

HIGHLIGHTING THE EPIDEMIOLOGY OF HIV VIRAL TROPISM IN HIGH BURDEN POPULATIONS

*Article Review by Abdu Abdullahi Adamu, Nigeria
(MBBS, MMSc-HIV Medicine Student of Texila American University)
Email: - audu86@yahoo.com*

SOURCE

J Int AIDS Soc. 2012; 15: 2. Published online Jan 26, 2012. doi: 10.1186/1758-2652-15-2

REVIEW OF LITERATURE

Human immunodeficiency virus type-1 (HIV-1) is one of the most complex microorganisms as it is known for its genetic heterogeneity. Currently knowledge based on molecular epidemiologic studies have clearly shown that the most prevalent forms of HIV 1 are subtypes (clades) C, B and A. In sub Saharan Africa and India, Subtype C accounts for about 50% of all infections thus making it the most common clade worldwide. However clade B is common in western countries.

HIV-1 subtypes differ by as much as 20-25% at the genetic level, and have varying biological characteristics, including differences in disease progression, pathogenicity, transmissibility and co-receptor usage.

HIV infection is dependent on the coreception present on the surface of the CD4 cell. And available studies have clearly established a relationship between HIV 1 coreceptor use and the disease stage. However most of these studies were conducted on HIV 1 subtype B.

In general, in the early stages of HIV infection and disease, it is associated with greater prevalence of only chemokine type 5 (CCR5)-tropic (R5) HIV-1, which is characterized with slower progression to AIDS while the emergence of C-X-C chemokine receptor type 4 (CXCR4)-using virus (X4) has been associated with greater treatment experience and higher risk of death, and coincides with more rapid CD4+ T-cell depletion and disease progression.

HIV 1 subtype B is most prevalent in high income countries of the west and consequently is the most studied in terms of receptor usage and its relationship to disease state. This relationship is not well understood for other subtypes especially A, C, and D which are common in Africa and South East Asia.

The introduction of the CCR5 antagonist; Maraviroc, has generated more interest in the study of tropism of this virus in sub Saharan Africa and Asia where most of the burden of the disease exist.

INTRODUCTION

The introduction of Maraviroc which is a CCR5 antagonists as an antiretroviral drug necessitates the need to study HIV tropism for other HIV 1 subtypes especially those present in other countries in South East Asia and Sub Saharan Africa which accounts for a majority of the burden of the infection. The study under review was undertaken to evaluate HIV-1 co-receptor tropism in the developing world where non-B subtypes predominate, in order to assess the therapeutic and prophylactic potential of CCR5 antagonists in these regions.

In this vain, this review aims to highlight the prevalence of R5 and X4-tropic HIV-1 among samples obtained from patients with HIV-1 subtype C infection from India and South Africa, and with subtype A/A1 and D infection from Uganda, and to explore the demographic and clinical characteristics associated with R5 infection. In addition, the review will also highlight the ability of the Trofile® assay to determine tropism of non-B subtypes of HIV-1, which previously had not been explored in a large study.

ARTICLE SUMMARY

In this study, HIV 1 infected patients were recruited into a prospective cross sectional observational study from Uganda, India and South Africa. The subtype infection was also established for each country as Indian and South Africa patients were infected with subtype C while Ugandan patients are infected with subtype D. Study protocols that were used were reviewed by the eithics board of each institution. However sites (institutions) were selected based on their experience with HIV management and research.

In all countries most of the respondents reported heterosexual contact as means of transmission however blood transfusion was reported as a means of transmission in 3 patients. The Indian patients had lower CD4 count than patients from other countries however viral load was consistent across all three countries. A total of 307 samples from India, 678 from Uganda, and 297 from South Africa were collected. All samples has HIV 1 RNA higher than 500 copies/mL.

R5 tropism were detected in 96% of treatment naïve and treatment experienced patients in India; 71% of treatment experience patients in South Africa, 71% of treatment naïve and treatment experience patients in Uganda. Dual/Mixed tropic HIV 1 was found in 4% of Indians, 25% of South Africans and 29% of Ugandans. Presence of R5 type virus correlates with high CD4 count.

ARTICLE STRUCTURE

The article was presented in a standard format with an abstract which gave an overview of the article. The abstract structured into various segments containing introduction, methodology, results and conclusion. The article was well elaborated with charts and statistical analysis summarized in tables. It gave correlates between R5 tropism and CD4 count across of the countries. The background gave a concise overview of tropism. The methodology was presented in a structured format under the following subheadings: Study design, Study methodology, Sample size and statistical analysis.

The results were also presented using a structured format which has tropism as a subheading as such making it much easier to access specific data.

ARTICLE CRITIQUE

AUTHORITY

The article is published in the Journal of the International AIDS Society which is a highly respectable journal with a good impact factor. It is a great source for scientific peer reviewed information about HIV. The article is an authentic one as it is backed with robust references.

ACCURACY

Information contained in the article is accurate and all of them are well referenced.

PERIOD

The article was published in 2012 however data was collected between 2007 and 2008.

RELEVANCY

The article was conducted alongside a team of expert all with very sound academic background. It is a very relevant article as information about viral tropism in South East Asia and Sub Saharan Africa is very essential giving that Maraviroc has been introduced as an antiretroviral drug. This drug requires tropism testing before commencement.

OBJECTIVITY

The information contained in the article is evidence based.

STABILITY

The article is published in a journal with international reputation and has been cited in several other articles.

ANALYSIS OF GRAPH/IMAGE/TABLE

Not applicable.

RECENT ADVANCES RELATED TO THE TOPIC

Not applicable at the moment.

CONCLUSION

This is a well written article in a reputable peer review journal that examined HIV 1 coreceptors in samples collected from India, Uganda and South Africa. This is important because treatment options are being developed that depends on Coreceptors being used by the viruses at time of initiation of treatment.

REFERENCE

1. Brumme ZL, Goodrich J, Mayer HB, Brumme CJ, Henrick BM, Wynhoven B, Asselin JJ, Cheung PK, Hogg RS, Montaner JS, Harrigan PR. Molecular and clinical epidemiology of CXCR4-using HIV-1 in a large population of antiretroviral-naive individuals. *J Infect Dis.* 2005;15:466–474. doi: 10.1086/431519. [PubMed] [Cross Ref]
2. Buonaguro L, Tornesello ML, Buonaguro FM. Human immunodeficiency virus type 1 subtype distribution in the worldwide epidemic: pathogenetic and therapeutic implications. *J Virol.* 2007;15:10209–10219. doi: 10.1128/JVI.00872-07. [PMC free article] [PubMed] [Cross Ref]
3. Cornelissen M, Mulder-Kampinga G, Veenstra J, Zorgdrager F, Kuiken C, Hartman S, Dekker J, van der HL, Sol C, Coutinho R. Syncytium-inducing (SI) phenotype suppression at seroconversion after intramuscular inoculation of a non-syncytium-inducing/SI phenotypically mixed human immunodeficiency virus population. *J Virol.* 1995;15:1810–1818. [PMC free article] [PubMed]
4. Coakley E, Petropoulos CJ, Whitcomb JM. Assessing chemokine co-receptor usage in HIV. *Curr Opin Infect Dis.* 2005;15:9–15. doi: 10.1097/00001432-200502000-00003. [PubMed] [Cross Ref]
5. de Roda Husman AM, Koot M, Cornelissen M, Keet IP, Brouwer M, Broersen SM, Bakker M, Roos MT, Prins M, de Wolf F, Miedema F, Goudsmit J, Schuitemaker H. Association between CCR5 genotype and the clinical course of HIV-1 infection. *Ann Intern Med.* 1997;15:882–890.[PubMed]

6. Hu DJ, Buve A, Baggs J, van der GG, Dondero TJ. What role does HIV-1 subtype play in transmission and pathogenesis? An epidemiological perspective. *AIDS*. 1999;15:873–881. doi: 10.1097/00002030-199905280-00002. [PubMed] [Cross Ref]
7. Kaleebu P, French N, Mahe C, Yirell D, Watera C, Lyagoba F, Nakiyingi J, Rutebemberwa A, Morgan D, Weber J, Gilks C, Whitworth J. Effect of human immunodeficiency virus (HIV) type 1 envelope subtypes A and D on disease progression in a large cohort of HIV-1-positive persons in Uganda. *J Infect Dis*. 2002;15:1244–1250. doi: 10.1086/340130. [PubMed] [Cross Ref]
8. Keet IP, Krijnen P, Koot M, Lange JM, Miedema F, Goudsmit J, Coutinho RA. Predictors of rapid progression to AIDS in HIV-1 seroconverters. *AIDS*. 1993;15:51–57. doi: 10.1097/00002030-199301000-00008. [PubMed] [Cross Ref]
9. Kijak GH, McCutchan FE. HIV diversity, molecular epidemiology, and the role of recombination. *Curr Infect Dis Rep*. 2005;15:480–488. doi: 10.1007/s11908-005-0051-8. [PubMed] [Cross Ref]
10. Nielsen C, Pedersen C, Lundgren JD, Gerstoft J. Biological properties of HIV isolates in primary HIV infection: consequences for the subsequent course of infection. *AIDS*. 1993;15:1035–1040. doi: 10.1097/00002030-199308000-00002. [PubMed] [Cross Ref]
11. Moyle GJ, Wildfire A, Mandalia S, Mayer H, Goodrich J, Whitcomb J, Gazzard BG. Epidemiology and predictive factors for chemokine receptor use in HIV-1 infection. *J Infect Dis*. 2005;15:866–872. doi: 10.1086/428096. [PubMed] [Cross Ref]
12. Moore JP, Kitchen SG, Pugach P, Zack JA. The CCR5 and CXCR4 coreceptors--central to understanding the transmission and pathogenesis of human immunodeficiency virus type 1 infection. *AIDS Res Hum Retroviruses*. 2004;15:111–126. doi: 10.1089/088922204322749567. [PubMed][Cross Ref]
13. Ranga U. Human immunodeficiency virus-1 subtypes: could genetic diversity translate to differential pathogenesis. *J Indian Inst Sci*. 2002;15:73–91.
14. Spira S, Wainberg MA, Loemba H, Turner D, Brenner BG. Impact of clade diversity on HIV-1 virulence, antiretroviral drug sensitivity and drug resistance. *J Antimicrob Chemother*. 2003;15:229–240. doi: 10.1093/jac/dkg079. [PubMed] [Cross Ref]
15. Thomson MM, Perez-Alvarez L, Najera R. Molecular epidemiology of HIV-1 genetic forms and its significance for vaccine development and therapy. *Lancet Infect Dis*. 2002;15:461–471. doi: 10.1016/S1473-3099(02)00343-2. [PubMed] [Cross Ref]