



COINFECTION OF HEPATITIS B, HEPATITIS C AND SYPHILIS AMONG HIV POSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY

Microbiology

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ABSTRACT

Introduction: Human Immunodeficiency Virus (HIV) affects the immune system causing body's normal defense to break down, leaving it vulnerable to a host of life threatening diseases. High risk behaviors and routes of transmission for HBV and HCV are identical with HIV and other sexually transmitted diseases (STDs). Hence this study is carried out to determine coinfection of Hepatitis B, Hepatitis C and Syphilis among HIV positive patients on Antiretroviral Therapy at Regional STI Training, Research and Reference Laboratory (RSTRRL), Department of Microbiology, Mumbai.

Aim and Objective: To determine seroprevalence of Hepatitis B, Hepatitis C and Syphilis coinfection in HIV patients on antiretroviral therapy.

Material and Methods: A retrospective study was conducted during April 2016 to March 2018 in RSTRRL. Blood samples received in laboratory from ART clinic for HBV, HCV and syphilis testing were included in study. HBsAg and HCV antibody ELISA and VDRL Calcutta antigen for syphilis were performed. All VDRL positive samples were also tested by TPHA.

Results: 2771 patients on ART attending ART centre were included in this study. Maximum patients were males (55.18%). 66.73% of these were in the age group of 26-45 years which is the reproductive age group. Seroprevalence of Hepatitis B, Hepatitis C and syphilis was 4.3%, 1.6% and 1.8% respectively. Co-infection of HBV and syphilis, HBV and HCV, HCV and syphilis were found to be 0.4%, 0.07% and 0.04% respectively.

Conclusion: Screening of Hepatitis B, Hepatitis C and syphilis should be included in diagnostic algorithm of HIV positive patients on ART as the antiretroviral drugs could be hepatotoxic. Hepatitis B screening and Hepatitis B vaccination should be given to HBsAg negative individuals attending ICTC should be initiated in the ICTC's.

KEYWORDS

HIV, Hepatitis B, Hepatitis C, Syphilis, Antiretroviral Therapy.

INTRODUCTION

The Acquired Immuno-Deficiency Syndrome (AIDS), which represents the final clinical stage of infection by the Human Immunodeficiency Virus (HIV) was reported for the first time in 1981.^[1]

HIV affects the immune system causing body's normal defense to break down, leaving it vulnerable to a host of life threatening diseases.^[2] High risk behaviors and routes of transmission for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) are identical with HIV and other sexually transmitted infections (STIs). Although HCV transmission mostly occurs through blood and blood products, sexual, vertical and accidental routes have been reported.^[2,3]

Due to the HAART (Highly Active Antiretroviral Therapy) life expectancy of people with HIV has increased.^[3] It has a major impact on HIV associated mortality in low and middle income countries and HIV is now identified as a chronic manageable condition. Although ART mediated CD4 recovery and reduction of HIV related immune activation and inflammation could contribute to HBV and HCV control, ART related toxicity is also a matter of great concern.^[4]

As people with HIV live longer on HAART, coexisting HBV and HCV infections can contribute to increasing morbidity and mortality become more prominent.^[5,6] HIV modifies the natural history of infection, leads to increased percentage of carrier state. It also hastens HBV and HCV related liver disease.^[3,6,7]

HIV infected persons are less likely to clear HCV viraemia, leading to rapid progression of liver disease which is becoming a leading cause of death.^[3,7] Similarly HCV infection is also associated with faster progression of HIV to AIDS, but HBV infection has no such impact.^[7,8] Moreover, ulcerative STIs provides great opportunity of HIV transmission. As there may be false negative serology in syphilis, treatment for all HIV positive patients with penicillin based regimen is suggested.^[3,8]

Chronic infection with HIV, HBV, HCV and STIs, currently pose major clinical and public health challenges.^[4,5]

In 2012, people living with HIV infection or AIDS were 35 million worldwide.^[1] Worldwide 240 million and about 150 million peoples are affected with chronic HBV and HCV infections respectively.^[4] About 1 million deaths per year are due to HBV and HCV infections, which represents 2.7% of combined causes of mortality. It has been estimated that worldwide around 30% of people with HIV are coinfecting with HBV or HCV.^[11]

India is the second most populous nation in the world. Indian subcontinent is classified under intermediate HBV endemic zone and has the second largest global pool of chronic HBV infections. India has a population of more than 1.2 billion.^[9] India is carrying a burden of 2.27 million HIV cases, 15 million HCV cases and 43 million HBV cases with 50 million of HBV carrier.^[9,10]

Considering the burden of HBV infected people in the country, this study was proposed to understand the coinfections of HBV and HCV with HIV among ART patients as disease severity, liver toxicity of ART and transmission of infections in the community and spouse can be monitored.

AIM AND OBJECTIVE

To determine seroprevalence of Hepatitis B, Hepatitis C and Syphilis and coinfection with HIV among patients on antiretroviral therapy.

MATERIAL AND METHODS

A retrospective analysis was conducted on data of the period April 2016 to March 2018 from Regional STI Training, Research and Reference Laboratory (RSTRRL), Department of Microbiology, Mumbai. Blood samples received in laboratory from ART clinic for HBV, HCV and syphilis testing, were included in study.

Serum samples from patients were tested for Hepatitis B surface

antigen (HBsAg) (Hepalisa, J. Mitra & Co. Pvt Ltd) and for anti-Hepatitis C virus (anti-HCV) antibody (SD HCV ELISA 3.0) by ELISA according to the manufacturer's instructions.

As per the recommendation of WHO and National AIDS Control Organisation (NACO), the testing strategy for the diagnosis of syphilis is followed in this Centre. Screening of all serum samples were performed for detection of cardiolipin antibodies by Venereal Disease Research Laboratory (VDRL) test using Calcutta antigen (VDRL antigen from Institute of Serology, Kolkata). After screening, samples which were reactive for VDRL antigen, then subjected to quantitative VDRL test. VDRL reactive sera were subject to confirmation with antitreponemal antibodies by TPHA test (IMMUTREP TPHA, Omega Diagnostics). VDRL and TPHA tests were performed as per the manufacturer's instructions.

RESULT

2,771 blood samples from patients on ART were received in the laboratory from April 2016 to March 2018. Of these 1529 (55.18%) were males, 1241 (44.79%) females and 1 patient was transgender. Maximum patients 66.73% were in 26-45 years age group which is the reproductive age group. The age and sex wise distribution of samples from patients on ART is given in Table 1.

Table 1: Age and sex wise distribution of HIV positive patients on ART attending ART centre.

Sex ↓	Age →	≤18 years	19-25 years	26-45 years	≥46 years	Total
M		81	103	937	408	1529 (55.18%)
F		52	74	912	203	1241 (44.79%)
TG		0	1	0	0	1 (0.03%)
Total		133 (4.8%)	178 (6.42%)	1849 (66.73%)	611 (22.05%)	2771 (100%)

M-Male; F-Female; TG-Transgender.

The result of HBV, HCV and VDRL and TPHA among HIV patients on ART are given in Table 2

Table 2: Number and percentage of HBV, HCV and VDRL and TPHA positive patients among HIV positive patients on ART (n=2771)

Sr.	Test	Number of positive	Percentage
1.	HBsAg ELISA	135	4.87%
2.	Anti-HCV Antibody ELISA	43	1.55%
3.	VDRL positive, TPHA positive	67	2.42%
4.	Only VDRL positive (Titre < 1:8)	6	0.22%

The following co-infection were found in the 2771 samples tested among HIV patients on ART are given in Table 3

Table 3: Coinfections among HIV positive patients on ART (n=2771)

Sr.	Co-infection	Number of positive	Percentage
1.	HIV + HBsAg	122	4.4%
2.	HIV + Anti-HCV Antibody	40	1.44%
3.	HIV + VDRL	61	2.2%
4.	HIV + HBsAg + Anti-HCV Antibody	2	0.07%
5.	HIV + HBsAg + VDRL	11	0.4%
6.	HIV + Anti-HCV Antibody + VDRL	1	0.04%

All VDRL positive samples were confirmed by TPHA

The following graph shows age wise distribution of seroprevalence of HBV, HCV and Syphilis co-infection among HIV positive patients on ART.

Statistical analysis

As coinfection was not seen in age group of ≤ 18 years (n=133) and TG (n=1), these patients were excluded from statistical analysis. Following table 4 shows gender wise distribution of presence or absence of coinfection. Odds ratio of 2.56 was obtained in the statistical analysis.

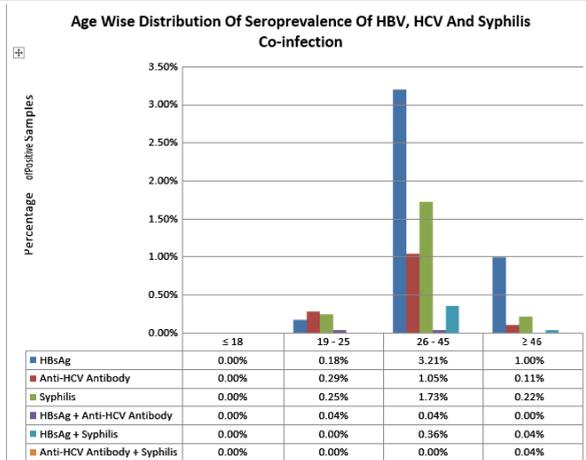


Table 4: Sex wise distribution of presence or absence of coinfection.

Sex ↓	Coinfection →	Present	Absent	Total
Male		176	1272	1448
Female		61	1128	1189
Total		237	2400	2637

Odds ratio = 2.56

Among 1448 males 12.15% (n=176) had coinfection compared to 5.13% (n=61) among 1189 females. Odds ratio is 2.56 which means males have 2.56 times more chances of getting coinfectd than females and prevalence of coinfection is significantly higher in males. [P value < 0.001; x² = 39.55]

Prevalence of coinfection among various age groups shown in table 5.

Table 5: Prevalence of coinfection among various age groups.

Age group (years)	Total number of patients	Number of coinfectd patients	Prevalence (%)
19 - 25	177	21	11.9
26 - 45	1849	171	9.3
≥ 46	611	39	6.4

Prevalence of coinfection is significantly more in between 19-25 years. [P value < 0.05 but > 0.02; x² = 7.02]

Distribution of coinfection among male and female within different age groups was done. In the age group of 19-25 years, frequency of coinfection in males were similar to that of females. [P value > 0.05; x² = 1.74] whereas in 26-45 years and ≥46 years, frequency of coinfection were significantly more in males. [P value < 0.001; x² = 26.896 (26-45 years) and x² = 12.24 (≥46 years)]

DISCUSSION

HIV is now considered a chronic condition affecting the immune system, due to which individual become vulnerable to other infections. HIV, HBV and syphilis share common routes of transmission. HCV is mainly transmitted through blood and blood products, sexual and vertical transmission have been reported. India is the second most populous country with second highest number of people living with HIV (PLHIV). Progression of HIV and enhanced immune suppression has effect on natural history and pathogenesis of these co-infections. Therefore monitoring is necessary for concurrent infections with HBV, HCV and syphilis in PLHIV. Failure to diagnose and treat these infections at early stage may results in complications such as increased disease severity, liver toxicity, cancer and even death.

Our study shows 66.73% (n=1849) of patients were in 26-45 years age group which is the reproductive age group. Males constituted 55.18% (n=1529) whereas females were 44.79% and only one was transgender (TG) in this study. Co-infection was probably not seen in ≤ 18 years as these may be adolescents who may have acquired HIV infection from parents and are on ART. Also, there is likely chance of adolescents being involved in high risk sexual activity.

Study done by Antala SK et al. also shows male preponderance (70%)

with maximum patients from 21-40 years (78%) of age group. Another study by Saravanan S et al. observed majority were male (86%) and 31-40 years of age group (39%) constitute major population. A study from Iran by Mohammadi M et al. showed 91.6% male and 52.1% patients from 31-50 years age group denoting majority. Similar study from Cambodia by van Griensven et al. showed 46% were male and predominant age group was 31-40 years and from Nepal by Ionita et al. found 51.3% were male and 78.4% patients belong to <30 years of age. All studies including ours showed male preponderance, reasons might be, lack of sex education and safe sex practices, lack of awareness about STIs and other communicable diseases and migration for employment due to financial burden of family.

In our study, prevalence of HBV, HCV and syphilis were found to be 4.4% (n=122), 1.44% (n=40) and 2.2% (n=61) respectively and

predominant age group was 26-45 years where prevalence of these infections was 3.21% (n=89), 1.05% (n=29) and 1.73% (n=48) respectively.

Out of total 2771 samples 251 samples shows positive result for at least one infection. Among 251 positive, 14 (5.58%) samples were positive for more than one co-infection. Prevalence of two infection was 0.51% (14/2771). 2 samples were positive for both HBsAg and Anti-HCV antibody shows 0.07% prevalence. Both HBsAg and VDRL positive samples were 11 with prevalence of 0.4%, while only 1 sample (0.04%) was positive for both Anti-HCV antibody and VDRL. None of the sample was positive for all three co-infection.

The following Table 6 shows prevalence of HIV, HBV, HCV and Syphilis co-infections from different studies.

Table 6

Co-infection ↓	Study done by →	Antala	Saravanan	Hussain	Munshi	Mohammadi	van	Ionita
		SK et al.	S et al.	T et al.	SU et al.	M et al.	Griensven et al.	et al.
HIV + HBV		19.5%	9%	0.2%	4.24%	14.5%	11%	4.4%
HIV + HCV		3%	2.2%	0%	1.69%	72%	5.3%	19.4%
HIV + Syphilis		6%	NA	1%	13.55%	NA	NA	NA
HIV + HBV + HCV		0.5%	0%	0.1%	NA	7.9%	0.4%	1%
HIV + HBV + Syphilis		1%	NA	0%	NA	NA	NA	NA
HIV + HCV + Syphilis		0%	NA	0%	NA	NA	NA	NA

NA – Not applicable for that study.

On literature search, limited studies found for co-infection of syphilis in HIV patients. Although the percentage of patients with co-infections is lower, but the combination of such infections are dangerous co-existence and may have a detrimental effect on the patient and the treatment outcome.

The strength of our study includes standard laboratory techniques, timely maintained and properly collected data as it was carried out in RSTRRL, Department of Microbiology, Mumbai. and large sample size.

A number of important limitations need to be acknowledged. The study was conducted with patients limited to a tertiary hospital and not of a community setting. We only tested for HBV by measuring HBV surface antigen, ideally full laboratory evaluation for HBV should be done. Therefore study did not differentiate HBV active infection from those of carriers. HCV diagnosis should be confirmed by a molecular test.

CONCLUSION:

Screening of Hepatitis B, Hepatitis C and syphilis should be included in diagnostic algorithm of HIV positive patients on ART as the antiretroviral drugs could be hepatotoxic. Timely treatment of these infections and management of drugs toxicity can prolong life of PLHIV. Hepatitis B screening and Hepatitis B vaccination should be given to HBsAg negative individuals attending ICTC should be initiated in the ICTC's.

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Conflict of interest

No conflict of interest to declare.

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