A DISSERTATION ON
TO PREDICT MORBIDITY AND MORTALITY IN HIV INFECTED INDIVIDUAL ON NACO ANTI RETROVIRAL THERAPY REGIMEN USING MODIFIED VETERANS AGING COHORT STUDY INDEX IN A TERTIARY CARE HOSPITAL

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CERTIFICATE OF GUIDE

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DECLARATION

I, **Dr. P.MARIKOMALA,** certainly declare that this dissertation titled, "**TO PREDICT MORBIDITY AND MORTALITY IN HIV INFECTED INDIVIDUAL ON NACO ANTI RETROVIRAL THERAPY REGIMEN USING MODIFIED VETERANS AGING COHORT STUDY INDEX IN A TERTIARY CARE HOSPITAL**", represent a genuine work of mine, done at the Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, under the supervision of **PROF.DR.P.SAMUEL DINESH, M.D.,D.,DNB., Chief** and Professor, Madras Medical College and Rajiv Gandhi Government General Hospital.

I, also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other university board, either in India or abroad.

This is submitted to The Tamil Nadu Dr. MGR Medical University, Chennai in partial fulfilment of the rules and regulations for the award of. M.D General Medicine

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LIST OF ABBREVIATIONS

NACO	National AIDS control Organization
AIDS	Acquired Immuno Deficiency Syndrome
HIV	Human Immunodeficiency Virus
WHO	World Health Organization
HAART	Highly Active Anti Retroviral Therapy
ART	Anti Retroviral Therapy
CVD	Cardio Vascular Disease
VACS	Veterans Aging Cohort Study
AZT	Azidothymidine
NACP	National AIDS Control Programme
RNA	Ribo Nucleic Acid
DNA	Deoxyribo Nucleic Acid
PCR	Polymerase Chain Reaction
RTI	Respiratory Tract Infection
TB	TuberClosis
CMV	CytoMegaloVirus
NNRTI	Non- Nucleoside Reverse Transcriptase Inhibitors
FI	Fusion Inhibitors
INSTI	Integrase Inhibitors
PI	Protease Inhibitors
NRTI	Nucleoside Reverse Transcriptase Inhibitors

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ABSTRACT

Background and Objectives

According to a global review of the AIDS epidemic, the World Health Organization (WHO) has reported 31.8 million adult patients as having been infected with the Human Immunodeficiency Virus estimated that the prevalence will be roughly 20.89 lakh in the year 2011, with 0.27% of those instances happening in the adult age group (15-49 years). The results of the EuroSIDA trial indicated that continued antiretroviral therapy (ART) considerably reduced the risk of death and progression to AIDS

Studies such as the SMART trial point to potential causes such as inflammation caused by HIV, which is connected with an increased risk of hypercoagulability, and organ system damage caused by ageing. The Veterans Aging Cohort Study Risk Index is a clear scoring system that was designed with the purpose of forecasting mortality rates in HIV patients who have been on treatment for a whole year.

Methods

This study was conducted in ART centre, Rajiv Gandhi Government General Hospital from June2022 to November 2022. A total 125 case were studied. The Haemoglobin, ALT, AST, serum creatinine, eGFR, FIB-4, HEPATITIS C, CD4 count were included and assessed. Data was entered in MS excel sheet and analysed using SPSS version 21.0. Chi square test and Fisher' s exact test was used for finding association

Results

In our study, around 18.4% were in the age group of 18-30 years, 24.8% 31-40 years, 21.6% 41-50 years, 27.2% 51-60 years and 8% more than 60 years and nearly 52.8% were males, and 47.2% were females. mean values of ALT of mean 24.58, and the median ALT levels were 14.50 (Minimum 11.0 to Maximum 27.25). The mean values of platelets were 203.66. The median platelets were 103.22 (145.0 to 258.50).

Conclusion

The VACS may be a useful indicator of physiologic frailty, indicating the need for more vigilant management or a comprehensive geriatric evaluation. The VACS Index may also assist in alerting healthcare providers and patients when life expectancy is low.

1. INTRODUCTION

To predict the morbidity and mortality in HIV infected individual on NACO Anti-Retroviral therapy Regimen using modified veterans aging cohort study index in a tertiary care hospital

Introduction

According to a global review of the AIDS epidemic, the World Health Organization (WHO) has reported 31.8 million adult patients as having been infected with the Human Immunodeficiency Virus. This number ranges from 30.1 million to 33.7 million (HIV). Among these patients, 1.9 million [1.7 million–2.1 million] people have been given their initial diagnosis of the condition (2013). (1)

As these data make clear, HIV/AIDS is still a huge threat to the health of people all over the world. This is especially true in developing countries. According to the data collected by the National AIDS Control Organization (NACO), India has the third highest number of HIV-positive people living within its borders of any country in the entire world. It is estimated that the prevalence will be roughly 20.89 lakh in the year 2011, with 0.27% of those instances happening in the adult age group (15-49 years). (2) In the context of HIV infection, highly active antiretroviral therapy, usually referred to as HAART, is an essential component of patient care. The results of the EuroSIDA trial indicated that continued antiretroviral therapy (ART) considerably reduced the risk of death and progression to AIDS when compared to

the early ART era, which was compared to the pre-ART treatment period and the later ART treatment period. In both the developed and developing worlds, the widespread use of antiretroviral therapy (ART) has led to a significant decrease in the incidence of the majority of diseases that define AIDS, as well as mortality rates. This change has been brought about by the widespread use of antiretroviral therapy (ART). (3) It is essential to suppress HIV replication in order to reduce the morbidity and mortality associated with HIV; doing so also improves the quality of life in those who have HIV infection. To achieve the level of HIV infection suppression that is required, antiretroviral medication must be utilised precisely in accordance with the instructions provided. (3) An increased risk of death has been observed in these individuals when compared to the controls that were the same age and gender, and this cannot be explained by metrics such as CD4 count alone. This remains the case despite the provision of the right treatment, which involves the use of ART. Studies such as the SMART trial point to potential causes such as inflammation caused by HIV, which is connected with an increased risk of hypercoagulability, and organ system damage caused by ageing. Both of these factors have been linked to an increased risk of bleeding. (5)There has been a growing body of evidence suggesting that the risk of serious conditions that are not related to AIDS is increased in people with HIV infection as compared to matched controls. These conditions include cardiovascular disease (CVD), renal or hepatic disease, and non-AIDS defining malignancies. In addition, the risk of serious conditions that are not related to AIDS has been shown to be increased in people

with HIV infection. These disorders include cardiovascular disease (often referred to as CVD), renal or hepatic disease, and cancers that are not defined by AIDS. [Further citation is required] (6) In order to monitor patients who may have risk factors that can be altered, a number of clinical studies have been conducted in order to investigate the link between non-traditional markers of inflammation and traditional markers of inflammation. These studies were carried out in order to investigate the link between non-traditional markers of inflammation and traditional markers of inflammation.

After treatment has begun, doctors who are providing care for patients who have HIV infection are routinely questioned about the prognosis of their patients as well as the quality of life they are experiencing. Several different prognostic systems have been developed in order to achieve the goals of standardisation and improvement in the accuracy of prognostic judgments. Risk factors, staging systems, statistical models, and computer algorithms are a few examples of the several types of systems that fall under this category. The Veterans Aging Cohort Study Risk Index is a clear scoring system that was designed with the purpose of forecasting mortality rates in HIV patients who have been on treatment for a whole year. This index was developed as part of the Veterans Aging Cohort Study (VACS). It was intended to take into account all of the various potential outcomes that HIV disease, comorbidities, substance addiction, and adverse pharmaceutical reactions related to therapy could have on the lives of HIV-positive people. (7)

Review of Literature

Since the first case of HIV was discovered in 1981, while the virus itself wasn't discovered until 1983, there has been substantial progress made in the field of research pertaining to HIV. These advancements include the creation of new diagnostic methods and treatment options. (10) The chemical known as azidothymidine (AZT) was the first medicine that was proven to have a therapeutic advantage in the treatment of HIV infection. This discovery came in the year 1987. After this, in 1992, combination retroviral medication became available to treat the virus that caused AIDS. (11) (12) In the year 1986, a serological investigation was carried out on commercial sex workers in the Indian state of Tamil Nadu, which is located in the southern region of India. This investigation was responsible for the identification of India's very first patient suffering from the condition. (13)

Epidemiology

The National AIDS Control Organization (NACO) has produced statistics that show India has the third highest number of people living with HIV infection of any country in the entire world. It is estimated that the prevalence will be roughly 20.89 lakh in the year 2011, with 0.27% of those instances happening in the adult age group (15-49 years). (2) It has been established that during the course of the last decade, there has been a reduction of 57% in the total number of annual new HIV

infections among the adult population of India. This decrease is a consequence of the effectiveness of the National AIDS Control Program (NACP), which was put into action by means of its interventional strategies and preventive programmes. (2) Tamil Nadu is the eleventh largest state in India when measured in terms of land extent, but its population density positions it seventh among all of India's states. (14) (15) It is estimated that there are 132,590 people living with HIV in Tamil Nadu (between 110,563 and 161,038), and approximately 3,148 new cases are identified each year in the state. (16)

HIV

The retrovirus family is home to the human immunodeficiency virus, more commonly referred to as HIV. Retroviruses are a family of viruses. The genetic information of retroviruses, as opposed to the genetic information of other viruses, is encoded by ribonucleic acids (RNA), as opposed to deoxyribonucleic acids (DNA). This sets retroviruses apart from other viruses (DNA). They are able to accomplish this by infecting CD4 T cells, which ultimately results in the death of the CD4 T cells. The human immunodeficiency virus, sometimes known as HIV, is the pathogen that leads to acquired immunodeficiency syndrome, more commonly known as AIDS (AIDS). The virus that causes AIDS, HIV, can be further subdivided into two subtypes, both of which are recognised to be responsible for the disease. HIV-1 is the virus that is principally responsible for the spread of the AIDS

epidemic around the world, while HIV-2 is a form of the virus that is considered to be less harmful and is found predominantly in West Africa. Since the virus was discovered approximately thirty years ago, the pandemic variant of HIV-1 has been diagnosed across all continents and countries; in addition, the illness affects people of all ages. The majority of the illness and mortality caused by HIV/AIDS has been experienced in developing countries. These countries have also suffered the majority of these effects. (8) The HIV-1 virus is composed of four distinct lineages, which have been labelled groups M, N, O, and P accordingly. Each of these groups has a specific subtype. In the end, the development of all four of these subgroups was finally caused by an event that was unrelated to each other and involved transmission across distinct species. Group M was the first subtype of HIV-1 to be discovered; today, it is understood to be the pandemic variety of HIV-1, and it may be located virtually anywhere in the world.

Methods by Which a Disease May Spread

• Sexual Percutaneous Perinatal routes

• Exposure at mucosal surfaces

The majority of people who become afflicted with AIDS do so between the ages of 6 and 9, which is a significant amount of time after their first infection with the HIV virus. AIDS can be broken down into its component parts, which are opportunistic infections, various illnesses or cancers that are frequently associated with HIV infection, and death from AIDS-related causes. The immunodeficiency that

underlies AIDS is the source of the spectrum of AIDS, and AIDS itself is the result of a chronic HIV infection in conjunction with a decline in CD4 cells.

ETIOPATHOGENESIS

HIV is capable of infecting a number of distinct cell lines, some of which include CD4+ T cells, dendritic cells, and macrophages, amongst others. The anogenital mucosa is the entry point into a host that the HIV-1 virus uses the great majority of the time. [Case in point:] [Case in point:] [Case in point:] [Dendritic cells have a molecule of CD4 that can be bound by the glycoprotein (GP)-120, which is the protein that makes up the envelope of the virus. Interstitial dendritic cells in the cervico-vaginal epithelium, as well as those in the tonsillar and adenoidal tissue, have the potential to be the initial target cells in an infection that is passed on through genital-oral sex. Likewise tonsillar and adenoidal tissue interstitial dendritic cells may also be the initial target cells. Transmission of macrophage-tropic viruses, as opposed to T-cell-tropic viruses, is the most common route by which newly acquired cases of HIV are brought about. T-cell-tropic viruses are less common. In order to enter cells, viruses require the cooperation of a number of different co-receptors. In order for the virus to enter macrophages, GP-120 needs to connect to both the CD4 receptor and the chemokine receptor CCR5. Only then will the virus be able to enter the cells. Macrophage-tropic viruses, on the other hand, are denoted by the letter R5, in contrast to T cell-tropic viruses, which are denoted by the letter

X4. The fact that macrophages include the CXCR4 receptor is what allows for the differentiation of these cells. Patients who are homozygous for a deletion in CCR5 are relatively resistant to R5 infection; nonetheless, incidences of X4 infection in these individuals have only very rarely been recorded. Patients who are homozygous for a deletion in CCR5 are relatively resistant to R5 infection.

When HIV-infected cells interact with CD4+ T cells, this leads to additional spread of the virus throughout the body. In as little as two days after mucosal exposure, HIV can be discovered in the lymph nodes of the region, and in as little as three days after that, it can be detected in the plasma of the individual. When a virus enters the bloodstream, it soon begins to spread to other organs throughout the body. These organs include the brain, the spleen, and the lymph nodes. The mucosa that lines the interior of the intestines is another primary target in the early stages of an infection. Memory CD4+ T cells are more likely to be destroyed than other types of T cells, and this can be triggered either by a direct infection or by a process that is known as apoptosis. Memory CD4+ T cells are more likely to be deleted. This can result in an early and excessive depletion of CD4+ T lymphocytes in the gastrointestinal compartment as compared to the blood found in the peripheral. This can be a consequence of the disease. It has also been hypothesised that the origin of persistent immunological activation in HIV infection may lie in the microbial translocation that takes place as a result of modifications in the mucosal barrier of the gut. This idea has been put forward as a possible explanation.

The submucosal CD4+ T cells, dendritic cells, and macrophages are the first cells that the virus infects after entering the body. It then moves on to the lymph nodes, and lastly, the plasma. When the virus penetrates the mucosal epithelium, this process is said to have begun. The time it took for viremia to become detected in the blood after experimental HIV exposure by intravaginal routes ranged from 5 to 30 days. A rapid increase in HIV RNA levels can be detected from the first detectable level all the way up to the peak level, which normally takes place at the same time as seroconversion in most cases. This can be seen from the beginning of the progression of HIV until it reaches the peak level. On the other hand, it is possible that a time of low-level viremia prior to a ramp-up viremia is more common than was previously supposed. This is something that was discovered after previous research was conducted. In order to determine whether or not low levels of viremia were present in samples that had previously been determined to be negative by prior quantitative PCR, a study was carried out using serial samples from patients who had a confirmed early HIV infection. This was done in order to evaluate whether or not low levels of viremia were present in samples. 23 out of 69 samples were found to be positive for the presence of the virus when they were retested using a sensitive qualitative reverse transcriptase PCR assay with a sensitivity of 4 copies / ml. This result was obtained after the samples were retested. These specimens were obtained nine to twenty-five days prior to the first sample that contained more than one hundred copies per millilitre. It is not known whether or not an infection can be caused by the low number of bloodborne pathogens seen in this sample.

It is possible to get a rough estimate of the cellular HIV reservoir by looking at the amount of HIV DNA that is detected in mononuclear cells that are located in the peripheral blood. This reservoir is generated quite fast after infection. In a study that involved 163 people who had been diagnosed with acute infection but had not started antiretroviral medication immediately following the diagnosis, researchers found that the level of HIV DNA and the initial CD4 cell count were independent indicators of disease progression. This was discovered in a trial that compared the two factors.

The progression of HIV into AIDS is preceded by an extended HIV infection and, as a result of this, a decrease in the number of CD4 cells that are present throughout the body. A CD4 cell count of fewer than 200 cells/L or the presence of any symptom that defines AIDS regardless of the CD4 cell count can both be used to identify a case of AIDS. However, the CD4 cell count is more commonly used. There is nothing wrong with either of these interpretations. When speaking of HIV infection, the condition that arises when the CD4 cell count drops below 50 cells / L is typically referred to as "advanced." This is because the term "advanced" is commonly used to characterise the situation. Opportunistic illnesses are illnesses that arise more frequently or more severely as a result of immunodeficiency. Opportunistic illnesses can be caused by either bacteria or viruses. These diseases are sometimes referred to as AIDS-defining disorders. All of these conditions are linked to uncontrolled HIV infection, and the most common types are opportunistic

infections (like Pneumocystis jiroveci) malignancies (such Kaposi's sarcoma and lymphoma), and illnesses that don't appear to have any other evident causes. AIDS-related illnesses were the primary cause of morbidity and mortality connected to HIV infection in the years leading up to the introduction of combination antiretroviral therapy (ART). ART is an acronym that stands for "antiretroviral therapy."

In this day and age of highly active anti-retroviral therapy (HAART), the causes of mortality include adverse events to therapy such as anaemia, hepatotoxicity, and immune reconstitution syndrome. These causes come on top of opportunistic illnesses like tuberculosis and pneumocystis jiroveci pneumonia, both of which are examples of opportunistic illnesses. These causes are more common than opportunistic illnesses. Therefore, there is a higher burden of mortality and morbidity in patients who are infected with HIV/AIDS due to both the disease and the medication; the necessity for monitoring in patients after the commencement of ART is just as important as it is in patients who have never received ART. This is because the disease and the medication both contribute to the situation. Patients who have advanced HIV infection (CD4 cell count of less than 50 cells/microl) have a median survival time of between 12 and 18 months if they do not receive antiretroviral treatment. The majority of people whose deaths are ascribed to complications caused by AIDS had CD4 cell levels that fell within this range. AIDS is an acronym for the human immunodeficiency virus.

In addition, opportunistic infections can be avoided or treated depending on the severity of the HIV infection, and other comorbidities such as haematological abnormalities such as leukopenia's or anaemia can be identified and treated appropriately provided that an effective screening programme is in place.

CLASSIFICATION OF AIDS

The clinical stages of AIDS have been categorised into four separate phases in accordance with the criteria established by the World Health Organization (WHO), with stage I being the least severe and stage IV being the most severe of the four stages. The stages consist of the following, as seen in digit nine:

Primary HIV infection is the first stage of HIV infection, and it can either be asymptomatic infection or an acute retroviral sickness. Both of these outcomes are referred to as primary HIV infection. A patient who has been exposed to the virus will often begin to develop symptoms of an acute retroviral syndrome 2–4 weeks later in the form of an acute febrile illness. These symptoms typically appear after the patient has been infected with the virus. In the majority of instances, it is also accompanied with lymphadenopathy, pharyngitis, and cutaneous symptoms. If there is a significant amount of HIV RNA in the blood, it may be possible to identify the core p24 antigen. A significant transitory lymphopenia is one example of an abnormality that can be identified in the blood. In most cases, a seroconversion from

an HIV antibody-negative status to an HIV antibody-positive status will take place during this phase.

Clinical Stage I: This stage can be asymptomatic or marked by persistent generalised lymphadenopathy. Persistent generalised lymphadenopathy is defined as lymph nodes that are enlarged to a size of more than one centimetre in two or more non-contiguous sites, excluding inguinal nodes, in the absence of a known cause. In this stage, lymph nodes can be enlarged to a size of more than one centimetre in two or more non-contiguous sites. This definition does not include the lymph nodes located in the inguinal region.

Patients are deemed to be in the clinical stage II when they show signs of a moderate (less than ten percent of their assumed or measured body weight) and unexplained weight loss. In addition to this, it can be differentiated from other normal infections by the presence of infections such as:

1. A recurrent RTI that is most likely caused by bacteria (two or more in any six-month period)
2. Herpes zoster
3. Angular cheilitis
4. Aphthous ulceration, which is characterised by a halo of inflammation and a yellowish-grey pseudo-membrane, and recurrent oral ulcerations that have occurred twice or more in the past six months.
5. Papular pruritic eruptions

6. Dermatitis seborrhoeica (Seborrheic)

7. Fungal paronychia

Clinical Stage III - This stage is distinguished by the presence of the following clinical characteristics:

1. Severe weight loss that cannot be accounted for (representing more than 10% of the body's supposed or measured weight).

2. Unexplained chronic diarrhoea for longer than one month.

3. a fever that cannot be explained, which can be either intermittent or chronic and lasts for more than a month.

4. Oral candidiasis

5. Oral hairy leucoplakia

6. Tuberculosis of the lungs (TBP) (current or in last two years)

7. Severe suspected bacterial infection (for example, pneumonia, meningitis, empyema, pyomyositis, infection of the bone or joint, bacteraemia)

8. Acute necrotizing ulcerative gingivitis or necrotizing ulcerative periodontitis.

9. Undiagnosed anaemia (less than eight grammes per decilitres), neutropenia (less than one thousand per millilitre), or thrombocytopenia (less than fifty thousand per millilitre) for more than one month.

Clinical Stage IV - This stage is distinguished by the following features and characteristics:

a. HIV Wasting Syndrome—Unexplained Weight Loss of More Than 10 Percent of Body Weight weight accompanied by visible thinning of face, waist and extremities;

in addition, either unexplained chronic diarrhoea (lasting > one month) or unexplained prolonged or intermittent fever (Documented temperature of 37.5 °C or more on occasions with no obvious foci of disease, negative blood culture, negative malaria slide and normal or unchanged CXR) for one month or more.

2. Pneumocystis pneumonia
3. Recurrent severe or radiological bacterial pneumonia (two or more episodes within one year)
4. Chronic herpes simplex virus (HSV) infection (orolabial, genital or anorectal of more than one month, or visceral of any duration)
5. Oesophageal candidiasis
6. Extra-pulmonary / Disseminated TB
7. Kaposi's sarcoma
8. CMV (retinitis or CMV infection of an organ other than liver, spleen or lymph nodes)
9. CNS toxoplasmosis
10. Cryptococcal meningitis or other extrapulmonary Cryptococcus infection
11. HIV encephalopathy
12. Disseminated non-tuberculous mycobacteria infection

13. Progressive multifocal leukoencephalopathy
14. Candidiasis of trachea, bronchi, lungs
15. Cryptosporidiosis (with diarrhoea lasting more than one month)
16. Isosporiasis
17. Any disseminated mycosis (e.g. coccidiomycosis, histoplasmosis, penicilliosis)
18. Recurrent non-typhoidal salmonella septicaemia (two or more episodes in last year)
19. Lymphoma (cerebral or B cell non-Hodgkin)
20. Invasive cervical carcinoma

u. Visceral leishmaniasis

Although it is common for opportunistic infections to become apparent when the CD4 cell count falls to levels of less than 200 cells/L, this is not always the case. Opportunistic infections can appear at any time. It is believed that the virus has a half-life in human serum of around 1.2 days, approximately 24 hours in an intracellular milieu, and approximately 6 hours when it is extracellular. These times were derived from estimates made using mathematical models. The amount of virus that is expelled from the body on a daily basis is equivalent to about 30 percent of the total viral load that is carried by the body. On the other hand, each and every day just six or seven percent of the total CD4 cells are replaced. As a consequence,

AIDS develops as a consequence of the persistent and high-level replication of HIV, which leads in the death of CD4 T cells as a consequence of immune-mediated processes. As a consequence, AIDS develops as a consequence of the persistent and high-level replication of HIV.

ANTI-Retroviral Agents

Within the context of HIV infection, highly active antiretroviral therapy, which is often referred to by its acronym HAART, is an essential component of patient care. The results of the EuroSIDA trial indicated that continued antiretroviral therapy (ART) considerably reduced the risk of death and progression to AIDS when compared to the early ART era, which was compared to the pre-ART treatment period and the later ART treatment period. In both the developed and developing worlds, the widespread use of antiretroviral therapy (ART) has led to a significant decrease in the incidence of the majority of diseases that define AIDS, as well as mortality rates. This change has been brought about by the widespread use of antiretroviral therapy (ART). (3) It is essential to suppress HIV replication in order to reduce the morbidity and mortality associated with HIV; doing so also improves the quality of life in those who have HIV infection. To achieve the level of HIV infection suppression that is required, antiretroviral medication must be utilised precisely in accordance with the instructions provided. (3) More than 25 antiretroviral medicines spanning six primary classes are currently available for use

in the treatment of HIV-infected individuals today. These pharmaceuticals are currently available for purchase. In order to determine which technique of therapy is the most effective, the efficacy of a broad variety of different combination regimens has been examined. This will allow for the identification of the method of treatment that is the most effective. Multiple comparative clinical trials have shown that combination therapy, which consists of two nucleoside reverse transcriptase inhibitor (NRTI) agents plus a third active drug from a different class, is the most effective treatment for suppressing HIV RNA, minimising drug toxicity, and/or reducing HIV-related morbidity and mortality. Combination therapy consists of two nucleoside reverse transcriptase inhibitor (NRTI) agents plus a third active drug from a different class.

This is a list of the primary classes of antiretroviral drugs, which are as follows:

1. Nucleoside reverse transcriptase inhibitors (NRTIs)
2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
3. substances that halt the action of proteases (PIs)
4. Integrase inhibitors (INSTIs)
5. Fusion inhibitors (FIs)

Antibodies that are directed against chemokine receptors (CCR5 antagonists)

Both in the United States (from 350 to 500 cells / mL) and in countries with moderate and low incomes (from 200 to 350 cells / mL), the CD4+ cell count

requirements for commencing HAART have recently been raised. In the United States, the new threshold is a higher CD4+ cell count. According to the data that is now available, the application of these guidelines will almost certainly result in a large increase in the number of people who will be in need of treatment and will require early HIV testing. Individuals who are new to treatment as well as those who have had previous treatment can benefit from the several successful therapy options offered by HAART. Each kind of antiviral medication is designed to combat the virus at a distinct stage in its life cycle after it has infected a CD4+ T-lymphocyte or another type of target cell. Primary elements that significantly control how these medicines are used include the ease or difficulty of taking these drugs in clinical practise, the side-effect profile, the efficacy based on clinical data, practise guidelines, and the preference of doctors.

When it comes to choosing a medicine and keeping it in place, clinicians confront substantial challenges in the form of medication resistance, adverse effects, pregnancy, and coinfection with the hepatitis B virus or the hepatitis C virus. These are just some of the challenges that they encounter.

The use of antiretroviral therapy is frequently connected with a number of toxic syndromes in settings where there is restricted access to resources. In order for us to have a better understanding of the risks and benefits that need to be taken into consideration prior to beginning treatment with these medications, a few of the adverse events that have been linked to the use of these pharmaceuticals have been outlined below in some detail. This will allow us to have a better understanding of

the dangers and advantages that need to be taken into consideration prior to beginning treatment with these medications.

Hyperlactatemia as well as the syndrome of lactic acidosis — The use of nucleoside reverse transcriptase inhibitors (NRTIs) over an extended period of time can eventually result in mitochondrial toxicity, which has been linked to both hyperlactatemia and the lactic acidosis syndrome. After using anti-retroviral medicine, patients living with HIV might develop the condition of hyperlactatemia, which causes symptoms. Clinical symptoms such as nausea, vomiting, stomach bloating, weariness, weight loss, and hepatomegaly are some of the potential outcomes of a significant increase in lactate levels in the serum. Other potential outcomes include hepatomegaly. While hyperlactatemia is characterised by increased lactate levels in patients and may induce symptoms, lactic acidosis is characterised by severe metabolic disarray as a consequence of unfavourable changes in systemic PH. This is in contrast to hyperlactatemia, which is characterised by increased lactate levels.

Any of the medications that fall into the NRTI family have the potential to cause mitochondrial toxicity if they are taken for a significant amount of time over an extended length of time. Through the course of a number of different trials, the drugs stavudine and didanosine have been singled out as being particularly associated with lactic acidosis. In addition, it was shown that utilising zidovudine for an extended period of time can result in lactic acidosis being produced in the body.

When combined, the antiretroviral drugs stavudine and didanosine provide a greater danger to the patient than when either of these medications is taken on its own. Other therapies, including as abacavir and the nucleotide tenofovir, have been related to extremely few incidences of mitochondrial toxicity; however, due to the economic constraints that exist in settings where resources are scarce, these agents are not utilised very frequently.

Female gender, obesity, and the use of stavudine have all been identified as potential risk factors for lactic acidosis in the industrialised world (17):

HIV-infected adults who were not previously treated with ART were started on NRTI-containing ART for the purpose of studying patients for ART-associated toxicities. During the course of the study and after nearly two years of follow-up, 2% of patients developed moderate to severe symptomatic hyperlactatemia, which was defined in the study as serum lactate greater than 4.4 mmol/L; lactic acidosis, which was defined in the study as symptomatic hyperlactatemia in addition to either a ketonuria or an acidosis, which was defined in the study as symptomatic hyperlactatemia in addition to either

(17) A research study that was conducted on 56 persons who had mitochondrial toxicity induced by the use of stavudine revealed that switching to an antiretroviral therapy (ART) regimen that contains zidovudine was found to be risk-free. The study was carried out in the United States.

(18) The availability of antiretroviral medication in many resource-depleted areas is mostly limited to older NRTIs, hence data of this kind may be useful in the process of selecting drugs to treat HIV infection.

Dideoxynucleoside analogues are the kind of antiretroviral medications that have been linked to study on pancreatitis the most closely. Examples of dideoxynucleoside analogues are didanosine and stavudine.

(20) A differential diagnosis for antiretroviral-induced pancreatitis includes pancreatitis caused by various etiologies, such as alcohol use, hyperlipidaemia, and cholelithiasis; antiretroviral-induced pancreatitis may be made worse by other causes, such as those mentioned above. Pancreatitis is characterised by severe cases of nausea and vomiting, severe cases of abdominal pain that spreads to the back, and severe cases of abdominal discomfort. It is possible for severe pancreatitis to be fatal, especially when it is accompanied by a condition that causes lactic acidosis. This is especially true when both conditions occur together. 17) Despite the fact that studies have shown that the overall rate of confirmed pancreatitis is fairly low in settings with limited resources, the ability to diagnose this complication may be hindered by the limited availability of diagnostic testing. Ten hundred and twenty-nine patients with advanced AIDS who were taking part in a home-based care programme in rural Uganda were evaluated for clinical symptoms of antiretroviral toxicity. This was done in the absence of any facilities for laboratory monitoring. (21) After observing a total of 11,268 patient-months, only 0.3 percent of patients

were given a clinical diagnosis of pancreatitis. This was after a total of 11,268 patient-months had passed. Despite the fact that almost all patients were started on antiretroviral medication (ART) that included stavudine, this was nevertheless the outcome. The incidence rate for clinical and/or chemical pancreatitis in individuals who were receiving stavudine-containing regimens varied from 0.77 to 1.84 per 100 person-years, which was significantly greater than the rate that was observed in the Uganda research. This was uncovered through an investigation into the past that was carried out in a setting that featured a plethora of available materials. (20) If you have a low body weight and you take didanosine, you may have a higher probability of having pancreatitis as a result of the combination of the two conditions. This is because didanosine is known to cause inflammation of the pancreas. All six cases of pancreatitis were reported in patients who were female, weighed less than 60 kilogrammes, and had received didanosine, either on its own (n = 1) or in addition to tenofovir (n = 5). This was the case among 575 patients who had been treated with tenofovir and didanosine (a combination that is no longer recommended), didanosine alone, or tenofovir alone. This was identified by conducting a review of the medical records of 575 individuals in the past. (22) Peripheral neuropathy — The antiretroviral medicines that are most frequently related with peripheral neuropathy are didanosine, nevirapine, and stavudine. Nevirapine and stavudine are followed closely by didanosine. (23) Peripheral neuropathy can also be caused by other reasons, including as severe HIV infection itself, getting older, diabetes, or nutritional deficiencies. Peripheral neuropathy can also be inherited. It's possible that

taking neurotoxic drugs like isoniazid at the same time could make your risk of developing peripheral neuropathy even higher.

Patients who acquire this problem should consider switching from stavudine to medications that are less toxic, such as tenofovir, whenever it is practicable for them to do so, since it is suggested that they do so. This is as a result of the fact that switch strategies to alternative agents have been related with advances in both the amount of mitochondrial DNA and the shape of mitochondria in resource-rich environments.
(29)

Implications for the functioning of the central nervous system It is possible for efavirenz to cause acute subjective neurologic symptoms; however, these symptoms normally only endure for a brief period of time, therefore this may have an impact on the patient's adherence to treatment.

It has been observed that the overall occurrence of this condition tends to vary according to racial group, and it is probable that this variation is the result of inherited influences on the metabolism of medications. The presence of the cytochrome (CYP)2B6 516G>T polymorphism, also referred to as the "T/T genotype," causes a reduction in the rate at which efavirenz is metabolised. This genetic variant is more common in people of African descent than it is in people of

Caucasian descent. According to one study, the T/T genotype was detected in 3% of European-Americans but in 20% of African-Americans. This difference was due to the genetic background of the two groups. This disparity can be attributed to the fact that African ancestry is more likely to be inherited by African ancestry in the case of African-Americans. (30) According to the findings of one more investigation, thirteen percent of HIV patients who were HIV infected in South Africa had this genotype. South Africans made up the entirety of the patient population. (31) The higher occurrence of the T/T genotype in Africans may explain, at least in part, reports of increased CNS toxicities such as depression, anxiety, and severe sleep disturbance in Africans. This is because increased symptoms are directly connected to higher serum drug concentrations. If CNS symptoms continue after the first month of treatment, nevirapine or some alternate medication should be sought. Nevirapine is one example of a treatment that falls under the alternative category.

If the typical dose of efavirenz, which is 600 milligrams, is increased to 800 milligrams per day, as is sometimes done to counteract the pharmacologic interactions between efavirenz and rifampin in patients with tuberculosis co-infection, the effects on the central nervous system may also become more severe. The standard dose of efavirenz is 600 milligrams. On the other side, this particular mode of dosage has been linked to greater toxicity in patient subsets that have the T/T genotype. In the event that a patient experiences substantial adverse effects on the central nervous system while receiving efavirenz at the dose of 800 milligrams, a

dose decrease should be explored, particularly in the event that viral suppression has already been achieved.

Anaemia - Since zidovudine frequently causes anaemia, it is recommended that the patient's haemoglobin levels be monitored. Anaemia is a common side effect of zidovudine medication, and it can either be completely asymptomatic (in which case, only macrocytosis would serve as a marker of zidovudine usage) or completely symptomatic. In the former scenario, only macrocytosis would serve as a signal of zidovudine use (in which case symptoms such as fatigue or dyspnoea would be present). In more severe circumstances, the anaemia that is caused by zidovudine has the potential to induce a disease called as aplastic crisis, which is a condition that is very dangerous to one's health.

At week 48 of the trial, 219 of the treatment-naive patients who were given zidovudine-containing regimens had severe anaemia (haemoglobin 6.5g/dL). This represents 6.6 percent of the patients who were enrolled in the study. Uganda and Zimbabwe were the two countries where the research was carried out. This percentage is substantially higher than what is seen in industrialised nations, and it may be a consequence of lower haemoglobin levels at baseline as a result of other infections that are occurring at the same time (such as hookworm or tuberculosis). Those individuals who were female and had a lower baseline haemoglobin level, CD4 cell count, or body mass index were at a significantly greater risk of having

severe anaemia. The fact that taking cotrimoxazole did not turn out to be a contributory factor in the development of this adverse event is reassuring news.

In circumstances where laboratory capabilities are available, it may also be required to assess for alternate causes of anaemia, such as iron deficiency, medication-induced hemolysis (such as dapsone), or bleeding from the gastrointestinal tract. The following are some examples of these reasons: In resource-limited settings, the infection known as parvovirus B19, which is another suspected cause of anaemia in HIV-infected individuals, has only rarely been implicated. However, this may be due to diagnostic limitations being a factor, as parvovirus B19 has only rarely been implicated. According to the findings of a study that was carried out in Brazil, 62.8% of 261 consecutive HIV-infected patients tested positive for parvovirus B19 IgG. The findings of this study indicated that seronegative patients can be at danger of infection during epidemic periods even when they did not have the virus. If there is a suspicion of bone marrow invasion (for example, by lymphoma or Mycobacterium avium complex) or suppression (for example, due to drugs), a bone marrow biopsy might be advised if it is possible to perform the procedure. However, this only applies if the procedure can be performed.

The use of zidovudine could be even more problematic in areas with a high incidence of certain parasite coinfections that can induce anaemia, such as malaria or hookworm. These coinfections can make anaemia more likely to occur. These diseases are prevalent in areas where there is also a high incidence rate of HIV. It is

possible that tuberculosis, rather than parasites, has a more substantial role in the development of anaemia in environments with a high prevalence of HIV and TB coinfection. In this specific case, the therapy for tuberculosis may lead to an overall improvement in the patient's anaemia. [Case in point] It would be advantageous to undertake baseline testing on the patient using a spun haematocrit even if there are constraints on the kinds of laboratory procedures that can be performed. This is due to the fact that after beginning zidovudine treatment, a patient who already has anaemia has a greater chance of experiencing a worsening of the severity of their anaemia.

When effective antiviral medicine was made available for the first time, tales of individuals with body shape anomalies such as central fat accumulation and peripheral fat loss began to emerge. This condition is known as lipodystrophy. It was shown that some patients had pure lipoatrophy, while other patients had fat build up, and a third subset of patients had a mixed picture of both of these morphologic features. Because of this, the term "HIV-associated lipodystrophy syndrome" was coined to describe the condition. In addition, issues with glucose and lipid metabolism have been connected in some patients to the development of lipodystrophy.

Physical traits that are stigmatised, such as malar atrophy, may be especially harmful to patients' commitment to therapy and overall well-being in settings in which discrimination is still institutionalised. [Citation needed] [Citation needed] It is

possible that zidovudine and stavudine use, as well as didanosine use, albeit to a lesser level, are factors that contribute to lipoatrophy.

It is likely that extensive usage of medications such as stavudine, which are known to promote metabolic and body shape alterations such as lipoatrophy, is to blame for the high prevalence of lipodystrophy in environments with limited access to resources. The fact that the occurrence of this condition is rather common lends credence to the validity of this idea. According to the findings of two separate research projects carried out in Africa, the prevalence rates for stavudine ranged anywhere from 30 to 70 percent.

Because of how infrequently this family of antiretrovirals is used, there is currently minimal information on the function that PIs play in lipodystrophy syndromes in settings with restricted resources. According to the findings of studies conducted in industrialised nations, the consumption of protease inhibitors (PIs) can be a major contributor to lipid deposition

Stopping the use of whatever medication or other substance is causing the lipoatrophy is the one and only effective treatment for the condition. Despite this, there has been very little visible improvement in the patient's clinical condition, and there is no assurance that they will make a full recovery.

Hepatotoxicity is a possibility whenever an antiretroviral treatment is taken; however, the risk that a specific medication will cause harm to the liver differs from drug to drug. The non-nucleoside reverse transcriptase inhibitors (NRTIs) stavudine and didanosine have the highest propensity to cause hepatotoxicity. This is almost certainly because of the effect that these medications have on the mitochondria. When ritonavir is used as a low-dose pharmacologic booster of other medications, rather than when it is taken at its maximum dose, the drug is typically associated with a lower risk of causing liver damage. This is due to the fact that ritonavir in full doses is the most hepatotoxic of the PIs; nonetheless, this medication is used at such high levels very infrequently these days. Because nevirapine is a non-nucleoside reverse transcriptase inhibitor, it is more likely to cause hepatotoxicity in those who have detectable viremia than efavirenz is. This is because efavirenz is a nucleoside reverse transcriptase inhibitor (NNRTI). Patients who have achieved viral suppression and are switched to nevirapine in circumstances in which there is an abundance of resources often have a reduced likelihood of experiencing side effects as a result of utilising this medicine.

Because of the possible hepatotoxicity of nevirapine, certain high-risk populations are more prone to experience side effects. According to the findings of a study that was carried out in Mozambique with the participation of 146 pregnant women, patients whose CD4 cell counts were fewer than 250 cells/mm3 were more likely to have severe hepatotoxicity. This was one of the key takeaways from the research.

The research was carried out in the form of a prospective cohort (6 percent versus 0 percent). It has been determined that having a CD4 count of more than 400 cells/mm3 in men is a risk factor for nevirapine hepatotoxicity; however, at the present time, this discovery is less relevant in resource-limited settings because patients who fall into this category rarely meet current WHO or national guidelines for the initiation of ART. [Citation needed] Patients who fall into this category rarely meet current WHO or national guidelines for the initiation of ART. [Citation needed]

There is a connection between having two different types of viral hepatitis at the same time and having an elevated risk of hepatotoxicity from ART treatment. For instance, in a study that was carried out in Nigeria and involving 1564 patients, the risk for serious hepatotoxicity 24 weeks after the initiation of ART was 3.1 percent in patients coinfected with HBV, whereas the risk was only 0.5 percent in patients who only had HIV. This finding was found in comparison to the fact that the risk was only 0.5 percent in patients who only had HIV. There was no correlation seen between hepatotoxicity and either the baseline HBV DNA concentration or the presence of HBeAg. Coinfection with hepatitis C is another substantial risk factor; nevertheless, this diagnosis has a tendency to be more common in locations that have an abundance of available resources.

Two additional risk factors for liver injury due to antiretroviral therapy are the concurrent use of other hepatotoxic drugs (such as ant tuberculous agents or herbal remedies), as well as the existence of abnormalities of aminotransferases at baseline (ART).

Nevirapine and abacavir have been associated with hypersensitivity responses, which are uncommon but could be lethal. Nevirapine and abacavir are the drugs that are linked to the most incidences of hypersensitive syndrome, despite the fact that practically any treatment has the potential to set off the condition in some patients. Before beginning patients on these medications, the practitioner should evaluate the patient for any warning signals that might indicate an increased chance of experiencing this adverse response. This should happen before the patient actually starts using any of these medications for treatment.

It is also possible for common concurrent medications, such as ant tuberculous therapies, trimethoprim-sulfamethoxazole (TMP-SMX), beta-lactam antibiotics, and herbal remedies, to set off hypersensitivity reactions (HSR). As a consequence of this, it is extremely important to consider the potential that any medication could be the root of the problem.

Nevirapine is the non-nucleoside reverse transcriptase inhibitor that is recommended to patients the most frequently in settings where there is restricted access to medical resources (NNRTI). (32)

The earliest signs of hypersensitivity responses, also known as HSRs, often appear within the first 16 weeks of treatment. These reactions, which are also known as HSRs, can take the form of a rash, fever, hepatitis, or eosinophilia. A total of 1029 people in Uganda were monitored for a period of 19 months with the purpose of determining the incidence of nevirapine-induced hypersensitivity responses. The incidence was 1.7%. There was a single person who passed away as a result of these reactions. (21) After a HSR has been completed, you should not proceed with a nevirapine challenge.

Nevirapine hypersensitivity reactions are more likely to occur in women with a CD4 cell count of less than 250 cells/mm3 and in men with a CD4 cell count of less than 400 cells/mm3, respectively. There is a relationship between the pre-treatment CD4 cell count, the presence of HIV viremia, and the possibility that nevirapine may cause HSR. This relationship exists in all patients. Even if the patient's CD4 count rises throughout the course of treatment to more than 250 cells per mm3, the nevirapine does not need to be discontinued in its administration to the patient. When viral suppression has already been achieved, the likelihood of an allergic reaction arising is significantly reduced. Therefore, switching a patient to nevirapine because of an adverse event associated with another treatment is far less likely to result in HSR if viral suppression has already been established. (33) It is recommended that a lead-in dose approach be utilised (for instance, taking 200 milligrams once day for a period of 14 days, and then increasing the dosage to 400

milligrams twice daily) in order to reduce the likelihood of having unfavourable side effects.

Abacavir: The presence of the HLA-B*5701 allele is associated with a significantly increased risk of a hypersensitive reaction (HSR) to abacavir, whereas the absence of this allele is associated with a significantly reduced risk of an immunologic reaction.

In many industrialised countries, testing for HLA-B*5701 has become standard practise. On the other hand, such testing is relatively unusual in settings with limited access to resources. It is fortunate that this haplotype is rare among Africans; as a result, it appears that abacavir can be used very securely in this population as long as careful monitoring is conducted. However, this does not negate the fact that it is important to perform such monitoring. Only two percent of the 599 patients in Uganda who were randomly assigned to receive abacavir experienced a HSR, which is a much lower percentage compared to the four point seven percent who were treated with nevirapine. (34)

Nephrotoxicity — There is reason for concern that the incidence of nephrotoxicity may increase when tenofovir, a nucleotide reverse transcriptase inhibitor, becomes more widely available in Sub-Saharan Africa. This is a cause for concern because it may increase the risk of kidney damage. Because of this, there is a greater chance that there will be a rise in the incidence of nephrotoxicity. Patients who already had

diabetes or hypertension before beginning therapy with tenofovir were more likely to develop renal insufficiency as a side effect of using tenofovir.

An observational research of 3316 treatment-naive patients in Zimbabwe and Uganda found that severe renal dysfunction at 96 weeks was uncommon. This was the case despite the high incidence of baseline mild to moderate renal insufficiency and the common use of tenofovir (74 percent). The improvement in baseline glomerular filtration rate that was seen with regimens that did not contain tenofovir was only minor. (35)

This discovery provides a great deal of solace when one considers that, before beginning treatment, 45 percent of the patient group had mild renal insufficiency and 7 percent of them had substantial renal insufficiency.

Patients in a number of different countries who have both HIV and HBV coinfection are routinely given tenofovir as a treatment option. South Africa and Nigeria are also examples of these countries. Tenofovir is effective against hepatitis B in two different ways.

Zidovudine therapy has been linked to an increased risk of side effects, one of which is a condition known as myopathy. It frequently presents itself as a slow onset of generalised muscle fatigue or a weakening of the muscles. Patients have to go through extensive history taking as well as physical examinations so that they can be monitored for any myopathy that may be related to zidovudine use. If laboratory monitoring is available, a creatine kinase test should also be performed on suspected

instances; if the test results show that the creatine kinase level is increased, a muscle biopsy may be performed. Creatine kinase is an enzyme that is produced by muscles. Zidovudine medication must be terminated promptly if there is even the tiniest likelihood that this diagnosis is accurate.

Rash is a common adverse reaction that can occur in patients taking non-nucleoside reverse transcriptase inhibitors (NNRTIs), such as efavirenz and nevirapine. In the course of a case-control research that was carried out in Thailand, a comparison was conducted between patients who developed a rash after initiating antiretroviral therapy (ART) that contained nevirapine and patients who did not develop a rash. (36) Both a previous history of drug allergy and a low body weight were factors that raised the probability of getting a rash as a reaction to the medication. Increasing CD4 cell counts was also associated with an increased risk of getting a rash (the odds ratio increased by 1.2 for every increment of 50 cells/mm3 in the total number of cells).

Even if the patient develops a rash, it is typically safe to continue the therapy with nevirapine or efavirenz as long as the patient is constantly followed. However, there are some cases in which it is not safe to continue the medication. It is essential, however, to differentiate between a self-limiting mild drug rash and a life-threatening, systemic reaction, such as Stevens-Johnson Syndrome (SJS) or hypersensitivity reaction (HSR), which have both been described in association with nevirapine and abacavir. A self-limiting mild drug rash is one that clears up on its

own, while a life-threatening, systemic reaction can be fatal. This differentiation is of the utmost importance. (37) Diagnostic of Stevens-Johnson syndrome is a rash that is accompanied by mucosal involvement (such as in the eyes or mouth), whereas constitutional symptoms, fever, and eosinophilia are indicative of hypersensitivity reaction (HSR).

Other potential causes of rashes, such as medications, concurrent infections (for instance, secondary syphilis), or an increase of eczematous rashes or eosinophilic folliculitis during ART-associated immune reconstitution, should also be taken into consideration.

Incompatibilities that impact the gastrointestinal tract — Diarrhea is a common side effect of taking protease inhibitors, and this effect may or may not resolve on its own. If the diarrhoea does not stop after treatment, it is especially crucial to rule out the possibility of opportunistic infections in patients who have significant immunosuppression. One example of an opportunistic infection is Mycobacterium avium intracellular.

Antiretroviral medication is associated with a number of adverse effects, including dyslipidaemia and metabolic disorders (ART). These adverse consequences include altered lipid profiles in the fasting state as well as decreased glucose tolerance.

(38) Within the NRTI class of medications, the likelihood of stavudine and zidovudine being associated with dyslipidaemia is higher than the likelihood of abacavir or tenofovir being associated with the condition. Nevirapine, which is associated with favourable increases in HDL-c, is less likely to produce

dyslipidaemia than the drug efavirenz, which has a higher risk of causing the condition. These two antiretroviral medications are both considered NNRTI medicines, which is a class of antiretroviral medication.

At 12 and 24 months after the start of antiretroviral treatment, the lipid profiles of 374 HIV patients in Uganda who were using stavudine, lamivudine, and nevirapine were analysed. The vast majority of these patients were taking all three of these medications (ART).

(39) After a period of 24 months of therapy with nevirapine, patients saw significant and proportionately bigger improvements in HDL-cholesterol levels than increases in total cholesterol or LDL-c levels. This was the case even though total cholesterol and LDL-c levels also increased. These results are almost certainly linked to the medication.

Incidences of conditions associated with cardiovascular disease — It is probable that traditional cardiovascular risk factors are on the rise in many parts of the world where resources are scarce but where cardiovascular disease is prevalent nonetheless. According to the World Health Organization (WHO), cardiovascular illnesses (which include coronary artery disease and cerebrovascular disease) are to blame for 15 percent of all deaths that take place in countries with poor incomes. This percentage is a considerable amount greater than the 5.7% of fatalities that are attributed to HIV/AIDS. (40) In South Africa, a survey was administered to persons living in both rural and urban areas to study the impact that urbanisation has had on people's nutritional status as well as their general health. (41) The findings of this

study showed that people who lived in urban areas had significantly higher levels of LDL-c and total cholesterol, significantly higher rates of obesity, and significantly higher proportions of people who had elevated systolic blood pressure than people who lived in rural areas. All of these factors contributed to an increased risk of cardiovascular disease.

Despite the fact that abacavir and didanosine have been associated with a significantly increased risk of myocardial infarction These associations continue to be controversial in a number of studies that were carried out in settings with an abundance of resources, and the processes that lie under the surface have not been completely explained. (42)

To evaluate the impact that antiretroviral medications have on the risk of cardiovascular disease in low-income nations that are undergoing changes in lifestyle as a result of industrialization, additional research is required.

Taking additional safety measures while carrying a child In contexts with limited resources, the proportion of women of reproductive age who are affected by HIV infection is disproportionately higher. Taking these precautions, especially during pregnancy, is of the utmost importance. There is a high prevalence of pregnancies due to the fact that there is a lack of effective contraception that is readily available, as well as because there are strong social pressures to procreate. Both of these factors contribute to the fact that many infected men and women continue to engage in sexual activity. (43) There are other places where a more in-depth discussion of

the teratogenic potential of other antiretroviral medicines as well as the use of nevirapine in pregnancy for the aim of maternal health or the prevention of mother-to-child transmission may be found. Efavirenz is a medicine that falls within the Pregnancy Category D category, meaning that it should be avoided by women who are either planning to get pregnant or who have a possibility of becoming pregnant in the future. This categorization was arrived at as a result of the neural tube defects that were identified in investigations involving monkeys as well as in a few clinical cases involving humans.

INFLAMMATORY IMMUNODEFICIENT SYNDROME

The term "immune reconstitution inflammatory syndrome" (IRIS) refers to a group of inflammatory illnesses that are associated with a paradoxical exacerbation of pre-existing infectious processes in HIV-infected patients following the beginning of highly active antiretroviral therapy. Patients with IRIS have an exacerbation of pre-existing infectious processes in their bodies after beginning HAART (HAART).

(44) Pre-existing infections in individuals who have IRIS may have been previously diagnosed and treated, or they may have been subclinical and were later unmasked by the host's regained capacity to mount an inflammatory response. Either way, these infections may have been present in the individual before they were diagnosed with IRIS. Alternately, the host may have regained the ability to mount an inflammatory response, which may have prevented these infections from being detected.

(45) Systemic or local inflammatory reactions may appear at the site or locations of the underlying illness if immune function improves rapidly following the beginning of HAART treatment. These reactions could affect the entire body or just a certain part of it. It just depends. In most cases, this inflammatory reaction will go away on its own, particularly if the illness that is causing it is successfully treated. On the other hand, there is always the possibility of long-term effects and catastrophic outcomes, particularly in cases when brain structures are compromised.

It is generally accepted that in order to make a diagnosis of IRIS, there needs to be a worsening of a recognised (also called "paradoxical") or unrecognised (also called "unmasking") pre-existing infection in addition to an improvement in immune function. This is required in order to meet the criteria for IRIS. The process of doing so is referred to as "unmasking" IRIS. It is required to notice the majority or all of the following qualities in order to arrive at an appropriate diagnosis, as they are as follows:

The presence of HIV infection in association with a low CD4 count prior to treatment (often less than 100 cells/microl). In regard to this overarching principle, there is a significant and noteworthy deviation in the form of tuberculosis. Those individuals who have a CD4 count that is higher than 200 and who have previously been infected with M. tuberculosis have an increased chance of getting IRIS.

●A positive virologic and immunological response to ART.

Following an appropriate examination for the clinical presentation, the lack of evidence of a drug-resistant illness, bacterial superinfection, drug allergy or other adverse drug reactions, patient noncompliance, or lower medication levels due to drug-drug interactions or malabsorption is considered acceptable.

The presence in a patient's clinical presentation of symptoms that are characteristic of illnesses linked with inflammation

There is a relationship between the first day of HAART treatment and the first day that clinical symptoms of the disease appear.

NATIONAL AIDS CONTROL PROGRAMME

Antiretroviral medication, also known as ART, has been provided to patients completely free of charge by the National AIDS Control Programme (NACP II) ever since April of 2004. There are around three hundred and fifty active antiretroviral therapy (ART) centres in India, which are home to more than five hundred thousand patients who are presently undergoing antiretroviral medication (ART). In the private sector, there are around 30,000 patients who are eligible to receive free antiretroviral therapy each year. (4) As a direct result of this, the number of deaths that can be directly attributed to AIDS has been continuously decreasing, and it is believed that antiretroviral medication has been responsible for the preservation of

1.5 lakh lives as of 2011. (2) The number of ART centres is undergoing a steady increase that will be carried out in phases as part of a staged expansion plan.

MORTALITY IN HIV / AIDS

The majority of HIV-positive people who are receiving adequate treatment with antiretroviral medication (ART) have HIV-RNA levels that are frequently undetectable using the tests that are currently available. This indicates that the prevalence of AIDS-defining events is relatively low in these people. In spite of receiving appropriate treatment with ART, it has been observed that these individuals have a greater mortality rate in comparison to controls of the same kind. It is not possible for a single variable, such as the CD4 count, to explain this occurrence. Studies such as the SMART trial point to potential causes such as inflammation caused by HIV, which is connected with an increased risk of hypercoagulability, and organ system damage caused by ageing. Both of these factors have been linked to an increased risk of bleeding. ART (continuous antiretroviral therapy) or therapy guided by CD4 T cell counts were the two treatment options that were randomly assigned to HIV patients who were infected with HIV and participated in this study. When compared to participants who received continuous therapy, those who were randomly allocated to undergo interrupted therapy had a significantly higher risk of both morbidity and mortality. Participants who received continuous therapy did not have this significantly increased risk. It was found that abruptly stopping ART regimens was associated

with a rapid increase in inflammatory and coagulation-related indicators, in addition to an increased risk of death, AIDS, and cardiovascular disease (CVD). The pathways that link HIV replication to inflammation, coagulopathy, and the progression of disease are still, for the most part, not fully understood. [Case in point:] [Case in point:] [Case in point:] [C (47) A growing body of evidence suggests that the risk of serious non-AIDS conditions, such as cardiovascular disease (CVD), renal or hepatic disease, and non-AIDS defining malignancies, is increased in people with HIV infection when compared to matched controls. These conditions include cardiovascular disease (CVD), renal or hepatic disease, and non-AIDS defining malignancies. These conditions include cardiovascular disease (CVD), renal or hepatic disease, and cancers that are not defined by AIDS. (6) A number of clinical experiments have been carried out in order to investigate the degree of connection that exists between non-traditional markers of inflammation and traditional markers of inflammation. The goal of these experiments is to monitor patients who have potentially modifiable risk factors.

INDEX OF THE VETERANS AGING COHORT STUDY (VACS)

The Veterans Aging Cohort Study (VACS) is a longitudinal, prospective, multi-site observational study of HIV infected and uninfected patients who were assessed in infectious disease and general medical clinics at Veterans Administration Medical

Centers. The study is being conducted by the Veterans Health Administration (VAMC).

(49) The Veterans Aging Cohort Study (VACS) Risk Index was designed using a simplified point system with the purpose of forecasting mortality rates in HIV patients who have been receiving treatment for one year. The index's target population is HIV patients. It was intended to take into account all of the potential interactions that HIV disease, comorbidities, substance addiction, and adverse medication reactions related to therapy could have on the outcome of HIV-infected patients. [Citation needed] (7) Given that the majority of patients would be receiving ART for extended periods of time, an on-treatment index was deemed to be more useful to health professionals and HIV positive persons, for the aim of monitoring prognosis after the onset of medication. [Citation needed] After the treatment had been initiated, there was also the possibility that previously established relationships between known biomarkers and mortality would shift as a result of the intervention. This was a potential outcome. (5) It was initially developed in HIV-positive veterans of the United States Armed Forces, and then it was validated in separate cohorts from the United States and Europe that were participants in the Antiretroviral Therapy Cohort Collaboration. (6) It is currently being studied in a number of other countries (ART-CC). (5) A cohort of more than 33,000 HIV-infected veterans was used to collect data for the purpose of developing prognostic indices. During the course of these veterans' normal clinical visits, beginning with the first visit, data on their inpatient and outpatient diagnoses, laboratory findings, and pharmacy

dispensations were recorded. The cohort was utilised in the construction of the indexes. The Veterans AIDS Care System (VACS) encompassed all HIV-positive Veterans who were already getting care from the Veterans Administration (VA). The development and validation datasets were combined in order to analyse index performance within relevant patient subgroups. This was done by pooling the datasets. Women, people whose HIV-1 RNA levels were lower than 500 copies/ml, and patients who had both HIV and Hepatitis C infections were divided into these categories (HCV). (5)

The VACS index takes into account a variety of different prognostic markers, some of which were the individual's age in years, CD4 count, HIV-1 RNA, haemoglobin, aspartate transaminase (AST) & alanine transaminase (ALT) levels, platelets, creatinine, and HCV status.

Following the dissection of the separate components of the VACS index into their respective constituent parameters, two composite indicators of hepatic injury (FIB-4) and renal injury (eGFR) were manufactured as a result of the data obtained from these parameters. Age, aspartate aminotransferase level, alanine aminotransferase level, and platelet count are the variables that are taken into consideration in the calculation of the fibrosis index (FIB-4). This index has been demonstrated to be a reliable indication of fibrosis in the liver. When a lower cut off value of 1.45 was used, there was a 90% likelihood that an individual with a FIB-4 score of less than 1.45 would have an inaccurate prediction of advanced fibrosis. (Ishak fibrosis score 4-6, which encompasses early-stage bridging fibrosis to cirrhosis.) If, on the other

hand, the FIB-4 score was greater than 3.25, this would indicate advanced fibrosis with a specificity of 97% and a positive predictive value of 65%. This formula was validated by using a patient cohort that contained at least seventy percent of patients who achieved outcomes that were either lower than or equal to 1.45.

The findings of the nine distinct component criteria that make up the VACS Index are combined into a single score by the VACS Index, which helps to reflect the patient's illness burden in a more precise manner. Composite indices, like the VACS index, have a number of major advantages over individual biomarkers that cannot be found in any other context. These advantages cannot be replicated using any other method. To begin, a score gives the doctor an overall impression of the patient's condition and has the potential to be used to make predictions regarding the development of the patient's clinical condition, such as an increased or decreased risk of morbidity or mortality. In addition, a score provides the patient with an overall impression of the doctor's assessment of their condition. Although it is possible to generate a prognosis by entering distinct numbers into a risk calculator, the convenience of interpreting a single number makes the usage of that single number more appealing. This is something that should be kept in mind by both the patient and the physician. Second, the levels of concern that are triggered by these variables that are routinely monitored have frequently been shown to be far greater than the levels that are identified by the index. The method of evaluating the cumulative impact of a number of biomarkers can be of assistance to physicians in

better comprehending the relevance of less severe abnormalities that may nonetheless be connected with disease. (5)

From the Literature

The Christian Medical College (CMC) in Vellore has been very active in providing HIV care as well as training for medical professionals ever since the beginning of the HIV epidemic in India in the year 1986. Medicine Unit I and Infectious Diseases currently provide medical care to more than 44,118 outpatients and 2217 hospitalised patients on an annual basis. An interdisciplinary infectious disease (ID) clinic provides comprehensive medical care to around 3873 HIV patients each year. This type of clinic also provides services in the areas of paediatrics, dermatology, STD, and social work. In addition, the division is responsible for organising get-togethers of support groups for those who test positive for HIV. These gatherings not only give patients and their families the chance to receive emotional support from one another, but they also contribute to the financial well-being of the facility. The Obstetrics and Gynecology department of the hospital runs a programme called the Prevention of Parent to Child Transmission (PPTCT). Through this programme, couples who go to the antenatal clinic have the opportunity to receive counselling on how to prevent the transmission of HIV to their children. Women who are HIV positive can get therapies that are geared toward lowering the likelihood that the virus will be passed on to their children. Antiretroviral therapy (ART) drugs can

now be provided at no cost to HIV-positive individuals thanks to the collaborative efforts of ACTFID (ACC-CMC Trust for Infectious Diseases) and NACO. (47)

AIM OF THE STUDY

To predict morbidity and mortality in HIV infected individuals who attended the ART center under NACO ART regimen.

To use this data to design and implement effective intervention to improve the outcome

MATERIALS AND METHODOLOGY

Study design : Prospective and retrospective study

Study setting: ART center ,Madras Medical College

Study population :

Inclusion criteria

1. Patients above 18 years of age
2. PLHIV started on first line NACO ART regimen from ART clinic one year back

Exclusion criteria

1. Age less than 18 yrs.
2. PLHIV started on ART before or after the specified period
3. PLHIV started on non NACO ART

Sample size (n) =Z2pq/d2

p= prevalence-29.7

d=Absolute precision (10)

Non responders-10%

Sample size = 1.96*1.96*8.8*100-8.8%10*10

=123

Sample size : 123

Approximately =125

Data entry and analysis

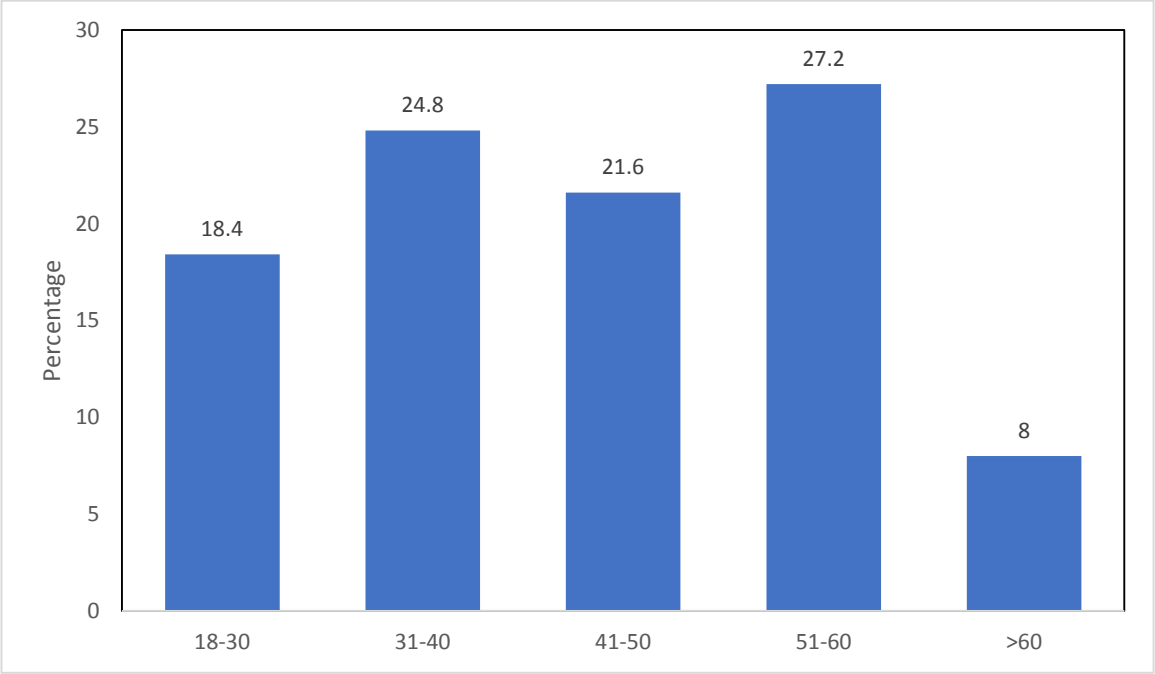
Data collected was entered in Microsoft excel and analyzed using SPSS version 24.0

RESULTS

Table 1: Distribution of age among the study participants (N=125)

Slno	Age	Frequency	Percentage
1	18-30	23	18.4
2	31-40	31	24.8
3	41-50	27	21.6
4	51-60	34	27.2
5	>60	10	8
Mean±SD		43.66±13.01	18 to 65

Figure 1: Distribution of age among the study participants (N=125)

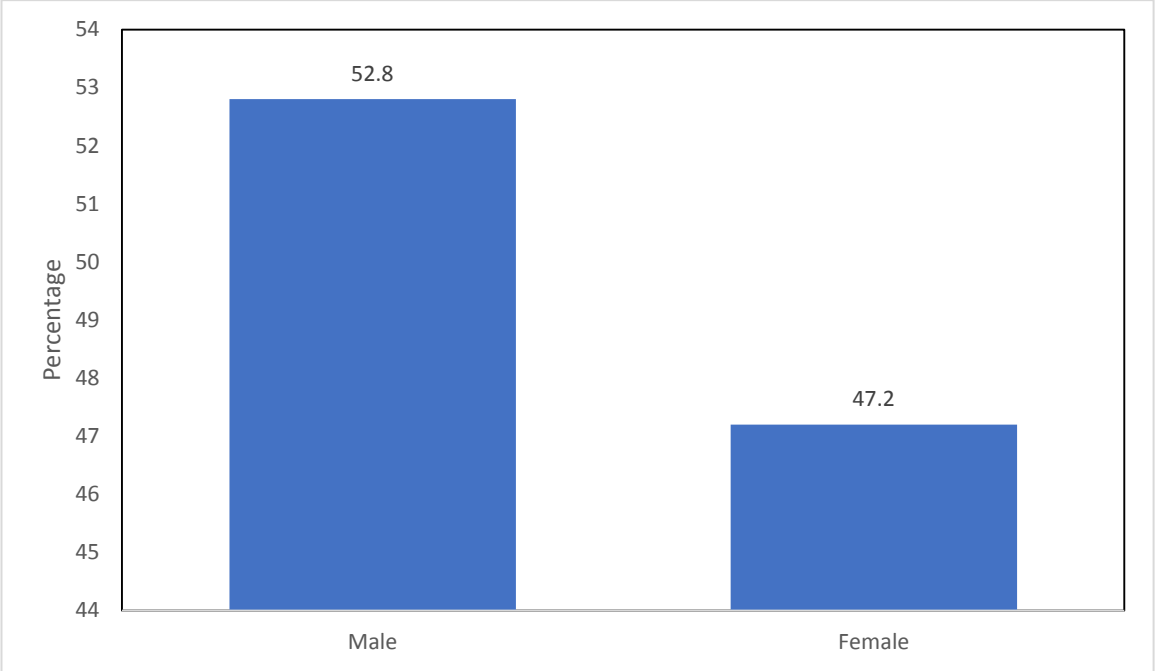


Around 18.4% were in the age group of 18-30 years, 24.8% 31-40 years, 21.6% 41-50 years, 27.2% 51-60 years and 8% more than 60 years.

Table 2: Distribution of gender among the study participants (N=125)

Slno	Gender	Frequency	Percentage
1	Male	66	52.8
2	Female	59	47.2

Figure 2: Distribution of gender among the study participants (N=125)

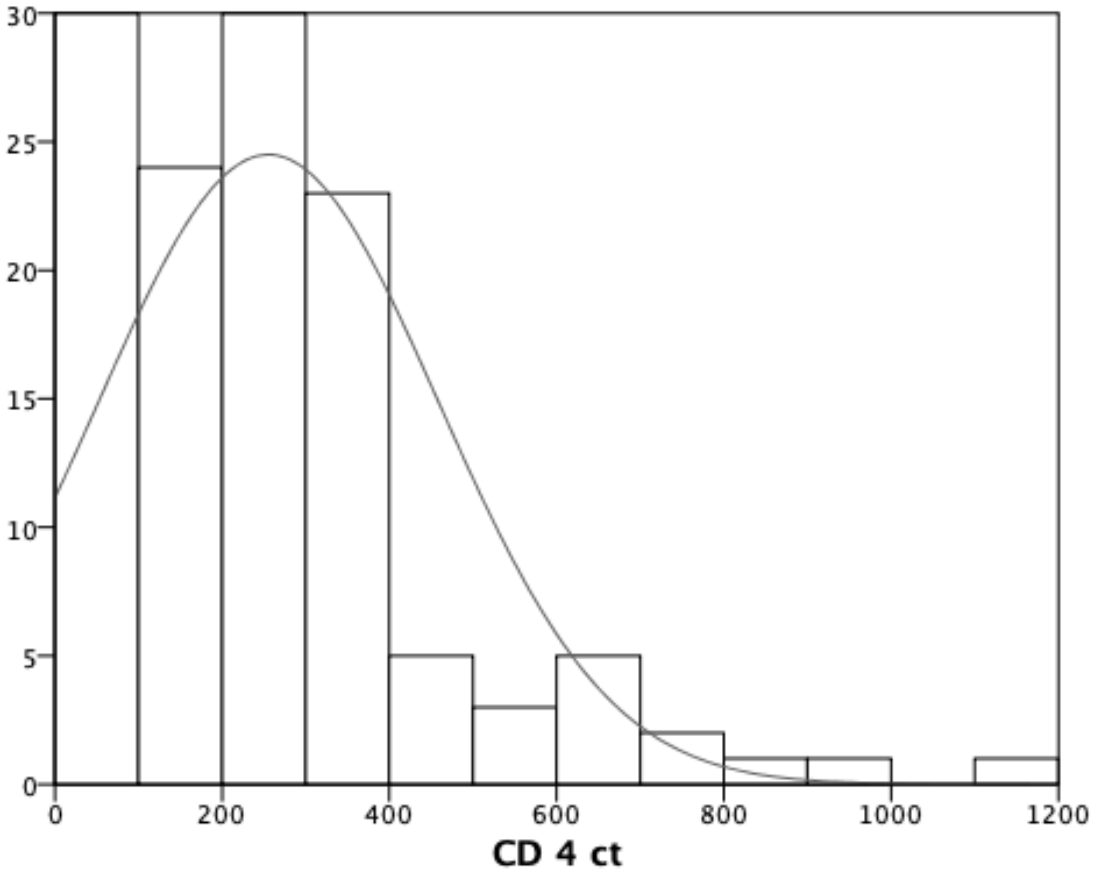


Around 52.8% were males and 47.2% were females.

Table 3: Distribution of CD4 count among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	CD4	255.36	230.00	107.00	230.00	322.50

Figure 3: Distribution of CD4 count among the study participants (N=125)

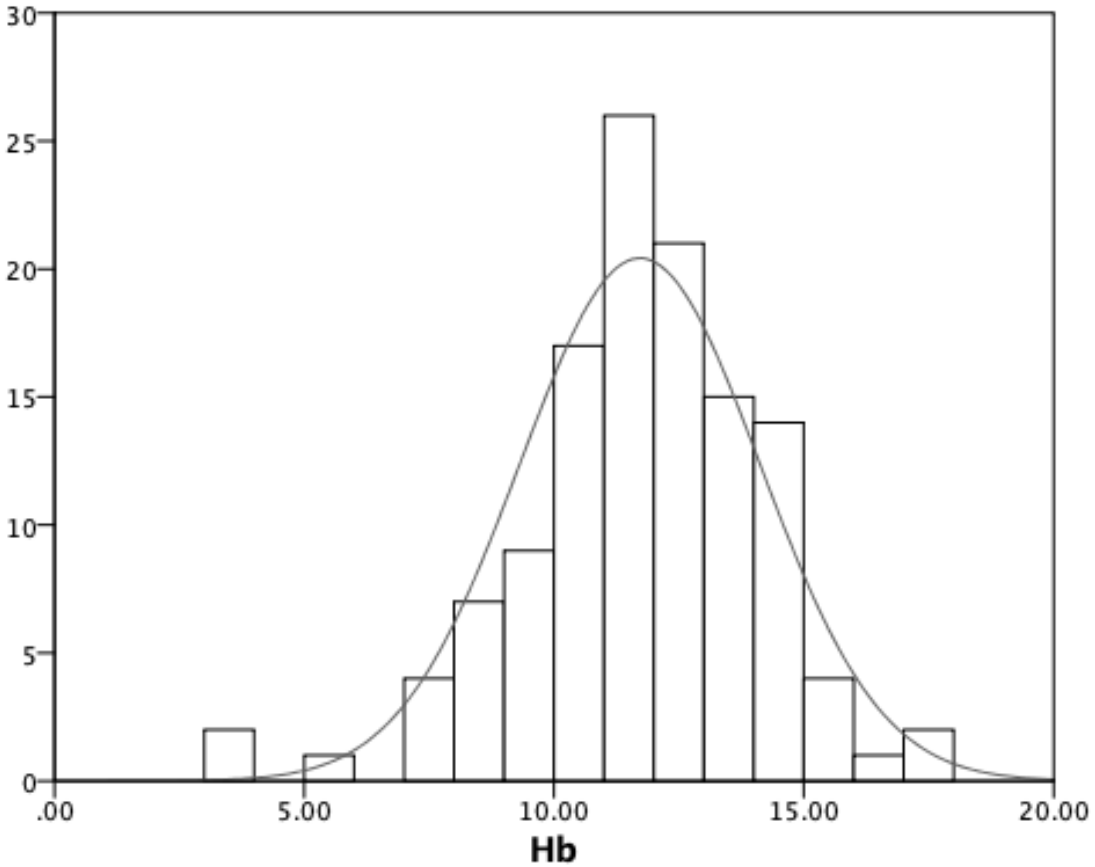


The median CD4 count is 230.00 (107.00 to 322.50).

Table 4: Distribution of hemoglobin among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	Hemoglobin	11.72	11.80	10.50	11.80	13.30

Figure 4: Distribution of hemoglobin among the study participants (N=125)

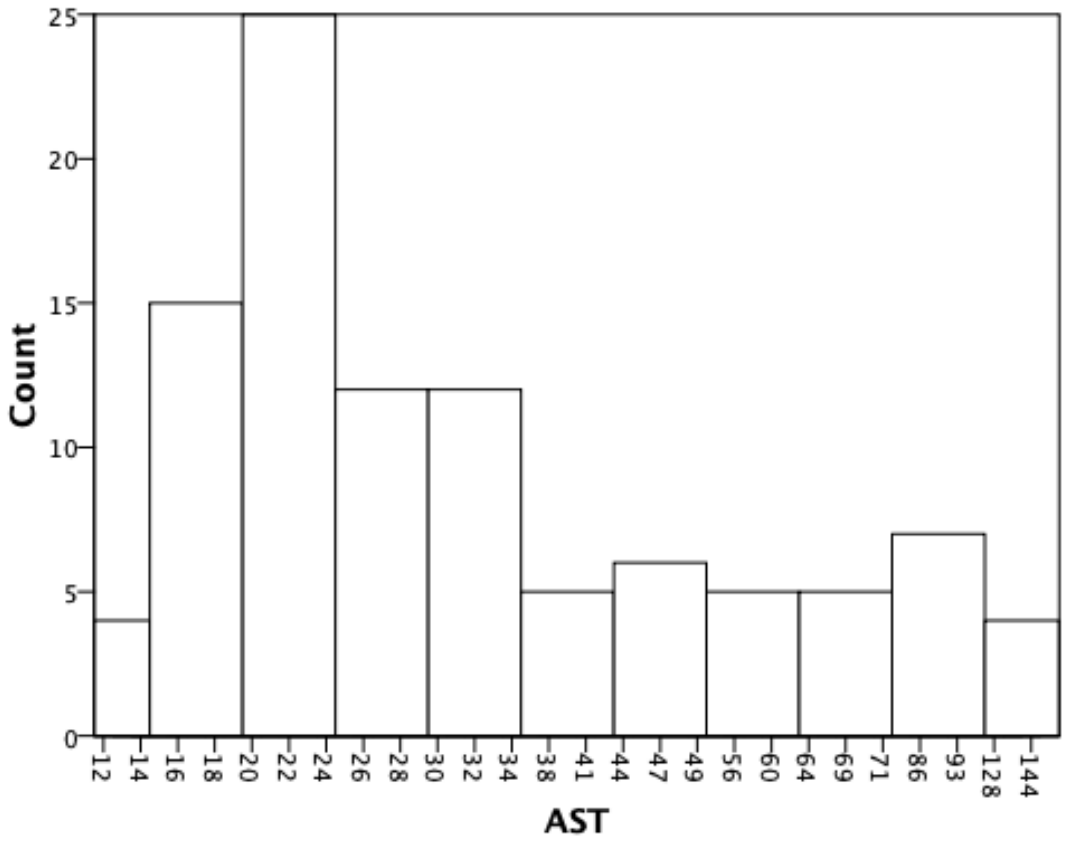


Median hemoglobin 11.80 (10.50 to 13.30).

Table 5: Distribution of AST among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	AST	38.51	27.00	20.25	27.00	44.75

Figure 5: Distribution of AST among the study participants (N=125)

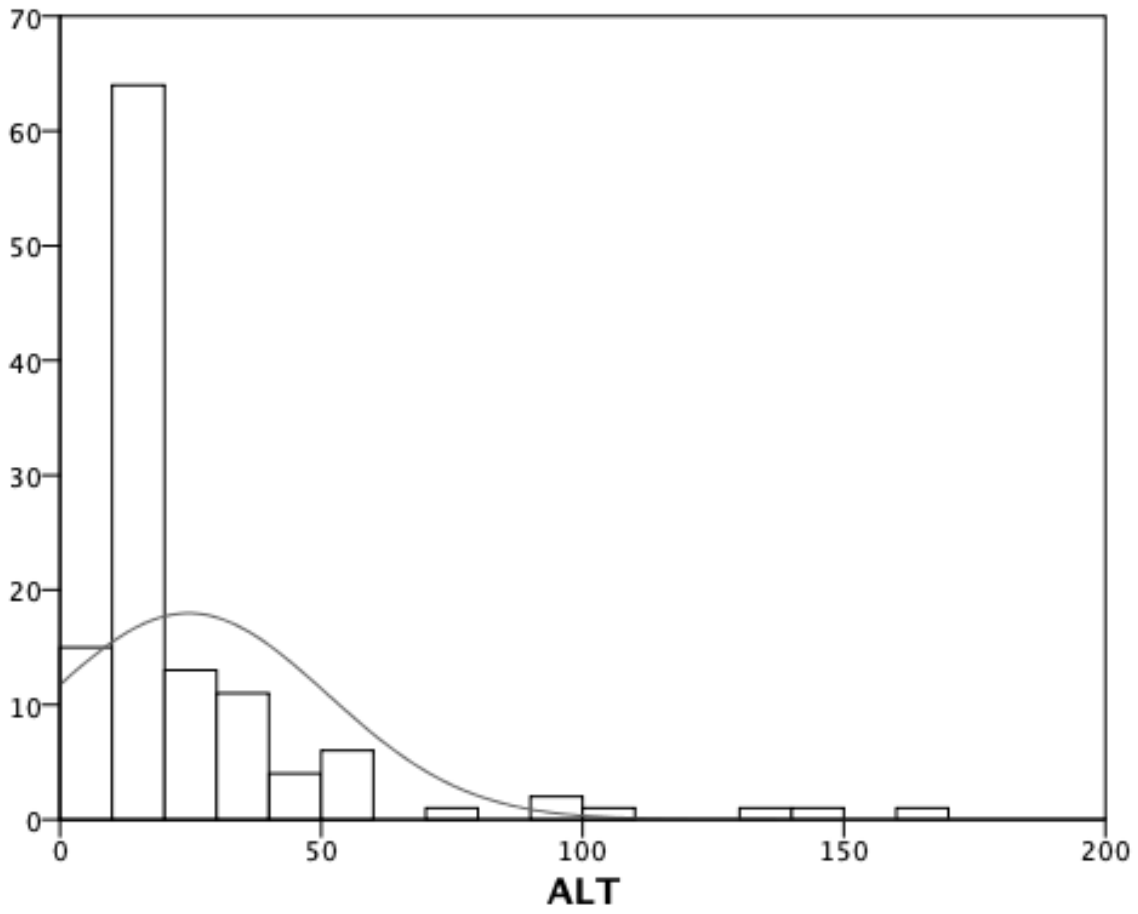


Median AST levels were 27.00 (20.25 to 44.75).

Table 6: Distribution of ALT among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	ALT	24.58	14.50	11.00	14.50	27.75

Figure 6: Distribution of ALT among the study participants (N=125)

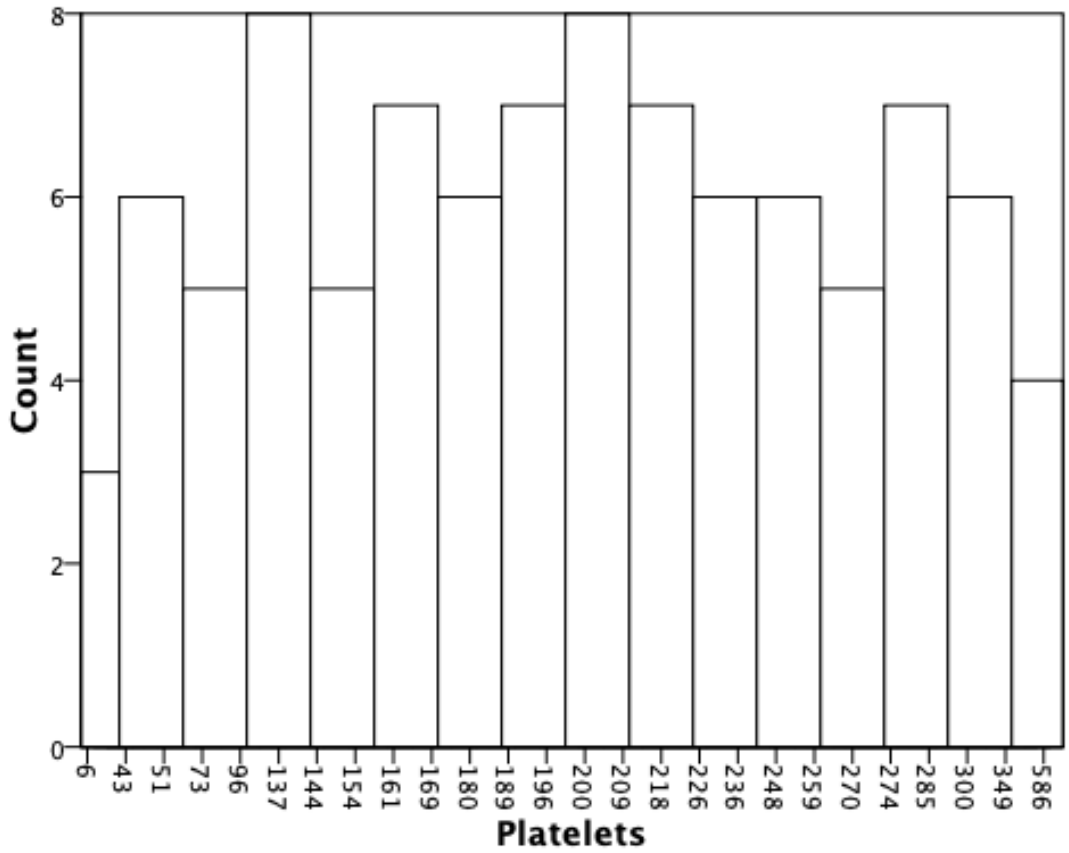


Median ALT levels were 14.50 (11.0 to 27.25).

Table 7: Distribution of platelets among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	Platelets	203.66	103.22	145.50	199.00	258.50

Figure 7: Distribution of platelets among the study participants (N=125)

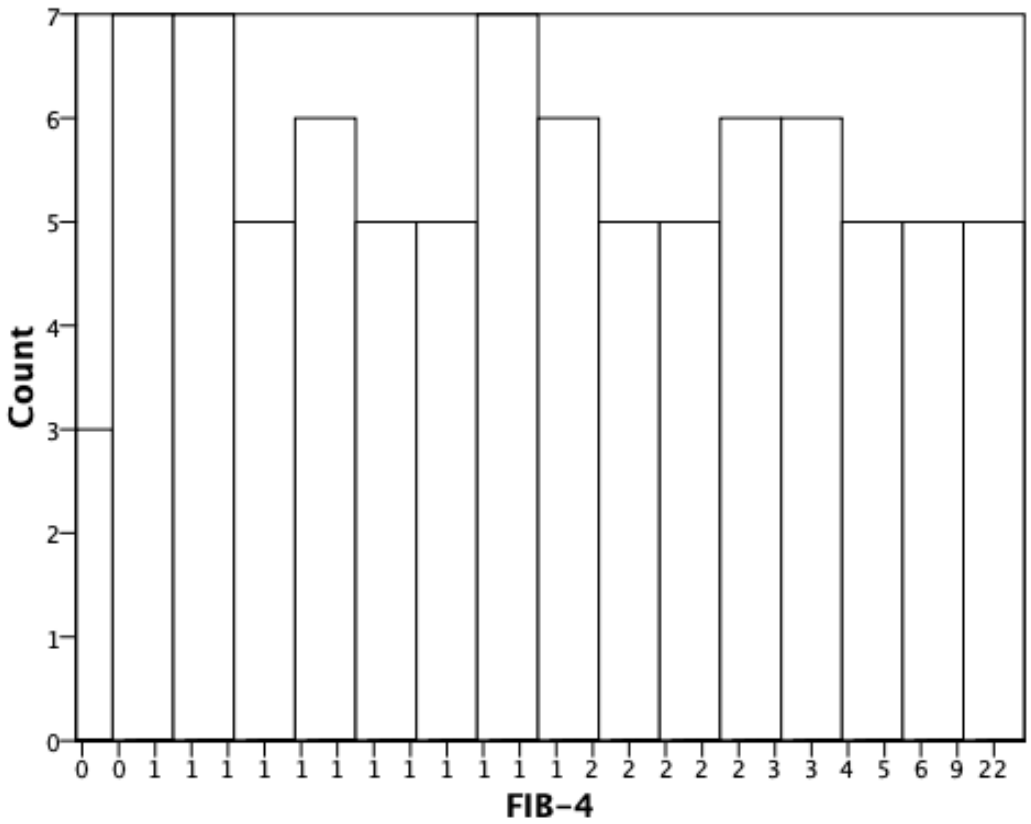


Median platelets were 103.22 (145.0 to 258.50).

Table 8: Distribution of FIB-4 among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	FIB-4	3.40	7.72	0.88	1.28	2.57

Figure 8: Distribution of FIB-4 among the study participants (N=125)

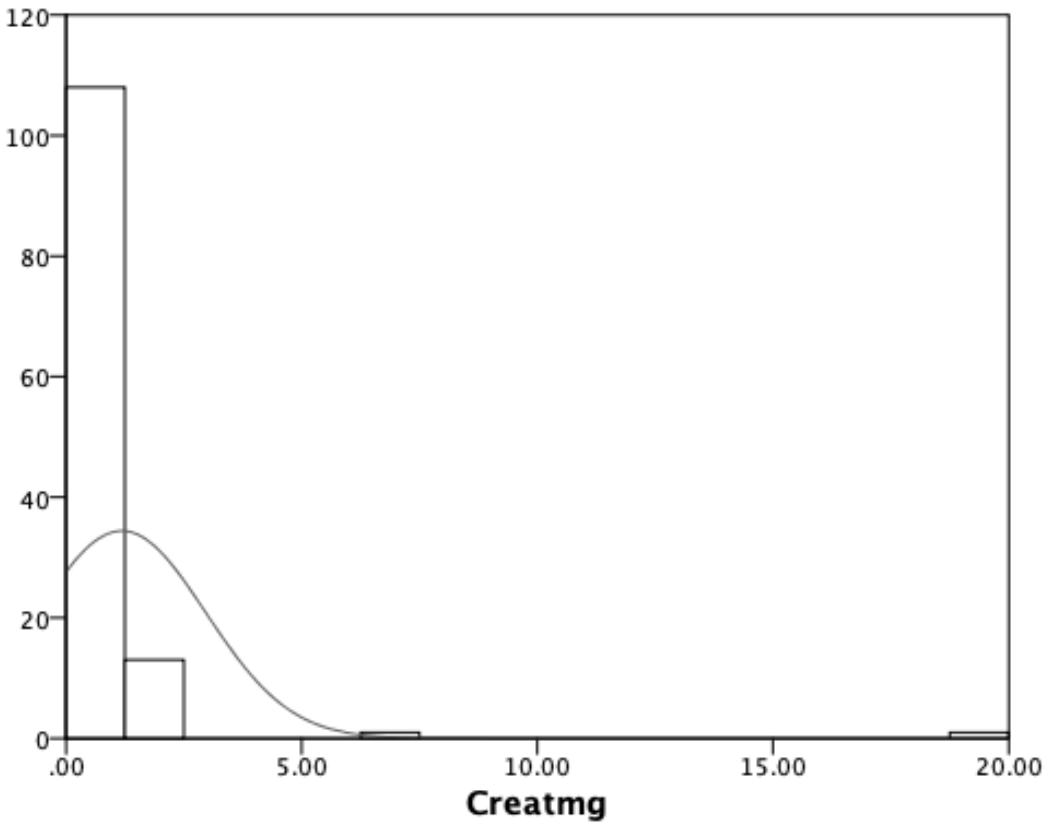


Median FIB-4 levels were 7.72 (0.88 to 2.57).

Table 9: Distribution of Creatinine mg among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	Creatinine mg	1.18	1.78	0.82	0.96	1.12

Figure 9: Distribution of Creatinine mg among the study participants (N=125)

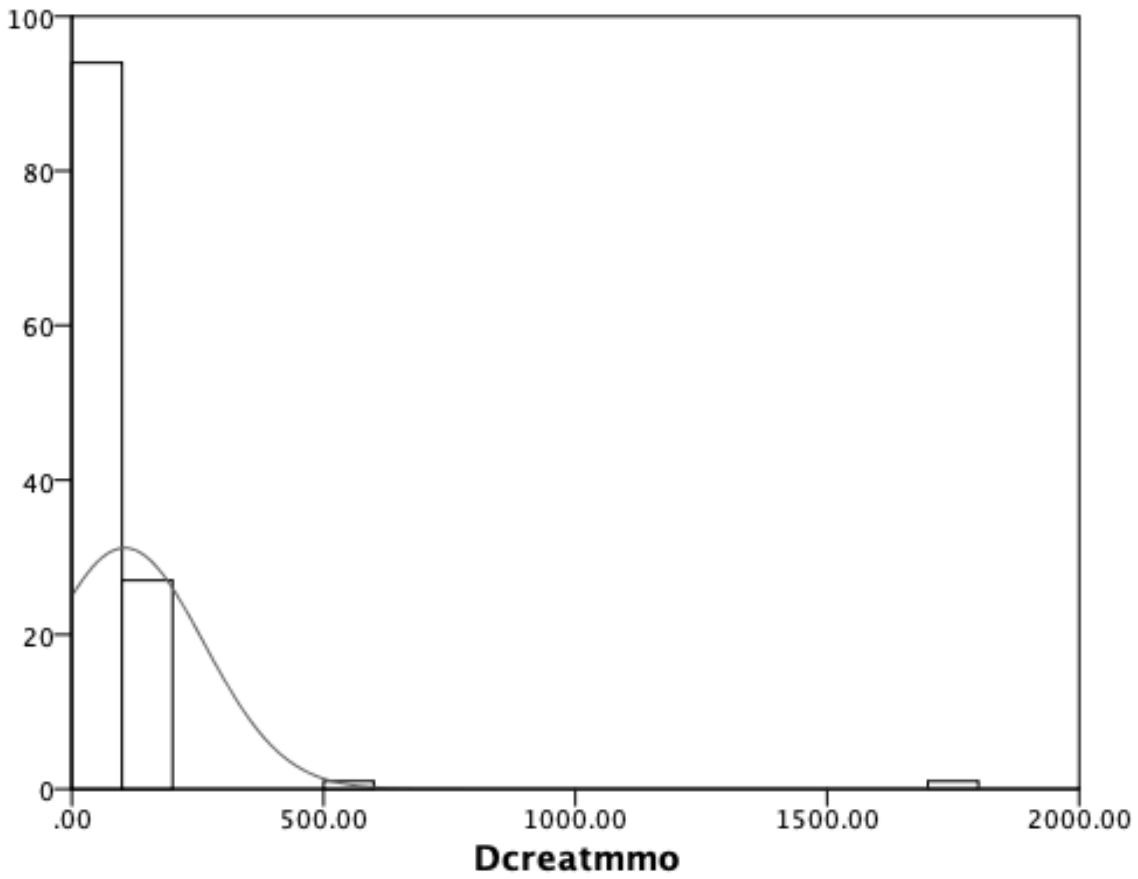


Median creatinine levels were 1.78 (0.82 to 1.12)

Table 10: Distribution of Creatinine mmol among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	Creatinine mmol	105.03	157.27	72.48	84.86	99.00

Figure 10: Distribution of Creatinine mmol among the study participants (N=125)

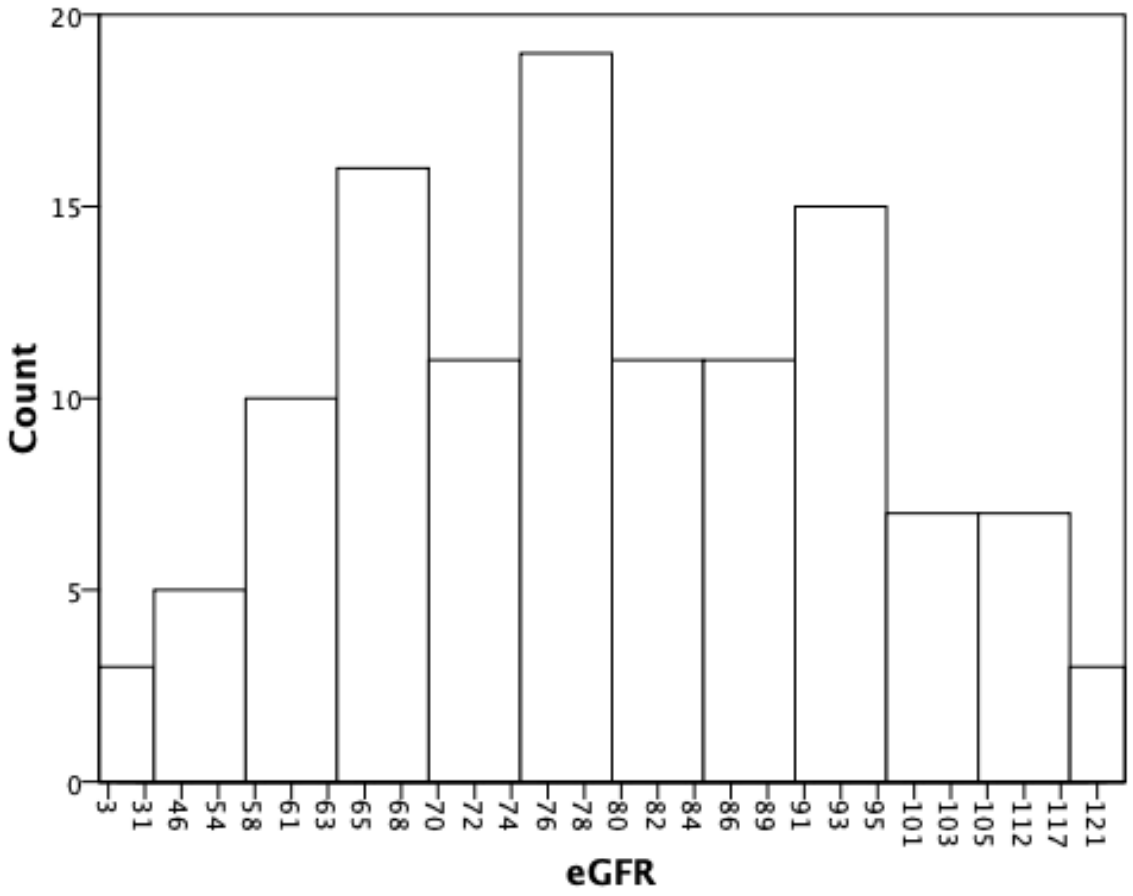


Median Creatinine mmol were 157.27 (72.48 to 99.00)

Table 11: Distribution of eGFR among the study participants (N=125)

Slno	Variable	Mean	Median	25	50	75
1	**e**GFR	79.03	19.61	68.00	78.00	91.00

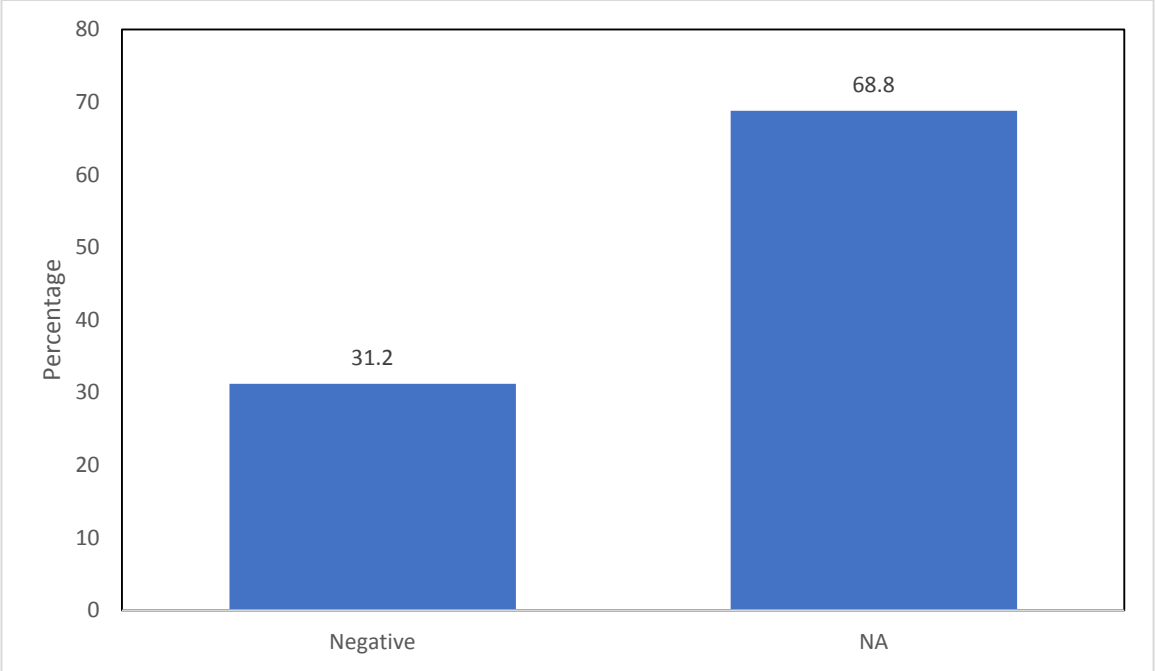
Figure 11: Distribution of eGFR among the study participants (N=125)



Median eGFR levels were 19.61 (68.00 to 91.00).

Table 12: Distribution of HCV among the study participants (N=125)

Slno	HCV	Frequency	Percentage
1	Negative	86	31.2
2	NA	39	68.8

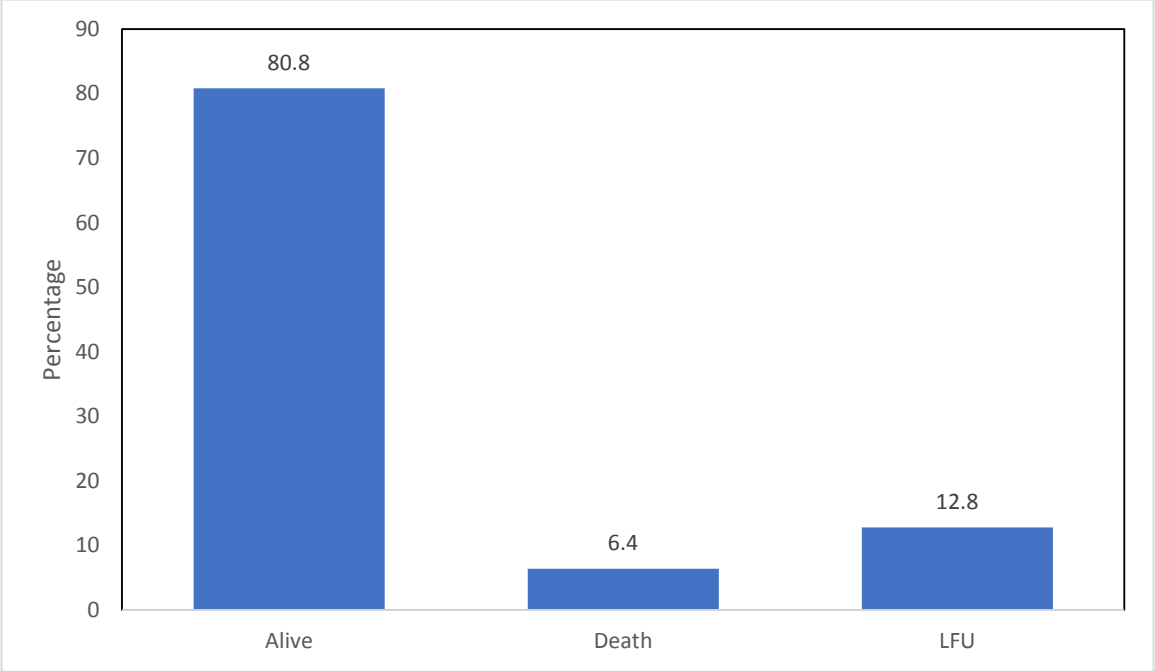


Around 31.2% were HCV negative.

Table 13: Distribution of outcome among the study participants (N=125)

Slno	Outcome	Frequency	Percentage
1	Alive	101	80.8
2	Death	8	6.4
3	LFU	16	12.8

Figure 13: Distribution of outcome among the study participants (N=125)

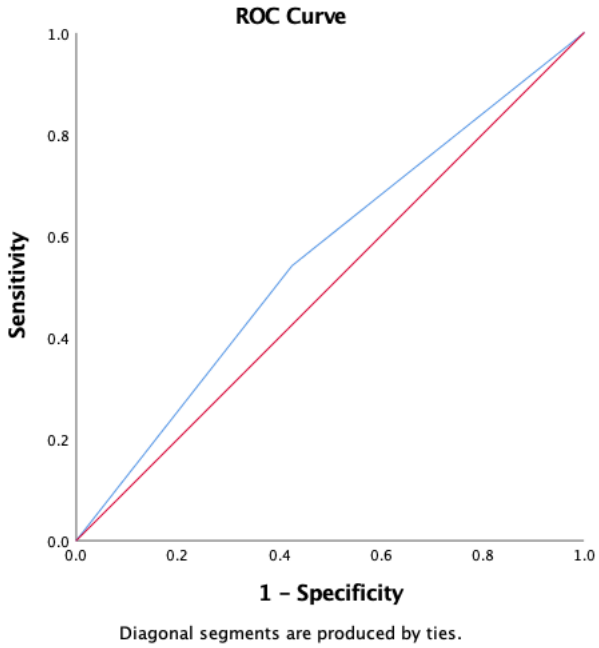


Around 80.8% were alive, 6.4% died and 12.8% LFU.

Table 14: Diagnostic accuracy outcome with probable cases among the study participants (N=125)

Slno	Probable	Outcome	
		Death+LFU	Alive
1	Death	19	43
2	Alive	5	58

Statistic	Value	95% CI
Sensitivity	79.17%	57.85% to 92.87%
Specificity	57.43%	47.19% to 67.21%
Positive Likelihood Ratio	1.86	1.37 to 2.52
Negative Likelihood Ratio	0.36	0.16 to 0.81
Disease prevalence	19.20%	12.71% to 27.21%
Positive Predictive Value	30.65%	24.56% to 37.49%
Negative Predictive Value	92.06%	83.93% to 96.26%
Accuracy	61.60%	52.48% to 70.16%



Area Under the Curve				
Test Result Variable(s)				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.558	.067	.384	.428	.689

DISCUSSION

Antiretroviral therapy has been extraordinarily effective in suppressing HIV infection, restoring immune function, and enhancing health, and it has led to dramatic reductions in morbidity and mortality in regions of the developing world with the highest prevalence of HIV infection. According to research from the ART in Lower Income Countries cohort and Malawi, Uganda, and India, 175 percent of HIV-infected patients receive fixed-dose combination (FDC) therapy with a nonnucleoside reverse-transcriptase inhibitor and have excellent viral suppression[48]. These remarkable achievements have prompted the global health priority of HAART expansion. More than 2 million people in the developing world are receiving HAART; the majority of these people are located in sub-Saharan Africa, which bears the brunt of the HIV epidemic.

The Veterans Aging Cohort Study Index (VACS Index) is composed of routine clinical laboratory tests that accurately and generally predict all-cause mortality in HIV-positive and HIV-negative individuals. Increasing evidence supports its use as a measure of physiologic frailty in HIV-positive older adults due to its associations with frailty-related outcomes, such as mortality, hospitalisation, fragility fractures, serious falls, pneumonia, cognitive decline, delirium, and functional decline.

So, we conducted the study to predict the morbidity and mortality in HIV-infected individuals on the NACO Anti-Retroviral therapy Regimen using modified veterans ageing cohort study index in a tertiary care hospital

In our study, around 18.4% were in the age group of 18-30 years, 24.8% 31-40 years, 21.6% 41-50 years, 27.2% 51-60 years and 8% more than 60 years and nearly 52.8% were males, and 47.2% were females.

According to Olaniyi O Taiwo et[49,] the CD4 counts (cells/ml) of this patient rose from 73 to 269 while the viral load (copies/ml) dropped from 514,298 to 288. In our study, the mean CD4 count is 255.36, and the median CD4 count is 230.00 (107.00 to 322.50).

A study by **AC Justice**[50] et al. revealed that after one year of ART, 77% of the entire sample had HIV-1 RNA < 500 copies/ml, 34% had haemoglobin values between 12–13.9 g/dL, 10% had haemoglobin values between 10–11.9 g/dL, 25% had FIB 4 consistent with fibrosis (>3.25), 6% had stage III renal insufficiency (eGFR <60mL/min), and 24% had HCV co-infection.I n our study, median haemoglobin ranges from 11.72 g/dL and Median hemoglobin 11.80 g/dL (Minimum 10.50 g/dL to Maximum 13.30 g/dL). According to AC Justice[50], age independently predicts biomarkers and outcomes associated with frailty and modifies a large number of additional predictors.FIB-4, which includes AST, ALT, platelets, and age, is used to estimate liver fibrosis. The mean values of ALT of mean 24.58, and the median ALT levels were 14.50 (Minimum 11.0 to Maximum 27.25). The mean values of platelets were 203.66. The median platelets were 103.22 (145.0 to 258.50).

CONCLUSION

In summary, we have demonstrated that a novel index composed of routine clinical data can predict mortality among HIV-infected individuals on ART with good to very good discrimination and consistent calibration across important subgroups. A universal frailty index may not be a realistic objective. Instead, the measure of frailty should be selected based on its intended application. The VACS may be a useful indicator of physiologic frailty, indicating the need for more vigilant management or a comprehensive geriatric evaluation. The VACS Index may also assist in alerting healthcare providers and patients when life expectancy is low and end-of-life planning are necessary. It outperforms other general risk indices in distinguishing mortality risk in a wide variety of patient settings in a reproducible and generalizable manner. It also predicts other frailty-related outcomes, is cross-sectionally associated with frailty-related biomarkers and differentiates mortality risk and other frailty-related outcomes among individuals of similar chronologic age.

LIMITATIONS OF STUDY

Small sample size and single institution study Hence results cannot be extrapolated to general population. Drugs that can cause hematological parameters changes were not addressed**.**

11. REFERENCES

1. Antiretroviral therapy in Indian setting: when & what to start with, when & what to switch to? - PubMed - NCBI [Internet]. [cited 2015 May 11]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22310814
2. Tate JP, Justice AC, Hughes MD, Bonnet F, Reiss P, Mocroft A, et al. An internationally generalizable risk index for mortality after one year of antiretroviral therapy. AIDS Lond Engl. 2013;27(4):563.
3. Neuhaus J. Markers of inflammation, coagulation, and renal function are elevated in adults with HIV infection. - PubMed - NCBI [Internet]. [cited 2015 May 11]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20446848
4. Does an Index Composed of Clinical Data Reflect Effects of Inflammation, Coagulation, and Monocyte Activation on Mortality Among Those Aging With HIV? [Internet]. [cited 2015 Jun 2]. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3297653/
5. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). - PubMed - NCBI [Internet]. [cited 2015 May 13]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/6189183
6. The Efficacy of Azidothymidine (AZT) in the Treatment of Patients with AIDS and AIDS-Related Complex — NEJM [Internet]. [cited 2015 May 13]. Available from: http://www.nejm.org/doi/full/10.1056/NEJM198707233170401

7. Combination therapy with zidovudine and dideoxycytidine in patients with advanced human immunodeficiency virus infection. A phase I/II study. - PubMed - NCBI [Internet]. [cited 2015 May 13]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/1345755

8. Evidence for HTLV-III infection in prostitutes in Tamil Nadu (India). - PubMed - NCBI [Internet]. [cited 2015 May 13]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3623641

9. WHO | Data and statistics [Internet]. [cited 2015 May 11]. Available from: http://www.who.int/hiv/data/en/

10. Annual Report Cover design approved A - NACO_English 2013-14.pdf [Internet]. [cited 2015 May 11]. Available from: http://naco.gov.in/upload/2014%20mslns/NACO_English%202013-14.pdf

11. National Health Mission – Tamil Nadu :: [Internet]. [cited 2015 May 13]. Available from: http://www.nrhmtn.gov.in/statglance.html

12. Census 2011 - census2011_tn.pdf [Internet]. [cited 2015 May 13]. Available from: http://www.census.tn.nic.in/whatsnew/census2011_tn.pdf

13. STATE HIV EPIDEMIC FACT SHEET.pdf [Internet]. [cited 2015 May 13]. Available from:

http://naco.gov.in/upload/2014%20mslns/STATE%20HIV%20EPIDEMIC%20FACT %20SHEET.pdf

14. Origins of HIV and the AIDS Pandemic [Internet]. [cited 2015 May 15]. Available from: http://perspectivesinmedicine.cshlp.org/content/1/1/a006841.full

15. Antiretroviral therapy in Indian setting: when & what to start with, when & what to switch to? - PubMed - NCBI [Internet]. [cited 2015 May 11]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22310814

16. Wester CW, Okezie OA, Thomas AM, Bussmann H, Moyo S, Muzenda T, et al. Higher-than-expected rates of lactic acidosis among highly active antiretroviral therapy-treated women in Botswana: preliminary results from a large randomized clinical trial. J Acquir Immune Defic Syndr 1999. 2007 Nov 1;46(3):318–22.

17. Bolhaar MG, Karstaedt AS. A high incidence of lactic acidosis and symptomatic hyperlactatemia in women receiving highly active antiretroviral therapy in Soweto, South Africa. Clin Infect Dis Off Publ Infect Dis Soc Am. 2007 Jul 15;45(2):254–60.

18. Forna F, Liechty CA, Solberg P, Asiimwe F, Were W, Mermin J, et al. Clinical toxicity of highly active antiretroviral therapy in a home-based AIDS care program in rural Uganda. J Acquir Immune Defic Syndr 1999. 2007 Apr 1;44(4):456–62.

19. Reisler RB, Murphy RL, Redfield RR, Parker RA. Incidence of pancreatitis in HIV- 1-infected individuals enrolled in 20 adult AIDS clinical trials group

studies: lessons learned. J Acquir Immune Defic Syndr 1999. 2005 Jun 1;39(2):159–66.

20. Martínez E, Milinkovic A, de Lazzari E, Ravasi G, Blanco JL, Larrousse M, et al. Pancreatic toxic effects associated with co-administration of didanosine and tenofovir in HIV-infected adults. Lancet Lond Engl. 2004 Jul 3;364(9428):65–7.

21. Ait-Mohand H, Bonmarchand M, Guiguet M, Slama L, Marguet F, Behin A, et al. Viral efficacy maintained and safety parameters improved with a reduced dose of stavudine: a pilot study. HIV Med. 2008 Oct;9(9):738–46.

22. Gerschenson M, Kim C, Berzins B, Taiwo B, Libutti DE, Choi J, et al. Mitochondrial function, morphology and metabolic parameters improve after switching from stavudine to a tenofovir-containing regimen. J Antimicrob Chemother. 2009 Jun;63(6):1244–50.

23. Haas DW, Ribaudo HJ, Kim RB, Tierney C, Wilkinson GR, Gulick RM, et al. Pharmacogenetics of efavirenz and central nervous system side effects: an Adult AIDS Clinical Trials Group study. AIDS Lond Engl. 2004 Dec 3;18(18):2391–400.

24. Cohen K, Grant A, Dandara C, McIlleron H, Pemba L, Fielding K, et al. Effect of rifampicin-based antitubercular therapy and the cytochrome P450 2B6 516G>T polymorphism on efavirenz concentrations in adults in South Africa. Antivir Ther. 2009;14(5):687–95.

25. Renaud-Théry F, Nguimfack BD, Vitoria M, Lee E, Graaff P, Samb B, et al. Use of antiretroviral therapy in resource-limited countries in 2006: distribution and uptake of first- and second-line regimens. AIDS Lond Engl. 2007 Jul;21 Suppl 4:S89–95.

26. Wit FWNM, Kesselring AM, Gras L, Richter C, van der Ende ME, Brinkman K, et al. Discontinuation of nevirapine because of hypersensitivity reactions in patients with prior treatment experience, compared with treatment-naive patients: the ATHENA cohort study. Clin Infect Dis Off Publ Infect Dis Soc Am. 2008 Mar 15;46(6):933–40.

27. Dart Trial Team. Twenty-four-week safety and tolerability of nevirapine vs. abacavir in combination with zidovudine/lamivudine as first-line antiretroviral therapy: a randomized double-blind trial (NORA). Trop Med Int Health TM IH. 2008 Jan;13(1):6–16.

28. Reid A, Stöhr W, Walker AS, Williams IG, Kityo C, Hughes P, et al. Severe renal dysfunction and risk factors associated with renal impairment in HIV-infected adults in Africa initiating antiretroviral therapy. Clin Infect Dis Off Publ Infect Dis Soc Am. 2008 Apr 15;46(8):1271–81.

29. Kiertiburanakul S, Sungkanuparph S, Charoenyingwattana A, Mahasirimongkol S, Sura T, Chantratita W. Risk factors for nevirapine-associated rash among HIV- infected patients with low CD4 cell counts in resource-limited settings. Curr HIV Res. 2008 Jan;6(1):65–9.

30. Rao N, White GJ. Successful treatment of Enterococcus faecalis prosthetic valve endocarditis with linezolid. Clin Infect Dis Off Publ Infect Dis Soc Am. 2002 Oct 1;35(7):902–4.

31. Mutimura E, Stewart A, Rheeder P, Crowther NJ. Metabolic function and the prevalence of lipodystrophy in a population of HIV-infected African subjects receiving highly active antiretroviral therapy. J Acquir Immune Defic Syndr 1999. 2007 Dec 1;46(4):451–5.

32. Buchacz K, Weidle PJ, Moore D, Were W, Mermin J, Downing R, et al. Changes in lipid profile over 24 months among adults on first-line highly active antiretroviral therapy in the home-based AIDS care program in rural Uganda. J Acquir Immune Defic Syndr 1999. 2008 Mar 1;47(3):304–11.

33. fs310_2008.pdf [Internet]. [cited 2015 Sep 6]. Available from: http://www.who.int/mediacentre/factsheets/fs310_2008.pdf

34. Vorster HH, Venter CS, Wissing MP, Margetts BM. The nutrition and health transition in the North West Province of South Africa: a review of the THUSA (Transition and Health during Urbanisation of South Africans) study. Public Health Nutr. 2005 Aug;8(5):480–90.

35. Worm SW, Sabin C, Weber R, Reiss P, El-Sadr W, Dabis F, et al. Risk of myocardial infarction in patients with HIV infection exposed to specific individual antiretroviral drugs from the 3 major drug classes: the data collection on adverse events of anti-HIV drugs (D:A:D) study. J Infect Dis. 2010 Feb 1;201(3):318–30.

36. Nebié Y, Meda N, Leroy V, Mandelbrot L, Yaro S, Sombié I, et al. Sexual and reproductive life of women informed of their HIV seropositivity: a prospective cohort study in Burkina Faso. J Acquir Immune Defic Syndr 1999. 2001 Dec 1;28(4):367–72.

37. DeSimone JA, Pomerantz RJ, Babinchak TJ. Inflammatory reactions in HIV-1- infected persons after initiation of highly active antiretroviral therapy. Ann Intern Med. 2000 Sep 19;133(6):447–54.

38. French MA. HIV/AIDS: immune reconstitution inflammatory syndrome: a reappraisal. Clin Infect Dis Off Publ Infect Dis Soc Am. 2009 Jan 1;48(1):101–7.

39. Operational guidelines for ART services.pdf [Internet]. [cited 2015 May 13]. Available from: http://www.naco.gov.in/upload/Publication/Treatment%20Care%20and%20su p port/Operational%20guidelines%20for%20ART%20services.pdf

40. Sandler NG, Wand H, Roque A, Law M, Nason MC, Nixon DE, et al. Plasma Levels of Soluble CD14 Independently Predict Mortality in HIV Infection. J Infect Dis. 2011 Mar 15;203(6):780–90.

41. Veterans Aging Cohort Study (VACS) [Internet]. [cited 2015 Jun 2]. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3049942/

42. Justice AC, Modur SP, Tate JP, et al; NA-ACCORD and VACS Project Teams. Predictive accuracy of the Veterans Aging Cohort Study index for

mortality with HIV infection: a North American cross cohort analysis. J Acquir Immune Defic Syndr **2013**; 62:149–63.

43. Kuller LH, Tracy R, Belloso W, et al; INSIGHT SMART Study Group. Inflammatory and coagulation biomarkers and mortality in patients with HIV infection. PLoS Med 2008; 5:e203.

44. Vasan RS**.** Biomarkers of cardiovascular disease: molecular basis and practical considerations. Circulation 2006;113(19):2335-62.

45. Salinas JL, Rentsch C, Marconi VC, Tate J, Budoff M, Butt AA, et al. Baseline, Time-updated, and Cumulative HIV Care Metrics for Predicting Acute Myocardial Infarction and All-Cause Mortality. Clin Infect Dis. 2016;63(11):1423-30.

46. Marquine MJ, Montoya JL, Umlauf A, Fazeli PL, Gouaux B, Heaton RK, et al. The Veterans Aging Cohort Study (VACS) Index and Neurocognitive Change: A Longitudinal Study. Clin Infect Dis. 2016;63(5):694-702.

47. CHRISTIAN MEDICAL COLLEGE - fhivmedpros.pdf [Internet]. [cited 2015 Jun 26]. Available from: http://www.cmch-vellore.edu/pdf/fhivmedpros.pdf

48. Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration, & ART Cohort Collaboration. (2006). Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. *The Lancet*, *367*(9513), 817-824.

49. Taiwo OO, Hassan Z. The impact of Highly Active Antiretroviral Therapy (HAART) on the clinical features of HIV - related oral lesions in Nigeria.

AIDS Res Ther. 2010 Jun 25;7:19. doi: 10.1186/1742-6405-7-19. PMID: 20579347; PMCID: PMC2903493.

50. Justice AC, Modur SP, Tate JP, Althoff KN, Jacobson LP, Gebo KA, Kitahata MM, Horberg MA, Brooks JT, Buchacz K, Rourke SB, Rachlis A, Napravnik S, Eron J, Willig JH, Moore R, Kirk GD, Bosch R, Rodriguez B, Hogg RS, Thorne J, Goedert JJ, Klein M, Gill J, Deeks S, Sterling TR, Anastos K, Gange SJ; NA-ACCORD and VACS Project Teams. Predictive accuracy of the Veterans Aging Cohort Study index for mortality with HIV infection: a North American cross cohort analysis. J Acquir Immune Defic Syndr. 2013 Feb 1;62(2):149-63. doi: 10.1097/QAI.0b013e31827df36c. PMID: 23187941; PMCID: PMC3619393.

12. ANNEXURE

INFORMATION SHEET

We are conducting a study titled " **TO PREDICT MORBIDITY AND MORTALITY IN HIV INFECTED INDIVIDUAL ON NACO ANTI RETROVIRAL THERAPY REGIMEN USING MODIFIED VETERANS AGING COHORT STUDY INDEX IN A TERTIARY CARE HOSPITAL"** among patients in ART Centre Rajiv Gandhi Government General Hospital, Chennai.

The purpose of this study is to examine patients who are diagnosed as Person living with HIV and AIDS to use haematological parameters to predict morbidity and mortality.

We are selecting certain cases and if you are found eligible, we may be using your blood samples to do certain tests.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator
Date:
Place:

Signature/ left thumb impression of
Participant/attender

PATIENT CONSENT FORM

TO PREDICT MORBIDITY AND MORTALITY IN HIV INFECTED INDIVIDUAL ON NACO ANTI RETROVIRAL THERAPY REGIMEN USING MODIFIED VETERANS AGING COHORT STUDY INDEX IN A TERTIARY CARE HOSPITAL

Participant Name :

Age:

Sex:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the questions and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety , advantage and disadvantage of the technique.
I understand that my participation in the study is voluntary and that I'm free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study.

I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study. I hereby consent to undergo complete physical examination, pathological and radiological investigation pertaining to the study.

Signature/Thumb Impression of Participant

PROFORMA

TO PREDICT MORBIDITY AND MORTALITY IN HIV INFECTED INDIVIDUAL ON NACO ANTI RETROVIRAL THERAPY REGIMEN USING MODIFIED VETERANS AGING COHORT STUDY INDEX IN A TERTIARY CARE HOSPITAL

NAME:

AGE:
SEX:
OCCUPATION:
RESIDENCE:
CONTACT NUMBER:
PRESENTING COMPLAINT

PAST HISTORY:
1.Diabetes Mellitus 2. Hypertension 3. Dyslipidemia 4. COPD 5. Bronchial Asthma
6. Renal Failure 7. Chronic Liver Disease 8. Rheumatic Heart Disease
9. Hypothyroidism 10. CCF 11. Illicit Drug 12. Ischemic Heart disease
13. Hyperthyroidism 14. Malignancy

PERSONAL HISTORY:

FAMILY HISTORY:

TREATMENT HISTORY:

GENERAL EXAMINATION:

Level of Consciousness
Pallor/Icterus/Cyanosis/Clubbing/Pedal edema/lymphadenopathy
Blood pressure
Pulse rate
Respiratory rate
Temperature
Body mass index

LOCAL EXAMINATION:

SYSTEMIC EXAMINATION:

CVS:
RS:
Abdomen:
CNS:

INVESTIGATIONS

Age	
Gender	
CD4 count	
Haemoglobin	
AST	
ALT	
Platelets	
Creatinine	
Hepatitis C coinfection	
HIV-1 RNA, copies/ml	
FIB-4	
eGFR	

MASTER CHART

S. No.	Age	SEX	CD 4 ct	Hb	AST	ALT	Platelets	FIB-4	Creat(mg/Dcreat(mmoeGFR)		eGFR	HCV	MVI	OUTCOME
1	31	MALE	42	14	94	35	5.11	2.31	0.97	86.325	63	Negative	45	Alive
2	44	FEMALE	159	11.2	28	50	1.45	1.36	1.04	92.354	69	Negative	52	Alive
3	35	MALE	200	7.4	15	11	4.7	1.24	18.9	1725.0	7	Negative	48	Alive
4	27	MALE	180	11.1	24	10	5.57	0.59	0.75	69.48	103	Negative	32	Alive
5	53	MALE	300	12	16	14	1.8	0.57	0.48	64.258	96	negative	38	Alive
6	52	MALE	92	13.5	33	52	2.22	0.71	0.94	85.615	74	Negative	19	Alive
7	37	MALE	400	14	15	79	2.98	0.82	0.68	73.582	82	positive	6.08	Alive
8	46	MALE	335	11.3	18	146	2.45	0.65	0.4	82.415	73	Negative	32	Alive
9	41	MALE	77	12.7	36	92	1.9	8.4	0.6	70.28	84	Negative	47	Alive
10	60	MALE	250	11.8	26	15	2.45	0.78	0.94	83.258	72	Negative	41	Alive
11	58	FEMALE	119	11	41	23	1.89	5.64	1.4	102.544	77	Negative	37	Alive
12	46	FEMALE	232	11.1	45	34	4.32	6.42	1.05	90.57	89	negative	47	Alive
13	54	MALE	61	15	73	45	1.26	1.32	1.18	99.065	57	Negative	14	Alive
14	52	MALE	225	10.1	42	17	7.9	0.36	1.47	124.358	62	negative	47	Alive
15	26	MALE	148	13.9	90	18	2.13	0.86	0.88	72.685	4	negative	16	Alive
16	60	MALE	152	9.1	88	39	6.5	21.65	1.34	116.253	74	Negative	45	Death
17	41	MALE	331	10.1	22	18	1.58	0.48	2.15	167.248	38	Negative	64	Alive
18	59	FEMALE	136	NA	45	46	4.76	2.84	0.4	70.72	116	negative	47	Alive
19	56	MALE	259	14.2	65	24	2.15	2.65	1.36	116.359	64	Negative	35	Alive
20	32	FEMALE	285	12.2	41	13	8	0.51	0.92	85.369	105	negative	25	Alive
21	57	MALE	310	14.9	86	42	1.35	0.34	0.65	52.301	93	Negative	6.7	Alive
22	30	FEMALE	88	13.1	57	23	6	1.64	0.8	72.52	104	Negative	19	Death
23	53	MALE	144	10.7	21	14	4.87	1.95	1.08	83.257	82	Negative	43	Alive
24	48	MALE	165	10.4	34	13	2.34	0.48	0.64	55.632	86	negative	54	Alive
25	32	MALE	521	12.8	18	39	3.45	0.64	0.74	66.0	94	negative	44	Alive
26	31	MALE	114	13.8	112	17	1.76	4.51	1.32	107.654	70	Negative	35	Alive
27	36	FEMALE	40	9.4	22	19	3.65	3.96	1.3	103.65	72	Negative	40	Alive

S. No.	Age	SEX	CD 4 ct	Hb	AST	ALT	Platelets	FIB-4	Creat(mg/Dcreat(mmoeGFR)		eGFR	HCV	MVI	OUTCOME
28	34	FEMALE	471	3.9	49	14	4	2.65	0.9	79.56	96	Negative	63	Alive
29	38	FEMALE	111	12.7	125	13	4.67	19.4	0.8	68.159	116	Negative	48	Alive
30	40	FEMALE	32	11.2	16	23	1.45	1.33	1.34	115.248	64	Negative	37	Alive
31	57	MALE	445	14	70	17	4.32	7.6	0.43	147.862	69	Negative	49	Alive
32	56	FEMALE	1123	13.5	45	37	4.56	7.65	1	82.5	92	Negative	46	Alive
33	65	FEMALE	135	12.9	52	13	3.45	0.99	1.17	106.354	48	negative	49	Alive
34	31	FEMALE	222	9.4	23	18	2.65	1.36	0.68	82.201	68	negative	60	Alive
35	38	FEMALE	550	12	54	54	1.95	4.69	0.74	67.248	94	Negative	54	Alive
36	46	FEMALE	333	12.5	26	15	1.23	2.78	1.9	93.265	62	positive	31	Alive
37	24	FEMALE	82	10.1	57	13	1.85	3.65	0.75	83.260	94	Negative	34	Death
38	54	FEMALE	169	13.5	62	14	3.98	2.64	6.48	541.263	82	Negative	37	Alive
39	49	MALE	456	10.8	26	24	1.54	1.65	1.09	93.320	60	negative	59	Alive
40	24	FEMALE	169	10.1	28	55	2.23	2.35	1.08	93.126	62	negative	67	Death
41	57	FEMALE	136	10	24	17	2.54	6.83	0.64	56.320	114	positive	52	Alive
42	52	MALE	265	7.9	58	23	1.65	6.79	0.94	75.213	80	Negative	76	Alive
43	49	FEMALE	349	3.3	12	18	2.45	9.85	1.4	113.025	68	Negative	52	Alive
44	51	FEMALE	253	11.4	26	14	2.78	2.48	0.9	81.367	92	negative	31	Alive
45	47	FEMALE	644	12.8	51	33	2.97	6.83	1.6	139.672	45	Negative	40	Alive
46	37	FEMALE	347	11.6	29	12	1.65	0.47	0.7	71.021	89	negative	32	Alive
47	53	FEMALE	268	11.2	18	15	2.63	0.19	0.84	72.158	83	negative	34	Alive
48	21	FEMALE	264	11.6	43	16	5	2.09	0.9	83.251	67	Negative	48	Alive
49	60	FEMALE	684	11.9	81	17	1.84	9.7	0.68	84.864	82	negative	37	Alive
50	56	MALE	174	12.4	73	24	4.73	5.14	1.28	110.308	64	Negative	24	Alive
51	48	MALE	20	14.2	16	13	1.72	1.92	0.67	63.895	104	Negative	6.8	Alive
52	65	MALE	369	12.6	20	105	2.59	1.74	1.04	94.236	68	Negative	52	Alive
53	61	MALE	741	10.6	19	18	2.64	6.83	0.6	53.04	70	negative	58	Alive
54	23	MALE	684	14.6	24	15	3.87	2.74	1.28	93.153	75	negative	62	Alive
55	47	MALE	237	15.1	27	14	2.28	2.45	1.36	106.325	68	Negative	57	Alive
56	30	MALE	19	13	48	48	1.64	8.16	0.45	69.693	114	Negative	53	Alive

S. No.	Age	SEX	CD 4 ct	Hb	AST	ALT	Platelets	FIB-4	Creat(mg/Dcreat(mmoeGFR)		eGFR	HCV	MVI	OUTCOME
57	53	MALE	281	12.8	27	15	4.59	1.4	1.01	88.410	82	Negative	59	Death
58	39	FEMALE	234	12.4	24	18	4.34	0.48	0.63	593498	123	negative	55	Alive
59	44	FEMALE	168	11.9	36	14	2.74	8.1	1.23	109.358	72	Negative	19	Alive
60	37	FEMALE	249	5.3	168	14	2.54	0.41	1.24	113.678	68	Negative	64	Alive
61	36	FEMALE	230	9.6	18	17	1.72	0.4	0.75	63.789	105	Negative	68	Alive
62	53	FEMALE	300	11.6	20	15	2.56	0.74	0.8	70.482	72	positive	25	Alive
63	44	MALE	275	13.8	11	13	2.95	8.0	0.85	62.158	90	negative	47	Alive
64	39	MALE	210	10.7	21	11	3.34	3.25	1.35	93.485	76	Negative	75	Alive
65	60	FEMALE	338	13.3	52	18	9.4	4.82	1.06	91.936	84	negative	38	Alive
66	41	MALE	53	12.7	55	12	2.62	1.5	0.94	93.482	92	Negative	24	Alive
67	59	MALE	46	14.7	49	164	2.69	7.3	0.81	73.520	78	Negative	15	Alive
68	22	MALE	50	15.2	33	20	1.76	3.46	1.05	91.258	84	Negative	18	Alive
69	47	MALE	302	11.6	21	13	1.89	1.43	0.92	82.147	90	Negative	23	Alive
70	43	FEMALE	65	11.2	70	11	2.28	57.3	0.9	72.541	96	Negative	37	Death
71	35	MALE	408	10.8	22	17	2.34	4.0	1.15	88.624	83	negative	40	Alive
72	33	MALE	231	10.6	33	13	3.98	1.27	1.74	128.205	56	negative	45	Alive
73	31	FEMALE	100	9.5	80	10	2.63	7.63	0.91	81.259	70	Negative	48	Death
74	52	FEMALE	232	13.9	36	19	3.25	2.25	1.2	109.827	64	Negative	51	Alive
75	48	MALE	341	14.2	69	25	3.75	4.80	1.3	106.08	53	Negative	54	Alive
76	33	MALE	17	12	37	47	4.34	6.01	1.08	94.248	76	Negative	58	Alive
77	26	MALE	384	14.9	70	25	4.85	6.75	0.80	64.865	92	Negative	61	Alive
78	45	MALE	311	11	22	49	1.08	0.71	0.9	72.536	76	Negative	56	Alive
79	24	FEMALE	3	11.3	32	24	192	0.21	0.41	34.693	60	positive	37	Alive
80	62	FEMALE	44	10.9	28	46	4.92	1.57	0.81	72.425	84	Negative	47	Alive
81	22	MALE	698	14.5	21	49	3.29	0.72	0.91	70.72	90	Negative	45	Alive
82	62	MALE	65	12.8	55	14	2.17	2.8	1.36	118.359	66	Negative	24	Death
83	51	FEMALE	46	11.9	19	17	1.82	1.15	1.09	90.425	70	Negative	27	Alive
84	29	FEMALE	341	11.5	22	15	2.95	2.48	1.03	91.036	64	negative	29	Alive
85	22	FEMALE	174	11.8	21	14	2.38	1.16	1.05	97.851	78	Negative	37	Alive

S. No.	Age	SEX	CD 4 ct	Hb	AST	ALT	Platelets	FIB-4	Creat(mg/Dcreat(mmoeGFR)		eGFR	HCV	MVI	OUTCOME
86	48	MALE	290	10.4	145	42	1.46	2.29	0.89	83.126	94	negative	53	Alive
87	54	FEMALE	195	8.2	18	14	1.57	1.44	1.15	94.259	78	Negative	75	Alive
88	42	FEMALE	218	11.3	30	15	1.84	1.6	0.69	61.435	60	positive	43	Alive
89	35	FEMALE	317	8.7	26	17	2.74	1.35	1.04	91.426	64	Negative	45	Alive
90	52	FEMALE	222	11.7	57	11	4.68	7.8	0.95	82.456	84	Negative	56	Alive
91	55	FEMALE	108	8.8	19	13	4.32	0.89	1.19	103.286	60	Negative	52	Alive
92	37	MALE	237	13.5	22	17	4.82	0.5	1.18	113.254	54	Negative	55	Alive
93	46	MALE	337	11.4	65	15	1.74	8.4	0.95	84.264	98	Negative	37	Alive
94	38	MALE	917	9.5	36	13	647	2.7	1.18	97.214	83	negative	43	Alive
95	36	FEMALE	49	11.3	29	16	2.58	6.4	0.79	79.354	106	Negative	31	Alive
96	32	FEMALE	298	10.9	66	13	2.34	9.7	1.33	108.321	74	Negative	35	Alive
97	50	FEMALE	65	12.6	119	31	1.8	6.33	0.48	64.211	120	Negative	38	Alive
98	49	MALE	187	13	28	47	3.86	0.75	0.77	68.068	94	Negative	42	Alive
99	53	MALE	769	14.3	115	39	5.52	3.7	NA	70.952	68	positive	45	Alive
100	24	MALE	99	14.5	23	56	4.75	0.71	0.84	81.203	94	negative	48	Alive
101	62	FEMALE	294	9.9	12	25	2.65	2.34	1.08	92.38	66	positive	54	Alive
102	40	FEMALE	498	11.6	30	33	4.34	1.02	1.16	104.324	74	negative	46	Alive
103	52	MALE	298	12.6	34	39	5.1	39.15	0.78	55.628	114	Negative	42	Alive
104	45	MALE	58	12.4	83	15	1.63	40.9	0.94	81.263	90	Negative	18	Alive
105	30	MALE	69	9.7	13	29	1.7	1.36	1.12	99.006	78	Negative	63	Alive
106	56	MALE	30	13.5	28	35	4.62	0.7	0.93	82.357	90	Negative	60	Alive
107	57	MALE	187	8.5	19	17	2.67	0.98	0.82	73.245	102	Negative	52	Alive
108	58	FEMALE	178	11.5	33	13	4.13	0.65	0.73	72.658	84	negative	45	Alive
109	33	MALE	68	13.8	29	107	1.54	8.17	0.94	84.93	67	Negative	25	Alive
110	65	FEMALE	339	7.8	45	23	1.76	7.19	0.72	64.352	93	Negative	54	Alive
111	60	MALE	215	12.4	28	63	5.16	1.65	0.77	62.359	88	Negative	64	Death
112	53	FEMALE	288	8.2	62	13	1.64	5.9	1.32	106.852	70	Negative	64	Alive
113	57	FEMALE	346	11.5	72	11	2.45	6.3	0.63	78.635	82	positive	31	Alive
114	62	FEMALE	316	10.5	41	17	2.61	1.42	0.82	72.604	80	Negative	45	Alive

S. No.	Age	SEX	CD 4 ct	Hb	AST	ALT	Platelets	FIB-4	Creat(mg/Dcreat(mmoeGFR)		eGFR	HCV	MVI	OUTCOME
115	20	MALE	64	14.8	32	20	4.71	1.09	0.96	84.864	70	Negative	47	Alive
116	51	MALE	40	14.6	64	24	1.75	2.65	1.9	169.578	90	Negative	27	Alive
117	25	MALE	337	14.5	63	130	3.75	1.4	1.87	103.469	56	positive	16	Alive
118	40	FEMALE	249	8.4	41	14	3.42	1.27	1.5	76.25	72	Negative	47	Alive
119	18	FEMALE	455	10.7	18	17	2.73	5.2	0.89	84.26	70	Negative	31	Alive
120	36	FEMALE	40	12.7	69	12	4.87	4.53	1.05	93.156	76	Negative	47	Alive
121	67	MALE	871	13.3	24	15	1.45	1.38	1.06	94.234	80	Negative	31	Alive
122	39	MALE	741	12.9	54	44	4.3	3.4	0.85	72.462	104	Negative	54	Alive
123	60	MALE	598	14.2	31	15	2.74	6.4	1.42	91.465	70	Negative	21	Alive
124	62	FEMALE	45	7.5	40	12	2.5	1.06	1.15	106.459	78	Negative	53	Alive
125	26	MALE	178	13.4	33	14	2.19	6.7	0.68	77.642	116	Negative	46	Alive

ETHICAL PERMISSION LETTER

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg. No(CDSCO).ECR/270/Inst./TN/2013/RR-20
EC Reg. No(DHR).EC/NEW/INST/2021/1618
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CERTIFICATE OF APPROVAL

To
Dr.P.MARIKOMALA,
Second Year Post Graduate, MD (General Medicine),
Madras Medical College,
Chennai-600003.

Dear Dr. P.MARIKOMALA,

The Institutional Ethics Committee has considered your request and approved your study titled **"TO PREDICT MORBIDITY AND MORTALITY IN HIV INFECTED INDIVIDUAL ON NACO ANTI RETROVIRAL THERAPY REGIMEN USING MODIFIED VETERANS AGING COHORT STUDY INDEX IN A TERTIARY CARE HOSPITAL"- NO.21082022.** The following members of Ethics Committee were present in the meeting held on **04.08.2022** conducted at Madras Medical College, Chennai 3.

1. Prof.P.V.Jayashankar,MS Orth.,D.Orth.,M.Ch Orth (Liverpool) :Chairperson
2. Prof.N.Gopalakrishnan,MD.,DM., FRCP, Director, Inst.of Nephrology,MMC,Ch. : Member Secretary
3. Prof. K.M.Sudha, Prof. Inst. of Pharmacology,MMC,Ch-3 : Member
4. Prof. Alagarsamy Jamila ,MD, Vice Principal, Stanley Medical College, Chennai : Member
5. Prof.Meena Suresh, MD.,DGO.,Prof.of Obst & Gynaec, IOG,Chennai : Member
6. Prof.S.Lakshmi, Prof. of Paediatrics ICH Chennai :Member
7. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
8. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
9. Thiru K.Ranjith, Ch- 91 : Lay Person

We approve the proposal to be conducted in its presented form.
The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003.

PLAGIARISM CERTIFICATE

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W	URL: https://1library.net/document/dy437e9z-validation-modified-infected-indian-population-initiate... Fetched: 2022-03-02 08:01:10	50
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To predict the morbidity and mortality in HIV infected individual on NACO Anti-Retroviral therapy Regimen using modified veterans aging cohort study index in a tertiary care hospital To predict the morbidity and mortality in HIV infected individual on NACO Anti-Retroviral therapy Regimen using modified veterans aging cohort study index in a tertiary care hospital Introduction
According to a global review of the AIDS epidemic,

CERTIFICATE - II

This is to certify that this dissertation work titled "**TO PREDICT MORBIDITY AND MORTALITY IN HIV INFECTED INDIVIDUAL ON NACO ANTI RETROVIRAL THERAPY REGIMEN USING MODIFIED VETERANS AGING COHORT STUDY INDEX IN A TERTIARY CARE HOSPITAL**" **of the candidate DR. P.MARIKOMALA with registration Number 200120100517 for the award of the degree of M.D. in the branch of Internal Medicine. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 11 percentage of plagiarism in the dissertation.**

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Guide & Supervisor sign with Seal.