

Hepatitis B and C Positivity in Various Categories of Human Immunodeficiency Virus Seropositive Individuals in a Regional STD Centre-an Eight-Year Evaluation of Trends and Risk Factors

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Abstract: Problem statement: Among the various infections whose incidence has increased since the advent of HIV/AIDS, Hepatitis B and C stand out clearly. This is so because the routes of transmission of these infections are essentially the same as those of HIV/AIDS, making co-infections a common occurrence. The risk of infection for Hepatitis B and C is several times more than it is for HIV/AIDS and the trends in incidence of hepatitis are changing over time, which is what prompted the following 8 year study. **Approach:** The study was carried out at a Regional STD Centre in Delhi, among various categories of HIV seropositive persons (patients with STDs, AIDS, Asymptomatic cases and contacts of HIV seropositives), who were tested for HBsAg and HCV antibodies using approved kits. **Results:** Of 3197 HIV sero-positive samples including males, females, children and transgenders, 1545 were tested for HBsAg and 1553 for HCV antibodies. Of these, 8.9% tested positive for HBsAg, 8.3% for HCV antibody and 0.4% for both. Hepatitis B co-infection was present in all categories of HIV seropositive patients. A large proportion of HBsAg positives were full blown AIDS cases, while HCV positivity was very common among IVDUs. The incidence of HBV and HCV cases over 8 years, seem to show a downward trend, the reasons for which are discussed. **Conclusion:** Although extensive sero-positivity data on Hepatitis B and C in HIV patients is available from all over the globe, studies involving the various categories of HIV sero-positive cases, especially from developing countries, are scarce. Detecting the presence of Hepatitis B and C markers in HIV positive individuals will not only help formulate better treatment protocols, but also improve prognosis, survival and management of these patients and fuel adequate measures for appropriate allocation of resources in eliminating HBV and HCV infections too.

Key words: Hepatitis B, hepatitis C, HIV seropositive, asymptomatic, STD patients

INTRODUCTION

The global AIDS epidemic has brought in its wake a host of opportunistic infections, making it a truly formidable foe of mankind with enormous public health significance. Among the various infections whose incidence has increased in the presence of HIV infection, Hepatitis B and C (HBV and HCV infections), stand out clearly. This is so, because the routes of transmission of these diseases are essentially the same as those of HIV/AIDS (Kottlilil *et al.*, 2005; Tankhiwale *et al.*, 2003). Although HBV and HCV infections in the HIV setting, are not listed as opportunistic infections by Center for Disease Control and Prevention (CDC), they are common co-existing infections (Thio, 2003). Hepatitis B is one of the

commonest infections worldwide, with about 300 million people infected with the virus (Arora and Mann, 2007) and two thirds of all liver cancers due to the virus (Lee, 1997). In India, nearly 4.7% of the general population are carriers of HBV surface antigen (HBsAg), with a carrier pool of around 43 million (Arora and Mann, 2007; Acharya, 1999). Studies have shown that histological damage of liver may progress more rapidly in HBV/HIV co-infected patients, leading to cirrhosis in a shortened timeframe (Zago *et al.*, 2007). Also, HIV sero-positive patients on antiretroviral drugs, frequently show liver enzyme elevations if co-infected with Hepatitis B virus, thereby requiring extreme caution in the use of ART drugs (Soriano *et al.*, 2005). Furthermore, vaccination is an option available for Hepatitis B prevention, which makes it relevant to

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screen for the infection in HIV seropositive individuals (Soriano *et al.*, 2005).

Hepatitis C is another important cause of chronic liver disease. One third of HIV-infected individuals worldwide suffer from chronic hepatitis C, but HCV affects more than 75% of HIV positive subjects infected by the parenteral route (Soriano *et al.*, 2006). Thus, co-infection of HIV with HCV is more common in people with exposure to contaminated blood, making IV drug users and haemophiliacs significant target groups (Chowdhury *et al.*, 2003). In India too, 1-1.5% of the population is positive for HCV antibodies (Chowdhury *et al.*, 2003; Baveja *et al.*, 2003) and the seroprevalence rate among blood donors in New Delhi, India is 1.85% (Panigrahi *et al.*, 1997).

The incidence of HIV positive persons being co-infected with Hepatitis B or C viruses, or both, is being increasingly reported all over the world, including India (Saha *et al.*, 2000). Even so, not all three infections enjoy the same importance as far as funding, research and clinical studies are concerned. The reasons for this are obvious- while Hepatitis B has an effective vaccine and treatment modalities, Hepatitis C has no vaccine but a fairly good treatment regimen. HIV/AIDS has no vaccine or cure, at best, an HIV infected person can only receive treatment to improve his symptoms and prolong life.

Hepatitis B and C infections are transmitted more easily than HIV. The risk of acquiring the infection after exposure through needlestick injury from an infected individual, is 33.3% for Hepatitis B and 1.9% for Hepatitis C, while it is only about 0.3% for HIV infection (Muralidhar and Muralidhar, 2006). Yet, the thrust has always been more on HIV/AIDS for reasons mentioned above.

The trends in incidence and risk factors for hepatitis B and C are clearly changing over time and this is what prompted the following study, carried out over a period of 8 years. Moreover, hardly any study has looked into the incidence of these co-infections in various categories of HIV positive individuals.

MATERIALS AND METHODS

The study was carried out over a period of 8 years from 1st January 2000 to 31st December 2007, at the VMMC and Regional STD Centre of Safdarjung Hospital, New Delhi, one of the largest tertiary care hospitals in India. The study group included the following categories of HIV sero-positive persons:

- Direct walk-in persons attending the Integrated Counseling and Testing Centre (ICTC) who

underwent HIV testing and were confirmed to be seropositive-Asymptomatic persons (AS) and contacts

- In-patients admitted to various wards in the hospital, with high degree of suspicion of AIDS (due to the presence of opportunistic infections), referred to the Centre for confirmation of their HIV status and found positive (AIDS patients)
- Patients found to be HIV sero-positive in private hospitals or laboratories outside, referred to the centre for confirmation of status and found to be positive (contacts and AS)
- Patients attending the male and female STD clinics for various STI/RTI symptoms and advised HIV testing and found to be sero-positive (STD patients)

In all the above four categories of patients, the HIV test was performed after appropriate pre test counseling and informed written consent.

A total of 39,131 blood samples were collected over 8 years from 1st Jan. 2000 to 31st Dec 2007, sera separated and tested for HIV antibodies by ELISA/Rapid/Simple (E/R/S) methods approved by National Aids Control Organization (NACO). ELISA method used was Microlisa for HIV by J. Mitra and Co. Ltd. Rapid test used was Retroquic-Qualpro Diagnostics or Acon-Acon Biotech, China or Capillus-(Trinity Biotech PLC, Ireland). The Simple test kits used were Combaids by Span Diagnostics Ltd. All testing strategies were the ones recommended by NACO guidelines and conforming to WHO standards.

In all, 3,197 samples were confirmed to be HIV sero-positive (8.2%). The sera of confirmed HIV sero-positive individuals were tested for HBsAg antigen using 3rd generation HEPALISA and for HCV antibodies using the HCV Microlisa kit (both manufactured by J Mitra and Co. Ltd. and having passed WHO phase I Geneva evaluation), after due formalities like, recording complete patient history and clinical details at the ICTC.

RESULTS

Of the 39, 131 sera samples tested for HIV antibodies, 3,197 were confirmed to be positive (8.2%). Out of these, 2 242 (70.1%) were males, 801 (25.1%) females, 80 (2.5%) male children, 52 (1.6%) female children and 22 (0.7%) transgenders. (Note: Although 22 transgender persons were included in the study, they were categorized as females as per their own submission during the counseling sessions) (Fig. 1).

Table 1: HIV sero-positivity over the 8 year period in various patient categories

HIV +	2000	2001	2002	2003	2004	2005	2006	2007	Total
STD cases	682 (62) 9.10%	656 (34) 5.20%	994 (43) 4.30%	629 (35) 5.60%	771 (45) 5.80%	763 (38) 5.00%	314 (24) 7.60%	527 (27) 5.10%	5336 (308) (5.80%)
AIDS cases	907 (67) 7.40%	848 (107) 12.60%	611 (127) 20.80%	854 (181) 21.20%	1242 (252) 20.30%	1524 (271) 17.80%	1134 (228) 20.10%	1471 (289) 19.60%	8591 (1522) (17.70%)
Contacts	602 (20) 7.30%	482 (22) 4.60%	689 (41) 5.90%	557 (30) 4.90%	445 (44) 10.10%	929 (68) 7.40%	1449 (101) 7.00%	349 (78) 22.30%	5502 (404) (7.30%)
Asymptomatic (AS)	2847 (85) 4.90%	2697 (102) 3.80%	3861 (144) 3.70%	1853 (137) 7.40%	1758 (113) 6.50%	2426 (118) 4.90%	1705 (96) 5.60%	2555 (168) 6.60%	19702 (963) (4.90%)
Total	5038 (234) 4.6%	4683 (265) 5.7%	6155 (355) 5.8%	3893 (383) 9.8%	4216 (454) 10.8%	5642 (495) 8.8%	4602 (449) 10.0%	4902 (562) 11.5%	39131 (3197) (8.2%)

Note: Figures in parentheses denote positive numbers

Table 2: Results of year-wise HBsAg and HCV antibody tests and their positivity

	2000	2001	2002	2003	2004	2005	2006	2007	Total
HBsAg tested	222	147	95	42	373	209	199	258	1545
Hepatitis B antigen positive	29 (13.1%)	16 (10.9)	4 (4.20%)	6 (14.3%)	44 (11.8%)	18 (8.6%)	9 (4.5%)	12 (4.7%)	138 (8.9%)
HCV tested	201	231	318	355	55	209	0	184	1553
HCV positive	13 (6.5%)	26 (11.3%)	35 (11.0%)	38 (10.7%)	4 (7.30%)	7 (3.30%)	0	6 (3.30%)	129 (8.3%)
HBsAg + HCV tested	190	132	95	42	55	209	0	184	907
HBsAg + HCV positive	2 (1.00%)	5 (3.80%)	1 (1.00%)	1 (2.40%)	1 (1.80%)	3 (1.4%)	0	0	13 (1.40%)

Note: Figures in parentheses indicate percentage positive

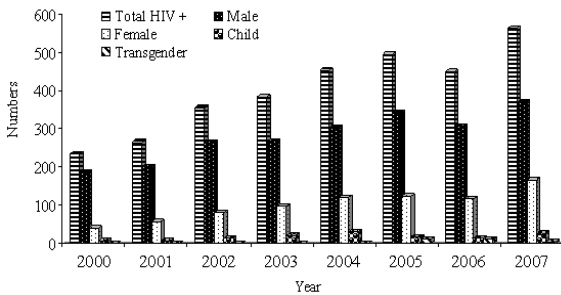


Fig. 1: Trend of HIV seropositivity over 8 years

The break up of these sample categories shows that, out of 3,197 HIV seropositive cases- 308 were STD cases (9.6%), 1522 suspected AIDS cases (47.6%), 404 contacts of HIV seropositive cases (12.6%) and 963 Asymptomatic HIV seropositive cases (30%) (Table 1).

There were 2,154 sera samples from patients belonging to more than one category (e.g., STD + AIDS in the same patient and so on), out of which 73 were HIV seropositive (3.4%).

Of the 3,197 HIV positive samples, only 1,545 were tested for HBsAg and 1,553 for HCV antibodies, due to insufficient specimen quantity/ loss of sera samples/ non availability of kits during certain periods. Also, only 907 sera samples were tested for both HBsAg and HCV antibody (Table 2).

Details of Hepatitis B positivity over the 8 year period are as follows:

Total number of samples tested for HBsAg were 1,545, of which 138 were positive (8.9%). Out of the positives, 117 (84.8%) were males, 17 (12.3%) females

and 4 (2.9%) children. The major mode of transmission was heterosexual route-128 (92.8%), while 5 (3.6%) cases of blood transfusion, 3 (2.2%) cases of IV drug use and one instance (0.7%) of mother to child transmission, were noted. There was one case where transmission mode could not be arrived at and men having sex with men (MSM) transmission was conspicuous by its absence.

Among the 138 cases positive for Hepatitis B surface antigen, 27 were diagnosed cases of STIs (19.6%), of which genital ulcers constituted 17 cases (12.3%), while other STDs were 10 (7.2%). Twenty five cases of HIV-TB were HBsAg positive (18.1%) and other opportunistic infections of AIDS cases totaled 89 (64.5%). There were 39 Asymptomatic cases (28.3%). Ninety nine cases had a combination of symptoms.

The 99 symptomatic cases were associated with the following combinations of illness:

- Genital ulcer cases + AIDS = 17 (19.1%)
- Other STDs (discharge/warts) + AIDS = 10 (11.2%)
- Tuberculosis in AIDS = 25 (24.7%)
- Other AIDS cases = 47 (diarrhoea, PGL, weight loss, fatigue, asthenia, prolonged fever)

Similarly, the details of Hepatitis C antibody positivity over the 8 year period, were as follows:

Total number of samples tested for HCV antibody were 1,553, of which 129 (8.3%) were positive. Out of the positives, 101 (78.3%) were males, 26 (20.2%) females and 2 (1.5%) were children. The commonest

mode of transmission was by heterosexual route-79 (61.2%), followed by IV drug users 44 (34.1%), while 4 (3.1%) cases of blood transfusion and 2 (1.6%) of mother to child transmission were noted. Once again, as in the case of HBsAg, MSM transmission was conspicuous by its absence.

Among the 129 cases positive for Hepatitis C antibody, 11 were diagnosed cases of STIs (8.5%), of which genital ulcers constituted 6 cases (4.7%), while other STDs totaled 5 (3.9%). Eighteen cases of HIV-TB were present (14%) and other opportunistic infections of AIDS cases totaled 25 (19.4%). There were 75 asymptomatic cases (58.1%).

Both HBsAg and HCV antibodies were tested in 907 samples of which 13 were positive (1.4%). (Males = 10, Females = 2 and Child = 1). Out of the 13 positives, 7 were IV drug users, 5 had tuberculosis and 5 had other features of AIDS (diarrhoea, fever, rash and PGL).

DISCUSSION

The present study revealed a steady increase in HIV seropositivity over the last 8 years (except a small dip in the year 2006). A similar trend was reported from this Centre in an earlier period of study too (Ray, 2004). Other studies from India also indicate this upward trend, which in turn points to an increase in high risk, as well as treatment seeking behavior over time.

Over the 8 year study, the incidence of Hepatitis B has shown a gradual decrease among HIV sero-positive cases, except in 2003, when there was an increase in cases, probably because the number of samples tested that year was not significant enough to make deductions and be indicative of the true incidence. This downward trend may be attributable to an increase in HBV vaccination status, which is being promoted actively, both in the Government as well as the private health sectors.

Hepatitis B co-infection was present in all categories of HIV seropositive patients viz. Asymptomatic cases, STD patients, IV drug users, post blood transfusion cases, contacts and children with parent to child transmission of HIV/AIDS. According to Dhanvijay *et al.* (1999) 28% of HIV infected individuals harbored Hepatitis B infection, while Ramanamma and Ramani (2000), in their study had 14.3% Hepatitis B positive cases. In this study, 8.9% of HIV positive subjects were HBsAg positive. While the previous two studies reflect the figures in Central and Southern states of India, respectively, our study was carried out in New Delhi, which is in the North and the capital of India. According to some studies (Soriano *et al.*,

2006), nearly 10% of HIV infected patients have Hepatitis B infection, which is nearly the same as our figures (8.9%), while in a Brazilian study the prevalence of chronic Hepatitis B virus infection was 3.8% (Zago *et al.*, 2007).

Like most other studies (Anvikar *et al.*, 2000; De los Angeles *et al.*, 2004; Konopnicki *et al.*, 2005) ours too had a distinct preponderance of male HIV positive patients associated with HBV and HCV infections as compared to females. In India, this may be attributed to the fact that female attendance in STD clinics is far less, because of socio-economic reasons. Females are busy taking care of children and the homefront and often neglect their own health. Also, being home makers and financially dependent, they usually rely on their male partners to take them to the health care facility.

The study by Anvikar *et al.* (2000) had a HBV carriage of 6.15%, solely in STD clinic attendees (Anvikar *et al.*, 2000), while it was 22.58% in a study by Dhanvijay *et al.* (1999). In the Brazilian STD clinic study, 37.6% of HIV positive attendees with STIs were positive for HBsAg (Zago *et al.*, 2007), while our study recorded 19.6%, which is closer to the figures in Indian studies.

Anvikar *et al.* (2000) reported that HBV positivity was highest in patients with ulcerative STDs compared to other types of STDs. This is corroborated in the present study too, where it was seen in 62.96% of patients with ulcerative STDs, compared to urethral discharge or other STDs. It is a well-known fact that genital ulcers facilitate the transmission of HBV by direct transfer of exudate through non-intact skin or mucous membrane (Anvikar *et al.*, 2000).

As regards the mode of transmission of Hepatitis B infection among HIV seropositive individuals (Soriano *et al.*, 2005), Soriano V *et al.* have reported close to 10% of HIV patients with HBV co-infection, among homosexual males (MSMs). Also, in the Brazilian study (Zago *et al.*, 2007), 13.6% of HBV cases were among MSMs. This group was conspicuous by its absence in our study. This again, may be attributed to the differences in socio-economic conditions between countries and regions. Hepatitis B positivity among IV drug users with HIV infection was 21.7% in the Brazilian study (Zago *et al.*, 2007), while our study had only 2.2%. Heterosexual route of transmission far outweighs other routes in the greater parts of the Indian subcontinent, for both HIV and HBV positivity.

As with Hepatitis B infection, the incidence of Hepatitis C, after an increase between 2000 and 2001, showed a steady fall over the next 5 years. This may

well be so, because the incidence of Hepatitis C infection is linked to exposure to parenteral transmission routes, like IV drug use and these practices, although existing, have probably reduced in number since the targeted intervention programme of the National AIDS Control Programme, in India, addressed the blood safety issues on a war footing.

Although heterosexual transmission route was highest in terms of sheer numbers, the incidence of Hepatitis C positivity, as seen in our study, was high in patients who were IV drug users (34.1%), a fact which several studies have corroborated (Arora and Mann, 2007; Soriano *et al.*, 2006). It is also quite common in STD patients, a finding noted by Bhattacharya *et al.* (2003) from South India.

Both HBV and HCV infections were uncommon in the paediatric HIV positive cases (2.9 and 1.5%, respectively). One of the reasons for this could be the infrequent occurrence of vertical transmission in India, especially for HBV infection, as shown by Acharya *et al.* (2006). As for HCV infections, there are hardly any reports in paediatric HIV positive cases from this part of the world. Moreover, HCV infection in India has a population prevalence of about 1% and occurs predominantly through transfusion or IV drug abuse (Acharya *et al.*, 2006), both of which are uncommon in children.

CONCLUSION

Although extensive sero-positivity data is available from all parts of the globe, well designed studies involving the various categories of HIV sero-positive cases, especially from developing countries, are scarce. While antiretroviral treatment needs to be given to the patient indefinitely, the treatment regimens for HBV and HCV infections are for a limited duration. This fact should be used to advantage in co-infected patients. Hence, it is important to detect presence of hepatitis B and C markers in HIV positive individuals to plan an appropriate treatment protocol, thereby improving prognosis, survival and management of HIV/AIDS patients. It is postulated that in case of HIV-HBV co-infected patients, HBV treatment may decrease the risk of HAART-related hepatotoxic events (Soriano *et al.*, 2006). Public health education, infection control practices and availability of an effective vaccine have led to a decline in HBV infections in developed countries. It remains a considerable cause of morbidity and mortality in HIV infected persons, requiring increased vigilance of physicians treating HIV patients (Brook *et al.*, 2008). The same is not true for Hepatitis C whose incidence is very high especially among IV

drug users. Useful data, made available from studies such as these, can fuel preventive measures and stimulate appropriate allocation of resources in eliminating HBV and HCV infections particularly in the much needed developing countries.

ACKNOWLEDGEMENT

The researchers are grateful to Ms. Renu Mehta (Senior technician) for valuable services rendered in the course of this study

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