

The Search for a Predictor of CD4 Cell Count Continues: Total Lymphocyte Count Is Not a Substitute for CD4 Cell Count in the Management of HIV-Infected Individuals in a Resource-Limited Setting

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Total lymphocyte count (TLC) has been recommended as a substitute for CD4 cell count for the management of HIV-infected individuals living in resource-limited settings. To confirm this, 151 TLCs and CD4 cell counts were obtained from 109 patients who had not yet started treatment and analyzed. CD4 cell counts of <200 cells/mm³ were found in 42 cases (37.8%) with TLCs of ≥1200 cells/mm³. Thus, 1 in 3 individuals would have been deprived of needed treatment. Therefore, in this setting, TLC is not a reliable predictor of CD4 cell count in HIV-infected individuals.

Monitoring individuals with HIV infection/AIDS involves the use of expensive tools, which are not readily available in resource-limited settings. In April 2002, the World Health Organization (WHO) recommended that, when a CD4 cell count is not available or is not affordable to obtain for affected individuals, a total lymphocyte count of less than 1000–1200 lymphocytes/mm³ in individuals with stage II or III disease be used as an indication to initiate antiretroviral therapy [1]. This recommendation was based on rigorous evaluation of data obtained almost exclusively from developed countries [2–4]. In 2001, Akanmu et al. [5] reported that total lymphocyte count could not be used as a surrogate for CD4 cell count in mon-

itoring response to antiretroviral therapy. There is limited information on the relationship between CD4 cell counts and total lymphocyte count and other hematological indices in resource-limited settings. This study was initiated to ascertain the reliability of total lymphocyte count as a substitute for CD4 cell count, determine the relationship of other hematological indices with CD4 cell count, and observe the influence of the person's sex, if any, on data collected.

Patients, materials, and methods. All consenting HIV-1-seropositive individuals, both symptomatic and asymptomatic, were recruited over a 12-month period and were investigated. Hematological indices, such as hematocrit, WBC count, and WBC differential count, were obtained using an automated cell counter (Advia-60; Advia). CD4 lymphocyte count was obtained using the Dynal Manual CD4 kit. Total lymphocyte count was calculated from the WBC count and the differential count for lymphocytes. The sensitivity and specificity of total lymphocyte count as a predictor of CD4 cell count were calculated together with the likelihood ratio [5]. Data are presented as mean ± SD with 95% CIs and are analyzed using differential statistics.

Results. A total of 151 results from 109 HIV-1-seropositive individuals with a mean age of 38.5 ± 11.6 years were analyzed. There were significantly more female patients than male patients (ratio of male to female patients, 1:1.4; *P* < .05). The mean hematocrit was 31.8% ± 7.0%, the mean WBC count was 4892 ± 2239 cells/mm³, the mean total lymphocyte count was 1966 ± 1079 lymphocytes/mm³, and the mean CD4 cell count was 225 ± 175 cells/mm³ (table 1). Table 2 shows that male subjects were significantly older than female subjects (45.4 ± 11 vs. 34.7 ± 10 years; *P* < .0001) and had a higher mean hematocrit than female subjects (34% ± 7% vs. 30% ± 6.5%; *P* < .01), but the other parameters showed no significant difference between the sexes.

Correlations between CD4 cell count and the other parameters (table 3) showed that total lymphocyte count (*r* =

Table 1. Measured parameters for 151 tests performed for 109 HIV-1-seropositive individuals in a resource-limited setting.

Parameter	Mean ± SD	95% CI
Age, years	38.5 ± 11.6	31.4–45.7
Hematocrit, %	31.8 ± 7.0	26.7–36.8
WBC count, cells/mm ³	4892 ± 2239	4112–5673
Total lymphocyte count, cells/mm ³	1966 ± 1079	1653–2280
CD4 cell count, cells/mm ³	225 ± 175	189–260

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Table 2. Measured parameters of 64 male and 87 female HIV-1-seropositive patients in a resource-limited setting.

Parameter	Male patients	Female patients	P
Age			<.0001
Mean years \pm SD	45.4 \pm 10.9	34.7 \pm 10.1	
No. of patients with data	31	56	
Hematocrit			<.001
Mean % \pm SD	34.1 \pm 7	30.1 \pm 6.5	
No. of results analyzed	64	87	
WBC count			NS
Mean cells/mm ³ \pm SD	4788 \pm 2090	4970 \pm 2351	
No. of results analyzed	64	87	
Total lymphocyte count			NS
Mean lymphocytes/mm ³ \pm SD	1973 \pm 1111	1962 \pm 1062	
No. of results analyzed	64	87	
CD4 cell count			NS
Mean cells/mm ³ \pm SD	222 \pm 189	227 \pm 165	
No. of results analyzed	64	87	

NOTE. NS, not statistically significant (i.e., $P > .05$).

0.431; $P < .001$) and hematocrit ($r = 0.373$; $P < .001$) had significant positive correlations. WBC count and age were not significantly correlated with CD4 cell count. Data on patient sex (table 4) showed that female sex had a stronger correlation ($r = 0.473$; $P < .001$) than did male sex ($r = 0.384$; $P < .01$) with total lymphocyte count and CD4 cell count. However the reverse was the case for hematocrit and CD4 cell count ($r = 0.453$ [$P < .001$] and $r = 0.340$ [$P < .01$], respectively). For 111 results (73.5%; 64 female and 47 male patients), the total lymphocyte count was ≥ 1200 lymphocytes/mm³; of these patients, 42 (37.8%; 21 female and 21 male) had a CD4 cell count of < 200 cells/mm³ (figure 1). The sensitivity of total lymphocyte count as a predictor of CD4 cell count was 45.5%, and the specificity was 62.2%. The likelihood ratio was 0.83.

Discussion. The mean values obtained in this laboratory-based study were similar to values reported elsewhere (table 1) [5, 6]. The correlation coefficient for CD4 cell count and hematocrit was not as strong as that for CD4 cell count and total lymphocyte count (table 3), and, therefore, hematocrit cannot be used as a predictor of CD4 cell count, particularly in patients with an advanced state of immunosuppression. Contrary to

expectation, total lymphocyte count did not correlate strongly with CD4 cell count, as was reported by Beck et al. [2] in 1996, and there was not a significant difference between male and female subjects with regard to CD4 cell count [7, 8]. Indeed, this study corroborates findings of other studies [5, 9] that total lymphocyte count was not a surrogate for CD4 cell count and that it was “an imperfect predictor of CD4 count” [9]. Again, support for this was provided by the sensitivity of total lymphocyte count as a predictor of CD4 cell count, which was $< 50\%$ in this study. It was also observed that ~ 1 of 3 results involving a total lymphocyte count of 1200 lymphocytes/mm³ had a CD4 cell count of < 200 cells/mm³. This means that, at diagnosis, too many individuals would have gone untreated if

Table 3. Correlation of CD4 cell count with other parameters.

Parameter	r	P
Age, years	0.0243	NS
Hematocrit, %	0.3733	<.001
WBC count, cells/mm ³	0.1458	NS
Total lymphocyte count, lymphocytes/mm ³	0.4309	<.001

NOTE. NS, not significant (i.e., $P > .05$).

Table 4. The influence of patient sex on the correlations between CD4 cell count, age, and measured hematological parameters.

Parameter, patient sex	r	P
Age, years		
Male	0.3973	<.05
Female	-0.0189	NS
Hematocrit, %		
Male	0.4534	<.001
Female	0.3399	<.01
WBC count, cells/mm ³		
Male	0.0620	NS
Female	0.209	NS
Total lymphocyte count, lymphocytes/mm ³		
Male	0.3837	<.01
Female	0.4732	<.001

NOTE. NS, not significant (i.e., $P > .05$).

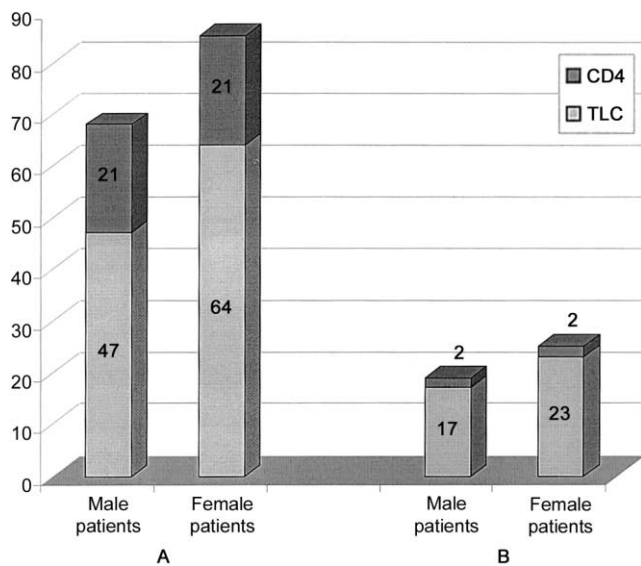


Figure 1. The number of results with a CD4 cell count of $<200\text{ cells/mm}^3$, despite a total lymphocyte count (TLC) of $\geq 1200\text{ lymphocytes/mm}^3$ (A), and vice versa (B).

the WHO guideline for the use of total lymphocyte count instead of CD4 cell count was implemented, and this would be unethical.

Total lymphocyte count is not a substitute for CD4 cell count in a resource-limited setting: 1 in 3 individuals would be deprived of needed medication if a total lymphocyte count of 1200 cells/mm^3 were used, as recommended by the WHO. CD4 cell counts per se were similar for male and female patients. Other hematological indices have not been found to be useful predictors of CD4 cell count, which will have to remain the gold standard for monitoring HIV-infected individuals, even

in a resource-limited setting, until another readily available surrogate marker is found. The search continues.

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