Epidemiology of HIV and selected blood-borne infections in East-Africa
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Prevalence and screening costs of hepatitis C virus among Ugandan blood donors

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Abstract

Background: Screening donated blood for hepatitis C virus (HCV) is important for HCV prevention and is routinely practiced in North America and Europe. However, in many African countries little is known about HCV prevalence or cost-effectiveness of HCV antibody (anti-HCV) screening.

Methods: We investigated 2592 plasma specimens collected consecutively from blood donors in central Uganda in 1999. Routine screening by the blood bank included human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), and syphilis. To assess HCV prevalence and cost-effectiveness of testing, specimens were additionally tested for anti-HCV IgG by enzyme immunosorbent assay (EIA). Specimens repeatedly reactive (RR) on EIA were tested with a recombinant immunoblot assay (RIBA).

Results: Overall, 107 (4.1%) specimens were HCV EIA RR. Fifteen EIA RR specimens (0.6%, 95% confidence interval = 0.3–0.9%) were RIBA positive and 47 (1.8%) were RIBA indeterminate. Most (80%) RIBA-positive specimens were non-reactive for HIV, HBsAg, and syphilis. RIBA positivity was not associated with donor age, sex, number of donations, HIV, or HBsAg positivity. Costs of screening donors for anti-HCV by using EIA were estimated at US$782 per potential transfusion-associated HCV infection (exposure to RIBA-positive blood) averted.

Conclusions: Current screening tests for other infections are ineffective in removing HCV-positive donations. Testing costs are considerable; cost-effectiveness of identifying HCV-infected donors will be critical in decision making about HCV screening in Uganda.
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Introduction

Infection with hepatitis C virus (HCV) was the main cause of transfusion-transmitted hepatitis in industrialized nations (Alter et al. 1989; Esteban et al. 1990) where it has been virtually eliminated now that donated blood is routinely screened for HCV (Schreiber 1996). Even though recommended by the World Health Organization (Global Surveillance and Control of Hepatitis C 1999) screening for HCV is far less common in resource-constrained settings. Beginning in 1989 Uganda introduced a successful national transfusion programme that greatly improved blood safety by screening for hepatitis B surface antigen (HBsAg), human immunodeficiency virus (HIV), and syphilis, by deferring candidate blood donors through standard questions aimed at identifying individuals at higher risk for such infections, and by reducing and later eliminating directed and paid donations. Screening for HCV has not been introduced as its prevalence in blood donors and the costs for screening are unknown. We determined the HCV prevalence in a sample of Ugandan blood donors and the costs for laboratory testing.

Methods

This evaluation was carried out at Nakasero Blood Bank (NBB), which supplies blood products for central Uganda. All blood donors are volunteer (both new and repeat) donors who donate directly at either the blood bank’s headquarters, a satellite donor recruitment site in Kampala, the capital city, or with one of NBB’s four mobile teams. These mobile teams visit schools, trading centres, or other public events in Kampala and throughout central Uganda. Candidate blood donors are first screened by questions related to recent transfusions, needle use, and medicine intake, liver disease, fever, or weight loss, number of sex partners, contact with commercial sex workers, and illness of spouse. Blood is then collected from eligible blood donors and stored at room temperature until returned to NBB the same day or stored at <9°C until returned to NBB the following day(s). Data collected include age, sex, and
number of previous blood donations. From April to May 1999, left-over specimens from 2592 blood donations were kept for a later evaluation of HCV infection. These had been consecutively collected from donors attending NBB’s main or satellite site in Kampala or from people who donated with one of the four mobile teams. As part of NBB’s routine screening programme, these blood donations were screened for HIV antibodies using an enzyme immunosorbent assay (EIA) [MUREX HIV-1.2.O, Murex Biotech Ltd, Kent, UK]. Non-reactive specimens were reported as HIV negative; repeatedly reactive (RR) specimens were reported as HIV positive. Specimens with discordant HIV EIA results were further evaluated using Uni-Form II plus O (Vironostika, Boxtel, The Netherlands) and Western blot. For HBsAg testing, the MUREX HBsAg assay was used; specimens reactive in duplicate were reported as positive, all others as negative. Screening for syphilis was made by the Venereal Disease Research Laboratory test; reactive specimens were confirmed by Treponema pallidum haemaggulinitation (TPHA) test.

Aliquotted specimens for HCV testing were stored at -20°C or colder. HCV testing was performed with ORTHO anti-HCV 3.0 EIA® (Ortho-Clinical Diagnostics, Inc., Raritan, NJ, USA) at NBB. Initially reactive specimens were re-tested with the same assay in duplicate as directed by the manufacturer. Only specimens that tested RR (defined as reactive in one or both duplicate tests) were considered EIA reactive. Testing was repeated and confirmed at the Centers for Disease Control and Prevention in Atlanta, GA, USA. EIA repeat-reactive specimens were further tested by CHIRON recombinant immunoblot assay (RIBA) 3.0® for IgG to four antigens. Specimens RIBA reactive to two or more antigens were classified as HCV positive. Specimens reactive to only one antigen were classified as HCV indeterminate. Specimens non-reactive in EIA screening or non-reactive by RIBA were classified as HCV negative. Screening costs were assessed using costs for EIA test kits only as RIBA was performed only for the purpose of estimating the proportion of EIA-reactive donations likely to be infectious (Alter et al. 2003). For the year 2000, the cost for ORTHO EIA was given as US$5.19 per test (R. Downing, personal communication). We
also included in our cost calculations information regarding blood banking practice at NBB and transfusion practice at Kampala’s largest hospital. A mean of 1.46 blood bags were yielded from each blood donation. At the hospital, an average of 1.2 blood bags were transfused within a single transfusion event. For transfusions with more than one blood bag, the probability that all bags were from the same donor was 20%. Costs related to re-transfusions during the same hospital stay but at a later time, blood bank costs for overhead, and indirect costs for discarding false HCV-seropositive donations as well as costs for treatment or prevention of illness or death by screening for HCV were not included.

Results

The median age of the 2592 donors tested was 23 years (range: 15–60). Eighty-two per cent were male. The prevalence for HIV was 2.2%, for HBsAg 3.0%, and for syphilis 0.2%. A total of 107 (4.1%) specimens were RR by HCV EIA; 15 were confirmed as anti-HCV positive by RIBA (0.6%, 95% confidence limits: 0.3–0.9%), 47 were indeterminate by RIBA, and 45 were negative by RIBA. There was no association between anti-HCV seropositivity and age, sex, or repeat donor status. Of the 15 RIBA-positive blood donations, three also tested positive for HIV, HBsAg, or syphilis and thus had been discarded. The remaining 12 (0.46%) specimens tested negative in all three routine screening tests already in place. These 12 anti-HCV-positive blood donations may have resulted in 16 patients transfused with HCV-seropositive blood. Applying the anti-HCV prevalence of 0.46% (anti-HCV positive but negative for HIV, HBsAg, and syphilis) to all donations in 1999, we estimate that 179 patients were exposed to HCV-seropositive transfusions out of an estimated total of 33,819 patients transfused (including patients re-transfused during same year). The risk of receiving an HCV-seropositive blood transfusion was estimated at approximately 0.4%. 
The anti-HCV screening costs per blood donation using EIA alone were estimated at US$5.95. Based on the 15 RIBA-positive donations (leading to an estimated 20 patients exposed to HCV-seropositive blood), the EIA screening costs per potential transfusion-associated HCV infection averted were estimated at US$782. These costs increase to US$938 if only HIV, HBsAg, or TPHA-negative donations (with approximately 16 patients exposed to HCV-seropositive blood) are considered. These costs compare to average screening costs of US$7.00 to prevent a patient being exposed to an HBsAg-positive transfusion, making screening for HCV 112 times more expensive than screening for HBV (detailed screening costs for HBsAg detection not shown).

Discussion

From a sample of 2592 Ugandan blood donors we estimated an anti-HCV prevalence of 0.6%. This prevalence is consistent with those found among blood donors from other Sub-Saharan African countries reported by studies that also used confirmatory testing to exclude false-positive screening test results (Ampofo et al. 2002; Etard et al. 2003; Fang et al. 2003). Prevalences of confirmed anti-HCV positivity from these studies ranged from 0.01% to 0.9%, two- to eightfold lower than prevalences based on screening test positive results alone.

Based on 1999 figures, routine screening for anti-HCV would have averted 179 transfusion recipients from being exposed to HCV-seropositive blood at a cost of US$782 per potential transfusion-associated HCV infection. The costs of HCV infection averted may be underestimated because (i) anti-HCV positivity may not represent viraemia as HCV clearance may have occurred in some donors, and (ii) using only the price of test kits for the cost analysis underestimated the overall costs of screening. Routine screening already in place for HIV, HBsAg, and syphilis removes approximately one-fifth of all HCV-seropositive donations. Although direct screening costs (per HCV-seropositive transfusion averted) are many times higher than those for HBsAg, this ratio...
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... may become smaller when including costs of HBV- and HCV-related disease averted. Many exposures to HBsAg-positive transfusions do not result in chronic infection and or HBV-related disease; in contrast, most HCV infections do result in chronic infection and liver disease (Alter & Seeff 2000).

Many countries do not have the resources to implement routine HCV testing of blood donors given the current cost of test kits. The performance of the currently available screening tests for detecting anti-HCV in sera from persons in African countries should also be further evaluated. Using different test formats and manufacturers, screening test positive rates ranged from 4.1% (in our study) to 8.4% in a study of blood donors in Ghana (Ampofo et al. 2002) to 10.3% in a sample of the general population in Tanzania (Tess et al. 2000); in contrast, RIBA-confirmed anti-HCV rates ranged from 0.6% to 0.9% to 1.2%, respectively.

In our study 1.8% of all blood donations and 44% of EIA-reactive donations tested indeterminate by RIBA. Other investigators have found similarly high rates of non-specific results, which seem to be unique to blood donors and other persons tested in this part of the world (Tess et al. 2000; Ampofo et al. 2002; Fang et al. 2003). In one study, none of the indeterminate samples were HCV RNA positive, suggesting that both the screening and confirmatory antibody assays may perform differently in these populations (Fang et al. 2003). Reducing the number of samples that test initially reactive will reduce the need to retest in duplicate, thus reducing not only the costs of testing but also costs associated with donor loss due to deferral. Further evaluation seems warranted to investigate the causes for the high frequency of non-specific test results in Uganda and elsewhere. Lower cost screening tests for anti-HCV will be critical before routine HCV screening appears feasible in a resource-constrained setting such as Uganda.
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