CROSS SECTIONAL STUDY OF PREVALENCE OF DYSLIPIDEMIA IN TREATMENT NAÏVE PLHA (PATIENTS LIVING WITH HIV/AIDS) AND ITS CORRELATION WITH CD4 COUNT

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M.D. (GENERAL MEDICINE) - BRANCH – I

GOVERNMENT KILPAUK MEDICAL COLLEGE

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BONAFIDE CERTIFICATE

This is to certify that "**CROSS SECTIONAL STUDY OF PREVALENCE OF DYSLIPIDEMIA IN TREATMENT NAÏVE PLHA (PATIENTS LIVING WITH HIV/AIDS) AND ITS CORRELATION WITH CD4 COUNT"** is a bonafide work performed by **Dr. GANESH ARAVIND. S.**, Post graduate student, Department of Internal Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in fulfilment of regulations of the Tamil Nadu Dr. M.G.R Medical University, for the award of M.D. Degree Branch I (General Medicine) during the academic period from May 2011 to April 2014.

Prof. Dr. N. Gunasekaran M.D., DTCD
Medical Superintendent & Director INCD,
Professor and HOD,
Department of Medicine,
KMC & GRH
Chennai

Prof. Dr. T. Ravindran M.D., DNB, Dip Diabetology
Professor and unit chief,
Department of Medicine
Kilpauk Medical College,
Chennai.

Prof. P. Ramakrishnan M.D., D.L.O
The DEAN
Govt.Kilpauk Medical College
Chennai - 600 010

DECLARATION

I solemnly declare that this dissertation "**CROSS SECTIONAL STUDY OF PREVALENCE OF DYSLIPIDEMIA IN TREATMENT NAÏVE PLHA (PATIENTS LIVING WITH HIV/AIDS) AND ITS CORRELATION WITH CD4 COUNT**" was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Dr. T. Ravindran M.D., DNB., Dip Diabetology,** Professor and Unit chief, Department of Internal Medicine, Government Kilpauk Medical College and Hospital, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfilment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

Place: Chennai-10

Date:

(Dr. S. GANESH ARAVIND)

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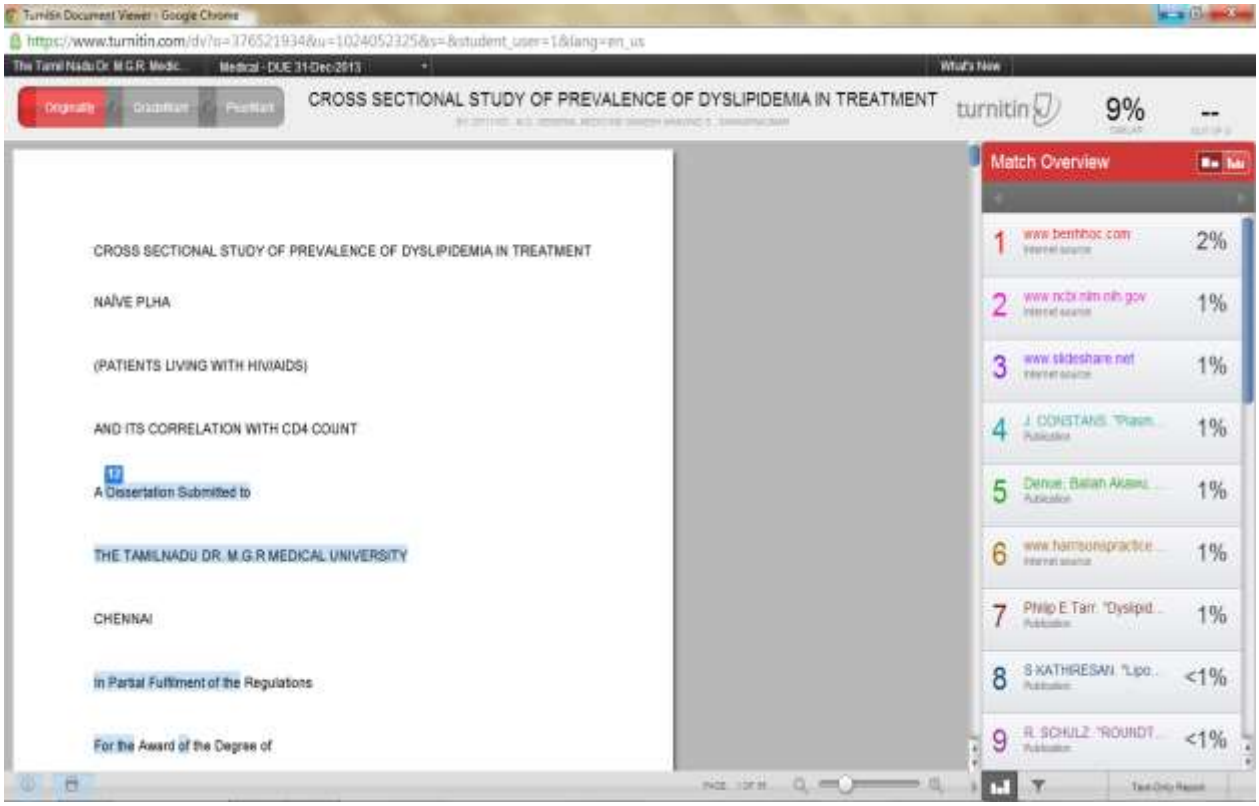
Finally, I wholeheartedly thank all my patients for their active co-operation in this study, without which this would not have become a reality.



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Abstract

Introduction:

HIV infection/AIDS is a global pandemic, with cases reported from virtually every country. Some studies have found a good correlation of Lipid profile and Body Mass Index (BMI) with advanced HIV infection.

Materials and Methodology:

In considering the above facts, a cross sectional study (using 50 PLHA and 50 controls) was conducted in Govt Kilpauk Medical College Hospital using various clinical and laboratory measures such as WHO clinical Staging, Anthropometry (BMI), lipid profile were done and they were compared with CD4 count of PLHA. Then it was analysed to check whether these parameters can be used as a surrogate marker for CD4 count to initiate ART and to monitor the therapy.

Observations and results:

In our study, good number of patients had a 'high risk' triglyceride range. Very high risk' cholesterol level is significantly higher among cases. PLHA had significantly lower level of LDL. HDL level was low among female cases.

There is no significant correlation between the CD4 count and the Levels of various parameters of lipid profiles. Apart from the intended correlation, we also attempted to correlate various other parameters and we came to a

conclusion that WHO categories correlates with CD4 count. Gender and HDL correlates well in our study population

Conclusions:

Although the CD4 count is used as “gold standard” test, WHO staging can be used as a surrogate marker for CD4 count to initiate ART in resource limited settings. Lipid profile can never be used as surrogate for CD4 count.

Keywords:

Patient living with HIV/AIDS(PLHA); CD4 count; Dyslipidemia; Cross section study; WHO categories; Lipid profile; Body Mass Index

INTRODUCTION

HIV infection/AIDS is a global pandemic, with cases reported from virtually every country. At the end of 2007, 33.2 million individuals were living with HIV infection (range: 30.6–36.1 million) according to the Joint United Nations Programme on HIV/AIDS (UNAIDS). More than 95% of people living with HIV/AIDS reside in low and middle-income countries of which 50% are female, and 2.5 million are children <15 years. In 2007, there were an estimated 2.5 million new cases of HIV infection worldwide, including 420,000 in children <15 years. In 2007, global AIDS deaths totalled 2.1 million (including 330,000 children <15 years). HIV incidence likely peaked in the late 1990s at >3 million new infections per year. Recent reductions in global HIV incidence likely reflect natural trends in the pandemic as well as the results of prevention programs resulting in behaviour change. Although the AIDS epidemic was first recognized in the United States and shortly thereafter in Western Europe, it very likely began in sub-Saharan Africa, which has been particularly devastated by the epidemic. More than two-thirds of all people with HIV infection (about 22.5 million) live in that region, even though sub-Saharan Africa is home to just 10–11% of the world's population .Within the region, southern Africa is worst affected. In eight southern African countries, available sero prevalence data shows that >15% of the adult population aged 15–49 is HIV-infected. In Asia, an estimated 4.9 million people were living with HIV at the end of 2007, of

2which 3.6 million people are in South East Asia. In 2007, there were 2.4 million people live with HIV/AIDS in India with an estimated adult HIV prevalence of 0.34%. The cost of combination ART has dropped in recent years as a result of generic medicines and differential pricing based on country need and ability to pay. The cost of diagnostic services to determine eligibility for treatment and to monitor treatment response has kept ART inaccessible to many, however. The US Department of Health and Human Services (DHHS) and the World Health Organization (WHO) recommend initiating ART therapy based on consideration of a patient's CD4 T-cell count when available. A CD4 cell count requires expensive laboratory equipment and trained technicians, which are absent in many areas of high HIV prevalence. The cost of monitoring HIV therapy may become more prohibitive than the cost of the medications themselves. In December 2003, the WHO broadened the recommendations for initiation of ART when CD4 testing is unavailable to include WHO stage III or IV or WHO stage II in combination with a TLC 1200 cells/mm3. Many studies have evaluated the use of TLC as a surrogate marker for CD4+ cell count with mixed results. Some studies have found a good correlation but others have not. In addition to low Lymphocyte count, Anaemia, Thrombocytopenia, Lipid profile and Body Mass Index (BMI) have been associated with advanced HIV infection.

In considering the above facts, a cross sectional study was conducted in Govt Kilpauk Medical College Hospital using various clinical and inexpensive

laboratory measures such as WHO clinical Staging, Anthropometry (BMI), lipid profile were done and compared with CD4 count. It is analysed that these parameters can be used as a surrogate marker for CD4 count to initiate ART and to monitor the therapy.

AIMS AND OBJECTIVES

AIM OF THE STUDY:

1. To study the prevalence of dyslipidemia in patient not started on Highly Active Anti-Retroviral Therapy.
2. To analyse the Lipid profile, CD4 count results and to check whether they are correlated with each other.

Review of literature

HIV disease – AIDS and related disorder

AIDS was recognised first in US 1981 when CDC reported unexplained occurrence of P. carinii pneumonia in five homosexual men. Later it was recognised in injection drug user blood transfusion recipients

1983 → HIV was isolated

1984 → HIV was demonstrated to be the causative organism for AIDS

1985 → ELISA

CDC categories persons on the basis of clinical conditions/ CD4 count. There are three clinical and three CD4 range categories. Therefore it is represented by a matrix of 9 mutually exclusive categories.

Using this system, any HIV individual with CD4 count<200/microliter has AIDS by defubutuib regardless of presence of symptoms/ opportunistic infection. Once patient lands in category B he cannot go back to category A clinical condition, even if the condition resolves. The same goes strongly true for category C clinical condition in relation to category B [1].

Category A

One / more of conditions in adolescent/ adult (>13 yrs.) with documented HIV infection

- Asymptomatic HIV infection
- Acute HIV infection with accompanying illness
- Persistent generalised lymphadenopathy

Category B

One/ more of following criteria in adolescent or adult

1) Condition attributed to HIV infection/ are indicative of defect in cell mediated immunity
2) Conditions are considered by physician to have a clinical course to require management that is complicated by HIV infection
    a. Bacillary angiomatosis
    b. Herpes zoster
    c. Candidiasis
    d. Listeriosis
    e. Pelvic inflammatory disease
    f. Peripheral neuropathy
    g. Constitutional Symptoms like fever/ diarrhoea >1 month

Category C

Conditions in AIDS Surveillance case definition

a. Candidiasis of bronchi, trachea, Lungs
b. Candidiasis of Oesophagus
c. Cervical Cancer – invasive
d. Extra pulmonary/ Disseminated coccidiodomycosis
e. Extra pulmonary/ Chronic intestinal cryptococcosis
f. CMV retinitis
g. HSV chronic ulcer/ Bronchitis pneumonia/ Esophagitis
h. Extra pulmonary/ Disseminated Histoplasmosis
i. Chronic intestinal isospora
j. Kaposi sarcoma
k. Burkitt's lymphoma/ Lymphoma of brain
l. Mycobacterium avium complex
m. Mycobacterium tuberculosis
n. Recurrent pneumonia
o. Pneumocystis jiroveci
p. Wasting syndrome due to HIV[2]

	A- Asymptomatic/ Primary HIV/ Persistent generalised Lymphadenopathy	B- Symptomatic individual	C- AIDS indicator condition
CD4 T cell count >500	A1	B1	C1
CD4 T cell count 200 – 499	A2	B2	C2
CD4 T cell count <200	A3	B3	C3

Etiologic agents

Human disease retroviruses are

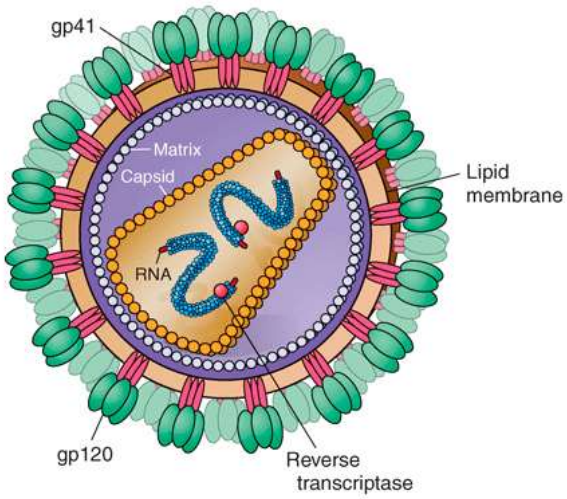
1) HTLV-1 } Transforming retrovirus
2) HTLV-2

3) HIV1 } Cytopathic effects directly/ indirectly
4) HIV2

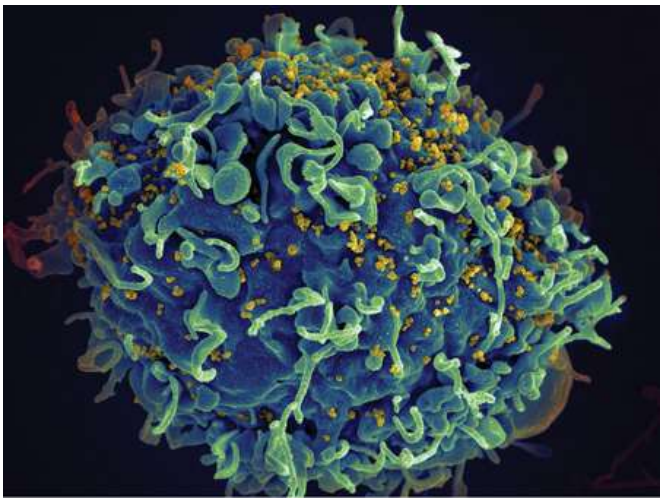
HIV1 (M,N,O,P) and HIV2(A,B,C,D,E,F,G) are from chimpanzees/ gorilla and sooty mangabeys respectively

AIDS pandemic is predominantly caused by HIV1 M group virus [3]

Morphology



Icosahedral with numerous spikes made of gp120 and gp40



Replication

Hall mark enzymes – Reverse transcriptase, integrase

I) The glycoprotein gp120 binds to CD4 molecule, then gp120 molecule undergo a conformational change and bind to one of the two major co-receptors CCR5/ CXCR5.

II) The glycoprotein gp120 then binds to DC sign(c-type lectin receptor in dendritic cell).

III) The glycoprotein gp41 penetrates plasma membrane of target.

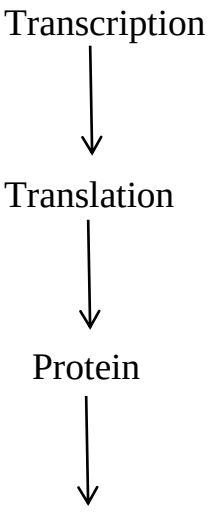
IV) Pre-integration complex (RNA, Enzymes, Capsid coat) is released onto cytoplasm and reaches nucleus.

V) Viral RNA → proviral HIV DNA. This stage is most vulnerable stage ApoBEC family of protein – inhibits viral replication by,

a. ApoBEC bind viral genome with subsequent reverse transcripts accumulation.

b. ApoBEC, through its deaminase activity causes hypermutation

VI) Proviral HIV DNA integrates with human chromosome



Post translational modification

(Glycosylation/ phosphorylation, myristoylation and cleavage)

Budding occurs through a specialised region in the host cell membrane (lipid bilayer) known as lipid rafts. Protease catalyses the cleavage of the gag-pol precursor to yield the mature virion [4]

Genome: - [46]

3 genes codes importantly for the structural proteins,

Gene ‘gag’ – Protein that form core of virion (p24)

Gene ‘pol’ – Reverse Transcriptase, protease, integrase

Gene ‘env’ – envelop glycoprotein (gp120, gp4)

6 other genes (tat, rev, nef, vif, vpr, vpu) which modifies host cell, thereby enhance the viral growth. HIV2 has vpx instead of vpu in HIV1

Circulating recombinant-forms are generated when an individual is injected by 2 subtypes that then recombine and create a virus with a selective advantage. [5]

Transmission:-

I. SEXUAL TRANSMISSION –most common mode

a) Factors
    a. Viral load
    b. STD

i. Ulcerative – Treponema pallidum, Hemophilus ducryei, HSV.
ii. Nonulcerative – Neisseria gonorrhoea, Chlamydia trochamatis, Trichomonas vaginalis.

b) URAI > Vaginal intercourse transmission, because of
    a. Direct inoculation into blood.
    b. Infecting langerhan cell in mucosa.
c) Viral load <1700 transmission is very rare. Therefore initiation ART(Anti-Retroviral Therapy) reduces plasma viremia thereby reducing transmission
d) Treatment of Sexually Transmitted Disease will prevent HIV transmission
e) Circumcision is associated with a lower risk of HIV infection for heterosexual men
    a. Fore skin contains high density of Langerhan cells
    b. Micro trauma to foreskin and glans penis
    c. Moist environment under foreskin
f) Oral contraceptive increase HIV transmission by affecting cervical mucosa

II. TRANSMISSION BY BLOOD/ BLOOD PRODUCTS

a) Blood/ blood product transfusion/ transplanted tissue

b) Sharing injection, paraphernalia such as needles, syringes, the water in which they are mixed

c) Few cases of HIV transmission via semen used in artificial insemination and tissues/organs used in organ transplantation have also been documented, prior to those screening procedures. At present, donors of such tissues are pre-screened for HIV infection.

In case of HIV-serodiscordant couples (HIV-infected male; HIV-uninfected female) who have desire to conceive a child, assisted reproductive techniques like sperm-washing to minimize the risk of transmission of HIV have been employed successfully, with only one well-documented failure of seroconversion (i.e., becoming infected with HIV infection) in the uninfected female partner, reported in 1990.[6]

III. TRANSMISSION OF HIV IN OCCUPATIONALLY VULNERABLE PERSON:

Procedures that place a health worker at potentially high risk of HIV transmission are

a) Percutaneous sharp injuries (e.g., a needle stick or cut with a sharp object) or

b) Contact of non-intact skin or mucous membrane (e.g., exposed skin that is abraded, diseased with dermatitis, or chapped) with blood, infected tissue, or other potentially risky body fluids. Large, meta

centric studies have shown that the risk of transmission of HIV infection following a skin puncture by needles or sharp things that were contaminated by blood from person who was documented with HIV infection is approximately about 0.3% and following a mucous membrane exposure is 0.09% if the injured and/or exposed health care worker was not treated with antiretroviral drugs within 24 hours.

c) Transmission of HIV infection following non-intact skin exposure has also been documented, but the mean risk of transmission via this route has not been appropriately determined.

The most attention attracting dramatic reports of transmission of HIV infection in health care setting was the transmission of HIV infection to 8000–10,000 children in Romanian orphanages in 1980s. Other largest incidents happened in health care setting/hospitals were in Russia and Libya in late 1980s and late 1990s, respectively. Each of these above incidents attracted considerable global attention and was likely related to repeated use of contaminated needles and/or provision of blood products which is contaminated by HIV infection. [50]

IV. MATERNAL-INFANT/ FOETAL TRANSMISSION:

HIV infection may be transmitted from infected mother to her foetus during her pregnancy, during parturition, or via breast feeding. This still remains an important modality of HIV transmission in certain developing/

underdeveloped countries, where the ratio of infected women to infected men was about 1:1. Virological analyses of aborted embryo/ foetuses denote that HIV infection can be transmitted from mother to the foetus/ embryo during first or second trimesters of the pregnancy. Despite this fact, maternal transmission to the foetus most commonly occurs in the peri-partum/ perinatal period. Two significant studies done in Rwanda and the former Zaire demonstrated the fact that approximate proportions of mother-to-child transmissions were 23–30% before delivery, 50–65% during parturition, and 12–20% through breast-feeding in post-partum period.

Short-duration prophylactic antiretroviral therapeutic regimens, such as single dose nevirapine given to the infected mother at the onset of parturition and one dose to the new born infant within 72 hrs of birth, are of significant relevance to low- to mid-income countries because of low cost of above antiretroviral regime and the fact that in those nations perinatal care is often not properly utilised/ not available and pregnant women are seen by the health care workers for first time near the time of delivery. These above factors increase the likelihood of HIV transmission. Apart from the above factors, others responsible for HIV transmission include detectable amount of HIV in breast milk, presence of mastitis, very low CD4+ T cell counts in mother and vitamin A deficiency in mother. The most important thing is that the risk of HIV

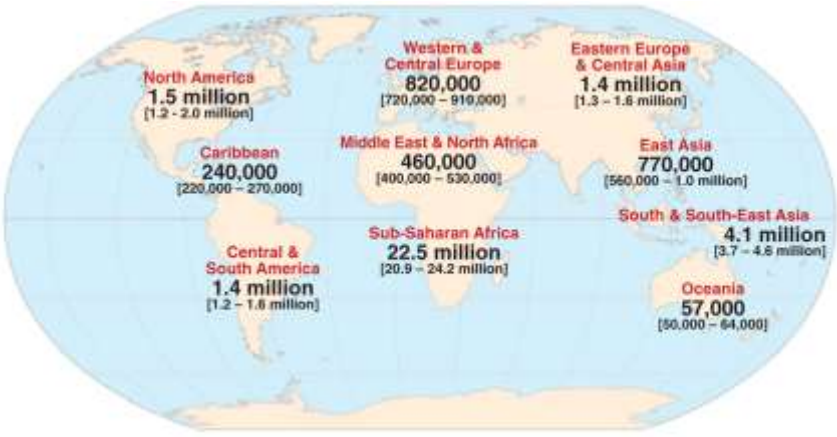
infection via breast milk feeding is much high during the initial months of breast-feeding.

EPIDEMIOLOGY:-

HIV Infection and AIDS Worldwide

AIDS is an emerging global pandemic, with many cases reported from different country. By 2009, estimated 33.3 million patients were living with HIV infection/AIDS, based on the statistics released by the Joint United Nations Programme on HIV/AIDS (UNAIDS).[47]

More than 95% of patients living with HIV/AIDS dwell in low- and middle-income countries; 50% were female, and 2.5 million were children <15 yrs.



Populations in many Asian nations are very large (especially India and China) that even very low infection rate and sero-prevalence rate result in apparently large numbers of people living with HIV/AIDS. [48]

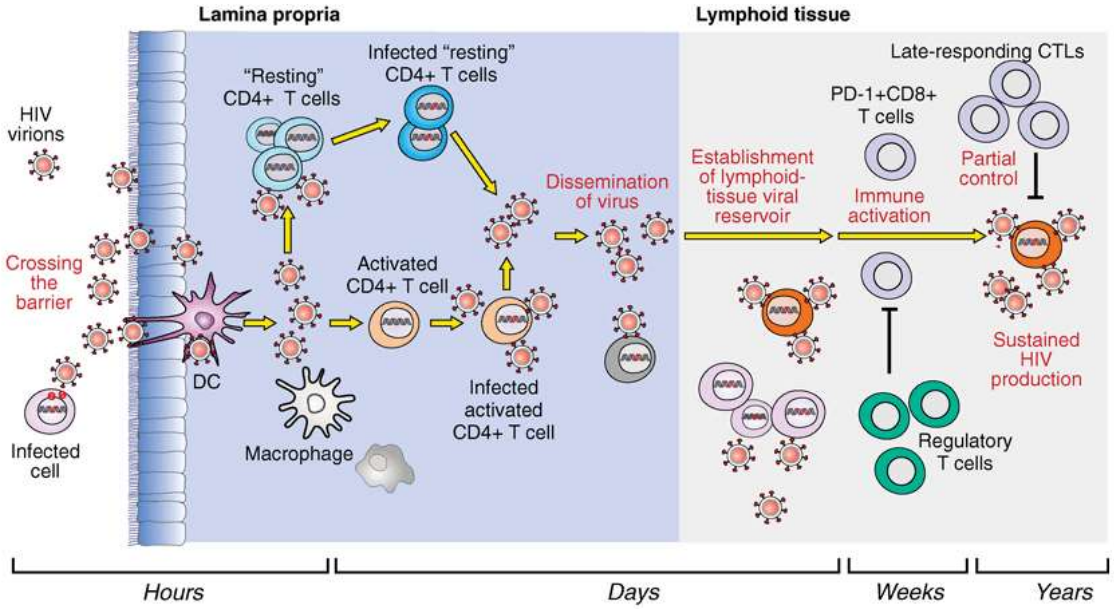
PATHOPHYSIOLOGY AND PATHOGENESIS:-

The hallmark of AIDS/HIV disease is a massive lacunae in the defence system (immunodeficiency) resulting primarily from a progressive qualitative and quantitative deficiency of a subset of 'T' lymphocytes termed to as 'helper T cells' occurring in the setting of polyclonal immune cell activation. The helper T lymphocytes are phenotypically defined by the presence on their surface by the CD4 molecule, which functions as the cell's primary receptor for the Human Immunodeficiency Virus. A co-receptor must be present in the T lymphocytes together with CD4 molecule for an efficient binding, effective fusion, and proper entry of HIV-1 into its target cells (i.e., T Lymphocytes). HIV exploits these two major co-receptors, CCR5 and CXCR4, for their fusion and entry; these co-receptors function as the primary receptors for chemo attractive cytokines called chemokines and these belong to seven-transmembrane-domain G protein coupled family of receptors. A number of other mechanisms are also responsible for depletion of immunological cells and/or immune dysfunction of CD4+ T lymphocytes have been shown in vitro. [49]These include direct infection of these cells by HIV followed by their destruction, and the indirect effects such as immunological clearance of the infected cells and immune exhaustion/fatigue due to an aberrant cellular activation, and activation-induced apoptosis (cell death). Patients with CD4+ T lymphocytes levels beneath certain levels are at increased risk of communicating a wide variety of opportunistic disorders, particularly the

opportunistic infections and neoplasms that are AIDS-defining diseases. Some features/ disorders occurring in HIV/ AIDS, such as Kaposi's sarcoma and certain neurological abnormalities, cannot be completely explained by the immune-compromise caused by HIV infection, since the above mentioned complications may occur well in advance to the development of severe immunologic disability.

Virtually there exists, in all patients living with HIV/AIDS, a pool of latently infected, dormant CD4+ T lymphocytes that serve, at least, as one of the important component of the dormant reservoir of virus. Such resting cells manifest post-integration latency (which means the HIV provirus integrates into the genome of the lymphocytes and can stay in this resting state until a provocative signal propels the expression/replication of HIV transcripts and ultimately replication-competent and infective virus).

The picture below shows the viral invasion through the mucosal surface.



Immunological system activation and variable extend of the inflammation are crucial and essential components of any immune response to a foreign substance/ antigen. However, the activation of the immune system and variable inflammatory response can be considered significantly aberrant in a patient living with HIV/AIDS and they play crucial role in pathogenesis of the HIV disease and other important chronic inflammatory conditions associated with HIV/ AIDS. Activation of the immune/ defence system and variable inflammatory response in the HIV-infected individual contribute substantially to

(1)The replication of HIV virion,

(2)Induction of the immune dysfunction, and

(3)Increased incidence of chronic inflammatory/ non-inflammatory conditions associated with continuous/persistent immunological activation and inflammation

- Bone fragility
- Accelerated aging syndrome
- Cardiovascular disease
- Cancers
- Kidney disease
- Diabetes
- Neurocognitive dysfunction
- Liver disease

Table 189-4 Mechanisms of CD4+ T Cell Dysfunction and Depletion	
Direct Mechanisms	**Indirect Mechanisms**
Loss of plasma membrane integrity due to viral budding	Aberrant intracellular signaling events
Accumulation of unintegrated viral DNA	Autoimmunity
Interference with cellular RNA processing	Innocent bystander killing of viral antigen–coated cells
Intracellular gp120-CD4 autofusion events	Apoptosis
Syncytia formation	Inhibition of lymphopoiesis
	Activation-induced cell death
	Elimination of HIV-infected cells by virus-specific immune responses

DIAGNOSIS OF HIV INFECTION IN SUSPECTED INDIVIDUAL/ AS A SCREENING PROCEDURE:-

The Centre for Disease Control had recommended that the screening for HIV infection should be performed as a matter of routine health care. The diagnosis/ detection of HIV infection/ AIDS depend on direct detection of the HIV or one of the viral components/ antigen and/ or demonstration of the antibodies to Human Immunodeficiency Virus. As shown above, antibodies to the HIV generally appear in the systemic circulation 3–12 weeks following the inoculation of the infection.

The standard serological screening test for detection of HIV infection is the Enzyme linked immunosorbant Assay (ELISA), which is also termed as an enzyme immunoassay (EIA). The above mentioned solid-phase assay is excellent and an extremely good screening measure with a sensitivity of about >99.5%. Most diagnostic laboratories utilise a commercial ELISA kit which contains antigens/components from both HIV-1 and HIV-2 and thus enable us to detect either infections. These kits utilise both recombinant and natural

antigens which are persistently updated to enhance their sensitivity to the newly discovered/ identified species, such as group O viruses. Fourth-generation ELISA test combines the detection of p24 antigen of Human Immunodeficiency Virus with the identification of the antibodies against HIV. ELISA tests are generally reported as positive (highly reactive), indeterminate (partially reactive) and negative (nonreactive).

Only 10% of the ELISA-positive subjects are subsequently confirmed to have incurred HIV infection. There is humpty number of factors associated with the false negativity for ELISA test. Among those factors

a) Antibodies to the class II antigens (may be seen after pregnancy, following blood transfusion, or transplantation),

b) Hepatic disease,

c) Autoantibodies,

d) Acute viral infections and

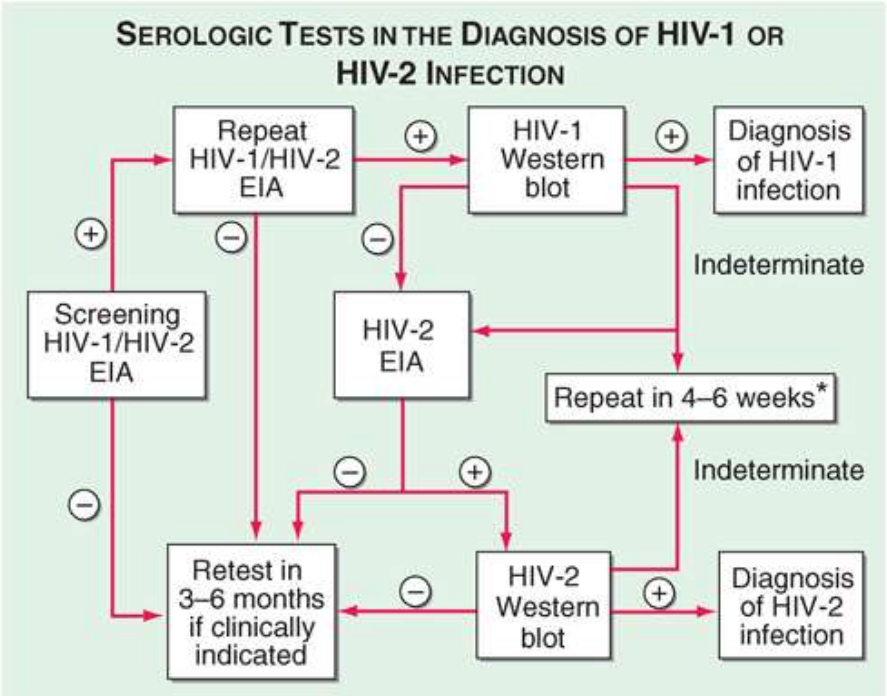
e) Recent influenza vaccination.

The confirmatory test that is most commonly used - Western blot. This immunological assay encompasses the advantage of the fact that multiple HIV components/ antigens of well-characterized molecular weights invoke the production of specific antibodies. Those components/ antigens can be isolated on the basis of their molecular weight, and antibodies to each of those components can be identified as discrete/ separate bands on the Western blot

test. A negative Western blot is defined as one in which there is no bands present at molecular weights corresponding to the HIV gene products. In a patient identified with a positive or indeterminate ELISA and negative Western blot assay, one can conclude with the certainty that ELISA reactivity was false positive. On the other side, a Western blot assay demonstrating the antibodies to the products of all the three of the major genes of HIV (*gag*, *pol*, and *env*) one can conclude with certainty that the individual had definite evidence of HIV infection. Criteria published by the US FDA (Food and Drug Administration) in the year 1993 for a positive Western blot assay state that the result is termed positive/ reactive if antibodies to HIV gene products exist to two of the three HIV Antigens/ proteins: p24, gp41, and gp120/160. Utilising these criteria, 10% of all the blood donators deemed positive for HIV-1 infection didn't have an antibody band to the *pol* gene product p31. Some 50% of the above positive blood donators were subsequently found to be false positives. Thus, the lack of the p31 band should increase the doubt that one may be dealing a patient with a false-positive western blot test result. In this setting it is intelligent to obtain an additional confirmation with a RNA-based test for HIV-1 virion and/or a follow up Western blot assay. By the definition, patterns of reactivity in western blot assay that do not fall into either the positive or the negative categories are termed as "indeterminate" group.

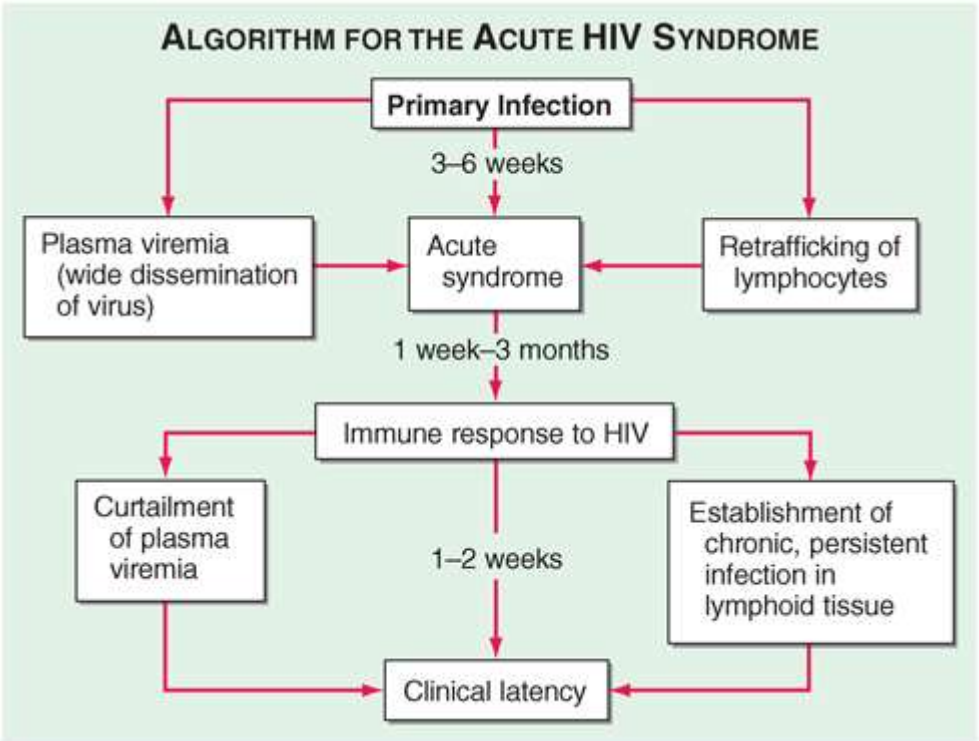
Other diagnostic tests/modalities (such as RNA-PCR, DNA-PCR, the assay for bDNA, or p24 antigen capture) may be done to confirm that these bands do not indicate early HIV infection.

FLOWCHART SHOWING THE STEPS INVOLVED IN THE DIAGNOSTIC PROTOCOL:-



ACUTE AIDS SYNDROME:-

Table 189-9 Clinical Findings in the Acute HIV Syndrome	
General	Neurologic
Fever	Meningitis
Pharyngitis	Encephalitis
Lymphadenopathy	Peripheral neuropathy
Headache/retroorbital pain	Myelopathy
Arthralgias/myalgias	Dermatologic
Lethargy/malaise	Erythematous maculopapular rash
Anorexia/weight loss	Mucocutaneous ulceration
Nausea/vomiting/diarrhea	



The Asymptomatic Stage—Clinical Latency

Although length of the time from initial infection to the development of the clinical disease (i.e., incubation of infection) varies widely, the median time

for untreated patients is roughly about 10 years. As already emphasized above, the HIV/AIDS with an active viral replication/ multiplication is on-going and progressive during this asymptomatic stage/ period of clinical latency. The rate of the progression of the disease is correlated directly with the levels of HIV RNA. Patient with a very high plasma level of HIV RNA may progress to more symptomatic disease much faster than do patient with low plasma levels of HIV-RNA.

Some patients are referred to as **'long-term non-progressors'** may show little if there is any decline in T cell CD4+ counts over an extended period of time. These long term non-progressive patients generally have significantly very low levels of HIV-RNA;

There is another subset of PLHA patients, termed as **'elite non-progressors'**, who exhibits HIV-RNA levels <50 copies per millilitre.

Certain patients remain entirely asymptomatic despite the fact that their T cell (CD4+) counts show a gradual/ steady progressive decline to significantly low levels. In this scenario, the appearance of an opportunistic disease (infection/ Malignancy) may be the primary manifestation of HIV infection/ AIDS.

During this asymptomatic period/ clinical latency of HIV infection, the median rate of decline of the CD4+ T cell is roughly measures 50/μL per year.

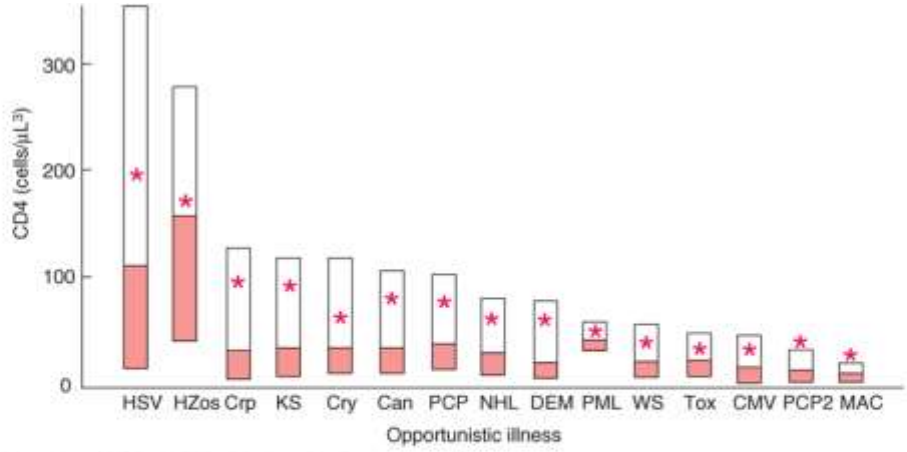
When CD4+ T cell count falls to significantly low level i.e., <200/µL, the resulting immunodeficiency state is significantly severe enough to place the patient at a higher risk for both opportunistic infections and neoplasms and, thereby leading to a clinically apparent disease (symptomatic disease).

Symptomatic Disease:-

Symptoms of the HIV disease (AIDS) can manifest at any point of time during the disease course of HIV infection. The spectrum of the illnesses may change widely as the CD4+ T cell count declines. The more severe and life-threatening complications of HIV infection are encountered in PLHA patients with significantly very low CD4+ T cell counts i.e., <200/µL. A diagnosis of HIV/AIDS is done in any patient with HIV infection and a CD4+ T cell count <200/µL and in anyone with HIV infection who develops one of the HIV-associated diseases considered to be indicative of a severe deficiency in cell-mediated immunity. While the etiological agents of these secondary infections are typically opportunistic organisms such as atypical mycobacteria, *P. jiroveci*, CMV, and many other organisms that do not generally cause diseases in the absence of a defective immune system, they also encompasses common bacterial, viral and mycobacterial pathogens. After the widespread use of HAART and institution of the appropriate guidelines for the prevention and treatment of opportunistic infections and their control, the incidence of these secondary infections have dropped down dramatically. Overall, the clinical

spectrum of HIV disease/AIDS is constantly varying as these patients live longer and new and better methodologies to prophylaxis and treatment of HIV disease are significantly emerging day by day. In addition to the classical AIDS-defining illnesses, patients living with HIV infection also have a dramatic raise in serious non-AIDS illnesses, including non-AIDS related carcinomas and, cardiovascular, metabolic, renal and liver disease. Non-AIDS incidences dominate the disease burden for these patients with HIV infection receiving HAART. Lesser than 50% of the deaths in AIDS patients are as a direct result of a classic AIDS-defining illness. The physician providing health care to the patient suffering from HIV infection must be well versed in general medicine as well as AIDS- related opportunistic diseases. In general, it should always be stressed that a key component of the treatment of symptomatic complications of the HIV/AIDS, whether they are primary or secondary, is achieving a good control of replication of HIV through the effective use of HAART and prescribing primary and secondary prophylaxis for opportunistic infections as and when indicated.

CD4 count and its relationship with the opportunistic infections:



Relationship between CD4+ T cell counts and the development of opportunistic diseases. Boxplot of the median (line inside the box), first quartile (bottom of the box), third quartile (top of the box), and mean (asterisk) CD4+ lymphocyte count at the time of the development of opportunistic disease. Can, candidal esophagitis; CMV, cytomegalovirus infection; Crp, cryptosporidiosis; Cry, cryptococcal meningitis; DEM, AIDS dementia complex; HSV, herpes simplex virus infection; HZos, herpes zoster; KS, Kaposi's sarcoma; MAC, *Mycobacterium avium* complex bacteremia; NHL, non-Hodgkin's lymphoma; PCP, primary *Pneumocystis jiroveci* pneumonia; PCP2, secondary *P. jiroveci* pneumonia; PML, progressive multifocal leukoencephalopathy; Tox, *Toxoplasma gondii* encephalitis; WS, wasting syndrome. *(From RD Moore, RE Chaisson: Ann Intern Med 124:633, 1996.)*

AIDS AND NON COMMUNICABLE DISEASES:-

Heart disease is relatively common post-mortem finding in patient infected with HIV/AIDS (25–75% in the autopsy series). The most common form of heart disease is the coronary artery heart disease. In one large series, the overall incidence of myocardial infarction (MI) was about 3.5/1000 patient-years, 28% of those events were fatal, and Myocardial infarction was responsible for about 7% of all deaths in the above cohort. In patients living with HIV infection, cardiovascular disease may be coupled with classical risk factors such as a direct consequence of HIV infection, smoking, or adverse reaction/ complication of HAART. Patients living with HIV infection have raised levels of triglycerides, reduced levels of high-density lipoprotein cholesterol, and a much raised prevalence of smoking than the cohorts of

individuals without HIV infection. The finding that the incidence of cardiovascular disease events was much lower in patients on antiretroviral therapy than in those randomized to undergo a treatment interruption recognised a clear correlation between HIV replication and cardiovascular disease risks. In one of the studies, a baseline CD4+ T cell count of <500/µL was detected to be an independent individual risk factor for any cardiovascular disease events comparable in magnitude to that attributable to smoking. While the exact/precise pathogenesis of this correlation remains unclear, it is likely related to the inappropriate immune activation and an increased tendency for coagulation seen as a result of HIV multiplication. Exposure to certain reverse transcriptase inhibitors and HIV protease inhibitors has been correlated with the increase in total cholesterol and/or myocardial infarction risk. Any increase in the risk of death from Myocardial Infarction resulting from the utilisation of certain antiretroviral drugs must be balanced (benefit/ risk ratio) against the marked increase in overall survival rate brought about by these dreadful/darling drugs.

Another form of the cardiovascular disease associated with HIV infection is dilated cardiomyopathy coupled with congestive heart failure (CHF) referred to as **'HIV-associated cardiomyopathy'**. This generally occurs as late complication of this viral (HIV) infection and, histologically, this depicts the elements of myocarditis. For this reason, some have advised treatment with IV

immunoglobulin (IVIg) which in-turn can subside/ allure the inflammation of myocardium. HIV can be demonstrated directly in the cardiac tissue in this setting, and there is a chronic debate over whether it plays a direct role in this condition. Patients present with typical findings of CHF including shortness of breath and edema. Patients with HIV infection may also develop cardiomyopathy as adverse effects of cytokines like IFN-α or drugs like nucleoside analogue therapy. Drug induced cardiomyopathy are reversible once therapy is put on red button.

Kaposi Sarcoma, Chagas' disease, Cryptococcosis, and toxoplasmosis can affect significantly the myocardium, leading to opportunistic infection associated cardiomyopathy. In one series of studies, most patients living with HIV infection and treatable myocarditis were found to have toxoplasmosis associated myocarditis. Most of those patients also had an evidence of toxoplasmosis affecting their central nervous system. Thus, double-dose contrast CT scan or MRI of the brain should be inculcated in the workup of any of the patient with advanced HIV infection, significantly low CD4 count and cardiomyopathy.

Lipid Profile

A wide variety of endocrine and metabolic dysfunctions are seen in the context of patients living with HIV infection. These may be a direct consequence from infection due to HIV, or secondary to opportunistic

neoplasms or infections, or related to therapeutic (anti-retroviral therapy) side effects. Between 33 and 75% of these patients with HIV infection receiving HAART develop a syndrome often termed as ‘lipodystrophy’, comprising of the elevations in plasma triglycerides, total serum cholesterol, and serum apolipoprotein B, as well as hyperglycaemia and hyperinsulinemia. Many of these patients have been noted to have characteristic set of body habitus changes associated with redistribution of fat, consisting of peripheral wasting coupled with truncal obesity. Truncal obesity is apparent as an increase in waist/abdominal girth related to increases in mesenteric fat, a dorso-cervical pad of fat ("buffalo hump") reminiscent of patients with Cushing's syndrome, and breast enlargement. The lipoatrophy, or peripheral wasting, is generally noticeable in the face and buttocks and by the venous prominence in the legs/ extremities. These changes may occur at any time ranging from 6 weeks to several years after the initiation of HAART. Approximately 20% of these patients living with HIV-associated lipodystrophy meet the criteria for the **metabolic syndrome** as defined by The U.S. National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) or The International Diabetes Federation (IDF). The lipodystrophy syndrome has been established in association with the regimens containing a variety of different anti-retro viral drugs, and while initially reported in setting of administration of protease inhibitor therapy, it also appears that similar changes can also be induced by potent and commonly used protease-sparing regimens. It has also been

suggested that these lipoatrophy changes are particularly much severe in patients receiving the thymidine analogues like stavudine and zidovudine. Guidelines established National Cholesterol Education Program (NCEP) should be followed in management of these lipid abnormalities. Due to these concerns regarding drug interactions, the most commonly utilized lipid-lowering agents in this setting are gemfibrozil and atorvastatin.

Immune Reconstitution Inflammatory syndrome. [53, 05]

Table 189-11 Characteristics of Immune Reconstitution Inflammatory Syndrome (IRIS)
• Paradoxical worsening of clinical condition is seen following the initiation of antiretroviral therapy
• Occurs weeks to months following the initiation of antiretroviral therapy
• Is most common in patients starting therapy with a CD4+ T cell count under 50/μL who experience a precipitous drop in viral load
• Is frequently seen in the setting of tuberculosis
• Can be fatal

LIPID:-

Screening:

Guidelines for the management and screening of lipid related disorders have been provided by the expert Adult Treatment Panel (ATP) convened by the National Cholesterol Education Program (NCEP) of the National Heart, Lung, and Blood Institute. The NCEP ATPIII panel guidelines which were published in 2001 recommend that all adults older than 20 years of age should have plasma levels of the cholesterol, triglyceride, LDL-Cholesterol, and HDL-

Cholesterol measured after a 12-hour overnight fasting. In most of the clinical laboratories, the total cholesterol and triglycerides in plasma are measured by enzymatic method, and then the cholesterol in the supernatant fluid is measured after the precipitation of apoB-containing lipoproteins to determine the HDL-Cholesterol (which is an apoA containing substance). The LDL-Cholesterol is estimated using the following formula:

(The VLDL-Cholesterol is estimated simply by dividing the plasma triglyceride by 5, reflecting the proportion of cholesterol to triglyceride in VLDL particles.)

This formula is reliable and accurate if the test results obtained are done in patients on fasting state and if the triglyceride level does not exceed more than 200 mg/dL; by convention the above formula cannot be used if plasma triglyceride level is >400 mg/dl; The accurate method for determination of LDL-Cholesterol levels in patients with triglyceride levels >200 mg/dL requires the application of ultracentrifugation techniques or any other direct assays for LDL-Cholesterol. If triglyceride level is more than 200 mg/dL, the guidelines recommend that the "non-HDL-C" be calculated by simple subtraction of HDL-C from total cholesterol and that this should be considered as a secondary target of therapy. Further treatment and evaluation is primarily based on the plasma

LDL-Cholesterol and secondarily on non-HDL-Cholesterol levels as well as the assessment of overall cardiovascular risk factors.

Diagnosis:-

The crucial first step in management of lipid disorder is the determination of the class or classes of lipoproteins that are increased or reduced in the patient. The Fredrickson scheme of classification for hyperlipoproteinemias, although less commonly used now-a-days than in the past, can be helpful in this regard. Once the hyperlipidemia is accurately diagnosed/ classified, efforts should be targeted to rule out any possibilities of secondary causes of the hyperlipidemia. Although many of the patients with hyperlipidemia have a genetic cause of their lipid disorder (primary), secondary factors may frequently contribute to hyperlipidemia. Fasting plasma glucose should be obtained in preliminary workup of all the subjects with a raised plasma triglyceride level. Nephrotic syndrome and chronic renal failure should be excluded first by obtaining urine protein level and serum creatinine. Liver function tests should also be performed to rule out cholestasis and hepatitis. Hypothyroidism can be ruled out by measuring the serum level of TSH. Patients with hyperlipidemia, especially hypertriglyceridemia, who drink excessive alcohol, should be promoted to decrease their alcohol intake. Obesity, Sedentary lifestyle and smoking are important risk factors which were associated with low HDL-Cholesterol levels, and patients should also be counselled about these risk factor issues.

Once these secondary causes for the raised lipoprotein levels have been ruled out, every possible attempt should be made to diagnose the primary lipid disorder since the underlying causative agent has a significant effect on the risk of developing Coronary artery Heart Disease, on response to the drug therapy, and on management of other family members. Often, determining correct diagnosis requires a detailed history, family medical status and, in some cases, lipid analyses in rest of the family members.

If fasting plasma triglyceride level is more than 1000 mg/dL, then the patient almost always has chylomicronemia and either has Type V or Type I hyperlipoproteinemia. The plasma triglyceride to total cholesterol ratio helps us to distinguish between the two possibilities and is much higher in Type I than Type V hyperlipoproteinemia. If the patient has Type I hyperlipoproteinemia, then post heparin lipolytic assay should be done to determine if the patient has Lipoprotein lipase or apoC-II deficiency. Type V is a much more common form of chylomicronemia in the adult patient than Type I. Often treatment of the secondary factors contributing to the hyperlipidemia (such as diet, glucose intolerance, obesity, alcohol consumption, estrogen therapy) will change a Type V into a Type IV pattern, reducing the significant risk of developing acute pancreatitis.

If levels of LDL-Cholesterol are very high (i.e., greater than a ninety-fifth percentile), it is very likely that the patient has a genetic form of hyperlipidemia

(hypercholesterolemia). The presence of the severe hypercholesterolemia, tendon xanthomas, and autosomal dominant pattern of inheritance are consistent with the diagnosis of Familial Hypercholesterolemia, FDB, or ADH-PCSK9. At present time, there is no forcing reason to perform molecular level studies to further refine the molecular diagnosis, because the treatment of FH and FDB is same. Recessive forms of severe hypercholesterolemia are very rare and if patient with severe hypercholesterolemia has parents with normal cholesterol levels, sitosterolemia should be considered; a diagnostic clue for the identifying sitosterolemia is the greater than expected response of the hypercholesterolemia to reductions in dietary cholesterol content or to treatment with either a cholesterol absorption inhibitor (ezetimibe) or to bile acid resins. Patients with a moderate hypercholesterolemia, which does not clump in the families, are likely to have polygenic hypercholesterolemia.

The most common error in the treatment and diagnosis of the lipid disorders occurs in patients with a mixed hyperlipidemia without any chylomicronemia. Elevation in the plasma levels of both cholesterol and triglycerides are seen in the patients with increased plasma levels of IDL (Type III) and of LDL and VLDL (i.e., Type IIB) and in patients with increased levels of VLDL (i.e., Type IV). The proportion of triglyceride to total cholesterol is higher in Type IV than the other two lipid disorders. The plasma levels of apoB containing lipids are highest in Type IIB. A beta quantification to determine the

VLDL-C/triglyceride ratio in plasma or a direct measurement of the plasma LDL-C should be performed at least once prior to initiation of lipid-lowering therapy to determine if the hyperlipidemia is due to the accumulation of remnants or to an increase in both LDL and VLDL.

Table 241-3. Clinical Identification of the Metabolic Syndrome—Any Three Risk Factors

Risk Factor	Defining Level
Abdominal obesity[a]	
Men (waist circumference)[b]	>102 cm (>40 in.)
Women	>88 cm (>35 in.)
Triglycerides	>1.7 mmol/L (>150 mg/dL)
HDL cho-lesterol	
Men	<1 mmol/L (<40 mg/dL)
Women	<1.3 mmol/L (<50 mg/dL)
Blood pressure	≥130/≥85 mmHg
Fasting glucose	>6.1 mmol/L (>110 mg/dL)

Table 241-2. LDL Cholesterol Goals and Cutpoints for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories

	LDL Level, mmol/L (mg/dL)		
Risk Category	**Goal**	**Initiate TLC**	**Consider Drug Therapy**
Very high	<1.8 (<70)	≥1.8 (≥70)	≥1.8 (≥70)
ACS, or CHD w/DM, or multiple CRFs			
High	<2.6 (<100)	≥2.6 (≥100)	≥2.6 (≥100) [<2.6 (<100): consider drug Rx]
If LDL <2.6 (<100)	[optional goal: <1.8 (<70)] <1.8 (<70)		
Moderately high	<2.6 (<100)	≥3.4 (≥130)	≥3.4 (≥130) [2.6–3.3 (100–129): consider drug Rx]
2+ risk factors (10-year risk, 10–20%)			
Moderate	<3.4 (<130)	≥3.4 (≥130)	≥4.1 (≥160)
2+ risk factors (risk <10%)			
Lower	<4.1 (<160)	≥4.1 (≥160)	≥4.9 (≥190)
0–1 risk factor			

ARTICLES SHOWING THE RELATIONSHIP BETWEEN THE CD4 COUNT AND IMMUNODEFICIENCY:-

The aim of the study conducted by Eric Walter Pefura Yone, Awa Foueudjeu Betyoumin, Andre Pascal Kengne, Francois Jerome Kaze Folefack and Jeanne Ngogang in Cameroon, was assessment of prevalence, and the characteristics of abnormalities of lipid profile in PLHA patient with or without ART that include nonnucleoside reverse transcriptase inhibitors (NNRTIs). They found that PLHA pts on first-line ART had high total cholesterol, LDL-c and TC/HDL-c ratio as compared with ART-naïve PLHA patients. Serum levels of HDL-c and triglycerides were not different between these two groups. The described derangements of lipid profile are potentially atherogenic.

The conclusion of the above study was WHO first-line cART regimens containing NNRTIs are correlated with potentially atherogenic adverse lipid profile in HIV1/AIDS patients compared to untreated or treatment naïve PLHA patients. This indicates the need for updating the current recommendations of WHO concerning biological monitoring of PLHA on first-line cART to include lipid analysis. Lipid levels and any other cardiovascular risk factors should be closely monitored in these patients on such therapy so that any potentially life threatening effects of ART can be optimally managed [7].

The conclusion of the study conducted by Dr. Christian Obirikorang, Dr. Francis Agyemang Yeboah, Lawrence Quaye et al., states that the lipid profile changes in PLHA can be correlated to the progression of the disease. Increase in

serum Triglycerides and the decrease in serum total Cholesterol, HDL cholesterol and LDL cholesterol could be helpful in the assessment of progression of disease, risk assessment for myocardial infarction and the clinical treatment of Ghanaian patients living with HIV/AIDS before introduction of HAART [8].

Previous studies conducted have shown that patients living with AIDS exhibit significantly abnormal complete lipid profile in plasma [9]. Few authors [10, 11] who calculated/collected the concentration of plasma triglycerides, total cholesterol and HDL-c in retrovirus infected individuals by the degree of immunological suppression according to the CD4 count, also came to a similar conclusion that, with an emergence or rise of immunological deficiency and clinical detoriation/ biochemical detoriation in the form of lipid profile derangement, indicated by an increase in triglyceride level and decreased concentrations of HDL cholesterol were intensified. The findings are also consistent with reports from Ducobu and Payen, 2000 [10] who declared that HIV infection induced an early lowering of cholesterol and a late rise of triglyceride with a lowering of HDL. The lipid profile changes are proportional to the decrease of CD4 count, which reflected the infection i.e., HIV infection severity, as was the case in this study. Shor-Posner *et al.*, (1993) [12] reported same findings in which they demonstrated significantly decreased levels of total cholesterol, HDL, LDL cholesterol in HIV/AIDS patients when compared with that of seronegative controls ($P < 0.05$). This decreased level of total, LDL,

HDL cholesterol was reported to be due to elevated levels of beta-2 microglobulin [4].

The reduced cholesterol levels are prevalent even during early stages of HIV infection and were correlated with a specific change in immune function [12]. The results of the study showed that increase of triglycerides in HIV positive patients occurs at a later stage of disease. This hypertriglyceridemia, demonstrated by other authors [13, 14] was correlated with opportunistic infections and interferon-α. The association between interferon-alpha (IFN-α) and triglycerides (TG) patients living with HIV/AIDS has been previously established by Grunfeld *et al* (1991) [8]. IFN-α may raise TG by two important mechanisms:

1) A reduction in TG clearance; and
2) A raise of *de novo* hepatic lipogenesis (lipid production) and increased VLDL production.

The hepatic lipogenesis may be enhanced by three cytokines as follows: Interleukin 1 and 6 (IL-1 and IL-6) tissue necrotic factor- alpha (TNF-α). IL1 and 6 increase hepatic levels of citrate; and IFN-α that does not increase hepatic citrate. Both depressed TG clearance and increased hepatic VLDL overproduction were found in patients living with HIV/AIDS, and the increased hepatic lipogenesis correlates to IFN-α [15].

Acute opportunistic/ any other infections might increase TG level by the increasing the level of hormones (steroids) or cytokines other than TNF-α or

IFN-α. Decrease in cholesterol, especially HDL-C occurs in HIV-seropositive patients at an earlier stage much more before the development of hypertriglyceridemia. These abnormalities of cholesterol metabolism have been suggested by others [12, 16]. TNF-α has been hypothesised/found to play a crucial role in the peroxidation of plasma lipoproteins and lipids in animals and in patients through stimulation of the production of oxygen reacting species [17]. Lipid peroxidation, in part, may explain the abnormalities of cholesterol metabolism in patient living with HIV/AIDS and these modifications would have important impact on the immune dysfunction. Studies show that dyslipidaemia in patients living with HIV/AIDS carries the very same degree of cardiovascular risk as in HIV-negative population [18].

The serum concentrations of TGL [19] and HDL-cholesterol are considered independent risk factors for coronary artery disease [20, 21]. Stampfer *et al.*, (1996) [22] in his study of TGL level and its association with risk of myocardial infarction concluded that raised triglyceride level, smaller LDL particle diameter and reduced HDL-cholesterol levels appear to indicate underlying metabolic perturbations with negative consequences for risk of myocardial infarction (MI); raised triglyceride levels may help us identifying high-risk individuals who are likely to develop Myocardial infarction.

With the introduction of HAART in late 1990s, HIV associated morbidity and mortality in patients receiving HAART, have significantly decreased so that

they no longer die due to opportunistic infections.[23] This is true, especially in developed countries which have significant health advances. The international donors and organizations have put a huge effort, which in turn have assisted in providing easy access to Highly Active Anti-Retroviral Therapy in most of the developing countries like Nigeria. However, patients living with HIV/AIDS are subjected to dyslipidaemia and other complications secondary to HAART which are often termed as HIV metabolic syndrome [24].

Even before the use/availability of HAART, studies in HIV infected individuals have demonstrated a variety of lipid abnormalities. [25, 2 6] Low levels of total cholesterol (TC), HDL - cholesterol and Low density Lipoprotein cholesterol (LDL) have been shown in HIV infection [25]. Mondy K et al reported low HDL and high TG in their study group in the US [27]. In Uganda, recent studies showed that HIV infected patients have infrequent rise in serum TC, LDL and TGL. [28]

The correlation between HAART especially Protease Inhibitor (PI) based regimen and the incidence of abnormal lipid and lipoprotein profiles is well known. [29] In another study, HIV-infected ART-naïve subjects had decreased concentrations of LDL and HDL and a higher concentration of TG than healthy controls. After receiving Protease Inhibitor based Anti-Retroviral Therapy, LDL-Cholesterol and TGL concentrations increased, while HDL-C concentrations remained unchanged [30]. However, Nevirapine based regimen

has shown to increase TC, HDL and these changes start even at 24 weeks of treatment. [31]

In Nigeria, Akpa MR et al, has studied the serum lipid profile levels in healthy Nigerians [32]. They found that mean TC and LDL concentrations were elevated but Triglyceride (TGL) and HDL were reduced. In a similar work i.e., lipid profile among patients with type 2 diabetes, several permutation and combinations of abnormal lipid concentration including reduced HDL and raised TG were noted. [33]

However, data about various patterns of lipid profile in treatment naïve HIV positive patients is very minimal. We hypothesized that treatment naïve patients living with HIV/AIDS in our environment, have various abnormal lipid profiles which were quite different from HIV negative persons. Secondly, even the short term treatment with HAART like post exposure prophylaxis has an impact on lipid level

Increased level of serum TG was recorded among patients living with HIV/AIDS, though this may not be significant. The levels of TG and HDL fit the criteria for dyslipidaemia as defined by the National Cholesterol Education Program (NCEP-ATP III), with serum level of less than 1.03mmol/l and greater than 2.3mmol/l respectively [35]. Although the mean LDL was significantly greater than the control, this did not reach dyslipidemic level. The finding of reduced HDL in treatment naïve patients living with HIV/AIDS was similar to

the Nutrition for Healthy Living (NFHL) cohort in the United States [36]. In that study, HIV patients who are not yet started on HAART have an adjusted OR of 2.7 for low HDL compared with that general population. This is strongly supported by recent studies in Spain [37]. This finding of decreased HDL is also similar to conclusion obtained among diabetics, diabetics and hypertensive in Nigeria [38].

Reduced HDL is a well-recognized important and independent risk factor for adverse cardiovascular disease events and this has been shown to be true in HIV infected patients, irrespective of any other associated risk factors [39].

An important finding is corroborated by the findings of Shor-Posner et al, where reduced cholesterol without or with raised triglyceride was seen in male patients with an early HIV -1 infection [39]. Decreased level of cholesterol has been shown in AIDS, early HIV infection and some other infections [40, 41]. This has been found to be inversely related to Tumor Necrosis Factor-alpha (TNF-alpha) [39], but the pathophysiological mechanisms are not yet clear [39].

The lack of correlation between any of the lipid parameters and hypertension may be associated to the duration of hypertension, the degree of the blood pressure control or extend of immune suppression. Even in previously diagnosed hypertensive patients, who have been on medications or those with a strong positive family history of adverse cardiovascular events in their first degree relative, there were no significant association between hypertension and

abnormal lipid profile, especially reduced HDL [38]. This may signify that HIV infection may contribute to an additional and independent cardiovascular risk factor in hypertensive patients.

The reason for lack of relationship between lipid parameters in the study group of patients living with HIV/AIDS and the immune status may be due to the close resemblance in the CD4 count as most these patients are in the CD4 count ranging from 50 to 220cell/mm3. Despite this, it has been shown that the decrease in HDL in HIV infection persists all along different CD4 levels from the beginning of infection [39]. Raised TGL was shown to directly correlate with interferon alpha levels, advanced / opportunistic infection when immunity is markedly compromised and delayed/slow clearance due to compromised lipoprotein lipase activity. [42, 43]

Case reports have described that the HIV-infected patients who were ApoE ε2 or ε4 carriers in whom severe hyperlipidaemia was triggered by the initiation of HAART [54]. ApoE ε4 carriage was already been linked to hypertriglyceridemia in advanced HIV infection in the pre-HAART era [54]
A more recent report showed an association of hypertriglyceridemia with variant alleles of ApoC3 in 60 men who all were treated with PI based HAART [51]. TG levels were higher in carriers of three variant ApoC3 alleles than in carriers of one or two variant alleles. An association of these ApoE and ApoC3

variants with hyperlipidaemia was recently reported in a longitudinal study of 329 HIV infected patients in the Swiss HIV cohort study [14].

The genetic variants were relatively common: 27.7% of patients were carriers of variant alleles of ApoE (i.e., ε2 or ε4 alleles), 17.9% were carriers of all three variants of ApoE, 5.8% were carriers of variants of both ApoC3 and ApoE; and these patients were at risk for extreme and sustained hypertriglyceridemia when exposed to RTI. The relative contribution of genotype and HAART to lipid levels was also evaluated. HAART containing a PI but no RTI, and RTI containing HAART were associated with increases in non –HDL-C of 0.29mmol/l (11mg/dl) and 0.65mmol/l (25mg/dl), respectively. The contribution of the ApoE ε4 allele was a non – HDL-C increase of 0.27 mmol/l (10.4mg/dl) i.e., quantitatively similar to the non-HDL-C increasing effect of PI treatment [14]. This study highlighted the issues of appropriate methodology and statistical power in genetic association studies. Longitudinal modelling of lipid levels in large numbers of patients may represent the most important and the powerful approach to quantitating the contributions of genotype and HAART to dyslipidaemia. Cross-sectional analyses of lipid levels at a single time point during HAART exposure may be underpowered to detect the genetic effects. [54]

CARDIOVASCULAR RISKS IN HIV-INFECTED PERSONS

Several cases of premature coronary Heart Disease (CHD) have been reported in HIV patients with dyslipidaemia associated with HAART [56-61]. In a cross sectional study, HIV infected individuals had more femoral or carotid artery atherogenic plaques than controls. However most of these patients had 1 or more established CHD risk factors like Diabetes mellitus, Smoking, Hypertension etc. A recent large cohort study showed higher age-adjusted rates of coronary Artery Heart Disease in the HIV infected individuals compared with HIV negative individuals (6-3 versus 2.9/1000 person years, respectively)[62]. The most solid data linking HAART exposure to an increased cardiovascular risk to date was provided by the DAD study. In the most recent analysis of DAD data, the adjusted risk of myocardial infarction (MI) was increased by 17% for each year of HAART exposure, 16-18% for each mmol/l increase in T-Cholesterol, and 39-48% for each doubling of the TG concentration [63]. It is clear that the benefits of HAART outweigh the small, absolute increase in cardiovascular risk that is presumably attributable to the HAART [64]. In the DAD study, the risk of MI was 1.39/1000 patient years in those not exposed to HAART. The risk increased 2.53/1000 in those <1year of exposure, and 6.07/1000 in those exposed to >6 years of HAART. The exact mechanisms by which premature atherosclerosis is mediated in HIV infected person is unclear. Support for direct pro-atherogenic effects is provided by studies showing that HAART and HIV infection itself may induce endothelial

dysfunction [65-67], an early indicator of atherosclerosis associated with diminished vasodilatory properties of the endothelium. A high proportion of HIV infected individuals can be classified as being at high 10-year cardiovascular risk. Among 3199 HIV-infected patients evaluated in Spain in 2004, 10% of women and 29% of men were considered to be at either moderately high or high 10 year CAD risk [68].

With the improved life expectancy since the introduction of HAART and the consequent ageing of the HIV-infected population, the number of patients at high cardiovascular risk is likely to increase. This has already been shown in the DAD cohort, in which the proportion of patients at high risk increased from 36.2% in 2000 to 44.7% in 2003 [69]. After adjusting for changes in cardiac risk factors, however, the MI risk was lower in 2003-2004 compared with 1999-2000. The exact reasons for this decrease in MI risk are not yet clear. Several changes over time have been noted in the DAD cohort, including a decrease in PI use (2000:47.4%, 2003: 40.1%), an increase in NNRTI use (2000:32.6%, 2003: 38.5%), an increase in patient receiving lipid-lowering therapy (2000: 4.0%, 2003: 8.1%), and an increasing proportion of ex-smokers (2000: 15.7%, 2003: 24.9%). Such trends have also been recorded in other studies, and suggest that physician awareness of cardiovascular risk is increasing [62, 70 and 71].

In a large cohort study from California, the use of d4T decreased, and the use of ATV and lipid-lowering therapy increased during the study period (1996-2004) [62]. More widespread use of lipid-lowering therapy in the most recent

years and a tendency to usage PIs more sparingly has also been noted in a study from Tennesse [72]. In the French Aquitaine Cohort of HAART-treated patients, a decrease in the prevalence of smoking, decreased PI use and an increase in the use of lipid lowering medication were noted between year 2000 and year 2004, along with significant decrease in the intimal media thickness [71]. Although the effect on cardiac outcomes remains to be confirmed, each of these studies suggests the feasibility and potential efficacy of interventions aimed at cardiovascular prevention in HIV-infected patients.

EFFECTS OF SWITCHING THE ANTIRETROVIRAL THERAPIES

The association between increased serum lipid levels and certain antiretroviral therapies had led to exchanging the potentially offending component for another drug. This switching strategy has the potential advantage of avoiding the pharmacologic intervention for elevations in lipid levels. However, because of the multifactorial nature of dyslipidemia in HIV infection, abnormalities may not resolve simply by switching drugs. Switching from a PI to nevirapine or abacavir has generally resulted in an improvement in total cholesterol and triglyceride levels [73-81], whereas switching to efavirenz has produced less consistent results [82]. These trials have generally depicted the persistent viral growth suppression for 6-12 months after switching regimens. In patients with a favourable treatment history (i.e., no previous intake of an RTI-based antiretroviral regimen that was less than fully suppressive and also it have

been shown that there was no virological rebound for patient receiving NRTI based ART regimen), switching from lipid raising Protease Inhibitor to abacavir or nevirapine may be more preferred than the pharmacologic intervention with a lipid lowering drug. In practice, however, many of the patients will have already received NNRTI therapy. Various studies comparing the different effects of therapies like switching of ART drugs to those of adding lipid lowering medications to on-going newer research level therapy have not yet been properly reported. Physicians should have to weigh the risks of newer treatment-related toxicities/ adverse effect and the possibility of viral relapse when switching between various antiretroviral drugs regimens. Clinician should also consider the risks of potential drug interactions and new treatment-related toxicities due to lipid-lowering agents when added to existing antiretroviral regimens.

MATERIALS AND METHODS

This is a cross sectional study conducted in Government Kilpauk Medical College Hospital, Department of medicine in collaboration with ART centre, for a period of 7 months. A total of 100 cases attended the out-patient department/ admitted in medical ward with HIV/AIDS and who were not on HAART were selected for the present study from May 2013 to November 2013.

Among 100 patients studied 50 cases are Patients living with HIV/AIDS who were not on HAART (as case) and rest 50 are those who attended outpatient department (as control)

Patients who fulfil inclusion and exclusion criteria were enrolled for the study after obtaining written informed consent. The study protocol was approved by the ethical committee of Govt. Kilpauk medical college hospital, Chennai-10 for research studies conducted on April, 2013.

Inclusion criteria

Patients admitted in medical wards/ attended outpatient department/ ART centre of Govt. Kilpauk medical college hospital,

- Patients in the age group of above 18 years
- Patients proven to have HIV/AIDS by ELISA/& western blot techniques (in cases only)

Exclusion criteria

Medical conditions and patients who were on drugs which alters the lipid profile are excluded from study like

1. Patient who don't have family history of dyslipidemia
2. Not a diabetic, hypertensive/ CAD/ CKD patient
3. Not on drugs causing dyslipidemia
4. Not started on Highly active antiretroviral therapy(in case only)
5. No history of any opportunity infection

Data collection

Detailed history was taken from the patients that includes onset of symptoms, past medical history and thorough physical examination and systemic examination was done and entered in proforma specially designed for this study.

Blood investigations

In all patients who are selected for the study, routine investigations like complete blood count and urine examination were done. Biochemical parameters like random blood sugar, fasting lipid profile and CD4 count for PLHA case were done. Body Mass Index was calculated for all the patients selected for the study

METHODOLOGY OF INVESTIGATIONS

HIV serology was done using micro ELISA kit.

CD_4 count was done with FACS count (Automated Counter) manufactured by Becton and Dickinson.

Lipid profile analysis was done on serum obtained after 12 hours of fasting. Total cholesterol, triglycerides and HDL-C are measured

Tests were done in a single laboratory by the same person. Therefore no interpersonal error was possible.

The normal values of the parameters taken for the study were assessed and listed below.

Total Cholesterol (TC)

Desirable TC is **less than 200mg/dl**

Borderline high TC is from 200-239mg/dl

High TC is greater than or equal to 240mg/dl

HDL Cholesterol (HDL-C)

Desirable HDL-C is greater than or equal to 40mg/dl (50mg/dl in female)

Low HDL-C is **less than 40mg /dl** (50mg/dl in female)

Triglycerides (TG)

Desirable Triglycerides is **less than 150mg/dl**

Borderline high TG is from 150 to 199mg/dl

High TG is from 200 to 499 mg/dl

Very-high TG is greater than 500mg/dl

Patient living with HIV/AIDS were grouped based on WHO Clinical Staging (National Aids Control Organisation)

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **statistics software (SPSS).**

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

Sensitivity, specificity, accuracy, positive predictive value and negative predictive values were calculated using the following formulae

$$\text{Sensitivity} = \frac{\text{True positive}}{\text{True positive + False negative}} \times 100$$

$$\text{Specificity} = \frac{\text{True negative}}{\text{False positive + True negative}} \times 100$$

$$\text{Accuracy} = \frac{\text{True Positive + True Negative}}{\text{Total cases}} \times 100$$

$$\text{Positive predictive value} = \frac{\text{True positive}}{\text{True positive + False positive}} \times 100$$

$$\text{Negative predictive value} = \frac{\text{True negative}}{\text{True negative + False negative}} \times 100$$

OBSERVATIONS AND ANALYSIS

Table 1

Age distribution among Cases and Controls

Age group	Cases	Controls
<30 yrs	0	3
30 - 39 yrs	6	9
40 - 49 yrs	18	14
50 - 59 yrs	18	15
>60 yrs	8	9

Out of 50 cases of Patient Living with HIV/ AIDS (PLHA) studied majority of patients belong to the

a) Age group of 40 to 49 (36%) and
b) Age group of 50 to 59 (36%).

Chart 1a

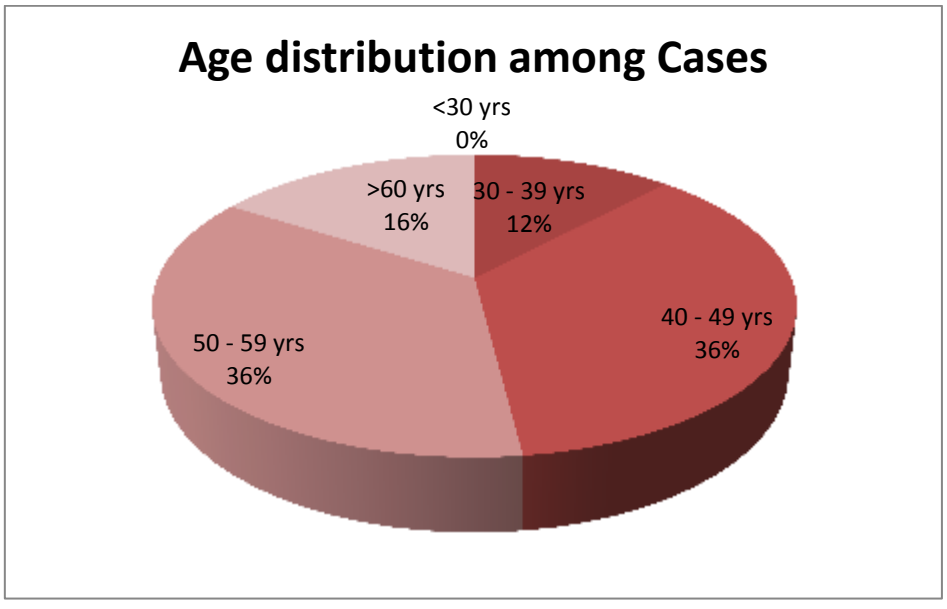
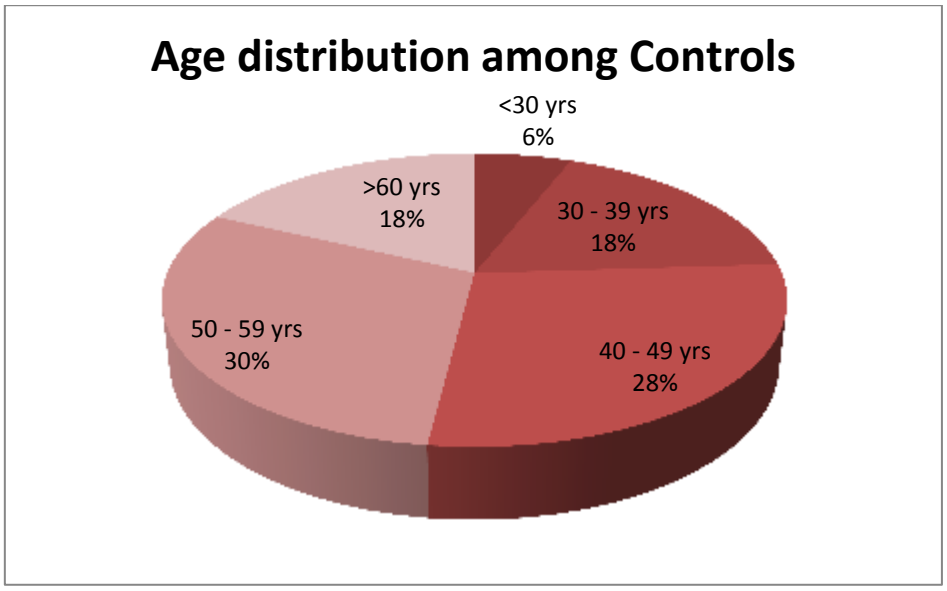


Chart 1b



Out of 50 normal persons (controls) studied majority of patients belong to the

a) Age group of 50 to 59 (30%) and
b) Age group of 40 to 49 (28%)

Table 2

Gender distribution among Cases and Controls:-

Gender	Cases	Controls
Male	21	19
Female	29	31

The gender distribution among the PLHA patients and normal persons compared in our study are matched appropriately as shown in the table above and the chart depicted below.

In our study the prevalence of disease appears to be more common in female

Chart 2

Gender distribution among Cases and controls

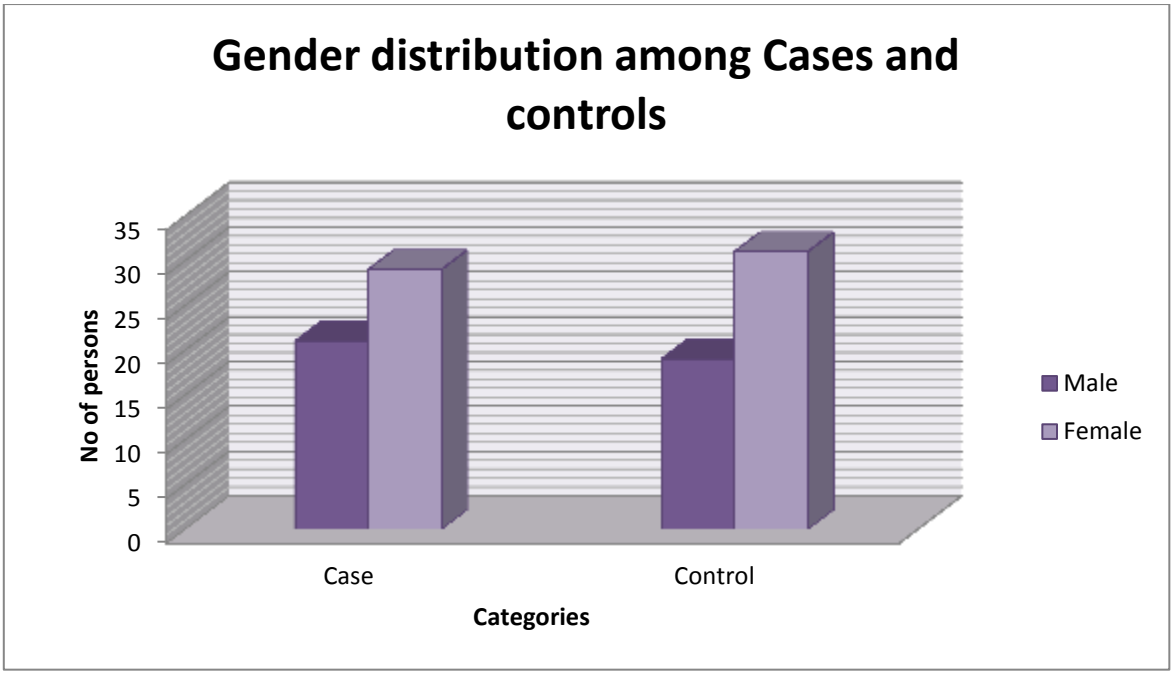


Table 3

Number of Cases based on WHO categories:-

WHO categories	No. of persons
I	14
II	14
III	12
IV	10

In our study, there was significantly higher number of Patients Living with HIV/AIDS in category I/II when compared with that of patient living in category III/IV

Chart 3

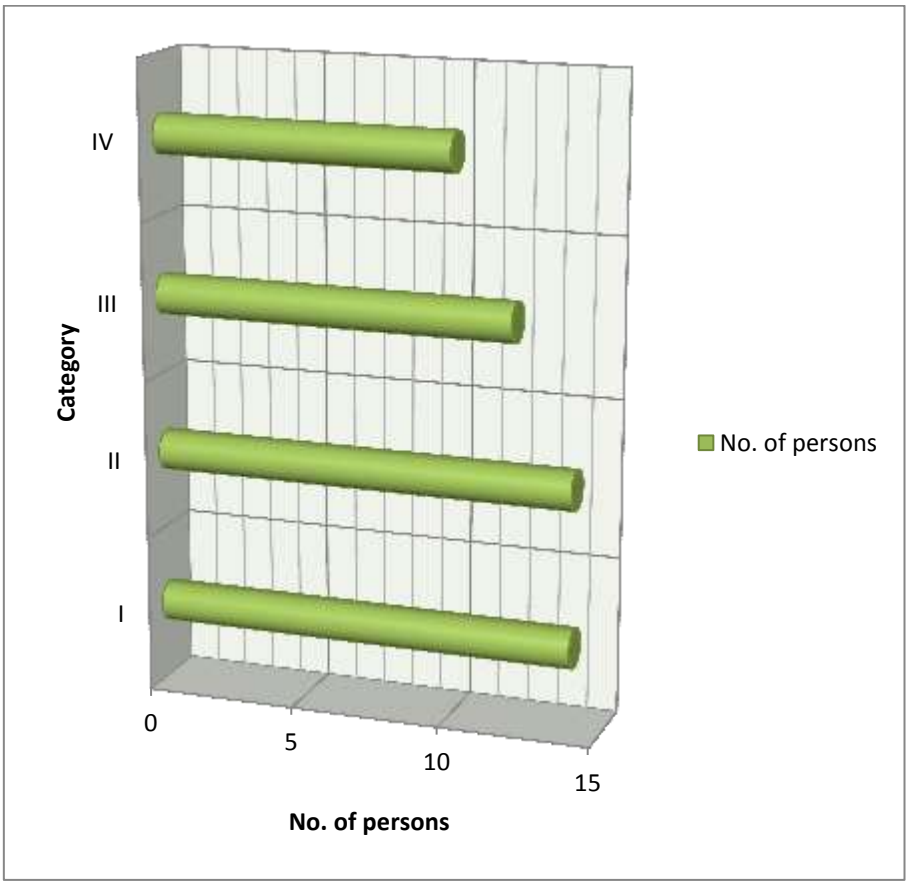


Table 4

Distribution of BMI among Cases and Controls:-

BMI	Cases	Controls
<18.5	1	0
18.5 to 24.9	31	26
25 to 29.9	18	23
>30	0	1

In our study, about 62% of the patients living with HIV AIDS were in the normal range of body mass index and 36% of cases were in pre-obesity range.

Among the control population, 52% of the persons were in normal range and 46% of persons were in pre-obesity range

Chart 4

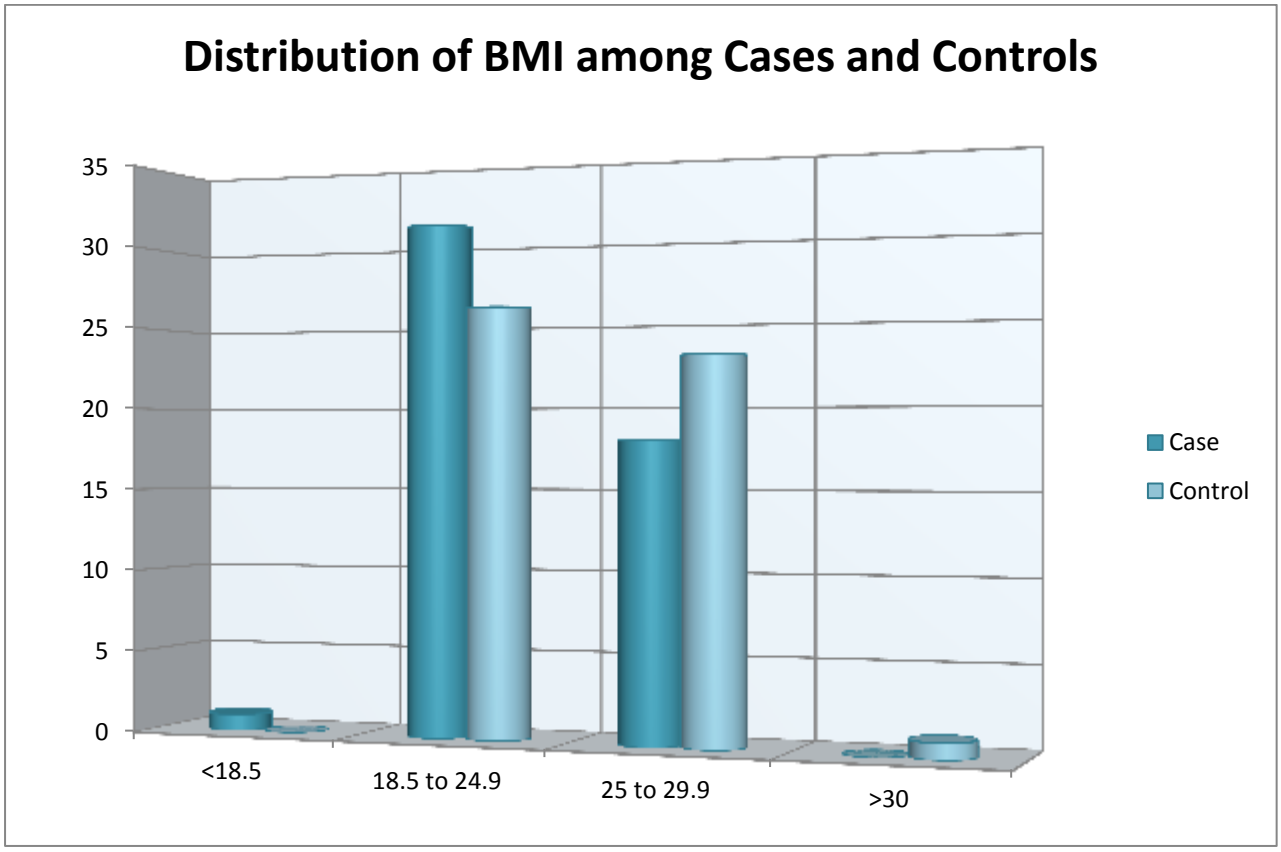


Table 5

CD4 count among the Cases:-

CD4 count	Case
>500	12
200 to 499	27
<200	11

In our study group, majority of the HIV infected population had a CD4 count in the range of 200- 499 (54%), where as 24% had CD4 count more than 500 and 22% had CD4 count less than 200

Chart 5

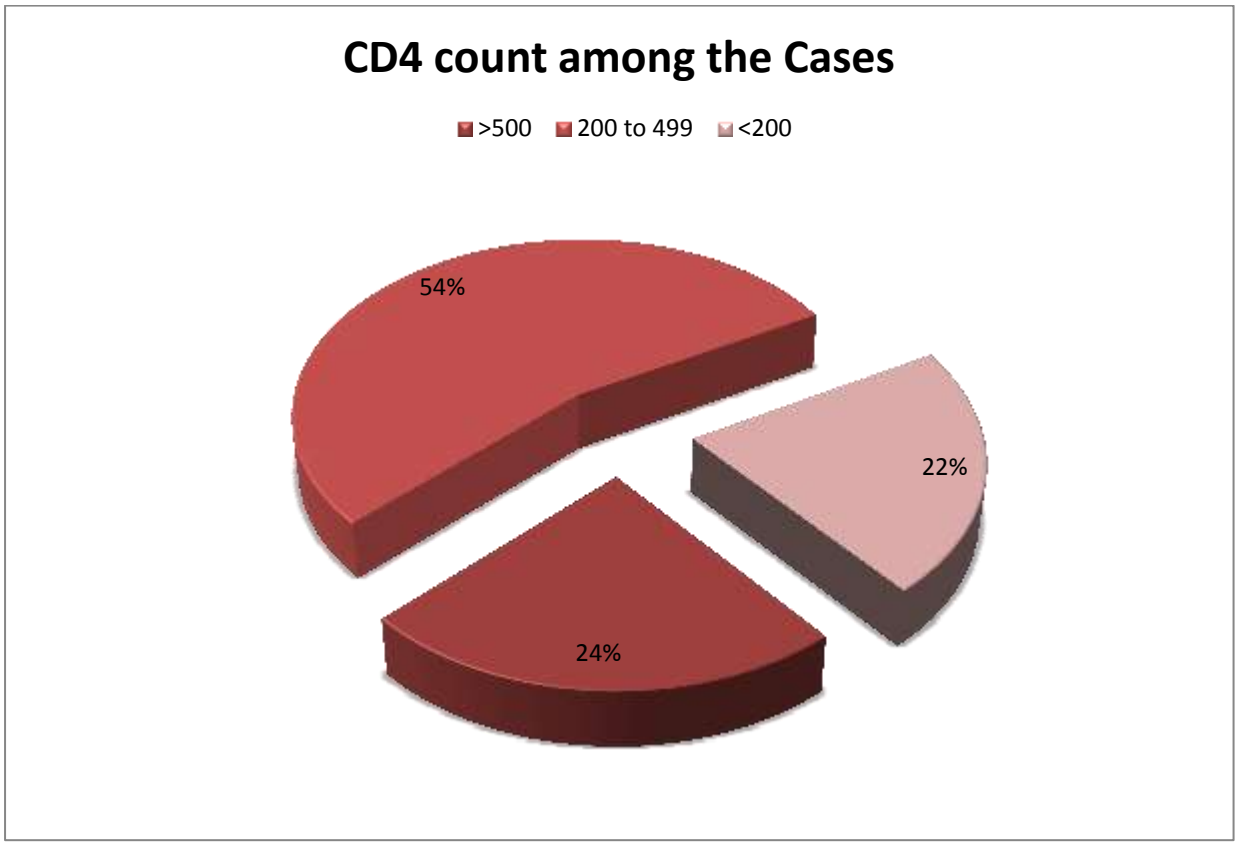


Table 6

Triglyceride distribution among Cases and Controls:-

TGL	Case	Control
<150(desirable)	9	19
150-199(borderline high risk)	11	21
200-499 (high risk)	27	10
≥500 (very high risk)	3	0

In our study group, among cases there is a very good number of cases (PLHA) had a high risk triglyceride range where as in control population, majority of population had a borderline high risk (42%) and desirable triglyceride range (38%)

Chart 6

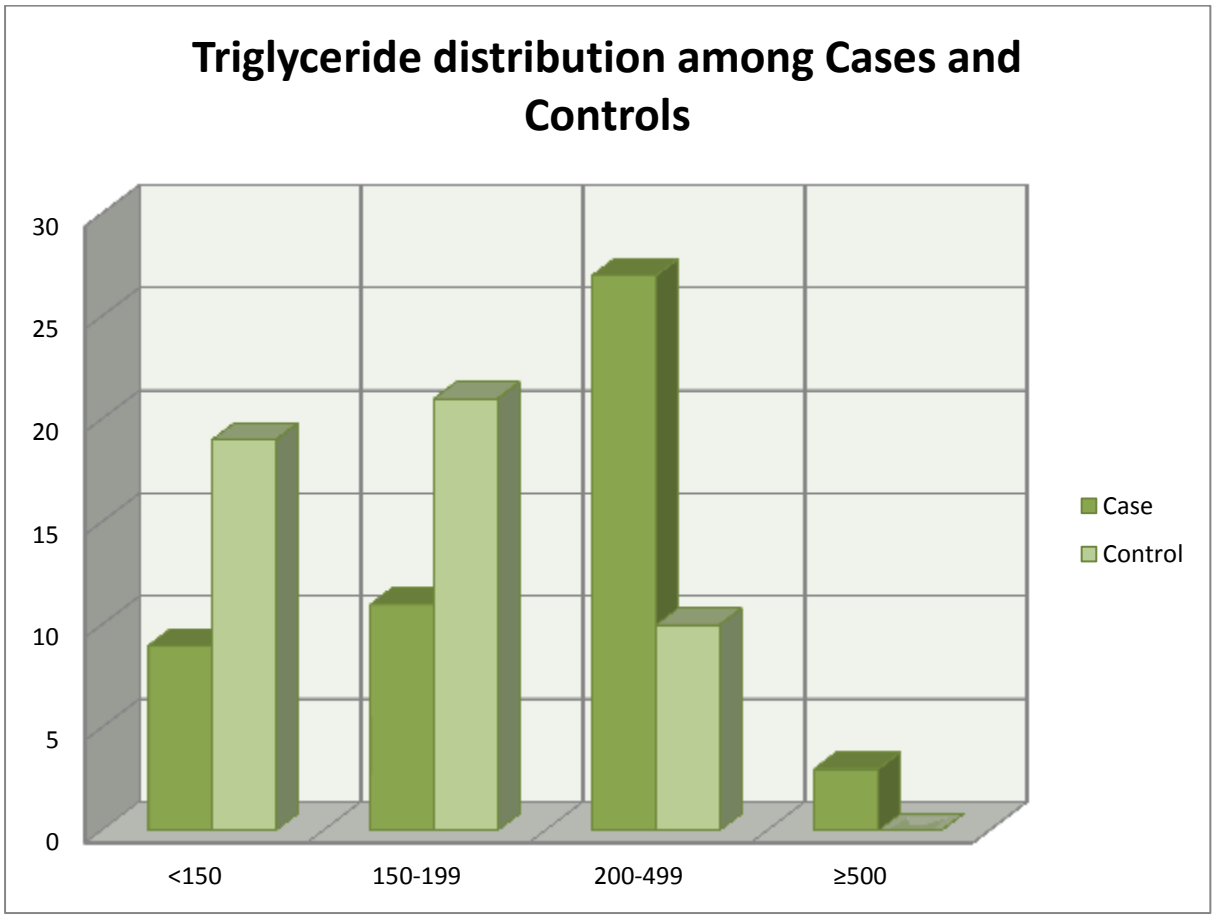


Table 7

Cholesterol distribution among Cases and Controls:-

CHO	Cases	Controls
<200	36	40
200-239	8	9
≥240	6	1

From the above chart, it is very clear that the percentage of population having desirable cholesterol level is higher among the controls (80%) when compared with that of the cases (72%). It is also shown that the patient having 'very high risk' cholesterol level is significantly higher among the cases (12%) when set side by side with that of controls.

Chart 7

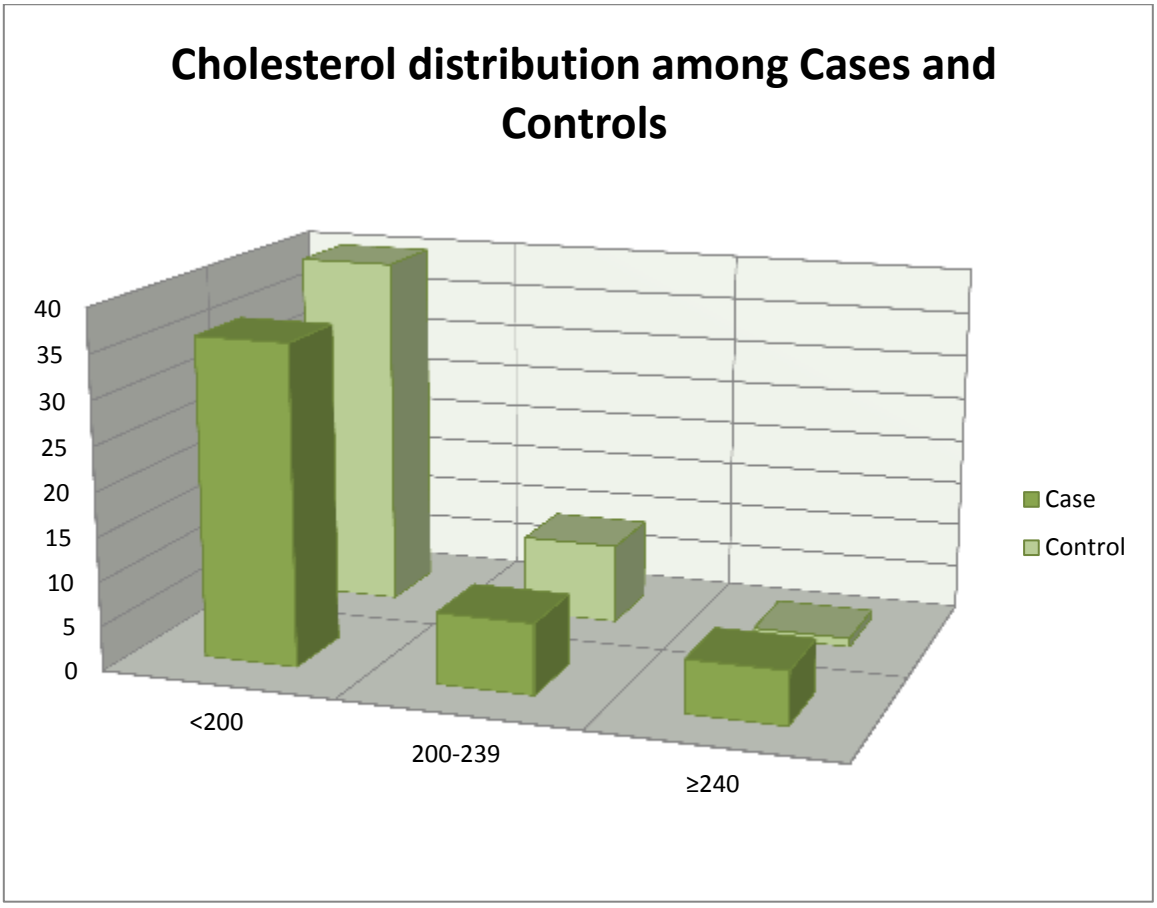


Table 8

LDL distribution among Cases and Controls:-

LDL	Cases	Controls
<100	32	21
100-129	11	21
130-159	4	8
160-189	2	0
≥190	1	0

The percentage of population having 'desirable' cholesterol is high in cases (62%) than controls (42%). It appears that HIV infected population had a significantly lower level of LDL when compared with that of normal population.

Chart 8

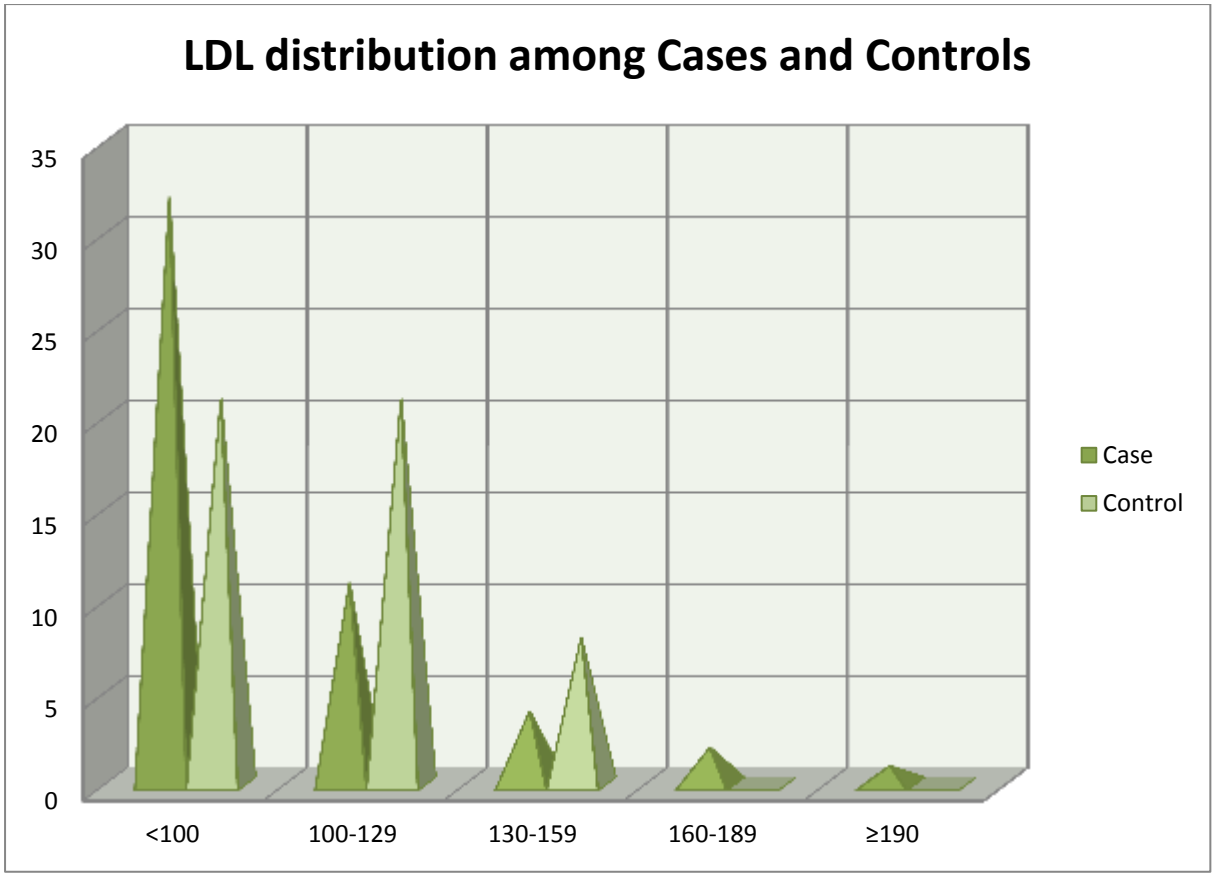


Table 9

HDL distribution among Cases and Controls:-

HDL	Case		Control	
	Male	Female	Male	Female
<40	**7**		**6**	
≥40	**14**		**13**	
<50		**24**		**27**
≥50		**5**		**4**

Among male cases 33% had riskier level of HDL level and the rest (66%) had protective level of HDL. This was comparable to that of control male population.

Among Female cases 82% had riskier level of HDL level while the rest (18%) had protective level. In control population (female) 87% of female are in the riskier range of HDL cholesterol.

Chart 9

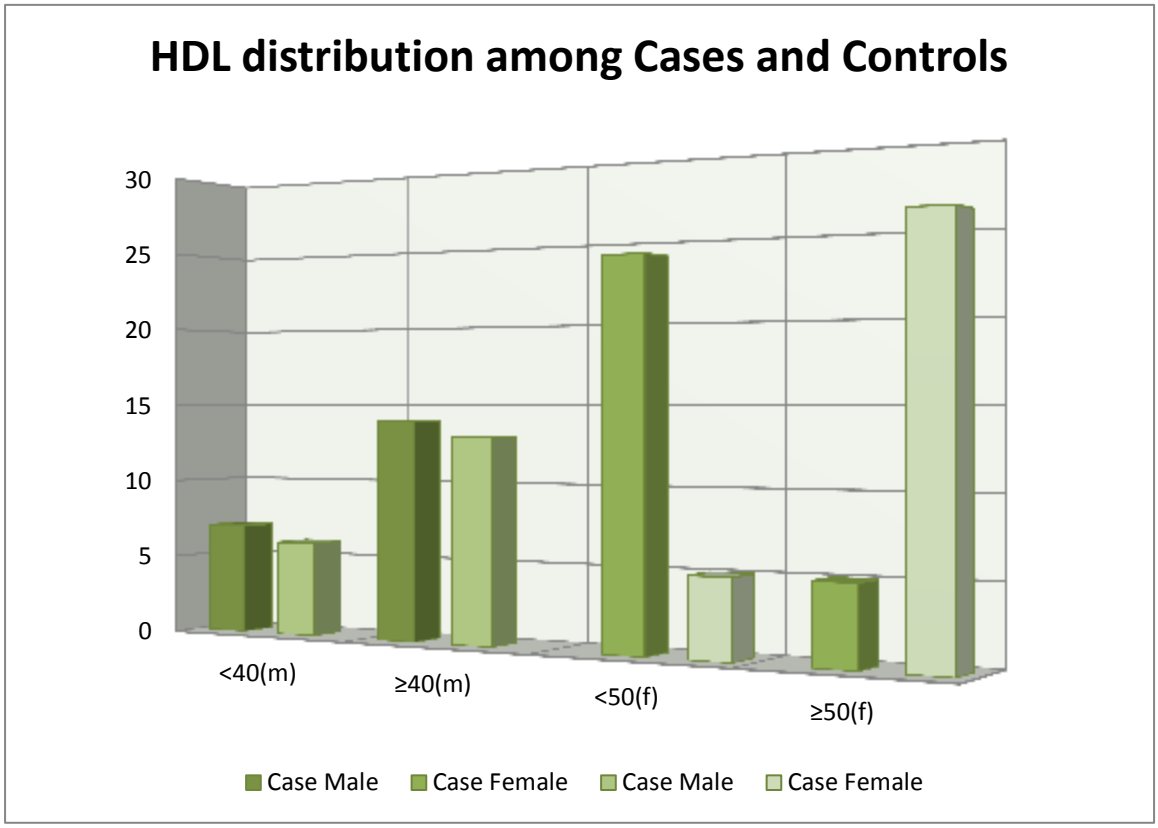


Table 10

Age VS Dyslipidemia in Cases and Controls:-

	Age	TGL				Cholesterol			HDL				LDL				
		<150	150 - 199	200 - 499	>500	<200	200-239	≥240	<40(m)	<50(f)	≥40(m)	≥50(f)	<100	100-129	130 -159	160 - 189	≥ 190
Cases	<30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 – 39	0	1	5	0	5	1	0	1	3	2	0	4	1	1	0	0
	40 – 49	5	5	7	1	13	2	3	2	6	8	2	8	4	2	3	1
	50 - 59	3	3	11	1	12	6	0	2	11	2	3	11	6	0	1	0
	>60	1	2	5	0	6	2	0	2	3	3	0	6	0	2	0	0
Controls	<30	1	1	1	0	3	0	0	1	1	1	0	1	1	1	0	0
	30 - 39	2	7	0	0	6	3	0	2	1	6	0	1	3	2	2	1
	40 - 49	7	3	4	0	13	1	0	1	5	6	2	1	6	6	1	0
	50 - 59	8	5	2	0	10	5	0	1	12	0	2	2	2	6	5	0
	>60	1	5	3	0	8	1	0	1	7	0	1	0	4	4	1	0

Chart 10a

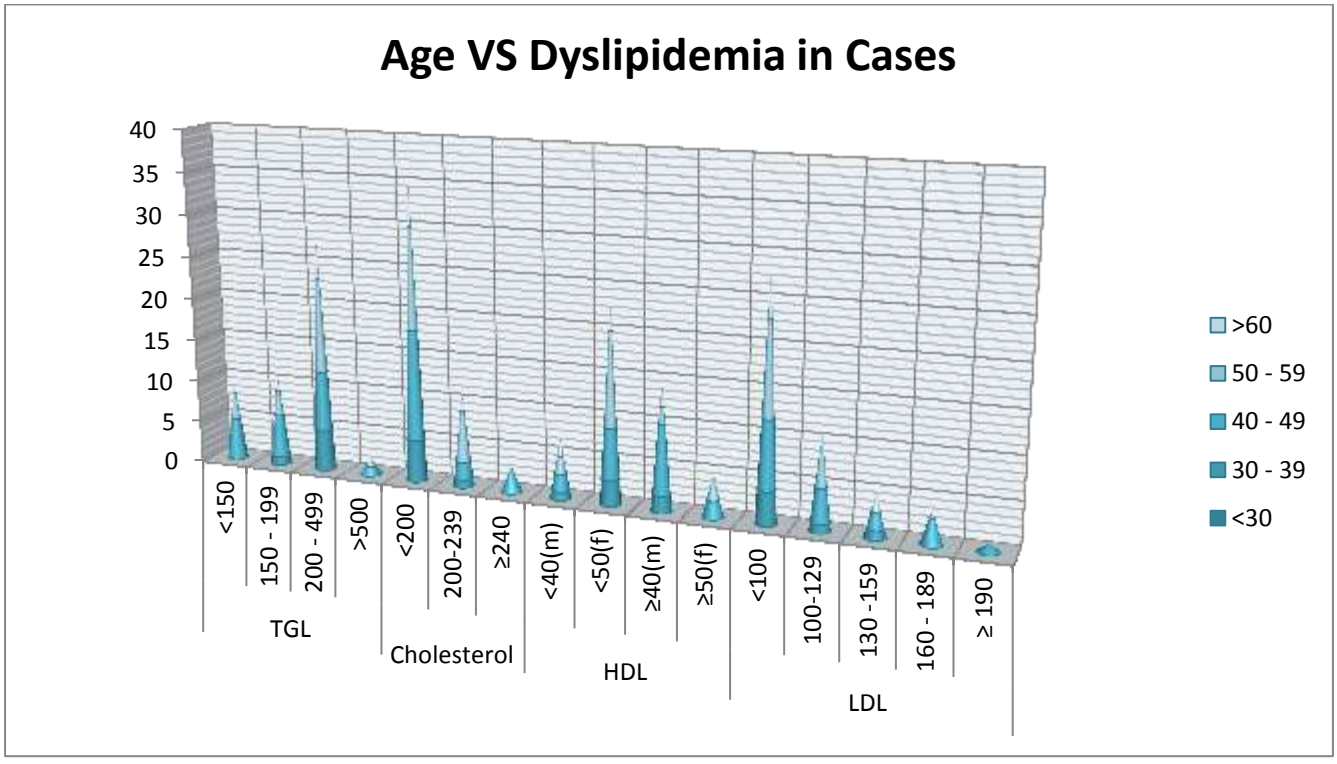


Chart 10b

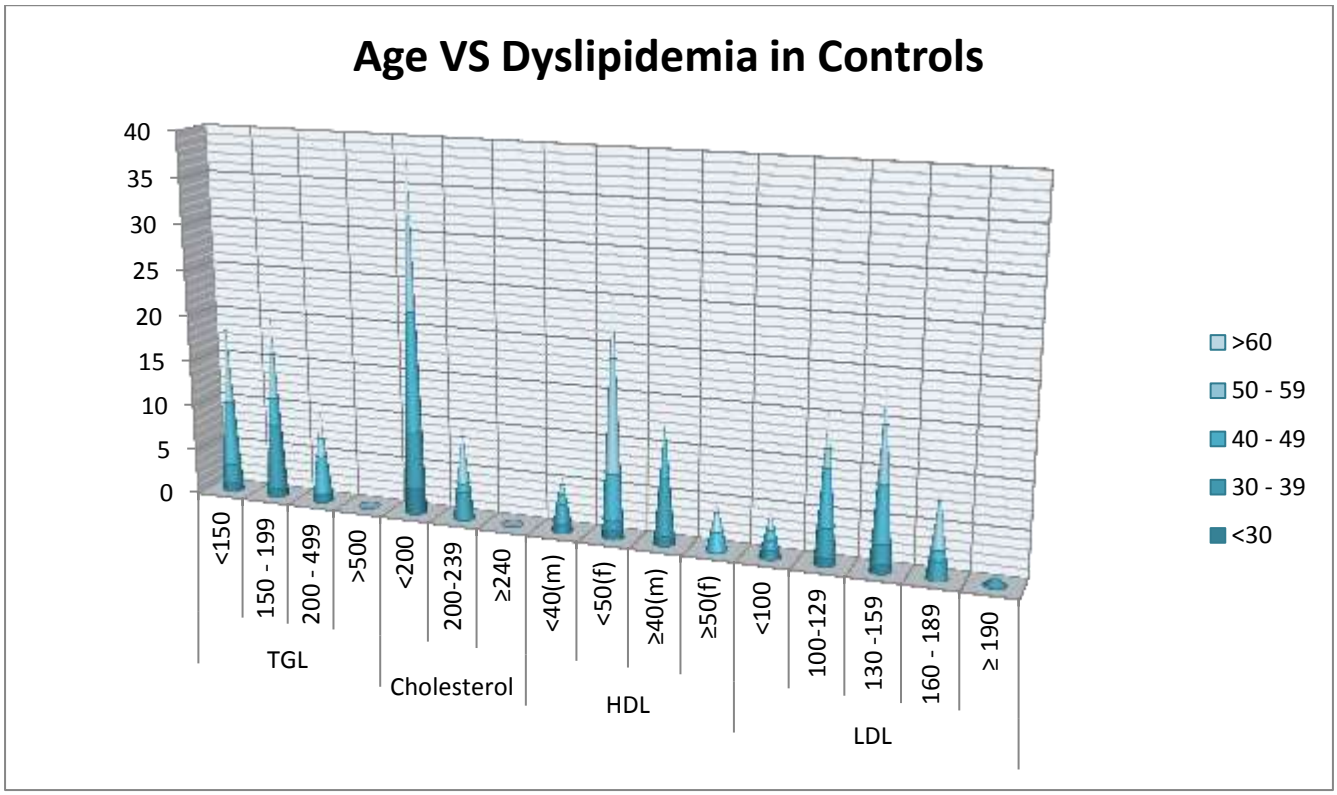

Age VS Dyslipidemia in Controls
40
35
30
25
20
15
10
5
0
<150
150 - 199
200 - 499
>500
<200
200-239
≥240
<40(m)
<50(f)
≥40(m)
≥50(f)
<100
100-129
130 -159
160 - 189
≥ 190
TGL
Cholesterol
HDL
LDL
>60
50 - 59
40 - 49
30 - 39
<30

Table 11

Gender vs Dyslipidemia in Cases and Controls:-

	Gender	TGL				Cholesterol			HDL				LDL			
		<150	150 -	200 -	>500	<200	200-	≥240	<40(m)	<50(f)	≥40(m)	≥50(f)	<100	100-	130 -	160 -
Cases	Male	5	4	12	0	14	4	3	7		14		11	5	4	1
	Female	5	8	14	2	22	4	3		23		6	20	6	1	1
Controls	Male	5	9	5	0	15	3	1	6		13		2	5	8	3
	Female	14	12	5	0	25	6	0		27		4	3	11	11	6

Chart 11a

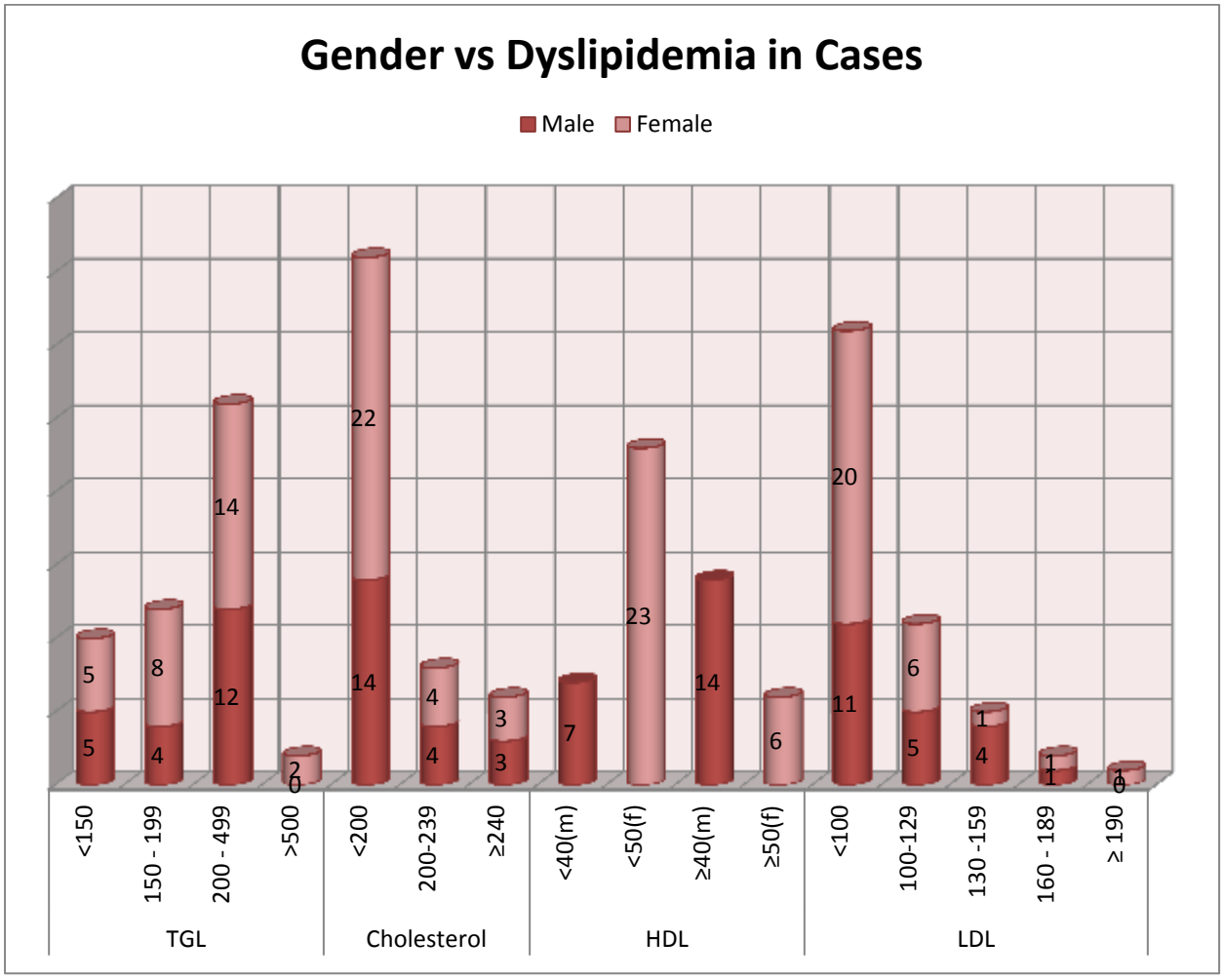


Chart 11b

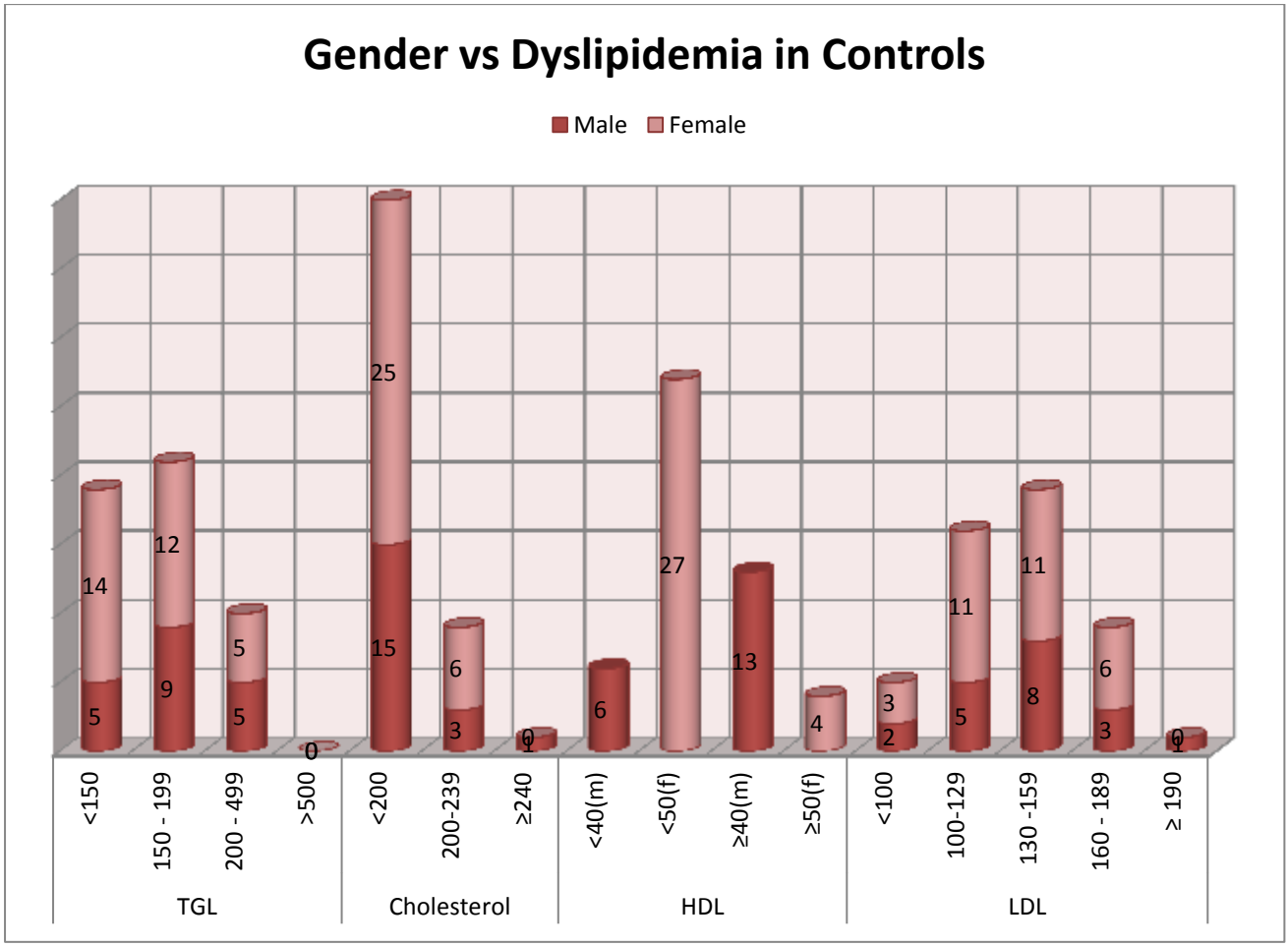

Gender vs Dyslipidemia in Controls
Male
Female
14
5
12
9
5
5
0
25
15
6
3
0
1
6
27
13
4
3
2
11
5
11
8
6
3
0
1
<150
150 - 199
200 - 499
>500
TGL
<200
200-239
≥240
Cholesterol
<40(m)
<50(f)
≥40(m)
≥50(f)
HDL
<100
100-129
130 -159
160 - 189
≥ 190
LDL

Table 12

Dyslipidemia distribution among various categories of HIV:-

Staging	TGL				Cholesterol			HDL				LDL				
	<150	150 -	200 -	>500	<200	200-	≥240	<40(m)	<50(f)	≥40(m)	≥50(f)	<100	100-	130 -	160 -	≥ 190
I	2	3	5	2	10	2	1	0	10	0	3	10	1	2	0	0
II	3	3	12	0	13	3	2	3	8	5	2	11	4	1	1	1
III	1	2	7	0	7	1	2	3	2	5	0	5	4	1	0	0
IV	3	2	4	0	6	2	1	1	4	4	0	6	2	0	1	0

Chart 12

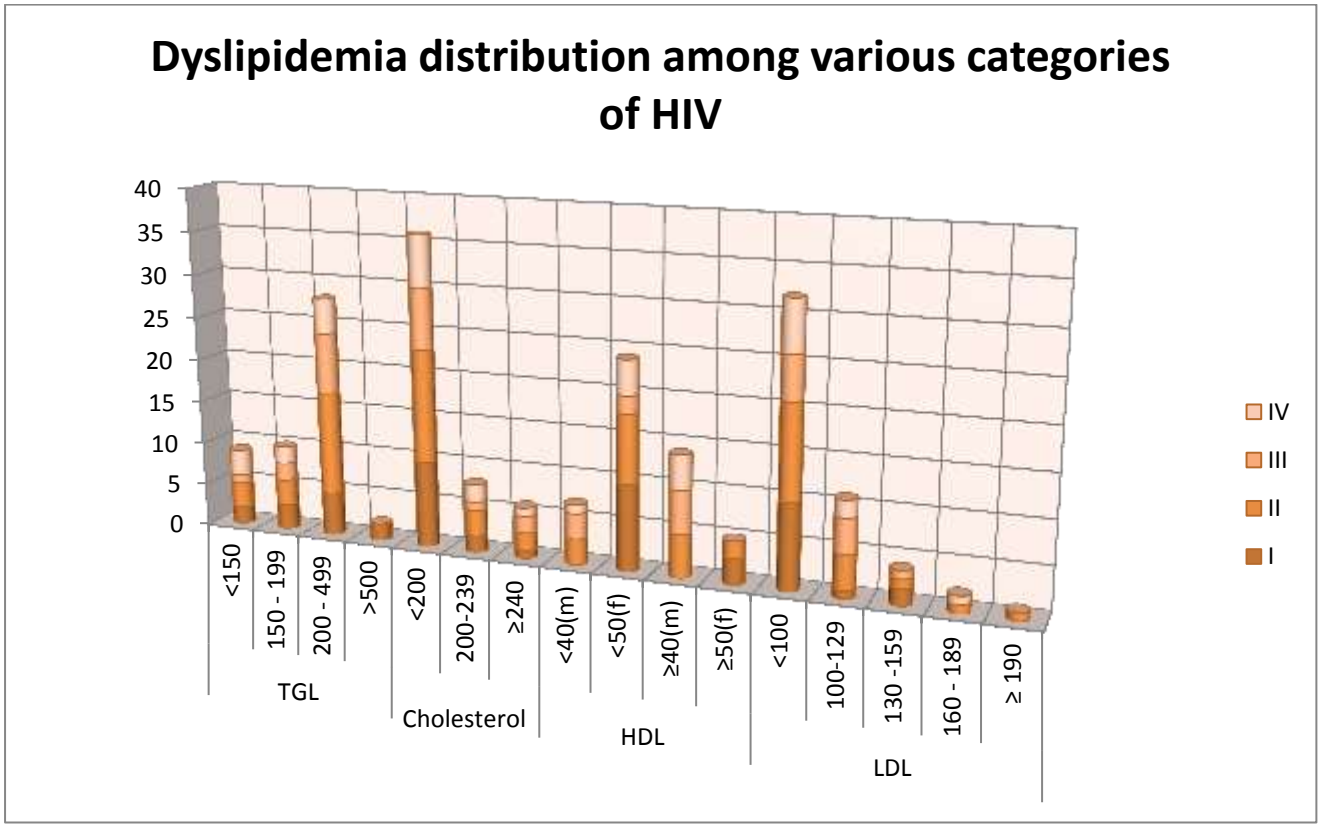


Table 13

BMI vs. Dyslipidemia in Cases and Controls:-

	BMI	TGL				Cholesterol			HDL				LDL				
		<150	150 -	200 -	>500	<200	200-	≥240	<40(m)	<50(f)	≥40(m)	≥50(f)	<100	100-	130 -	160 -	≥ 190
Cases	<18.5	0	0	1	0	1	0	0	0	0	1	0	1	0	0	0	0
	18.5 to 24.9	6	8	17	0	19	9	3	7	12	10	2	18	9	2	2	0
	25 to 29.9	3	3	10	2	13	3	2	0	12	3	3	13	2	2	0	1
	>30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Controls	<18.5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	18.5 to 24.9	10	10	6	0	23	3	0	4	16	6	0	12	12	2	0	0
	25 to 29.9	9	10	4	0	17	6	0	1	14	5	3	9	8	6	0	0
	>30	0	1	0	0	1	0	0	0	1	0	0	0	1	0	0	0

Chart 13a

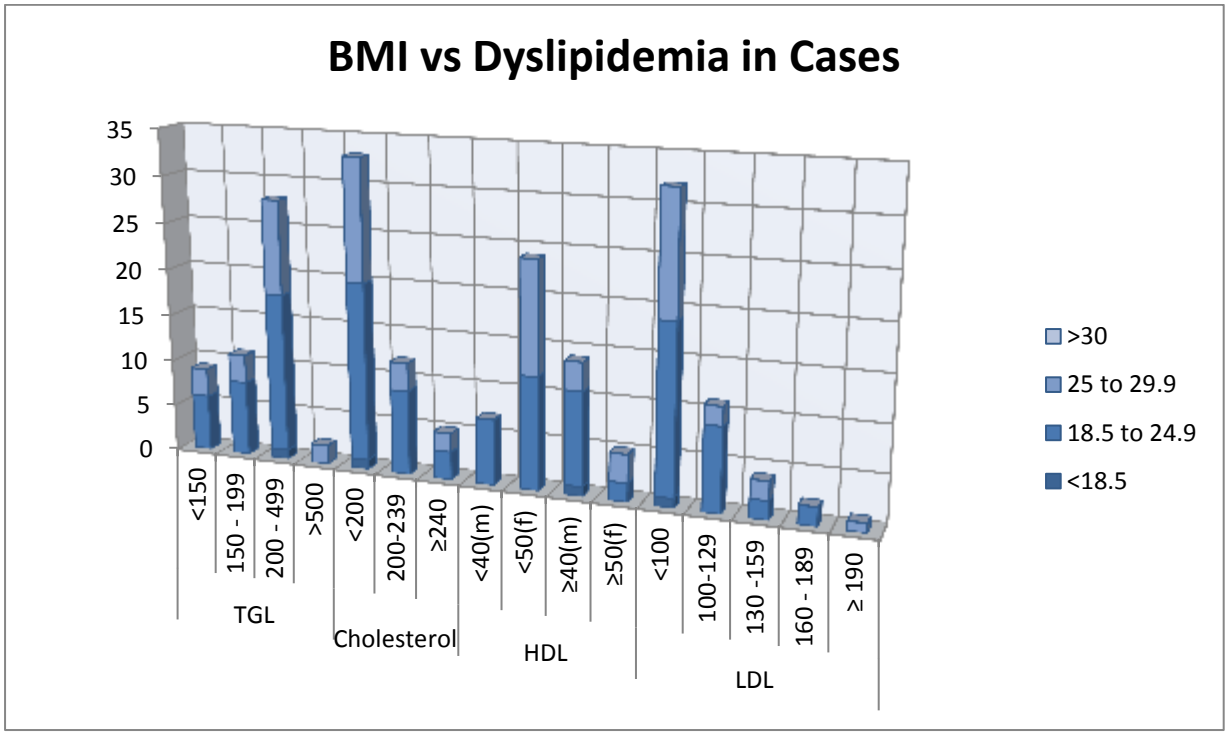


Chart 13b

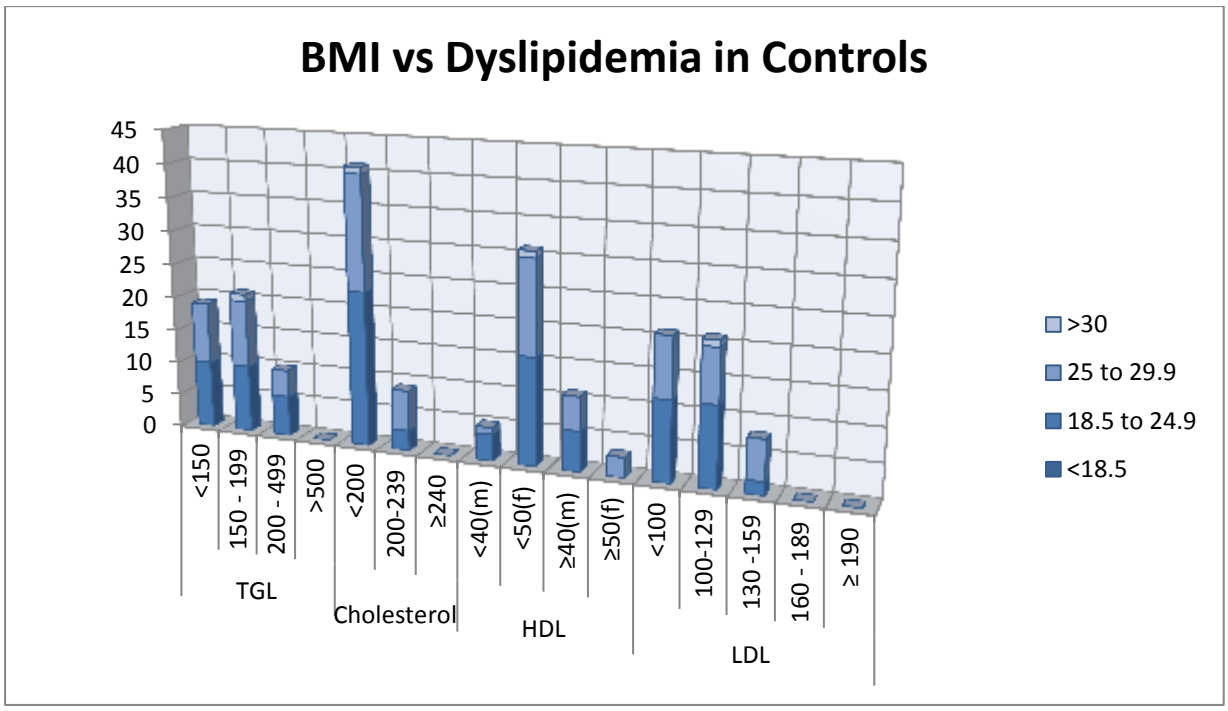

BMI vs Dyslipidemia in Controls
45
40
35
30
25
20
15
10
5
0
<150
150 - 199
200 - 499
>500
<200
200-239
≥240
<40(m)
<50(f)
≥40(m)
≥50(f)
<100
100-129
130 -159
160 - 189
≥ 190
TGL
Cholesterol
HDL
LDL
>30
25 to 29.9
18.5 to 24.9
<18.5

Table 14

Dyslipidemia distribution in HIV patients categorised based on CD4 count:-

CD4 count	TGL				Cholesterol			HDL				LDL				
	<150	150 -	200 -	>500	<200	200-	≥240	<40(m)	<50(f)	≥40(m)	≥50(f)	<100	100-	130 -	160 -	≥ 190
<200	2	4	6	0	7	2	3	3	3	5	1	8	2	1	1	0
200 - 499	7	2	16	2	23	4	0	3	15	7	2	18	7	2	0	0
≥ 500	0	5	6	0	6	2	3	1	6	2	2	6	2	1	1	1

Chart 14a

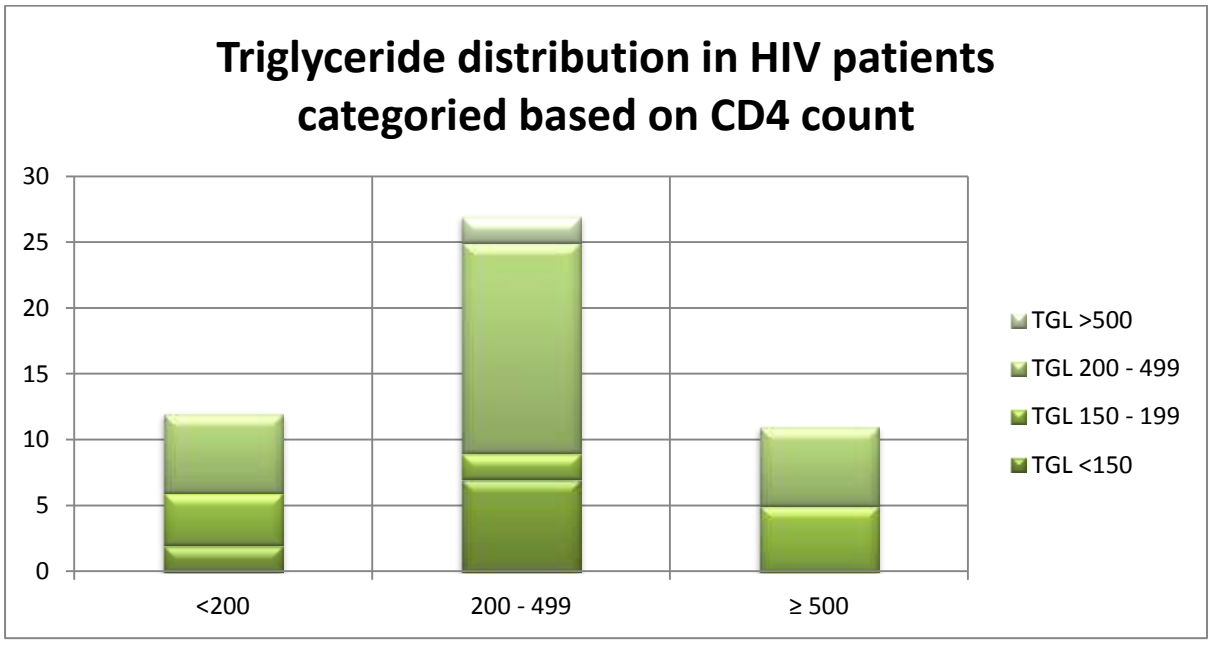


Chart 14b

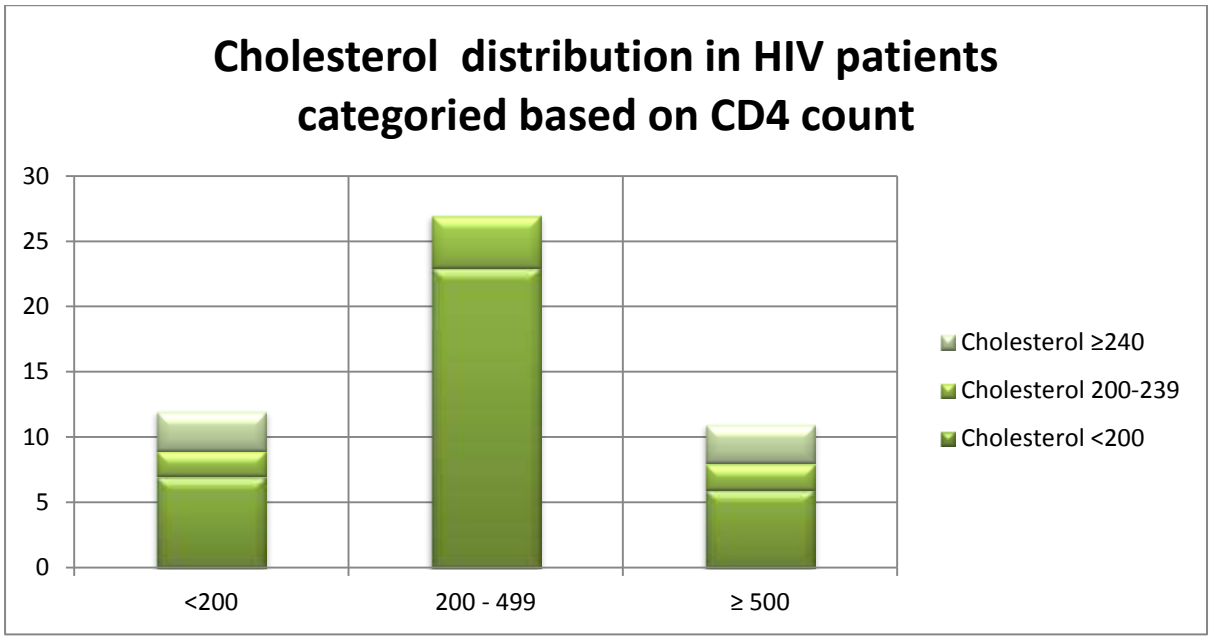


Chart 14c

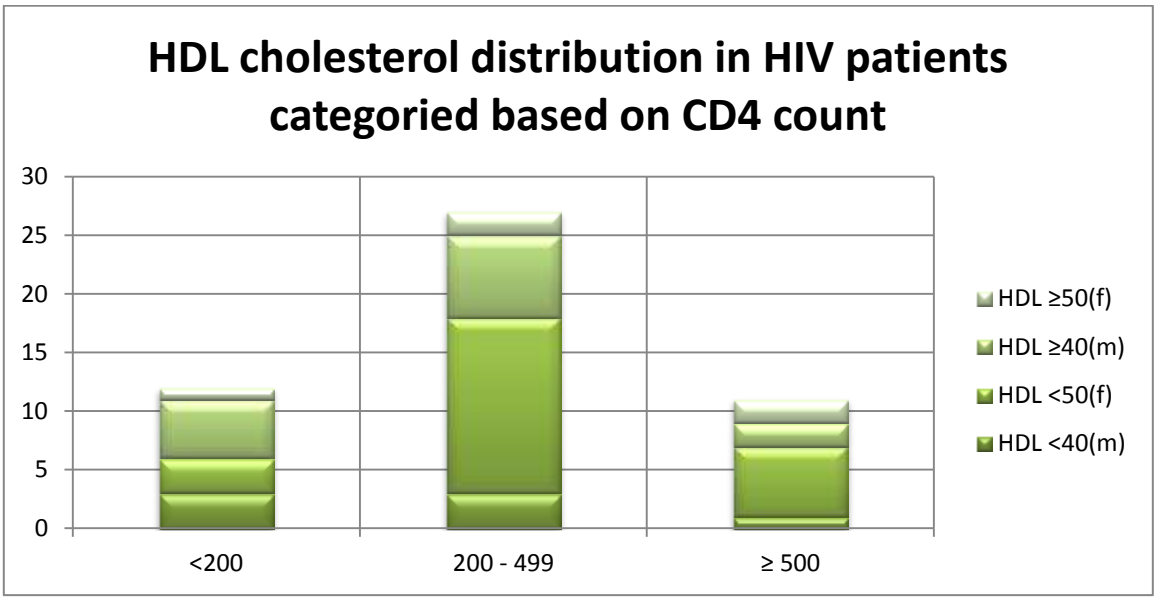


Chart 14d

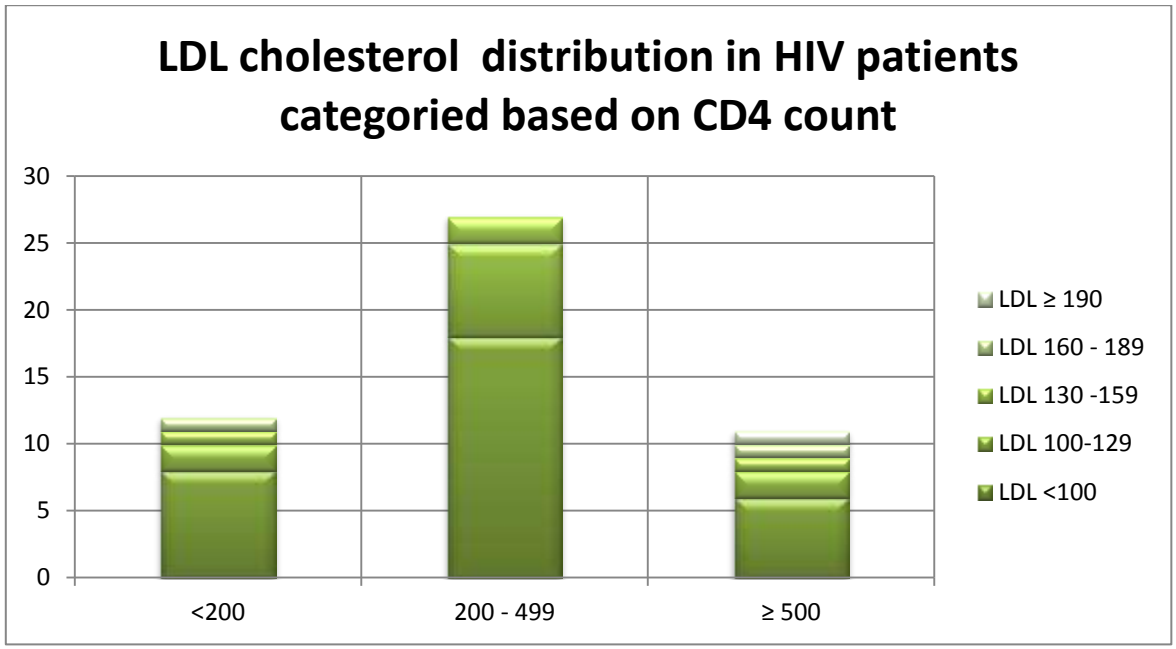

LDL cholesterol distribution in HIV patients categoried based on CD4 count
30
25
20
15
10
5
0
<200
200 - 499
≥ 500
LDL ≥ 190
LDL 160 - 189
LDL 130 -159
LDL 100-129
LDL <100

Table 15

Correlation of CD4 count with BMI:-

CD4 count	BMI			
	<18.5	18.5 - 24.9	25 -29.9	>30
<200	0	9	3	0
200 - 499	1	17	9	0
≥ 500	0	5	6	0

Among the cases in our study, it is very clear from the above tabular column that irrespective of CD4 categorisation, majority of case population have normal body mass index.

And also we could appreciate in our study that the distribution of HIV infected person was found to reside significantly in 200 to 499 range of CD4 count category.

Chart 15

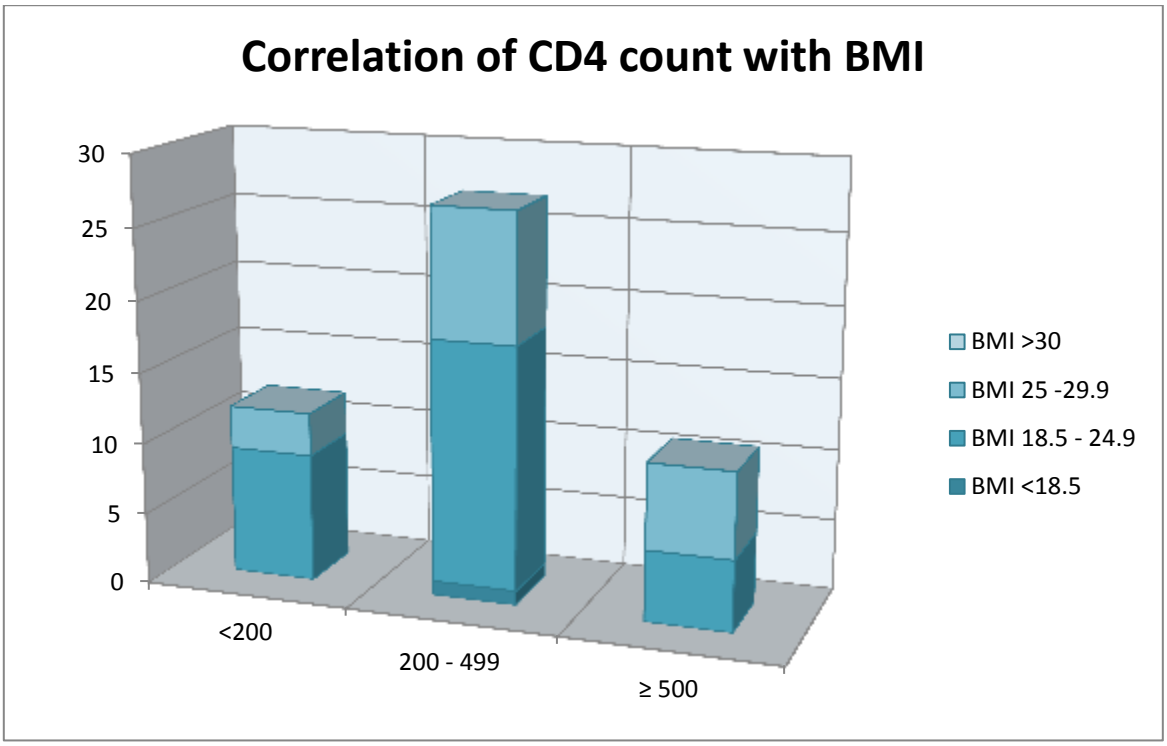


Table 16

Correlation of CD4 count with HIV categories:-

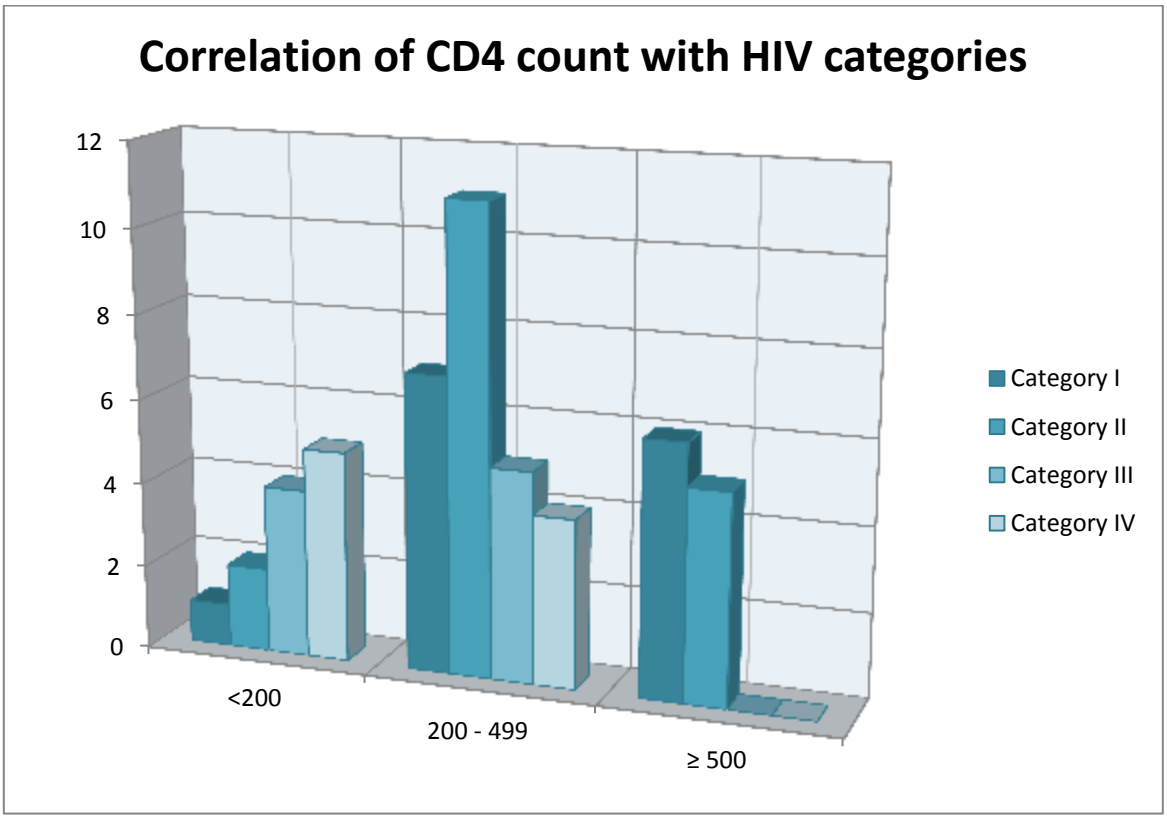
CD4 count	Category			
	I	II	III	IV
<200	1	2	4	5
200 - 499	7	11	5	4
≥ 500	6	5	0	0

Among cases,

Majority of patients in category III and IV have CD4 count < 500 while majority of patient in Category I and II have CD4 count more than 200

Similarly, majority of population with CD4 count <200 are in category III and IV whereas majority of population with CD4 count > 200 are in category I and II

Chart 16



STATISTICS AND ANALYSIS:-

Age distribution among cases and controls

	Group	N	Mean	Std. Deviation	P value
Age in years	Controls	50	47.94	11.304	0.271
	Cases	50	50.20	8.985	

There is no significant difference in the age distribution among cases and controls. That is, in my study, age distribution was matched between cases and controls.

CD4 count Vs. Lipid profile

		N	Mean	Std. Deviation	Range		P- value
					Minimum	Maximum	
TGL	Up to 199	12	272.67	146.052	76	492	0.807
	200-499	27	245.56	121.378	94	553	
	500 and above	11	246.73	97.683	162	456	
	Total	50	252.32	121.190	76	553	
TC	Up to 199	12	191.08	44.874	115	254	0.129
	200-499	27	166.22	32.032	110	226	
	500 and above	11	203.18	93.971	126	439	
	Total	50	180.32	55.262	110	439	
HDL	Up to 199	12	42.08	6.921	33	58	0.848
	200-499	27	43.19	5.609	24	51	
	500 and above	11	43.09	3.986	39	50	
	Total	50	42.90	5.560	24	58	
LDL	Up to 199	12	94.467	44.8088	41.8	178.2	0.148
	200-499	27	73.926	40.0038	15.4	145.0	
	500 and above	11	110.745	84.8076	44.6	328.0	
	Total	50	86.956	54.7916	15.4	328.0	
VLDL	Up to 199	12	54.533	29.2104	15.2	98.4	0.807
	200-499	27	49.111	24.2756	18.8	110.6	
	500 and above	11	49.345	19.5367	32.4	91.2	
	Total	50	50.464	24.2379	15.2	110.6	

There is no significant correlation between the CD4 count and the Levels of various parameters of lipid profiles

Gender vs. BMI distribution:-

		Group		Total	P- value
		Control	Cases		
Male	Count	19	21	40	
	% within Sex	47.5%	52.5%	100.0%	
Female	Count	31	29	60	
	% within Sex	51.7%	48.3%	100.0%	
Total		50	50	100	0.683

The distribution of BMI among different sex groups in cases and controls are not statistically significant.

This implies that the sex has effect on Body Mass Index in neither cases nor control.

WHO categories Vs. CD4 count

	N	Mean	Std. Deviation	Range		P value
				Minimum	Maximum	
I	13	499.23	206.306	209	882	
II	18	419.61	192.319	17	837	
III	10	205.80	114.858	42	398	
IV	9	197.89	92.826	76	318	<0.001**
Total	50	357.64	207.865	17	882	

There was a very significant correlation between CD4 count and WHO categories for HIV infection

Post Hoc test (Tukey HSD test)

WHO Categories	N	Subset for alpha = .05	
		1	2
IV	9	197.89	
III	10	205.80	
II	18		419.61
I	13		499.23
Sig.		.999	.673

This above post hoc test demonstrates that there is a significant difference between the distributions of CD4 count among WHO categories I, II and III, IV. This also shows that as the patient deteriorates down the WHO categories, the CD4 count significantly comes down

WHO categories Vs. Dyslipidemia

Dyslipidemia	WHO categories	No. of cases	Mean	Std. Deviation	Range		P- value
					Minimum	Maximum	
TGL	I	13	264.15	156.019	120	553	
	II	18	251.72	96.328	94	412	
	III	10	242.30	102.913	76	441	
	IV	9	247.56	146.397	110	492	
	Total	50	252.32	121.190	76	553	0.978
TC	I	13	169.08	43.786	131	279	
	II	18	187.50	74.136	110	439	
	III	10	181.40	47.596	115	254	
	IV	9	181.00	35.746	136	246	
	Total	50	180.32	55.262	110	439	0.847
HDL	I	13	44.85	4.059	40	50	
	II	18	42.83	4.706	35	51	
	III	10	41.10	9.012	24	58	
	IV	9	42.22	3.930	38	50	
	Total	50	42.90	5.560	24	58	0.438
LDL	I	13	71.400	41.7051	24.4	147.8	
	II	18	94.322	74.2478	15.4	328.0	
	III	10	91.840	40.2504	41.8	157.8	
	IV	9	89.267	41.1178	43.4	178.2	
	Total	50	86.956	54.7916	15.4	328.0	0.702
VLDL	I	13	52.831	31.2037	24.0	110.6	
	II	18	50.344	19.2657	18.8	82.4	
	III	10	48.460	20.5826	15.2	88.2	
	IV	9	49.511	29.2794	22.0	98.4	
	Total	50	50.464	24.2379	15.2	110.6	0.978

In our study, from the above table, it is very clear that the distribution of various parameters in lipid profile has no pattern/ statistical correlation among the various WHO categories of the HIV infected person. (P values correlating various parameters and WHO categories are very much higher than 0.05)

BMI Vs. Dyslipidemia in cases and controls

		N	Mean	Std. Deviation	Range		
					Minimum	Maximum	
TGL	Normal	26	188.38	77.964	126	412	
	Overweight	23	172.13	60.474	122	420	
	Obese	1	152.00	.	152	152	
	Total	50	180.18	69.466	122	420	0.66
TC	Normal	26	170.58	26.297	126	210	
	Overweight	23	182.22	27.709	120	240	
	Obese	1	178.00	.	178	178	
	Total	50	176.08	27.044	120	240	0.32
HDL	Normal	26	40.42	2.436	34	46	
	Overweight	23	41.13	3.494	34	54	
	Obese	1	40.00	.	40	40	
	Total	50	40.74	2.940	34	54	0.68
LDL	Normal	26	92.477	34.7206	17.6	144.0	
	Overweight	23	106.661	30.8317	27.0	158.4	
	Obese	1	107.600	.	107.6	107.6	
	Total	50	99.304	33.0666	17.6	158.4	0.32
VLDL	Normal	26	37.677	15.5928	25.2	82.4	
	Overweight	23	34.426	12.0948	24.4	84.0	
	Obese	1	30.400	.	30.4	30.4	
	Total	50	36.036	13.8932	24.4	84.0	0.66

		N	Mean	Std. Deviation	Range		P value
					Minimum	Maximum	
TGL	Underweight	1	312.00	.	312	312	
	Normal	31	227.71	100.394	76	458	
	Overweight	18	291.39	147.025	110	553	
	Total	50	252.32	121.190	76	553	0.185
TC	Underweight	1	168.00	.	168	168	
	Normal	31	175.77	44.134	110	254	
	Overweight	18	188.83	72.399	131	439	
	Total	50	180.32	55.262	110	439	0.718
HDL	Underweight	1	42.00	.	42	42	
	Normal	31	42.26	6.298	24	58	
	Overweight	18	44.06	4.108	38	51	
	Total	50	42.90	5.560	24	58	0.554
LDL	Underweight	1	63.600	.	63.6	63.6	
	Normal	31	87.974	44.8676	15.4	178.2	
	Overweight	18	86.500	71.1788	24.0	328.0	
	Total	50	86.956	54.7916	15.4	328.0	0.911
VLDL	Underweight	1	62.400	.	62.4	62.4	
	Normal	31	45.542	20.0788	15.2	91.6	
	Overweight	18	58.278	29.4050	22.0	110.6	
	Total	50	50.464	24.2379	15.2	110.6	0.185

There is no significance in the correlation of BMI with dyslipidemia in either cases or controls The P value of these correlations are well above 0.05 which signifies that there is no correlation between BMI and dyslipidemia in case and control.

Gender VS Dyslipidemia

For controls,

	Sex	N	Mean	Std. Deviation	P value
TGL	Male	19	180.11	59.091	0.995
	Female	31	180.23	76.070	
TC	Male	19	181.05	28.066	0.314
	Female	31	173.03	26.395	
HDL	Male	19	40.00	2.925	0.166
	Female	31	41.19	2.903	
LDL	Male	19	105.032	32.2544	0.343
	Female	31	95.794	33.5882	
VLDL	Male	19	36.021	11.8182	0.995
	Female	31	36.045	15.2140	

There is no significance in the correlation of various parameters of lipid profile with that of sex among the control population

For cases,

	Sex	N	Mean	Std. Deviation	P- value
TGL	Male	21	225.24	104.282	0.181
	Female	29	271.93	130.330	
TC	Male	21	180.90	44.208	0.950
	Female	29	179.90	62.832	
HDL	Male	21	40.95	6.756	0.034*
	Female	29	44.31	4.072	
LDL	Male	21	94.905	38.7801	0.388
		29	81.200	64.0140	

	Female				
VLDL	Male	21	45.048	20.8565	0.181
	Female	29	54.386	26.0661	

All except HDL has no correlation with gender among the case population. HDL cholesterol has a significant correlation (P – Value -0.034 i.e., <0.05) with the gender among the cases but not among the controls.

Gender Vs. CD4 count

	Sex	N	Mean	Std. Deviation	P- value
CD4 Count	Male	21	296.71	211.409	0.07
	Female	29	401.76	197.204	

Correlation between the CD4 count and Gender is not significant in the case population

Gender Vs. BMI,

For controls,

	Sex	N	Mean	Std. Deviation	P- value
BMI	Male	19	23.737	3.0339	0.164
	Female	31	24.968	2.9607	

BMI has no correlation with the gender among the controls.

For cases,

	Sex	N	Mean	Std. Deviation	P-Value
BMI	Male	21	22.941	2.3901	<0.001*
	Female	29	25.657	2.3473	

BMI has very high significant correlation with the gender among the case population.

CD4 count Vs. BMI,

			Level of BMI			Total	P- value
			Underweight	Normal	Overweight		
CD4 Count	Up to 199	Count	0	9	3	12	
	200-499	Count	1	17	9	27	
	500 and above	Count	0	5	6	11	
Total		Count	1	31	18	50	0.529

BMI	N	Mean	Std. Deviation	Range		P- value
CD4 count				Minimum	Maximum	
Up to 199	12	23.828	2.2501	18.6	26.4	
200-499	27	24.594	2.5642	17.6	28.9	
500 and above	11	25.079	3.4983	18.9	29.6	
Total	50	24.517	2.7044	17.6	29.6	0.538

From the above chart, it is made clear that there is no significant correlation between CD4 count and BMI.

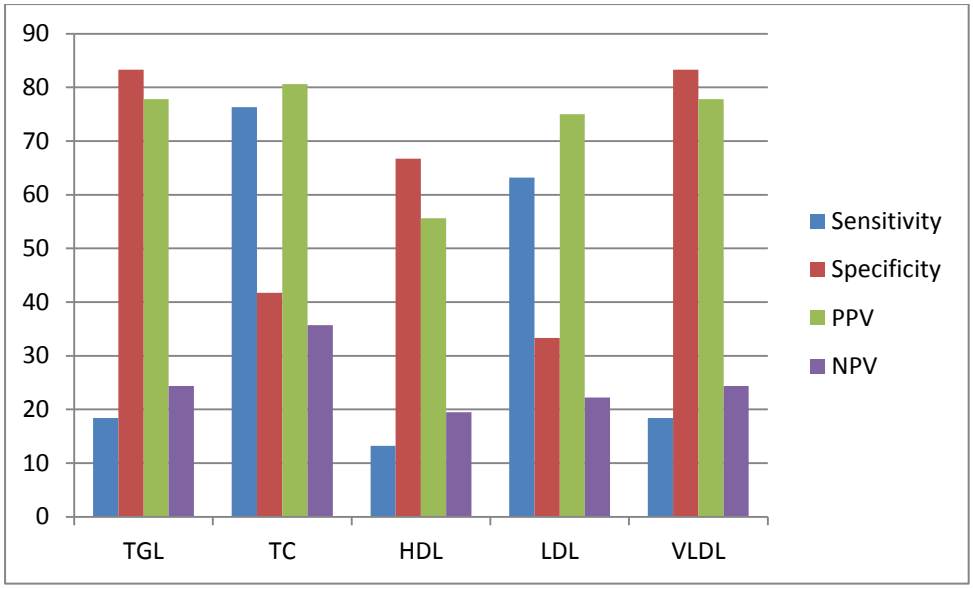
CD4 Vs Duration of illness

CD4 count	N	Mean	Std. Deviation	Range		P-value
				Minimum	Maximum	
Up to 199	12	3.75	1.658	1	6	0.821
200-499	27	3.54	1.704	1	8	
500 and above	11	3.91	1.868	1	7	
Total	50	3.67	1.701	1	8	

There is no significant association between CD4 count and Duration of illness.

Sensitivity/ specificity/ PPV/ NPV of lipid profile for predicting CD4 count < (or) ≥200

Lipid Profile	Sensitivity	Specificity	PPV	NPV
TGL	18.4	83.3	77.8	24.4
TC	76.3	41.7	80.6	35.7
HDL	13.2	66.7	55.6	19.5
LDL	63.2	33.3	75	22.2
VLDL	18.4	83.3	77.8	24.4



From the above chart, it is very clear that TGL, HDL-cholesterol and VLDL has a good Specificity and Positive Predictive Value, whereas Total cholesterol and LDL cholesterol has good sensitivity and Positive Predictive Value. All parameters in lipid profile have very poor negative predictive value.

Discussion

This study included data on 50 HIV positive patients and 50 HIV negative controls that were matched in age and gender parameters. HIV positive patients ,has shown in this study, has a variety of lipid abnormalities including elevation of TGL, total cholesterol and reduced level of HDL and LDL compared with HIV negative controls but were not significant. Higher level of serum TGL was also recorded among HIV positive patients, though this is not significant. The level of TGL, TC, HDL and LDL meet the criteria for dyslipidemia as defined by the National Cholesterol Education Program Adult treatment Panel III(NCEP-ATP III), with mean serum level of greater than 150mg/dl, 200mg/dl, lesser than 40mg/dl(m) or 50mg/dl(F) and greater than 100mg% respectively. Even though the mean LDL was significantly lower than control, it did not reach dyslipidemic level. The finding of low HDL in treatment naïve patients was slightly lower than the Nutrition for Healthy Living (NFHL) control in our study. In a study based in US, HIV patients who are not yet started on HAART have an adjusted OR of 2.7 for low HDL compared with general population. This is equally supported by recent study in Spain. This finding of low HDL is also similar to results obtained among diabetics, diabetics and hypertensive patients.

Low HDL is a very well recognised risk factor for poor/adverse cardiovascular outcomes and this has also been shown to be true in HIV infected individuals, irrespective of other associated risk factors.

In this study, we found no significant association between mean values of lipid parameters, BMI and CD4 count.

In Many studies, Hypocholesterolemia has been reported in HIV infection. In this study Cholesterol is higher in HIV positive patients than control but it is not that significant. However, male patients with HIV had an elevated level of Total Cholesterol compared with females. This finding is supported by the findings of Shor-Posner et al, where occurrence of hypercholesterolemia with or without hypertriglyceridemia was found in male patients with early infection with HIV -1. Reduced level of cholesterol has been demonstrated in early HIV infection, AIDS and some other infections. Relatively low cholesterol has been found to be negatively related to Tumor Necrosis Factor-alpha, but the mechanisms are not yet clear.

The reason for lack of association between lipid parameters in HIV positive patients and the immune status may be related to the close similarity in the CD4 count as most patients are in the CD4 count range 200 –499 cell/mm3. Despite this, it has been demonstrated that the reduction in HDL in HIV infection persist along all ranges of CD4 levels from the beginning of infection. Elevated TG was shown to have positive correlation with interferon alpha,

advanced / opportunistic infection when immunity is markedly reduced and delayed clearance due to reduced lipoprotein lipase activity.

Tuberculosis is a common infection in HIV/AIDS patients with a prevalence of 12.7% in Ile Ife, and 28.1% in Ibadan. With co infection, there is a synergism between the two infections leading to progression of the two diseases and ultimately death, if not treated. As revealed in a study done in African country, HIV patients co infected with TB had a significantly higher mean LDL compared with HIV positive patients who were not co- infected. This may indicate an exaggerated state caused by HIV/TB co infection. This needs further study to show that there is a prevalence of dyslipidemia in PLHA co-infected with Tuberculosis.

Despite these limitations, our findings indicate that HIV infected individuals have a host of variations in their lipid profiles compared with HIV negative control in our environment. Low HDL, reaching the dyslipidemic range, low LDL and high TGL were found compared with controls. This derangement in the lipid profile among Patient living with HIV/AIDS can lead to increased adverse vascular event

BODY MASS INDEX:

In our BMI has sensitivity 80%, specificity 54% ,accuracy 64%, PPV 57%and NPV 76% in predicting CD4 count < 200 cells/µL.

Caroline Costello, MPH, Kenrad E. Nelson, MD, Predictors of

LowCD4Count in Resource-Limited Settings .In this study BMI< 18.5 kg/ m^2 has specificity of 95.6% and sensitivity of 13.4% in predicting CD4 count < 200 cells/µL.

In our study BMI is more sensitive but less specific when comparing with above study in predicting CD4 count < 200 cells/µL. Normal BMI is more prevalent in our study population, which in turn decrease the specificity. The BMI is normal in our study because most of our patients are in WHO staging II and III.

BMI <18.5kg/m^2 is more common in stage III and IV when CD4 count is <200 cells/ µL .Thus it is useful in predicting CD4 count <200 cells/µL

AGE

The mean age of patients in control was 48$\pm$11 and the mean age in cases was 50$\pm$9. There was no statistical significance found between Age and dyslipidaemia in both the groups.

SEX DISTRIBUTION

In our study the prevalence of dyslipidaemia was found to be more among females than males in both the groups. But there was no statistically significant correlation found between gender and dyslipidaemia.

There are no studies available to suggest the correlation of Age / Gender with dyslipidaemia in HIV – infected patients.

TOTAL CHOLESTEROL

Majority of the patients in our study were found to have normal Cholesterol levels in both the groups. Only 20% of patients in control and 28% of patients in case population were documented to have high Cholesterol levels i.e., more than 200mg%.

In our study, only 12.0% of patients among cases were found to have Cholesterol level > 240mg% whereas in DAD study, the prevalence of Cholesterol > 240mg/dl among persons living with HIV/AIDS was 27%

	Present Study	**DAD Study**	**Galli et al**
Prevalence of Cholesterol >240mg/dl	12.0%	27.0%	10%

HDL CHOLESTEROL

Majority of patients in our study were found to have normal HDL-C levels only 38% of patients among case population and 34% among control population were documented to have HDL-C <40mg/dl.

Hypertriglyceridemia in association with Low HDL-C was commonly observed in HIV infected patients before the initiation of HAART

In DAD study, the prevalence of HDL-C <35mg/dl among HIV infected persons was 27.1%.

	Present Study	DAD Study
Prevalence of HDL-C < 40mg/dl	16%	
Prevalence of HDL-C < 35mg/dl		27.1%

TRIGLYCERIDES

Majority of patients in our study were found to have high Triglyceride levels in both the groups (62% among controls & 82% among cases)

In our study, the prevalence of Triglycerides > 200mg/dl were 20.0% among control and 60.0% among cases whereas Galli et al, observed that the prevalence of TGL> 200mg/dl was 23% in patients

	Present Study	Galli et al
Prevalence of Triglycerides >200mg/dl in HIV infected patients	60%	23%

Hypertriglyceridemia in association with Low HDL-C was commonly observed in HIV – infected persons before the HAART. In our study also, 20% of patients among Group 1 found to have elevated TG level >200mg/dl before starting HAART.

Both hypertriglyceridemia and hypocholesterolemia are associated with progressive HIV disease. These abnormalities may be a non-specific response to chronic infection as indicated by the well-documented relationship between Triglycerides concentration and levels of inflammatory cytokines.

DYSLIPIDAEMIA

There was no major or significant alterations in TGL, Total Cholesterol& LDL-C levels observed in both the groups, whereas HDL-Cholesterol level, was found to have a significant difference between male and female gender.

In our study, Dyslipidaemia was defined as alteration in any one of the three parameters namely Total Cholesterol, Triglyceride and HDL-c alone or combination of these abnormalities.

In our study, there was no statistical significance observed between CD_4 count and dyslipidaemia. But there was a significant correlation between CD4 count and WHO group.

LIMITATIONS OF THE STUDY

1. Sample size was small so further studies with bigger sample size has to be done to further verify the results.
2. Our study has been done among the population attending Kilpauk medical college hospital OPD and there can be a bias in selecting such a group of population, so this study has to be done among the general population or it has been done at multiple centres and meta-analysis of those studies can provide a significant conclusion of this issue among patient living with HIV/AIDS.
3. WHO clinical staging in our cases were done on presumed clinical basis and some basic laboratory investigations, so some of the patients may be wrongly staged/ categorised.

CONCLUSION

1. The prevalence of dyslipidemia in our study is as follows
    a. Good number of patients had a 'high risk' triglyceride range
    b. 'Very high risk' cholesterol level is significantly higher among cases
    c. PLHA had significantly lower level of LDL
    d. HDL level was low particularly among female cases
2. In our study, majority of the HIV infected population had a CD4 count in the range of 200- 499 (54%), where as 24% had CD4 count more than 500 and 22% had CD4 count less than 200.
3. There is no significant correlation between the CD4 count and the Levels of various parameters of lipid profiles
4. Apart from the intended correlation, we also attempted to correlate various other parameters and we came to a conclusion that
    a) WHO categories correlates with CD4 count i.e., as the staging increases, CD4 count decreases.
    b) Gender and HDL correlates well in our study population

Although the CD4 count is used as "gold standard" test, WHO staging can be used as a surrogate marker for CD4 count <200 cells/µL to initiate ART in resource limited settings. Lipid profile can never replace CD4 count in areas where appropriate facilities are not available.

Annexures

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List of abbreviations used

AHA – American Heart Association

AIDS – Acquired Immune Deficiency Syndrome

Apo C3/ Apo E – Apoprotein C3/ Apoprotein E

ART – Anti Retroviral Therapy

ATP – Adult Treatment Panel

BMI – Body Mass Index

BMI – Body Mass Index

CAD – Coronary Artery Disease

cART – Combined AntiRetroviral Therapy

CCR/CXCR – Cysteine-Cysteine Receptor/ Cysteine-x-Cysteine Receptor

CD – cluster differentiation

CDC – Centre for Disease Control

CHF – Congestive Heart Failure

CHO – cholesterol

CMV –CytoMegalo Virus

CT – Computer Tomography

DNA – Deoxyribo Nucleic Acid

ECG – Electrocardiogram

EIA – Enzyme Immuno Assay

ELISA – Enzyme Linked ImmunoSorbent Assay

ESR – Erythrocyte Sedimentation Rate

FDB – familial defective apolipoprotein B

FH – familial hypercholesterolemia

gp – Glycoprotein

HAART – Highly Active Antiretroviral Therapy

HDL-C – High Density Lipoprotein Cholesterol

HIV – Human Immunosuppression Virus

HSV – Herpes Simplex Virus

HTLV – Human T-Lymphotropic Virus

IDL – Intermediate Density Lipoprotein

IRIS – Immune Reconstitution Inflammatory Syndrome

IVIg – Intra Venous Immunoglobulin

LDL-C – Low Density Lipoprotein Cholesterol

MI – Myocardial Infarction

MRI – Magnetic Resonance Imaging

NCEP – National Cholesterol Education Programme

PCSK-9 - Proprotein Convertase Subtilisin/Kexin Type 9

PLHA – Patient Living with HIV/ AIDS

RNA – Ribo Nucleic Acid

STD – Sexually Transmitted Disease

TC – Total Cholesterol

TGL – Triglycerides

TLC – Total Leucocyte Count

TSH – Thyroid Stimulating Hormone

UNAIDS – United Nation Programme on HIV/AIDS

URAI – Unprotective Receptive Anal Intercourse

WHO – World Health Organisation

PROFORMA

H/o Drug use

H/o viral hepatitis, Jaundice, Liver disease

H/o alcohol consumption /drinking pattern

NAME: **UNIT**

NO.: **I.P.NO.:**

AGE/SEX:

OCCUPATION: **DATE**

OF ADMISSION:

ADDRESS: **DATE OF DISCHARGE:**

CONTACT NO:

COMPLAINTS:

HISTORY:

PAST HISTORY:

Duration of HIV

Complaint for which he/she was done HIV screening

Diabetes/ Hypertension/ Dyslipidemia/ CAD/ CKD

FAMILY HISTORY: Dyslipidemia

PERSONAL HISTORY: Chewing Tobacco/ Smoking/ Alcohol/ Drug Abuse

TREATMENT HISTROY (DRUGS):

GENERAL PHYSICAL EXAMINATION:

HT: **WT:** **BMI:**

VITALS:

BP: **PR:** **RR:**

SYSTEMIC EXAMINATION:

CVS:

RS:

P/A:

CNS:

Others

INVESTIGATIONS:

LIPID PROFILE

Triglycerides	Total Cholesterol	HDL- C	LDL-C	VLDL-C

RENAL PROFILE

Random sugar	Urea	Creatinine

Complete Hemogram

TC	DC	ESR	HB	Platelet count

CD4 cell count

CD4	

ECG all leads

Sl No	Name	Age	Sex	Duration of Illness	WHO Categories	Ht (cms)	Wt(kgs)	BMI	waist circ	TGL	TC	HDL	LDL	VLDL	CD4 Co	Reason for screening
1	Rajaram	47	Male	3	II	159	58	22.9	84	94	138	42	77.2	18.8	388	Fatigability
2	Willson	47	Male	4	II	175	70	22.8	86	211	226	40	143.8	42.2	368	FUO
3	Kanagaraj	52	Male	2.5	IV	157	60	24.3	97	112	176	50	103.6	22.4	275	FUO
4	Rangan	74	Male	6	III	164	58	21.5	81	316	254	33	157.8	63.2	155	PGL
5	Murugesan	64	Male	5	III	158	63	25.2	96	269	159	42	63.2	53.8	142	FUO
6	Narayanasami	67	Male	6	III	168	60	21.2	86	76	115	58	41.8	15.2	42	Fatigability
7	Kuppan	48	Male	3	III	156	40	24.65	88	151	199	41	127.8	30.2	52	LOA/LOW
8	Vasanthan	60	Male	4	III	154	58	24.45	90	441	251	36	126.8	88.2	162	PGL
9	Sivakumar	55	Male	2	II	158	62	24.83	92	412	212	35	94.6	82.4	17	FUO
10	Mani	48	Male	5	IV	161	63	24.3	88	182	136	46	53.6	36.4	138	FUO
11	Kamalakannan	51	Male	6	IV	172	70	23.66	89	287	217	38	121.6	57.4	268	PGL
12	Arumugam	49	Male	5	II	174	68	22.46	94	350	186	36	80	70	325	Fatigability
13	Murugaiya	48	Male	4	II	168	67	23.73	91	100	194	45	129	20	433	dysphagia
14	Magesan	48	Male	3	III	156	60	24.65	86	249	126	24	52.2	49.8	233	FUO
15	Ravi	50	Male	2	III	172	58	19.6	88	217	150	47	59.6	43.4	288	LOA/LOW
16	Rani	55	Female	1	II	152	48	27.2	83	121	183	51	107.8	24.2	493	PGL
17	Jothi	52	Female	2	I	161	65	25	85	456	279	40	147.8	91.2	882	FUO
18	Sharon	47	Male	2	II	145	51	24.2	80	185	252	41	174	37	837	Fatigability
19	Saraswathi	45	Female	4	I	155	63	26.2	80	125	214	44	145	25	423	FUO
20	Lutmary	50	Female	3	I	150	52	28.8	82	209	209	43	124.2	41.8	690	PGL
21	Jayalaxmi	51	Female	7	I	158	72	28.8	91	320	165	50	51	64	209	Fatigability
22	Renuka	47	Female	5	II	150	63	28	95	335	439	44	328	67	517	PTB
23	Rajeswari	39	Female	5	II	151	62	27.1	83	355	167	46	50	71	570	LOA/LOW
24	Girija	51	Female	1	I	144	49	23.6	81	187	140	50	52.6	37.4	588	PGL
25	Vijayalaxmi	48	Female	2	IV	150	62	27.5	90	298	175	42	73.4	59.6	303	PGL
26	Indira	46	Female	4	I	147	64	29.6	94	167	131	50	47.6	33.4	795	Fatigability
27	Govindammal	42	Female	3	II	149	55	24.77	78	313	150	43	38.4	62.6	384	PTB
28	Parasakthi	50	Female	3	I	145	58	27.5	88	553	183	48	24.4	110.6	254	PGL
29	Kalaivani	44	Female	5	I	149	61	27.4	91	210	136	45	49	42	420	FUO
30	Padmavathy	68	Female	7	I	155	60	24.9	95	162	140	40	67.6	32.4	556	Fatigability
31	Parvathy	51	Female	2	II	146	47	22	82	313	150	43	38.4	62.6	384	LOA/LOW
32	Kottiswari	42	Female	4	I	153	63	26.9	91	553	183	48	24.4	110.6	254	PGL
33	Rajam	63	Female	2	I	147	53	24.5	81	210	136	45	49	42	420	Fatigability
34	Muniyamma	55	Female	3	I	153	62	26.4	93	162	140	40	67.6	32.4	556	PGL
35	Hamsa	39	Female	8	II	163	57	28.9	95	350	132	38	24	70	448	Altered Sensorium
36	Siddiqa	63	Male	5	IV	153	62	26.4	92	160	164	44	88	32	119	PGL
37	Thenmozhi	50	Female	1	IV	150	55	24.4	85	458	175	40	43.4	91.6	113	PTB
38	Sembammal	58	Female	1	III	145	50	23.7	86	240	210	42	120	48	289	Fatigability
39	Malliga	47	Female	3	II	152	43	18.6	66	186	180	50	92.8	37.2	86	LOA/LOW
40	Savithri.S	53	Female	2	II	155	60	24.9	98	282	120	42	21.6	56.4	446	PTB
41	Kaliamma	52	Female	4	I	151	55	24.12	85	120	142	40	78	24	443	PGL
42	Nagapandiammal	64	Female	5	II	151	55	24.12	84	268	110	41	15.4	53.6	295	Fatigability
43	Sarasamma	52	Female	4	II	152	57	24.67	87	160	198	42	124	32	289	FUO
44	Logeswari	45	Female	3	IV	150	55	24.44	85	129	246	42	178.2	25.8	76	PTB
45	Balamma	58	Female	2	IV	152	60	25.96	89	492	202	38	65.6	98.4	171	PGL
46	Tamilselvi	32	Female	3	III	163	64	24.08	72	152	182	46	105.6	30.4	297	FUO
47	Kumar	40	Male	4	IV	152	58	25.1	88	110	138	40	76	22	318	Fatigability
48	Anandan	36	Male	2	III	174	52	17.57	80	312	168	42	63.6	62.4	398	LOA/LOW
49	Devendran	32	Male	5	II	164	52	19.33	82	284	212	41	114.2	56.8	646	FUO
50	Srinivasan	35	Male	6	II	178	60	18.94	84	212	126	39	44.6	42.4	627	Fatigability

Sl No	Name	Age	Sex	Ht (m)	Wt(kgs)	BMI	waist circumference	TGL	TC	HDL	LDL	VLDL
1	Bagavaan	36	Male	1.72	63	21	88	130	160	38	96	26
2	Ramesan	37	Male	1.68	78	28	90	**152**	196	40	125.6	30.4
3	Gopalakrishna	38	Male	1.71	72	25	85	140	150	42	80	28
4	Moorthy	39	Male	1.7	69	24	84	**160**	126	46	48	32
5	Prasanth	40	Male	1.72	72	24	76	148	184	40	114.4	29.6
6	Dhananjeyan	38	Male	1.74	76	25	86	**158**	**202**	38	132.4	31.6
7	Murugan	41	Male	1.65	67	25	86	**202**	166	42	83.6	40.4
8	Balasubraman	40	Male	1.65	80	29	90	**210**	192	40	110	42
9	Gopinath	42	Male	1.66	70	25	84	**160**	**206**	41	133	32
10	Palanivel	39	Male	1.57	72	29	90	**198**	**240**	42	158.4	39.6
11	Natesan	45	Male	1.73	72	24	85	130	160	44	90	26
12	Jayaram	46	Male	1.73	63	21	80	**152**	196	40	125.6	30.4
13	Prasath	49	Male	1.75	80	26	83	140	156	34	94	28
14	Ayyasamy	52	Male	1.67	58	21	78	**260**	192	38	102	52
15	Ramanujam	70	Male	1.55	57	24	85	**210**	196	34	120	42
16	Sakthi	53	Female	1.64	58	22	86	140	**210**	38	144	28
17	Pandi	52	Female	1.63	58	22	81	**290**	**202**	42	102	58
18	Sarasu	63	Female	1.7	80	28	85	**202**	**200**	40	119.6	40.4
19	Ramayee	50	Female	1.71	68	23	83	142	196	42	125.6	28.4
20	Rani.S	53	Female	1.62	60	23	84	**168**	182	42	106.4	33.6
21	Rosy	51	Female	1.65	79	29	87	**192**	**220**	38	143.6	38.4
22	Frabella	64	Female	1.66	77	28	80	**190**	186	44	104	38
23	Sumathra	53	Female	1.67	74	27	81	140	**202**	40	134	28
24	Prabha	52	Female	1.66	68	25	82	138	160	42	90.4	27.6
25	Sujitha	73	Female	1.6	50	20	83	**156**	142	42	68.8	31.2
26	Madhavi	62	Female	1.65	80	29	80	**162**	148	40	75.6	32.4
27	Mythili.M	50	Female	1.66	70	25	85	**159**	168	54	82.2	31.8
28	Kamala	47	Female	1.54	55	23	82	**170**	174	38	102	34
29	Reeshma	48	Female	1.52	56	24	84	**316**	130	40	26.8	63.2
30	Vidhya	50	Female	1.51	54	24	84	126	190	42	122.8	25.2
31	Suganya	51	Female	1.59	67	27	82	130	120	42	52	26
32	Abhinaya sund	52	Female	1.57	59	24	78	142	138	44	65.6	28.4
33	Chellama	53	Female	1.51	68	30	84	**152**	178	40	107.6	30.4
34	Ruby	53	Female	1.58	50	20	81	148	182	42	110.4	29.6
35	Tamilarasi	67	Female	1.74	85	28	83	122	198	42	131.6	24.4
36	Geetha	39	Female	1.58	48	19	81	**190**	140	40	62	38
37	Vasanthi	42	Female	1.47	57	26	85	124	162	42	95.2	24.8
38	Kokila	41	Female	1.53	53	23	82	136	156	40	88.8	27.2
39	Porkodi	43	Female	1.51	67	29	85	130	182	42	114	26
40	Mythili.M	43	Female	1.67	70	25	84	148	198	41	127.4	29.6
41	Rani	46	Female	1.58	57	23	86	**412**	138	38	17.6	82.4
42	Annalakshmi	70	Female	1.53	56	24	86	**152**	154	40	83.6	30.4
43	Ghanthi	62	Female	1.59	67	27	84	**162**	188	42	113.6	32.4
44	Parimala	53	Female	1.52	65	28	83	**180**	**202**	40	126	36
45	Radha	63	Female	1.73	80	27	85	**420**	149	38	27	84
46	Lakshmi Sundari	23	Female	1.51	51	22	86	148	169	40	99.4	29.6
47	Manikandan	27	Male	1.33	36	20	80	**162**	180	40	107.6	32.4
48	n	26	Male	1.52	44	19	78	**382**	136	39	20.6	76.4
49	K.Balaji	34	Male	1.63	56	21	84	**156**	**210**	40	138.8	31.2
50	M. Maniyannan	36	Male	1.74	61	20	80	**172**	192	42	115.6	34.4

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.1223/ME-1/Ethics/2013 Dt:07.03.2013.
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on cross sectional study of prevalence of dyslipidemia in treatment NAIVE PLHA patient and its correlation with CD4 count" for Project work submitted by Dr. S.Ganesh Aravind, MD (GM), PG Student, Govt. Kilpauk Medical College, Chennai.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

CHAIRMAN, 19/4/13
Ethical Committee
Govt.Kilpauk Medical College,Chennai

GOVT. KILPAUK MEDICAL COLLEGE
19 APR 2013
Kilpauk, Chennai-10.