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Prevalence of Occult Hepatitis B Infection among HIV Infected Patients at an Innercity Clinic

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Abstract

Considering higher morbidity and mortality associated with HIV/HBV coinfected patients compared to monoinfected patients, it is imperative to determine the prevalence of occult HBV (OHB) infection, in such population.630 unique HIV-infected patients, during the defined study period, were screened for evidence of occult HBV infection serology. 82 patients (13%) were found to have evidence suggestive of OHB infection of which 57 had HBV DNA testing available and comprised the final study population. Data on demographic variables, Hepatitis C antibody status, antiretroviral therapy (ARV), CD4 count and HIV viral load was also collected. Among the final study population, 7% (n=4) patients met the OHB definition. All 4 (100%) with OHB had HIV RNA levels > 50 copies/ml. OHB was found in 4 (22%) of 18 patients not on ARV, but in none of 39 patients on ARV (p=0.007). All patients on ARV were on a regimen with anti HBV activity. 75% of patients with OHB tested positive for HCV compared to 47% in isolated anti HBc positive but HBV DNA negative population (p= 0.58). With an OHB prevalence of 7% in our community clinic, clinicians should have a high index of suspicion for OHB among HIV patients whose hepatitis panel is positive only for anti HBc only and start them on HAART regimen containing ARVs with anti-HBV activity.

Keywords: Occult Hepatitis B; HIV

Background

More than two decades since the recognition of Occult Hepatitis B virus (OHB) infection, there is still limited information in terms of its prevalence, clinical significance, pathological and infective potential and the need for treatment and follow up. Occult HBV infection has been defined as the presence of Core alone positive HBV serology [positive Hepatitis B core antibody (anti HBc) with negative Hepatitis B surface antigen (HBs Ag) and surface antibody (HBs Ab)], along with detectable HBV DNA. It is a form of chronic HBV infection. Occult hepatitis B has been reported in patients with chronic hepatitis C infection, cirrhosis, end stage renal disease on dialysis, and Human Immunodeficiency virus (HIV) infection [1,2].

The presence of chronic Hepatitis B co-infection is associated with greater morbidity and mortality among HIV-infected patients [3-5]. It is important to know the prevalence of occult or core alone positive Hepatitis B coinfection in HIV-infected patients as it is another form of chronic Hepatitis B infection, which may also potentially negatively affect patient outcomes. Limited published research data in one of the seminal studies in United States on HIV positive but ARV naive patients by Shire et al. [6] suggested a prevalence of 11%. However the prevalence of occult HBV infection among HIV-infected populations in this era of HAART has not been studied before.

Objective

To determine the prevalence and patient characteristics of occult hepatitis B infection in HIV infected patients attending an outpatient HIV clinic in New York City.

Methods

Harlem Hospital Center Infectious Diseases Clinic, located in the Harlem neighborhood of New York City, NY, has a large HIV outpatient clinic with over 1000 patients seen annually. Patient information from all visits is stored in an electronic database (Discoverer Plus). After obtaining Institutional review board (IRB) approval from Columbia University Medical Center this electronic database was screened to identify potential study participants. A total of 630 unique HIV-infected patients had a clinic visit during the defined study period - June 1, 2007 and January 31st 2009. Of these 630 patients, 82 (13%) were found to have serological evidence suggestive of occult HBV infection (HBsAg-, HBsAb-, anti HBc+). Serologic evaluation for HBsAg, anti-HBs, and total anti-HBc was performed using enzyme immunoassay test kits from Abbott Laboratories (Abbott Park, IL), in accordance with manufacturer's specifications). HBV DNA testing was available on 57 patients and they comprised the final study population in whom a more detailed chart review was performed. Samples were tested for HBV DNA using the Roche COBAS Amplicor HBV Monitor assay, which is a PCR amplification-based assay). In addition to demographic variables, information on Hepatitis C antibody (HCV Ab), antiretroviral therapy (ARV), most recent CD4 count and HIV viral load were collected and entered into a MS Excel Spreadsheet. Statistical analysis was performed using EpiInfo 3.5.3.

Results

Among the final study population (n=57) (Table 1), the majority were males (n=36, 63.2%), African American (n=50, 87.7%), Hispanic (n=6, 10.5% and Caucasian (n=1, 1.7%), with a mean age of 48.7 ± 6.2yrs. In terms of their HIV infection, 70.2% were on ARV (n=39), 75.4% had CD4 cell counts > 200 cells/mm3 (n=43), and 40.4% had HIV RNA levels < 50 (n=23). Nearly half of the study population (n=28, 49%) tested positive for HCV antibodies. Only 7% (n=4) of the final study population met the definition of occult HBV infection. Of these patients with occult HBV infection, 50% (n=2) were males, 100% (n=4)

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	n	%
Male Gender	36	62.2
Race/ Ethnicity		
African American	50	87.8
Hispanic	6	10.5
Caucasian	1	1.7
Age (mean ± s.d.)	48.7±6.2 yrs	
On antiretroviral medications	39	70.2
CD4 cell count >200	43	75.4
Mean CD4 cell count	461.4	
HIV RNA level < 50	30	52.6
HCV co-infection	27	47.4
Occult HBV	4	7

Table 1: Descriptive Characteristics of Study Population (N= 57).

	n	%
Male	2	50
Female	2	50
African American	4	100
HCV antibody+	3	75
Mean CD4 cell count	408 ± 280 cells/mm^3	
CD4 <200	2	50
CD4 > 200	2	50
VL <50	0	0
VL>50%	4	100
On ARV	0	0
Not on ARV	4	100

Table 2: Characteristics of patients with HBV DNA positive (N=4).

were African American, mean CD4 count was 408 ± 280 cells/mm3, 100% (n=4) had HIV RNA levels > 50 copies/ml, 100% (n=4) were not on ARV (Table 2). Overall, detectable HBV DNA was found in 4 (22%) of 18 patients not on ARV, but in none of the patients who were on ARV (n=39) (p=0.007). All patients on ARV (n=39) were on a regimen with NRTI backbone including Tenofovir, Emtricitabine or Lamivudine that had anti HBV activity. 75% of patients with occult HBV tested positive for HCV compared to 47% in isolated anti HBc positive but HBVDNA negative population (p= 0.58).

Conclusions and Discussion

HBV infection has traditionally been associated with HIV as a coinfection as they share the same transmission modes [3,5,7-9]. The prevalence of occult Hepatitis B varies significantly between geographical regions (<10% to up to 25%) [5], among various patient populations tested as well as the sensitivity of the assay used [3,4,10,11].Though the overall prevalence of occult HBV in our community clinic (7%) is lower than the historical reported prevalence of 11%, the prevalence was much higher (22%) among hose not on ARV. This is concerning as occult HBV has not only been associated with increased liver enzymes and pathology but also implicated with HBV transmission; reactivation of HBV and hepatocellular carcinoma (HCC) [3,12-15].

The use of ARV in this study was significantly associated with the lack of detectable HBV viremia. None of the patients on ARV tested positive for occult infection. All of the patients on ARV were on a regimen which was active against Hepatitis B, with regimens including Lamivudine, Tenofovir and Emtricitabine. This actually might have caused HBV suppression and contributed to a lower prevalence in our study as compared to the historical prevalence.

A high proportion of patients with occult HBV infection also tested positive for HCV Ab (75%). This increased prevalence of occult HBV with HIV and HCV coinfection has been reported before [16-18]. It has been postulated that HCV either facilitates or induces mutation in HBV resulting in inefficient replication of HBV, a phenomenon known as interference and this inhibitory effect is mediated by HCV core protein [19].

Apart from viral factors, host factors like defective or insufficient immune response to infection due to HIV/HCV and/or immunosuppressive state have also been suggested for this discrepancy in HBV serology [20]. Finally Occult HBV infection has also been reported to adversely affect the treatment response to HCV though this effect is debatable [21].

Our study did not find any association between presence of occult HBV infection and CD4 Counts unlike an association with lower CD4 counts reported by Stuart et al. [22]. The strength of our study was a mixed population in terms of age and sex distribution. Also our study population included HIV-infected individuals both on and off ARVs. However our study mainly consisted of African American population, only looked into the presence/absence of HBV DNA at the time of positive core only Hepatitis B serology, and did not include long term follow-up of the study populations.

Prior studies have documented variable hepatitis B viremic states in other HIV-infected populations affected by multiple factors such as presence of other immunosuppressive states, compliance with ARVs, presence/absence of HCV infection and particular genotype, response to HCV treatment, HBV genotype, and HDV coinfection. Also since the study included only patients that had total HBV serology, including DNA levels available and excluded the rest, the final prevalence could have been an underestimate.

In conclusion, clinicians should have a high index of suspicion for occult HBV among HIV-infected patients whose hepatitis panel is positive only for Hepatitis B core antibody (anti HBc). All such patients should be screened with HBV DNA, particularly if they also have HCV co-infection. It is now recommended that HIV-infected patients who need treatment for hepatitis B should be started on a full HAART regimen containing ARVs with anti-HBV activity.

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