Human T-cell lymphotropic virus 1/2 and human immunodeficiency virus antibodies identification among transactional sex workers and drug users in the Dominican Republic

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Received 25 September 2018; revised 9 February 2019; editorial decision 15 February 2019; accepted 15 February 2019

Background: Human immunodeficiency virus (HIV) increases the risk of acquiring human T-cell lymphotropic virus (HTLV) and subsequently HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). Existing data have exclusively reported generalized rates of HIV and HTLV-1 chronic viral infections in the Dominican Republic. To our knowledge, no published studies have focused on the rates of HTLV-1/2 in transactional sex workers and drug users, both higher risk groups, in the Dominican Republic.

Methods: From December 2012 to April 2013 we conducted a study to estimate the seroprevalence of HTLV-1/2 immunoglobulin G (IgG) and HIV antibodies among transactional sex workers and intravenous drug users in Santo Domingo, Dominican Republic. Serological status was analysed with behaviour and demographic data.

Results: We collected and analysed plasma from 200 participants with a mean age of 27.4 y in men and 25.2 y in women. The overall weighted seroprevalence of HTLV-1/2 IgG antibodies was 13.91% (95% CI 7.59 to 20.23) in men and 10.59% (95% CI 4.05 to 17.13) in women. The overall weighted seroprevalence of HIV-1 was 13.91% (95% CI 7.59 to 20.23%) in men and 17.65% (95% CI 9.55 to 25.75) in women. Male intravenous drug users had an exceptionally high rate of HTLV-positive HIV co-infection, at 75% (95% CI 44.99 to 105.01). Although there association has been found between HTLV/HIV co-infections and sex work, the adjusted odds revealed a confounding role of HIV infection.

Conclusions: The results highlight the urgent need for enhanced public health preventive strategies among high-risk populations in the Dominican Republic and other resource-constrained Caribbean settings, as well as global adoption of routine screening for HTLV-associated infections, particularly in these high-risk, underserved populations.

Keywords: Dominican Republic, drug users, HIV, HTLV, sex workers, transactional sex

Introduction

Human T-lymphotropic viruses (HTLVs) are T-cell CD4+ lymphotropic human retroviruses capable of remaining in the infected host for an undetermined length of time and >90% of infected individuals remain asymptomatic carriers of the virus throughout life. The first human retrovirus discovered was HTLV-1 by Poiesz et al. in 1980. Present day studies estimate 5–10 million persons are infected worldwide. While primarily asymptomatic, HTLV-1 plays a causative role in adult T-cell leukaemia/lymphoma (ATL), HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP), uveitis and infective dermatitis and is associated with other less well-defined conditions. HTLV-2 is closely related to HTLV-1, is less pathogenic and can lead to the development of a range of neurological diseases. More recently, HTLV-3 and HTLV-4 have been found in central African populations, but their modes of transmission, pathogenesis and clinical manifestations are not yet well defined. At the moment, there are no serological tests for HTLV-3/4 screenings.
There is a strong association between HTLV-1 proviral load and the clinical status of infected individuals with chronic diseases such as ATL and TSP/HAM. Evidence has shown that a strong cytotoxic T lymphocyte (CTL) response to HTLV-1 is associated with a low proviral load and a low risk of the inflammatory disease. Viral persistence of HTLV in CTLs and Tax protein transcription and activation cause chronic hyperantigenaemia, leading to constant antigenic stimulation and CTL impairment. The spread of HTLV-1 from within the CTL requires cell-to-cell contact, as lymphocytes infected with HTLV-1 produce low levels of HTLV-1 virions.

The Caribbean is classified as an endemic region for HTLV-1, but its prevalence has been underestimated, with only Jamaica and Haiti being the main foci of studies. Jamaica has a high seroprevalence ranging from 1.7 to 17.4% depending on sex and age, while rural Haiti has shown a prevalence of 3.8–4.3%. Cuba, on the other hand, reports the lowest prevalence in the region. The overall prevalence of HTLV-1 and HTLV-2 in the Caribbean region ranges from 1 to 10%. HTLV-1 and HTLV-2 combined with human immunodeficiency virus (HIV) are common in endemic areas due to their shared routes of transmission, and HIV/HTLV-1 co-infection is associated with accelerated progression to acquired immune deficiency syndrome. A common finding in HTLV/HIV co-infection studies is an increase in CD4+ cell count not associated with improved immune protection. HTLV/HIV co-infection suggests involvement in high-risk behaviours, such as unprotected sex, multiple sex partners, intravenous drug use and men who have sex with men ( MSM). The prevalence of HIV-1/HTLV-1 co-infection in Trinidad and Tobago was 6%, this being the first study (1987) to report HTLV/HIV co-infection prevalence in the Caribbean compared with the prevalence of HTLV/HIV co-infection in Jamaica of 5% in 2003. A foundational study conducted in 1992 of nearly 4000 samples belonging to high-risk populations and patients diagnosed with leukaemia or lymphoma as well as with neurological disease found a rate of seropositivity of 1–5% for high-risk populations in the Dominican Republic. The latest study of HTLV in the Dominican Republic was conducted in 2008, where the prevalence of HTLV/HIV was 1.7% (95% confidence interval [CI] 0.2 to 3.5).

Intravenous drug users (IDUs) and MSM are high-risk groups for HTLV infection. Among IDUs globally, there was a significant increase in HTLV-1 prevalence from 6.6% in 1988 to 52% in 2004 and a notable decrease of HTLV-2 prevalence from 0.7% in 1989 to 3.2% in 2011. The prevalence of HTLV-2 among MSM in Peru was estimated at 1.3% in 2006. Among high-risk Argentinian populations, the HTLV-1 and HTLV-2 prevalence was 19.1% for IDUs and 0.4% (3/282) for MSM. Comparatively, in Italy, the frequency of HTLV-2 infection was 6.7% among HIV-positive subjects and 1.1% among HIV-negative subjects. A study conducted in Washington (USA) in 2006 found that HTLV-2 infection was detected in 7.4% of IDUs. In southern Brazil it was determined that injecting cocaine users were 5.2 times (95% CI 2.5 to 10.7) more likely to be HTLV-1 or HTLV-2 positive than non-injecting cocaine users. In Stockholm in 1994, the prevalence of HTLV-2 infection among IDUs was 3.2%. The Dominican Republic lacks studies of HTLV in these vulnerable populations. However, there are some studies that have evaluated the role of intravenous drug use and sex work among MSM and other high-risk groups with a substantial risk of HIV infection.

These figures suggest that there is wide variability in HTLV-1 and HTLV-2 rates over time, across nations and in high-risk populations. Therefore generalizability across settings is limited, warranting ongoing prevalence studies in endemic areas. As a result, we aim to assess the prevalence of HTLV and HIV co-infections in key populations of marginalized communities, namely transactional sex workers and IDUs, in the Dominican Republic.

Methods

Study settings

During a period of 5 months from December 2012 through April 2013, a group of stakeholders belonging to key populations were identified through social workers and community representatives. These stakeholders were invited to inform the planning of the surveillance and sampling strategy of this study, employing a community-based participatory approach. After the identification of high-burden geographic regions of commercial sex work and drug use, four communities on the outskirts of the capital city, Santo Domingo, were selected as priority sites based on expected elevated prevalence. Persons who inject drugs or those who identified as transactional sex workers were identified by snowball sampling and recruited by community-based stakeholders belonging to the same region. All participants gave their written informed consent. The Ethics Committee of the Universidad Iberoamericana (UNIBE), Santo Domingo, Dominican Republic, approved this study.

Assuming a medium effect size (w=0.30), a level of significance of 0.05, 1 degree of freedom and a power (1-β error probability) of 0.98, the minimum sample size required was found to be 179. Expecting a 10% attrition rate, 200 participants >16 y of age were recruited. Of the 200 participants, 115 (57.5%) were men and 85 (42.5%) were women. All participants received pre- and post-study counselling on HIV and HTLV transmission and all results were provided on an individual basis by a physician and referral to care was provided. Plasma samples were screened for HTLV-1/2 immunoglobulin G (IgG) antibodies using the ImmunoComb II HTLV 1&2 test (Orgenics, Yavne, Israel) and for HIV antibodies with the ImmunoComb II HIV 1&2 BiSpot test (Orgenics, Israel) and for HIV antibodies with the ImmunoComb II HIV 1&2 BiSpot test (Orgenics, which differentiated between HIV-1 and HIV-2 as two separate spots in solid phase cards. HTLV- and HIV-positive samples were confirmed with western blot (MP Biomedicals, Santa Ana, CA, USA).

Risk factors, behaviours, demographic data and serological results were analysed using SPSS Statistics for Mac version 20.0 (IBM, Armonk, NY, USA) to individualize risk factors for HTLV infection and HTLV–HIV co-infection.

Results

Overall weighted seroprevalence of HTLV-1/2 IgG antibodies was 13.91% (95% CI 7.59 to 20.23%) in men and 10.59% (95% CI 4.05 to 17.13%) in women (Table 1). The mean age was 27.44 y (95% CI 23.02 to 31.86) for men and 25.22 y (95% CI 20.79 to 29.65) for women (Table 2). HTLV prevalence was...
equally associated among differing sexual orientation in men (Table 3). The overall weighted seroprevalence of HIV-1 was 13.91% (95% CI 7.59 to 20.23) in men and 17.65% (95% CI 9.55 to 25.75) in women, with a mean age of 28.13 y (95% CI 24.19 to 32.07) for men and 30.87 y (95% CI 27.07 to 34.67) for women. Correlation of HTLV and HIV antibodies was χ²(p=0.000; odds ratio [OR] 7.5789 (95% CI 3.0268 to 18.9770), χ²(1)=23.041, p=0.00001). High HTLV prevalence and co-infection with HIV was reported in lower socio-economic status communities/low-resource areas of Santo Domingo.

Of HTLV-positive men, 50% were co-infected with HIV (95% CI 25.5 to 74.5) while 44.44% of HTLV-positive women were co-infected with HIV (95% CI 11.98 to 76.9). Infection of HIV was strongly associated with sex work in this sample (OR 2.876 (95% CI 1.308 to 6.328), χ²(1)=7.289, p=0.007) (Tables 1 and 3). However, HTLV infection was not associated with sex work in this sample (OR 1.789 [95% CI 0.771 to 4.153], χ²(1)=1.868, p=0.172). Adjusting for confounding factors and the common OR was calculated (OR 6.301 [95% CI 2.051 to 15.875], χ²(1)=20.014, p=0.000). Additionally, an equal association can be seen in co-infected male sexual workers of various sexual orientations (Tables 1 and 3). Although an association between HTLV/HIV co-infections and sex work was found, the adjusted OR revealed a confounding role of HIV infection.

The majority of participants indicated that they used condoms, particularly those indicating they engaged in sex work (Table 1). Notably the greatest prevalence of HIV co-infected individuals occurred in male IDUs (75% [95% CI 44.99 to 105.01]). In the analysis of the type of drug used, marijuana represented the highest percentage among those with HTLV IgG (75% in males [95% CI 53.78 to 96.22], 77.78% in females [95% CI 50.62 to 104.94]) and HIV antibodies (75% in males [95% CI 53.78 to 96.22], 53.33% in females [95% CI 28.08 to 78.58]). Cocaine closely followed (Table 1).

### Table 1. Demographic and seroprevalence characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Male (n=115)</th>
<th>Female (n=85)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>HTLV positive</td>
<td>16</td>
<td>13.9</td>
</tr>
<tr>
<td>Co-infection with HIV</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Reported condom use</td>
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<td>74.8</td>
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<tr>
<td>Sexual preference</td>
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<tr>
<td>Heterosexual</td>
<td>85</td>
<td>73.9</td>
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<tr>
<td>Homosexual (MSM/WSW)</td>
<td>18</td>
<td>15.6</td>
</tr>
<tr>
<td>Bisexual</td>
<td>12</td>
<td>10.4</td>
</tr>
<tr>
<td>Reported drug use</td>
<td>115</td>
<td>100</td>
</tr>
<tr>
<td>Marijuana</td>
<td>94</td>
<td>81.7</td>
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<tr>
<td>Cocaine</td>
<td>65</td>
<td>56.5</td>
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<td>Heroin</td>
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<td>2.6</td>
</tr>
<tr>
<td>Crack</td>
<td>16</td>
<td>13.9</td>
</tr>
<tr>
<td>MDMA</td>
<td>3</td>
<td>2.6</td>
</tr>
<tr>
<td>Sex workers</td>
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<td>25.2</td>
</tr>
<tr>
<td>HTLV positive</td>
<td>8</td>
<td>7.6</td>
</tr>
<tr>
<td>Co-infection with HIV</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Reported condom use</td>
<td>26</td>
<td>89.7</td>
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<tr>
<td>Heterosexual</td>
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<tr>
<td>Homosexual (MSM/WSW)</td>
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<tr>
<td>Bisexual</td>
<td>8</td>
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<tr>
<td>IDUs</td>
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</tr>
<tr>
<td>HTLV positive</td>
<td>10</td>
<td>14.3</td>
</tr>
<tr>
<td>Co-infection with HIV</td>
<td>6</td>
<td>8.6</td>
</tr>
</tbody>
</table>

MDMA: 3,4-methylenedioxyamphetamine; WSW: women who have sex with women.

### Discussion

Data on HTLV prevalence is scarce and most likely is underestimated in the Caribbean. Also, many health professionals are unaware of HTLV and its pathological complications, there is a low accuracy of diagnosis and there is a lack of treatment options for HAM/TSP. Likewise, surveillance efforts are either non-existent or infrequent in most endemic countries. For these reasons, some experts have argued that HAM/TSP, and by extension HTLV, is a neglected disease.

Our findings demonstrate a high prevalence of HTLV among high-risk populations in the Dominican Republic, which supports previous studies that have characterized the Caribbean as an endemic region for HTLV. The data on gender, sexual orientation and condom use show equally distributed seropositivity. However, it remains unknown whether infection is the result of repeated exposure to the virus or after activation of HTLV-infected cells that were acquired at birth or an early age. HTLV seroprevalence in Dominican pregnant women has not been reported. In a broad study of the Caribbean region, the seroprevalence of HTLV in pregnant women was 2.0–3.8% and in Haiti it ranged from 2.2 to 4.2%. Another potential source of transmission that has not been explored is blood transfusions. In general, the blood supply in the Dominican Republic is considered unsafe and lags behind neighbouring Caribbean countries in screening 100% of donated blood. These gaps in the literature should be addressed in future studies to inform policy changes and amendments to current blood screening protocols.

Similar to what has been reported in other Latin American countries, a high prevalence of HTLV and co-infection with HIV was seen in low socio-economic status communities. The latest nationwide surveillance report revealed that in these areas in Santo Domingo, those who have the highest sexually transmitted infection prevalence are sex workers and IDUs. Among the sex workers surveyed, 20.1% had chlamydia, 6.2% had gonorrhea, 6% had syphilis, 1.7% had hepatitis B, 0.8% had hepatitis C, 7.8% had trichomoniasis, 7.4% had bacterial vaginosis and 1.7% had candidiasis. Among IDUs surveyed, 7.2% had syphilis, 3.1% had hepatitis B and 0.8% had hepatitis C. This disproportionate burden of both HIV and HTLV can be attributed to the nature of sex work, where risky behaviours include having multiple partners, engaging in unsafe sex practices, improper or inconsistent condom use and intravenous drug use. These findings could reflect greater engagement in these risky behaviors.
behaviours and the necessity for more public health preventive strategies among key populations living in these communities.

It should be noted that 75% of HIV co-infected individuals were male IDUs. In the Dominican Republic, IDUs have not previously been observed to have high levels of HTLV infection. The high frequency of seropositivity indicates increased accessibility to and popularity of intravenous drugs, as well as a potentially emerging outbreak in a country that lacks needle exchange programs and drug rehabilitation centres. Additionally, the majority of both male and female HIV co-infected individuals indicated they participate in sex work. Since parental transmission is traditionally associated with HTLV-2, while sexual transmission is strongly associated with HTLV-1, this outcome highlights the importance of further investigations to serotype HTLV in the Dominican Republic.

In the past decade, the recognition of HIV has changed from a death sentence to that of a manageable chronic condition. As of 2015, approximately 17.0 million people living with HIV (PLWH) are on antiretroviral therapy (ART), which is a 33% increase over the previous 2 y. Furthermore, with more people in the general population on stable regimens of ART, the number of PLWH has plateaued, but HTLV continues to be overlooked. Although the long-term effect of this co-infection is still being debated, there is greater consensus that HTLV-1/HIV-1 co-infection results in reduced survival time in both adults and children, and despite elevated CD4+ T cell counts, it does not delay the onset of opportunistic infections.

Also, the presence of HIV stimulates HTLV-1 by affecting gene expression and increasing production of pro-inflammatory cytokines interleukin 2 and interferon γ, thereby stimulating the production of T helper type 1 cytokines. Consequently, this chronic immune activation may induce prominent metabolic complications.

Therefore it is all the more important to consider the long-term implications of this co-infection, particularly in high-prevalence countries such as the Dominican Republic, and to demystify the associated complications. Results also call attention to the need for more investigations on the neurological complications experienced, to show the clinically relevant effect of HTLV-1 and HTLV-2 on HIV-1-positive patients.

Authors’ contributions: RP conceived the study and designed the study protocol. RP, LT, CRM, JPR and HB drafted the revised manuscript. All the authors contributed to interpretation of the data, critically revised the manuscript for intellectual content and approved the final manuscript. RP is the guarantor of the paper.

Acknowledgements: We express our sincere gratitude to Dr Aida Mencia-Ripley for her thoughtful guidance on the development and revision of this article and to the University of Alabama at Birmingham Sparkman Center for Global Health for their ongoing commitment to improving the health of high-risk populations in resource-constrained settings.

Funding: This work was supported by Universidad Iberoamericana internal funding for competitive innovation (FICU-UNIBE).

Competing interests: None declared.

Ethical approval: The Ethics Committee of Universidad Iberoamericana, Santo Domingo, Dominican Republic, approved this study.

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