International Journal of Current Research in Medical Sciences

ISSN: 2454-5716

www.ijcrims.com

Coden: IJCRPP(USA)

Research Article

http://s-o-i.org/1.15/ijcrms-1-5-4

Study on the variations in CD4+, CD8+ and CD4; CD8 Ratio in HIV-infected children in Umuahia; Abia state.

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Abstract

The variations in CD4+, CD8+ and CD4:CD8 in HIV-infected children was investigated at the HIV/AIDS clinic Federal Centre Umuahia. A total number of one hundred and twenty six (126) were recruited for the study, being children within the age of 2-12 years. They were grouped into three {3} of forty two (42) each of equal number of males and females. The control (group 1} were apparently healthy children, group II were HIV-infected children on therapy (HAART) while group III were HIV-infected children without therapy (HAART). The blood samples of the subjects were collected and analyzed for CD4, CDS while CD4:CD8 was calculated. The result revealed a significantly lower value of CD4+ and CD4:CD8 ratio P<0.05 of group III (456±131 cells/ml; 0.6±0.1) when compared with groups I (905±183cells/ml; 1.310.1) and II {745±240 cells/ml; 0.8+0.2). And the CD8+ of group III was significantly higher (905±184 cells/ml) when compared with groups I (6831128 cells/ml) and II (838+169 cells/ml) P<0.05.The CDS* showed a significant strong negative correlation with CD4 and CD4:CD8 which suggested an increase in oxidative stress with subsequent numerical and functional decline in CD4+.

Keywords: CD+, CD8+ , CD4: CD8 RATIO, HIV-Infected children.

Introduction

HIV infection is characterized by progressive immunodeficiency whose immunologic hallmark is both numerical and functional decline in CD4+ T cells (Lizette et al., 2003} with increase production of CD8+ (Abram et al., 2010), induced by oxidative stress. The development of both impaired respohsiveness and enhanced apoptosis in T cells have been reported to be through tumor necrosis factor (TNF)- X- related mechanism (BUttke and Sandstorm, 1994).The Viral fat protein liberated by HIV have a direct interference with calcium homeostasis activation of caspases and the induction of mitochondrial generation, all being important events in the apoptotic cascade of several cell types (lizette et al., 2003). The increase in level of CDS in HIV ser positive patients have been shown to correlate with a number of the makers of sever

Materials and Methods

A total number of one hundred, and twenty six(126) subjects aged 2-12years were recruited for the study after their oral and written informed consent. Control (group 1) are the apparent healthy children, group ii are HIV - infected children on therapy (HAART) and group iii are those screened HIV positive for the first time but had not been exposed HIV disease, including viral load (Froebel et al., 200). According to Resino et al. (2003), in as much as highly active antiretroviral therapy reduces the level of COSb and boost immunity, not all HAART-based treatment are successful. And the work done by zijenah, (2005) have shown the diagnostic importance of CD4: COS Ratio, its high, prediction of HIV infection or treatment failure in children and the need for its inclusion in monitoring HIV infected children especially in developing countries where virologic testing is unavailable. The objective of this study is to ascertain the variations on the CD4, CD8 and CD4;CD8+ ratio following HIV infection and the role CD4;D8 ratio can play in the effective management of children infected with HIV and the monitoring of treatment failure and/or success to any antiretroviral drug and no AIDS indicator conditions. The three groups were made up of 42 subjects each of equal number of males and females. And those reactive to any other viral infection and/or any underling chronic illness were excluded from the study. The study was carried out at Federal Medical Center Umuahia Nigeria

Sample collection

About 2ml of blood was collected from each subject and dispensed into dipotassium ethylene diamine tetrocetic acid (EDTA) vacutainer (Beckson, Dickson and company USA). And the CD4 and CDS counts were done written 2hours of blood collection using flow cytometer (partec compaqy Ltd Germany)

Stast1cal analysis

The result was expressed as mean ± SD. The stastical analysis was done using One Way Analysis of Variance (ANOVA) and Pearson correlation at 5% Level of significance with the statistic package for social science (SPSS) version 17.

HIV Screening and confirmation

The HIV statuses of the subjects were established using unigold test kit (Trinity Biotech PLC), Stat Pak kit (ChemBio Diagnostic System inc U.S.A) and Determine kit (Alere Determinem Japan) and confirmatory was done using Western Blot assay method.

Table l mean ± SD of CD4+ CD+ and CD4; CDS of the studied population

Groups	CD4+	CD8+(Cells/ml)	CD4:CD8
1	905 ±183	683± 128	1.3 ±0.1
II	745 ±240*	838 ±169*	0.8+0.2*
III	456 ±131**	905±184**	0.6+0.1**

d*= significantly ifferent from group i
**= significantly different from group I & ii at p <0.05

Discussion

The observed decline in the CD4+ counts of both groups ii and iii may be based on the fact that HIV infection is characterized by numerical and functional decline in CD4 cells, which underlines the immunodeficiency that result to acquired immunodeficiency syndrome (ADIS) (suresh et al., 2009). Multiple mechanism are implicated in the depletion of CD4 ranging from impaired thymic production of naive CD4, direct lysis and killing of infected cells(salmen and berrueta, 2012). The cytotoxic cell (CD8) acts and forms pores in the target's cell plasma membrane

thereby allowing granzymes-protease enzyme, to gain entry into the target cell activating series of cysteine protease leading to the apoptosis of the infected CD+. The decline can also arise from virus itself as it has both direct and indirect pathogenic effects on both mature CD4+ and the progenitor cells from which they arise (Me cune, 2001). The direct effects arises from excessive accumulation of unintegrated viral DNA from viral replication, which is cytotoxic hence induce death signal. Also the viral proteins (Nef, Env and Tat) have been suggested to increase the level of CD95 (Fas) and FasL which increase susceptibility of infected CD4+ cells to fas-mediated apoptosis (Judi et al., 2003).

Furthermore , the infected CD4+ cells constitute short-lived lymphocyte population with a half-life of 1.2days while other HIV infected cells such as the Macrophages constitute the long-live population with an average half-life of 14days (sanjay et al., 2009}

As the disease spreads to the naive CD4+ cells in the thymus, it progressively surpasses the capacity to produce new cells leading to immune deficiency.

The CD4+ of group III was significantly lower than that of group II, showing more immunosuppression in this group. This proves the finding that within six months and one year of institution of HAART in children with HIV infection, they had an increase in CD4+ counts, although CD4+ and CDS'" T cells never reached control group values (Resino et al., 2004).

This irnmunosuppression observed in group Hi could be explained on the basis that, as the HIV progresses, there is a shift in the cytokine response from type -1 cellular immune response (IFN-Y, TNF-ct and IL-12), to a type -2 humoral response (IL-4, IL-5, IL-10, and IL-13) {Geoffrey and Dana, 2005). Therefore the loss of the anti-apoptic cytokines -INF-Y, and IL-12 during disease progression and increase in the pro-apoptotic cytokines - IL-4 and IL-10 shows the role of apoptosis in the numerical and functional decline in CD4+ cells with consequent impairment in the response to diverse pathogens and the elimination of antigens by immune cells, giving rise to opportunistic infections. In this study, it was observed that the depletion of CD4 T- cells in HIV infected children was accompanied by an increased levels of CD8+ T cells which shows that a key feature of the immune system of patient with HIV infection is an expansion of the CDS T - cells pool in a setting of CD4 depletion (Marta et al., 2011). The highest CD8+ mean level was observed in group HI than in other groups, indicating highest activation of immune cells during asymptomatic phase as observed by Krishna et al. (2006). The increased level of CD8+ observed could be based on the functions of CD4+ among others, the induction of cytotoxic T cells. Once the CD8+ is activated, it undergoes clonal expansion with the help of interleukin -2 (IL-2) which is a growth and differentiator factor for T cells (Milstein et al., 2011), this therefore increases the number of the CD8+ cells in circulation for the infected CD4+ cells. The CD4:CD8 ratio was observed to decrease in HIV infected children when compare with control, this can be explained on the basis that, as HIV infection causes a decline in CD4+ with expansion of CD8+ the ratio in negatively affected because researchers have shown that in healthy children, CDS cells account for about 30% of the total lymphocytes while the CD4+ cells account for about 60% (Zijenah et al., 2005) which usually gives ratio of greater than one. Therefore as the CD4+ decreases with CDS* expansion, it causes the ratio to tend towards zero as the disease progresses as shown in the present study.

In the study of Zijenah et al., (2005), CD4:CD8 ratio has been suggested as a useful diagnostic tool where virologic testing is unavailable, since it has been proven to have greater than 98% specificity in identifying HIV infection in children and infants, as well as its cost effectiveness (Emmanuel et al., 2010).

Conclusion

This study showed an expansion in CD8+ which favours its high circulation, depletion in CD4+ and CD4:CD8 ratio consequent to chronic immune activation and oxidative stress.

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