CONCISE COMMUNICATION

The Relationships between Ethnicity, Sex, Risk Group, and Virus Load in Human Immunodeficiency Virus Type 1 Antiretroviral-Naive Patients

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This cross-sectional study examined the relationships between ethnicity, sex, risk group, and virus load in human immunodeficiency virus type 1 (HIV-1) antiretroviral-naive patients. HIV-1 RNA levels were measured in 322 patients attending St. Thomas’ Hospital between May 1997 and February 1999. By univariate analyses, only clinical status and CD4⁺ cell count were related to virus load. In multivariate analysis, variables independently related to virus load were CD4⁺ cell count (P = .001), being black African (P = .001), having a nonsexual risk for HIV infection (P = .03), and having AIDS (P = .05). Neither sex nor age was a significant predictor of initial virus load after adjusting for other variables. For a given CD4⁺ cell count, black Africans and people who contracted HIV nonsexually presented with a virus load lower than that of patients in other groups. Because virus loads may need to be interpreted differently according to ethnicity, this may affect decisions on when to initiate antiretroviral therapy and how to interpret clinical trial results.

Plasma virus load is an important marker for predicting the progression of disease in human immunodeficiency virus type 1 (HIV-1) infection [1]. Virus loads are used in combination with CD4⁺ lymphocyte count to estimate the stage of disease and to guide such therapeutic decisions as when to start and when to change highly active antiretroviral therapy. It is unclear, however, to what extent virus load varies according to factors such as sex and ethnicity.

Studies of the effect of a person’s sex on virus load suggest that virus load may be lower in women than in men early in infection, but as the infection progresses and immune deficiencies increase, sex differences tend to disappear [2, 3]. Few studies have compared virus load among ethnic groups. In a study of white, black, and Hispanic Americans, HIV-1 RNA levels were not associated with race or ethnicity [4]. However, a more recent study indicated that nonwhites have lower HIV-1 RNA levels [2]. A comparison of Ethiopian immigrants with HIV-1 subtype C infection and non-Ethiopian Israelis with subtype B infection found that, within given CD4⁺ categories, virus loads were very similar [5]. Studies have indicated a lower virus load among injection drug users (IDUs) than in gay men [2, 6]. However, other work that compared virus load between male and female IDUs and homosexual men concluded that any differences observed by risk group were driven chiefly by sex or by CD4⁺ cell percentage differences [7].

The objective of this study was to examine the relationships between ethnicity, sex, risk group, and virus load in HIV-1–seropositive patients attending a major HIV unit in south London. In 1998, 48% of newly diagnosed HIV-positive patients presenting to this unit were from sub-Saharan Africa, the majority of whom had non-B HIV-1 subtypes.

Subjects and Methods

All HIV-1–seropositive patients presenting at St. Thomas’ Hospital, London, between May 1997 and February 1999 who were antiretroviral naive at the time of their initial virus load measurement and who had virus load measured within 3 months of a CD4⁺ lymphocyte count were included in the study. Because of possible differences between virus load assays and because some other assays used at the time were thought to be less able to detect the virus in persons infected with non-B subtypes, only those in whom virus load was measured by branched-chain DNA (bDNA) assay were included in the analysis.

Medical records were reviewed for each patient, and the following information was retrieved: initial virus load, CD4⁺ lymphocyte
count, sex, age at diagnosis, ethnicity, probable mode of exposure to HIV, source of referral for HIV testing, and whether the patient had a diagnosis of AIDS at presentation. A diagnosis of AIDS was based on the Communicable Disease Surveillance Centre definition [8]. By this definition, a CD4⁺ cell count <200 cells/µL is not classified as AIDS defining.

**Laboratory assays.** HIV-1 RNA was measured in blood samples taken between 1 May 1997 and 31 September 1998 (279 samples) by the bDNA Chiron Quantiplex HIV RNA 2.0 assay (lower limit of quantification, 500 copies/mL). For blood samples taken after 1 October 1998 (43 samples), HIV-1 RNA was measured by the Chiron Quantiplex HIV RNA 3.0 assay (lower limit of quantification, 50 copies/mL).

**Statistical methods.** Data analysis was performed with SPSS for Windows, version 7.5.2. Virus load values were log₁₀ transformed for analysis. Univariate comparisons of virus load between patient groups were done by using unpaired Student’s t tests and analysis of variance. Univariate comparisons of CD4⁺ lymphocyte counts between patient groups were made by Mann-Whitney U and Kruskal-Wallis tests. Factors independently associated with virus load were identified by using a multiple linear regression model with a forward stepwise procedure. CD4⁺ lymphocyte count and age at diagnosis were included in the model as continuous variables, and sex and clinical status (AIDS/no AIDS) at the time of presentation as binary variables. Dummy variables were created to represent other categorical variables: ethnicity (white/black African/other), HIV risk group (homosexual/heterosexual/other), and source of referral (self-referred/general practitioner/hospital/other).

**Results**

**Demographic and clinical characteristics.** In total, 322 HIV-1-infected patients were included in the study. Of these subjects, 54% were white. Of the white group, 72.3% were gay men, and 12.7% were women. Black Africans formed the second largest ethnic group (35.1%): All had a heterosexual risk for infection, and 63.7% were women. Sixteen patients were thought to be infected with HIV through other, nonsexual routes, of whom 12 were infected via injection drug use. An initial diagnosis of AIDS was made at the time of presentation in 19.6% of patients.

**Virus load and CD4⁺ lymphocyte counts in relation to different patient characteristics.** Univariate analyses revealed no difference in initial virus load (log₁₀ copies/mL) with respect to ethnicity (P = .34), sex (P = .77), or risk group (P = .23) (figure 1). As expected, patients with AIDS had higher virus loads than those without AIDS (means of 4.73 and 4.04 log₁₀ copies/mL, respectively; P < .001), and there was a strong correlation between the CD4⁺ lymphocyte count and virus load (Spearman r = -0.47; P < .001). In addition, there was a relationship between virus load and source of referral (P = .04), with patients referred through a hospital department having virus loads higher than those of other patients. The initial CD4⁺ lymphocyte count was significantly different with respect to ethnicity (white patients had higher CD4⁺ lymphocyte counts than other patients; P < .001) and risk group (CD4⁺ lymphocyte counts

![Figure 1. Relationship between virus load (VL) and CD4⁺ lymphocyte count (in cells per microliter) by patient characteristics (top, ethnicity; center, sex; bottom, risk group). CI, confidence interval.](image-url)
were higher in gay men than in other patients; \(P < .001\). There was no significant difference between men and women with respect to CD4⁺ lymphocyte count (\(P = .07\)). Median CD4⁺ lymphocyte counts were as follows: all cases, 290 \(\times 10^3\) cells/L; black Africans, 220 \(\times 10^3\) cells/L; whites, 360 \(\times 10^3\) cells/L; and other ethnic groups, 210 \(\times 10^3\) cells/L. Median CD4⁺ lymphocyte counts were 360 \(\times 10^3\) cells/L for gay men, 240 \(\times 10^3\) cells/L for heterosexual men and women, and 230 \(\times 10^3\) cells/L for people in other risk groups.

**Multivariate analysis.** Table 1 shows results of the multivariate analysis. Variables that significantly contributed to the model were CD4⁺ lymphocyte count, being black African, belonging to the “other” risk group, and having an AIDS diagnosis at the time of presentation. After adjustment for all other variables in the model, the virus load was estimated to be 0.18 \(\log_{10}\) lower for every 100-cell-higher CD4⁺ lymphocyte count (\(P < .001\)), 0.32 \(\log_{10}\) lower among black Africans than among non-Africans (\(P = .001\)), and 0.44 \(\log_{10}\) lower among patients in the “other” risk group (\(P = .03\)), compared with patients in a heterosexual or homosexual risk group. In addition, the virus load was estimated to be 0.26 \(\log_{10}\) higher for patients who had an initial AIDS diagnosis.

Neither sex nor age at diagnosis significantly contributed to the model after adjustment for these factors. The analysis was repeated separately for heterosexual men and women and black Africans and yielded similar results. For heterosexual men and women, significant predictors of virus load were CD4⁺ lymphocyte count (estimate, \(-0.21\); \(P < .001\)), having an initial AIDS diagnosis (estimate, 0.39; \(P = .02\)), and being black African (estimate, \(-0.28\); \(P = .04\)). For black Africans, significant predictors of virus load were CD4⁺ lymphocyte count (estimate, \(-0.20\); \(P < .001\)) and having an initial AIDS diagnosis (estimate, 0.45; \(P = .02\)). When the analysis was repeated, either by excluding the 3 samples that were measured by the ultrasensitive assay and were <500 copies/mL or by setting the values to the lower limit of quantification for the less sensitive assay (500 copies/mL), the conclusions were similar.

**Discussion.**

Our results show that, for a given CD4⁺ cell count, black Africans present with a virus load lower than that of white patients. The majority of HIV-infected black Africans in the United Kingdom (UK) are infected by clade A and C HIV subtypes, whereas white patients are predominantly infected by the clade B subtype. Therefore, in this study, ethnicity was a marker not only of race but also of non-clade B HIV subtypes. The results could, therefore, be explained by a difference in rates of disease progression relating to HIV subtype. However, 2 European studies failed to find evidence for this; 1 study showed no difference in the plasma HIV-1 RNA levels between persons infected with subtypes A–D [9], and both studies indicated that non-B clades show rates of progression to AIDS similar to those of clade B [9, 10]. Of note, however, studies of non-B clades in Africa suggest that plasma HIV-1 RNA levels and rates of disease progression may differ between subtypes [8, 11].

The differences found in this study may indicate that the assay used does not give true results for black Africans. The accuracy of assays in measuring non-B subtypes has been a matter of concern in the past, and data indicate that HIV-1 subtype variation can have a major influence on virus load quantitation by different methods [12]. Nevertheless, this study included only samples measured by a single assay that is effective in measuring non-B HIV-1 subtypes [13]. Two different versions of the assay were used, and, although the later version is much more sensitive [13], similar conclusions were reached from the multivariate analysis after using an HIV-1 RNA count of <500 copies/mL as a cutoff for all values. Therefore, it appears unlikely that the differences in virus load between ethnic groups found in this study are a function of the choice of assay or the compatibility of assay versions.

If the assay is accurate, these findings suggest that virus load should be interpreted differently for different ethnic groups. This has implications for using virus load in black Africans as an indicator for when to initiate or to change antiretroviral therapy, and it suggests that treatment may need to be initiated at a lower virus load for black Africans than for whites. Furthermore, the interpretation of clinical trial results needs to take into account the ethnic makeup of the trial patient population.

Overall, there was no relationship between sex and virus load. The lack of any effect of sex in the subanalysis of black Africans suggests this conclusion. It has been established that virus load in women is lower initially and then converges with that in men over a period of 5–7 years. The sex difference seen in previous US cross-sectional studies may reflect the fact that the HIV-1 epidemic in the United States started in men earlier than in women, and thus women were infected later in calendar time than were men [3]. The same would not be true of persons who became infected in the African HIV epidemic.

There was no age effect after adjusting for other variables. Those patients not in a heterosexual or homosexual risk group, the majority of whom were IDUs, had a significantly lower virus load for a given CD4⁺ cell count. Given the small number of patients and the diversity of risk factors represented in this group, these results are difficult to interpret. Although IDUs have had lower virus loads in other studies, it is unclear what the biologic reason may be [7].

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Estimate</th>
<th>(P)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
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<tr>
<td>Constant</td>
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<td>&lt; .001</td>
<td>4.19 to 4.99</td>
</tr>
<tr>
<td>CD4⁺ cells/100 cells</td>
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<td>&lt; .001</td>
<td>-0.23 to -0.14</td>
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<td>.001</td>
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</tr>
<tr>
<td>Other risk group</td>
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<td>.03</td>
<td>-0.84 to -0.04</td>
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<tr>
<td>AIDS diagnosis</td>
<td>0.26</td>
<td>.05</td>
<td>0.004 to 0.51</td>
</tr>
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In this study, in the absence of information on the date of seroconversion, CD4⁺ cell count was used as a surrogate for disease progression and duration of infection. Although this is accepted clinical practice, it is important to be aware that CD4⁺ cell levels differ significantly by sex in seronegative men and women and after HIV-1 infection [14]. Ethnic differences have also been found in CD4⁺ cell levels [15]. A UK study indicated similar rates of CD4⁺ lymphocyte count decline in HIV-infected Africans and non-Africans in London [10]; however, a US study suggested that nonwhite persons have a decline in CD4⁺ cell counts slower than that in whites [2].

Further comparative studies that include people with known seroconversion dates may help to resolve the questions arising from this study. Such studies would indicate whether virus load differs between ethnic and risk groups for a given time after seroconversion, independently of the CD4⁺ cell count.

References