# A STUDY OF RENAL FUNCTION ABNORMALITIES IN PATIENTS WITH HIV INFECTION /AIDS

## CROSS SECTIONAL STUDY

*Dissertation Submitted for*

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**Chennai – 600 032.**

# MADURAI MEDICAL COLLEGE, MADURAI.

## CERTIFICATE

This is to certify that this dissertation titled "**A STUDY OF RENAL FUNCTION ABNORMALITIES IN PATIENTS WITH HIV INFECTION /AIDS"** submitted by **DR. K.PREMKUMAR** to the faculty of General Medicine, **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by him under our direct supervision and guidance.


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# DECLARATION

I, **Dr.K.Premkumar** solemnly declare that the dissertation titled "**A STUDY OF RENAL FUNCTION ABRNORMALITIES IN PATIENTS WITH HIV INFECTION AND AIDS"- CROSS SECTIONAL STUDY** has been prepared by me.

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

Place : Madurai

Date: Dr.K.Premkumar

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## CONTENTS

# INTRODUCTION

## HUMAN IMMUNODEFICIENCY VIRUS DISEASE

AIDS was first recognized in the United States in 1981, when the U.S. Centers for Disease Control and Prevention (CDC) reported the unexplained occurrence of *Pneumocystis jiroveci* (formerly *P. carinii*) pneumonia in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma (KS) with or without *P. jiroveci* pneumonia in 26 previously healthy homosexual men in New York and Los Angeles. Within months, the disease became recognized in male and female injection drug users (IDUs) and soon thereafter in recipients of blood transfusions and in hemophiliacs. Then it became clear that an infectious agent transmissible by sexual (homosexual and heterosexual) contact and blood or blood products was the most likely etiologic cause of the epidemic.[ref1]

In 1983, human immunodeficiency virus was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated clearly to be the causative agent of AIDS. In 1985, a sensitive enzyme-linked immunosorbent assay (ELISA) was developed, which led to an appreciation of the scope and evolution of the epidemic at first in the United States and other developed nations and ultimately among developing nations throughout the world .

## DEFINITION

Using the current CDC3 classification, any HIV infected individuals with a CD4+ T cell count of < 200/µL has AIDS by definition, regardless of the presence or absence of symptoms or opportunistic diseases.[ref1]

## EPIDEMIOLOGY

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; ~50% are female, and 2.5 million are children .[ref1]

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 totaled 2.1 million (including 330,000 children <15 years). UNAIDS estimates that global HIV prevalence has been level since 2001. 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 behavior change.[ref1]

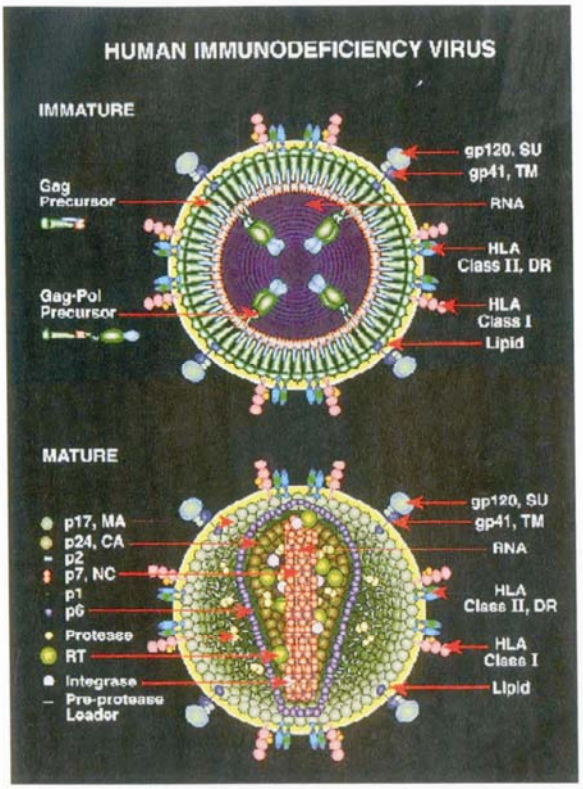
HIV prevalence in India is~3.6% amounting between 2 and 3.1 million people. On an average it comes to 2.5 million. The prevalence for adult female is 0.29% and for males 0.43%. Prevalence high in age group 15- 49 years. [ref2] Among IDU's it is as high as 8.71% while it is 5.69% and 5.38% among MSM and FSW respectively.[ref2]
In AndhraPradesh Karnataka, Maharasthra and Tamilnadu HIV is transmitted mainly through heterosexual route and is largely linked to commercial sex work. Indeed, according to selected surveys more than half of sex workers have become infected with HIV.

In India knowledge about HIV is still scant and incomplete. In a 2001 national behavioral study of nearly 85000 people, only 75% of respondents had heard of AIDS and awareness was particularly low among rural women in Bihar, Gujarat and West Bengal. Less than 33% of all respondents had heard of sexually transmitted infections and only 21% were aware of the links between sexually transmitted infections and HIV.

The etiologic agent of AIDS is HIV ,which belongs to the family of Human \retroviruses (Retroviridae) and the subfamily of lentiviruses. The HIV virion is an icosahedral structure containing numerous external spikes

formed by the two major envelope proteins ,the external gp120 and the transmembrane gp41.

## ETIOLOGIC AGENT




- **Gag Proteins and Precursor (p55)**
  - Capsid Structural Protein (CA, p24)
  - Matrix Protein (MA, myristylated, p17)
  - RNA Binding Protein (p9)
  - RNA Binding Protein ( proline-rich, p7)
  - Other Gag Proteins( p6, p2, p1)
- **Viral Encoded Enzymes**
  - Polymerase (p61,p55)
    - Reverse Transcriptase
    - Rnase H
  - Protease (p10)
  - Integrase (p32)
- **Envelope Proteins**
  - Surface Glycoprotein (gp120)
  - Transmembrane Glycoprotein (gp41)
- **Accessory and Regulatory Proteins**
  - Tat
  - Rev
  - Nef
  - Vif (Viral Infectivity Factor)
  - Vpr
  - Vpu
  - Vpx
  - Tev
- **Nucleic Acids**
  - HIV RNA

[ref 13]

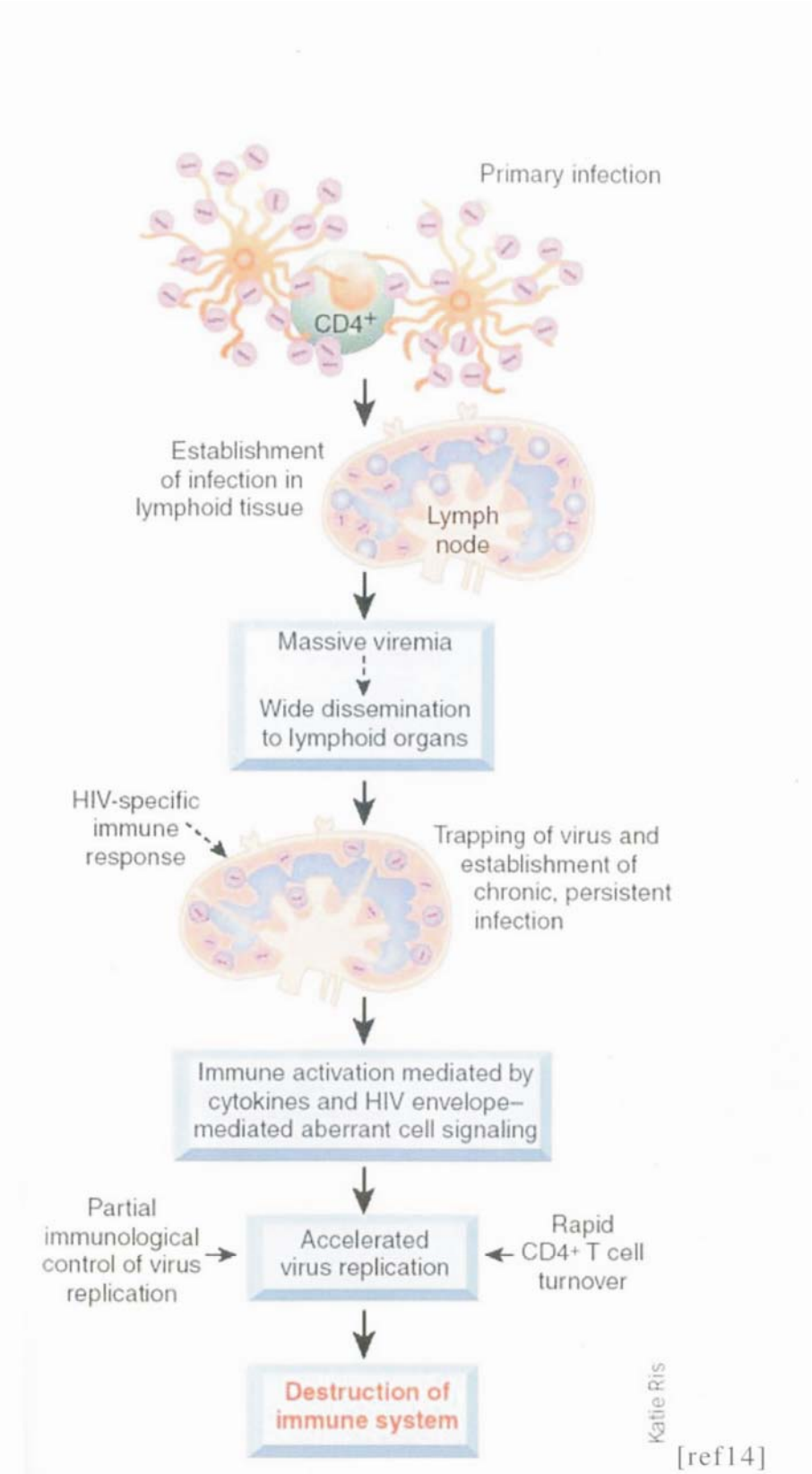
## TRANSMISSION

HIV is tranmitted by both homosexual and heterosexual contact; by blood and blood products and by infected mother to infants either intrapartum, perinatally or via breastmilk.

## PATHOPHYSIOLOGY AND PATHOGENESIS

The hallmark of HIV disease is a profound immunodeficiency resulting primarily from a progressive quantitative deficiency of the subset of T lymphocytes referred to as helper T cells. When the number of CD4+ cells declines below a certain level, the patient is at high risk of developing a variety of opportunistic diseases, particularly the infections and neoplasms that are AIDS- defining illnesses. Some features of AIDS, such as KS and neurologic abnormalities cannot be explained completely by the immunosuppressive effects of HIV ,since these complications may occur prior to the development of severe immunologic impairment.

The combination of viral pathogenic and immunopathogenic events that occurs during the course of HIV disease from the moment of initial (primary) infection through the development of advanced stage disease is complex and varied. It is important to appreciate that the pathogenic mechanisms of HIV disease are multifactorial and multiphasic.[ref1]

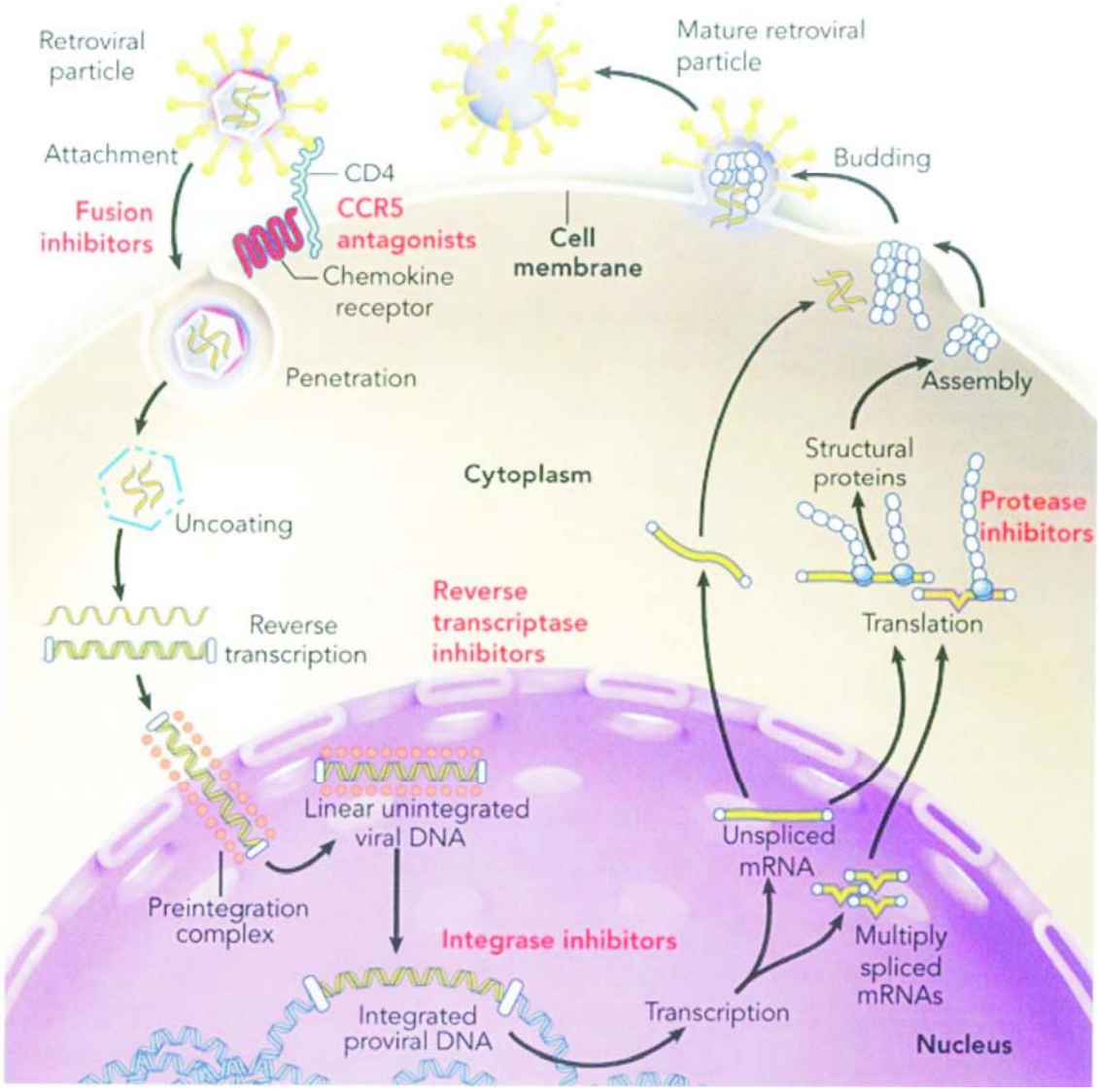

Primary infection
CD4+
Establishment of infection in lymphoid tissue
Lymph node
Massive viremia
Wide dissemination to lymphoid organs
HIV-specific immune response
Trapping of virus and establishment of chronic, persistent infection
Immune activation mediated by cytokines and HIV envelope–mediated aberrant cell signaling
Partial immunological control of virus replication
Accelerated virus replication
Rapid CD4+ T cell turnover
Destruction of immune system
Katie Ris

[ref14]

# ANTIRETROVIRALTHERAPY

The best time to initiate antiretroviral treatment (ART) remains controversial. It is best to weigh the benefits of viral suppression against side effects of the drugs for each patient. In general, treatment for asymptomatic HIV disease should be initiated when the CD4 cell count drops below 350 cells/micL or symptomatic HIV disease. Patients with rapidly dropping CD4 counts or very high viral loads (>100,000/micL) should be considered for earlier treatment. For these patients who might have difficulty adhering to treatment or who are at higher risk for toxicity (eg. Underlying liver disease), waiting until the CD4 count nears 200 cells/micL may be a better strategy.

## ANTIRETROVIRAL THERAPY



**Antiretroviral Drugs Used in the Treatment of HIV Infection**

| Drug | Toxicity |
|---|---|
| Zidovudine (AZT) | Anemia, granulocytopenia, myopathy, lactic acidosis, hepatomegaly with steatosis, headache, nausea |
| Didanosine (ddI) | Pancreatitis, peripheral neuropathy, abnormalities on liver function tests, lactic acidosis, hepatomegaly with steatosis |
| Zalcitabine (ddC) | Peripheral neuropathy, pancreatitis, lactic acidosis, hepatomegaly with steatosis, oral ulcers |
| Stavudine (d4T) | Peripheral neuropathy, pancreatitis, lactic acidosis, hepatomegaly with steatosis, ascending neuromuscular weakness, lipodystrophy |
| Lamivudine (3TC) | Hepatotoxicity |
| Emtricitabine | Hepatotoxicity |
| Abacavir | Hypersensitivity reaction (can be fatal); fever, rash, nausea, vomiting, malaise or fatigue, and loss of appetite |
| Tenofovir | Potential for renal toxicity |
| Delavirdine | Skin rash, abnormalities in liver function tests |
| Nevirapine | Skin rash, hepatotoxicity |
| Efavirenz (Sustiva) | Rash, dysphoria, elevated liver function tests, drowsiness, abnormal dreams, depression |
| Etravirine | Rash, headache, dizziness, nausea, diarrhea |
| Saquinavir mesylate | Diarrhea, nausea, headaches, hyperglycemia, fat redistribution, lipid abnormalities |
| Fortovase | Diarrhea, nausea, abdominal pain, headaches, hyperglycemia, fat redistribution, lipid abnormalities |
| Ritonavir | Nausea, abdominal pain, hyperglycemia, fat redistribution, lipid abnormalities, may alter levels of many other drugs, including saquinavir |
| Indinavir sulfate | Nephrolithiasis, indirect hyperbilirubinemia, hyperglycemia, fat redistribution, lipid abnormalities |
| Nelfinavir mesylate | May contain traces of the potential carcinogen/teratogen ethyl methane sulfonate |
| Amprenavir | Nausea, vomiting, diarrhea, rash, oral paresthesias, elevated liver function tests, hyperglycemia, fat redistribution, lipid abnormalities |
| Fosamprenavir | |
| Lopinavir/ritonavir | Diarrhea, hyperglycemia, fat redistribution, lipid abnormalities |
| Atazanavir | Hyperbilirubinemia, PR prolongation, nausea, vomiting, hyperglycemia, fat maldistribution |
| Tipranavir | Diarrhea, nausea, fatigue, headache, skin rash, hepatotoxicity, intracranial hemorrhage |
| Darunavir | Diarrhea, nausea, headache |
| Enfuvirtide | Local injection reactions, hypersensitivity reactions, increased rate of bacterial pneumonia |
| Maraviroc | Hepatotoxicity, nasopharyngitis, fever, cough, rash, abdominal pain, dizziness, fever, musculoskeletal symptoms |
| Raltegravir | Nausea, rash |

# REVIEW OF LITERATURE

## Introduction

The renal manifestations of HIV infection occurs commonly during all stages of infection. Renal Manifestations of HIV infection occurs in 6-10% of HIV seroperative individuals . Fluid, electrolytes and acid-base, abnormalities, as well as acute renal failure, have been observed frequently, mainly as a consequence of drug toxicity or opportunistic infections .

Disorders of kidney may be due to

- a direct of consequence of HIV infection
- neoplasm
- related to drug toxicity

The most clinically relevant disorder is chronic renal failure progressing to end stage renal disorder (ESRD), which has also been observed with a high frequency in some centers. Caused by HIVAN - HIV associated immune mediated renal disease .

The progression of HIV disease is more rapid in patients with renal failure, particularly those with pre-existing end-stage renal disease who become infected with HIV as a result of hemodialysis or renal transplantations. [ref4]

The susceptibility of blacks, men, and persons with a H/o IDU suggests both genetic and environmental factors may modulate the development of HIV-associated renal disease.

1. **Classification[ref5]**
2. **Acute renal failure and fluid & electrolyte disorders**

    i. Acute renal failure

    ii. Disorders of osmoality

    iii. Potassium disorders

    iv. Acid-base disorders

3. **Glomerular renal disease**
4. HIV associated nephropathy

    i. Other renal lesions

    ii. End stage renal disease

II. **Acute renal failure and fluid and electrolyte disorders**

(i) **Acute renal failure**

III. **Causes**

5. **Prerenal**:

1. Volume depletion – Diarrhoea
    I. Bleeding
    II. Decreased intake
    III. NSAID's
2. Sepsis

3. Early obstructive uropathy

(A) **Renal**:

1. Acute tubular Necrosis:

- Ischemia / hypoperfusion
- Sepsis/endotoxemia
- Radiocontrast exposure
- Nephrotoxic antibiotics

Amphotericin B,

Aminoglycosides

Pentamidin

Foscarnet

Acyclovir

Cidofovir

Tenofovir

2. **Acute interstitial nephritis**

- Sulfamethxazole
- Dapsone
- NSAIDs
- Rifampin

3. **Glomerular disease**

- HIVAN

- HCV – MPGN (Mesangio proliferative glomerulo nephritis)

- other primary glomerulo nephropathies

4. **Infiltrative lesions**

- Kaposis sarcoma

- Renal cell carcinoma
- Lymphoma
- Amyloidosis

5. **Vasculitis**
   - Hemolytic – uremic syndrome
   - Thrombotic – thrombocytopenic purpura
   - renal cortical infarction

6. **Systemic infections**
   - Mycobacterium species
   - Candida species
   - Cryptococcus species
   - Aspergillosis
   - Cytomegalovirus
   - Bacterial endocarditis
   - Renal microabscess formation

7. **Miscellaneous**

   HAN (Heroin associated nephropathy)

   Nephrosarca (renal oedema with severe hypoalbuminemia)

Chemical interference with the creatinine assay

Trimethoprim – sulfamethoxazole

Cephalosporins

Cimetidine

**(B) Post Renal / Obstruction**

1. Drugs causing crystalluria

   Sulfadiazine

   Indinavir

   Acyclovir

2. Malignancy

**Mild ARF:** Defined as a peak serum creatinine >=2.0mg/dl. Occurs in upto 20% of hospitalized HIV infected patients . This percentage compares to an incidence rate of 4-5% in hospitalized non-HIV infected patients [ref5]. Patients with ARF on admission to the hospital are likely to have a prerenal cause related to hypovolemia. In patients who develop during the hospitalization, the likely cause is acute tubular necrosis from hypotension or drug nephrotoxicity. Common causes of ATN include sepsis, hypotension, and medications commonly used in the treatment of HIV-related infections such as aminoglycosides, pentamidine, acyclovir, foscarnet, amphotenicin B, tenofovir, adefovir and cidofovir, NSAIDs, rifamicin, trimethoprim – sulfamethoxazole . Both foscarnet and tenofovir are associated with development of nephrogenic diabetes insipidus.

**Severe Renal Failure:**

In HIV infected patients, sepsis contributes to the development of severe renal failure, defined as a peak creatinine >=6.0mg/dL, in upto 75% of cases severe renal failure in HIV –infected patients may be associated with terminal conditions in which acute dialysis would be inappropriate.

When the acute underlying illness is reversible, however, ARF will usually reverse with dialysis and conventional supportive care. Because the overall prognosis is favourable .

Acute interstitial nephritis has been found in 13% of autopsies done in patients with renal dysfunction, and an inciting agent is usually not identified [ref5].

Obstructive uropathy may be the result of abdominal adenopathy or sludge formation in the collecting system due to crystallization of protease inhibitors and Acyclovir. Rare opportunistic infections such as isolated renal mucormycosis, have also been described .

Renal function generally is restored once rigorous hydration is administered and the inciting agent is discontinued.

**Reversible causes of renal insufficiency**

Kidney infection

Exposure to nephrotoxic antibiotics or radiologic contrast

Endotoxemia

Hypoperfusion

**Progressive renal insufficiency**

Result from parenchymal infiltration with Kaposisarcoma or lymphoma. Urinalysis is extremely helpful in differential diagnosis of ARF in HIV patients. Urine sediment should be

(1) prerenal patients - normal

(2) ATN - muddy brown, granular casts and/or renal tubular cells and casts.

(3) Ac. Interstitial nephritis - predominately show WBCs, WBC casts, and a small amount of proteinuria and hematuria.

**(ii) Disorders of Osmolality:**

Among the electrolyte abnormalities observed in HIV patients, two- hyponatremia and hyperkalemia – are of most significance. [ref6]

**Hyponatremia**:

1) Most common electrolyte disturbance

2) Have been reported in 30-60% of hospitalized symptomatic HIV patients or AIDS and

3) Severe hyponatremia may be associated with increased morbidity and mortality in HIV infected patients it is a poor prognosis.

4) Volume depletion due to diarrhoea or vomiting is the usual cause of hyponatremia present at the time of hospital admission. In most of cases, when normal ECF volume is restored, the hyponatremia is corrected .

5) Excess body water is attributed either to hypovolemia with physiologic stimulation of ADH, administration of hypotonic fluids, or the SIADH. SIADH is the likely culprit in those who develop hyponatremia during hospitalization .

SIADH is usually associated with common pulmonary and intracranial diseases, such as

- Pneumocystis pneumonia,
- toxoplasmosis and
- Tuberculosis

Plasma ADH concentration, when measured in some of these patients, has been inappropriately elevated for the degree of hyponatremia and hypo-osmolality lending strong support for this being the mechanism underlying the hyponatremia .[ref7]

6) The initial treatment of SIADH consists of fluid restriction and treatment of underlying infection or malignancy.

7) In a few patients, evidence of adrenal insufficiency has accompanied the hyponatremia, and treatment with glucocorticoid hormone has improved the serum sodium concentration .

AIDS patients have a high incidence of adrenal abnormalities. Adrenal pathology, particularly CMV infection is found common in patients who have died from AIDS .

Other pathologic lesions that have been noted frequently include hemorrhage;

infection with toxoplasma,

Cryptococcus,

mycobacterium tuberculosis,

MAC;

infiltration with kaposi’s sarcoma and lymphoma .

Several drugs that are used commonly in the treatment of patients with AIDS are known to alter adrenal function or steroid hormone metabolism.

1. **Ketaconazole** inhibits cortisol synthesis and could lead to adrenal insufficiency, particularly in patients with limited adrenal reserve.
2. **Rifampin** enhances cortisol metabolism, which can result in adrenal insufficiency in patients with Addison’s disease who are on maintenance gluocorticoid therapy.

**(iii) Potassium Disorders**

Both hypokalemia and hyperkalemia commonly develop in HIV infected patients.

**Hypokalemia** is predictably seen secondary to gastrointestinal losses of potassium in HIV patients with gastrointestinal infections.

Amphotericin-B, frequently used to treat fungal infections in patients with AIDS can cause tubular dysfunction resulting in hypokalemia.

**Hyperkalemia** may occur as a result of the effect of

1) High doses of trimethoprin – sulfamethoxazole or IV pentamidine.

The underlying mechanism with both drugs consists of inhibition of distal nephron sodium transport, leading to a decrease in distal protein secretion .

Trimethoprim shares structural similarity with the potassium sparing diuretic triamterene.

2) Hyperkalemia and hyponatremia may also be a manifestation of mineralocorticoid deficiency due to adrenal insufficiency or the syndrome of hyporeninemic hypoaldosteronism .

3) Severe acute or chronic renal insufficiency may also contribute to the development of hyperkalemia due to potassium retention. Treatment of hyperkalemia should be guided by the cause and severity; it should respond to cessation of offending drugs or to treatment with loop diuretics or with fludrocortisone for adrenal causes .

A systemic abnormality in potassium equilibrium, which favours the development of hyperkalemia by a mechanism unrelated to renal potassium excretion, has also been identified in HIV – infected individuals .

**(iv) Acid Base Disorders**

HIV patients may present with a variety of simple and mixed acid-base disorders. Commonly due to infections or drugs.

Respiratory alkalosis and respiratory acidosis may occur in opportunistic infections of the lungs or CNS. Both high and non anion gap metabolic acidosis are also seen.

Causes of non anion gap metabolic acidosis [ref5]

- Stool base losses from diarrhoea
- adrenal insufficiency
- the syndrome of hyporeninenic hypoaldosteronism,
- drug toxicity (Amphotericin B – related renal tubular acidosis)

High anion gap metabolic acidosis in this population results from

- CRF
- Type A lactic acidosis due to tissue hypoxia (sepsis)
- Type B lactic acidosis

Type B lactic acidosis presents with markedly elevated blood lactate levels possibly caused by drug-induced mitochondrial dysfunction – “Mitochondrial myopathy” causing in interruption of normal mitochondrial respiration in skeletal muscle. This disorder been reported with .

Zidovudin

Didanosin

Zalcitabine

Lamivudin

Stavudin

These patients have no evidence of hypoxemia, tissues hypoperfusion, malignancy or sepsis. Recognition of this entity rests with a severe metabolic acidosis with an increased anion gap; blood lactate levels when measured, have been greater than 5, and frequently greater than 10 mmol/l .

Although life threatening acidosis is rare, 5-25% of treated patients may develop mildly elevated lactate level (2.5-5mmol/L) without acidosis.

Survival is shortened in these patients .

**III GLOMERULAR RENAL DISEASE**

**(A) HIV associated Nephropathy (HIVAN)**

**a. Epidemiology**

1. HIVAN is a unique clinical and histopathological entity and it is thought to develop as a result of HIV gene expression in renal tissue. HIVAN may be the initial manifestation of HIV infection.

2. HIVAN was first described in IDUs and was initially thought to be IDU nephropathy in patients with HIV infection. The disease now recognized as HIVAN was first described in patients with AIDS in 1984. But the

occurrence of this lesion in infants and children with AIDS from vertical transmission indicates that drug use is not necessary for its development .

3. HIVAN represents a major complication of HIV infection. Its natural history has been well defined – the development of nephrotic syndrome initially, then relentless progression to end-state renal disease (ESRD) in most patients [ref8].

HIVAN has become the most common single diagnosis in HIV infected patients with renal insufficiency.

The true prevalence of HIVAN is not known. HIVAN is more common in urban centres, with a prevalence of about 10%. The geographic distribution of HIVAN is not uniform, and depends on specific risk factors, which include race, gender, and drug use.

HIVAN, worldwide, over 90% of reported cases have occurred in people of African descent as is also true for focal segmental glomerulosclerosis (FSGS) associated with intravenous drug use (IVDU) .

HIVAN is 7-10 times more common in men than women, men comprises 80 to 90% of cases and 30-60% of people with HIVAN have a H/o IVDU . The remainders are either homosexual or originate from regions where HIV infection is endemic . In approximately 10% patients – no

specific risk factor for HIV can be identified . Black men have increased risk [ref4,9].

Thus, in the United States, the typical patient with HIVAN is a young African American male with a H/o IVDU.

Unfortunately, most patients who develop HIVAN do not have early signs or symptoms that would provide a clue to this diagnosis prior to the onset of progressive nephropathy.

HIVAN is recognized throughout the spectrum of HIV disease.

Clinical presentation typically includes

- Proteinuria but no hematuria on urinalysis

- high grade proteniuria, usually in nephrotic range (>3.5gms/day)

Proteinuria is the hall mark of HIVAN. Over all, microalbuminuria is seen in ~ 20% of untreated HIV infected patients; significant proteinuria is seen in closer to 2% [ref1] Hypoalbuminemia disproportionate to the degree of proteinuria.

- Normal or large kidneys with increased echogenicity on diagnostic ultrasound.[ref10].

- Note worthy is the rarity of hypertension and peripheral oedema in these patients despite the severity of the renal failures and proteinuria . Prognosis may depend on the clinical status of HIV infection, the presence of ESRD or both. [ref11].

- HIVAN has poor prognosis, most patients progress quickly to ESRD within 2 to 6 months.

Until the factors that precipitate HIVAN are identified and randomized drug trials performed, its therapy will remain empiric and be limited to suppression of viral proteins.

**b. Pathogenesis**

1. The pathogenesis of HIVAN has been studied intensely over the past 15 yrs. A central question in the pathogenesis of HIVAN is whether the disease can be attributed to direct viral effects or to HIV related changes in the cytokine milieu.

2. HIV appears to be trophic for specific cell types, including lymphocytes (T cells) and epithelial cells of colon, CNS and kidneys. The basis for tropism is complex and is not simply related to the presence of a surface $CD_4$ receptor on susceptible cells .

3. HIVAN is caused by HIV gene expression in renal tissue, resulting in injury of glomerular and tubular epithelial cells. This accounts for leakage of filtered proteins. (nephrotic syndrome) and renal failure.

4. Since HIV proliferation appears to be the major determinant of cytotoxicity, factors that precipitate viral replication within the kidney could explain the sudden onset of the disease.

5. HIV proliferation is regulated by at least two genes, *nef* and *vif*, with opposing action. Minor mutation in either of these could lead to rapid viral proliferation and death of the host cell. Concomitant infection with viral hepatitis, syphilis or CMV, could induce HIV replication.

6. CMV may promote viral proliferation through a mechanism that is dependent on tumor necrosis factor (TNF) .

7. Concomitant viral infections might remove inhibition to HIV replication by depleting $CD_4$ lymphocytes, further depressing the immuno system.

8. HIV is a potent stimulator of transforming growth factor -β a cytokine strongly implicated in the development of fibrosis. The transgenic mouse model (Tg 26) suggests that activation of the cytokine could well be the basis for the extensive interstitial fibrosis and glomerular sclerosis that are the hall marks of HIVAN .

9. There are evidences to indicate a strong association between. HIV and HIVAN. HIV DNA and protein markers specific for HIV have been demonstrated in tubular epithelium, glomerular epithelial cells, and mesangeal cells by a variety of techniques in vitro and in renal biopsy tissue of HIV patients .

10. HIV DNA has also been identified in the tissue of HIV patients without any renal disease .

11. Studies with transgenic mouse model (Tg 26)showed HIVAN with intact vpr gene .the transgenic mice bearing a simplified proviral DNA (encoding tat and vpr )developed renal disease characterized by FSGS in which vpr protein was localized to glomerular and tubular epithelia by immunohistochemistry.[Virology vol 322,issue1,Apr2004].

12. HIV infection may involve epithelial cells from multiple segments of the nephron, including proximal tubule, thick ascending loop of Henle, and collecting duct. This pattern of involvement may explain the tubular dilatation seen in kidney biopsy specimens of patients with HIVAN .

13. Despite undetectable viral levels in the serum, a case report described a patient who continued to express HIV in renal epithelial cells as determined by RNA in situ hybridization . Active replication of HIV occurs in kidney epithelium, possibly producing HIV strains in the kidney microenvironment,

that differ from HIV circulating in the blood. This suggests that kidney may serve as a viral reservoir harboring HIV strains that have evolved under tissue-specific selection pressures .

**(c) Clinical manifestation**

Renal manifestations of HIV infection occurs in 6-10% of HIV seropositive individuals.

Proteinuria is the hall mark of this disorder. Most patients (89%) excreted 1gm or more of protein / day .[ref12].

**Clinical presentation of HIVAN**

Source: Adapted from JJ Bourgoignie, R.Meneses, C. Ortiz, et al.,

| **PRESENTATION** | **% OF PATIENTS** |
|---|---|
| **Azotemia** | **64** |
| **Proteinuria** | **19** |
| **Azotemia &proteinuria** | **9** |
| **Electrolyte imbalance** | **6** |
| **Gross hematuria** | **3** |

**Features consistent with diagnosis of HIVAN include**

- Absence of hypertension
- A characteristic urine sediment
- Normal or large kidneys
- Hypoalbuminemia disproportionate to the degree of proteinuria and rapidly progressive renal insufficiency.

**(d) Histopathology**

HIVAN is associated with characteristic glomerular, tubulointerstitial and ultrastructural lesions. Autopsy data demonstrate that 90% of patients with the clinical diagnosis of HIVAN have focal and segmental glomerulosclerosis (FSGS).[ref12]. FSGS is a pattern of renal response to a variety of insults and is not specific for HIVAN. Renal biopsy may confirm the clinical diagnosis of HIVAN.

**Light microscopic features include**

- Collapsing focal segmental glomerulosclerosis or mesangial hyperplasia, a probable precursor lesion to FSGS
- Cystic tubular dilatation;

- Interstitial odema;
- Cellular infiltration by lymphocytes or monocytes;

Dilated degenerating proximal tubules filled with eosinophilic material, possibly representing cast formation in situ.[ref13].

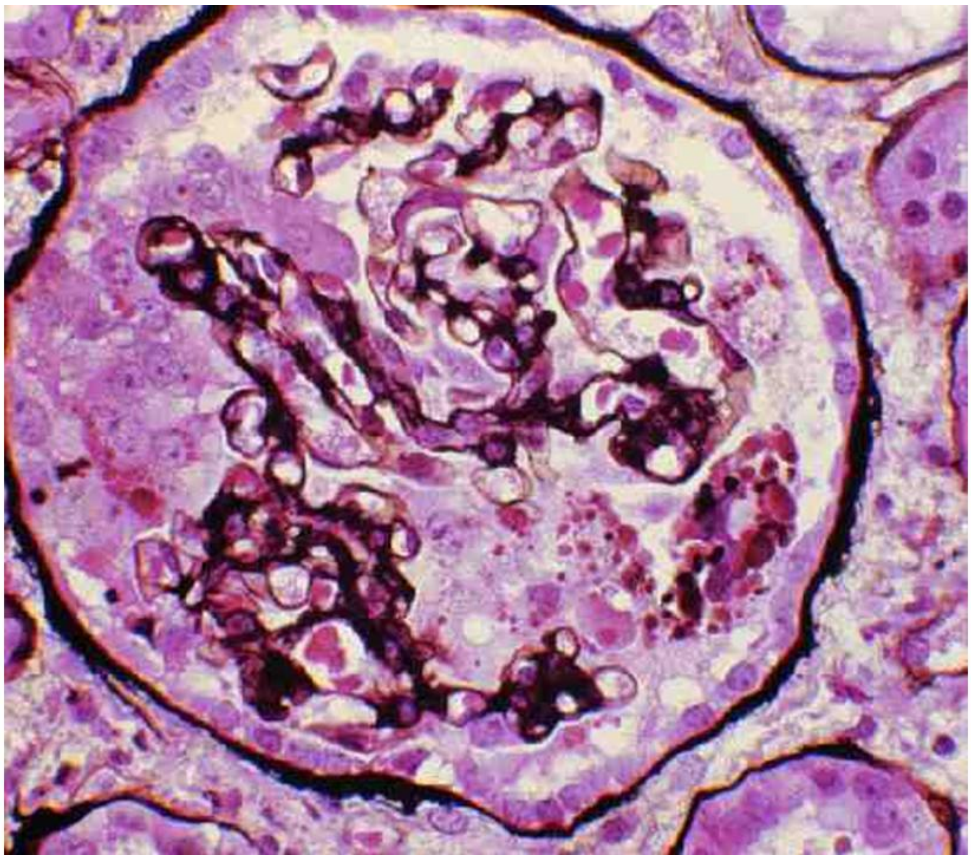
**Electron Microscopy**

The presence of numerous tubuloreticular inclusions (TRI) within endothelial cells is another important finding in HIVAN . TRI's are more common and more numerous in HIVAN than in HAN or idiopathic FSGS.[ref13]

A more than 10-fold increase in the number of TRIs per glomerular capillary was noted in HIVAN. Finding numerous TRIs in capillary endothelial cells in a patient with FSGS prompts some pathologists to request HIV antibody testing.TRI's may be a component of interferon or reflect a cellular response to interferon, but not represent particles of HIV.

Although renal tissue may stain for IgM, C1q, C3 and Kappa or lamda light chains in areas of focal sclerosis, immunologic mechanisms are probably not central to genesis of HIVAN . Both immuno globulin and complement can be trapped nonspecifically by sclerosing glomeruli

## COLLAPSING FOCAL SEGMENTAL GLOMERULOSCLEROSIS



**(e) Investigations**

Examination of urine sediment in HIVAN often reveals evidence of severe proteinuria with oval fat bodies and frank lipiduria. Large number of broad (giant) waxy casts have also been observed in some patients.

1. **Proteinuria**: Proteinuria is the hall mark of this disorder. Overall, microalbuminuria is seen ~20% of untreated HIV infected patients. Significant proteinuria is seen in closer to 2%. Fever, exercise, hyperglycemia, and severe hypertension can transiently cause proteinuria. To precisely quantitate and qualitatively analyze the amount and composition of urinary proteins, an examination of a 24 hour collection of urine is usually required. The normal 24 hours urine protein executed in the adult ranges from 30 to 150 mg. children and adolescents may excrete as much as twice this amount. In HIVAN, nephrotic range proteinuria is usually seen (>3.5gm / 24 hrs.). A urinary protein creatinine concentration ratio on the first voided morning urine sample is useful substitute for repeated 24 hours urine protein estimation. Normal spot urinary protein creatinine ratio on random samples generally fall below 2. Values >3 suggest the presence of nephrotic range proteinuria. Microalbuminuria indicates excretion of albumin of 20-200 μgm

per minute (albumin excretion rate of AER) of a daily excretion of albumin in the range of 30-300mg.

2. The dramatic decline observed in serum albumin concentration (to ≤ 1gm /dl) with moderate albuminuria (<10gm/day) may be caused by malnutrition or a defect in hepatic albumin synthesis or both. But in HIVAN, hypoalbuminemia will be disproportionate to the degree of proteinuria.

**Serum Electrophoresis:** (Proteins)

| | | |
|---|---|---|
| Nephrotic syndrome | alb ↓ | α2 Glo↑ |
| Chronic liver disease | | |
| with cirrhosis | alb ↓ | γ Glo↑ |
| Malnutrition | alb ↓ | |
| Acute febrile illness | α1 ↑ | |
| Hyperlipidemia | β Glo ↑ | |

3. Azotemia, proteinuria or both are the presenting feature in >90% of HIV infected patients.

In HIVAN, progression to end-stage renal disease occurred in an average of 1.9 weeks from the onset of mild azotemia .

4. **Renal Ultrasound** in patients with HIVAN typically shows normal or enlarged renal silhouette (>12.3 cm) with increased echogenicity, even with advanced renal failure. [ref10].

Renomegaly may be the result of

– insufficient time for global sclerosis and fibrosis given the rapid progression of renal disease.

– Marked dilatation of the tubules with numerous microcysts, in contrast to the tubular collapse frequently seen in other forms of chronic renal injury and interstitial oedema.

5. **Renal biopsy** may confirm the clinical diagnosis of HIVAN. Histopathology has already been discussed earlier. Biopsy in HIV infected patients with proteinuria finds the typical features of HIVAN in about 60% of cases; and a variety of other disease entities are also found in association with factors such as hepatitis and drug use.

**Diagnosis in HIV infected patients with proteinuria**

- 60% have typical features of HIV associated nephropathy on biopsy → FSGS and microcystic tubulointerstitial disease.
- Other common diagnosis

- FSGS alone (additional 10% - 15%)
- MPGN (10%)

- Tubulointerstitial disease (7%)
- Minimal change disease (5%)
- Membranous glomerulopathy (4%)
- Lupus like nephritis (3%)
- Amyloidosis (3%) [ref13]

**(f) Clinical course and Treatment**

The clinical course of HIVAN is rapid progression to ESRD in 6-12 months [ref4] with limited treatment options which include

- Anti retroviral therapy (ART) [ref14].
- Steroid treatment
- ACE inhibitors (ACE-Is) [ref15].

(i) **ART**: Because of the possible direct role HIV in the pathogenesis of HIVAN, ART would be expected to have beneficial effects. There have been case reports of dramatic improvements in renal function with initiation of combination ART but no prospective studies have shown a benefit in the course of HIVAN. Retrospective studies and case reports suggest that monotherapy with zidovudin may slow or even reverse the rapid deterioration associated with HIVAN . The AIDS Clinical Trials Group

(ACTG) is currently developing a clinical trial to compare treatment with an angiotensin receptor blocker (Valsartan) plus ART to ART alone in patients with HIVAN.

(ii) **Steroid Treatment**: There is 20 to 40% response rate of corticosteroids. Prednisolone 60mg/day for 2 to 11 wks leads to a significant reduction in serum creatinine and 24-hours urine protein excretion (due to reversal of interstitial inflammation) and 80% reduction in risk of progressive azotemia [ref1].

(iii) **ACE – inhibitors:** (Captopril and Fosinopril) Angiotensin II increases the cellular synthesis of transforming growth factor – beta (TGF-Beta) which has been implicated in the pathogenesis of HIVAN; ACE – inhibitors are effective in slowing the progression of renal insufficiency by reducing production of TGF-Beta in both humans and HIV-transgenic mice. Studies suggest that ACE-Is initiated early may offer renal survival benefits in HIVAN .

**(g) Current recommendations for treatment of HIVAN:**

Renal biopsy should be offered to patients as the treatment implications and prognosis vary according to the biopsy results.

**Risk factors** for progressive renal disease include

- $CD_4$ count <200 cells /μl [ref16].
- Detectable HIV RNA level
- Hypertension
- Low albuminemia
- Elevated serum creatinine

Combination ART should be initiated early in these patients. Because serum viral loads do not necessarily reflect the severity or rate of progression of HIVAN .The degree of renal insufficiency should influence the choice and dose of individual antiretroviral agents.

ACE-Is should certainly be the antihypertensive drug of choice in HIV infected patients with renal disease and hypertension, and should be considered in normotensive HIV infected patients with renal disease.

The role of corticosteroid treatment remains controversial, but may be considered in patients with HIVAN and early HIV disease whose renal failure is progressing rapidly.

**(B) Other Renal Lesions**

HIVAN is rare in non-African Americans. HIV associated immune mediated renal disease is the most common glomerular disease found on renal biopsy in series reported from Italy and France .

The patterns of glomerular involvement seen in these patients include,

- IgA nephropathy
- Membranous nephropathy
- Membrane proliferative GN
- Mesangial proliferative GN
- Diffuse proliferative GN
- Crescentric GN

Immune complex deposition in glomeruli leads to a proliferative glomerulonephritis and renal insufficiency.

The important forms of immune complex GN in HIV infection are

- IgA nephropathy
- Hepatitis – C Virus (HCV) related renal disease

HIV has been implicated as a stimulus for immune complex formation in IgA nephropathy; immune complexes with HIV antigen have been identified in the circulation and renal tissue eluates of HIV infected patients with IgA nephropathy and with other immune complex GN .

HIV – associated immune mediated renal disease usually presents with

- Mild to no renal insufficiency
- Low grade proteinuria and hematuria
- Patients rarely progress to ESRD

The exception is HCV – cryoglobulinemic GN.

HCV infection is almost universal in HIV patients with a H/o IVDU

HCV associated cryoglobulinemic GN presents with

- Nephrotic syndrome (Membrano proliferative GN)
- Hypertension
- Purpura
- Arthralgias
- Peripheral neuropathy

- Depressed complements levels
- Circulating cryoglobulins
- Rapidly progressive renal insufficiency
- respond to treatment with interferon - α

The association of membranous nephropathy in HIV-infected patients may be explained by the high incidence of HBV infection, malignancies and syphilis in this population .

Other renal diseases reported less commonly include

- Minimal change disease
- Amyloidosis
- Hemolytic urenic syndrome
- Tumour invasion of the kidneys

**(C) End-Stage Renal Disease (ESRD)**

HIVAN has become the third leading cause of ESRD among African Americans aged 20-64 yrs .[ref4].

Management options for these patients include

- Hemodialysis

- Peritoneal dialysis

- Transplantation

Each modality has advantages and disadvantages.

(i) **Improved survival of the HIV positive ESRD patient:** In HIV infected population, ART has led to dramatic improvements in survival. However, the improvement in survival seems to be attenuated in HIV patients with ESRD .

(ii) HIV infected patients dialysed at San Francisco General Hospital,[ref17].

| **$CD_4$ counts** | **Survival** |
|---|---|
| > 200 cells /μl | 33.4 months |
| < 200 cells <μl | 7.7 months |

Currently there is no reason to withhold renal replacement therapy from patients solely on the basis of HIV infection .

**(ii) Hemodialysis:**

- Most common modality for HIV patients

- Disadvantage includes

o Risk of infections from temporary catheters and grafts

o Risk to dialysis providers of blood and needle stick exposure

**(iii) Infection control in Hemodialysis:**

1. Careful adherence to universal body substance precautions by dialysis providers.

2. Routine infection control precaution and routine cleaning with sodium hypochlorite solution of dialysis equipment and of surfaces that are frequently touched are sufficient.

3. Isolation of HIV infected patients from other dialysis patients are unnecessary and could violate medical confidentiality.

4. Dialysate should be treated as a potentially contaminated body fluid.

The size of the HIV particle is much larger than most dialyzers membrane pore sizes; therefore, the HIV particle most likely does not cross the dialyzer membrane into dialyzate or ultrafiltrate.

**(iv) Peritoneal dialysis:**

Peritoneal dialysate fluid should be handled as a contaminated body fluid .

**Advantages**

- Reduced T-cell activation and cytokine release (Mediators of HIV proliferation) attributed to hemodialysis membrane.
- Enhanced humoral immune function.
- Improved nitrogen balance from glucose absorption.
- Permits larger doses of antiretroviral agents in patients with membrane associated leukopenias.
- Higher average hematocrit
- Lower risk of transmitting HIV infection.

**(v) Medical Management:**

The standard Dialysis Outcome Quality Initiative (DOQI) recommendations should be followed for HIV-infected patients with ESRD .

- HIV patients with ESRD respond well to erythropoietin therapy.
- HCV coinfection is very common in HIV infected ESRD patient. HIV/HCV coinfected patients should be discouraged from alcohol use and should be vaccinated for Hepatitis A and B

# AIMS AND OBJECTIVES

**TO DETERMINE THE RENAL FUNCTION ABNORMALITIES IN PATIENTS WITH HIV INFECTION / AIDS**

# MATERIALS AND METHODS

**Setting:** All HIV patients who were attending ART centre and patients admitted in STD ward,GRH,Madurai.

**Collaborating Departments :** Anti retroviral therapy centre

Department of STD

Madurai Medical College

Madurai.

**Design of the study** :Cross sectional study

**Period of study** :01.05.2008 – 31.10.2008.

**Sample size** **:145**

**Ethical committee approval** : obtained

**Consent** :Informed consent was obtained

**Financial support** : Nil

**Selection and Details of Study Subjects**

145 HIV patients who were attending ART centre and Dept of STD Govt. Rajaji Hospital during the period from 01.05.2008. to 31.10.2008 were included in study .

**Inclusion criteria**

All HIV patients attending ART centre and HIV positive patients admitted as inpatients in Dept. of STD were taken for study.

**Exclusion Criteria**

1. Patients with pre-existing hypertension , diabetes mellitus , chronic kidney disease , chornic liver disease , coronary artery disease and on nephrotoxic drugs were excluded from the study .
2. Conditions that likely to produce *Proteinuria* like acute febrile illness, pneumonia were exculed from the study.
3. Only Adult patients were included and patients with age < 12 years excludedfromstudy.

   The total number of cases screened were 250 of which 105 cases were excluded from the study. After exclusion of these patients, the total number of patients who were taken up for study was 145.

145 patients were grouped into patients with elevated renal parameters (Sr.Creatinine >1.5 mg/dL) and without elevated renalparameters.

All the patients in the study were not on Anti retrovival therapy or any other medications for Tuberculosis.

Most patients were on Prophylactic therapy with cotrimoxazole for pneumocystis jirovecii pneumonia prophylaxis and on Tab.Fluconazole for oral candidiasis.

These patients were investigated with Blood samples for Blood Urea, Sr.Creatinine , Serum electrolytes, Urine for spot PCR and 24 hrs urinary protein excretion and ultrasonography of abdomen for kindney size and for other abdominal organ pathology.

The collected data was analysed using epidemiological information package 2002[EPI 2002] developed by centre for Disease control (CDC) Atlanta in colloboration with WHO. Chi square test was used for test of significance. The data was compared with previous literatures.

## RESULTS AND OBSERVATIONS

### A: PROFILE OF CASES STUDIED

**Table 1 : Age Distribution**

| Age Group | RF cases | | Non RF cases | |
|---|---|---|---|---|
| | No | % | No | % |
| < 20 years | 1 | 2.2 | 1 | 1 |
| 21-30 | 11 | 24.4 | 29 | 29 |
| 31-40 | 25 | 55.6 | 50 | 50 |
| 41-50 | 6 | 13.3 | 14 | 14 |
| Above 50 | 2 | 4.4 | 6 | 6 |
| Total | 45 | 100 | 100 | 100 |
| Mean | 35.7 | | 34.9 | |
| SD | 8.3 | | 8.7 | |
| 'p' | 0.4512 Not Significant | | | |

In our study 145 patients were analysed, who were grouped into patients with HIV infection/AIDS

with elevated renal parameters (serum creatinine > 1.5mg/dl) and

without elevation of serum creatinine (<1.5mg/dl).

Analysing the above table,

Out of 145 patients

2.4% of patients belong to less than 20 yrs of age,

28% belong to 21-30 yrs,

52% belong to 31-40 yrs,

14% belong to 41-50 yrs, .3.6% belong to more than 50 yrs.

The mean age distribution was 35.3. with insignificant ‘p’ value.

**Table 2 : Sex Distribution**

| **Sex** | **RF cases** | | **Non RF cases** | |
|---|---|---|---|---|
| | **No** | **%** | **No** | **%** |
| Male | 33 | 73.3 | 61 | 61 |
| Female | 12 | 26.7 | 39 | 39 |
| Total | 45 | 100 | 100 | 100 |
| ‘p’ | 0.219 Not Significant | | | |

In our study 64.8% were males and 35.2%were females with insignificant ‘p’ value.

**Table 3 : Quantitative Parameter**

| Variable | RF cases | | Non RF cases | | 'P' | Significant |
|---|---|---|---|---|---|---|
| | **Mean** | **SD** | **Mean** | **SD** | | |
| Urine Spot PCR | 2.18 | 0.75 | 1.3 | 0.64 | **0.0001** | **Significant** |
| Creatinine Clearance | 19.9 | 9.11 | 98.2 | 9.29 | **0.0001** | **Significant** |
| 24 hours Urinary Protein | 1.93 | 1.03 | 0.3 | 0.32 | **0.0001** | **Significant** |
| Serum Na | 125.4 | 6.5 | 138.9 | 5.6 | **0.0001** | **Significant** |
| Serum K | 5.16 | 0.67 | 4.12 | 0.53 | **0.0001** | **Significant** |
| CD4 Count | 132.4 | 99.3 | 396.5 | 172.4 | **0.0001** | **Significant** |

The mean urine spot PCR,24 hrs urine protein excretion was elevated in renal failure group compared to non renal failure group with significant 'p' value.

There was hyponatremia and hyperkalemia in renal failure group compared with non renal failure group with significant 'p' value.

The mean CD4 count was <150 in renal failure group and The mean CD4 count was <400 in non renal failure group.

## Table 4 : Quantitative Parameter

| Variable | RF cases | | Non RF cases | | 'p' | Significance |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| **Urine Spot PCR** | | | | | | |
| Normal(.2) | 0 | 0 | 0 | 0 | | |
| Abnormal (>.2-3) | 41 | 45.6 | 100 | 100 | **0.0001** | **Significant** |
| Nephrotic range (>3) | 4 | 8.9 | - | - | | |
| **Creatinine Clearance(ml/min)** | | | | | | |
| Stage0-- >90 | - | - | 93 | 93 | | |
| stageII 60-89 | - | - | 7 | 7 | | |
| stageIII 30-59 | 6 | 13.3 | - | - | **0.0001** | **Significant** |
| stageIV15-29 | 25 | 55.6 | - | - | | |
| stageV< 15 | 14 | 31.1 | - | - | | |
| **24 Hour Urinary Protein(gms/day)** | | | | | | |
| <= 0.15 | - | - | 64 | 64 | | |
| 0.16-1 | 10 | 22.2 | 36 | 36 | **0.0001** | **Significant** |
| 1-3.5 | 31 | 42.2 | - | - | | |
| >=3.5 | 4 | 35.6 | - | - | | |
| **Sodium** | | | | | | |
| Normal | 3 | 93.3 | 28 | 28 | **0.0001** | **Significant** |
| Hypo | 42 | 6.7 | 59 | 59 | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Potassium** | | | | | | |
| Normal | 19 | 2.2 | 100 | 17 | **0.0001** | **Significant** |
| Hyper | 26 | 57.8 | - | - | | |
| **USG Abdomen** | | | | | | |
| Normal Study | - | - | 67 | 67 | **0.0001** | **Significant** |
| Bil. Renomegaly | 45 | 100 | 33 | 33 | | |

**Analysing the tables**

24 hrs urine protein excretion in renal failure group—10 pts had <1gm/day

31pts had>1-<3.5gm/day

4 pts in nephrotic range.

In non renal failure group -- normal protein excretion in 64 pts

Protein excretion<1gm/day in 36pts

With significant 'p' value between two groups.

Creatinine clearance – in RF group – stage III (30-59) in 6 pts

Stage IV (15-29) in 25 pts

Stage V (<15) in 14 pts

In non-RF group—normal (>90) in 93 pts

Stage II(60-89) in 7 pts

Significant hyponatremia and hyperkalemia seen in RF group compared to non-RF group with significant "p" value.

Bil.renomegaly present in all cases of RF group and 33 pts in non-RF group with significant "p" .

**Table 5 : Creatinine Clearance Stage and CD4 Count**

| Creatinine Clearance(ml/mt) Stage(ml/mt) | CD4 Count | |
|---|---|---|
| | **Mean** | **SD** |
| >90 | 402.8 | 176.5 |
| 60-89 | 312 | 61.3 |
| 30-59 | 116.5 | 30.9 |
| 15-29 | 147.3 | 116.9 |
| <15 | 112.7 | 82.7 |
| **'p'** | **0.0001**<br>**Significant** | |

The mean CD4 count in pts with stage III(30-59)—stage V(<15) --<150 cells. Showing increased risk for renal failure in HIV pts with reduction in CD4 count.

**Table 6: 24 Hours Urinary Protein and CD4**

| **24 Hours Urinary Protein (gms/day)** | **CD4 Count** | |
|---|---|---|
| | **Mean** | **SD** |
| < 0.15 | 396.3 | 162.6 |
| 0.16-1 | 366.7 | 189.2 |
| >1-<3.5 | 125.4 | 20.3 |
| >=3.5 | 62.2 | 19.5 |
| **'p'** | **0.0001 Significant** | |

This table shows increased proteinuria with decreased CD4 count

## DISCUSSION AND COMPARATIVE ANALYSIS

In our study 145HIV seropositive patients were analysed for renal function abnormalities and compared with the available literature. The age incidence showed a median age of 35.3 yrs. 2.4% of patients belong to less than 20 yrs, 28% belong to 21-30 yrs, 52% belong to 31-40 yrs, 14% belong to 41-50 yrs, 3.6% belong to more than 50 yrs.

The age wise prevalence in India(AIDS AND HIV INFORMATION AVERT.org) 4% in less than 20 yrs, 24% belong to 21-30 yrs, 35% belong to 31-40 yrs, 27% belong to 41-50 yrs, 15% belong to more than 50 yrs. HIV prevalence in India is 3.6%. the prevalence for adult female is 0.29% and for males 0.43%

In our study 64.8% were males and 35.2% were females with insignificant ‘p’ value. In our study, both renal failure group and non renal failure group had proteinuria with mean spot PCR of 2.18 for RF group and a mean of 1.3 for Non-RF group with significant ‘p’ value.

24 hours urine protein excretion had a mean of 1.93gm/day for RF group 0.3gm/day for Non-RF pts.with significant increase of proteinuria in pts. With renal failure.

- Nearly 100% pts. in RF group had increased proteinuria and 36% of pts in non-RF group had proteinuria.
- The overall (RF& Non-RF) percentage of pts with proteinuria was 55.86% with 31.7% pts with less than 1gm/day.
- No pts in Non-RF group had proteinuria more than 1 gm/dayor nephrotic range (>=3.5 gm/day).
- In RF group 21.4% had proteinuria >1gm/d-<3.5 gm/d. 0.09% had nephrotic range proteinuria.
- Proteinuria was increased in RF group in comparision to non-RF group with significant ‘p’ value.
- Patients with normal24 Hrs. proteinuria had a mean CD4 cell count of 396.3 cell/micL.
- Pateints with proteinuria less than 1gm/day had mean CD4 count of 366.7 cells/micL.
- Patients with more than 1gm/day and less than 3.5 gm/day had mean CD4 of 125.4 and pts. with nephrotic range had 62.2 cells/micL.
- In Sczezch et al study,32% had proteinuria. The predictors of proteinuria in his study was

- Absolute CD4 count <= 200cells/micL. and high HIV RNA level. This study establishes association between decreasing CD4 count and high HIV RNA levelwith the presence of proteinuria and occurrence of renal failure.

Han et al reported 24% of HIV pts with persistent microalbuminuria were proved to be having HIVAN by renal biopsy. Renal biopsy may be considered in HIV patients with persistent microalbuminuria with low CD4 count irrespective of good renal function.

In our study nephrotic range proteinuria was seen in 4 patients ( 0.09%) of RF group.All these pts. Had high serum creatinine value (mean 4.4mg/dL) and low CD4 count (mean- 45 cells/micL) with mean serum creatinine clearance of 12.84 mL/min showing association between increasing proteinuria with low CD4 count ,high serum creatinine and reduced creatinine clearance consistent with above study.

Alma et al conducted a study to document the histopathologic diagnosis in HIV pts with and without nephrotic range range proteinuria and to evaluate the predictive value of both nephrotic range proteinuria and CD4 count in diagnosing HIVAN.

In his study 53% of biopsy proven HIVAN had nephrotic range proteinuria . the patients with HIVAN had significantly higher serum creatinine (8.2 mg/dL)and lower CD4 count (158cells/micL ) at the time of biopsy.

Shri Ganesh R Barnela et al, study with 102 pts renal dysfunction in 39.21%. 19.6% had proteinuria of which 8.82% had nephrotic range proteinuria , HIVAN in 5.8%.

In our study,hyponatremia was seen in 93% of pts in RF group and 59% of pts in non-RF group. Overall 69.6% pts had hyponatremia .The mean serum sodium in RF group was 125.4 and in non-RF group was 138.9 with significant ‘p’ value.

In our study, hyperkalemia was present in 55% of RF group. No pts in non-RF had hyperkalemia.The mean serum potassium in RF group is 5.16 and in non-RF 4.12 Both hyponatremia and hyperkalemia occur commonly due to vomiting or diarrhoea. May also be manifestation of mineralocorticoid deficiency resulting from adrenal insufficiency or the syndrome of hyporeninemic hypoaldosteronism.

Perazalla MA, Wright FS et al described hyperkalemia in patients on Trimethoprim/sulfamethoxazole Prophylaxis . Trimethoprim may act like amiloride and blocks apical membrane sodium channels in the distal nephron.

Decreased potassium excretion leads to hyperkalemia in substantial number of patients treated with trimethoprim containing drugs.

In our study creatinine clearance had a mean of 19.9mL/min in RF group and 98.2mL/min in non-RF group.

The analysis between 24 hours urine protein ,serum creatinine , creatinine clearance and CD4 count showed a correlation of increased proteinuria with high serum creatinine , low CD4 count and reduced creatinine clearance. Mocroft A, Kirk et al showed 3.5% with end stage renal diseasehad lower CD4 cell count (median-80 vs 137 cells/micL).

In our study CD4 count in pts in

stage III CKD—116.5 cells

Stage IV CKD—147.3 cells

Stage V CKD—112.7 cells

All patients in RF group were in stage III to stage V with mean CD4 count of 125.5 showing clearly the risk of progressive renal failure with lower CD4 count.

In Non-RF group , the creatinine clearance was stage 0(>90ml/min)—stage II (60-89ml/min) with mean CD4 count in stage 0-402.8cells/micL

stage II-312cells/micL showing decreased creatinine clearance with lower CD4 count .

In our study, ultrasound abdomen showed bilateral enlarged kidneys in all (100%) patients with renal failure and 33% of non-renal failure group. Overall percentage of patients with bilateral enlarged kidneys was 53.8%.

Di Forti et al study showed 20% of HIV associated nephropathy patients with bilateral enlarged kidneys and 38% with decreased cortico medullary differentiation. In his study increased echogenicity and a heterogenous echopattern were the most common finding seen in 75% of cases. Globular morphology and loss of renal sinus fat in about half of patients.

# CONCLUSION

1. The presence of proteinuria in our study group was 55.86%

2. Patients with high proteinuria had high serum creatinine values and low CD4 (< 150 cells) count and reduced creatinine clearance.

3. Nephrotic range proteinuria was present in 0.09% of HIV seropositive patients with CD4 count =< 50 cells/micL.

4. Bilaterally enlarged kidneys were present in 53.8% of patients with increased proteinuria.

Limitations:

In our study only small number of patients (145) were involved and since it was a cross sectional study , the causal relatioship could not be identified using a cross sectional analysis.

Renal biopsy could not be done because of ethical problems.

# SUMMARY

The study " **A STUDY OF RENAL FUNCTION ABNORMALITIES IN PATIENTS WITH HIV INFECTION/ AIDS"** was done in 145 patients who were attending the Antiretroviral Therapy centre and patients who were admitted as inpatients in Department of STD, Govt. Rajaji Hospital, Madurai. Selected patients were divided in to two groups , patients with Renal failure (sr.creatinine>1.5mg/dl) and without Renal failure (<1.5mg/dl).

Selected patients were subjected to urine analysis for proteinuria with urine for spot PCR, 24 hours urine protein excretion. Blood investigations for blood urea,serum creatinine, serum electrolytes and ultrasound abdomen for kidney size.Out of 145 patients, 2.4% belong toless than 20 yrs, 28% belong to 21-30 yrs,52% belong to 31-40 yrs,14% belong to 41-50yrs and 3.6% belong to above 50 yrs.

In our study 64.8% were males and 35.2% were females.Proteinuria was present in 55.86% of patients with 31.7% with less than 1gm/day.21.4% of patients had proteinuria more than 1gm/day but less than 3.5 gm/day 0.09% had nephrotic range proteinuria.

No patients in Non renal failure group had proteinuria more than 1gm/day or nephrotic range proteinuria .CD4 cell count in patients with normal 24 hours protein excretion showed mean CD4 cell count of 396.3 cells.Patients with less than 1gm/day of proteinuria had a mean of 366.7 cells.Patients with more than 1gm/day and less than 3.5 gm/day had a mean of125.4 cells.

Patients with nephrotic range proteinuria had mean CD4 count of 62.2 cells.The above data analysis shows significant relationship between high proteinuria and low CD4 count.

In our study analysis of proteinuria, serum creatinine, creatinine clearance and CD4 cell count showed increased proteinuria with high serum creatinine , low CD4 count and decreased creatinine clearance. Ultrasound abdomen showed bilaterally enlarged in patients with high proteinuria .53.8% of patients in our study showed bilaterally enlarged kidneys.

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# GLOSSARY

| | |
|---|---|
| ADH | -Anti Diuretic Hormone |
| AER | -Albumin Excretion Rate |
| AIDS | -Acquired Immunodeficiency Syndrome |
| ARF | -Acute Renal Failure |
| ART | -Antiretroviral Therapy |
| ATN | -Acute Tubular Necrosis |
| CDC | -Centre For Disease Control |
| DNA | -Deoxy RiboNucleic Acid |
| ECF | -Extra Cellular Fluid |
| ELISA | -Enzyme Linked Immunosorbent Assay |
| ESRD | -End Stage Renal Disease |
| GRH | -Government Rajaji Hospital |
| HIV | -Human Immunodeficiency Virus |
| HIVAN | -Human Immunodeficiency Virus Associated Nephropathy |
| IDU | -Injection Drug Users |
| KS | -Kaposi's Sarcoma |
| MPGN | -Membrano Proliferative Nephropathy |
| NSAIDS | -Non Steroidal Anti Inflammatory Agents |
| RF | -Renal Failure |
| RNA | -RiboNucleic Acid |
| SIADH | -Syndrome of Inappropriate Anti Diuretic Hormone Secretion |
| Spot PCR | -Spot Protein Creatinine Ratio |
| Tg26 | -Transgenic Mice |
| TRI | -Tubulo Reticular Inclusions |
| UNAIDS | -Joint United Nations Programme on HIV/ AIDS |

# PROFORMA

Sl.No :

Name :

Age / Sex : IP. No :

Address :

Socioeconomic Status :

Disease Status - HIV-1 / HIV -2 / AIDS

CD4 count - CD4 % :

Height: Weight:

Blood Pressure -

CLINICAL DETAILS:

INVESTIGATIONS:

Urine - Spot Protein / Creatinine Ratio:

Urine - Albumin: Sugar : Deposit:

24 Hrs. Urine protein:

Blood - Sugar: Urea:

**Sr. Creatinine** -

Sr. Electrolytes – Na :

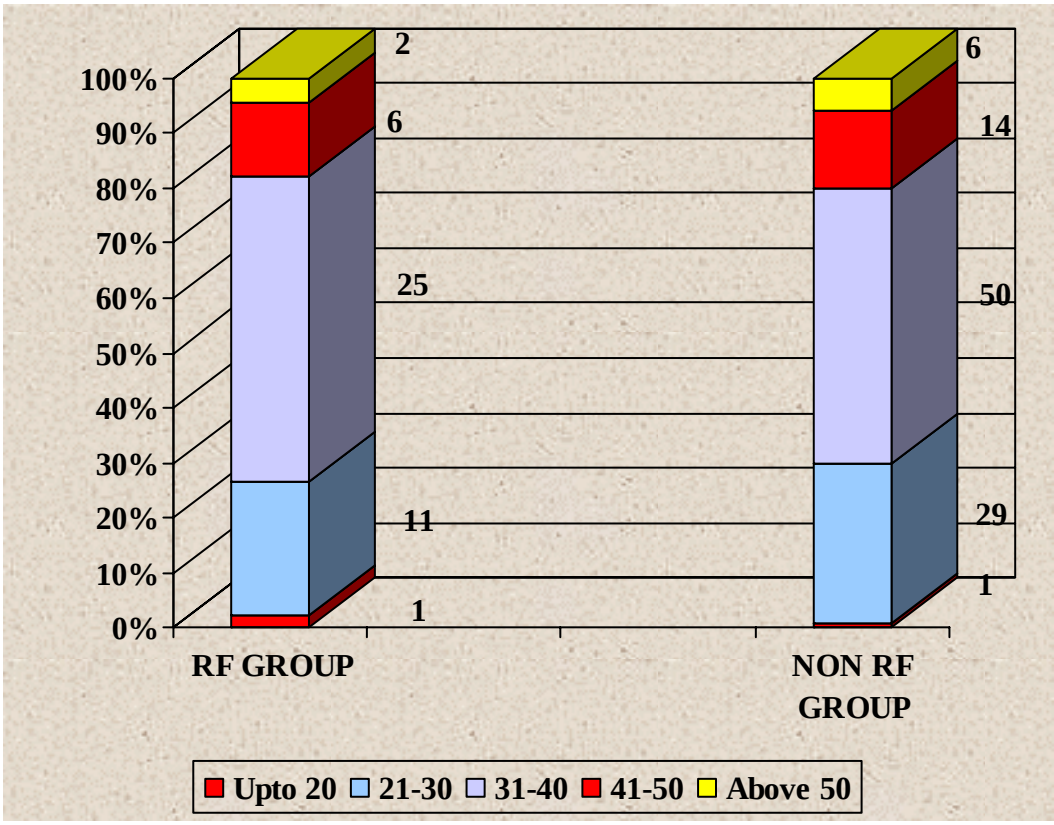
K :

HCO3 :

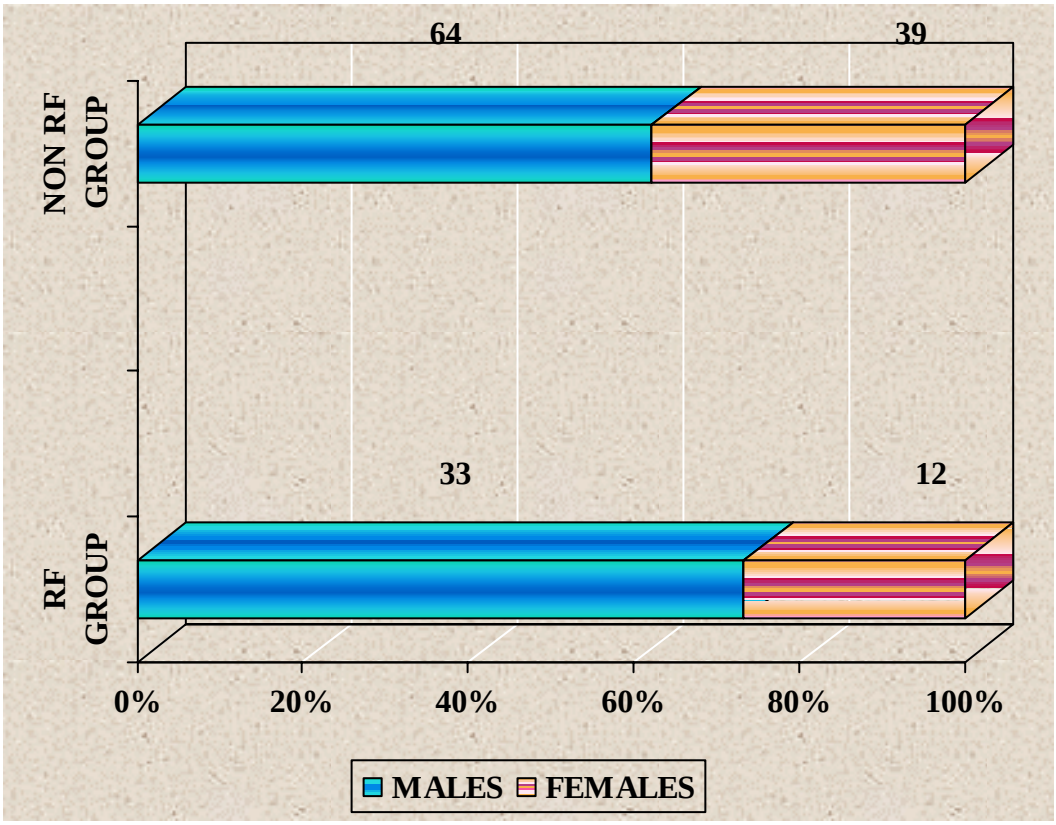
Cl :

USG. Abdomen & Pelvis :

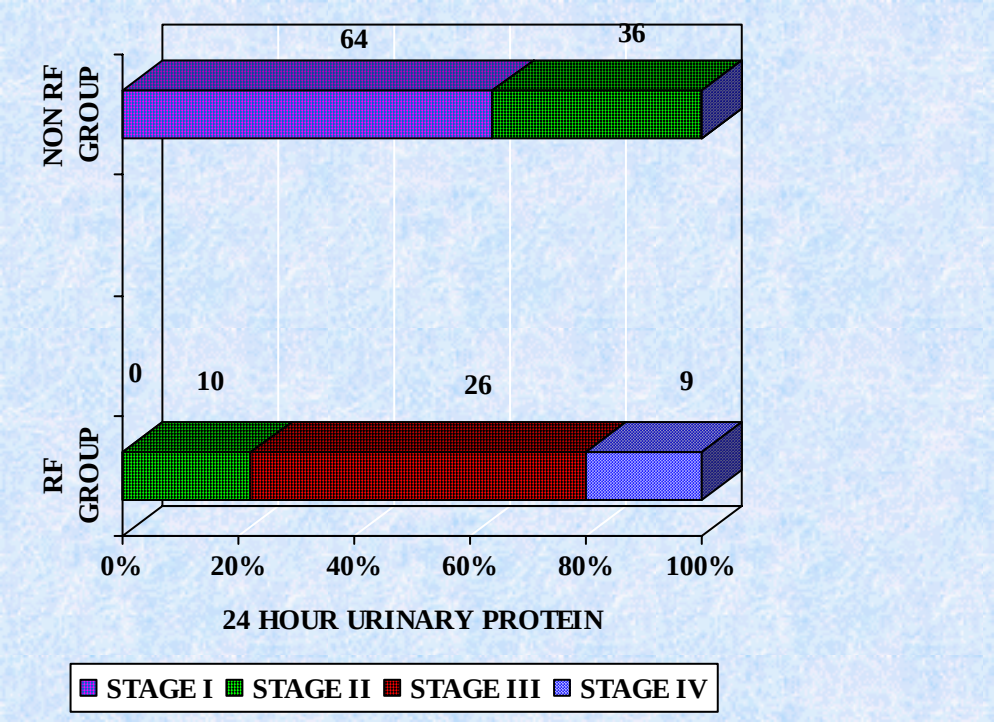
# AGE DISTRIBUTION



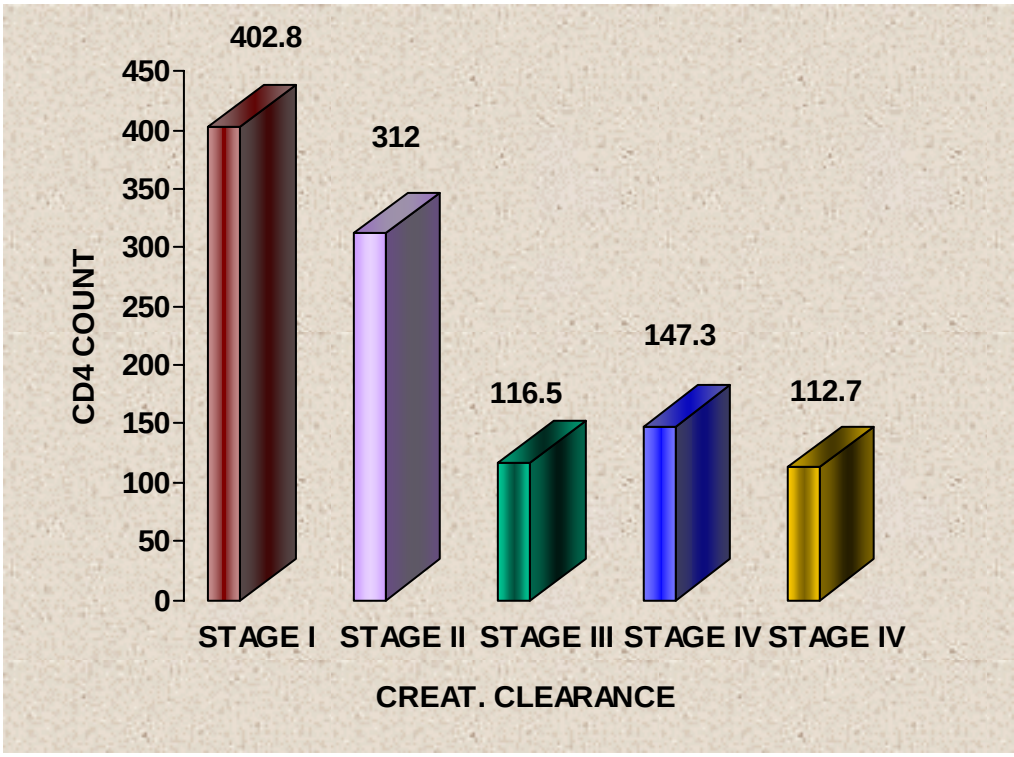
# SEX DISTRIBUTION



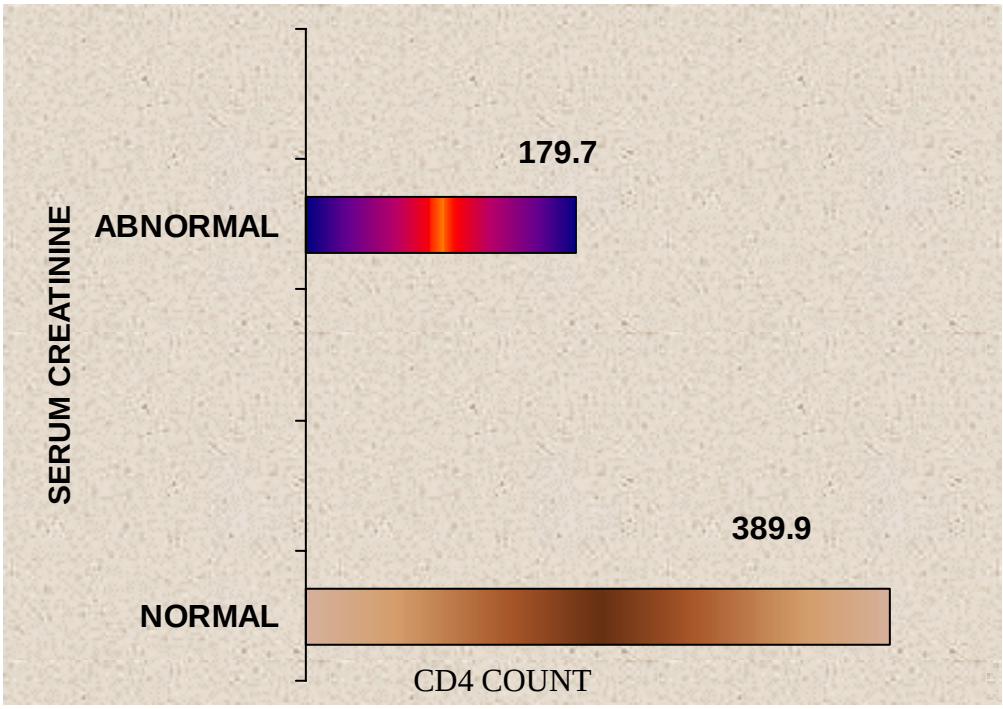
# 24 HOUR URINARY PROTEIN



# CREATININE CLEARANCE STAGE & CD4 COUNT



# SERUM CREATININE & CD4 COUNT




**The above graph shows lower CD4 COUNT (<200 cells) in patient with renal failure**

| HIV PT. WITHOUT RENAL FAILURE | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Serum | | | | |
| S.No. | Age | Sex | urine spot PCR | Urine Alb. Sug. Dep/HPF | Creatinine clearance (ml/min) | Urinary protein 24 hrs (gms) | Bl.Urea | S.Creatinine | Na | K | $HCO_3$ | Cl | USG Abd. |
| 1 | 40 | M | 0.3 | Alb(+)<br>N<br>N | 95.5 | 0.032 | 32 | 0.8 | 135 | 4.3 | 23 | 110 | Normal study |
| 2 | 35 | F | 0.5 | Alb(+)<br>N<br>N | 94 | 0.035 | 28 | 0.8 | 140 | 3.6 | 18 | 102 | Normal study |
| 3 | 32 | M | 0.45 | Alb(+)<br>N<br>N | 112.5 | 0.135 | 36 | 0.9 | 138 | 4.2 | 20 | 106 | Normal study |
| 4 | 33 | M | 0.8 | Alb(+)<br>N<br>N | 91.5 | 0.045 | 40 | 1 | 142 | 4.8 | 22 | 110 | Normal study |
| 5 | 24 | F | 2.5 | Alb(++)<br>N<br>N | 93.5 | 0.850 | 35 | 0.7 | 128 | 5 | 17 | 104 | Bil.renomegaly |
| 6 | 27 | M | 2.2 | Alb(++)<br>N<br>N | 110 | 0.950 | 38 | 1 | 130 | 4.5 | 22 | 115 | Bil.renomegaly ,<br>Ascites,<br>Bil.pleural effusion |
| 7 | 32 | M | 0.55 | Alb(+)<br>N<br>N | 112.5 | 0.038 | 40 | 0.8 | 139 | 4.4 | 19 | 98 | Normal study |
| 8 | 40 | M | 0.9 | Alb(+)<br>N<br>N | 98.5 | 0.082 | 26 | 0.8 | 142 | 4.9 | 20 | 102 | Normal study |
| 9 | 32 | M | 2 | Alb(++)<br>N<br>N | 101.5 | 0.750 | 32 | 0.9 | 132 | 5 | 17 | 110 | Bil.renomegaly |
| 10 | 24 | F | 0.28 | Alb(+)<br>N<br>N | 99 | 0.080 | 29 | 0.8 | 137 | 3.9 | 21 | 105 | Normal study |
| 11 | 33 | M | 0.3 | Alb(-)<br>N<br>N | 98.5 | 0.075 | 33 | 0.9 | 147 | 4.7 | 20 | 100 | Normal study |
| 12 | 22 | F | 0.85 | Alb(-)<br>N<br>N | 100.5 | 0.035 | 38 | 0.8 | 138 | 3.9 | 22 | 96 | Normal study |
| 13 | 27 | F | 0.35 | Alb(-)<br>N<br>N | 97.5 | 0.055 | 35 | 0.9 | 146 | 3.8 | 19 | 112 | Normal study |
| 14 | 32 | M | 0.5 | Alb(-)<br>N<br>N | 98 | 0.075 | 30 | 0.7 | 138 | 4.3 | 18 | 106 | Normal study |
| 15 | 33 | M | 0.45 | Alb(-)<br>N<br>N | 94.5 | 0.065 | 31 | 0.9 | 135 | 3.4 | 20 | 95 | Normal study |
| 16 | 60 | F | 2.75 | Alb(++)<br>N<br>N | 97.5 | 0.850 | 33 | 0.8 | 125 | 4.5 | 22 | 99 | Bil.renomegaly |
| 17 | 42 | F | 0.35 | Alb(+)<br>N<br>N | 93.5 | 0.086 | 24 | 0.8 | 143 | 5 | 21 | 104 | Normal study |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 18 | 30 | F | 2 | Alb(++)<br>N<br>N | 91.5 | 0.900 | 36 | 0.9 | 138 | 4 | 17 | 110 | Bil.renomegaly |
| 19 | 43 | M | 1.2 | Alb(+)<br>N<br>N | 98.5 | 0.015 | 34 | 0.7 | 136 | 3.3 | 18 | 94 | Normal study |
| 20 | 31 | F | 2.5 | Alb(++)<br>N<br>N | 105.5 | 0.875 | 28 | 1 | 137 | 4.6 | 24 | 97 | Bil.renomegaly ,<br>Ascites,<br>Bil.pleural effusion |
| 21 | 35 | M | 1.8 | Alb(++)<br>N<br>N | 98.5 | 0.950 | 32 | 0.9 | 130 | 4.2 | 23 | 106 | Bil.renomegaly |
| 22 | 38 | M | 0.3 | Alb(+)<br>N<br>N | 103.3 | 0.085 | 38 | 0.8 | 143 | 3.4 | 21 | 108 | Normal study |
| 23 | 52 | M | 1.9 | Alb(++)<br>N<br>N | 109 | 0.500 | 40 | 0.8 | 141 | 4.4 | 19 | 112 | Bil.renomegaly |
| 24 | 40 | F | 1.75 | Alb(++)<br>N<br>N | 105 | 0.750 | 33 | 0.8 | 137 | 4.7 | 20 | 114 | Bil.renomegaly |
| 25 | 35 | M | 1.1 | Alb(+)<br>N<br>N | 90.5 | 0.080 | 36 | 1 | 149 | 3.9 | 18 | 103 | Normal study |
| 26 | 40 | F | 1.2 | Alb(-)<br>N<br>N | 92 | 0.090 | 39 | 1 | 140 | 3.4 | 24 | 109 | Normal study |
| 27 | 55 | M | 0.3 | Alb(-)<br>N<br>N | 91 | 0.018 | 30 | 0.8 | 139 | 3.8 | 21 | 116 | Normal study |
| 28 | 33 | M | 1.2 | Alb(-)<br>N<br>N | 100.3 | 0.090 | 27 | 0.8 | 135 | 3.5 | 19 | 103 | Normal study |
| 29 | 36 | M | 0.8 | Alb(-)<br>N<br>N | 112 | 0.150 | 29 | 1 | 143 | 4.6 | 17 | 100 | Normal study |
| 30 | 35 | F | 0.5 | Alb(-)<br>N<br>N | 107 | 0.038 | 34 | 0.9 | 146 | 4 | 22 | 105 | Normal study |
| 31 | 40 | M | 1.5 | Alb(+)<br>N<br>N | 98 | 0.050 | 38 | 0.9 | 145 | 3.8 | 20 | 109 | Normal study |
| 32 | 30 | F | 1.25 | Alb(++)<br>N<br>N | 113 | 0.360 | 40 | 1 | 141 | 4.9 | 17 | 113 | Bil.renomegaly |
| 33 | 21 | F | 1.8 | Alb(-)<br>N<br>N | 112 | 0.030 | 37 | 0.8 | 139 | 3.7 | 22 | 104 | Normal study |
| 34 | 40 | M | 0.9 | Alb(+)<br>N<br>N | 97 | 0.080 | 40 | 1 | 140 | 4.8 | 18 | 112 | Normal study |
| 35 | 25 | M | 1.2 | Alb(-)<br>N<br>N | 109 | 0.015 | 36 | 1 | 146 | 4.5 | 23 | 109 | Normal study |
| 36 | 26 | F | 1.75 | Alb(++)<br>N<br>N | 105 | 0.450 | 35 | 0.9 | 133 | 4.5 | 21 | 96 | Bil.renomegaly |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 37 | 36 | F | 0.8 | Alb(+)<br>N<br>N | 93 | 0.150 | 33 | 0.9 | 147 | 3.2 | 19 | 100 | Normal study |
| 38 | 35 | F | 1.5 | Alb(++)<br>N<br>N | 95 | 0.950 | 39 | 0.7 | 136 | 3.7 | 18 | 97 | Bil.renomegaly |
| 39 | 21 | F | 1.8 | Alb(+)<br>N<br>N | 109 | 0.065 | 28 | 0.9 | 144 | 3.5 | 20 | 115 | Normal study |
| 40 | 35 | F | 1.8 | Alb(++)<br>N<br>N | 97 | 0.780 | 32 | 0.7 | 125 | 5 | 24 | 103 | Bil.renomegaly,<br>Ascites,<br>Bil.pleural effusion |
| 41 | 35 | M | 0.9 | Alb(-)<br>N<br>N | 93.3 | 0.098 | 39 | 1 | 140 | 3.3 | 17 | 106 | Normal study |
| 42 | 37 | M | 0.45 | Alb(-)<br>N<br>N | 97.6 | 0.076 | 35 | 0.7 | 138 | 4.1 | 22 | 108 | Normal study |
| 43 | 45 | F | 1.3 | Alb(-)<br>N<br>N | 91.5 | 0.140 | 32 | 0.9 | 135 | 4.7 | 19 | 102 | Normal study |
| 44 | 33 | M | 1.5 | Alb(-)<br>N<br>N | 93.8 | 0.100 | 37 | 0.8 | 133 | 4.9 | 21 | 98 | Normal study |
| 45 | 32 | M | 1.5 | Alb(-)<br>N<br>N | 95.3 | 0.135 | 23 | 0.7 | 145 | 4.5 | 22 | 96 | Normal study |
| 46 | 25 | F | 0.85 | Alb(+)<br>N<br>N | 93.5 | 0.125 | 31 | 0.9 | 135 | 3.6 | 20 | 114 | Normal study |
| 47 | 32 | M | 1 | Alb(+)<br>N<br>N | 98.3 | 0.450 | 29 | 0.9 | 139 | 3.9 | 18 | 105 | Bil.renomegaly |
| 48 | 45 | M | 1.5 | Alb(++)<br>N<br>N | 91.5 | 0.550 | 33 | 0.8 | 138 | 4.2 | 23 | 95 | Normal study |
| 49 | 29 | M | 0.8 | Alb(+)<br>N<br>N | 112.3 | 0.140 | 27 | 0.9 | 136 | 4.2 | 19 | 100 | Normal study |
| 50 | 39 | F | 1.9 | Alb(+)<br>N<br>N | 94.3 | 0.460 | 39 | 0.7 | 139 | 3.6 | 17 | 94 | Bil.renomegaly |
| 51 | 34 | M | 0.76 | Alb(+)<br>N<br>N | 91.4 | 0.145 | 35 | 1 | 145 | 4.7 | 21 | 95 | Normal study |
| 52 | 35 | M | 0.85 | Alb(+)<br>N<br>N | 94.5 | 0.130 | 40 | 0.9 | 140 | 4.3 | 23 | 100 | Normal study |
| 53 | 26 | F | 1.75 | Alb(++)<br>N<br>N | 105.3 | 0.550 | 39 | 0.8 | 134 | 4 | 19 | 110 | Bil.renomegaly |
| 54 | 25 | M | 1.8 | Alb(++)<br>N<br>N | 110.4 | 0.600 | 33 | 0.7 | 125 | 4.8 | 20 | 112 | Bil.renomegaly |
| 55 | 23 | F | 2.2 | Alb(++)<br>N<br>N | 107 | 0.970 | 27 | 0.8 | 143 | 3.5 | 22 | 114 | Bil.renomegaly |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 56 | 24 | F | 0.9 | Alb(-)<br>N<br>N | 113 | 0.086 | 29 | 1 | 147 | 4.5 | 16 | 104 | Normal study |
| 57 | 25 | M | 1.5 | Alb(-)<br>N<br>N | 112 | 0.090 | 33 | 0.8 | 148 | 3.9 | 22 | 109 | Normal study |
| 58 | 53 | M | 1.2 | Alb(-)<br>N<br>N | 94 | 0.135 | 37 | 0.9 | 145 | 4.2 | 19 | 106 | Normal study |
| 59 | 30 | M | 1.8 | Alb(-)<br>N<br>N | 105 | 0.140 | 30 | 1 | 139 | 3.7 | 18 | 110 | Normal study |
| 60 | 32 | M | 0.3 | Alb(-)<br>N<br>N | 103 | 0.035 | 35 | 1 | 135 | 3.2 | 23 | 98 | Normal study |
| 61 | 25 | M | 0.6 | Alb(+)<br>N<br>N | 110 | 0.050 | 34 | 0.8 | 147 | 3.9 | 21 | 95 | Normal study |
| 62 | 45 | M | 1.75 | Alb(++)<br>N<br>N | 93 | 0.850 | 39 | 0.8 | 142 | 3.6 | 17 | 102 | Bil.renomegaly |
| 63 | 42 | M | 1.5 | Alb(++)<br>N<br>N | 91.3 | 0.650 | 31 | 0.9 | 132 | 4.8 | 20 | 105 | Bil.renomegaly |
| 64 | 27 | F | 1.6 | Alb(+)<br>N<br>N | 103 | 0.075 | 37 | 0.9 | 134 | 5 | 22 | 110 | Normal study |
| 65 | 32 | M | 1.2 | Alb(+)<br>N<br>N | 95 | 0.090 | 40 | 1 | 140 | 3.5 | 21 | 106 | Normal study |
| 66 | 37 | M | 1.5 | Alb(+)<br>N<br>N | 94 | 0.135 | 32 | 0.9 | 142 | 4 | 17 | 112 | Normal study |
| 67 | 41 | M | 0.9 | Alb(+)<br>N<br>N | 92 | 0.145 | 29 | 0.8 | 149 | 3.2 | 22 | 115 | Normal study |
| 68 | 32 | M | 1.5 | Alb(++)<br>N<br>N | 98 | 0.950 | 38 | 0.7 | 146 | 3.9 | 20 | 106 | Bil.renomegaly |
| 69 | 42 | M | 0.85 | Alb(+)<br>N<br>N | 91 | 0.100 | 30 | 0.8 | 145 | 3.6 | 18 | 102 | Normal study |
| 70 | 36 | M | 1.8 | Alb(++)<br>N<br>N | 93 | 0.875 | 39 | 0.8 | 136 | 4.7 | 19 | 115 | Bil.renomegaly |
| 71 | 44 | M | 1.4 | Alb(-)<br>N<br>N | 90.5 | 0.080 | 40 | 0.9 | 129 | 4.5 | 24 | 99 | Normal study |
| 72 | 36 | M | 0.65 | Alb(-)<br>N<br>N | 92 | 0.075 | 29 | 0.7 | 142 | 4.2 | 20 | 107 | Normal study |
| 73 | 25 | F | 1.2 | Alb(-)<br>N<br>N | 98 | 0.095 | 33 | 1 | 135 | 4 | 19 | 110 | Normal study |
| 74 | 35 | M | 1.5 | Alb(-)<br>N<br>N | 91 | 0.090 | 37 | 0.8 | 139 | 3.7 | 21 | 115 | Normal study |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 75 | 30 | F | 0.9 | Alb(-)<br>N<br>N | 110 | 0.085 | 39 | 0.7 | 145 | 3.5 | 22 | 100 | Normal study |
| 76 | 41 | M | 1.5 | Alb(+)<br>N<br>N | 93 | 0.135 | 40 | 0.8 | 138 | 5 | 24 | 102 | Normal study |
| 77 | 65 | M | 1.6 | Alb(+)<br>N<br>N | 66.5 | 0.125 | 30 | 0.9 | 146 | 4.3 | 23 | 108 | Normal study |
| 78 | 50 | F | 1.85 | Alb(++)<br>N<br>N | 91 | 0.775 | 34 | 0.9 | 131 | 3.3 | 18 | 96 | Bil.renomegaly,<br>Ascites,<br>Rt.pleural effusion |
| 79 | 35 | M | 0.5 | Alb(+)<br>N<br>N | 93 | 0.140 | 29 | 0.8 | 139 | 3.7 | 20 | 108 | Normal study |
| 80 | 25 | F | 1.65 | Alb(++)<br>N<br>N | 107 | 0.900 | 31 | 0.7 | 133 | 3.8 | 22 | 110 | Bil.renomegaly |
| 81 | 23 | F | 0.85 | Alb(+)<br>N<br>N | 110 | 0.100 | 35 | 1 | 136 | 3.4 | 19 | 115 | Normal study |
| 82 | 37 | M | 2.5 | Alb(++)<br>N<br>N | 98 | 0.250 | 30 | 0.8 | 144 | 3.9 | 17 | 104 | Bil.renomegaly |
| 83 | 30 | M | 2.3 | Alb(++)<br>N<br>N | 107 | 0.350 | 29 | 0.9 | 138 | 4.1 | 22 | 100 | Bil.renomegaly |
| 84 | 31 | M | 0.8 | Alb(+)<br>N<br>N | 109 | 0.140 | 40 | 0.7 | 136 | 4.5 | 17 | 96 | Normal study |
| 85 | 47 | M | 1.4 | Alb(+)<br>N<br>N | 93 | 0.120 | 39 | 0.8 | 132 | 4.8 | 23 | 105 | Normal study |
| 86 | 28 | M | 1.8 | Alb(-)<br>N<br>N | 99 | 0.080 | 31 | 0.9 | 146 | 4.3 | 21 | 110 | Normal study |
| 87 | 32 | M | 1.3 | Alb(-)<br>N<br>N | 102 | 0.075 | 29 | 0.7 | 141 | 3.9 | 24 | 100 | Normal study |
| 88 | 34 | F | 0.9 | Alb(-)<br>N<br>N | 106 | 0.085 | 37 | 0.8 | 145 | 5 | 19 | 95 | Normal study |
| 89 | 18 | M | 1.2 | Alb(-)<br>N<br>N | 112 | 0.095 | 40 | 0.9 | 140 | 3.8 | 22 | 98 | Normal study |
| 90 | 28 | F | 0.5 | Alb(-)<br>N<br>N | 99 | 0.075 | 29 | 0.7 | 135 | 4.3 | 20 | 110 | Normal study |
| 91 | 38 | M | 1.65 | Alb(++)<br>N<br>N | 87 | 0.750 | 33 | 0.8 | 136 | 4.6 | 19 | 106 | Bil.renomegaly |
| 92 | 38 | M | 2.2 | Alb(+)<br>N<br>N | 85 | 0.325 | 37 | 0.9 | 142 | 3.6 | 18 | 105 | Normal study |
| 93 | 31 | M | 2.5 | Alb(++)<br>N<br>N | 89 | 0.450 | 27 | 0.8 | 144 | 3.6 | 20 | 110 | Bil.renomegaly |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 94 | 41 | M | 2.8 | Alb(++)<br>N<br>N | 85 | 0.550 | 31 | 0.7 | 128 | 4.8 | 18 | 102 | Bil.renomegaly |
| 95 | 40 | F | 2 | Alb(++)<br>N<br>N | 90 | 0.850 | 29 | 0.9 | 130 | 4.2 | 22 | 108 | Bil.renomegaly,<br>Ascites,<br>Bil.pleural effusion |
| 96 | 39 | F | 2.3 | Alb(++)<br>N<br>N | 95 | 0.755 | 38 | 1 | 135 | 3.8 | 20 | 97 | Bil.renomegaly |
| 97 | 42 | F | 0.9 | Alb(+)<br>N<br>N | 93 | 0.100 | 33 | 0.8 | 140 | 3.5 | 18 | 110 | Normal study |
| 98 | 27 | F | 1.8 | Alb(++)<br>N<br>N | 113 | 0.950 | 35 | 0.9 | 142 | 4 | 22 | 95 | Bil.renomegaly |
| 99 | 58 | F | 0.8 | Alb(+)<br>N<br>N | 67 | 0.160 | 30 | 0.7 | 138 | 3.5 | 20 | 110 | Normal study |
| 100 | 40 | F | 2.2 | Alb(++)<br>N<br>N | 69 | 0.800 | 47 | 0.8 | 145 | 5 | 16 | 115 | Bil.renomegaly |
| | | | | | | | | | | | | | |
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| | | |
| **CD4 COUNT** | | |
| 217 | | |
| 364 | | |
| 701 | | |
| 281 | | |
| 238 | | |
| 342 | | |
| 229 | | |
| 237 | | |
| 247 | | |
| 270 | | |
| 376 | | |
| 678 | | |
| 240 | | |
| 376 | | |
| 428 | | |
| 442 | | |
| 289 | | |

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|---|---|---|
| 475 | | |
| 441 | | |
| 209 | | |
| 327 | | |
| 344 | | |
| 344 | | |
| 549 | | |
| 310 | | |
| 753 | | |
| 399 | | |
| 269 | | |
| 331 | | |
| 323 | | |
| 460 | | |
| 559 | | |
| 628 | | |
| 280 | | |
| 511 | | |
| 357 | | |

| | | |
|---|---|---|
| 354 | | |
| 274 | | |
| 293 | | |
| 384 | | |
| 292 | | |
| 679 | | |
| 163 | | |
| 576 | | |
| 693 | | |
| 896 | | |
| 487 | | |
| 209 | | |
| 363 | | |
| 225 | | |
| 480 | | |
| 274 | | |
| 509 | | |
| 275 | | |
| 498 | | |

| | | |
|---|---|---|
| 463 | | |
| 499 | | |
| 525 | | |
| 346 | | |
| 421 | | |
| 284 | | |
| 1225 | | |
| 259 | | |
| 617 | | |
| 377 | | |
| 339 | | |
| 477 | | |
| 508 | | |
| 386 | | |
| 275 | | |
| 481 | | |
| 272 | | |
| 674 | | |
| 214 | | |

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|---|---|---|
| 614 | | |
| 382 | | |
| 216 | | |
| 592 | | |
| 339 | | |
| 789 | | |
| 349 | | |
| 376 | | |
| 256 | | |
| 332 | | |
| 239 | | |
| 168 | | |
| 187 | | |
| 466 | | |
| 150 | | |
| 480 | | |
| 306 | | |
| 248 | | |
| 369 | | |

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| 343 | | |
| 284 | | |
| 379 | | |
| 268 | | |
| 424 | | |
| 382 | | |
| 320 | | |
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