RESEARCH NOTE

Gender differences in human immunodeficiency virus (HIV) RNA and CD4 cell counts among new entrants to HIV care

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ABSTRACT

Clinic database extraction identified 806 new entrants to human immunodeficiency virus (HIV) care in Cleveland, OH, USA. At entry, women had higher CD4 counts and lower HIV RNA levels than men (mean, 388 vs. 310 cells/μL, and 8.94×10^4 vs. 1.27×10^5 copies/mL, respectively), but the proportion of entrants with category C illnesses, category B conditions, sexually transmitted diseases and CD4 counts <200 μL did not differ between genders. Hepatitis B seroprevalence was higher in men (8.7% vs. 0.6%), but there was no difference in hepatitis C prevalence. Whether women in Cleveland seek HIV care earlier, or whether early markers of HIV disease differ between the genders, remains to be determined.

Keywords CD4 counts, gender differences, hepatitis B seroprevalence, human immunodeficiency virus, RNA levels, sexually transmitted disease

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According to the US Department of Health and Human Services guidelines, $CD4^+$ cell counts and plasma human immunodeficiency virus (HIV)-1 RNA levels (viral load, VL) should be used to guide initiation of anti-retroviral treatment [1]. The definition of AIDS is also based partly on $CD4^+$ counts, with $CD4^+$ counts <200/μL and/or category C symptomatic conditions used to define patients with AIDS [2]. Since cut-off points do not take gender into account, the above guidelines and definition are based on the assumption that $CD4^+$ cell counts and VL are comparable for both genders. The aim of the present study was to examine possible differences in $CD4^+$ cell counts and VL between HIV-infected men and women new to HIV care in the era of highly active anti-retroviral therapy (HAART).

Database extraction identified 1066 patients who sought treatment for the first time at the Case Western Reserve University/University Hospitals of Cleveland Special Immunology Unit (Cleveland, OH, USA) during the period 1995–2002. Of these, 806 patients with no history of AIDS-defining illnesses in the 3 months before presentation and no previous anti-retroviral exposure were included in the present study. Information was obtained concerning demographics, category C AIDS-defining illnesses and category B symptomatic conditions (CDC Revised Classification System [2]) occurring before the initial visit and up to 6 months afterwards, previous or current sexually transmitted diseases (i.e., gonorrhoea, syphilis, chlamydia, herpes genital/anal, trichomoniasis, genital or anal warts, molluscum contagiosum; history and/or serology), presence of hepatitis B surface antigen and antibody (HBsAg/HBsAb; Immulite 2000 Chemiluminescence Immunoassay; Immulite, Los Angeles, CA, USA), hepatitis C antibody (HCV Ab; Ortho HCV 3.0 ELISA; Ortho, Raritan, NJ, USA), $CD4^+$ lymphocyte counts (flow cytometry) and VL (Amplicor HIV-1 Monitor Assay; Roche, Branchburg, NJ, USA) at baseline. The VL detection limit was 50 copies/mL. Data were analysed using the *t*-test for independent groups and χ^2 (SPSS v. 11.5; SPSS Inc., Chicago, IL, USA). Analysis of co-variance (ANCOVA) was used to assess the association of CD4 and VL after controlling for various co-variates.

In accordance with individuals living with HIV/AIDS in northeast Ohio, most (632; 78%) of the 806 patients included in the study were men, 39% were non-Hispanic whites, 55% were African-Americans, and 4% were Hispanics. The median age was 36.3 years (range, 16.3–

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75.1 years). Males were older than females (mean ± SD: 37.3 ± 8.7 vs. 35.1 ± 9.0 years, respectively; p 0.005). Homosexual/bisexual men represented 56% of the study group, and 33% had a history of drug use.

The known duration of infection (time from first positive HIV test to seeking care for the first time) was similar for men and women (412 ± 596 vs. 374 ± 529 days, respectively; p 0.541) The cumulative proportions of patients presenting with category C AIDS-defining illnesses or category B conditions were similar among men and women (Table 1). There was no significant difference in the frequency of sexually transmitted diseases between males and females. The overall seroprevalences of hepatitis B ($HBsAg^+$) and hepatitis C infections were 7% and 18%, respectively, with an overall prevalence of HBsAb of 31%. The seroprevalence of hepatitis B was higher in men, but there was no significant difference in hepatitis C antibody (Table 1).

$CD4^+$ cell counts and plasma HIV RNA in new entrants were 327 ± 253 cells/μL and $1.22 \times 10^5 \pm 2.08 \times 10^5$ copies/mL. Women had higher $CD4^+$ counts and lower HIV RNA VL than men at baseline, and these differences persisted after controlling for age, race and other baseline characteristics. Approximately one-third (36%) of new entrants to care had $CD4^+$ cell counts <200/μL, and this proportion did not differ significantly between genders (Table 2). Further analysis divided patients into sub-populations: (1) according to the absence (group Ia) or presence (group Ib) of category C symptomatic conditions; and (2) according to whether $CD4^+$ cell counts were ≥200/μL (group IIa) or <200/μL (group IIb) at presentation. The gender difference in $CD4^+$ counts was preserved for groups Ia and IIa, but not for groups Ib and IIb. There was no difference between the genders for HIV RNA VL in any of the above groups (Table 2).

Table 1. CDC category C AIDS-defining illnesses, category B symptomatic conditions, sexually transmitted diseases and markers for hepatitis B and C viruses among male and female new entrants to human immunodeficiency virus care

	Males (*n* = 632)	Females (*n* = 174)	p
Patients with category C illnesses, *n* (%)	100 (15.8)	21 (12.0)	0.23, NS
Patients with category B conditions, *n* (%)	176 (27.8)	52 (29.8)	0.63, NS
Patients with current or past STDs, *n* (%)	112 (17.7)	26 (14.9)	0.42, NS
Patients with positive HBsAg, *n* (%)	45/515[a] (8.7)	1/153[a] (0.6)	<0.001
Patients with positive HCV Ab, *n* (%)	97/515[a] (18.8)	24/153[a] (15.6)	0.405, NS

STD, sexually transmitted disease; NS, non-significant; HBsAg, hepatitis B surface antigen; HCV Ab, hepatitis C virus antibody.
[a]Patients screened for HBsAg/HBsAb and HCV Ab.

Table 2. $CD4^+$ cell counts and plasma HIV RNA levels in males and females at presentation

	Men (*n* = 632)	Women (*n* = 174)	p
$CD4^+$ cell count, cells/μL ± SD			
All patients	310 ± 242	388 ± 282	0.003
Group Ia: Category C^-	351 ± 239	430 ± 280	0.014
Group Ib: Category C^+	90 ± 124	109 ± 122	0.62, NS
Group IIa: $CD4^+ \geq 200/\mu L$	455 ± 194	512 ± 238	0.031
Group IIb: $CD4^+ < 200/\mu L$	72 ± 63	81 ± 70	0.49, NS
HIV RNA, $\times 10^4$ copies/mL ± SD			
All patients	12.65 ± 20.05	$8.94 \times 10^4 \pm 16.82$	0.048
Group Ia: Category C^-	10.38 ± 18.53	7.74 ± 16.41	0.21, NS
Group Ib: Category C^+	26.34 ± 23.26	19.34 ± 19.26	0.31, NS
Group IIa: CD4 ≥ 200/μL	6.08 ± 12.21	3.74 ± 8.83	0.12, NS
Group IIb: CD4 < 200/μL	23.62 ± 25.22	21.58 ± 23.94	0.67, NS
Entrants with $CD4^+$ < 200/μL, *n*(%)	197/507[a] (37.8)	43/141[a] (30.4)	0.114, NS

HIV, human immunodeficiency virus; NS, non-significant.
[a]Patients with available $CD4^+$ cell counts at baseline.

The beneficial effects of HAART are well-established [3,4], and the overall mortality and incidence of severe opportunistic infections have declined significantly since 1995 [5], perhaps motivating more individuals at risk to be screened for HIV infection. In the present study, women presenting for the first time for HIV care had lower plasma VL and higher $CD4^+$ cell counts than did new male entrants to care. However, women could be presenting earlier for HIV testing and care than men, and additional data concerning seroconversion are needed to investigate this possibility. On the other hand, although women had higher $CD4^+$ cell counts, this difference was only apparent in individuals presenting at an early stage of the disease (without category C conditions and with $CD4^+$ cell counts >200/μL), which could be interpreted as suggesting differences in cellular support for HIV replication between men and women at this early stage. This possibility is also suggested by a recent study [6] indicating gender differences in HIV vertical acquisition, although the mechanisms for this possible gender-dependent susceptibility remain unknown.

There are conflicting reports concerning the existence of gender-dependent differences in VL and $CD4^+$ cell counts. Some studies have found median VLs in women to be only 38–65% of those in men [7–10], while others [11,12] have found no gender differences. The EuroSIDA study [10]

reported higher $CD4^+$ cell counts in women, while Farzadegan *et al*. [7] found very similar counts for both genders. Since the present findings do not apply to individuals presenting with category C conditions or $CD4^+$ cell counts $<200/\mu L$, it would seem that there is no need to establish gender-dependent thresholds in this population to guide initiation of treatment. However, it might be worth reconsidering the threshold for asymptomatic women presenting with $CD4^+$ counts $>200/\mu L$ so that they receive highly active antiretroviral therapy at an earlier stage in the disease.

There are several limitations to these findings. First, self-reported data are subject to recall bias or to other reporting errors. Second, as in all retrospective studies, some data may be missing or incorrectly entered. Third, this study population, considered to represent patients seeking care for the first time, may also include a small number of people who had sought care elsewhere and, in the absence of preceding AIDS-defining illnesses, were not treated with anti-retroviral therapies. Nevertheless, this retrospective analysis found that new female entrants to HIV care had higher $CD4^+$ cell counts and lower VLs, and were less likely to be seropositive for hepatitis B infection. Whether women in Cleveland seek HIV testing earlier, or whether early markers of HIV disease differ between the genders, remains to be determined.

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RESEARCH NOTE

Combined treatment with ceftriaxone and linezolid of pneumococcal meningitis: a case series including penicillin-resistant strains

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ABSTRACT

This study evaluated the role of linezolid in the treatment of patients suffering from pneumococcal meningitis. Treatment included ceftriaxone (4000 mg every 24 h), linezolid (600 mg every 12 h) and dexamethasone (8 mg every 6 h). Linezolid was withdrawn if a penicillin-susceptible isolate of *Streptococcus pneumoniae* was identified. Of 16 patients studied, seven were infected with penicillin-non-susceptible isolates of *S. pneumoniae*, two died, and three reported sequelae. No

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