Hepatitis B virus co-infection is less common in HIV positive Indian patients

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Abstract

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) frequently coexist with HIV virus due to its common routes of transmission and associated liver disease which tends to challenge HIV treatment. The ethnic variations and data from the Asian subcontinent on this aspect are not available to our knowledge.

The aims of this paper are to study the prevalence of HBV and HCV infections in HIV positive patients and the mode of their acquisition. The study was conducted at the National Institute of Communicable Diseases (NICD), New Delhi from June 2003 to January 2004. All the study patients provided consent. A detailed questionnaire, routine hematological and bio-chemical tests and clinical examination of these patients were done. All patients were HIV ELISA Rapid positive and confirmed by western blot. Serological markers, HBsAg, HbeAg, Anti Hbe and Anti-HCV, were done with third generation ELISA kits and HBV DNA quantified using the bDNA technique. The data was subsequently analysed using SPSS software.

100 HIV positive patients were included in our study whose mean age was 32.74 ± 9.4 years, male:female=71:29 and BMI was 19.66 ± 3.2. 13 patients (13%) were HBV co-infected (M:F=10:3), of which 8 patients were HBeAg positive, 3 were positive for Anti Hbe and 2 patients were negative for both HBeAg and Anti HBe. None of the patients were found to be Anti HCV positive. Mode of transmission in all HIV positive patients was predominantly by sexual route (91%; n=91). 12 out of 13 HBV co-infected patients were also found to be infected by sexual route (p=0.65). Multivariate analysis with respect to HBV infection was done with the following variables—Education, occupation, per capita income, wt loss and clinical symptoms—and they were found to be statistically insignificant. Our data suggest that HBV is less prevalent with HIV as reported in Western countries and the relevant reasons need to be considered.
Keywords: human immunodeficiency virus, Hepatitis B virus, co-infection, prevalence.

1 Introduction

1.1 Prevalence of Hepatitis B

Hepatitis B nowadays is a major leading cause of chronic liver disease and hepatocellular carcinoma in the world. Over 370 million people around the world have already been infected with Hepatitis B virus (HBV).

1.1.1 Prevalence of HBV and HIV co-infection

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) frequently coexist with HIV virus due to its common routes of transmission and associated liver disease which tends to challenge HIV treatment. Diseases of the hepatobiliary system are major problems in HIV infected people. It has been estimated that approximately one third of deaths in HIV positive patients is in some way related to liver disease. In the USA, Western Europe, and Australia, both the human immunodeficiency virus (HIV) and Hepatitis B virus (HBV) are transmitted by sexual or parenteral routes [1]. There was only one study from the Indian subcontinent which has evaluated the spectrum of liver disease in HIV infected patients [2]. There is much less data available from India on this aspect [3].

1.1.2 Sero-prevalence of HBV in HIV positive patients

Over 95% of HIV-infected individuals have evidence of exposure to HBV infection. Also, HIV has significant impact on the course of HBV infection. It is associated with approximately a threefold increase in the development of persistent antigenemia [4]. The epidemiologies of the two infections overlap such that ≥90% of persons with the acquired immunodeficiency syndrome (AIDS) have markers of past or current HBV infection [1]. Hepatitis B surface antibody (anti-HBs) or hepatitis B core antibody (anti-HBc), are found in approximately 90% of AIDS patients. Further, there is increased infectivity for chronic HBV in HIV-positive persons regardless of their clinical state or laboratory evidence of immunosuppression. i.e. HbsAg was found 10 times and VDRL reactivity 6 times more often in HIV positive donors as compared to HIV negative donors [5]. This was because of a higher prevalence of both HBeAg and HBV-DNA in the serum of chronic HBV carriers with concurrent HIV infection. At least two mechanisms could produce clinically significant interactions between these two viruses. First, both have a stage of reverse transcription in their replication cycles, which may be important in doubly infected cells. Second, destruction of HBV-infected hepatocytes with consequent clearance of the hepatitis B virus is thought to be mediated by cytotoxic lymphocytes [6–8]. Also HIV infection predisposes HBV carrier state to as high as three fold than in only HBV infected individuals. This is because HBV clearance is dependent upon normal functioning of the immune system specially T-Helper cells, which is the primary defect in HIV positive patients. Alternatively, HBV infection resolution may be dependent upon other components like cytotoxic T lymphocytes, which in turn are dependent upon T-Helper cells [8]

Since there is a paucity of data from developing countries, we therefore undertook the present study to examine the sero-prevalence and risk factors for HBV in AIDS patients.

2 Materials and methods

The study was conducted at the National Institute of Communicable Diseases (NICD), New Delhi and Dept. of Gastroenterology, G. B. Pant Hospital, New Delhi where all the HIV positive patients, by ELISA Rapid Simple and confirmed by Western Blot, coming for CD4 counts in the AIDS laboratory were included. The study period was from June 2003 to January 2004. The patients were interviewed, examined and investigated with written consent. A total of 100 patients agreed to give interviews, submit to examination and investigation and were included in the study.

The questionnaire and examination comprised of information regarding identification data, clinical features, mode of transmission, anthropometric measurements, and general physical and systemic examination.

The questionnaire was pre-tested, pre-coded and semi-open ended. Information was collected on the following major aspects:

1) Sociodemographic data: age, sex, education, income, occupation, address including socio-economic status according to modified Kuppuswamy classification.
2) General physical examination including anthropometric measurements
3) Mode of transmission
4) Clinical manifestations by history and examination
5) Stage of the disease
    a. Acute HIV syndrome
    b. Asymptomatic stage
    c. Symptomatic stage
6) Viral Investigations
    a. Anti HIV 1 and 2 (confirmed with western blot)
    b. HBsAg
    c. HBeAg
    d. Anti-HBe
    e. Anti HCV
    f. HBV DNA quantification

The data was subsequently entered into the computer in MS.EXCEL and analysed using software SPSS. Chi-square test, T-test and logistic regression and P values less than 0.05 were taken to be significant.

3 Results

As depicted in table 1, out of all HIV positive patients, the maximum number were illiterate followed by high school and only one patient was a postgraduate.

Only 3% of all HIV positive patients were professional. Most of them were unemployed followed by businessmen. Unskilled workers were the least represented. In the socio-economic status of HIV positive patients as per modified Kuppuswamy classification, the majority of them belonged to class IV (52%) followed by class III and there was no one in class I.

Table 1: Socio-economic status according to education, income and occupation of study subjects.

EDUCATION STATUS	N=100
1. Illiterate	21
2. Primary Education	16
3. Middle school	17
4. High school	16
5. Graduate	14
6. Post-Graduate	1
OCCUPATION	N=100
1.Unemployed	37
2. Unskilled worker	2
3. Semi-skilled worker	15
4. Skilled worker	9
5. Businessmen	23
6. Semi- Professional	11
7. Professional	3
INCOME per capita per month	N=100
<450 Rs	5
450-1349 Rs	52
1350-2249 Rs	31
2250-3374 Rs	8
3375-4499 Rs	4
4500-8999 Rs	0
>8999 Rs	0
SOCIO-ECONOMIC STATUS	N=100
V	11
IV	52
III	31
II	6
I	0

Figure 1 shows the socio-economic status of HBsAg positive and HBsAg negative subjects.

Table 2 shows the distribution of study subjects according to their age, sex, height, weight and BMI shows male to female ratio of 71:29, mean age was 31.8 yrs, mean height of 1.58 m, mean weight of 51.7 kg and BMI of 20.4 was found. On application of logistic regression analysis, taking HBsAg as dependent variable and education, income, weight, BMI as independent variable only BMI was found to be marginally significant.

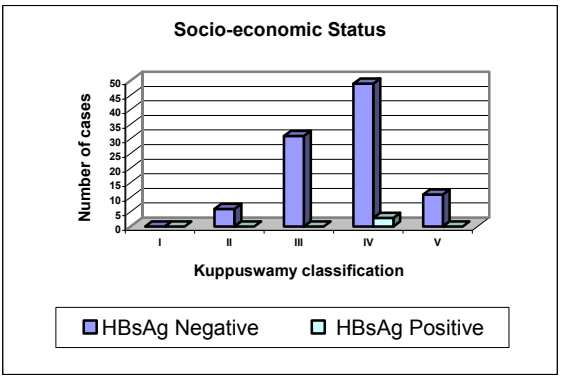

Figure 1: The socio-economic status of HBsAg positive and HBsAg negative subjects.

Table 2: The baseline characteristics of study subjects.

SEX (Male: Female)	71:29
AGE(Years)	31.8±9.4
HEIGHT(m)	1.58±0.1
WEIGHT(Kg)	51.7±14.9
BMI(Kg/m^2)	20.4±4.3

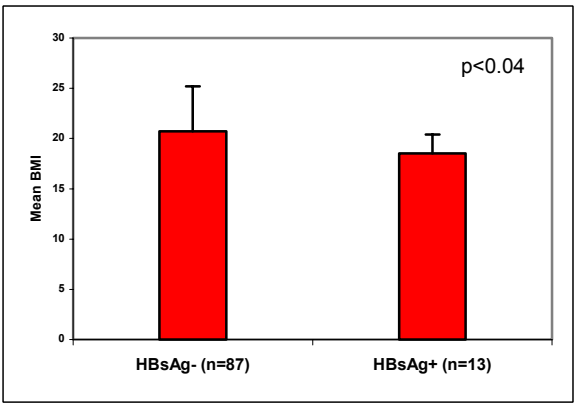

Figure 2.

Figure 2 shows that BMI is significantly related with respect to HBsAg.

As shown in table 3, the group with HBsAg positive subjects has less risk i.e. odds ratio of 0.615 as compared to HBsAg negative group for BMI (which is not significant). This means that if there is an increase of 1 unit in BMI then the risk of HBsAg positive subjects is decreased by 0.615 times.

Table 3: The significance of socio-economic status, weight and BMI with respect to HBsAg.

		B	S.E.	Validity	Degree of freedom	Significance	Exp(b)
Step 1 (a)	Education			3.459	6	.749	
	Illiterate	.953	1.133	.708	1	.400	2.594
	Primary Education	1.495	1.053	2.015	1	.156	4.460
	Middle school	-.282	1.353	.044	1	.835	.754
	Intermediate	- 9.401	34.816	.073	1	.787	.000
	Graduation	.078	1.287	.0040	1	.952	1.081
	Post-Graduation	-.955	173.325	.000	1	.996	.385
	Occupation	.144	.265	.296	1	.586	1.155
	Income		2.986	2.986	4	.560	
	<450 Rs	-2.700	1.712	2.487	1	.115	.067
	450 to 1349 Rs	-3.015	1.712	2.487	1	.087	.049
	1350 to 2249 Rs	-10.719	55.326	.038	1	.846	.000
	2250 to 3374 Rs	-10.750	71.517	.023	1	.881	.000
	Weight	.082	.073	1.239	1	.266	1.085
	BMI	-.486	.247	3.866	1	.049	.615
	Constant	5.548	3.139	3.123	1	.077	256.779

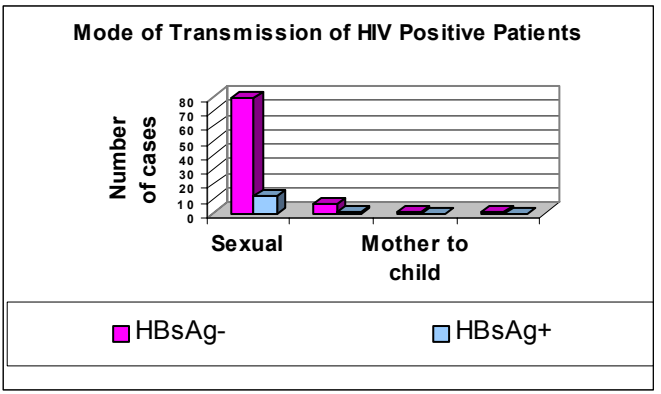

Figure 3.

Figure 3 shows the mode of transmission in HbsAg positive and HbsAg negative subjects. The majority of study subjects have a sexual route as the mode of transmission.

Table 4: The clinical manifestations of study subjects.

VARIABLE	(N=100)
Weight loss	45
Chronic Diarrhea	36
Chronic Fever	60
Persistent Cough	41
Tuberculosis	36
Generalized Pruiritis	18
Recurrent Herpes Zoster	1
Oropharyngeal Candidiasis	31
Generalized Lymphadenopathy	20
Chronic Herpes Simplex	7
Neurological impairment	4
Jaundice	9
Pneumonia	5
Anorexia	18
Joint Pain	4
Insomnia	2

The majority of the subjects had a history of fever, weight loss and diarrhea for more than one month and a history of prior pulmonary tuberculosis with or without sputum positive for Mycobacterium.

In table 5, most of the patients were in the symptomatic stage and only 9% were in the acute HIV Syndrome stage and 19% in the asymptomatic stage.

Table 5: HIV stages according to CDC (Centre for Disease Control).

STAGE	(N=100)
Acute HIV Syndrome	9
Asymptomatic stage	19
Symptomatic stage	72

Table 6: Serological analysis of study subjects.

MARKER	No. of Positive subjects (N=100)
HBsAg	13/100
HBeAg	8/13
Anti-HBe	3/13
Anti-HCV	0
HBV DNA	5/13

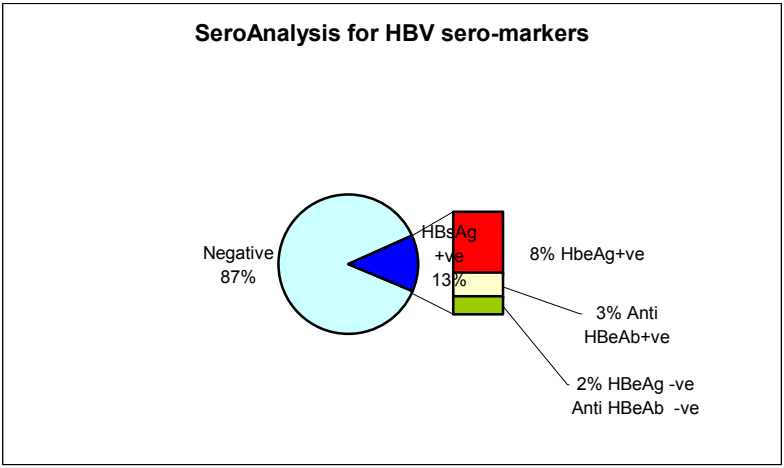

Figure 4: The distribution of HBsAg, HbeAg and AntiHBeAb in HIV positive subjects.

Out of the 100 HIV positive patients, only 13% were found to be HBsAg positive and out of these 13, 8 were HBeAg positive with a high replicative state. In the HIV patients, HBV DNA quantitative levels were much lower as only 5 patients had quantifiable DNA.

3.1 Discussion

Hepatitis B virus and hepatitis C virus frequently co-exist with the HIV virus due to its common routes of transmission and associated liver disease tends to challenge HIV treatment. HIV continues to spread in India mainly through heterosexual intercourse unlike the western world where it spreads relatively more among homosexual men and IV drug users and rarely through blood transfusion. It is due to the government of India ruling, which has mandated since 1992 the screening of donor blood for HBV and HCV infection along with HIV.

4 HBV co-infection in the world

When we compared our data of HIV co-infection with HBV infection with that of western data, the parameters such as mean age, icteric illnesses were found to be similar to that of our data [17]. Also our findings were in concordance with the fact that both HIV and HBV are mainly transmitted by sexual and parenteral routes and least by blood transfusion or mother to child transmission [7, 17]. Neil et al has shown has shown a high prevalence of HBV DNA in the serum of chronic Hepatitis B carriers with concurrent HIV infection whereas no such significant association was found in our Indian co-infected patients. One of the possible explanations for this low prevalence could be the interaction between

HBV DNA, HIV RNA and human genome. This causes some mutation in HBV genome, which either inhibits the HBV co-infectivity or promotes human resistance to HBV or HIV or both. Viral as well as host factor interactions must be studied to understand the underlying mechanisms in HIV and HBV co-infection.

5 HIV and HBV co-infection in India

The majority of reports on the spectrum of liver disease in HIV infected individuals have originated from the west. From India, there are many studies available on the prevalence of HIV, HBV and HCV infection individually in blood donors and high-risk population groups which do not have relevance to our study of co-morbidity [18]. To date there are very few studies available from the Indian subcontinent, which have shown the prevalence of HBV and HCV co-infection in HIV infected patients [2]. Our results from Central Northern India is similar to Rathi et al with HBsAg positivity of 13%, but contradicts Anti HCV positivity of 0%. This discrepancy with respect to Anti HCV may be solved by performing HCV RNA qualitative polymerized chain reaction, results of which are shortly to conclude on HCV co-infection in Indian HIV patients.

Thus we conclude, 13% of HIV infected patients were found to be co-infected with HBV infection with high replicative state in 8/13 (61.5%) HBeAg positive and low HBV DNA levels, most of them were found to be infected by sexual route.

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