

## CLINICAL RESEARCH

### Effectiveness of homoeopathic medicines in HIV patients - A clinical trial

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Targeted therapy for HIV treatment is the antiretroviral therapy but varied types of drug toxicities and adverse reactions are quiet common. Homoeopathy is popularly known for its unique methods to tackle the infection especially in viral diseases. The study was an open clinical trial using individualized homoeopathic medicines selected through repertorization. The aim of study was to observe the changes in CD4 and Viral load volumes after intervention of individualized homoeopathic medicines. 90 seropositive patients were enrolled in two study centers of Central Council for Research in Homoeopathy (CCRH). 72 patients, who completed the follow up period of six months, were assessed. There was significant change in Viral load volume as compared to the baseline data (95% CI, 0.16, 1.24,  $p=0.012$ ), but no significant changes was observed in CD4 cells (95% CI, -9.31, 57.84,  $p=0.154$ ). The other parameters like Body Mass Index (BMI) (95%, -1.12, -.57,  $p<0.001$ ) showed significant improvement. After homoeopathic intervention, WHO-QOL (Quality of Life) parameters showed statistical significant changes at  $p<0.05$  in physical health, psychological and environmental domains but in social domain no significant change was noted.

**Keywords:** HIV; antiretroviral therapy; homoeopathic medicines; viral load; CD4 cells; BMI; WHO-QOL

#### Introduction

An alternative to antiretroviral therapy (ART) is not yet established in Complementary and Alternative Medicines (CAM) including Homoeopathy due to inadequate research. Currently ART is considered to be the target therapy for the HIV viral suppression. With the introduction of this therapy, quality of life of HIV patients has improved because of reduced opportunistic infections.<sup>1,2</sup> Mortality rate has come down drastically due to this intervention.<sup>3-6</sup> However, all the different regimens of ARTs have been associated with varied degrees of adverse drug reactions and toxicities in the HIV infected individuals.<sup>7-11</sup> Since adverse reactions are inevitable with antiretroviral drugs, models of safe and suitable therapies need to be tested. Homoeopathy is one of the emerging complete medical system which offers relief in many incurable disease conditions in the most individualized and holistic manner without any known adverse effects. Various studies have been conducted whose results have undoubtedly proven the efficacy of

this system despite the controversy on undetectable medicinal matter and principle of individualization.<sup>12</sup>

As the HIV infection spreads, number of hypothetical observations have come up regarding the treatment option in Homoeopathy. Some study reports have suggested the use of *Phytolacca americana* and Cyclosporine-A due to similarity of its symptomatology and HIV infection.<sup>13,14</sup> But later a study conducted by Brewitt et al suggested the immuno-modulatory effects of homoeopathic medicines.<sup>15</sup> Another trial using the combination of homoeopathic medicines has shown reasonable improvement in CD4 cells counts followed by reduction of viral load in ART administered patients.<sup>16</sup> A double blind placebo controlled trial conducted by Rastogi DP et al (1999) suggested statistically significant changes in one group but the other group did not yield any results.<sup>17</sup> Some of the study reports underlined the principle of individualization whereas some others were done with combination therapies, basically non-homoeopathic in approach. Where the individualization was the main focus, those studies have failed to pin point any particular medicine for this potentially incurable condition. This may be the fundamental difference when conducting research in Homoeopathy in comparison to conventional clinical trials.

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Thus CCRH of Department of AYUSH, Ministry of Health and family Welfare, Govt. of India has initiated a multi centre open clinical trial using homoeopathic medicines to observe the changes in plasma viral load in comparison to CD4 changes in HIV infected patients of non targeted ART group. The study was undertaken after due consideration of ethical issues. The institutional ethical committee has approved non targeted ART populations of HIV carriers for the trial.

### Aims and Objectives

The study was carried out to ascertain the therapeutic role of homoeopathic medicines in checking or delaying the progression of HIV infection. This was monitored by clinical evaluation of the action of homoeopathic medicines on immune system by measuring changes in CD4 count; by ascertaining changes in HIV plasma viral load and by comparing whether the HIV viral load changes are relative to change in CD4 cell counts under homoeopathic therapy; and to ascertain the changes in physiological functions and quality of life amongst HIV infected individuals under homoeopathic therapy.

### Materials and Methods

#### Study design

This was an open-label observational prospective multi centre study of 1½ years duration. The samples were selected from the confirmed patients of HIV, who reported for homoeopathic treatment at the Outpatient Department of Regional Research Institute of Homoeopathy, Mumbai and Clinical Research Unit of Homoeopathy, Chennai. The age of the enrolled patients was between 18 to 50 years. Details of the study and the possible effects and side effects of

therapy were explained and the availability of ART was also intimated prior to the enrollment of the participants in the study. An informed consent was obtained from the HIV patients prior to the enrollment in the study.

Preliminary assessment of health status of each patient was done as a pre-requisite for the enrollment as per the inclusion and exclusion criteria (Table1). All the prerequisite Laboratory investigations were also done at base line. The impact of the intervention on Quality of Life (QOL) was assessed on WHO-QOL instrument by the patients at entry and at the end of trial. All four domains of WHO-QOL were tested using WHO-QOL BREF, having 26 questions in Hindi and in Tamil language considering the predominance of local language. A medico social worker was engaged to monitor the same. Viral load assessment was done at the baseline and at the end of trial. Body Mass Index (BMI) was calculated at the baseline as well as at the end of the study. Apart from the virological and immunological assessment, Complete Blood Count (CBC), ESR, Liver Function Tests (LFT), Renal Function Tests (RFT), Mantoux test, VDRL and X-ray of chest were done at the baseline. The same were repeated at the end of the study except the X-ray, VDRL and Mantoux test. CBC and LFT were repeated after three months.

Those patients who fulfilled the inclusion criteria were enrolled for the trial. Detailed case history of each patient was taken in a predefined recording format, includes various aspects of the patient for individualization to get the similitum.

90 patients of various categories of HIV infection as per the CDC classification were enrolled in the trial.

**Table 1:** Inclusion and exclusion criteria

<p><i>Inclusion criteria</i></p> <ul style="list-style-type: none"><li>• Positive antibody test for HIV as per NACO (India) guidelines.</li><li>• Both sexes between 18 and 50 years of age</li><li>• CD4 count 250/cu.mm and above</li><li>• Viral Load assay report</li></ul> <p><i>Exclusion criteria</i></p> <ul style="list-style-type: none"><li>• Undergoing treatment for systemic disease viz. diabetes, hypertension etc. and is on regular conventional treatment</li><li>• VDRL-Reactive</li><li>• Hepatitis B positive</li><li>• Active mycobacterium tuberculosis infection</li><li>• Continuing drug abuse</li><li>• Having taken any conventional antiretroviral drugs in the past 12 weeks</li><li>• Pregnant and lactating mothers</li><li>• CD4 count below 250/cu.mm</li></ul>
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Out of 90, 13 patients were loss to follow up and, therefore dropped from the study, 5 patients were withdrawn due to deficient post intervention viral load testing and CD4 assessment owing to delayed follow up reporting. Only 72 patients were analyzed who completed the required follow up of six months in which 40 (55.56%) patients were in A1 category, 30 (41.67%) in A2 and one each in B1 and B2 category. Homoeopathic medicines, were procured from M/s. Sharda Boiron Laboratories Pvt. Ltd. Sahibabad, U.P. Both the centers used the same batch of the medicines. The follow up was scheduled every two weeks. This study allowed the concerned investigators to prescribe the medicines after the repertorization by using Complete Repertory of CARRA version 4 software and medicines were finalized for prescription after considering various factors such as thermal modalities, constitutional features and other specific features which are not covered in the repertorization process but significant to the patient. This ensured the *individualization* of the case as far as possible and negated the possibility of a predefined prescription. The medicines were prescribed in 6C, 12C, 30C,

200C, 1M and 10M potencies. For acute complaints acute remedies were allowed to be prescribed as and when required but restricted to the potencies mentioned earlier. No diet restriction was instructed unless it was warranted for any specific clinical conditions.

The outcome was analyzed through various statistical methods using SPSS software (ver. 16). The data was statistically evaluated using the 't' test.

## Results

Of the 90 patients enrolled under this study, 72 were followed up for a period 6 months having mean age of  $33.86 \pm 5.635$ , 21 were males and 51 were females. 65 (90.28%) patients belonged to low socio-economic background and only 7 (9.72%) were from middle income group. Of the 72 HIV patients, 24 (33.3%) patients were labourers, 18 (25%) were house wives, 17 (23.6%) were working in nongovernmental organizations (NGO), 6 (8.3%) were in agriculture, 4 (5.6%) patients were drivers and 3 (4.2%) were in Government jobs (Table 2).

**Table 2 :** Demographic characteristics

Characteristics	Frequencies (percentage) (n=72)
<b>Age</b>	
20-30 years	21 (29.2)
31-40 years	42 (58.3)
41-50 years	9 (12.5)
<b>Sex</b>	
Male	21 (29.1)
Female	51 (70.8)
<b>Socio-economic status</b>	
Low income group	65 (90.3)
Middle income group	07 (9.7)
<b>Occupation</b>	
Agriculture	06 (8.3)
Laborer	24 (33.3)
Driver	04 (5.6)
NGO worker	17 (23.6)
House wife	18 (25.0)
Govt. employee	03 (4.2)

Mean body weight at entry was 58.33±12.63 and at the end of the trial was 57.9±13.67. The mean BMI calculated at the entry was 22.79±4.43 and at the end of study was 22.95±4.30 and showed significant ( $p=0.001$ ) improvement in weight by medicines.

Table 3 shows the homoeopathic medicines prescribed during the trial period. The frequently used medicines were *Lycopodium clavatum* (n=12), *Natrum muriaticum* (n=11), *Phosphorus* (n=11) and *Pulsatilla*

(n=11). Only *Lycopodium clavatum* (n=12) has shown statistically significant result in the trial ( $p=0.045$ ) as an individualized medicine prescription.

The post intervention CD4 data was compared to the baseline (95% CI, -9.31, 57.84,  $p=0.154$ ) which was not significant. But the viral load change was significant (95% CI, 0.16, 1.24,  $p=0.012$ ) after the intervention.

**Table 3:** Frequently prescribed medicines

Name of the medicine	Mean ± SD of viral load		P value
	At entry	At end	
Calcarea carbonica	9.36 ± 1.96	8.97 ± 2.06	0.357
Lycopodium clavatum	10.02 ± 1.64	8.53 ± 2.03	0.045*
Natrum muriaticum	8.29 ± 2.10	8.66 ± 2.39	0.650
Phosphorus	9.50 ± 3.16	9.46 ± 2.69	0.969
Pulsatilla	8.92 ± 2.66	7.77 ± 2.38	0.188
Rhus toxicodendron	11.36 ± 1.45	11.81 ± 1.81	0.356
Sepia	9.37 ± 0.56	8.39 ± 2.67	0.615
Sulphur	11.18 ± 1.36	9.83 ± 2.04	0.122

\*Using paired 't' test (symptoms score before and after treatment) P value <0.05 was significant.

QOL domains tested were physical health (D1), psychological health (D2), social relationships (D3) and environmental (D4). QOL Domains score were analysed before and after the treatment by using paired 't' test and showed significance in physical

health ( $p=0.012$ ), psychological health ( $p=0.001$ ) and environmental ( $p=0.000$ ) but in social ( $p=0.114$ ), does not showed significant change in domain score (Table 4).

**Table 4:** WHO QOL Domains

Name of the medicine	Mean ± SD of viral load		P value
	At entry	At end	
Physical health	24.56±3.827	27.00±7.510	0.012*
Psychological	19.88±3.696	21.42±3.782	0.001*
Social	10.74±2.421	11.72±5.217	0.114
Environmental	26.94±5.307	28.67±5.366	0.000*

\*Paired 't' test  $p<0.05$  is significant

All other tests has not shown any positive change in the trial except Serum Alkaline Phosphatase which had significant reduction within the normal range which has no significance in the less advanced HIV infection.

### Discussion

The Homoeopathy system of treatment is embroiled in controversy since its discovery due to unconventional approaches and rejecting essential existence of material doses for curing or relieving any disease conditions. Since *individualization* is the target in every homoeopathic prescription, focusing a particular medicine for a specific diagnosis will derail the purpose of curing disease condition. Within the limited scope of individualization this clinical trial was done to explore the possibilities of using individualized homoeopathic medicines in HIV infected cases.

Though limitations do exist in conducting research in the conventional methods, we tried to explore the evidence based data which have evolved during this trial. This study is such where the data procured pre and post interventions were analyzed using various statistical methods. Though this was an open trial without a control arm, the principle of *individualization* was maintained throughout the study.

70.8% of the patients were female in the study, one of the trends emerging in India, seeking medical care in HIV. This is because they are in the receiving end of infection due to the promiscuous behavior of their partners and inability in decision making capacity in their sexual preferences due to male dominance and various other socio-cultural compulsions.<sup>18</sup> This is again leading to vertical transmission of the infection to their newborn infants.<sup>19</sup>

CD4 cell counts have not shown significant change in this trial in post intervention ( $p=154$ ) period, it has been observed that the decline in CD4 cell counts was very minimal from baseline ( $549.56 \pm 186.62$ ) to at the end ( $525.29 \pm 200.89$ ) of the study (Table 5). But the viral load has responded to the therapy ( $p<0.012$ ) significantly. The reason for this shift in viral load irrespective of the changes in CD4 needs further study. Some possible explanation accounting for viral load reduction may be the Cytotoxic lymphocyte response.<sup>20</sup> The loss of correlation between viral load and CD4 cell count was also reported cases where there was co-infection with Human T Lymphotropic Virus-1 (HTLV-1) which was not assessed in this study.<sup>21</sup>

**Table 5:** Mean baseline value and mean end value

Investigations	Mean Baseline variables (SD) (N=72)	Mean variables at end (SD) (N=72)
CD4	549.56 ± 186.62	525.29±200.89
Viral load	9.6174 ± 2.34294	8.9153±2.55332
Body weight	58.33 ± 12.63	57.90±13.69

In support of the significance of the viral load changes observed we have taken into consideration the Quality of Life through the WHO-QOL instrument. The different domains are significantly shifted in favour of improved quality of life of the patient. The physical well being (Domain1) scoring had maximum shift which is indicative of the effectiveness of the modality of treatment used in the trial ( $p=0.012$ ). The overall improvement indices would have been better if the follow-up period was more than six months. The QOL was self administered and the same was provided in the regional languages. The physical well being is indirectly observed again through the comparison of baseline BMI and post intervention BMI ( $p = 0.0001$ ).

Since the BMI is simple and direct predictor of the progression of HIV, the outcome significantly proves the effectiveness of the current intervention.<sup>22-24</sup>

All the ART therapies are destined for inhibition in various stages of viral replications and the outcome was predictive due to its targeted quality. Whereas trial medicines used in this study had neither any targeted action on viral replication nor any inhibitive properties as such. The remedy selection was made purely on the basis of symptoms expressed by the patients. The data has significance in the light of failure of vaccination trials in HIV and drug resistance in prolonged ART usage due to failed adherence and mutation of virus all over the world.<sup>25-29</sup> Thus an

alternative option like application of homoeopathic medicines is to be developed to treat HIV infection.

During the trial period patients were advised to take only homoeopathic medicines though they were given the liberty to take other medications in case of any acute infections like fever, cold etc.

### Limitations of the study

Despite the significant results, this study has certain limitations. This was an open trial and no control was used in this study.

### Conclusion

The study has shown significant changes in viral load volume which was one of the objectives of the study. However no change was observed in respect to CD4 cells. There were significant changes in the QOL and BMI. The study has underlined the effectiveness of the trial which is required to be replicated using a control arm in larger sample size.

### Acknowledgement

We are grateful to Dr. M.S. Menon and Dr. (Mrs.) Jayanthi Shastri, consultants of the project for their active support and advice. We do acknowledge the contribution of Mrs. Maya Nambiar, Statistician for compilation and analysis of data. We are thankful to all technical staff of Regional Research Institute (Homoeopathy), Mumbai and Clinical Research Unit (Homoeopathy), Chennai for their co-operation. Lastly we are greatly indebted to our patients who have enrolled in the study.

### References

1. Buchacz Kate, Baker Rose K, Palella Frank J Jr, Chmiel Joan S, Lichtenstein Kenneth A, Novak Richard M, Wood Kathleen C, Brooks John T, and the HOPS Investigators. AIDS-defining opportunistic illnesses in US patients, 1994-2007: a cohort study. <http://www.who.int/3by5/publications/briefs/countries/en/index.html> accessed on 27.09.2010
2. Sharma Surendra K, Dhooria Sahajal, Prasad KT, George Ninoo, Ranjan Sanjay, Gupta Deepak, Sreenivas Vishnubhatla, Kadhiravan Tamilarasu, Miglani Sunita, Sinha Sanjeev, Wig Naveet, Biswasa Ashutosh, Vajpayee Madhu. Outcomes of antiretroviral therapy in a northern Indian urban Clinic. *Bull World Health Organ.* 88, 2010:222-226 doi:10.2471/BLT.09.068759
3. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, Aschman DJ, Holmberg SD

Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection: HIV Outpatient Study Investigators. *N Engl J Med.*; 338(13), 1998 Mar 26:853-60. PMID: 9516219 Abstract Accessed on 21.10.2010

4. Mocroft A, Vella S, Benfield TL, Chiesi A, Miller V, Gargalianos P, d'Arminio Monforte A, Yust I, Bruun JN, Phillips AN, Lundgren JD. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group, *Lancet.* 352(9142), 1998 Nov 28:1725-30. PMID: 9848347 Abstract accessed on 21.10.10
5. Severe P, Leger P, Charles M, Noel F, Bonhomme G, Bois G, George E, Kenel-Pierre S, Wright PF, Gulick R, Johnson WD Jr, Pape JW, Fitzgerald DW. Antiretroviral therapy in a thousand patients with AIDS in Haiti. *N Engl J Med.* 353(22), 2005 Dec 1:2325-34. PMID: 16319381 Abstract accessed on 21.10.10
6. Stringer JS, Zulu I, Levy J, Stringer EM, Mwango A, Chi BH, et al. Rapid scale-up of antiretroviral therapy at primary care sites in Zambia: feasibility and early outcomes. *JAMA.* 296, 2006:782-93. doi:10.1001/jama.296.7.782 PMID: 16905784 Accessed on 21.10.2010
7. Herman JS, Easterbrook PJ. The metabolic toxicities of antiretroviral therapy. *Int J STD AIDS.* 12(9), 2001 Sep:555-62; quiz 563-4. PMID: 11516363 Accessed on 25.10.2010
8. Heath KV, Montaner JS, Bondy G, Singer J, O'Shaughnessy MV, Hogg RS. Emerging drug toxicities of highly active antiretroviral therapy for human immunodeficiency virus (HIV) infection. *Curr Drug Targets.* 4(1), 2003 Jan:13-22. PMID: 12528986 Accessed on 25.10.10
9. Roca B. *Front Biosci.* Adverse drug reactions to antiretroviral medication. 14, 2009 Jan 1:1785-92. PMID:19273162
10. Marfatia YS, Makrandi Smita. Adverse drug reaction (ADR) due to Antiretrovirals (ARV):Issues and challenges. *Indian J Sex Transm Dis.* Vol. 26 No. 1, 2 2005. Accessed on 21.10.2010
11. Nihalani Umesh, Shah Asha, Kavina Burzin, Amin Bipin, Derasari Urvi, Purohit Hemang, Mankad Bankim, Prajapati Sanjeev, Prajapati Girish and Shevkani Manoj. NRTIs (ZDV and d4T) side effects in PLHAs attending the antiretroviral treatment centre of B. J. Medical College Aad Civil Hospital At Ahmedabad, Gujarat, India: Poster presentation accessed on 19.10.2010
12. Guna S.r.l., Via Palmanova 71. Homoeopathy: the scientific proofs of efficacy: [http://www.atms.com.au/homeopathy/Homeopathy 20the%20scientific%20proofs%20of%20efficacy.pdf](http://www.atms.com.au/homeopathy/Homeopathy%20the%20scientific%20proofs%20of%20efficacy.pdf) ISBN 88-85076-40-8 Publisher, Milan, Italy. Accessed on 05.02.2008

accessed on 05.02.2008

FitH Accessed on 18.01.2011

13. Irwin MKS, MBCHB, DIP OBS, MFHOM. Acquired immunodeficiency syndrome: Is *Phytolacca Americana* homoeopathic to the acquired immunodeficiency syndrome?, *The British Homoeopathic Journal*. Vol.77, October 1988:219-223.
14. Finnegan MJB, BA, MB, BCH. MFHOM. Cyclosporin: Similimum for AIDS? *The British Homoeopathic Journal* Vol.77, October 1988:215-218.
15. Dana Ullman. M.P.H. Controlled Clinical Trials Evaluating the Homeopathic Treatment of People with Human Immunodeficiency Virus or Acquired Immune Deficiency Syndrome. *The Journal of Alternative and Complementary Medicine*. Volume 9, Number 1, 2003:133-141. Accessed on 19.11.2007
16. Maria Da Gracas da Mota Silvera Sasaki, Professor of Community Health Department, Infectology Service of Clinicas Hospital of the Federal University of Parana. Randomized Placebo Controlled Clinical trial to apprise the effectiveness and safety of Immunomodulator Canova® in the therapeutics of patients who have HIV/AIDS on antiretroviral use; 2001.
17. Rastogi DP, Singh VP, Singh V, Dey SK and Rao K. Homeopathy in HIV infection: a trial report of double blind placebo controlled study. *British Homeopathic Journal*. 88, 1999:49-57.
18. HIV transmission in intimate partner relationships in India; UNAIDS November 2009 : URL available at [http://www.unaids.org.in/Publications\\_HIV\\_Transmission\\_Intimate\\_Partner\\_Relationships\\_In\\_India.pdf](http://www.unaids.org.in/Publications_HIV_Transmission_Intimate_Partner_Relationships_In_India.pdf) Accessed on 20.01.2011
19. Country progress report 2010, UNGASS, India. [http://www.unaids.org/es/dataanalysis/monitoring\\_countryprogress/2010progressreportsubmittedbycountries/file,33667,es.pdf](http://www.unaids.org/es/dataanalysis/monitoring_countryprogress/2010progressreportsubmittedbycountries/file,33667,es.pdf) Accessed on 10.01.2011
20. Gab Jung Kim, Hak Sung Lee, Kee-Jong Hong, Sung Soon Kim. Dynamic correlation between CTL response and viral load in primary human immunodeficiency virus-1 infected Koreans. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2949841/pdf/1743-422X-7-239.pdf> Accessed on 11.1.11.
21. Bhatt NB, Gudo ES, Semá C, Bila D, Mattei P Di, Augusto O, Garsia R, Jani I. Loss of correlation between HIV viral load and CD4+ T-cell counts in HIV/HTLV-1 co-infection in treatment naïve Mozambican patients. Accessed on 29.09.2010
22. Jones Clara Y, Hogan Joseph W, Snyder Brad, Klein Robert S, Rompalo Anne, Schuman Paula, and Carpenter Charles C. Overweight and Human Immunodeficiency Virus (HIV) Progression in Women: Associations HIV Disease Progression and Changes in Body Mass Index in Women in the HIV Epidemiology Research Study Cohort : [http://cid.oxfordjournals.org/content/37/Supplement\\_2/S69.full.pdf#page=1&view=](http://cid.oxfordjournals.org/content/37/Supplement_2/S69.full.pdf#page=1&view=)
23. Christian Erikstrup, Per Kallestrup, Rutendo Zinyama, Exnevia Gomo, MSc, PhD, Boniface Mudenge, Jan Gerstoft, Henrik Ullum. Predictors of Mortality in a Cohort of HIV-1-Infected Adults in Rural Africa. *Journal of Acquired Immune Deficiency Syndrome*. 44, 2007:478. Accessed on 18.01.2011
24. Langford Simone E, Ananworanich Jintanat and Cooper David A. Predictors of disease progression in HIV infection: a review. *AIDS Research and Therapy*. 4, 2007:11, <http://www.aidsrestherapy.com/content/4/1/11>. Accessed on 18.01.2011
25. El-Khatib Z, Ekstrom AM, Ledwaba J, Mohapi L, Laher F, Karstaedt A, Charalambous S, Petzold M, Katzenstein D, Morris L. Viremia and drug resistance among HIV-1 patients on antiretroviral treatment: a cross-sectional study in Soweto, South Africa. *AIDS*; 24(11), 2010 Jul 17:1679-87.
26. Steegen K, Luchters S, Dauwe K, Reynaerts J, Mandaliya K, Jaoko W, Plum J, Temmerman M, Verhofstede C. Effectiveness of antiretroviral therapy and development of drug resistance in HIV-1 infected patients in Mombasa, Kenya. *AIDS Res Ther*. 6, 2009 Jun 16:12.
27. Pachamuthu B, Shanmugam S, Nagalingeswaran K, Solomon SS, Solomon S. HIV-1 drug resistance among untreated patients in India: Current Status. *J Postgrad Med*. Vol 52 Issue 3, September 2006 [PubMed ID : 16855318] Accessed on 06.01.2011.
28. U Shankarkumar, A Pawar, K Ghosh. HIV-1 evolution, drug resistance, and host genetics: The Indian scenario Virus Adaption and Treatment.1, 2009:1-4. Accessed on 13.01.2011 (*National Institute of Immunohaematology (ICMR), KEM Hospital, Parel, Mumbai, Maharashtra*)
29. Kandathil AJ, Kannangai R, Verghese VP, Pulimood SA, Rupali P, Sridharan G, Grant P, Pillai D, Abraham OC. Drug resistant mutations detected by genotypic drug resistance testing in patients failing therapy in clade C HIV-1 infected individuals from India. *Indian Journal of Medical Microbiology*. 27(3), 2009:231-6. Accessed on 13.01.2011.