Int J Biol Med Res. 2012; 3(1): 1263-1266

BioMedSciDirect Publications

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

A Laboratory Analysis of HIV-2 over a Period of Five years in a Tertiary Care Hospital and Review of Literature

Ajantha GS[a*], Kulkarni RD[b], Kalabhavi AS[c], Shetty PC[c], Pavithra AJ[d]

[a]Associate Professor, Professor & Head[b], Assistant Professor[c], Tutor[d], Department of Microbiology, SDM College of Medical Sciences & Hospital, Sattur, Dharwad – 580 009, India.*

ARTICLE INFO

Keywords:
AIDS
Human Immunodeficiency Virus
HIV
HIV-2
India

ABSTRACT

Introduction: Human immunodeficiency virus (HIV) has rapidly spread all over the world. HIV-1 is the most common type but the less spoken HIV-2 is present in many places including India. Methods: The data of HIV serological assays performed on serum samples at our hospital between the years 2006 and 2010 were analyzed with special reference to HIV-2. Results: A total of 47,876 serum samples were tested for HIV infection, of which 1537 were reactive for HIV antibodies. Among them, 1509 were HIV-1, 23 were HIV-2 and five were reactive for antibodies of both HIV-1 and HIV-2. Conclusions: HIV-2 exists in this part of India also. The overall HIV infection rate has decreased over the five year period in our hospital. Though the control measures appear to be effective, rigorous control measures must be continued without any place for complacence.

1. Introduction

The dreadful spread of Human immunodeficiency virus (HIV) among the human race, after its first recognition in 1981, is still continuing with speed [1]. Now, it is one of the most pressing challenges to the stewards of health care management as well as to the researchers. After three decades, we have gained enormous information on this virus but it is not enough to design an effective vaccine or a curative therapy yet. The two human immunodeficiency viruses responsible are HIV-1 and HIV-2 but they are not closely related. Though there is up to 60 % sequence homology, their immunopathogenesis, drug susceptibility and epidemiological behaviour show important differences [2].

Though HIV-1 is more common and more dangerous than HIV-2, we need to observe the HIV-2 disease carefully. The spontaneity of the microbes to mutate into virulent strains cannot be underestimated. Today it is more important than before to generate and monitor the baseline data about prevalence of various types of infectious agents in any geographical area. As there are no previous data from this area, the present study was undertaken to know the

2. Materials and Methods

We are a tertiary care hospital in the North of Karnataka, India. The serum samples tested at our hospital over a period of five years between the year 2006 and 2010 were reviewed for HIV-2 reactivity. The samples were tested for HIV-1 and HIV-2 antibodies by three different tests as per the National AIDS Control Organization (NACO) guidelines [3]. The three different kits used in the study were NACO approved tests. To differentiate between HIV-1 and HIV-2, the results of HIV Tridot (J Mitra & Co. Pvt Ltd., New Delhi, India) were referred.

4. Results

A total of 47,876 persons were tested for the presence of HIV antibodies during the study period of which 1537 cases were reactive for HIV antibodies. On an average, 307.4 samples were reactive for HIV antibodies every year. The year-wise seropositivity rates of HIV-1 and HIV-2 are shown in Table-1. The statistical analysis of the decreasing HIV infections over the five-year period is shown in Table-2.

* Corresponding Author : Ajantha GS
Associate Professor, Department of Microbiology,
SDM College of Medical Sciences & Hospital, Sattur,
Dharwad – 580 009, India.
Tele: +91836-2477374, 2477257
E-mail: ajju_dwd@rediffmail.com

Table-1: Year-wise detection rates of HIV infections

Year	Samples tested	Total HIV reactive cases	Total HIV negative cases
2006	5207	322 (6.2%)	4885
2007	6414	308 (4.8%)	6106
2008	9077	292 (3.2%)	8785
2009	12115	330 (2.7%)	11785
2010	15063	285 (1.9%)	14778
Total	47876(100%)	1537(3.8%)	46339 (96.8%)

Table 2: Statistical analysis showing the significance of decreasing rates of HIV

Period	Chi Square Test Value	Degree of Freedom	p-value	Statistical significance
2006-2007	10.71	1	p□0.005	High
2007-2008	25.63	1	p□0.001	Very high
2008-2009	4.43	1	p□0.05	Significant
2009-2010	21.01	1	p□0.001	Very high
Total	293.9	4	p□0.001	Very high

Bar diagram-1: The decreasing rates of HIV infections over five years

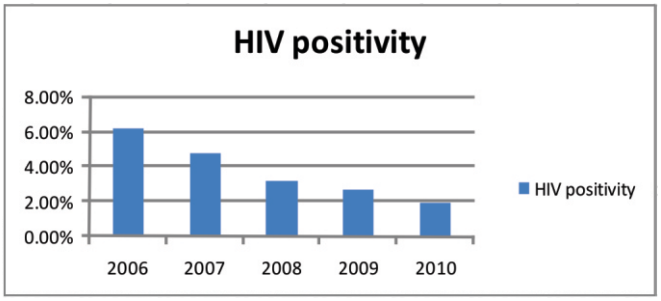

Table-3: HIV-1 and HIV-2 infections over the five years period

Year	HIV-1	HIV-2	Both
2006	318	4	Nil
2007	299	7	2
2008	283	7	2
2009	325	4	1
2010	284	1	Nil
Total	1509	23	5
(N=1537)	(98.2%)	(1.5%)	(0.3%)

Among these HIV-positive cases as shown in table 3, 1509 cases were reactive for HIV-1 and 23 were for HIV-2. Five of the tested sera were reactive for both HIV-1 and HIV-2 antibodies.

Less than one-third of the HIV-2 seropositives (8/23) belonged to the age group of 15-45 years while more than two-third belonged to the age group of 45-65 years (15/23). None of the HIV-2 cases were recorded from individuals below 15-years or above-65-years of age. The s ex distribution was almost equal (12 males and 11 females). We noted only one case of HIV-2 infection with pregnancy. Majority of the cases had history of heterosexual exposure and were form low socioeconomic group.

5. Discussion

HIV/AIDS (Acquired Immunodeficiency Syndrome), in spite of being only few decades old, has amplified into a monstrous health problem. HIV has infected millions of people by now all over the world. Roughly, 33.4 million people are living with HIV/AIDS. An estimated 2.27 million people in India are living with HIV/AIDS [4]. In the present study, the average HIV positivity among the tested was 3.8% and HIV-1 was responsible for 98.2% of these infections. The seropositivity has steadily decreased over the five years period from 6.2% to 1.9%, which is very highly significant ($p < 0.001$). By observation (Bar diagram-1) as well as statistical analysis (Table-2), it can be concluded that the HIV positivity rate is showing a consistent decline which is evenly spaced over the five year period. One of the main reasons for this significant decrease could be the increasing awareness among the public as well as effective implementation of the control programs. This phenomenon of declining rate of infections is observed in India as well as other parts of the world [1-4].

HIV-2, similar to HIV-1, has a limited host range and is restricted to humans. HIV-2 gained entry into the human population around 1940 and like HIV-1, has simian origin. Compared to HIV-1, there are more similarities between HIV-2 and SIVsmm (Simian immunodeficiency virus indigenous to feral sooty mangabey monkeys). Humans are in close contact with monkeys in West Africa where humans hunt them for food or keep them as pets. Now, it is globally accepted that HIV-2 has originated from cross-species migration of SIVsmm from monkeys to humans in West Africa [5]. Eight HIV-2 subgroups, A through H, have been recognised but only subgroups A and B commonly cause human infections [6]. HIV-1 is widespread and prevalent everywhere whereas HIV-2 is largely confined to West Africa because of low transmission rate [7]. However, the ability of HIV-2 to spread rapidly within a defined population has been observed in India [8].

Though HIV-2 is geographically restricted mainly to West Africa, it is prevalent in India also. The occurrence of this virus in India has been attributed to the past socio-economic link with Portugal [7]. This virus was first reported from India in 1991 [9]. There are only few reports about this virus from India and the rate among HIV-reactive individuals in different reports ranges from zero to 7% [2, 10-14]. In the present study, 1.5% of the HIV-reactive individuals were infected with HIV-2.

HIV-2 is very rare in pregnant women [15]. In our study also, only one case belonged to this category. The perinatal transmission rate of this viral type is also very low due to lower maternal RNA levels [15]. HIV-2 is generally more common in older individuals, as opposed to HIV-1 [16]. In our study, the same phenomenon was noted where 65.2 % of HIV-2 cases were from the age group of above 45 years.

The infection with HIV-2 may either result in long-term non-progression or in few cases, may progress to clinically evident AIDS [2]. HIV-2 infection does not protect against HIV-1 infection. Because long-term non-progression is very common in HIV-2 infection and also because of low mortality, the infected person has the risk of acquiring a second HIV infection. However, there is no evidence suggesting a worse outcome in cases co-infected with HIV-1 and HIV-2 [7]. As the present study was a retrospective analysis and no long-term follow up of HIV-2 infections, we are unable to comment on the progression of the disease or about a second HIV infection.

The low transmissibility and an attenuated clinical course of HIV-2 compared to HIV-1 are well known. Similar observations have been made in SIV infections of sooty mangabeys from where HIV-2 originated [17]. Majority of HIV-2 cases have near-normal CD4+ T cell counts, low viremia and non-progressive disease. The reasons are not clear though it may be due to a better immune response. Most HIV-2 infected individuals show powerful cytotoxic response to Env and Gag proteins along with broad neutralizing antibodies [6]. The CD8+ cytotoxic T lymphocyte responses also play important role. The slower disease progression in HIV-2 patients has been attributed to the antiviral cytokines (Interferon-γ), unidentified antiviral factors (CAF) and virus entry-blocking β-chemokines secreted by CD8 T-cells along with their perforin-based cellular cytotoxicity [18].

The less virulent course may also be due to a lower state of immune activation. This is probably related to the immunosuppressive activity of the C2-V3-C3 envelope region which is lacking in the homologous C2-V3-C3 region in the HIV-1 envelope [6]. The low plasma RNA levels in HIV-2 infected patients, when compared to HIV-1, in spite of comparable cellular proviral DNA levels could be because of better immune control [19]. Though in vitro cytopathocity is similar, HIV-1 can multiply more efficiently than HIV-2 under similar conditions [19, 20].

The mixed infections are detected in areas where both HIV-1 and HIV-2 are prevalent. But, due to cross-reacting antibodies between them, accurate diagnosis of actual mixed infection poses difficulty. The gold standard test to diagnose mixed infection is PCR, but false-negative results are known to occur because HIV-2 provirus load can be very low in advanced mixed infection [7]. The mixed infections were noted in five cases (0.3 % of HIV-reactive samples) of our study, but we could not confirm the results by molecular methods. In one of the South Indian hospitals, the number of mixed infections was more than that of HIV-2 infection alone [11]. In one more study from Karnataka, 18 % of HIV-reactive cases showed mixed positivity and 7 % were only HIV-2 reactive [13]. There are no data on the problem of antibody detection tests giving false negative results in advanced stages of the disease. This could be because the numbers of the less common HIV-2 infections progressing to advanced stage are very few.

It is important to identify and differentiate HIV-1, HIV-2 or mixed infections accurately, particularly those requiring ART, as there are differences in drug susceptibility between HIV-1 and HIV-2. First generation non-nucleoside reverse transcriptase inhibitors (NNRTIs) and some protease inhibitors (PIs) are ineffective against HIV-2. Although nucleotide reverse transcriptase inhibitors (NRTIs) are active against this virus, higher concentrations may be required to inhibit HIV-2 compared to HIV-1. 21 The CD4 counts also may not increase to the expected levels following therapy [2]. Thus, therapeutic options are limited and outcome is unpredictable for the needy patients. At present, there is no standard HIV-2 viral load assay to monitor therapy [21]. At the same time, HIV-2 is given less importance in vaccine research as most efforts are focused on HIV-1 vaccine which is the global epidemiological problem. Current vaccine research is directed at a T-cell based vaccine with the intention to protect from disease progression rather than to prevent the infection [18].

We have to hope and wait for more effective drugs or novel approaches like the latest innovation, DRACO (Double stranded RNA Activated Caspase Oligomerizer), for resistant viruses like HIV-2. DRACO drugs are supposed to be broad-spectrum antiviral agents and have been shown to be effective against many enveloped and non-enveloped viruses containing DNA, dsRNA, positive-sense ssRNA and negative-sense ssRNA genomes which replicate in the cytoplasm or in the nucleus. They are chimeric proteins where one protein has the function of binding only to long dsRNA which is produced only in virus-infected cells and one more protein for inducing rapid apoptosis. Thus, the drugs act by selectively inducing apoptosis of virus-infected cells only. However, these drugs are still under evaluation against various viruses and have yet to be tested against HIV-2 which is intrinsically resistant to some antiviral agents [22].

We have already witnessed a natural event of recombination of influenza viruses in pigs leading to the birth of a new virus and its transcontinental spread. Recombination of attenuated oral polio vaccine virus and wild polio viruses is also speculated. Similarly, there is always a fear that HIV-1 and HIV-2 viruses co-infecting the same host might recombine resulting in a more aggressive pathogen. At present, there is no evidence supporting this hypothesis in natural infections. However, HIV-1 and HIV-2 recombination has been shown to occur in vitro [23]. The most noteworthy example supporting this phenomenon would be the SIV from which HIV evolved. SIVcpz (SIV of chimpanzees) may perhaps be the result of recombination between SIVgsn (SIV of greater spot-nosed monkey) and SIVrcm (SIV of red capped mangabey) in a west central African monkey species which chimpanzees prey [5]. Therefore, continuous vigilance and monitoring of the behaviour of HIV-2 in the nature, in humans, in laboratory as well as through research is important for avoiding any future hitch in the ongoing gradual success of HIV control.

6. Conclusions

HIV infection appears to be gradually coming under control, though there is no cure or vaccine, because of effective preventive measures. We should not rest on the laurels but strive to achieve more. HIV-2 exists in this area also; we should be watchful and should study this virus more carefully. Better accessibility of quality diagnostic methods will help in accurate identification of HIV-2. This will prove helpful in directing appropriate therapy. Highly active antiretroviral therapy has made HIV/AIDS a manageable chronic disease but drug resistance due to inaccurate therapies may hamper this progress. Before this happens, responsible agencies and persons should take all the necessary steps. Researchers should aim for innovation of not only broad-spectrum antiviral agents like the brilliant invention of DRACO but also broad-spectrum vaccines. Such talented inventions would certainly provide a breakthrough in achieving major and rapid control over the HIV menace one day.

Acknowledgement:

We are thankful to Dr. Praveenchandra, Associate Professor, Department of Community Medicine, SDM College of Medical Sciences & Hospital, Sattur, Dharwad – 580 009 for the help in statistical analysis of the study.

7. References

[1] World Health Organization. Global health sector strategy on HIV/AIDS 2011-2015. Geneva: WHO Press, 2011, pp 3-6.

[2] Chiara M, Rony Z, Homa M, Bhanumati V, Ladomirska J, Manzi M, et al. Characteristics, immunological response & treatment outcomes of HIV-2 compared with HIV-1 & dual infections (HIV 1/ 2) in Mumbai. Indian J Med Res. 2010;132:683-689.

[3] National AIDS Control Organisation. Detection of HIV infection. Guidelines on HIV testing. New Delhi: NACO, Ministry of Health and Family Welfare; 2007; 8-53.

[4] Hart TA. Need for Improved Access to HIV Prevention Programmes. Indian J Med Res. 2010;132:653-655.

[5] Freed EO, Martin MA. HIVs and Their Replications. In: Knipe DM, Howley PM, editors. Fields Virology, 5th ed. Philadelphia: Lippincott Williams & Wilkins. 2007; 2107-2285.

[6] Barroso H, Borrego P, Bartolo I, Marcelino JM, Familia C, Quintas A, et al. Evolutionary and Structural Features of the C2, V3 and C3 Envelope Regions Underlying the Differences in HIV-1 and HIV-2 Biology and Infection. PLoS ONE 2011;6:e14548.

[7] De Silva TI, van Tienen C, Rowland-Jones SL, Cotten M. Dual Infection with HIV-1 and HIV-2: Double Trouble or Destructive Interference? HIV Ther. 2010;4:305-323.

[8] Grez M, Dietrich U, Balfe P, Briesen HV, Maniar JK, Mahambre G, et al. Genetic Analysis of Human Immunodeficiency Virus Type 1 and 2 (HIV-1 and HIV-2) Mixed Infections in India Reveals a Recent Spread of HIV-1 and HIV-2 from a Single Ancestor for Each of These Viruses. J Virol. 1994;68:2161-168.

[9] Rubsamen-Waigmann H, von Briesen H, Maniar JK, Rao PK, Scholz C, Pfutzner A. Spread of HIV-2 in India. Lancet. 1991;337:550-551.

[10] Solabannavar SS, Baragundi MC, Sonth SB, Patil CS. Seroprevalence of the Human Immunodeficiency Virus (HIV) 1 and 2 infections in a Tertiary Care Hospital. Journal of Clinical and Diagnostic Research 2010;4:3383-3387.

[11] Kannangai R, Ramalingam S,Castillo RC, Babu PG, John TJ, Sridharan G, Schwartz DH. HIV-2 status in southern India. Trans. R Soc Trop Med Hyg. 1999;93:30-31.

[12] Kannangai R, Nair SC, Sridharan G, Prasannakumar S, Daniel D. Frequency of HIV type 2 infections among blood donor population from India: A 10-year experience. Indian J Med Microbiol. 2010;28:111-3.

[13] Bairy I. Shivananda PG. Seroprevalence of HIV in Manipal. Indian J Med Sci. 2001;55:257-62.

[14] Solomon S, Kumarasamy N, Ganesh AK, Amalraj RE. Prevalence and risk factors of HIV-1 and HIV-2 infection in urban and rural areas in Tamil Nadu, India. Int J STD AIDS. 1998;9:98-103.

[15] Enders G. Viral infections of the fetus and neonates, other than rubella. In: Mahy BWJ, Muelen V, editors. Topley and Wilson's Microbiology and Microbial Infections- Virology. 10th ed. London: Hodder Arnold Publishers. 2005;1443-1497.

[16] Buve A, Bishikwabo-Nsarhaza K, Mutangadura G. The spread and effect of HIV-1 infection in sub-Saharan Africa. Lancet. 2002;359:2011-2017.

[17] Sodora DL, Allan JS, Apetrei C, Brenchley JM, Douek DC, Else JG, et al. Toward an AIDS vaccine: lessons from natural simian immunodeficiency virus infections of African nonhuman primate hosts. Nat Med. 2009;15:861-865.

[18] http://www.who.int/vaccine_research/diseases/soa_std/en/index4.html#]. Accessed on12th Aug 2011

[19] Lopes AR, Jaye A, Dorrell L, Sabally S, Alabi A, Jones NA, et al. Greater CD8_ TCR Heterogeneity and Functional Flexibility in HIV-2 Compared to HIV-1 Infection. J Immunol. 2003;171;307-316.

[20] Sagoe KWC, Mingle JAA, Affram RK, Britton S, Dzokoto A, Sonnerborg A Virological Characterization of Dual HIV-1/HIV-2 seropositivity and infections in southern Ghana. Ghana Medical Journal. 2008;42:16-21.

[21] Campbell-Yesufu OT, Gandhi RT. Update on Human Immunodeficiency Virus (HIV) - 2 Infection. Clin Infect Dis. 2011;52:780-787.

[22] Rider TH, Zook CE, Boettcher TL, Wick ST, Pancoast JS, et al. Broad-Spectrum Antiviral Therapeutics. PLoS ONE. 2011;6:e22572.

[23] Motomura K, Chen J, Hu WS: Genetic recombination between human immunodeficiency virus type 1 (HIV-1) and HIV-2, two distinct human lentiviruses. J Virol. 2008;82:1923-1933.