

SHORT REPORT

A trend towards increasing viral load in newly diagnosed HIV-infected inpatients in southeast China

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SUMMARY

Peripheral blood viral load is an important indicator of viral production and clearance. Previous studies have suggested that viral load might predict the rate of decrease in CD4⁺ cell count and progression to AIDS and death. Here, we conducted a retrospective analysis of the trends in HIV-1 viral load in southeast China. Among inpatients newly diagnosed with HIV infection, we found that viral load has increased over the past decade from 4·20 log₁₀ copies/ml in 2002 to 6·61 log₁₀ copies/ml in 2014, with a mean increase of 0·19 log₁₀ copies/ml each year. However, the CD4⁺ cell count was stable and insensitive to changes in viral load. Thus, increasing viral load appears to be an emerging trend in newly diagnosed HIV-infected inpatients.

Key words: HIV, increasing trends, viral load.

The peripheral blood viral load is an important indicator of viral production and clearance, as long as clearance is relatively constant [1, 2]. Consequently, HIV-1 plasma RNA viral load has been directly correlated with HIV disease progression and is inversely associated with the HIV-specific cytotoxic T-lymphocyte immune response [3]. Previous research has suggested that CD4⁺ T cells are effectors of HIV-1 virus clearance in peripheral blood [4]. Furthermore, CD4⁺ T cells appear to be required for the induction of HIV-specific cytotoxic T-lymphocyte activity [3], a concept based on the identification of a specific population of CD4⁺ T cells that are protective against acute disease and associated with reduced viral replication. CD4⁺ cell count is the best surrogate marker of the viral replication rate and HIV

disease progression and has been historically used to manage and monitor patients with HIV infection [2, 5, 6]. Thus, high viral load is associated with low CD4⁺ cell count, or with more rapid decreases in CD4⁺ cell count. However, the current study indicates that there is actually some variability in this cell count. To our knowledge, this is the first comprehensive data regarding viral load and CD4⁺ cell count changes in newly diagnosed HIV-infected inpatients in China. In this study, we retrospectively analysed viral load trends over the past 13 years in newly diagnosed HIV-infected inpatients in southeast China.

This was a cohort study conducted between January 2002 and December 2014 at the HIV inpatient unit of the Fuzhou Infectious Disease Hospital in southeast China. The study population comprised inpatients who were identified as being serologically positive for HIV infection for the first time between January 2002 and December 2014. All newly identified cases of HIV were confirmed by Western blot and reported to the Centers

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Table 1. Baseline characteristics of inpatients newly diagnosed with HIV infection in southeast China, from 2002 to 2014

Year	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
Case numbers	17	16	31	16	31	37	50	67	84	118	138	156	132	893
Female (%)	3 (17.6)	7 (43.8)	13 (41.9)	3 (18.8)	7 (22.6)	10 (27.0)	12 (24.0)	16 (23.9)	19 (22.6)	30 (25.4)	25 (18.1)	33 (21.2)	20 (15.2)	198 (22.2)
Male (%)	14 (82.4)	9 (56.2)	18 (58.1)	13 (81.2)	24 (77.4)	27 (73.0)	38 (76.0)	51 (76.1)	65 (77.4)	88 (74.6)	113 (71.9)	123 (78.8)	112 (84.8)	695 (77.8)
Average age (yr)	39.2 ± 5.8	37.0 ± 9.6	39.0 ± 9.2	43.0 ± 7.9	41.0 ± 9.6	37.6 ± 8.2	43.0 ± 9.5	42.0 ± 10.0	42.5 ± 9.5	39.0 ± 9.3	40.0 ± 9.8	41.1 ± 11.3	41.6 ± 11.5	40.8 ± 10.1
Mean viral load (log ₁₀)	4.20 ± 0.55	5.12 ± 1.18	5.20 ± 0.64	5.26 ± 0.46	5.42 ± 0.46	5.45 ± 0.46	5.89 ± 0.46	5.84 ± 0.45	6.38 ± 0.61	6.25 ± 0.57	6.36 ± 0.54	6.42 ± 0.57	6.61 ± 0.49	6.18 ± 0.66
Mean CD4 ⁺ count (cells/μl)	41.7 ± 23.6	58.4 ± 40.6	61.9 ± 42.1	52.6 ± 31.6	54.0 ± 31.6	56.5 ± 44.5	40.9 ± 44.0	55.8 ± 56.8	39.4 ± 40.8	57.5 ± 59.9	55.4 ± 63.3	57.2 ± 60.8	49.3 ± 56.3	52.8 ± 53.9
CD4 ⁺ count ≤ 50 (%)	14 (82.4)	9 (82.4)	17 (54.8)	7 (43.8)	18 (58.0)	23 (62.2)	40 (80.0)	48 (71.6)	68 (81.0)	87 (73.6)	106 (76.8)	114 (73.1)	102 (77.2)	653 (73.1)
CD4 ⁺ count 51–200 (%)	3 (17.6)	3 (17.6)	14 (45.2)	9 (56.2)	11 (35.5)	13 (35.1)	7 (14.0)	13 (19.4)	13 (15.5)	22 (18.6)	22 (15.9)	27 (17.3)	20 (15.2)	180 (20.2)
CD4 ⁺ count ≥ 201 (%)	0 (0.0)	1 (6.3)	0 (0.0)	0 (0.0)	2 (6.5)	1 (2.7)	3 (6.0)	6 (9.0)	3 (3.5)	9 (7.6)	10 (7.3)	15 (9.6)	10 (7.6)	60 (6.7)

for Disease Control (Fuzhou, China). Patients were excluded if they had previously received any antiretroviral therapy. The investigated population is shown in Table 1.

The initial measurements of viral load and CD4⁺ cell count were taken within 24 h of confirmation of the primary HIV infection. The plasma viral load was quantified through real-time polymerase chain reaction using a commercial diagnostic kit for HIV-1 quantification (Daan Gene Co. Ltd, China). The peripheral blood CD4⁺ cell count was measured by flow cytometry using a BD MultiTEST IMK kit (BD Biosciences, USA). SPSS v. 12.0 (SPSS Inc., USA) was used for statistical analysis, and differences between the groups were considered statistically significant at *P* < 0.05.

A total of 893 inpatients with primary HIV were enrolled in the cohort; the baseline characteristics of these inpatients are given in Table 1. Figure 1 summarizes the viral load and CD4⁺ cell count trends. As shown in Figure 1*a*, the annual mean value of log₁₀ HIV-1 viral load increased slightly each year from 4.20 log₁₀ copies/ml in 2002 to 6.61 log₁₀ copies/ml in 2014, with a mean increase of 0.19 log₁₀ copies/ml each year. Interestingly, the CD4⁺ cell count did not change in newly diagnosed HIV-infected inpatients during the same period (Fig. 1*b*). Statistically significant differences in viral load between 2002 and 2014, but not in CD4⁺ cell count, were found in newly diagnosed HIV-infected inpatients. Similarly, viral loads were not different in individuals with CD4⁺ cell counts of ≤ 50, 51–200 or ≥ 201 cells/μl (Table 1, *R*² = 0.0188), and the correlation of viral load with CD4⁺ cell count was non-significant. Thus, we anticipate increased HIV-1 viral load in newly diagnosed HIV-infected inpatients.

Previously published data indicated that the HIV-1 viral load and CD4⁺ cell count are negatively correlated in those with HIV infection or AIDS [7], but our data indicate that, over time, CD4⁺ cell counts have remained stable in newly diagnosed HIV-infected inpatients and that increases in viral load have not affected CD4⁺ cell count or disease progression. Notably, during the 13-year study period, CD4⁺ cell counts did not decrease as HIV-1 viral load increased, and this finding agrees with other antiretroviral therapy data from newly diagnosed HIV inpatients. However, our study is the first to report an epidemiological shift in newly diagnosed HIV-infected inpatients.

The possible reasons for a gradual increase in viral load in newly diagnosed HIV-infected inpatients in southeast China are unclear. In interpreting our

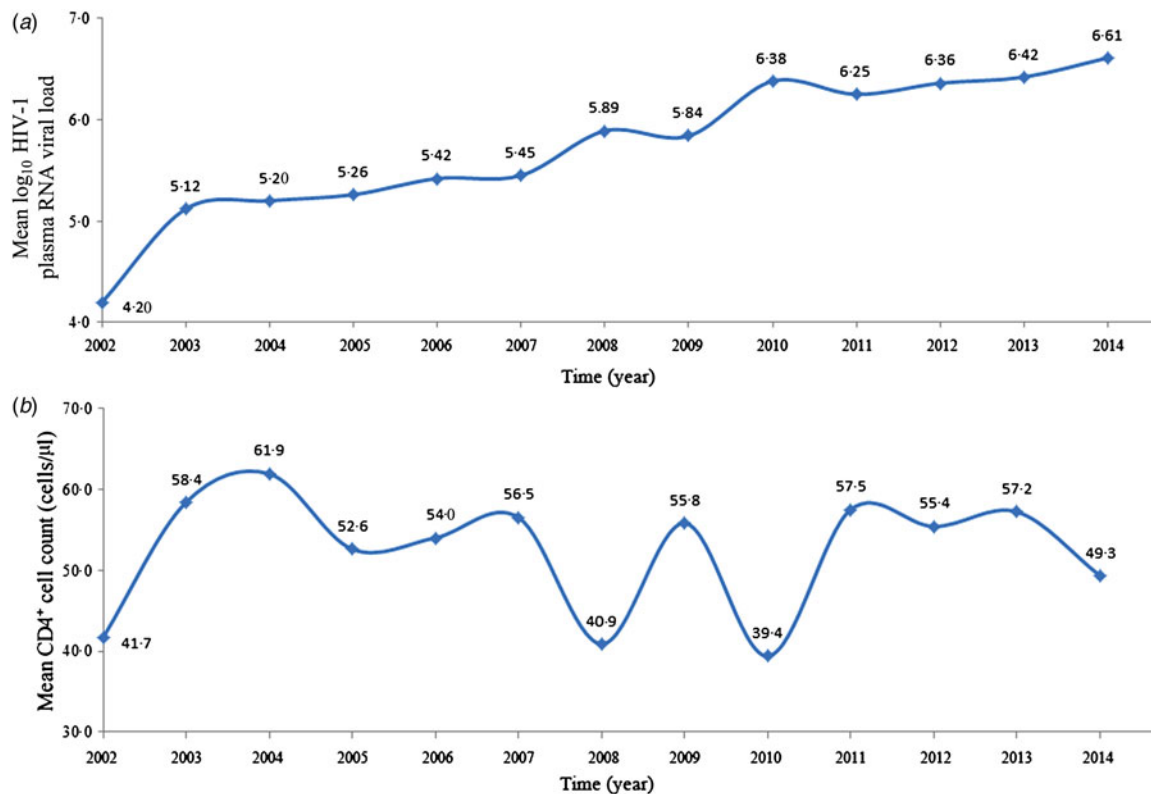


Fig. 1. Distributions of mean \log_{10} HIV-1 plasma viral load (a) and CD4⁺ cell count (b) of inpatients newly diagnosed with HIV infection in southeast China from 2002 to 2014.

findings, it is now difficult to ignore the mounting evidence that HIV adapts to the host immune system. It is possible that some of these molecular adaptations and continuous selection might reduce viral virulence which could explain the epidemiological changes observed in our study. Based on our results, transmission of HIV with a high viral load does not tend to result in more rapid CD4⁺ decline in the recipient; hence, HIV-infected individuals with stable CD4⁺ counts tend to have viruses with low virulence. These data suggest that viral evolution is occurring relatively rapidly, and that adaptations of HIV may contribute to a lowering of viral replication capacity at the population level and a consequent reduction in HIV virulence over time. There are two processes that might have influenced HIV virulence over the course of the epidemic: first, viral evolution in response to HLA-mediated selection pressure, and second, the widespread use of antiretroviral therapy [8–10].

Although there is no consensus on HIV-1 virulence trends, it is interesting to assess the direction of HIV virulence over the course of an epidemic [5, 8]. HIV virulence has been implicated as a factor in the

progression to AIDS in untreated infections, which itself might be correlated with the replicative capacity of HIV [8]. Primary infection with low-virulence HIV is likely to cause an infection with a high viral load, according to our data and that of other studies [5, 8–10]. By contrast, increasing viral load trends are consistent with the theory that viral infectivity diminishes over time due to viral evolution in the host. However, it is also possible for these trends to be the result of unmeasured biological or behavioural factors in the individual cohorts assessed.

In summary, we observed a new trend in HIV viral load in newly diagnosed HIV inpatients in Fujian Province (southeast China). Additional studies with larger populations are required to confirm our findings and assess the significance of these data.

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DECLARATION OF INTEREST

None.

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