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Examination of Co-infection of HIV, Hepatitis B, and Hepatitis C in Zambia

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ABSTRACT

Zambia's initiative on antiretroviral therapy (ART) has grown speedily in the public sector. Nonetheless, resource limitations have hampered the habitual screening for hepatitis B virus (HBV) and hepatitis C virus (HCV), and further inhibited its integration into the country's HIV treatment guidelines. This paper therefore carried out a cross-sectional study of adults seeking HIV care and treatment at the University Teaching Hospital (UTH) in Lusaka. The UTH Department of Internal Medicine manages one of the country's oldest ART programs, founded in 2001by the Ministry of Health. Respondents were screened for ART eligibility based on the Zambia's national guidelines which are similar to those of the World Health Organization (WHO). The participants consisted of adolescents and adults who are above 16 years of age, with confirmed HIV infection and identified as ART eligible. Trained study staff carried out the survey. Only adults who were ART naïve were considered, unless the previous ART use was deliberately transient, as with postexposure prophylaxis or perinatal HIV prevention. All participants were asked to complete a 28-question survey, administered in the language of their choice: English, Nyanja, or Bemba. Questions covered demographic characteristics, medical history, socioeconomic history, and risk factors for hepatitis B and/or C acquisition. Findings indicate that co-infection with HCV was uncommon at approximately 1%. The study did not observe any clinically useful predictors for viral hepatitis, suggesting that routine screening should be considered in settings with appropriate resources. Therefore, lower cost screening modalities for viral hepatitis are an urgent need to upgrade HIV care in resource-limited settings.

Keywords: HIV, Hepatitis B, ART, Hepatitis C, Health.

INTRODUCTION

In Zambia, the initiative on antiretroviral therapy (ART) has grown speedily in the public sector dating back to 2004 [1]. Owing to serious resource limitations, nonetheless, the habitual screening for hepatitis B virus (HBV) and hepatitis C virus (HCV) has not been integrated into the country's HIV treatment guidelines. Understanding the extent of these dual epidemics is critical to the optimization of HIV treatment. Several antiretroviral drugs – most notably nevirapine and lopinavir – are associated with liver failure among patients with HBV or HCV infection [2]. Conversely, tenofovir and lamivudine have been shown to inhibit HBV replication and could be used to improve long-term clinical outcomes. Studies of HBV surface antigen (HBsAg) prevalence among HIV-infected adults have provided varying estimates in Zambia. In a 1996 survey, Oshitani and colleagues detected HBsAg in the serum samples of 24 of 340 (7.1%) HIV-infected pregnant women [3]. In 2002, Kasolo et al. estimated HBsAg seropositivity in 31.3% among HIV-infected adults hospitalized at a tertiary care institution.[4] This study therefore, examined co-infection rates among adults starting ART in a primary care setting, as well as HCV-HIV co-infection prevalence in Zambia.

Materials and Methods

A cross-sectional study of adults seeking HIV care and treatment at the University Teaching Hospital (UTH) was conducted in Lusaka. The UTH Department of Internal Medicine manages one of the country's oldest ART programs, founded in 2001by the Ministry of Health.[5] Individuals who present to the clinic are screened for ART eligibility based on the Zambian national guidelines that are similar to those of the World Health Organization (WHO). The study participants consisted of adolescents and adults who are above 16 years of age, with confirmed HIV infection and identified as ART eligible. Trained study staff carried out the survey. Only

adults who were ART naïve were considered, unless the previous ART use was deliberately transient, as with postexposure prophylaxis or perinatal HIV prevention. All participants were asked to complete a 28-question survey, administered in the language of their choice: English, Nyanja, or Bemba. Questions covered demographic characteristics, medical history, socioeconomic history, and risk factors for hepatitis B and/or C acquisition. Blood specimens were drawn for viral hepatitis screening, while enzyme immunoassays was used to detect HBsAg for acute HBV (Axsym HBsAg™, version 2; Abbott MaxPlanck, Wiesbaden, Germany) and anti-HCV antibodies for HCV infection (Axsym HCV™, version 3; Abbott Max-Planck, Wiesbaden, Germany). Baseline alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were analyzed using an automated chemistry analyzer (Cobas Integra 400™; Roche, Mannheim, Germany). Liver enzyme elevation was based on guidelines set forth by the Division of AIDS, U.S. National Institutes of Health.[6]. Liver enzyme elevations were graded according to the highest results between ALT or AST as follows: ALT and/or AST of 50–100 U/L mild elevation; 101-200 U/L moderate elevation; >200 U/L severe elevations. To compare categorical variables, Pearson's chi-square test and Fisher's exact test, was considered appropriate. For continuous variables, statistical comparisons were made using Wilcoxon's rank sum tests. Sample size was based on an estimated HBV prevalence of 31% [4] with a precision ±5%. All analyses were performed using SAS™, version 9.1.3 (SAS Institute, Cary, NC, USA).

RESULTS

From December 12, 2007 to June 13, 2008, a total of 323 ART-naïve adolescents and adults >16 years of age were enrolled for the study. The median age was 37 years (IQR=32, 44); median CD4+ cell count was 118 cells/μL (IQR=59, 199); and 174 (54%) were women. Of the 323 participants, 32 (9.9%; 95% confidence interval [CI]: 6.7–13.2%) were HBsAg positive while four (1.2%; 95% CI: 0.03–2.4%) were anti-HCV antibody seropositive. No one was co-infected with hepatitis B and C. Patients with active HBV and HIV co-infection were more likely to be <40 years of age (84.4%) when compared to those who were not co-infected (63.9%; P=0.02). No differences in prevalence were noted according to sex, baseline WHO stage, or CD4+ cell count. A history of blood transfusion, that of tattooing, reported sexual partners in the past year, and past history of sexually transmitted infections were also not associated significantly with HBV. Mild to moderately elevated liver transaminases (AST or ALT) were more likely to be observed among patients with HBV co-infection (P=0.003). A severe elevation of liver enzymes (≥200 IU/L) was uncommon in this population (7 of 290; 2.4%) and similar between the HIV/HBV co-infected and non-co-infected groups (3.4% vs. 2.3%; P=0.5). No statistically significant predictors of hepatitis C infection were identified, though the statistical power to observe differences was very low with only four HCV infected persons.

DISCUSSION

As the HIV epidemic in Zambia moves forward in the ART era, new data on hepatitis coinfection are clearly needed to guide health policy. In this study, it was found that active HBV coinfection (HBsAg seropositivity) occurred in 9.9% of ART-naïve HIV-infected patients. In contrast, HCV occurred in only 1.2% of HIV-infected persons, a finding consistent with the primarily heterosexual transmission of HIV and low intravenous drug use. This study's estimate of HBV prevalence was lower than the 31% reported in 2003 at UTH, a figure upon which this research sample size had been based. In that study, Kasolo and colleagues had targeted hospitalized patients and this likely contributed to the unusually high prevalence observed among HIV-positive adults [7]. The results of this research are more consistent with studies in South Africa (4.8%), Nigeria (11.9%), Senegal (16.8%), and Tanzania (17.3%) [8] that targeted HIV-eligible patients in an outpatient setting. It also approximated disease prevalence among HIV-infected pregnant women in Zambia (7.1%) [3]. With the initiation of antiretroviral therapy and subsequent immune reconstitution, a concern is a paradoxical exacerbation of inflammatory-related pathology in persons with HBV who may not know their status. In the study's HIV infected population, patients with HBV co-infection were more likely to have moderately elevated ALT but not severely elevated aminotransferase levels. Prior studies have found that among HBV-infected individuals, HIV co-infection is actually associated with lower ALT levels but higher risk of progression to cirrhosis [9]. This finding may be related to the impairment of immunity in advanced HIV, which – despite higher rates of HBV replication – results in less inflammation and necrosis. Indeed, in HIV-infected patients, HBV co-infection is an independent predictor for cirrhosis, hepatocellular carcinoma, and mortality [10]. To prevent this excess morbidity and mortality associated with HIV/HBV co-infection, treatment guidelines in upper income nations recommend screening all HIV-infected adults for viral hepatitis.[11] Recently updated guidelines from the WHO recommend that all patients who require treatment for HBV co-infection initiate ART, regardless of the CD4 count or WHO clinical stage.[12] Such an approach has also been adopted by the Zambian Ministry of Health.

HBsAg is now recommended as part of eligibility screening for ART. For HBsAg-positive individuals with CD4 counts higher than 350 cells/μL, ART can be initiated if liver transaminases are elevated or if HBsAg positivity remains persistent for at least 6 months. Although this represents an important step forward in health policy, the limited availability of hepatitis B screening countrywide – particularly in rural areas – represents a significant

challenge to its implementation. With knowledge of HBV-HIV co-infection, ART regimens could be tailored to treat both conditions. Screening information could also be helpful early in the course of ART, to better understand the development of the immune reconstitution inflammatory syndrome. Validated algorithms to triage high-risk patients for HBV screening could help improve the cost-efficiency of screening programs, but data from this study suggest that there may be few well-performing demographic or medical predictors. For example, 16 out of 29 (55%) of HBV co-infected patients would be missed if mildly elevated liver enzymes alone were used to triage screening. In contrast with HBV screening, the low disease prevalence of HCV-HIV co-infection suggests that universal screening for HCV is not likely to be cost-effective in our setting. Several antiretroviral drugs for HIV treatment are known to inhibit HBV replication, including lamivudine, emtricitabine, and tenofovir. [13] As tenofovir–lamivudine and tenofovir– emtricitabine "backbones" gain a widespread use in Africa – as they have in Zambia[14-15] – a large proportion of co-infected patients will receive "empiric" treatment for HBV regardless of formal diagnosis. In this scenario, the initial ART regimen could be used as a criterion to triage HBV screening, so that testing is performed when tenofovirbased regimens are contraindicated or unavailable. While this approach considers only one benefit of HBV screening, such strategies should be considered in settings where universal hepatitis screening is not feasible. Control strategies for HBV in Zambia have focused on blood bank screening and childhood vaccination. HBV and HCV screening is now universal in transfusion centers across the country, based on guidance from the Ministry of Health. Zambia has also incorporated HBV vaccination into the routine childhood schedule in 2005, and the WHO–UNICEF estimated a coverage of 80% in 2009.[30] Childhood vaccination is especially important given the presumed mode of HBV transmission as horizontal (from family or other close contacts) during early childhood [15].

CONCLUSION/ RECOMMENDATION

To conclude, active HBV co-infection was diagnosed among nearly 10% of HIV-infected adults eligible for ART at a tertiary care center in Lusaka, Zambia. Conversely, co-infection with HCV was uncommon at approximately 1%. This research did not observe any clinically useful predictors for viral hepatitis, suggesting that routine screening should be considered in settings with appropriate resources. Therefore, lower cost screening modalities for viral hepatitis are an urgent need to upgrade HIV care in resource-limited settings.

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