

Trend in CD4+ Cell Counts at Diagnosis in Human Immunodeficiency Virus-Infected Persons in Korea

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At the beginning of the acquired immunodeficiency syndrome (AIDS) epidemic, it had a significantly high mortality rate. However, advancements in antiretroviral therapy (ART) have considerably changed the natural history of human immunodeficiency virus (HIV) infection and have reduced its associated morbidity and mortality. It has been well known that in people living with HIV, CD4+ cell counts decrease progressively and that after 8-10 years of infection, CD4+ cell counts go below 200/mm³. 'Presentation with advanced HIV disease' is the diagnosis of HIV infection at an advanced stage, defined as a CD4+ cell count <200/mm³. From an individual perspective, patients who present at an advanced stage of immune deficiency are at higher risks of developing clinical disease and death, as well as being more likely to achieve poorer outcomes when they receive ART [1]. Persons presenting with advanced HIV infection need to start ART, but there are some pertinent issues among these patients. They are more prone to opportunistic infections. There is the risk for drug-drug interactions and overlapping toxicities of medications used to treat opportunistic infections and antiretroviral agents. The risk of immune reconstitution inflammatory syndrome is significantly increased in patients who start ART in the advanced stage.

From a public health perspective, the costs of treating late presenters are high and delayed diagnosis increases the risk of onward HIV transmission in the community [2].

Since the first reported case of HIV infection in Korea in 1985, the number of newly diagnosed people with HIV infection has been increasing every year. As of December 2015, the cumulative number of people with HIV infection in Korea was 10,502 [3]. Although the prevalence of HIV in Korea is low compared to that in other countries, there are some concerns regarding its epidemiology. First, contrary to the global trend, the annual number of newly diagnosed persons has been increasing so far (219 in 2000, 327 in 2005, 680 in 2010, and 1,018 in 2015). The incidence of HIV infection is decreasing globally, especially in Africa [4]. Second, the proportion of persons presenting with advanced HIV disease has increased over time. There have been a number of studies that revealed the proportion of persons with late presentation among individuals with newly diagnosed HIV infection in Korea [5-7]. In one study, the proportion of persons presenting with advanced HIV disease increased from 31% in 1987-1998 to 43% in 1999-2008 [5]. In another study conducted from 2000 to 2007, the proportion was 37.3% (858/2,299) [7]. The risk factors for presentation

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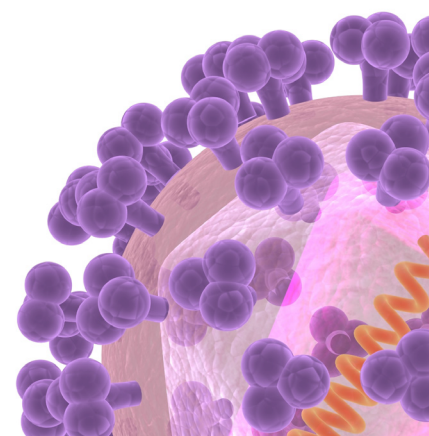
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with advanced HIV disease have been investigated in several studies and included old age, testing at hospital compared to testing at public health center, testing due to clinical manifestations compared to health check-ups, male sex, infection by heterosexual contact compared to a homosexual contact, and diagnosis after 1999 compared to before 1998 [5-7].

In this issue of *Infection & Chemotherapy*, Kim et al. reported the trend in CD4+ cell counts at diagnosis and initiation of highly active antiretroviral therapy (HAART) between 1992 and 2015 [8]. This is a report from the Korea HIV/AIDS Cohort study, which was initiated in 2006 and prospectively collected the data of HIV-infected patients from 21 tertiary and secondary hospitals in Korea. CD4+ cell counts and HIV RNA titers at the diagnosis of HIV infection and HAART initiation were analyzed by three-year time intervals. They found that the median values of CD4+ cell counts at diagnosis and HAART initiation were 247/mm³ and 181/mm³, respectively. The median values of HIV RNA titers at diagnosis and HAART initiation were 39,436 copies/mL and 83,500 copies/mL, respectively. Overall, the proportion of patients presenting with advanced HIV disease was 34.4% (467/1,356) and increased gradually to the 2010-2012 period, which was consistent with the results of previous studies [5-7]. This study had an advantage in that CD4+ cell counts at the time of HAART initiation were analyzed, which had not been investigated before. The median values of CD4+ cell counts at the time of HAART were 181/mm³ and showed a decreasing pattern before the 2010-2012 period. Of note is the proportion of patients presenting with advanced HIV disease during the 2013-2015 period was decreased to 34% compared with 51% during the 2010-2012 period. The Korea HIV/AIDS Cohort is the largest one in Korea, but this study analyzed only 1-15% of newly diagnosed individuals in Korea, which is a pitfall of this study. In fact, the number of patients analyzed during the 2013-2015 period comprised 3.2% of newly diagnosed individuals in Korea. Further studies are required to identify whether or not the proportion of late presenters will decrease in future.

The proportion of patients presenting with advanced HIV disease varies between countries. In developed countries, the CD4+ counts of HIV patients at first presentation have not increased significantly over the past 20 years [9]. Recently the proportion of late presenters has decreased significantly in several countries in Asia. For example, the proportion of patients presenting with advanced HIV disease decreased from 88.5% in 2006 to 49.6% in 2011 in China [10]. As mentioned above, late presentation has adverse effects on individuals and the community, and we have to make efforts to decrease its

occurrence. Education is one key effort aimed at achieving early diagnosis among HIV-infected individuals. Barriers to early HIV testing include a lack of perception of HIV risk factors, a lack of knowledge about HIV testing and treatment, fear of positive results, disclosure, and stigma. Late presentation tends to be less common among men who have sex with men because they have a higher perceived risk. Second, easy access to testing for HIV infection is essential for early diagnosis as exemplified by anonymous voluntary testing. Third, opt-out screening should be considered to identify HIV-infected individuals who are unaware of their status. In the USA, HIV screening is now recommended for patients aged 13-64 years in all health-care settings after the patients are notified that testing will be performed unless they decline. The prevalence of HIV in Korea is below 0.1%, and there is no consensus about implementing opt-out screening, but this should be considered.

The prevalence of HIV infection is relatively low in Korea. However, we have to pay attention to the annually increasing number of newly diagnosed persons with HIV infection and the proportion of persons presenting with advanced HIV disease.

Conflicts of Interest

No conflicts of interest.

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