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CCR5 CO-RECEPTOR EXPRESSION ON CIRCULATING CD4+LYMPHOCYTES IN HIV-1 PATIENTS ON HAART AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET-KENYA

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ABSTRACT

HIV-1 continues to be a major public health problem globally and particularly in Sub-Saharan Africa. The expression of CCR5 co-receptors and its influence on HIV-1 entry into host cells and tissues has been studied mostly in developed countries outside Africa. The impact of HAART on the expression of CCR5 co-receptor on host cells is little studied in Sub-Saharan Africa. This study focused on expression of CCR5 co-receptor on circulating $CD4^+$ T cells in HIV-1 patients on HAART. A cross-sectional study design of 48 adult HIV-1 patients on HAART and an equal number of HAART naïve were recruited. Blood samples were assayed for $CD4^+$ T cells and CCR5 co-receptor by FACS Calibur® while viral loads were quantified by COBAS® Amplicor version 2. The median expression (%) of CCR5 co-receptors on $CD4^+$T were1.32 and 0.80 in patients on HAART and HAART naïve respectively, p=0.003. The median in the viral loads (copies/ml) were 111.5 and 39301 in patients on HAART and the HAART naïve respectively, p=0.001.This study concluded that HAART up-regulates CCR5 co-receptor expression in HIV-1 infected participants compared to HIV-1 infected but HAART naïve counterparts.

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INTRODUCTION

The CCR5co-receptors are low molecular weight proteins that play a role in leukocyte chemotaxis, emigration, and activation during inflammation. The CCR5 co-receptor is commonly expressed on T Lymphocytes, Monocytes, macrophages, dendritic and microglia cells (Mehandru, 2007). The Human Immunodeficiency Virus-1 (HIV-1) has been shown to utilize predominantly CCR5 and CXCR4 to attach to CD4 T cells before viral fusion and entry (Zhang *et al*., 2006). The possible impact of antiretroviral therapy on the expression of CCR5 co-receptors has not been well documented in developing countries. So far studies on CCR5 co-receptors expression levels in HIV-1 infected individuals on HAART have been carried out in developed countries outside Africa where they concentrated on HIV sub-type B (Samantha *et al*., 2010).

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A small study in Uganda, demonstrated up-regulation of CCR5 expression in early stages ofHIV-1 infections with clades A and D but a down-regulation of the co-receptor in late stages infections with the same clades (Wright *et al*., 2011). The predominant HIV subtypes in Kenya include subtypes A, D and other recombinant types (Brito *et al*., 2007). There is limited data in Kenya on the expression levels of the CCR5 co-receptors in HIV-1/AIDS patients on HAART. The CCR5 co-receptor is an important target of HIV-1 and understanding its expression characteristics may help direct development of therapies. The present HAART regimens only ameliorate the symptoms and signs of AIDS and do not take into account their influence on CCR5 expression (Ostrowski *et al*., 2015). We sought to determine and compare the differences in expression of CCR5 co-receptors on $CD4^+$ T lymphocytes in patients on HAART and the HAART naïve patients at Moi Teaching and Referral Hospital in western Kenya.

Table 1. Participants'CD4, CCR5and viral load Characteristics

Characteristic	Study population Median (IQR) n=96	Median(IQR) of HAART n=48	Median (IQR) of HAART Naïve n=48	P- values
CD4(cells/µl)	301.5(228.3, 449.8)	269.5(220.8, 449.8)	315(229.3, 451.0)	p=0.626
CCR5(% counts)	0.0119(0.005, 0.185)	1.32(0.88, 2.24)	0.80(0.26, 1.38)	p=0.003
Viral Load(copies/ml)	2281(40.3, 58442)	111.5(<20,5599.5)	39301.5(1072.5,88247)	p=<0.001

MATERIALS AND METHODS

A cross-sectional study was conducted at the Academic Model for Providing Access to Healthcare (AMPATH) of Moi Teaching and Referral Hospital. The AMPATH is a partnership of Moi University College of Health Sciences, Moi Teaching and Referral Hospital in Uasin Gishu County of western Kenya and a consortium of North American Medical Schools led by Indiana University School of Medicine. Consecutive sampling technique was utilized to recruit 48 HIV-1 positive on HAART and 48 HIV-1 positive, HAART naïve participants. Ethical approval and informed consent were obtained before the study begun. Blood sample was collected from each of the 48 HAART exposed and 48 HAART naïve participants and divided into two portions. One portion of sample was used to determine $CD4^+$T cells and CCR5 co-receptors expression levels using a cocktail of fluorescent labeled antibodies according to the manufacturer's protocol as follows: FITC CD195 (5µl), PE CD4 (5µl), PerCP Cyt5.5 CD3 (5µl) and PBS-FCS 1% (5µl) to add up to 20µl per tube (BD Biosciences, Pharmingen™). The FACS data were then analyzed on BD cell-quest ®program of the FACS Calibur®. The second portion of each blood sample was used for viral load determination using COBAS® Amplicor version 2 for the RNA of the HIV-1 virus in plasma with detection limit of 20 HIV-1 RNA copies/ml. Participants were matched by gender and age. Data was analyzed using Statistical Package for Social Scientists (SPSS) 16 version. Non-parametric tools, Mann-Whitney U and Spearman's coefficient tests were utilized in deriving inferential statistics between those on HAART and the HAART naïve; while for descriptive statistics the median and inter-quartile ranges were employed because data was skewed. All *P*-values were two-tailed and values ≤ 0.05 were considered statistically significant.

Limitations of the study

This study did not take into account diurnal variations among the study participants which may have affected immunological parameters.

RESULTS

A total of 96 HIV-1 positive participants were recruited into the study of whom 48 had received HAART for ≥ 6 months and an equal number were HAART naïve. The median (IQR) ages was 41(36.3, 46) comprising of 60.4%females. Majority of the participants on HAART 39(81 %) were on first-line regimen (Lamivudine, Zidovudine and Efavirenz or Nevirapine), while 9 (19 %) were on second-line regimen. Many patients on HAART 21(43.8%) were in W.H.O. Clinical stage III, while a majority 31(64.6%) of HAART naïve patients were in the W.H.O. Clinical stage II. The table below shows that CCR5 co-receptor expression and viral loads varied significantly between HAART and HAART naïve patients. There was insignificant variation in the CD4 counts between the two groups of participants; p-value was <0.005 and p=0.626 respectively.

DISCUSSION

The patients seen in this study were of similar median ages but higher (315 versus 217 cell/µl) median $CD4^+$ T cell counts in the HAART naïve than the Asian studies, (Jiajie Fang *et al*., 2013; Zhou *et al*., 2010). These differences could be due to the fact that patients in Kenya sought for medical care late in the disease stage than their Asian counterparts. Even though the median$CD4^+$T cells and viral loads in patients on HAART were lower than HAART naïve, the trend of distribution is similar to earlier study (Tang *et al*., 2011). The HAART drugs effectively suppress HIV-1 replication, rebuild the immune system and considerably improve the prognosis of patients (Jin *et al*., 2012). HIV-1 positive patients on HAART demonstrated a higher median CCR5 co-receptor levels than the HAART naïve group. With the progression of the disease, HIV-1 virus enters $CD4^+$ T cells where it may remain latent, with resultant up-regulation of CCR5 co-receptors (Stanley *et al*., 1996). In this study the CCR5 co-receptor expression seems to increase as CD4 cell count declined similar to an earlier study by Stanley *et al.* (1996), which contrasts with findings from other studies which consistently show that patients on HAART have a corresponding up-regulation of CCR5 co-receptors and an increase in the $CD4^+$ T cells population (Wright *et al*., 2011). The observation in this study may be due to the pathological changes in immune reconstitution syndrome that may occur in some individuals when initially commenced on HAART (Ledergerber *et al*., 1999). These could also have been due to suppression of immune activation and inflammation in late stage HIV-1 infection (Carsenti-Dellamonica *et al*., 2011).

Conclusion and Recommendations

This study indicates that HAART appears to up-regulate CCR5 co-receptor in participants on HAART than the HAART naïve. A prospective, large study may help to elucidate the pattern of CCR5 co-receptors expression on $CD4^+$ T cells of patients on different regimens of first-line and second-line HAART.

Author's contribution

Simiyu Ben, Mining Simeon and Diero Lameck conceived the idea to publish this work.
Simiyu Ben, Ndede Isaac and Emonyi Wilfred coordinated data collection, analysis,
Namasake Dominic and Masengeli Nathan revised the consecutive drafts.

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REFERENCES

Brito, A., Almeida, A., Gonsalez, C.R., Mendonça, M., Ferreira, F. and Casseb, J. 2007. Successful HAART is associated with high B-chemokine levels in chronic HIV type 1-infected patients. *AIDS Res Hum Retroviruses,* 23(7):906-12.

Carsenti-Dellamonica, H., Saïdi, H., Ticchioni, M., Guillouet, de Salvador, F., Dufayard, C. J. and Gougeon M.L. 2011. The suppression of immune activation during enfuvirtide-based salvage therapy is associated with reduced CCR5 expression and decreased concentrations of circulating interleukin-12 and IP-10 during 48 weeks of longitudinal follow-up. *HIV Med*., 12(2):65-77.

Jiajie Fang, Shi Bai, Lijuan Wu, Xuanwen Zhu, Xiaolin Yao Changzhong Jin and Chaojun Wang, 2013. Impact of highly active antiretroviral treatment on expression of HIV-1 coreceptors and ligand levels in peripheral blood from HIV-1 infected patients in China. *Journal of International Medical Research,* 0(0) 1–10.

Jin, C., Zhang, F. and Wu, L. 2012. Immune activation and CD127 expression on T lymphocyte subsets of a Chinese cohort of pediatric aids patients with different viral responses. *Curr HIV Res.,* 10: 584–591.

Ledergerber, B., Egger, M., Erard, V., Weber, R., Hirschel, B., and Telenti, A. 1999. AIDS-related opportunistic illnesses occurring after initiation of potent antiretroviral therapy: the Swiss HIV Cohort Study. *JAMA*, 282(23):2220-2226.

Mackay, C. R. 2011. Chemokines: Immunology's high impact factors, *Nature publishing;* Available at *http://www. immunol.nature.com*

Mehandru, S. 2007. The gastrointestinal tract in HIV-1 infection: questions, answers, and more questions! *The PRN Notebook.*; 12:1-10.

Ostrowski, M. A., Justement, S. J., Catanzaro, A., Hallahan, C. A., Ehler, L. A., Mizell, S. B., and Fauci, A. S. 2015. Expression of Chemokine Receptors CXCR4 and CCR5 in HIV-1-Infected and Uninfected Individuals. *The Journal of Immunology*, 161:3195-3201.

Samantha, J .W., Graeme, J .M. and Nesrina, I. 2010. Nature and Function of CCR5 in Immune Activation, HIV-1 Entry, and Targeted Therapeutics. *J Viral Entry*; 4(1):1–10.

Stanley, S. K., Ostrowski, M. A., Justement, J. S., Gantt, K., Hedayati, S. and Fauci, A. S. 1996. Effect of immunization with a common recall antigen on viral expression in patients infected with human immunodeficiency virus type 1. *New England Journal of Medicine*, 334(19), 1222-1229

Tang, L.L., Jin, C.Z. and Wu, L.J. 2011. *The impact of highly active antiretroviral treatment on the blood profiles of patients with acquired immune deficiency syndrome. J Int Med Res; 39: 1520–1528.*

Wright, E., Mugaba, S., Grant, P., Parkes-Ratanshi, R., Van der Paa Lieve, and Kaleebu, P. 2011. Co-receptor and Cytokine Concentrations May Not Explain Differences in Disease Progression Observed in HIV-1 Clade A and D Infected Ugandans. Plos One.

Zhang, Z.N., Shang, H., Jiang, Y.J., Liu, J., Dai, D. and Wang, Y.N. 2006. Activation and coreceptor expression of T lymphocytes induced by highly active antiretroviral therapy in Chinese HIV/AIDS patients. *Chin Med J (Engl).*, 119(23):1966-71.

Zhou, H.Y., Zheng, Y.H., He, Y., Chen, Z., and Liu, C. 2010. Evaluation of a 6-year highly active antiretroviral therapy in Chinese HIV-1-infected patients. Intervirology.; 53(4):240-6. *Epub* 2010 Mar 30.

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