultaneous infection of HDV with HBV does not necessarily produced increased clinical severity compared with HBV infection alone.

Screening for the HDV is not often requested routinely. Few studies have been done to monitor the number of persons with hepatitis delta infection in Malaysia. Two studies published in the Institute for Medical Research, Kuala Lumpur found that in 1985[5], 17.8% (4 of 27) and in 1989[6], 20% (7 of 35) of the HBsAg positive intravenous drug users (IDU) screened were anti-HDV positive. An earlier study in 1985[7] did not detect the hepatitis delta virus in 176 HBsAg positive blood samples screened in the University Hospital, Kuala Lumpur.

This study was done to look at a number of hepatitis B surface antigen (HBsAg) positive IDU who also had the HDV as well as to study the presence of HBeAg/Ab and the human immunodeficiency virus (HIV) in this population.

Method

Between 1990 and 1992 blood from 3,138 intravenous drug users (IDU) was sent for HBsAg screening to the Blood Services Centre, Hospital Kuala Lumpur. Of those screened 12.3% (386) were found positive for HBsAg. Samples from 44 HBsAg positive IDU which had sufficient serum were chosen to test for anti-HDV by the competitive enzyme immunoassay (EIA) from Abbott Laboratories; HBsAg, HBeAg and anti-HBe were screened using the Abbott Radioimmunoassay kits, and anti-HIV 1 antibody was detected using the Wellcozyme EIA kits. No attempt was made to look for delta antigen in the serum because it occurs only in the early phase of infection[1]. The serodiagnosis of hepatitis delta therefore rests on the detection of delta antibody. In any case the presence of delta antibody in serum reflects ongoing delta replication in the liver.

Results

This study shows that out of the 44 HBsAg positive IDU, 15 (34%) were found to have antibodies to the HDV. These 44 were all males of whom 25 were Malays, 13 Chinese, five Indians and one Albanian. They were between 19 and 61 years old with the majority in the 20 to 31 age group (see Table I). Thirty-nine per cent (17 out of 44) were HBeAg positive, 41% (18 out of 44) were anti-HBe positive and 19 had no HBe markers. Table II shows the markers of IDU who were delta antibody positive and HBeAg/Ab positive – 47% and 53% respectively. There is no difference in HBe positivity (indicating viral replication in the liver) and anti-HBe positivity among delta positive persons and HBsAg positive persons screened.

Only three out of 44 (6.8%) tested were anti-HIV positive and all three were from 1992 samples reflecting the increasing prevalence of HIV infection in IDU population in Malaysia. Two of the three HIV carriers were also delta antibody positive. Table III shows the prevalence of anti-HIV in IDU screened at HKL has increased from 2.5% in 1990 to 16.5% in 1992 (unpublished data).

In 1990 blood samples from 19 IDU with HBsAg positivity were screened and seven (36.8%) were anti-delta positive. In 1991 there were only four samples and one (25%) was anti-delta positive. In 1992, 21 IDU with HBsAg positivity were screened and six (28.6) were anti-delta positive.

Discussion

The numbers are small in this study but they do suggest that more than 25% of HBsAg positive IDU tested have HDV infection. More of the IDU may have been infected by the delta virus but as circulating delta antigen and delta antibody are often undetectable once HBsAg disappears, retrospecting sero-diagnosis

Table I
Delta antibody in HBsAg positive IDU

Age (years)	Tested	No. Positive (%)
10 - 19	1	0
20 - 29	20	8 (53%)
30 - 39	19	7 (47%)
40 - 49	1	0
50 - 59	2	0
60 - 69	1	0
Total	44	15 (34%)

Table II
HBeAg/Ab markers in HBsAg positive IDU

	HBeAg positive	Anti-HBe positive	No. HBe markers	Total screened
HBsAg Positive	17 (39%)	18 (41%)	9	44
Delta Ab +ve (%)	7 (47%)	8 (53%)	0	15

Table III
IDU screened for anti-HIV at HKL 1990 - 1992

Year	1990	1991	1992
No. tested	509	1074	1474
Anti-HIV positive	13	116	244
Percentage	2.5 %	10.8 %	16.5 %

cannot be made as HDV markers usually do not outlast a resolving HBV infection.

Unfortunately, further information on these patients could not be obtained, therefore the reasons for the increased risk for both delta and anti-HIV 1 viruses in 1992 could not be identified.

Some of the possibilities may be that these IDU were more frequent users of injected drugs or were infected from a common HDV infected source locally, or had travelled overseas and got infected.

The recognition that HDV may influence the liver pathology[2] in carriers of the hepatitis B surface antigen should make testing for the antibody to HDV in the sera done for HBsAg positive patients with liver pathology. In patients with chronic HBV and HDV coinfection, the HDV supresses HBV replication without significant effect on the expression of HBsAg[7]. Thus HBV inhibitory mechanism of HDV, if

Table IV
Number of HIV infected persons detected in Malaysia: 1985 - 1993

Year	Total
1985	0
1986	4
1987	5
1988	23
1989	183
1990	662
1991	1686
1992	2417
1993	2516

identified, could provide a new treatment for chronic HBV infection[2].

HBV and HIV infection coinfection may occur because the risk factor for the two viruses are similar. The liver disease in such coinfection is usually mild, despite active HBV replication (with HBeAg positivity). On the other hand, HBV may enhance HIV replication[2]. In this study there were three cases with HBV and HIV coinfection.

HIV carriers in the IDU screened in HKL increased from 2.5% in 1990 to 16.5% in 1992 (Table III). A similar increased is seen in the Ministry of Health data on HIV infected persons in Malaysia, as shown in Table IV. Eighty per cent of the HIV carriers in Malaysia are IDU (Figure 1). It is therefore not surprising that more HIV carriers were admitted to the hospital for treatment since 1990. Therefore all health care workers should practice Universal Precautions to protect themselves from HIV and Hepatitis.

In 1985, How *et al*[7] did not detect delta infection from 176 HBsAg positive serum samples. A subsequent study in 1986[5] showed that four (17.8%) of 27 IDU had delta markers. In 1989[6] of the 35 IDU tested, seven (20%) had evidence of delta infection. In this study, 15 out of 44 (34%) HBsAg positive IDU were anti-HDV positive (Table V). Thus there is a progressive increase in the number of delta antibody detected. While the numbers studied so far are small, they do suggest an increase in the incidence of delta infection in IDU population in Malaysia.

A surveillance on prevalence of HDV in IDU should be maintained to monitor the risk of delta infection in the Malaysian population.

The campaign by the Ministry of Health to vaccinate all newborns for hepatitis B will protect the next generation of Malaysians against not only hepatitis B, but also the delta virus, and substantially reduced the risk of delta virus causing liver damage.

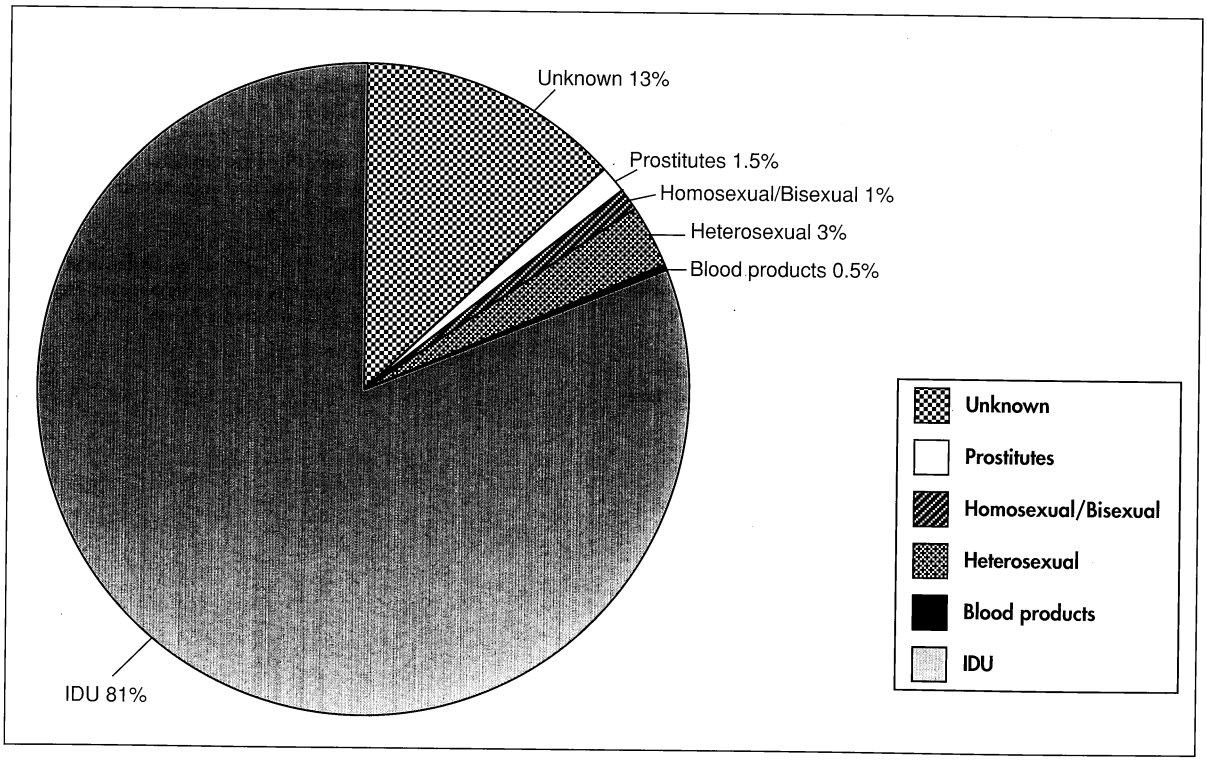

Fig. 1: Distribution of HIV by risk behaviour in Malaysia

Table V
HBsAg positive IDU tested for delta antibody: 1985 – 1992

Year	No. exam HBsAg	Delta Ab positive	Reference
1985	176	0	6 (UH)
1986	27	4 (17.8%)	4 (IMR)
1987	35	7 (20%)	5 (IMR)
1990–1992	44	15 (35%)	Present study (HKL)

Acknowledgement

We would like to express our thanks to the Director General of Health and Director of Hospital Kuala Lumpur for permission to publish this paper and to Encik Amran and staff of HIV/Hepatitis Lab for their assistance in this study.

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