

Correlation Between Viral Load And Immunity Of HIV Carriers - An Experimental Study

P Devi, N Parameswari, S Murugan

Citation

P Devi, N Parameswari, S Murugan. *Correlation Between Viral Load And Immunity Of HIV Carriers - An Experimental Study*. The Internet Journal of Health. 2008 Volume 9 Number 1.

Abstract

A series of forty HIV carriers of both sexes and age group from 26 to 45 years were selected for the present study. Their blood samples were collected and analyzed for their viral load and immunoglobulins IgG, IgA and IgM. Their results showed that an increase in the levels of viral load and IgG and normal levels of IgA and IgM. This study indicated that there was no decrease in the level of immunoglobulins IgG, IgA and IgM, though there was increase in the level of viral load.

INTRODUCTION

AIDS (Acquired Immunodeficiency Syndrome) is a particularly unpleasant fatal disease caused by infection with the human immunodeficiency virus (HIV) ¹. The major feature of the disease is the destruction of the immune system which is normally the body's way of fighting disease. HIV is actively wiped out the cells that form the body's immune system, resulting in the disease known as AIDS ².

There are currently two types of HIV: HIV-1 and HIV-2. Worldwide, the predominant virus is HIV-1, and generally when people refer to HIV without specifying the type of virus they will be referring to HIV-1. However, HIV-2 is less easily transmitted, and the period between initial infection and illness is longer in the case of HIV-2. Both HIV-1 and HIV-2 appear to cause clinically indistinguishable AIDS. HIV-1 strains can be classified into two groups, group M and group O and Group M consists of at least ten genetically distinct subtypes A to J. A declining titer of IgA antibodies against gp160, gp120 and p²⁴ antigens may be associated with disease progression ³. Serum IgA (SIgA) may play a role in the invitro neutralization of HIV-2

⁴.

The HIV-positive subjects had HIV-specific serum IgG and IgA; the sero negative persons had HIV-specific serum IgA in the absence of IgG. Testing of the sero negative persons one year after the interruption of sex with HIV patients showed that no IgG seroconversion had occurred and that HIV-specific IgA serum concentrations had declined. The

immunologic picture for resistance to HIV infection should include HIV-specific cell-mediated immunity as well as HIV-specific IgA-mediated mucosal and systemic immunity ⁵.

About 25% of the children of untreated HIV-infected mothers are later determined to be HIV-infected. At birth, all of the children of HIV-infected mothers have HIV-IgG antibody, which is transferred trans- placentally from the mothers to their children, and infected children produced HIV-IgG antibody in response to their infection. Most infected children have detectable HIV-IgA by 3 months of age ⁶. The presence of IgG, serum IgA and secretory IgA antibodies capable of mediating antibody dependent cellular cytotoxicity may be critical in maintaining a functional immune response in al stages of HIV infection ⁷.

HIV-1 infection induces the expression of high level of gm2 ganglioside on infected cells and IgM antibody (AB) against GM2 can cause complement mediated cytolysis of HIV-1 infected cells. There is a positive correlation between the anti-GM2 IgM antibody Ab titer and CD4+ cell count but a negative correlation between the anti-GM2 IgM Ab titer and HIV RNA load. Therefore, the amount of IgM Ab against GM2 may be related to the prognosis of HIV-1 infected patients ⁸.

The in vivo IgM to IgG isotype switch and affinity maturation may be important for protection and long-term survival in certain HIV-1 infected individuals ⁹. So the present study was carried to assess the viral load in the blood, estimate the immunoglobulins IgG, IgA and IgM and

correlate the viral load and immunity of HIV carriers

MATERIALS AND METHODS

Forty HIV carriers of both sexes and age from 26 to 45 years who came to Kovai Medical Centre and Hospital (KMCH), Coimbatore, Tamil Nadu for regular checkup were selected for this study. Forty healthy subjects of both sexes and corresponding age group free from HIV infection were chosen as controls. 15ml of Heparinised blood and stored in a vacutainer blood collection tube also 5ml of blood is collected from the HIV carriers and serum is separated and stored in a vial. The viral load was estimated by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) aimed at amplifying the RNA of the virus. The quantification of viral load was done at Specialty Ranbaxy Limited, a clinical reference laboratory in Mumbai, India.

Pathogen diagnosis by the polymerase chain reaction (PCR) is based on the amplification of specific regions of the pathogen genome. In real-time PCR, amplified product is detected via fluorescent dyes. These are usually linked to oligonucleotide probes which bind specifically to the amplified product. Monitoring the fluorescents intensities during the PCR run (i.e. in real time) allows the detection and quantification of the accumulating product without having to re-open the reaction tube after the PCR run.

The determination of human IgG, IgA and IgM are based on the specific reaction between antigen and corresponding antibody. IgG, IgM are based on the specific reaction between antigen and corresponding antibody. IgG, IgA and IgM in the serum were determined by Radical immunodiffusion test as described by Fahey and Muckelvey¹⁰ and Mancini et al.¹¹. The levels of significance in the variation of above biochemical parameters in blood among HIV patients were determined by performing student's 't' test.

RESULTS AND DISCUSSION

The mean HIV load was increased in the HIV carriers when compared to the control. The mean HIV load was 30788.70 ± 22811.43 copies / ml in the HIV carriers and 0 copies / ml in the control. Increase in the HIV load was statistically significant at 1% level. This supports the statement of Sabin et al¹² and Dianzani et al.¹³. According to them, the blood HIV load is increased in HIV carriers.

The mean IgG level was remarkably increased when compared to the control. The mean IgG level was 2325.25 ± 394.41 mg/dl in the HIV carriers and 1112.38 ± 219.45

mg/dl in the control. Increase in the mean IgG level was statistically significant at 1 percent level. Similar observation was made by Lawoko et al.¹⁴ that there is an increased IgG binding in HIV -1 infected individuals.

When the mean viral load 30788.70 ± 022811.43 copies/ml was increased, the mean IgG level 2325.25 ± 394.4mg/dl was also increased. But this elevation is not useful in the prevention of disease progression. This statement is supported by Daniel et al.¹⁵ and Olivos et al.¹⁶. Oliva et al¹⁶ reported that following primary infection with HIV – 1, antibodies against HIV – 1 auto antibodies, also arise. Such auto antibodies have an important role in the pathogenesis of HIV – 1 infection.

Figure 1

Table 1: The values of various parameters in the blood of HIV carriers

S.No	Parameters	Units	Mean ±SD		Groups compared	't' value	indication
			Control group (A)	HIV carriers(B)			
1.	Viral load	Copies/ml	0±0	30788.7± 22811.43	A vs B	4.235**	Increased
2.	IgG	mg/dl	1112.38± 219.45	2325.25±394.41	A vs B	9.322**	Increased
3.	IgM	mg/dl	192.65± 49.79	186.37± 43.84	A vs B	0.395NS	Normal
4.	IgA	Mg/dl	244.9±43.12	241.87± 148.73	A vs B	0.355 NS	Normal

Significance level: * = $P < 0.05$; ** $P < 0.01$; NS not significant

The mean IgG level was normal when compared to the control. The mean IgA level was 241.87± 148.73 mg/dl in the HIV carriers and 224.9± 43.12 mg/dl in the control. There was no significant variation in the mean IgA level in the HIV carriers. Koziowski and Jackson³ stated that IgA level is increase in early in infection and remained elevated throughout disease progression. But the present study contradicted the statement of Koziowski and Jackson³.

When the mean viral load 30788.70±28811.43 copies /ml were increased, the mean IgA level 241.87 ±148.73 mg / dl were not increased. Koziowski and Jackson³ reported that the IgA level was increased early in infection and remained elevated throughout disease progression. But the present study contradicted the statement of Koziowski and Jackson that the IgA was not increased.

The mean IgM level was normal when compared to the control. The mean IgM level was 186.37 ± 43.84 mg/dl in the HIV carriers and 192.65 ±49.70 mg / dl in the control. There was no significant variation in the mean IgM level in

the HIV carriers. Wu et al.⁸ reported that HIV – 1 infection induces the expression of high level of IgM antibody. But the current study was contradictory to the statement of Wu et al.⁸. When the mean viral load 30788.70 ± 22811.13 copies/ml was increased, the mean IgM level 186.37 ± 43.84 mg / dl was not increased. The above statement is supported by Toran et al.⁹ and Daniel et al.¹⁵.

Any immune stimulation may increase the viral load, and specific immunization may lead to enhancement of infection. High mutation rate and high turnover rate, which are the characteristics of the virus explains in part why the immune response alone is unable to control the infection.

CONCLUSION

The current study was done in HIV carriers who were healthy and who did not turned to full blown AIDS. Their results showed that an increase in the level of immunoglobulin IgG and viral load and normal levels of IgA and IgM. Though there is an increase in viral load, the immunoglobulin IgA and IgM level were found to be normal in HIV carriers. Due to chronic infection of HIV, IgG level was found to be increased. The current study indicated that even though there was an increase in the viral load, there was no decrease in the levels of immunoglobulins IgG, IgA and IgM. A study might be needed with large sample size concentrating on the IgA anti HIV antibodies binding to envelope glycoproteins of HIV in carriers. Since the non-specific IgA in plasma are involved in every stages of HIV infection, but the mechanism is not known so far. The polymeric nature of the IgA antibodies against env glycoproteins might be studied promptly by analyzing the same in carriers as well as AIDS patients which may help us to assess the role of the antibody in every stages of the disease. Since elevated levels of GM2 ganglioside on infected cells producing IgM antibody against the same have correlation with CD4 + cell count and HIV RNA load and these may be related to the prognosis of HIV – 1 infected patient. They might be correlated with the other T cells also. These studies might be needed for the enhancement of immune response against those viruses to prolong the life of the infected persons.

CORRESPONDENCE TO

Dr. P. Uma Devi, Assistant Professor, School of Biotechnology, Karunya University, Coimbatore-114.Tamilnadu, India. Mobile:+91 9994583372 e - Mail: umadevipongiya@rediffmail.com

References

1. Roitt, M.I. & Peter, J. Immunodeficiency. Essential immunology; 10th edition, Blackwell Science Ltd. 2002; 305-321
2. Kozlowski, P.A. & Jackson, S. Serum IgA subclasses and molecular forms in HIV infection; selective increase in monomer and apparent restriction of the antibody response to IgA 1 antibodies mainly directed at envelope glycoproteins. AIDS Research Human Retroviruses 1982; 8(100): 1773-1780.
3. Pieterse, J. Aids and HIV symptoms what is the difference? 2001.
4. Lizeng, Q., Skott, P., Soural, S., Nilsson, C., Andersson, S.S., Ehnlund, M., Taveira, N. & Bjorling, E. Serum immunoglobulin A (IgA)- mediated immunity in human immunodeficiency virus type -2 (HIV-2) infection. Virology 2003; 308(20): 225-232.
5. Mazzoli, S., Lopalco, L., Salvi, A., Trabattoni, D., Lo Caputo, S., Semplici, F., Biasin, M.B.C., Cosma, A., Pastori, C., Meacci, F., Mazzotta, F., Villa, M.L., Siccardi, A.G. & Clerici, M. Human immunodeficiency virus (HIV) specific IgA and HIV neutralizing activity in the serum exposed seronegative partners of HIV-seropositive persons. Journal of Infectious Disease 1990; 180 (30): 871-875.
6. Sever, J.L., Rakusan, T.A., Campos, J.M., O'Donnell, R.M. & Price, V.A. HIV antibody responses in children of HIV infected mothers. Pediatrics AIDS HIV Infection 1996; 7(4): 246-253.
7. Black, K.P., Cummins, J.E Jr. & Jackson, S. Serum and secretory IgA from HIV infected individuals mediate antibody dependent cellular cytotoxicity. Clinical Immunology Immunopathology 1996; 81(20): 182-190.
8. Wu, X., Okada, N., Goto, M., Iwamoto, A. & Okada, H. The IgM antibody level against ganglioside GM2 correlates to the disease status of HIV-1 infected patients. Microbiology and Immunology 2000; 44(95): 405-410.
9. Toran, J.L., Kremar, I., Sanchez-Pulido, L., de Alboran, I.M., del Real, G., Llorente, M., Valencia, A., de Mon, M.A. & Martinez, A.C. Molecular analysis of HIV-1 gp 120 antibody response using isotype IgM and IgG phage display libraries from a long term non progressor HIV-1 infected individual. Ur Journal Immunology, 1999; 29 (9): 2666-2675.
10. Fahey, J.L. & Mckelvey, E.M. Quantitative determination of serum immunoglobulins in antibody agar plates. Journal of Immunology 1965; 94: 84.
11. Mancini, G., Carbonara, A.O. & Heremans, J.F. Immunochemical quantification of antigens by single radial immunodiffusion. Immunochemistry 1965; 2: 235.
12. Dianzani, F., Antonelli, G., Riva, E., Turriziani, O., Antonelli, I., Tying, S., Carrasco, D.A., Lee, H., Nguyen, D., Pan, J., Poast, J., Cloyd, M. & Brown, S. Is human immunodeficiency virus RNA load composed of neutralized immune complexes? Journal of Infectious Disease 2002; 185(8): 1051-1054.
13. Sabin, C.A., Devereux, H., Phillips, A.N., Janossy, G., Loveday, C. & Lee, C.A. Immune markers and viral load after HIV-1 seroconversion as predictor of disease progression in a cohort of haemophilic men. AIDS 1998; 12(11): 1347-1352.
14. Lawoko, A., Johansson, B., Rabinarayan, D., Pipkorn, R. & Blomberg, J. Increased immunoglobulin G, but not M binding to endogenous retroviral antigens in HIV-1 infected persons. Journal of Medical Virology 2000; 62(4): 435-444.
15. Daniel, V., Susal, C., Weiner, R., Zipperle, S., Kropelin, M., Zimmermann, R., Huth – Kulne, A. & Opelz, G.

Sequential Occurrence of IgM, IgM / IgG and gp 120-IgM/IgG complement complexes on CD4+ lymphocytes in relation to CD4+ blood lymphocyte depletion in HIV+ hemophilia patients: results of a 10 year study. Immunology Letter 1995; 47(1-2): 97-102.

16. Olivos, I.P., Moreno-Altamirano, M.M., Sanchez-Colon, S., Masso Rojas, F. & Sanchez-Garcia, F.J. Connectivity and HIV -1 infection role: role of CD4+ T-cell counts and HIV-1 RNA copy number. Scandinavian Journal of Immunology 2000; 52(6): 618-627.

Author Information

Pongiya Uma Devi, M.Sc., M.Phil., Ph.D

Assistant Professor, School of Biotechnology, Karunya University

N. Kannika Parameswari, M.Sc., M.Phil.

Lecturer, PG Research Department of Biochemistry, Dr. D.G.P. Arts and Science College

Sevanan Murugan, M.Sc., Ph.D

Lecturer, School of Biotechnology, Karunya University