



CD4 Population Dynamics In Response To Antiretroviral Therapy In Some Cases Reported At Federal Medical Centre, Keffi, North Central Nigeria

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ABSTRACT

The study was carried out on patients presenting with HIV/AIDS at the Federal Medical Center, Keffi. The study aimed at assessing the immune response of such individuals to Highly Active Antiretroviral Therapy (HAART). The study covered 118 HIV-infected, treatment-naïve individuals; 96 females and 22 males. The Cyflow Counter was used to quantitatively analyse the blood samples for the total CD4⁺ count. The CD4⁺ lymphocyte count was repeated after three months. The results were analyzed using Regression and Correlation Analysis. It was discovered that 57% of the individuals had an increase in CD4 count after 3 months' therapy while 43% had a decrease. For those who had an increase, the mean CD4 was 72.1 cells/μl while for those who had a decrease, the mean CD4 decrease was 62.3 cells/μl. This research shows that although there was a general increase in CD4 count of the patients in response to the antiretroviral treatment after three months on therapy, however, there was no statistically significant positive effect of the treatment on the immune system within the same period.

Keywords: CD4, lymphocyte count, HIV/AIDS, HAART, Treatment Naive, Response

INTRODUCTION

Since the discovery of Human Immunodeficiency Virus (HIV), several attempts have been made to find a cure for the infection. The introduction of Highly Active Antiretroviral Therapy (HAART) has helped in curbing most of the scourge, but the eradication of HIV infection cannot be achieved with the available antiretroviral regimens yet. The primary goal of the treatment is to reduce HIV-related morbidity and prolong survival, keep the HIV level in the blood constantly at a low level, restore and preserve immunologic function and also prevent vertical transmission (Adler, 2001).

The immune system is a network of cells, tissues and organs that work together to defend the body from "foreign" invaders (USDHHS, 2003). To this end, it relies on two functional branches: the innate and the acquired, both involving a diversity of blood-borne factors (complement, antibodies and cytokines) and cells (macrophages, polymorphonuclear cells and lymphocytes) (Marcos *et al.*, 2003).

The human body has a collection of defense cells referred to as CD cells- a short form for cluster of differentiation cells. The cluster of differentiation (CD) is a protein expressed on the surface of the surface of the cells of the hematopoietic system. The expression of these proteins is used in lymphocyte nomenclature (WHO, 2007). Cluster of differentiation molecules can act in numerous ways, often, acting as receptor or ligands important to the cell. A signal cascade is usually initiated, altering the behavior of the cell. Some CD proteins do not play a role in cell signaling, but have other functions, such as cell adhesion. Over 300 CD molecules have been reported so far. Only a fraction of the known CD molecules has been thoroughly characterized and most of them have an important function. In the example of CD4⁺ and CD8⁺, these

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molecules are critical in antigen recognition (Wikipedia, 2009).

CD4⁺ T-lymphocytes occupy the central position in regulating immune functions (WHO, 2007). They are fundamental to the development of specific immune responses to infection, particularly intracellular pathogens. Cluster differential counts are important indicators of HIV disease progression and for initiating and monitoring antiretroviral treatment (ART) (Perez-Santiago *et al.*, 2016). As the primary target of HIV, their depletion severely limits the host response capacity (Langford *et al.*, 2007). The primary receptor for HIV is the CD4 molecule on the human T-helper cells.

HAART refers to antiretroviral drugs taken in combination of three (or more) of the treatment of HIV infection. Several treatment guidelines for HIV recommend initiation of antiretroviral therapy in advanced stages of the disease. Nevertheless, there is still concern that immune recovery may not be complete once CD4 T-cells have decreased below a certain threshold (Garcia *et al.*, 2004). Before initiating therapy, patient counseling and education should be conducted. The essence of this is to help the patients understand the potential risk of antiretroviral therapy, including short and long term adverse drug effect and the need for long term commitment and adherence to the prescribed treatment regimen.

The study assessed the immune response of HIV-infected individuals to Highly Active Antiretroviral Therapy (HAART), evaluated the impact of HAART on CD4 count in HIV-infected individual and critically examined in statistical and analytical terms, the outcomes of the findings.

METHODOLOGY

Study area and population

The study area was Keffi town, located in the Northern part of Nigeria. It is about 68km from Abuja (Federal Capital Territory). It is situated on latitude 8°5'N and longitude 7°5'E. Keffi is at an altitude of 850m above sea level and it is North-west of Lafia, the Capital of Nasarawa State (Akwa *et al.*, 2007). Human populations from Wamba, Kokona, Mararaba, Karu, Masaka, Toto, Akwanga, Doma, Obi, Nasarawa and Garaku all attend the medical

facility in Keffi. The research work was carried out at the Federal Medical Center Keffi. A total of 118 results were obtained for this study, comprising of 22 males and 96 females.

Collection of blood specimens

Blood specimens were collected by venipuncture. The arm of the patient was tied with a tourniquet and the position of the veins disinfected using cotton wool soaked with methylated spirit. Using a vacutainer needle, blood specimens were collected into appropriately labelled microtitre tube containing Ethylene Diamine Tetraacetic Acid (EDTA). A different needle was used for each specimen collected. The blood specimens were collected at the phlebotomy and then transported to the laboratory for analysis.

Test procedure

The Cyflow Counter (Partec, Germany) was used to quantitatively analyse the blood samples for the total CD4⁺ count. All reagents were brought to room temperature prior to the commencement of the test. 20µl of the CD4⁺ antibody (Partec GmbH, Germany), was dispensed into each Rohren tube after which 20µl of blood was added to the tube all, by means of sterile microtitre tubes after thorough but carefully mixing the blood sample in each case. The Rohren tubes were then incubated in the dark at room temperature for 15 minutes. After incubation, 800µl of no-lyse dilution buffer (Partec GmbH, Germany), was dispensed into the tubes and analysis using Partec Cyflow counter was carried out.

Statistical Analyses

Data obtained from the test results were subjected to statistical analysis using Regression and Correlation Analysis with the help of Statistical Package for Social Sciences (SPSS).

RESULTS

After treatment for three months, 67 (56.8%) subjects had an increase in CD4 cell count while 51(43.2%) subjects had a decrease. Correlation and regression analysis of the data obtained indicated a fairly strong correlation between the initial CD4 count and the CD4 count after treatment (for those who had an increase in CD4 count), a 43.8 increase in CDA count after treatment for three months

for the general data and a 72.1 increase in CD4 count (after treatment) for each CD4 count

Figure 1 shows a Bar chart for initial CD4 counts of all the individuals in the study. From the chart, 17 individuals had an initial CD4 count within the range 0-99, 14 individuals within the range 100-199, 19 individuals fell within 200-299 while 20 individuals fell within 300-399, 21 individuals fell within 400-499, 11 individuals within 500-599, 9 individuals within 600-699 and 7 individuals fell within 700-799. This means that majority of the individuals had a baseline CD4 count within the range 400-499 while only a few individuals (7) fell within the range 700-799.

Figure 2 shows a Bar chart for the follow-up CD4 counts of all the individuals in the study, 3 individuals had a follow-up CD4 count within the range 0-99, 13 individuals fell within 100-199, 18 individuals within 200-

299, 28 individuals 300-399 and 29 individuals fell within 400-499. 18 individuals had a follow-up CD4 count within the range 500-599 while 3 individuals fell within 600-699, 4 individuals fell within 700-799 and 2 individuals fell within the range 800-899. From this chart, it is observed that majority of the individuals (29) had a follow-up CD4 count within the range 400-499 closely followed by 300-399 (28). Very few individuals fell within 800-899 and 0-99 (2 and 3 respectively).

Figure 3 is a merged line chart for the initial and follow-up CD4 counts of all the individuals in the study. This bar chart is therefore a comparison of the CD4 counts. From this chart, majority of the individuals presented with CD4 counts between 400-499, while even more had follow-up CD4 counts between 400-499.

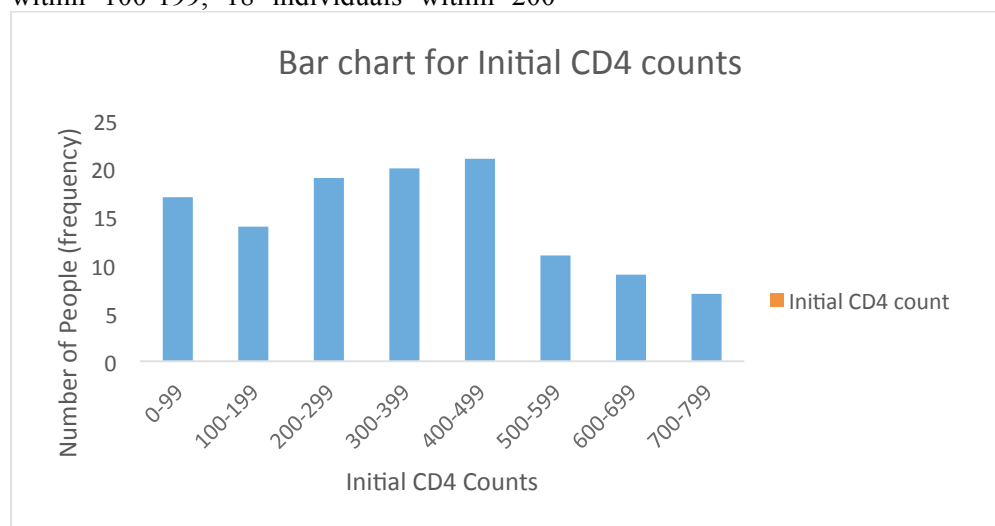


Figure 1: Bar Chart for Initial CD4 Counts

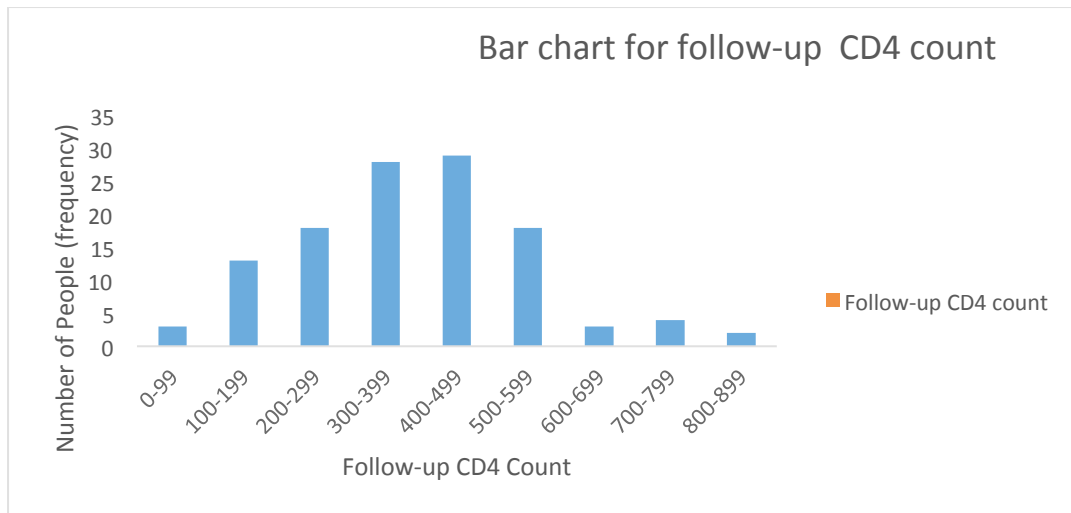


Figure 2: Bar Chart for Follow-Up CD4 Counts

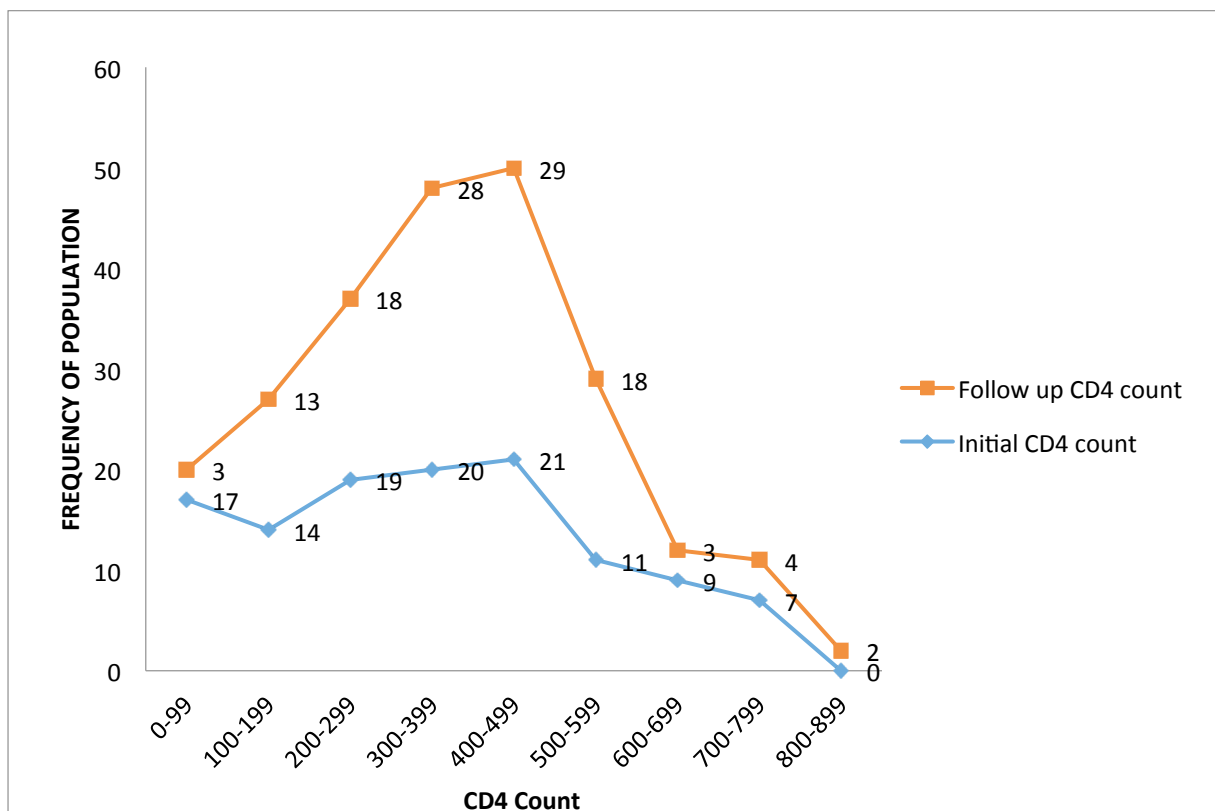


Figure 3: Line chart for initial and Follow up CD4 count

DISCUSSION

Results obtained implies that there was a strong correlation between the initial and follow-up CD4 counts, for both those who had an increase or a decrease in the CD4 count after three months of therapy. An increment in CD4 count affords the patient clinical benefits as there is a lower risk of clinical progression of HIV disease. This was observed in a study

Loutfy *et al.*, (2005) to assess the relationship between 12 months CD4 cell count response and clinical outcome in HIV infected individuals despite receiving antiretroviral therapy. The researchers concluded that a 25cell/ μ l increase in CD4 cell count was associated with a 21% reduction in the risk of an AIDS defining event or death. Low CD4 counts are associated with an elevated risk of

both opportunistic illnesses and non-AIDS related diseases (Highleyman, 2009).

From the general data obtained, there was an increase of 43.8 cells/ μ l. This is higher. In comparison to values obtained in a similar studies in Port Harcourt (39 cells/ μ l) (Erhabor *et al.*, 2006a). However, the value obtained in this study is quite low compared to 122 cells/ μ l increase obtained in a different study in Port Harcourt to assess the HAART-dependent CD4 lymphocyte response based on Pre-therapeutic CD4 lymphocyte count in HIV-infected Nigerians (Erhabor *et al.*, 2006b). In another study in Lagos to assess the response to HAART of the elderly and young HIV/AIDS patients, the mean CD4 increase was 98 cells/ μ l, in subjects older than 55 years and 64 cells/ μ l, in subjects less than 55 years of age (Ekong *et al.*, 2004).

The initial and follow-up counts after three months therapy are shown in figure 1. From this figure, it is observed that for 57% of the cases, follow-up counts were higher than the initial counts while for 43%, it was the reverse. It therefore means that, from simple arithmetical analysis, the effect of antiretroviral therapy was pronounced. For those cases which follow-up counts were lower, it can be concluded that there was no positive response to therapy. The reasons for this could be diverse and not fully understood. The immune system could be grossly decapitated at initiation of therapy. Prolonged damages to the immune system of patients in an advanced stage of the disease may lead to qualitative (cellular dysfunction) and/or quantitative (lack of CD4 cell increase) defects. The impaired immunological recovery following HAART may be related to a reduced thymic function (Florence *et al.*, 2003). Another factor which poses a great challenge to immune recovery is low nutritional status. Optimal nutritional statuses as well as adequate vitamin levels are known to be, by themselves, enough to prevent the development of AIDS in people who react positively to the tests for HIV. The higher rates of HIV progression and vertical transmission in developing countries coincide with similarly higher rates of malnutrition and vitamin deficiencies, indicating that HIV infection may be modified by nutritional status (Giraldo, 2002). Non-adherence to therapy could lead to poor response to HAART. Poor

adherence to HAART may result in treatment failure and death (Abaasa *et al.*, 2008). Factors associated with poor adherence include a poor patient-clinician relationship, high pill burden, forgetfulness, mental depression, lack of patient education, inability of patients to identify their medications, drug toxicities and being too ill (WHO, 2007). There are several biological mechanisms that may underlie poor immunological response to HAART, related to both failure to produce new CD4 cells (for example, due to deficiencies in thymic activity or bone marrow or altered levels of cytokines such as interleukin-7) and excessive CD4 cell destruction (due to CD4 cell hyperactivation, ongoing HIV replication, persistent antigenic stimulation, or altered immune system regulation). Furthermore, individual genetic factors appear to also play a role (Highleyman, 2009).

The total initial and follow-up CD4 counts for males in the study, as shown in figure 2, are 7252 and 8342 respectively. The total initial and follow-up CD4 counts for females in the study, as shown in figure 3, are 32190 and 37202 respectively. In both cases, the total follow-up CD4 counts were higher than the total initial CD4 counts, indicating a general tendency of the subjects to respond positively to the treatment.

Conclusion

In the present work, there was a general increase in CD4 count i.e. a general positive difference in the response to the antiretroviral treatment after three months on therapy although this was not statistically significant. However, better response could be achieved after treatment for a longer period.

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Conflict of interest

The authors declared no conflict of interest.

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