AN INTERVENTIONAL STUDY OF HEALTH RELATED QUALITY OF LIFE OF PEOPLE LIVING WITH HIV/AIDS BEFORE AND AFTER ANTIRETROVIRAL THERAPY FOR THREE MONTHS AT GOVERNMENT HOSPITAL OF THORACIC MEDICINE, TAMBARAM, CHENNAI.

Dissertation Submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfillment of the regulations

for the award of the degree of

M.D. (Community Medicine)
BRANCH – XV

MADRAS MEDICAL COLLEGE
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.

MARCH 2007

CERTIFICATE

This is to certify that the dissertation entitled "**AN INTERVENTIONAL STUDY OF HEALTH RELATED QUALITY OF LIFE OF PEOPLE LIVING WITH HIV/AIDS BEFORE AND AFTER ANTIRETROVIRAL THERAPY FOR THREE MONTHS AT GOVERNMENT HOSPITAL OF THORACIC MEDICINE, TAMBARAM, CHENNAI"** is the bonafide original work of **Dr. PRIYA SENTHILKUMAR** in partial fulfillment of the requirements for **M.D. (Community Medicine) BRANCH – XV** examination of the Tamilnadu Dr. M.G.R. Medical University to be held in March 2007.

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DECLARATION

I, **Dr. PRIYA SENTHILKUMAR** solemnly declare that dissertation titled, "**AN INTERVENTIONAL STUDY OF HEALTH RELATED QUALITY OF LIFE OF PEOPLE LIVING WITH HIV/AIDS BEFORE AND AFTER ANTIRETROVIRAL THERAPY FOR THREE MONTHS AT GOVERNMENT HOSPITAL OF THORACIC MEDICINE, TAMBARAM, CHENNAI"** is a bonafide work done by me at Madras Medical College during 2004-2007 under the guidance and supervision of **Dr. K. MARY RAMOLA, M.D.,** Department of Community Medicine, Madras Medical College, Chennai-600 003.

The dissertation is submitted to Tamilnadu, Dr. M.G.R. Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (BRANCH – XV) in Community Medicine.**

Place : Chennai.

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ACKNOWLEDGEMENT

I express my profound gratitude to **Dr. KALAVATHY PONNIRAIVAN, M.D.,** The Dean of Madras Medical College, Chennai-600 003 for permitting me to use all the needed resources for this dissertation work.

I sincerely express my grateful thanks to **Dr. K. MARY RAMOLA,** Director i/c, Academics, Institute of Community Medicine, Madras Medical College for her unstinted support and advice rendered throughout my study.

It is with a deep sense of gratitude that I acknowledge my profound indebtedness to **Dr. A.K. RAJENDRAN, M.D.,** Professor of Community Medicine, Chengalpet Medical College for his valuable guidance.

I sincerely thank **Dr. S. RAJASEKARAN, M.D., D.T.C.D.,** for the inspiration and encouragement he has provided.

I express my sincere thanks to the Assistant Professors **Dr. R. NAGARANI, M.D., and Dr. ARUNMOZHI, M.D.,** for their co-operation and kind help.

I express my thanks to **Mr. A. VENKATESAN**, Lecturer in Statistics, Institute of Social Paediatrics, Stanley Medical College, Chennai for providing statistical software support.

Above all I thank my husband **Dr. T. SENTHIL KUMAR, Fellow in HIV / AIDS** without whom I would not have been able to accomplish this.

CONTENTS

LIST OF ABBREVIATION

1)	3TC	:	Lamivudine
2)	ABC	:	Abacavir
3)	AIDS	:	Acquired Immune Deficiency Syndrome
4)	ART	:	Anti Retroviral Therapy
5)	ATT	:	Anti-Tuberculosis Treatment
6)	AZT	:	Zidovudine
7)	CDC	:	Centre For Disease Control
8)	D4T	:	Stavudine
9)	EFV	:	Efavirenz
10)	HIV	:	Human Immune Deficiency Virus
11)	HRQOL	:	Health Related Quality of Life
12)	NACO	:	National AIDS Control Organization
13)	NACP	:	National AIDS Control Programme
14)	NVP	:	Nevirapine
15)	PI	:	Protease Inhibitors.
16)	PLHA	:	People Living with HIV / AIDS
17)	PPTCT	:	Prevention of Parent to Child Transmission
18)	QOL	:	Quality Of Life
19)	SACS	:	State AIDS Control Society
20)	TDF	:	Tenofovir
21)	WHO	:	World Health Organization

INTRODUCTION

HIV / AIDS in India is moving from high risk groups to the more vulnerable segments among the general population. There are an estimated 5.7 million HIV positive cases in 2005[1].

Political commitment has shifted significantly in favour of providing access to antiretroviral therapy for people living with HIV / AIDS. Treatment is now perceived as a critical component of a comprehensive programme to combat HIV / AIDS, along with prevention and the improvement of health care infrastructure for the delivery and monitoring of care and support.

'The Call to Action' at the UN general assembly special session on HIV / AIDS pushed forward s new global consensus on the need for Antiretroviral Therapy. World Health Organization released guidelines for antiretroviral use in resource constrained settings in April 2002 and added 10 ART drugs to its list of essential medicines for all countries. WHO declared the lack of access to ARV treatment for HIV / AIDS a 'Global Health Emergency' in September 2003 and announced that it would release an emergency plan to scale up access to ARV treatment for atleast three million people by the end of 2005 (popularly known as the 3 by 5 initiative).

Role of Antiretroviral Therapy:

ART is no cure for HIV / AIDS. Effective antiretroviral regimens inhibit the efficient replication of the HIV virus and reduces viraemia to undetectable levels. Lower frequency of opportunistic infections significantly reduces the cost of management of HIV. This helps people to lead more productive lives, with perceptibly reduced stigma and discrimination. Success achieved in terms of ART delaying the onset of AIDS has now transformed the common perception about HIV from being an immediately fatal source to a some what more manageable, chronic illness, although devastatingly debilitating in the long run.

JUSTIFICATION

HIV / AIDS is an infectious disease that is also considered to be chronic disorder. The health related quality of life or health status has become an important consideration in the treatment of patients with chronic disorders. The purpose of medical intervention for chronic diseases is defined as improvement in both the quantity and quality of life. The former corresponds to an improvement in mortality, where as the latter indicates improvement in the (HRQOL) Health related quality of life. The importance of HRQOL as a health index especially in the evaluation of health care services for the treatment of chronic disorders, has long been emphasized. However, there have been few reports examining the HRQOL in AIDS patients.

Anti-retroviral increase the AIDS - free time, delay and decrease opportunistic infections but may have intolerable side effects and the effect of anti-retroviral on long-term survival is unclear. So it would be just to examine the quality of life of patients on anti-retroviral therapy and compare it with their pre ART quality of life.

REVIEW OF LITERATURE

MILE STONES:

1981- Acquired immunodeficiency syndrome (AIDS) was first recognized as a new disease in the United States when clinicians in New York, Los Angeles, and San Francisco began to see young, homosexual men with Pneumocystis carinii pneumonia (PCP) and Kaposi's sarcoma (KS), unusual diseases for young adults not known to be immunosuppressed. The first report in the medical literature that alerted the world to this new immunodeficiency syndrome appeared in June of 1981 and described five young, homosexual men in Los Angeles with PCP[2].

1983- Human Immunodeficiency Virus (HIV) was first isolated in France in 1983 by Françoise Barré-Sinoussi in the laboratory of Luc Montaignier as lymphadenopathy-associated virus (LAV)[3].

1984- The virus was also isolated in San Francisco in 1984 by Jay Levy and named it AIDS Associated retrovirus[4].

1986 - First case of HIV infection was detected in India among commercial sex workers in Madras.

1986- Discovery of HIV – 2 virus in West Africa by Montaignier's group [5].

1986- National AIDS Committee was formed to guide and advice the Govt. of India in Prevention and Control of HIV/AIDS.

1987- National AIDS Control Programme (NACP) was launched.

1992- National AIDS Control Organisation (NACO) was setup as a semi- autonomous body by the Govt. of India.

1992- Launching of NACP Phase I (1992-1999) with following objectives:

1. Involve all States and Union Territories in developing HIV/AIDS preventive activities with a special focus on the major epicenters of the epidemic.

2. Attain a satisfactory level of public awareness on HIV transmission and prevention.

3. Develop health promotion interventions among risk behaviour groups.

4. Screen all blood units collected for blood transfusions.

5. Decrease the practice of professional blood donations.

6. Develop skills in clinical management, health education and counselling, and psychosocial support to HIV seropositive persons, AIDS patients and their associates.

7. Strengthen and control of Sexually Transmitted Diseases (STD) and

8. Monitor the development of the HIV/AIDS epidemic in the country.

1999- Launching of NACP Phase II (1999-2006) with the following objectives:

1. To shift the focus from raising awareness to changing behaviour through interventions, particularly for groups at high risk of contracting and spreading HIV.

2. To support decentralization of service delivery to the State and Municipalities and a new facilitating role for National AIDS Control Organization. Program delivery would be flexible, evidence-based, participatory and to rely on local programme implementation plans.

3. To protect human rights by encouraging voluntary counseling and testing and discouraging mandatory testing.

4. To support structured and evidence-based annual reviews and ongoing operational research, and

5. To encourage management reforms, such as better managed State level AIDS Control Societies and improved drug and equipment procurement practices. These reforms are proposed with a view to bring about a sense of 'ownership' of the programme among the States,

Municipal Corporations, NGOs and other implementing agencies.

2003- The "3 by 5" initiative, launched by UNAIDS and WHO in 2003, was a global TARGET to provide three million people living with HIV/AIDS in low- and middle-income countries with life-prolonging antiretroviral treatment (ART) by the end of 2005. It was a step towards the GOAL of making universal access of HIV/AIDS prevention and treatment accessible for all who need them as a human right.

2004- The government on the eve of the World AIDS Day, 2003, announced its programme for free distribution of ARVs in selected states. In June 2004, the Global Fund on AIDS, TB and Malaria awarded a financial grant of US $ 165 million to provide ART in the public sector and through public-private partnershipsfor 1,00,000 people living with AIDS over a five year period.

2006- NACP Phase III(2006-2011). The overall goal of NACP III is to halt and reverse the epidemic in India over the next 5 years by integrating programmes for prevention,

care, support and treatment. This will be achieved through four strategic objectives namely:

1. Prevention of new infections in high risk groups and general population through:

a. Saturation of coverage of high risk groups with targeted interventions (TIs)

b. Scaled up interventions in the general population

2. Increasing the proportion of people living with HIV/AIDS who receive care, support and treatment.

3. Strengthening the infrastructure, systems and human resources in prevention and treatment programmes at the district, state and national levels.

4. Strengthening a nation-wide strategic information management system.

BURDEN OF THE DISEASE:

There are an estimated 38.6 million people living with HIV world wide – 4.1 million newly infected in 2005, 2.8 million died of AIDS in 2005[1].

In India the estimated number of cases is 5.7 million HIV cases and 2.7 to 6.8 lakh deaths (2005) due to AIDS.

The national adult prevalence is 0.8 % of the 35 states of India 6 states, four in southern India (Andhra Pradesh, Tamil Nadu, Maharastra, Karnataka) and two in north eastern India (Manipur and Nagaland) have generalized epidemic with HIV prevalence rate of above 1% among pregnant women[1].

The prevalence in Tamil Nadu has dropped to below 1 % (2005 sentinel surveillance report NACO). These six states account for nearly 80 % of all reported AIDS cases in the country.

India has a large number of people living with HIV/AIDS, second to South Africa.

NATURAL HISTORY OF THE DISEASE:

The natural history of any disease refers to the stages through which a disease passes, in the absence of any intervention. Clear knowledge of natural history of a disease helps in identifying the stages at which appropriate intervention for prevention or control of the disease can be undertaken.

Pre-pathogenesis period

The Agent

Human Immune deficiency Virus (HIV)

- HIV belongs to the family of retro viruses
- There are two types of HIV virus: Type 1 and Type 2
- Both types are prevalent in India, Type 1 is more frequently reported.
- HIV Type 1 is a more virulent pathogen than type 2.
- HIV type 2 is generally milder, slower to progress and poorly transmitted vertically.
- Virus is found in almost all body fluids and organs.

- But they are present in very large numbers in semen, vaginal and cervical secretions and blood.
- The central nervous system, testes, lymph nodes act as reservoirs of HIV.
- The highest concentration of HIV among the body fluids is found in cerebrospinal fluid.

HOST FACTORS

AGE AND SEX

The spread of HIV infection occurs most frequently in the sexually active and economically productive age group of 15 to 44 years. Globally during 2004 the male to female ratio is nearing equal. In India according to NACO, however, the male to female ratio is 3:1. APAC sponsored community prevalence study in Tamil Nadu during 1998 shows the HIV infected cases between males and females to be equal.

Factors involved in the risk of acquisition of infection

- Number of sexual partners
- Frequency of "at risk" sexual exposures
- Local HIV prevalence rates among core groups and bridge population, etc.

- Consistent use of condoms
- Presence of sexually transmitted diseases in any of the partners.

High-risk behaviors

Based on the epidemiological characteristics of HIV infection, certain high-risk behavior groups, who are likely to be harboring infection more frequently than the general population, have been identified.

- People with multiple sex partners (Commercial sex workers, men who are away from their families for long periods, as they are likely to have extra marital sex) and homosexuals.
- Injecting drug users, because they share needles and syringes.
- People requiring frequent transfusions of blood e.g. hemophiliacs, thalassemics etc.

Transmission routes

1. **Sexual Transmission**

   The current worldwide expansion of AIDS epidemic is primiarily driven by sexual transmission of HIV-1. In the most populous regions of the world, sexual transmission among hetro sexuals is the dominant mode of spread[6] sexual transmission among homosexual men is still a significant part of epidemic spread in United States and Europe[7].

2. **Injection Drug Usage**

HIV could be isolated from blood – contaminated needles, syringes and injection paraphernalia which provides a biologic rationale for HIV transmission among IDU[8]. This is an important route of transmission in North Eastern States of India.

3. **Transmission by Blood, Blood Products, Tissue Transplantation and Artificial Insemination.**

Transmission of HIV-1 can occur following transfusion of a blood product derived from an infected person's blood and processed into a blood component (i.e. whole blood, packed cells, fresh frozen plasma, cryoprecipitate and platelets[9].

4. **From infected mother to her baby**

Transmission from infected pregnant mother to the baby mainly during the perinatal period and through breast milk.

5. **Needle stick exposure**

Accidental exposure in health care settings or in procedures like tattooing etc., Needle stick / sharp injuries are a comparatively rare mode of transmission. There are only few such cases reported in the world despite the fact that millions of health care workers are knowingly or unknowingly handling HIV infected individuals. Despite

such a low risk, the unrealistic fear remains as a major hurdle in extending health care to the HIV infected individuals. The risk depends upon the concentration of virus in those body fluids, the depth of injury, the type of needle (with solid or hollow bore) Immunogenic status of the patient and the precautions followed thereafter.

EFFICACY OF VARIOUS MODES OF TRANSMISSION

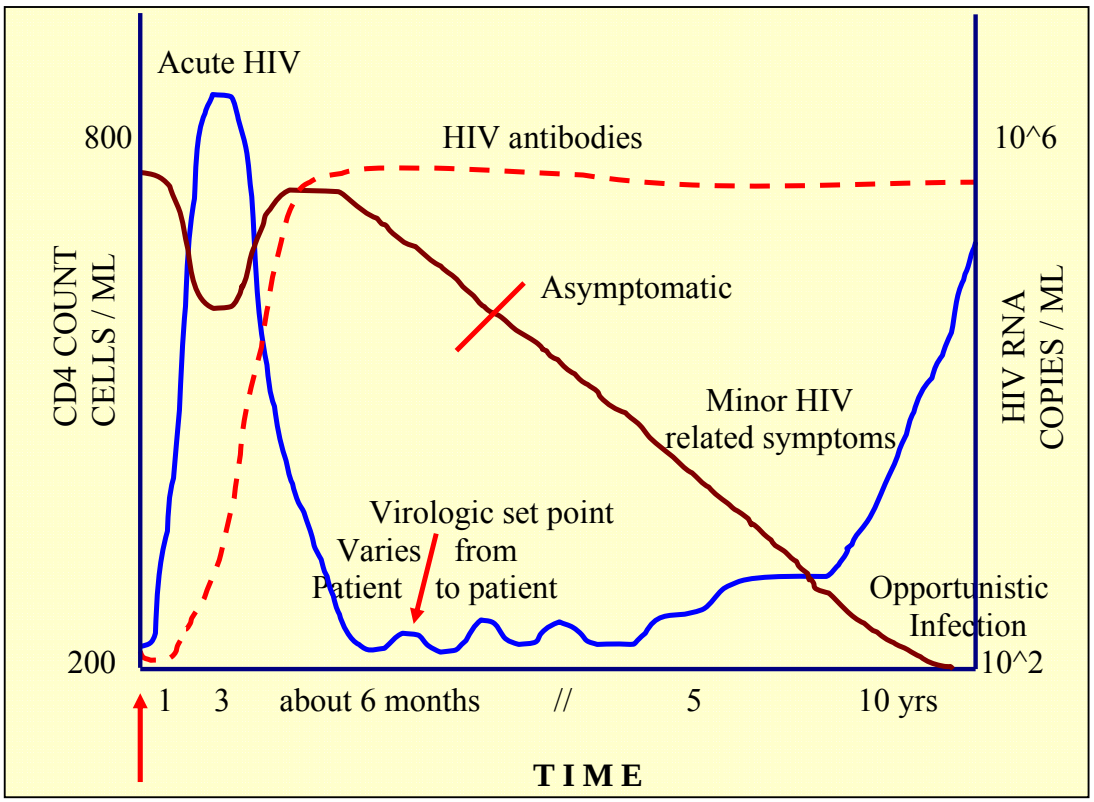
Sl. No.	Modes of transmission	Efficacy	Source of infection
1	Sexual intercourse	0.1 – 1.0%	80 - 86%
2	Blood transfusion	90 – 95%	3 – 5%
3	Perinatal	20 – 40%	2 – 3%
4	Injecting drug use	0.5 – 1.0%	3 – 5%
5	Needle stick exposure	Less than 0.1%	

Pathogenesis

The natural history of HIV infection begins as soon as virus enters the body of a susceptible host through any of the routes of transmission as discussed earlier (sexual, parenteral and perinatal)

- HIV infects predominantly T helper (CD4) Lymphocyte
- As the numbers and functions of CD4 cells decline, immune deficiency sets in

- As immune deficiency progresses, the subject develops secondary (opportunistic) infections and malignancies and further constitutional signs and symptoms of the diseases contracted
- 5-10% of HIV individuals are long-term non-progressor and live for more than 10 years.



TYPICAL COURSE OF HIV INFECTION IN AN UNTREATED PERSON

Upto three months of HIV infection, there is often an asymptomatic viraemia, during which period although patients are infective, ELISA test for HIV antibodies are negative. Progression to symptomatic disease i.e., the amount of time it takes from HIV infection to become full blown AIDS depends on the general health and nutritional status before and during the time of HIV infection [10].

WINDOW PERIOD

Lasts for 6 weeks to 12 weeks

HIV antibodies reach a high titer approximately 3 months after the virus has entered the body. If the tests like RAPID test, ELISA & Western Blot are performed within three months, they may be reported as negative. This is known as the window period. However the patient will be in a carrier state transmitting the disease to others by all routes mentioned.

CD4 COUNT AND VIRAL LOAD:

Depletion of CD4+ T lymphocytes is the hall-mark and the apparent source of the central immune defect of HIV disease, determination of the CD4 lymphocyte count (or percentage) has been the most important laboratory marker of disease progression. Absolute

CD4 lymphocyte count or percentage correlates strongly with AIDS – defining disease, has been included in the surveillance case definition of AIDS since 1993, and has been used to set indications for therapy. The CD4 lymphocyte count declines from a normal value of around 1,000 cells to an AIDS-defining level of 200/μL over a mean of about 8 to 9 years in a young adult, but there is a great deal of individual variability in this general pattern.

The measurement of the number of viral copies per milliliter of peripheral blood (commonly known as "viral load") has been made possible by the development of sensitive assays using polymerase chain reaction or nucleic acid sequence – based amplification of the viral source or branched DNA amplification of the signal that can detect virus down to a few hundred copies per milliliter in the most commonly used tests and down to a few copies per milliliter in the latest ultrasensitive tests. I was known from earlier viral detection tests, such as assays for p24 antigen and quantitative assays for the antibodies to the p24 antigen, that measures of viral activity were strong predictors of AIDS in asymptomatic HIV-infected persons independent of the CD4 lymphocyte count[11,12]. The newer measures of viral quantity are even stronger predictors of disease and provide a clinically useful range of values that can monitor the effectiveness of antiviral therapies in

controlling viral replication. Their prognostic usefulness has been demonstrated in prospective studies by associating levels of viral quantity in peripheral blood and changes in viral quantity with subsequent development of AIDS and death[13]. The association has been shown in both recent seroconverters and asymptomatic HIV-infected persons and in subjects from different HIV transmission groups[14]. Plasma HIV RNA levels are orders of magnitude lower in long-term non-progressors than in subjects with progressive disease. Undetectable HIV RNA in peripheral blood is associated with stable CD4 lymphocyte counts and increases in HIV RNA correlate with rate of CD4 lymphocyte cell decline[14,15]. Peripheral blood viral load is changed by anti-retroviral therapy, often dropping below the level of assay detection in persons who begin receiving combination therapy[16].

WHO CLINICAL STAGING[17] :

Clinical stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical stage 2

- Unexplained moderate weight loss (<10% of presumed or measured body weight)
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical stage 3

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for longer than one month

- Unexplained persistent fever (above 37.5^{o}C intermittent or constant for longer than one month
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia,)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8 g/dl *)*, neutropenia (<0.5 x 10^{9} /L) and or chronic thrombocytopenia (<50 X 10^{9} /L^{3})

Clinical stage 4

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)

- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis

ANTI-RETROVIRALS

The advent of ART in the late 1980's began a revolution to change HIV from being a killer disease to one of manageable chronic illness. The primary aim of ART strategies is to suppress viral replication. Successful viral suppression restores the immune system, slows or halts disease progression and improves quality of life. Studies

in Brazil have shown that there is an improvement in AIDS related mortality and morbidity due to universl accesses of ART in Brazil. Quality of life in individuals receiving Anti-retroviral therapy is related to adherence[18].

Adherence is a major factor which can determine the success of ART programme as well as to prevent development of HIV drug resistance. Adherence is necessary to ensure sustained viral suppression on the available first line regimen, because when resistance occurs treatment becomes increasingly complicated and costly.

The Government of India launched a free ART programme on 1st April 2004 and has since adopted the public health approach to administration and distribution of ART[17]. Section of first line regimen is determined on the basis of a number of considerations such as potency, profile of side effects, ability to keep future treatment options open, ease of adherence, cost, risk during pregnancy and potential of resistant viral strains. The current global recommendation in all circumstances is a trifle drug regimen[19].

KEY GOALS OF THE NATIONAL CARE AND TREATMENT PROGRAMMES:

- To provide long term ARV Therapy to eligible patients
- To monitor and report treatment outcome

- To attain individual drug adherence rates of 95% and more
- To increase the lifespan and quality of life of PLHAS.

Eligibility for ART:

The national programme offers antiretroviral therapy to following group of people:

- All persons with HIV infection who are clinically eligible to receive ART
- Those who are already on ART (outside the national programme) and want to get enrolled into the National ART programme according to the available national ART regimens after written informed consent

Strengthening of linkages and referrals with the Prevention of Parent to Child Transmission (PPTCT) programme will be done in order to expand treatment access to women as well as children living with HIV/AIDS. The national programme will link with other programmes such as the Revised National TB Control Programme (RNTCP), Reproductive and Child Health (RCH), National Rural Health Mission (NRHM) and others.

Goals of Therapy

- **Clinical Goals:** Prolongation of life and improvement in quality of life.
- **Virologic Goals:** Greatest possible reduction in viral load for as long as possible.
- **Immunologic Goals:** Immune reconstitution that is both quantitative and qualitative.
- **Therapeutic Goals:** Rational sequencing of drugs in a fashion that achieves clinical, virologic and immunologic goals while maintaining treatment options, limit drug toxicity and facilitate adherence.
- **Epidemiologic Goals:** Reduce HIV transmission.

When to start antiretroviral therapy in adults and adolescents[17]

All persons registered for care and treatment at the ART centers should have a full history and clinical examination which include clinical staging. The principle for initiation of ART is based on clinical staging with CD4 to guide treatment and follow-up. Lack of a CD4 result should not delay initiation of ART if the patient is medically eligible for this, but a CD4 test should be done as soon as possible.

The following group of persons will undergo a CD4 test to screen for ART eligibility[17]:

- All positive persons with WHO clinical stages 3 and 4.
- All persons tested HIV positive 6-8 years ago
- PLHAs with history of pulmonary TB and/or herpes zoster in the past.
- If CD4 has been done from private lab and is less than 350 cells/mm^3
- HIV infected partners of AIDS patients
- All pregnant HIV-positive women
- All HIV positive children (< 15 years old)

WHO Clinical classification of established HIV infection[17]

HIV associated symptomatology	WHO clinical stage	Treatment Guideline
Asymptomatic	1	CD4 guided
Mild symptoms	2	CD4 guided
Advanced symptoms	3	CD4 guided
Severe/advanced symptoms	4	Treat irrespective of CD4

Treatment Guideline as per CD4 Count[17]

CD4 (cell /mm3)	Actions
< 200	Treat irrespective of clinical stage
200 – 350	Offer ART for symptomatic patients **Initiate before drop below 200 cells/mm^{3*}**
>350	Defer treatment in asymptomatic persons

***** If CD4 is between 200-250, this should be repeated in 4 weeks and treatment to be considered in asymptomatic patients. Current global evidence and WHO guidelines recommend that patients be initiated on ART before CD4 drops below 200 cells/mm$^{3.}$

What to start:

Currently, the national programme will make a limited number of first line regimen combinations available. Drug combinations available under the National Programme are:

(i) Stavudine(30mg)+Lamivudine(150mg)+ Nevirapine(200 mg)

(ii) Stavudine(40 mg)+Lamivudine(150mg)+ Nevirapine(200 mg)

(iii) Zidovudine(300mg)+Lamivudine(150mg)+ Nevirapine(200 mg)

(iv) Stavudine(30 mg) + Lamivudine(150mg)

(v) Stavudine(40 mg) + Lamivudine(150mg)

(vi) Zidovudine (300mg) + Lamivudine(150mg)

(vii) Efavirenz (600mg)

(viii) Nevirapine (200 mg)

Fixed dosed combinations (FDCs) are preferred because they are easy to use, have distribution advantages (procurement and stock management), improves adherence of intake of ARVs and thus reduces the changes of development of HIV drug resistance. Current national experience showed that BID (twice a day) regimens with FDCs are well tolerated and complied with.

The first-line ART regimens recommended under the national programme are:

AZT (Zidovudine)		Nevirapine (NVP)
Or	+ Lamivudine (3TC) +	Or
D4T (stavudine)		Efavirenz (EFV)

The recommended choices of first line regimens should be given in the following priority[17]:

a. **AZT + 3TC + NVP/EFV** (for patients with Hb > 8 g/dl) for (60% of total patients)

b. **d4T + 3TC + NVP/EFV** (for 40% of total patients)

c. **TDF + 3TC + NVP/EFV.** This combination is for special situations only when there is toxicity/other contraindications to AZT or d4T. This combination will be provided on a case-to-case basis at SACS level for a limited number of patients. This will be decided by an

expert panel at SACS consisting of two physicians with experience in ART, one SACS representative and one INP representative. (To be discussed with DG)

Efavirenz (EFV) should be given to following group of persons:

a. PLHA receiving concurrent anti-tuberculous drugs (ATT) for the duration of the anti-TB treatment
b. Where there is clinical or laboratory evidence of hepatic dysfunction eg. due to hepatitis B/C co-infection or other causes

EFV is contraindicated in pregnant HIV – infected women during the first trimester of pregnancy because of concerns of teratogenicity.

CLINICAL AND LABORATORY MONITORING[17]

With the advent of scaling up of treatment nationally as well as increased awareness of HIV and access to counseling and testing services, it is envisioned that there would be an increase in PLHAs not requiring ART as many more would have presented in an earlier stages of disease. Experience of current ART centers showed that there is a need to emphasize good HIV (pre-ART) care and support so as to maintain wellbeing.

a) **Pre-ART care:** is defined as the period where a HIV positive person is well and does not medically require initiation of ART. It is expected that with the scaling up of the national programme and

numbers of Counseling and testing centers, the shift from AIDS patients to HIV persons will occur. For PLHAs who do not need ART, they should be advised and counseled to maintain healthy/ positive living.

In order to follow up and monitor these patients such that early detection of opportunistic infections (OIs) and initiation of ART before the CD4 declines to below 200 cells, the following is recommended as routine monitoring of patients who are not yet eligible for ART:

1. Comprehensive clinical evaluation:
2. Laboratory work up of pre- ART care patients:
    - HIV-infected persons should have a baseline screening CD4 where possible.
    - Laboratory work-up:
        i. Mandatory: CBC, ALT/AST, ALP, serum creatinine, CXR, VDRL/TPHA; urinalysis
        ii. For women: PAP smear screening annually or acetic acid cervical screening at district healthcare facilities
        iii. Screen HBsAg and HCV for IDUs/ transfusion-associated infections or those with liver enzyme elevations
        iv. Attention should be given to screen TB

Services to be offered for pre-ART Care patients should include family screening and counseling of partners and children as well as follow-up of discordant couples, support, linkages, tracing defaulters etc.

These patients should be registered in the NACO Pre-ART Register .

b) Routine Monitoring of patients on ART

a) Recommendations on the follow up and monitoring schedule for patients on ART in the national programme:

Monitoring and follow up schedule for patients on ART[17]

	Day 0 (baseline)	**At 15 days**	**At 1 month**	**At 2 month**	**At 3 month**	**At 6 month**
Clinical and adherence counseling	X	X	X	X	X	X
Hb	X	X (if on AZT)	X (if on AZT)		X	X
ALT	X	X (in on NVP)	X (if on NVP)		X *	X*
Urinalysis	X					X (if on TDF)
Lipid profile	X (if on EFV and PI)					X (if on d4T, EFV or PI)
Random Blood sugar	X					X (if on PI)

Pregnancy testing for women with pregnancy potential (if planning for EFV)

* For HBV and/or HCV co-infected patients, 3-monthly screening of liver function is recommended.

FOLLOW UP OF CD4 SCHEDULE

CD4 count	Repeat CD4 every
< 350	3 months
> 350	6 months
on ART	6 months
> 500	For operational research or consider suggesting annually which allows for recording a steep decline in some cases

- If CD4 between 200 to 250, the repeat in 4 weeks and consider treatment

Once a patient is on an effective and stable regimen at 6 months, quarterly follow up is recommended where adherence is reasonably ascertained.

b) Clinical follow up of patients on ART : follow with high index of clinical suspicion to Screening new opportunistic infections (OI) and adverse drug reactions appropriate to the regimen given.

Major toxicities of first line ARV regimens and drug substitutions

Regimen	Toxicity	Drug Substitution
D4T/3TC/NVP	• d4T – related neuropathy or pancreatitis • d4T –related lipoatrophy • NVP –related severe hepatotoxicity • NVP – related severe rash (but not life threatening) • NVP –related life threatening rash (Stevens – Johnson syndrome)	• Switch d4T to ZDV • Switch d4T to TDF or ABC (if available) • Switch NVP to EFV (except in pregnancy) • Switch NVP to EFV • Switch NVP to PI
AZT/3TC/NVP	• ZDV –related persistent GI intolerance or severe haemtological toxicity • NVP –related severe hepatoxicity • NVP –related severe rash (but not life threatening) • NVP –related life threatening rash (Stevens - Johnson syndrome)	• Switch ZDV to d4T • Switch NVP to EFV (except in pregnancy. In this situation switch to NFV, LPV/r or ABC.) • Switch NVP to EFV • Switch NVP to PI
D4T/3TC/EFV	• d4T –related neuropathy or pancreatitis • d4T –related lipoatrophy • EFV –related persistent CNS toxicity	• Switch d4T to ZDV • Switch d4T to TDF or ABC • Switch EFV to NVP
AZT/3TC/EFV	• ZDV –related persistent GI intolerance or severe hematological toxicity • EFV – related persistent CNS toxicity	• Switch ZDV to d4T • Switch EFV to NVP

Note: Substituting D4T (ie. patient is off D4T) may not reverse lipodystrophy but may slow its progression. Besides AZT - TDF, ABC or ddI are acceptable alternatives but may not be available in the national programme.

ADHERENCE TO ANTIRETROVIRAL THERAPY[17]

Studies of drug adherence in the developed world have suggested that higher levels of drug adherence are associated with improved virological and clinical outcomes and that rates 95% are desirable to maximise the benefits of ART. It is a challenge to achieve rates this high over a long period of time. Interventions that improve treatment adherence and safe behaviour are:

(i) The decision to enroll a patient into the ART programme should be based on the patient's medical and psycho-social parameters.

(ii) Education and counseling: Once the person is enrolled in the ART programme, the physician and counselor should educate the persons about the possible side effects of drugs, follow-up dates and importance of adherence to ARV treatment and consequences of non-adherence. During every follow-up visit to ART clinic, the patient should also be asked to bring drugs along with him so that the pills can be counted in order to assess the level of adherence.

(iii) ART clinic counselors should maintain a register of all visits. During every visit the patient should be counselled on adherence of ARV treatment and in case of any side effects of drugs the patients should be referred to treating physician. Counselors

should be part of the training programme on ARV treatment and they should be trained properly in monitoring of adherence to ARV treatment. Counselor should also emphasize that ART is merely a treatment and not a cure and the need to practice safe sexual behaviour, with consistent condom use. It might be useful to ensure condom availability during every visit of the HIV/AIDS patients on ARV treatment.

(iv) Participation of Family Members / guardian: Patient should be motivated to bring a family member or guardian along at the time of commencing ARV treatment. The guardian should be educated about the illness and the need for lifelong treatment and adherence to drugs. They should be encouraged to accompany patients on the follow-up visit, if possible. All efforts should be made to encourage guardian supported ARV treatment so that the adherence of therapy could be ensured.

(v) Reminders in case of drop out: In case the patient does not visit the ARV treatment unit on the scheduled fixed date, NGOs/Networks of PLHAs should be involved to contact the patient or guardian in a confidential manner to mobilize the patient to continue treatment. The role of communities and NGOs in mobilizing communities to support adherence is

extremely important. Maintaining confidentiality and privacy are of utmost importance.

(vi) Involvement of Primary Health Care Systems: A patient residing in a rural area would find it difficult to re-visit the district hospital for follow-up.

(vii) Depending upon the patients attached to a PHC/CHC, ARV drugs should be made available by the district hospital. However, patient should be referred from PHC/CHC to district hospital once in six months for laboratory investigations and opinion of the treating physician.

(viii) Treatment adherence may be more difficult in pregnant women and in immediate post partum period. Pregnancy associated morning sickness and gastro-intestinal upset may complicate ART and this may be further complicated by side effects associated with ARV drugs. Family support would be essential for ensuring adherence to ARV treatment.

(ix) Treatment adherence in children is a special challenge, particularly if family unit is disrupted by health or economic conditions. As currently, pediatric formulations are not widely available for all ARV drugs, WHO recognizes that until appropriate formulations can be made more widely available, the

splitting of adult dose formulation of ARV drugs, should be considered

Key to successful adherence strategies is the proper education of the patient before the initiation of therapy, support ARV initiation as patient first starts medications and continuously monitor and support adherence. Reinforcement of adherence principles to the patient by treatment supporters (guardian), relatives, friends and community support personnel is of great help.

QUALITY OF LIFE:

Quality of life is a term that is popularly used to convey an overall sense of well being and includes aspects such as happiness and satisfaction with life as a whole[19].

World Health Organisation has defined QOL as individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, standards, expectations and concerns[20].

Health Related Quality of life (HR – QOL) refers to a patient's physical and mental well being over time. It is defendant on disease symptoms, treatment efficacy in relieving symptoms and treatment

related side effects[21]. The evaluation of HR-QOL originated with the European Organization for Research and Treatment of Cancer (EORTC) which designed instruments to assess patient well being during cancer clinical trials[22].

Assessment of QOL has been traditionally done in chronic diseases like cancer, diabetes, schizophrenia and in patients who have undergone surgeries. But in recent years, health relative QOL has been an important consideration in virtually all situations resulting in deviation from normal health including QOL assessment in HIV infected individuals. Studies have been carried out to see the effect of antiretroviral therapy particularly on the major changes in the life of HIV infected individuals who can now look forward to many more years in life[23]. But these extra years of life include a large pill burden, life style modification to accommodate the dosage schedules and to cope with various side effects[24]. All these factors make it necessary to evaluate quality of life of HIV infected individuals, which provides valuable insights into how the disease and treatment affect the patients.

Several instruments have been specifically developed to assess the QOL of people living with HIV and AIDS. Some of these includes Medical Outcome Questionnaire[25]. The AIDS Health Assessment

Questionnarie[26], the general health assessment[27] and the multidimensional quality of life questionnaire for HIV / AIDS[28].

In addition a number of generic instruments are also available like SF-36[29] the sickness impact profile[30] and the WHOQOL-100.

Studies have been conducted to validate the QOL instruments like MOS (HIV)[31], SF-36[29] and WHOQOL-HIV[31].

The WHOQOL-HIV was pilot tested among 900 persons from six culturally diverse centres (Australia, Brazil, Thailand, India (New Delhi and Bangalore) and Zimbabwe) Subsequently, this module was further field tested. Statistical analyses show that persons with HIV / AIDS should poorer quality of life.

Cross-cultural applicability of instruments is a major limitation for their widespread use. The WHOQOL is the only quality of life instrument that has been simultaneously developed in a wide range of cultures. It is a cross-cultural measure that may be particularly useful for measurement of quality of life across different areas[32,33]. The Hindi, Tamil and Kannada versions of WHOQOL-HIV Brief are available.

METHODOLOGY

STUDY DESIGN:

An interventional study design -"Before and After" Comparison study without control.

STUDY POPULATION:

People Living with HIV/AIDS attending Government Hospital of Thoracic Medicine, Tambaram, Chennai.

INCLUSION CRITERIA:

Adults above the age of 18 years, of both sexes, Tamil speaking, who have been screened and found fit to receive Antiretroviral therapy.

METHOD OF SCREENING FOR ART:

PLHAs who are in Clinical Stage IV disease and PLHA's whose partner is already receiving ART were counselled regarding ART and importance of adherence. If they are willing to take ART they are subjected to the following tests – CD4 count, Heamoglobin, HBsAg, LFT, RFT, X-Ray chest and Sputum for AFB.

If their CD4 count is <200, or >200 but <350 and clinically Stage IV and if LFT, RFT are within normal limits they are considered fit for Antiretroviral therapy. These patients are registered for ART.

SAMPLE SIZE CALCULATION:

Wig et al[34] have reported mean (SD) total score of quality of life as 48.83(11.18) .

Expecting a better quality of life after ART at the end of 3 months, that is, a change of minimum 7.5 units (increase) in the total score, with alpha and beta errors at 5 % and 10 % level respectively.

The required sample size will be:

$$N = \frac{2 \times SD^2 \times [Z_{(1-\alpha/2)} + Z_{(1-\beta)}]^2}{(\text{mean}1 - \text{mean}\ 2)^2}$$

Where SD is 12

mean 1 – mean 2 = 7.5

n = 54

Expecting a 10% drop out rate the sample to be studied will be 60.

SAMPLING TECHNIQUE:

Simple random sampling by lottery method at the rate of three persons per day of PLHA's who have been registered for ART till the required sample size was reached from 18.04.06 to 12.05.06. On an average 10 new cases are registered for ART every day.

METHOD:

After obtaining permission from the Director, Institute of Community Medicine, Madras Medical College, Chennai and from The Superintendent, Government Hospital of Thoracic Medicine, Tambaram, Chennai, the study was started.

The purpose of the study was explained, confidentiality was assured and oral consent obtained from the participants.

The pre-tested Tamil version of WHOQOL-HIV BREF was introduced and they were requested to fill up without leaving any question. If they were not sure of any answer they were asked to fill up the nearest possible one which comes to their mind. For those who could not read, the questionnaire was read out, and in case of doubts, they were clarified by a single interviewer. Their height and weight were noted.

The patients' address, contact phone numbers was obtained. The mode by which they preferred to be contacted was noted. The phone number of the investigator was also given to everyone. Some of them did not want letters to be written to them as their HIV status was not known to people around them. They preferred to call the investigator to intimate their visit dates. They were requested to meet the investigator who would be present 20.07.06 to 20.08.06 at GHTM, Tambaram.

On their follow-up visit after three months (for investigations and collecting drugs) the WHOQOL HIV BREF was reintroduced, the procedure to fill being the same as before. Logistically it is not possible to ascertain that they have really taken their drugs. So an 'intention to treat' analysis was done.

During the first contact 64 PLHA's were enrolled for the study. 49 came for follow up between 20.07.06 and 20.08.06. Four died before July 2006. The remaining 11 were contacted over phone and or post as per their initial preference. Three preferred to have the questionnaire sent by post and five wanted to answer over the phone. One person did not return the questionnaire. The remaining three could not be contacted by phone or by post. So, finally 56 persons were followed up.

The questionnaire has 31 questions pertaining to 6 domains namely- Physical (4 questions), Psychological (5 questions), Level of Independence (4 questions), Social (4 questions), Environmental (8 questions), Personal Beliefs (4 questions), one question regarding their rating of their QOL and one question regarding their level of satisfaction about their health. Each question has a score range of 1 to 5. Twenty four questions have answers in such a way that the score reflects QOL. Seven questions have Reverse scoring. Eg. - For the Question No.3 –

To what extend do you feel that physical pain prevents you from what you need to do?

Not at all	A little	A moderate amount	Very much	An extreme amount
1	2	3	4	5

A score of 1 indicates the best and 5 indicates the worst.

For such questions the modified score is got by subtracting the obtained score from 6 (6- Obtained score)

Thus, if the patient writes 1(Not at all), then the Modified score would be 6-1=5.

Overall scores could range from 31 to155, with a higher score indicating better Quality of life.

STATISTICAL ANALYSIS:

Statistical analysis was performed using Statistical Analysis software SPSS. Descriptive variables such as mean and standard deviation are used. One-way analysis of variance (ANOVA) was performed for finding out significant difference between domain scores and demographic characteristics. Paired t-test was performed for finding out significant difference between pre and post-ART Quality of life scores. Pearson Correlation was performed to find out the correlation between BMI and CD4 and QOL.

RESULTS

The Demographic Profiles of the sample population is as below;

TABLE – 1

SEX DISTRIBUITION

Sex	No. of Cases
Male	34 (60.7%)
Female	22 (39.3%)

TABLE – 2

AGE DISTRIBUTION

Age in years	No of Cases	Percentage
21-30	14	25%
31-40	28	50%
41-50	10	17.9%
51-60	4	7.1%

Mean Age is 36.89 and SD is 7.88

TABLE-3

MARITAL STATUS OF THE STUDY PATIENTS

Marital Status	No.	Percent
Single	6	10.7%
Married	28	50.0%
Living as married	1	1.8%
Separated	4	7.1%
Widowed	17	30.4%

TABLE – 4

PERCEPTION OF STATE OF HEALTH

Health Status	No.	Percent
Very Poor	1	1.8%
Poor	18	32.1%
Neither poor nor good	24	42.9%
Good	11	19.6%
Very Good	2	3.6%

TABLE-5

MODE OF TRANSMISSION

	Gender		Total
Mode	**Male**	**Female**	
Sex with man	2	21	23
Sex with women	31	0	31
Blood products	1	1	2
Total	34	22	56

Heterosexual transmission was seen in 52 (92.86%) subjects, homosexual in 2 (3.57%) and transmission through blood products was seen in 2 (3.57%)

TABLE-6

YEARS AFTER DIAGNOSIS AND PRE-ART QOL

	N	**Mean**	**Std. Deviation**	**Oneway ANOVA F-test**
0-1	21	62.0952	11.09912	F=0.74 P=0.53
2-3	19	64.1579	7.51490	
4-5	13	67.2308	11.11421	
6-7	3	63.3333	2.51661	
Total	56	64.0536	9.71301	

Based on One-way ANOVA and F-test there is no statistically significant difference in years after diagnosis and pre ART QOL. So, the groups may be considered as homogenous.

TABLE-7

	Mean	Std Deviation	Minimum	Maximum
Pre ART	64.05	9.71	42.00	85.00
Post ART	101.48	8.55	72.00	123.00

Pre and

Post-ART overall QOL scores

Paired t-test

t=32.45 P=0.001 (Highly Significant)

There was a Highly Significant improvement in the Quality of Life scores after ART.

TABLE - 8

DOMAIN-WISE PRE AND POST-ART SCORES

		Mean	Std. Deviation	Paired t-test
Pair 1	Pre_Physical	2.2902	.87097	t=15.99 P=0.001
	Post_Physical	3.9330	.60395	
Pair 2	Pre_Psychological	2.3500	.69308	t=16.10 P=0.001
	Post_Psychological	3.7429	.62285	
Pair 3	Pre_Level of independence	1.8348	.76615	t=14.71 P=0.001
	Post_Level of independence	3.2188	.65028	
Pair 4	Pre_Social	2.4196	.60134	t=16.11 P=0.001
	Post_Social	3.4420	.54144	
Pair 5	Pre_Environmental	2.4821	.45566	t=23.97 P=0.001
	Post_Environmental	3.6942	.45222	
Pair 6	Pre_Personal beliefs	2.9375	.67798	t=19.25 P=0.001
	Post_Personal beliefs	4.2634	.51217	

CORRELATION BETWEEN BMI AND POST TEST SCORE

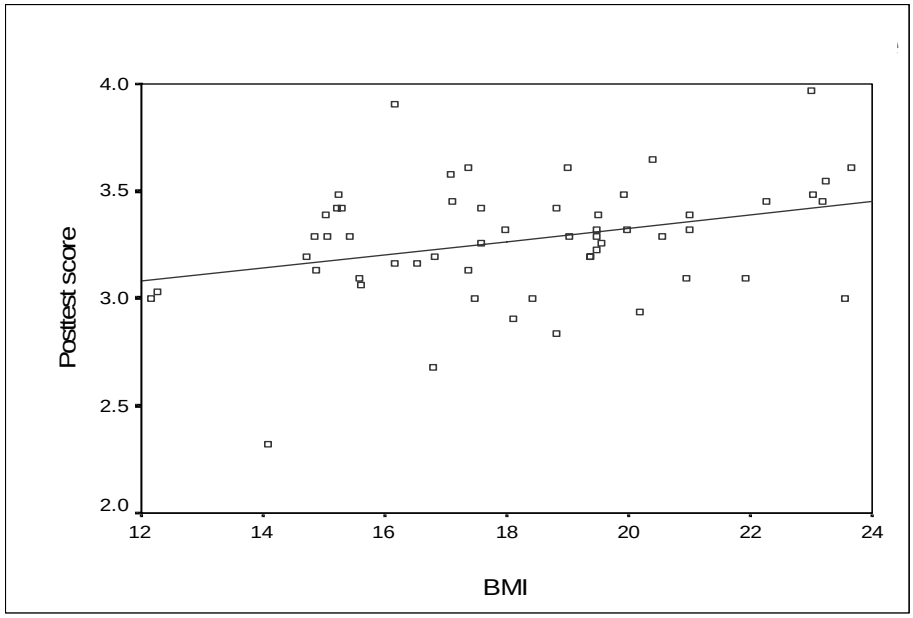


TABLE-9
CORRELATIONS

		Pretest score	**Posttest score**
BMI	Pearson Correlation	.239	.321(*)
	Sig. (2-tailed)	.076	.016
	N	56	56

* Correlation is significant at the 0.05 level (2-tailed).

0-0.2 poor

0.2-0.4 fair

0.4-0.6 moderate

0.6-0.8 good

0.8-1.0 very good

TABLE – 10

COMPARISON OF MALE AND FEMALE PRE AND POST ART SCORES

	Gender	**N**	**Mean**	**Std. Deviation**	**Student t-test**
Pre total	Male	34	64.7941	9.44451	t=0.70
	Female	22	62.9091	10.23025	P=0.48
Post total	Male	34	102.5000	8.19183	t=1.10
	Female	22	99.9091	9.04438	P=0.27

There was no statistically significant difference between men and women in the baseline QOL scores.

There was no statistically significant difference between those living with spouse and those without (One-way ANOVA).

Based on One-way ANOVA the patients' perception of his/her status of health correlated well ($p<0.05$) with the physical, psychological and Level of Independence domains but not with Social, Environmental and Personal Beliefs.

TABLE-11
CORRELATION BETWEEN CD4 AND QOL

		Base line QOL
CD4	Pearson Correlation	0.433(**)
	Sig. (2-tailed)	0.001
	N	56

** Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

WHO has defined quality of life as 'individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'. Quality of life is often regarded as a concept that is too nebulous to be measured reliably with a structured questionnaire and is subject to too much variability across cultures and individuals to have any useful validity. However, WHOQOL questionnaire developed in the WHOQOL project demonstrated that QOL could be conceptualized and defined in a uniform way across cultures. Its constituent core domains and facets can be assessed using structured questionnaire methodology, and cross-cultural as well as intra-cultural comparisons can be made.

Physical domain assesses pain, impact of disease on activities of daily living, lack of energy and sleep.

The psychological domain assesses the patients' own thoughts, about body image and appearance, positive feelings like enjoyment, ability to concentrate, personal satisfaction and negative feelings like despair, anxiety and depression.

Level of independence assesses medical treatment, mobility, performance of activities of living and capacity for work.

The Social domain assesses acceptance, personal relationships, social support and sexual activity.

Environment does play a major role in determining health states. Environmental domain assesses influence of factors like financial resources, the work environment, accessibility to health and social care, freedom, security and participation and opportunities for leisure activities on the QOL

The domain on Personal beliefs assesses the feelings like meaningfulness in life, discrimination, fear of future and death.

The study shows that there is a significant improvement in the QOL of patients after three months of starting ART. This is in line with other studies[35]. Other studies have shown that women have lower QOL than men[34]. Such a difference was not observed in this study.

Levels of Independence, physical and psychological wellbeing seem to play an important role in one's perception of one's health status more than social and environmental factors.

As in other studies the CD4 count has a positive correlation with QOL.

SUMMARY AND CONCLUSION

An interventional study to find the improvement in Quality of Life of People Living with HIV/AIDS was done. The Tamil version of WHO QOL-HIV BREF was used. The scores were compared with the demographic charecteritics and the difference between pre ART and post ART scores were compared.

There was a highly significant improvement in the Quality of Life of People Living with HIV/AIDS due to Anti retroviral therapy.

Thus based on his study it can be concluded that Antiretroviral therapy not only prolongs life it also improves the quality of life of people living with HIV/AIDS.

LIMITATIONS

A single 3 month follow-up to assess the impact of ART on QOL is not sufficient.

This group should be followed up every three months to study the effects of delayed complications, and effect of resistance of the virus to the drugs on the QOL. Due to time constraints this kind of continued follow-up could not be done.

The validity of the study would have been better if there was a control group which did not receive ART and again due to time constraints and ethical constraints this could not be done.

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ART CENTRE AT GHTM, TAMBARAM

INTERVIEWING AN ILLITERATE PLHA