

# Effect of Antiretroviral Therapy on CD4+/CD8+ Ratio in HIV Patients in Immune Recovery Stages at a Tertiary Care Hospital in Riyadh

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**Abstract:** - This HIV infection is not a common in Saudi Arabia. The enumeration of CD4+ and CD8+ remains a fundamental method to measure HIV disease progression, and the CD4+/CD8+ ratio is a reflection of the immune system's health. The aim of this study was to determine the effect of antiretroviral therapy on the CD4+/CD8+ ratio in patients suffering from HIV infection in Saudi Arabia. Retrospective data of thirty HIV cases were collected from the electronic medical records in a tertiary care hospital in Riyadh (King Abdul-Aziz Medical City) during 2005-2012. The number of CD4+ and CD8+ cells by flow Cytometry technique was studied for each patient over several visits. The viral load measured by PCR, antiretroviral therapy data was documented for these patients and the data analyzed by parametric data analysis using the appropriate statistical software. Our results showed that 40% of the patients had improved CD4+/CD8+ ratio after ART therapy. 17% of these patients maintained a constant rate and 43% had a severe drop in the CD4+/CD8+ ratio. Our finding showed that using the CD4+/CD8+ ratio is useful to determine the disease progression and the effectiveness of ART therapy. However, more studies are needed with a large number of patients to support our findings.

**Key-Words:** - HIV, AIDS, Infection, CD4+, CD8+, CD4+/CD8+, antiretroviral therapy.

## 1 Introduction

As you Human immunodeficiency virus (HIV) is a lentivirus which is one of the retrovirus families that causes acquired immunodeficiency syndrome (AIDS) [1]. HIV is transmitted to humans through vaginal, anal, mouth, eyes, and skin tissue secretions [2, 3]. AIDS is a human disease that causes severe progressive failure of the immune system, and it perpetuates life-threatening, opportunistic infections and cancers [4, 5, 6].

HIV infection and AIDS were discovered in 1981 in Los Angeles and New York. Typical AIDS symptoms were first described in homosexual men [7, 8]. The lab results of these patients showed a severe decrease in T-helper cells mainly CD4+ cells, which are considered as a significant part of the immune system. AIDS is a developing stage of HIV

infection, therefore the real definition of AIDS is the actual reduction of CD4+ cells count (<200 cells/mm<sup>3</sup>) or any complications of HIV infection which include a diversity of so-called "opportunistic infections," cancers, neurologic symptoms, and wasting syndromes [9, 10].

HIV attacks the important immune cells such as CD4+ T helper cells, dendritic, and macrophages. HIV infection decreases CD4+ T cells levels through three major mechanisms: Firstly, the virus directly kills the infected cells. Secondly, the virus increase apoptosis rate in infected cells. Moreover, finally, CD8+ cytotoxic lymphocytes kill infected CD4+ T cells. When CD4+ T cell number drops off under a critical value, the cell-mediated immunity is diminished, and the body increasingly grows to be at risk for opportunistic infections [11,

19]. Individuals with CD4+ cells less than 200 cells per mm<sup>3</sup> are particularly at risk of HIV-specific complications. Thus the immune system does not function adequately and is considered severely suppressed. A declining number of CD4+ cells also means that HIV disease is advancing and signals that the person is at risk of many opportunistic infections. Also, the actual CD4+ cell count indicates which specific therapies should be initiated to prevent subsequent infections [20].

The CD4+/CD8+ ratio is an indication of immune system health which normally ranges between 1 to 4 and CD4+ cell count usually exceeds CD8+ cell count. However, CD4+/CD8+ ratio reduces in old age when the defense mechanisms of the body are compromised. People with autoimmune diseases have an increased CD4+/CD8+ ratio, while those with viral infections have a low CD4+/CD8+ ratio. In general, within six months of seroconversion, the CD4+ count declines by approximately 30% and the CD8+ count enhances by nearly 40%. Therefore CD4+/CD8+ ratio is usually less than 1. CD4+/CD8+ ratio is also affected by tuberculosis, corticosteroid use, seasonal variations, and changes in the CD4+ analysis [12].

HIV infection is characterized by progressive depletion of CD4+ T-cells because of reduced production and increased destruction, and a marked activation and expansion of the CD8+ T-cell compartment. Effective antiretroviral therapy (ART) suppresses HIV replication allowing progressive CD4+ T-cell recovery that is usually accompanied by persistent expansion of CD8+ T-cells. As a consequence, there is an incomplete restoration of the CD4/CD8 T-cell ratio, which very often remains inverted (1,2). Low CD4/CD8 ratios have been associated with T-cell activation and immune senescence(3,4) with higher morbidity and mortality, mainly due to frequent occurrence of non-AIDS events.

In Zimbabwe, a study to assess the CD4+/CD8+ ratio as an interpreter of HIV infection in infants under 18 months of age [14] established that PCR was negative for sixty out of sixty-one infants who had a CD4+/CD8+ ratio  $\geq 1$ . In another study, CD4+/CD8+ ratio was found to be  $< 1$  [13]. Overall, the CD4+/CD8+ ratio had  $\geq 98.7\%$  sensitivity and 98.3% specificity for recognized infant HIV-1 infection (all subtype C) and 100% sensitivity and specificity when looking only at the 12 to 18-month infant subset population [14, 15]. With this background, we aimed to conduct this study to determine the effect of antiretroviral therapy on CD4+/CD8+ ratio in HIV patients at

immune recovery stages in a tertiary care Hospital in Riyadh, Saudi Arabia.

## 2 Materials and Methods

A retrospective cohort study was done for all HIV cases at a tertiary care hospital in Riyadh (King Abdul-Aziz Medical City) during 2005-2012. The collected data included 30 patients (8 females and 22 males) between the ages of 8-74 years who received antiretroviral therapy at King Abdul-Aziz Medical City (KAMC) complex in Riyadh, Saudi Arabia. The records collected included HIV viral load, CD4+ and CD8+ absolute B-lymphocytes count at different time periods. Antiretroviral therapy data was obtained from the patient's records and correlated with viral load at the same period.

HIV viral load was detected with real-time reverse transcription polymerase chain reaction (PCR) using homozygous fluorescence detection method as described by Holmes H, et al. 2001 and Davis C, et al. 2003 (Abbot Real-Time HIV-1 Assay System, USA) at Molecular Microbiology laboratory at KAMC [16, 17].

The viral load values were expressed as log<sub>10</sub> of the viral copies/ml. The absolute number of CD4+ and CD8+ (T suppressors) was enumerated using the flowcytometer auto-analyzer in the flowcytometry lab at KAMC (FACS Canto II; Becton Dickinson and Company, San Jose, CA, USA) [18].

Data was retrospectively collected and tabulated and analyzed using student sample t-test in Microsoft Excel 2007 sheets and Statistical Package for the Social Sciences (SPSS ver. 19).

## 3 Result

The CD4+/CD8+ ratio obtained from treated and a non-treated cohort of patients within 7 years is shown in Table 1, where it has been divided into 12 visits and expressed as mean  $\pm$  SD.

Our results have been divided to two groups. Group A shows the comparison of viral load in treated and non-treated patients. Group B demonstrates the improvement of CD4+/CD8+ ratio in patients undergoing antiretroviral therapy among different periods of time.

The comparison in group A, of the viral load in treated (1.80  $\pm$  0.1) and untreated patients (5.5  $\pm$  5.7) showed differences in long term therapy over the last period ( $P < 0.05$ ). However, no such observation was noted in the comparison of

CD4+/CD8+ ratio between treated and non-treated patients for the same periods. (Table 2, Figure 1)

The improvement of CD4+/CD8+ ratio in patients under antiretroviral therapy "GROUP B" displayed three types of cases. Case #1 showed that 40% of patients treated with antiretroviral therapy had improved CD4+/CD8+ ratio (Fig 2a. Case #1).

However, Case #2 exemplified that 17% of these patients maintained a constant rate with antiretroviral therapy (Fig 2b Case #2).

Moreover, Case #3 illustrated that 43% of patients had a severe drop in the CD4+/CD8+ ratio after treatment (Fig 2c Case #3). This trend was not observed in untreated HIV patients.

## 4 Discussion

The accurate description of the HIV in the Middle East has been slow due to social, cultural, taboo and religious factors. Since 1984 HIV screening was made routine for particular groups of individuals, including suspected patients with HIV/AIDS, risk-related contacts of HIV-infected persons, blood donors, staff in certain occupations, new migrants, and intravenous drug users [19]. Pre-marital and prenatal HIV testing programs were established. Notification of HIV/AIDS cases in KSA was made mandatory by the government in the late 90's [20].

This study is the first in Saudi Arabia to determine the effect of antiretroviral therapy on the CD4+/CD8+ ratio in patients suffering from HIV infection.

Our findings show that 40% of patient improvement in CD4+/CD8+ ratio with antiretroviral therapy, while 16% of patient showed no effect of the therapy on CD4+/CD8+. A significant number (44 %) of patients showed depression of CD4+/CD8+ ratio with treatment. Through this study, we strived to provide insight into different factors affecting the treatment therapy in our clinical settings.

In other studies, in Australia and France, the effect of ART on CD4+/CD8+ ratio in adult HIV patients was positive and patients showed considerable progression and improvement which is similar to our results [21].

Also, our finding showed that using the CD4+/CD8+ ratio is a useful tool to determine the patient health progression. However, since the number of patients in our study was low, more studies are needed with large number of patients to confirm the usefulness of CD4+/CD8+ ratio in monitoring the antiretroviral therapy in HIV patients.

We used data from the patients records hence patient compliance to treatment cannot be assessed which is one of the limitations of our study. Another important limitation of this study is that the number of HIV patients are generally limited in our country in comparison to other countries hence the effect could be assessed in a restricted number of patients seen in this tertiary care hospital. More large scale studies are needed with a high number of patients to confirm the usefulness of CD4+/CD8+ ratio in monitoring the antiretroviral therapy in HIV patients.

## 5 Conclusion

Although HIV infection is not so common in Saudi Arabia however, antiretroviral therapy has a favourable effect on CD4+/CD8+ ratio with positive patient outcomes. So, effective antiretroviral therapy is a plus for the effective management of HIV patients.

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