Hematologic and Biochemical Changes Associated with Human T Lymphotropic Virus Type 1 Infection in Jamaica: A Report from the Population-Based Blood Donors Study

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**Objective.** We investigated changes in hematologic and biochemical parameters associated with human T lymphotropic virus type 1 (HTLV-1) infection, antibody titer, and provirus load. Additionally, on a subset of participants, we assessed the epidemiologic relationship of HTLV-1 with *Strongyloides stercoralis*.

**Methods.** Among volunteer blood donors in Jamaica, HTLV-1 carriers were frequency matched with HTLV-1 negative subjects by age, sex, and date of blood donation. HTLV-1 antibody titer, provirus load, *S. stercoralis* IgG antibodies, complete blood cell count, blood chemistry, and urinalysis parameters were measured.

**Results.** HTLV-1 carriers, compared with HTLV-1–negative individuals, had elevated levels of cleaved lymphocytes (24.5% vs. 16.4%), any lymphocyte abnormalities (atypical, cleaved, and reactive lymphocytes combined, 45.7% vs. 35.4%), and γ-glutamyl transferase levels (21.2 vs. 19.6 IU/L), as well as lower eosinophil count (2.6% vs. 3.1%). Among carriers, HTLV-1 antibody titer was inversely correlated with mean corpuscular volume and positively correlated with levels of total protein, phosphorus, and lactate dehydrogenase. HTLV-1–provirus load was higher among carriers with cleaved lymphocytes and any lymphocyte abnormalities. Provirus load was inversely correlated with hemoglobin, mean corpuscular volume, neutrophil, and eosinophil levels and was positively correlated with lactate dehydrogenase levels. Provirus load was significantly higher among male than female subjects.

**Conclusions.** Markers of HTLV-1 infection (infection status, antibody titer, and provirus load) are associated with hematologic and biochemical alterations, such as lymphocyte abnormalities, anemia, decreased eosinophils, and elevated lactate dehydrogenase levels.

Human T lymphotropic virus type 1 (HTLV-1) causes adult T cell leukemia/lymphoma (ATL) and HTLV-1–associated myelopathy (also known as “tropical spastic paraparesis”) [1, 2]. Worldwide, HTLV-1 is endemic in southern Japan, the Caribbean, and parts of West Africa [1, 2]. The majority of HTLV-1 infections are asymptomatic, and the lifetime risk of developing ATL or HTLV-1–associated myelopathy/tropical spastic paraparesis is <5% [3, 4]. Previous studies have reported various alterations in hematologic and biochemical parameters among asymptomatic HTLV-1 carriers [5–11]. These include the presence of “flower cells,” which are abnormal lymphocytes with cleaved or lobulated nucleus that resemble ATL cells [12], anemia [5, 7, 11], elevated lymphocyte and platelet counts [6, 9], de-
creased eosinophil counts [6, 7, 9], and increased levels of creatine kinase (CK) and lactate dehydrogenase (LDH) [9, 10]. Whether these alterations are also associated with HTLV-1 titer and provirus load, 2 strong predictors of HTLV-1–associated disease risk [12, 13], has not been previously studied.

Mild, subclinical immunosuppression induced by HTLV-1 is believed to increase susceptibility to opportunistic infections [14, 15]. Clinical studies have shown that infection with Strongyloides stercoralis, an intestinal nematode, is common among HTLV-1 carriers [14–18]. When infected with S. stercoralis, HTLV-1 carriers appear to manifest more-severe parasite dissemination [14, 15]. Conversely, chronic antigen stimulation associated with S. stercoralis coinfection may also alter the clinical course of HTLV-1 infection [14, 19–22]. Few studies have assessed the epidemiologic relationship of S. stercoralis with HTLV-1 antibody titer and provirus load. Furthermore, the impact of S. stercoralis coinfection on hematologic and biochemical parameters among HTLV-1 carriers has not been previously addressed.

In this study, we examined hematologic and biochemical changes associated with HTLV-1 infection status and with antibody titer and provirus load among carriers. Additionally, with a subset of the study participants, we assessed the association of S. stercoralis with HTLV-1 infection, antibody titer, provirus load, and hematologic and biochemical changes.

MATERIALS AND METHODS

Study Subjects
We included participants in the Jamaica Blood Donors Study, a cross-sectional study of HTLV-1 infection. Between June 2001 and June 2006, individuals who donated blood at the National Transfusion Center or at the University of West Indies blood bank in Kingston were invited to participate in the study. Five hundred fifty-five subjects who were HTLV-1 seropositive, as determined by blood bank screening, were frequency matched with 357 HTLV-1–seronegative donors by age (± 5 years), sex, and date of blood donation (± 3 months). Using a standardized questionnaire, a trained study nurse collected past and current medical history and demographic information. All participants underwent physical examination, electrocardiography, urinalysis, and phlebotomy. All study procedures were conducted by personnel blind to the HTLV-1 status of the subject. The study was approved by the University of West Indies and National Cancer Institute institutional review boards.

Laboratory Methods

HTLV-1 assays. Plasma and PBMCs were separated in the HTLV-1 laboratory at University of West Indies and were stored at −70°C at National Cancer Institute’s central biospecimen repository until use. The blood bank initially determined HTLV-1 status with use of a whole-virus EIA (Vironostika). HTLV-1 status was then confirmed in the National Cancer Institute–Science Applications International Corporation laboratory (Frederick, MD) with use of a western blot (HTLV blot 2.4; Genelabs Diagnostics), as described elsewhere [23]. Briefly, individuals were considered to be HTLV-1 positive when 3 bands corresponding to p19, p24, and rpg46-I were present at >1 intensity [23]; patients for whom all 3 bands (p19, p24, and rpg46-I) were absent were considered to be HTLV-1 negative [23]. Individuals with bands for p24 and rpg46-II were classified as HTLV-II positive, and individuals with bands for other patterns were considered to be HTLV indeterminate [23]. HTLV-1 antibody titer was measured using a 5-fold end point dilution method (HTLV-1 microelisa system; Vironstika). Quantitative provirus DNA load in PBMCs was measured using a real-time automated TaqMan PCR method [24]. Provirus load was normalized to the number of endogenous retrovirus type 3 copies, to adjust for DNA input [24]. HTLV-1 carriers with undetectable provirus load were assigned a value of 5 copies per 10⁴ cells, which is one-half of the lower limit of detection.

Strongyloides assay. IgG antibodies to S. stercoralis were detected in plasma with use of an EIA, as described elsewhere [25]. Samples with an antibody level of 0%–7% were considered to be negative, and those with a level ≥8% were considered positive [25].

Complete blood cell count (CBC), blood chemistry, and urinalysis. CBC and blood chemistry were determined using standard automated assays at University of West Indies. Blood smears were used to detect the presence of atypical lymphocytes, cleaved lymphocytes, and reactive lymphocytes (≥1% defined as positive). Subjects positive for atypical lymphocytes, cleaved lymphocytes, or reactive lymphocytes were considered to be positive for any lymphocyte abnormalities. Urinalysis included dipstick detection of blood, glucose, and protein; a result of − or −/+ was considered to be negative, and +/+ ++/ +++ was considered to be positive. The C-reactive protein level was measured using an immunoturbidimetry assay (Dade Behring), and results were dichotomized as normal (<0.5 mg/dL) and abnormal (≥0.5 mg/dL).

Statistical Analyses
Of the 912 (555 HTLV-1–positive and 357 HTLV-1–negative) subjects enrolled in the study, we excluded 44 HTLV-1–indeterminate subjects from all analyses. Additionally, we excluded 31 subjects who were HTLV-II positive (29 among HTLV-1–positive and 2 among HTLV-1–negative subjects). Thus, the analyses were based on 837 subjects (482 HTLV-1–positive and 355 HTLV-1–negative subjects). S. stercoralis serology assays were performed for all participants with available specimens who were recruited into the study before December 2004 (288 [34.4%] of 837 participants; 134 of whom were HTLV-1 positive and 154 of whom were HTLV-1 negative).
Table 1. Associations of clinical parameters and *Strongyloides stercoralis* antibody with human T lymphotropic virus type 1 (HTLV-1) status among blood donors in the Jamaica Blood Donors Study.

<table>
<thead>
<tr>
<th>Categorical variables</th>
<th>No. (%) of subjects</th>
<th>HTLV-1 negative (N = 355)</th>
<th>HTLV-1 positive (N = 482)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical lymphocytes</td>
<td></td>
<td></td>
<td></td>
<td>.08</td>
</tr>
<tr>
<td>Negative</td>
<td>299 (84.7)</td>
<td>385 (80.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>54 (15.3)</td>
<td>96 (20.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaved lymphocytes</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Negative</td>
<td>295 (83.6)</td>
<td>363 (75.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>58 (16.4)</td>
<td>118 (24.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reactive lymphocytes</td>
<td></td>
<td></td>
<td></td>
<td>.63</td>
</tr>
<tr>
<td>Negative</td>
<td>324 (91.8)</td>
<td>438 (91.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>29 (8.2)</td>
<td>43 (8.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any lymphocyte abnormalities</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.01</td>
</tr>
<tr>
<td>No</td>
<td>228 (64.6)</td>
<td>261 (54.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>125 (35.4)</td>
<td>220 (45.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-reactive protein level</td>
<td></td>
<td></td>
<td></td>
<td>.67</td>
</tr>
<tr>
<td>Normal</td>
<td>306 (86.2)</td>
<td>409 (85.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>49 (13.8)</td>
<td>71 (14.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrocardiography findings</td>
<td></td>
<td></td>
<td></td>
<td>.35</td>
</tr>
<tr>
<td>Normal</td>
<td>312 (90.7)</td>
<td>433 (92.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>32 (9.3)</td>
<td>36 (7.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Strongyloides stercoralis</em></td>
<td></td>
<td></td>
<td></td>
<td>.79</td>
</tr>
<tr>
<td>Negative</td>
<td>136 (88.3)</td>
<td>117 (87.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>18 (11.7)</td>
<td>17 (12.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** Values in boldface are statistically significant at P < .05. Results were unavailable from 2 subjects for C-reactive protein level, 3 subjects for all complete blood cell count results, and 17 subjects for electrocardiography findings.  
* P values are adjusted for age and sex.  
**b** Includes subjects with atypical lymphocytes, cleaved lymphocytes, or reactive lymphocytes.  
**c** Normal level, <0.5 mg/dL; abnormal level, ≥0.5 mg/dL.  
**d** Includes subjects with bradycardia, tachycardia, T-wave inversion, left ventricular hypertrophy, sinus rhythms, and ventricular extra systole.  
**e** *S. stercoralis* results were available for 288 subjects.

Nonnormally distributed continuous virologic, CBC, and blood chemistry results were transformed on either the log10 scale (HTLV-1 antibody titer, provirus load, WBC, and platelet levels) or the natural log (Ln) scale (mean corpuscular volume [MCV], monocyte percentage, eosinophil percentage, and potassium, total CO2, urea, total protein, total bilirubin, and alkaline phosphatase, γ-glutamyl transpeptidase [GGT], serum glutamic oxaloacetic transaminase, calcium, phosphorus, and LDH level) to achieve approximate normality. For all analyses, CBC and blood chemistry results were used as the dependent variables. Associations of HTLV-1 status and *S. stercoralis* serostatus with categorical CBC and blood chemistry results were assessed using logistic regression after adjustment for age and sex. Associations of HTLV-1 status and *S. stercoralis* serostatus with continuous CBC and blood chemistry results were assessed using multiple linear-regression models. From these models, we report age- and sex-adjusted means and SDs. For ease of interpretation, except for HTLV-1 titer and provirus load, we present adjusted geometric means and SDs after back-transformation to the original scale.

Among HTLV-1 carriers (n = 482), associations of HTLV-1 antibody titer (n = 482) and provirus load (n = 326) with categorical CBC and blood chemistry results were assessed using logistic regression. We calculated age- and sex-adjusted Pearson’s partial correlation coefficients to assess the degree of correlation of HTLV-1 titer or provirus load with continuous CBC and blood chemistry results. All analyses were performed using SAS software, version 9.1 (SAS), and because of the exploratory nature of this study, corrections for multiple comparisons were not performed.

**RESULTS**

**Hematologic and biochemical alterations associated with HTLV-1 infection status.** A significantly higher proportion of HTLV-1 carriers had cleaved lymphocytes (24.5% vs. 16.4%; P < .01) and any lymphocyte abnormalities combined (45.7% vs. 35.4%; P < .01) than did HTLV-1–negative subjects (table 1). HTLV-1 carriers also had a significantly lower mean eosinophil percentage (2.62% vs. 3.16%; P < .01), lower mean potassium level (4.18 vs. 4.34 mmol/L; P < .01), and significantly higher mean GGT level (21.2 vs. 19.6 IU/L; P = .04) than did HTLV-1–negative subjects (table 2). Atypical lymphocytes, WBC counts, and alkaline phosphatase and serum glutamic oxaloacetic transaminase levels were marginally higher among HTLV-1 carriers than among HTLV-1–negative subjects (tables 1 and 2). Levels of other parameters evaluated were similar between HTLV-1–positive and –negative subjects.

**Hematologic and biochemical alterations associated with HTLV-1 antibody titer.** Among 482 HTLV-1 carriers, the mean log10 HTLV-1 antibody titer (± SD) was 3.23 ± 0.82. Mean HTLV-1 antibody titer did not significantly differ by sex (table 3). Antibody titer was not associated with the presence of atypical, cleaved, or reactive lymphocytes, either separately or combined as any lymphocyte abnormalities (table 3). HTLV-1 antibody titer was inversely correlated with MCV (r = −0.10; P = .02) and total carbon dioxide levels (r = −0.11; P = .03) (table 4). Antibody titer was positively correlated with levels of total protein (r = 0.16; P < .01), phosphorus (r = 0.12; P < .01), and LDH (r = 0.24; P < .01) (table 4). Antibody titer was marginally associated with decreased neutrophil count and increased calcium level.

**Hematologic and biochemical alterations associated with HTLV-1 provirus load.** Among 326 HTLV-1 carriers with available provirus load, the mean log10 provirus load (± SD) was 2.92 ± 1.14. Provirus load was significantly higher among
male than female subjects (3.06 copies/10^5 cells vs. 2.71 copies/10^5 cells; \(P<.01\)) (table 3). Provirus load was significantly higher among carriers with cleaved lymphocytes (3.24 vs. 2.86 copies/10^5 cells; \(P = .01\)) and any lymphocyte abnormalities (3.12 vs. 2.78 copies/10^5 cells; \(P<.01\)) than among carriers without the respective lymphocyte abnormality (table 3). Provirus load was inversely correlated with hemoglobin level (\(r = -11; \ P = .04\)), MCV (\(r = -0.15; \ P<.01\)), neutrophil count (\(r = -0.12; \ P = .02\)), and eosinophil level (\(r = -0.19; \ P<.01\)) and was positively correlated with potassium (\(r = 0.11; \ P = .03\)) and LDH (\(r = 0.12; \ P = .02\)) levels (table 4). Provirus load was marginally associated with increased proportion of atypical lymphocytes, increased bilirubin level, and decreased GGT level. Carriers with missing provirus load data had sex and age distributions similar to those for carriers with available provirus load.

**S. stercoralis associations.** Overall prevalence of *S. stercoralis* antibody was 12.1% (35 of 288 subjects), and prevalence was similar between HTLV-1 carriers and HTLV-1–negative subjects (12.7% vs. 11.7%; \(P = .79\)) (table 1). Among HTLV-1 carriers (\(n = 134\)), the mean log_{10} HTLV-1 antibody titer (3.22 in coinfected subjects vs. 3.26 in subjects infected with HTLV-1 only; \(P = .61\)) and mean log_{10} HTLV-1 provirus load (2.98 copies/10^5 cells in coinfected subjects vs. 2.84 copies/10^5 cells in subjects infected with HTLV-1 only; \(P = .53\)) did not differ by *S. stercoralis* coinfection status (table 3).

Among subjects with *S. stercoralis* data (\(n = 288\), *S. stercoralis*–seropositivity was not associated with age or sex. *S. stercoralis*–seropositive subjects had a higher mean eosinophil percentage (4.11% vs. 2.70%; \(P = .08\)) and total bilirubin level (12.74 vs. 8.57 μmol/L; \(P = .01\)) and a lower mean creatinine level (74.51 vs. 84.10 μmol/L; \(P = .05\)) and a marginally lower mean uric acid level (0.29 vs. 0.31 mmol/L; \(P = .19\)) than did *S. stercoralis*–seronegative subjects. Among HTLV-1 carriers (\(n = 134\), *S. stercoralis*–seropositive subjects had significantly higher mean eosinophil percentage (4.11% vs. 2.70%; \(P = .01\)), higher mean bilirubin level (12.12 vs. 8.57 μmol/L; \(P = .01\)), marginally higher mean hemoglobin concentration (13.40 vs. 12.91 g/dL; \(P = .05\)), and marginally lower mean creatinine level (74.51 vs. 84.10; \(P = .06\)) than did *S. stercoralis*–seronegative subjects. Among HTLV-1 carriers (\(n = 134\), *S. stercoralis*–seropositive subjects had significantly higher mean eosinophil percentage (4.11% vs. 2.70%; \(P = .01\)), higher mean bilirubin level (12.12 vs. 8.57 μmol/L; \(P = .01\)), marginally higher mean hemoglobin concentration (13.40 vs. 12.91 g/dL; \(P = .05\)), and marginally lower mean creatinine level (74.51 vs. 84.10; \(P = .06\)) than did *S. stercoralis*–seronegative subjects. **Table 2.** Associations of hematologic and biochemical parameters, with human T lymphotropic virus type 1 (HTLV-1) status among blood donors in the Jamaica Blood Donors Study. 

<table>
<thead>
<tr>
<th>Continuous variables</th>
<th>HTLV-1 negative (N = 355)</th>
<th>HTLV-1 positive (N = 482)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count, cells (\times 10^9/L)</td>
<td>5334.57 ± 753.83</td>
<td>5536.05 ± 790.01</td>
<td>.09</td>
</tr>
<tr>
<td>Hemoglobin concentration, g/dL</td>
<td>13.05 ± 0.97</td>
<td>13.10 ± 0.98</td>
<td>.45</td>
</tr>
<tr>
<td>Mean corpuscular volume, fl</td>
<td>87.44 ± 5.75</td>
<td>86.80 ± 5.71</td>
<td>.10</td>
</tr>
<tr>
<td>Platelet count, cells (\times 10^9/L)</td>
<td>251,420.10 ± 25,071.34</td>
<td>246,263.47 ± 24,818.67</td>
<td>.19</td>
</tr>
<tr>
<td>Neutrophils/bands/segments, %</td>
<td>49.10 ± 12.74</td>
<td>49.48 ± 12.83</td>
<td>.66</td>
</tr>
<tr>
<td>Lymphocyte percentage</td>
<td>40.06 ± 11.63</td>
<td>40.27 ± 11.71</td>
<td>.80</td>
</tr>
<tr>
<td>Monocyte percentage</td>
<td>5.60 ± 3.09</td>
<td>5.56 ± 3.09</td>
<td>.85</td>
</tr>
<tr>
<td>Eosinophil percentage</td>
<td>3.16 ± 2.33</td>
<td>2.62 ± 1.95</td>
<td>.01</td>
</tr>
<tr>
<td>Potassium level, mmol/L</td>
<td>4.34 ± 0.58</td>
<td>4.18 ± 0.57</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Total CO₂ level, mmol/L</td>
<td>23.78 ± 3.27</td>
<td>23.35 ± 3.23</td>
<td>.11</td>
</tr>
<tr>
<td>Creatinine level, μmol/L</td>
<td>86.96 ± 20.80</td>
<td>85.92 ± 20.75</td>
<td>.47</td>
</tr>
<tr>
<td>Total protein level, g/L</td>
<td>75.24 ± 6.93</td>
<td>75.53 ± 6.90</td>
<td>.55</td>
</tr>
<tr>
<td>Total bilirubin level, μmol/L</td>
<td>10.14 ± 6.06</td>
<td>10.33 ± 6.22</td>
<td>.64</td>
</tr>
<tr>
<td>Alkaline phosphatase level, IU/L</td>
<td>59.25 ± 21.82</td>
<td>62.09 ± 23.05</td>
<td>.06</td>
</tr>
<tr>
<td>SGOT level, IU/L</td>
<td>19.60 ± 11.10</td>
<td>21.22 ± 12.13</td>
<td>.04</td>
</tr>
<tr>
<td>Calcium level, mmol/L</td>
<td>2.37 ± 0.17</td>
<td>2.35 ± 0.17</td>
<td>.32</td>
</tr>
<tr>
<td>Phosphorus level, mmol/L</td>
<td>0.92 ± 0.24</td>
<td>0.91 ± 0.24</td>
<td>.96</td>
</tr>
<tr>
<td>LDH level, mmol/dL</td>
<td>167.73 ± 53.19</td>
<td>167.03 ± 53.23</td>
<td>.84</td>
</tr>
</tbody>
</table>

**NOTE.** Values in boldface are statistically significant at \(P<.05\). Results were unavailable from 3 subjects for all complete blood cell count results, 3 subjects for total protein and γ-glutamyl transpeptidase levels, 5 subjects for bilirubin and phosphorus levels, 7 subjects for alkaline phosphatase level, 10 subjects for uric acid level, 31 subjects for lactate dehydrogenase level, 110 subjects for chloride level, and 257 subjects for total carbon dioxide level. GGT, γ-glutamyl transpeptidase; SGOT, serum glutamic oxaloacetic transaminase.

\(a\) \(P\) values, means, and SDs are adjusted for age and sex.
Table 3. Associations of clinical variables with HTLV-1 antibody titer and provirus load among human T lymphotropic virus type 1 (HTLV-1) carriers in the Jamaica Blood Donors Study.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Log₁₀ HTLV-1 antibody titer (n = 482)</th>
<th>Log₁₀ HTLV-1 provirus loada (n = 326)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean OR (95% CI)b</td>
<td>Mean OR (95% CI)b</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3.30 1.00</td>
<td>2.71 1.00</td>
</tr>
<tr>
<td>Male</td>
<td>3.19 0.90 (0.77–1.05)</td>
<td>3.06 1.42 (1.10–1.84)</td>
</tr>
<tr>
<td>Atypical lymphocytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>3.24 1.00</td>
<td>2.87 1.00</td>
</tr>
<tr>
<td>Positive</td>
<td>3.22 0.99 (0.75–1.31)</td>
<td>3.22 1.30 (0.99–1.69)</td>
</tr>
<tr>
<td>Cleaved lymphocytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>3.21 1.00</td>
<td>2.86 1.00</td>
</tr>
<tr>
<td>Positive</td>
<td>3.29 1.11 (0.86–1.43)</td>
<td>3.24 1.39 (1.07–1.80)</td>
</tr>
<tr>
<td>Reactive lymphocytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>3.25 1.00</td>
<td>2.92 1.00</td>
</tr>
<tr>
<td>Positive</td>
<td>3.10 0.81 (0.54–1.21)</td>
<td>3.04 1.09 (0.78–1.51)</td>
</tr>
<tr>
<td>Any lymphocyte abnormalitiesc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.22 1.00</td>
<td>2.78 1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>3.25 1.05 (0.84–1.31)</td>
<td>3.12 1.30 (1.07–1.59)</td>
</tr>
<tr>
<td>C-reactive protein leveld</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3.21 1.00</td>
<td>2.97 1.00</td>
</tr>
<tr>
<td>Abnormal</td>
<td>3.37 1.19 (0.88–1.62)</td>
<td>2.77 0.92 (0.71–1.20)</td>
</tr>
<tr>
<td>Electrocardiography findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3.24 1.00</td>
<td>2.93 1.00</td>
</tr>
<tr>
<td>Abnormala</td>
<td>3.08 0.79 (0.51–1.22)</td>
<td>2.92 0.95 (0.68–1.33)</td>
</tr>
<tr>
<td>Strongyloides stercoralisf</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>3.22 1.00</td>
<td>2.98 1.00</td>
</tr>
<tr>
<td>Positive</td>
<td>3.26 1.04 (0.54–1.84)</td>
<td>2.84 0.89 (0.57–1.41)</td>
</tr>
</tbody>
</table>

**NOTE.** Values in boldface are statistically significant at P < .05. Results were unavailable from 1 subject for all complete blood cell count results, 2 subjects for C-reactive protein, and 9 subjects for electrocardiography findings.

a Provirus load results were available for 326 of 482 HTLV-1 carriers.

b Includes subjects with atypical lymphocytes, cleaved lymphocytes, or reactive lymphocytes.

c Includes subjects with bradycardia, tachycardia, T-wave inversion, left ventricular hypertrophy, sinus rhythms, and ventricular extra systole.

d Normal level, <0.5 mg/dL; abnormal level, ≥0.5 mg/dL.

DISCUSSION

Among healthy volunteer blood donors in Jamaica, we show that hematologic and biochemical changes, such as increased presence of lymphocyte abnormalities (particularly cleaved lymphocytes), decreased eosinophil count, and elevated GGT level, are associated with HTLV-1 infection status. Furthermore, unlike previous investigations that were limited to examinations of health effects associated with HTLV-1–infection status [5–11], we extended our analyses to include an evaluation of hematologic and biochemical changes associated with both HTLV-1 antibody titer and provirus load, 2 strong predictors of HTLV-1–associated disease risks among carriers [12, 13]. Our analyses show that alterations such as increased presence of lymphocyte abnormalities, anemia (decreased hemoglobin concentration and MCV), decreased eosinophil count, and elevated LDH level are correlated with HTLV-1 antibody titer and/or
Table 4. Associations of biochemical variables with human T lymphotropic virus type 1 (HTLV-1) antibody titer and provirus load among human T lymphotropic virus type 1 (HTLV-1) carriers in the Jamaica Blood Donors Study.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>( \text{Log}_{10} ) HTLV-1 titer ((n = 482))</th>
<th>( \text{Log}_{10} ) HTLV-1 provirus load(^c) ((n = 326))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( r )</td>
<td>( P^b )</td>
</tr>
<tr>
<td>WBC count, cells ( \times 10^3 )/L</td>
<td>-0.04</td>
<td>.29</td>
</tr>
<tr>
<td>Hemoglobin concentration, g/dL</td>
<td>-0.01</td>
<td>.77</td>
</tr>
<tr>
<td>Mean corpuscular volume, fl.</td>
<td>-0.10</td>
<td>.02</td>
</tr>
<tr>
<td>Platelet count, cells ( \times 10^3 )/L</td>
<td>0.02</td>
<td>.55</td>
</tr>
<tr>
<td>Neutrophils/bands/segments, %</td>
<td>-0.07</td>
<td>.08</td>
</tr>
<tr>
<td>Lymphocyte percentage</td>
<td>0.07</td>
<td>.10</td>
</tr>
<tr>
<td>Monocyte percentage</td>
<td>-0.02</td>
<td>.61</td>
</tr>
<tr>
<td>Eosinophil percentage</td>
<td>&lt;0.01</td>
<td>.92</td>
</tr>
<tr>
<td>Potassium level, mmol/L</td>
<td>0.01</td>
<td>.67</td>
</tr>
<tr>
<td>Total CO(\text{II}) level, mmol/L</td>
<td>-0.11</td>
<td>.03</td>
</tr>
<tr>
<td>Urea level, mmol/L</td>
<td>-0.03</td>
<td>.44</td>
</tr>
<tr>
<td>Creatinine level, ( \mu )mol/L</td>
<td>-0.05</td>
<td>.23</td>
</tr>
<tr>
<td>Total protein level, g/L</td>
<td>0.16</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Total bilirubin level, ( \mu )mol/L</td>
<td>0.01</td>
<td>.82</td>
</tr>
<tr>
<td>Alkaline phosphatase level, IU/L</td>
<td>-0.03</td>
<td>.45</td>
</tr>
<tr>
<td>GGT level, IU/L</td>
<td>-0.02</td>
<td>.64</td>
</tr>
<tr>
<td>SGOT level, IU/L</td>
<td>0.06</td>
<td>.14</td>
</tr>
<tr>
<td>Calcium level, mmol/L</td>
<td>0.08</td>
<td>.05</td>
</tr>
<tr>
<td>Phosphorus level, mmol/L</td>
<td>0.12</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>LDH level, mmol/dL</td>
<td>0.24</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

\(^a\) Pearson’s partial correlation coefficient adjusted for age and sex.
\(^b\) \( P \) value from linear-regression models, with adjustment for age and sex.
\(^c\) Provirus load results were available for 326 of 482 HTLV-1 carriers.

NOTE. Values in boldface are statistically significant at \( P < .05 \).

Because HTLV-1 antibody titer and provirus load reflect the burden of infection in an individual better than does infection status alone, our results suggest that HTLV-1 infection is directly responsible for these hematologic and biochemical alterations.

We found higher HTLV-1 provirus loads among male than female subjects. Although consistent with previous reports from Japan [26, 27], this is the first observation of a significant sex difference in provirus load from the Caribbean [24]. Our current results should be interpreted in the context of HTLV-1–associated disease incidence in that part of the world [24]. As previously noted, ATL incidence is significantly higher among men than women in Japan [26, 27], whereas such differences have not been noted in the Caribbean [24]. It is possible that our previous studies in the Caribbean, in which the overwhelming majority of participants were female [28], did not have sufficient statistical power to detect sex differences in HTLV-1 provirus load. Age at infection is an important risk factor for ATL, with younger ages at infection conferring higher risk [1]. Furthermore, previous studies have shown that HTLV-1 provirus load among individuals infected perinatally may continue to increase with increasing duration of infection [29]. Given that HTLV-1 is transmitted in infancy by breast-feeding and that, among adults, it is transmitted predominantly sexually from men to women [30], the average age at infection in our cohort was presumably much younger in male than in female subjects. Thus, a higher provirus load among male subjects in our cohort may have arisen from a higher proportion of subjects perinatally infected among male subjects, compared with female subjects. This observation, however, warrants replication in future studies.

Our observations of a higher proportion of lymphocyte abnormalities (particularly atypical and cleaved lymphocytes) among HTLV-1–positive subjects, the associations of lymphocyte abnormalities with high antibody titer and provirus load, and the positive correlation of LDH level with antibody titer, as well as provirus load, are consistent with increased leukocyte turnover caused by HTLV-1 infection [6, 9–11, 13]. Extending previous reports of increased anemia associated with HTLV-1 infection [5, 7, 11], we show that levels of hemoglobin and
MCV are negatively correlated with high antibody titer and/or provirus load among carriers, which suggests a direct role of HTLV-1 in causing anemia.

Increased mortality from liver cancer and heart disease has been previously reported among HTLV-1 carriers [31, 32]. In this study, HTLV-1 infection status was not associated with abnormal C-reactive protein levels or electrocardiography findings, but HTLV-1 infection status was associated with significant elevations in levels of GGT and marginally significant elevations in levels of alkaline phosphatase and serum glutamic oxaloacetic transaminase, markers of cardiac and hepatic damage. However, because HTLV-1 antibody titer and provirus load were not associated with changes in alkaline phosphatase, GGT, or serum glutamic oxaloacetic transaminase levels, it is unclear whether HTLV-1 infection is directly responsible for these alterations. Murphy et al. [7] previously reported a higher prevalence of self-reported hepatitis among HTLV-1–positive food handlers in Jamaica than among HTLV-1–negative individuals. Thus, it is possible that these observations are confounded by other factors, such as coinfections with hepatitis B and hepatitis C viruses [31].

HTLV-1 infection status and antibody titer and provirus load were significantly associated with decreased eosinophil counts. A decrease in the eosinophil count induced by HTLV-1 infection is believed to increase susceptibility to parasitic infections among carriers [6, 7, 9, 14]. We found that *S. stercoralis* infection was independent of HTLV-1 infection status, antibody titer, and provirus load. This lack of association between HTLV-1 carriage and *S. stercoralis* is consistent with previous seroepidemiologic studies from this region [17, 33]. Although HTLV-1 and *S. stercoralis* were independent, coinfection with *S. stercoralis* among HTLV-1 carriers was associated with increased eosinophil counts, highlighting the opposing effects of HTLV-1 and *S. stercoralis* on eosinophil levels. This opposing effect on eosinophil counts, coupled with the cross-sectional nature of our study, make it particularly difficult to address whether increased susceptibility to parasite coinfection among HTLV-1 carriers arises from decreased eosinophil counts.

We note the limitations of our study. Our results for the epidemiologic association of HTLV-1 carriage with *S. stercoralis* infection must be interpreted with caution because *S. stercoralis* results were available for only a subset (34.4%) of subjects recruited into the study. Furthermore, because we relied solely on serologic tests for determination of *S. stercoralis* infection status, our results warrant cautious interpretation. Concomitant stool examination for determination of *S. stercoralis* larvae would have been ideal for distinguishing current infections and evaluating the possible impact of parasite burden [14, 17]. The cross-sectional nature of our study curtails any conclusions regarding temporality of associations. Although we observed that several biochemical changes were significantly associated with HTLV-1 infection status, titer, and provirus load, the majority of these alterations were within clinical limits. Additional longitudinal studies with additional intermediate markers of clinical outcomes are required to address whether these alterations correlate with future disease risks. We could not adjust analyses for important confounders, such as socioeconomic status. Finally, discrepancies in associations of HTLV-1 infection status, antibody titer, and provirus load with hematoLogic and biochemical parameters may have arisen from differences in statistical power across comparisons.

In conclusion, markers of HTLV-1 infection (infection status, antibody titer, and provirus load) are associated with hematologic and biochemical alterations, such as lymphocyte abnormalities, anemia, decreased eosinophil counts, and elevated LDH level. Future studies addressing the longitudinal changes in subclinical health effects among healthy HTLV-1 carriers may aid in a better understanding of HTLV-1–associated disease pathogenesis.

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