A STUDY OF RENAL AND ELECTROLYTE DISTURBANCES IN HIV INFECTED PATIENTS

DISSERTATION SUBMITTED FOR

M.D GENERAL MEDICINE

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TAMILNADU, INDIA

CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled ***"A STUDY OF RENAL AND ELECTROLYTE DISTURBANCES IN HIV INFECTED PATIENTS"*** *is the bonafide work of* ***Dr.RAMESH.N*** *in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for* ***M.D General Medicine Branch I*** *examination to be held in* ***April 2017.***

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CERTIFICATE FROM THE HOD/GUIDE

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DECLARATION

I, ***Dr.RAMESH.N ,*** *declare that, I carried out this work on* **"A STUDY OF RENAL AND ELECTROLYTE DISTURBANCES IN HIV INFECTED PATIENTS"** *at the Department of Medicine, Govt. Rajaji Hospital during the period February2016 to July2016. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree or diploma to any other University, Board either in India or abroad. This is submitted to The Tamilnadu Dr.M.G.R.Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D degree examination in General Medicine.*

Place : *Madurai* ***DR.RAMESH.N***

Date*:27.09.16*

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ABBREVIATIONS

HIV	Human Immunodeficiency Virus
AIDS	Acquired Immunodeficiency Syndrome
PLHA	People Living With HIV and AIDS
HAART	Highly Active Antiretroviral Therapy
PCP	Pneumocystis carrnii Pneumonia
OIs	Opportunistic Infections
DCM	Dilated cardiomyopathy
CDC	Centre for Disease Control
WHO	World Health Organisation
ELISA	Enzyme Linked Immunosorbent Assay
Cart	Combibation antiretroviral therapy
CD4	Cluster of Differentiation 4
Na+, K+	Sodium,Potassium
CRF	Circulating Recombinant Forms
HAD	HIV associated dementia
EBV	Epstein barr virus
CMV	Cytomegalovirus
PHT	Pulmonary hypertersion
HIVAN	HIV associated nephropathy

CONTENTS

INTRODUCTION

Human immune deficiency virus infection was first identified in the year 1986 at Madras. Subsequently cases of HIV infection and AIDS identified all over India.HIV virus when infects a person over time causes AIDS(Acquired Immuno Deficiency Syndrome) .AIDS is a condition which causes progressive failure of the body's immune system allows life-threatening opportunistic infections and certain cancers to thrive. There are numerous clinical manifestations of AIDS. In India there are many studies dealing with various aspects of AIDS cases. Eventhough few studies available on various organ involvement in HIV infection and AIDS, they do not describe renal involvement in AIDS cases. So I hereby made an attempt to study renal and electrolyte disturbances in HIV affected individuals.

INCIDENCE AND PREVALENCE IN INDIA:

INDIA is world's third largest population suffering from HIV/AIDS. In our country ,as per 2015,there are 2.1 million people living with HIV. Adult (15–49 years) HIV prevalence is estimated as 0.3% .There are 68,000 people died of AIDS related illnesses in India in 2015.There occurs about 86,000 new HIV infections by the year 2015. Overall India's HIV epidemic is falling down.HIV prevalence in India varies geographically. The 5 states with highest prevalence are Nagaland, Mizoram, Manipur, Andhra Pradesh and Karnataka.

AIMS AND OBJECTIVES

1) To find out the prevalence of Renal and electrolyte disturbances in Patients with HIV irrespective of ART.

2)To explore the mechanism for renal involvement through literature

REVIEW OF LITERATURE

HISTORY AND PROBLEM STATEMENT

AIDS (Acquired immunodeficiency syndrome), recognised as an emerging disease in early 1980s.It then has evolved from a mysterious illness to a global pandemic by infecting tens of million in less than twenty years. In 1981, AIDS was recognised in US recognised that HIV was the causative agent for AIDS.

According to estimates by WHO at the end of 2015, around 36.7 million people were living with HIV worldwide and around 11.7 million people had access to antiretroviral therapy in low and middle income countries. Over 28 million people are eligible for antiretroviral therapy, under WHO.

TYPES OF HIV EPIDEMICS

WHO and UNAIDS define the different types of HIV epidemics as below.

Low level epidemics	HIV prevalence not consistently exceeded more than 5% in any defined subpopulation
Concentrated epidemics	HIV prevalence consistently exceeded more than 5% in atleast one subpopulation but < 1% in pregnant women.
Generalised HIV in	HIV prevalence consistently exceeded more than 5% in

epidemics	any defined subpopulation and > 1% in pregnant women.

HIV PREVALENCE STATEMENT IN (SEAR) COUNTRIES,2007

COUNTRY	ESTIMATED NUMBER OF PLHA	PERCENTAGE OF ADULT POPULATION INFECTED WITH HIV
BANGLADESH	12,000	<0.1%.
BHUTAN	<500	<0.1%.
INDIA	24,00,000	0.3%
INDONESIA	2,70,000	0.2%
MALDIVES	<100	0.1%
MYANMAR	2,40,000	0.7%
NEPAL	70,000	0.5%
SRILANKA	3,800	<0.1%
TAILAND	6,10,000	1.4%

HIV PREVALENCE IN INDIA

Based on sentinel surveillance data, HIV prevalence classified into three groups.

GROUP I – HIGH PREVALENCE STATES

>5% in high risk groups and 1% or > 1% in pregnant women

-Tamilnadu, Maharastra, Karnataka.

-Andhra pradesh, Manipur, Nagaland.

GROUP II - MODERATE PREVALENCE STATES

>5% in high risk groups and <1% in pregnant women

- Gujarat, Goa, Pondicherry.

GROUP III - LOW PREVALENCE STATES

<5% in high risk groups and <1% in pregnant women

-other states.

DEFINITION AND CLASSIFICATION

The current CDC (Center for disease control and prevention) classified the HIV infected person based on clinical condition and CD4 cell count .

HIV patient is will have AIDS when the CD4 count <200/microlitre irrespective of presence of symptoms, signs and opportunistic infections.

CD4+ T cell count (per µL),	Category A – asymptomatic/ acute HIV/ PGL	Category B – symptomatic	Category C – AIDS indicators
>500	A1	B1	C1
200 – 400	A2	B2	C2
<200	A3	B3	C3

CATEGORY A : consists of patients with one or more of the following conditions , but conditions enumerated under category B or C must not have occurred. These include :

Asymptomatic infection
Generalised lymphnode enlargement (present persistently)
Acute HIV infection with associated illness or history of acute HIV infection.

CATEGORY B: Includes Patients with one or more of following conditions, but those under category C must not have occurred plus the condition is related to HIV or defect in cell mediated immunity. These include[11] :

❖ Bacillary angiomatosis,
❖ Oral thrush,
❖ Vulvovaginal candidiasis recurrent/ non responsive to treatment,
❖ Cervical dysplasia/ carcinoma in situ,
❖ Fever/ diarrhoea > 1 month,
❖ Oral hairy leukoplakia,

❖ >1 episode/ >1 dermatome – Herpes zoster,
❖ Idiopathic thrombocytopenic purpura,
❖ Listeria infection,
❖ PID like tubo ovarian abscess,
❖ Peripheral neuropathy.

Category c-AIDS defining illness

❖ Invasive candidiasis (esophagus, trachea, lung or bronchi),
❖ Invasive cervical malignancy,

❖ Coccidioidomycosis,
❖ Cryptococcosis,
❖ Chronic intestinal Cryptosporidiosis / Isospora infection,
❖ CMV retinitis,
❖ HIV encephalopathy,
❖ Herpes simplex infections (bronchitis, pneumonia, esophagitis),
❖ Histoplasmosis,
❖ Kaposi sarcoma,
❖ Primary CNS lymphoma,
❖ Burkitt's lymphoma,

❖ Pulmonary or extrapulmonary TB,
❖ Mycobacterium Avium Complex infection.
Pneumocystis carinii pneumonia,
❖ Progressive multifocal leukoencephalopathy (PML),
❖ CNS toxoplasmosis,

❖ AIDS cachexia,
❖ Recurrent pneumonia/ Salmonella sepsis.

HIV VIRUS

HIV virus is classified under family of retroviridae and subfamily of lentivirus. Two subtypes of HIV virus have been identified. HIV 1 is most common subtype in worldwide. HIV virus is easily killed by the heat and it is readily inactivated by ether, acetone, ethanol 20% and betapropionolactone. It is relatively resistant to ionizing radiation and UV light.

MORPHOLOGY

Spherical in shape and enveloped virus

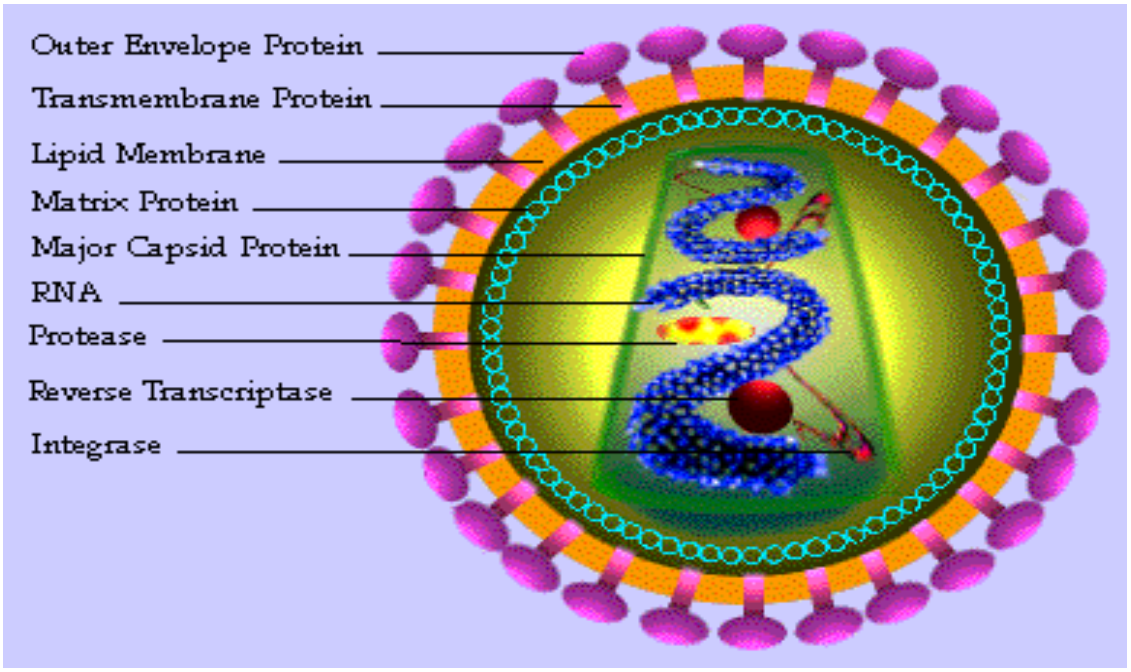
90-120nm in size

Genome contains two identical single strandard +one RNA copy and Reverse transcriptase

Three structural genes –gag, pol and env

Non-structural and regulatory genes - tat, nef, rev, vif, vpu

STRUCTURE OF THE HIV VIRUS



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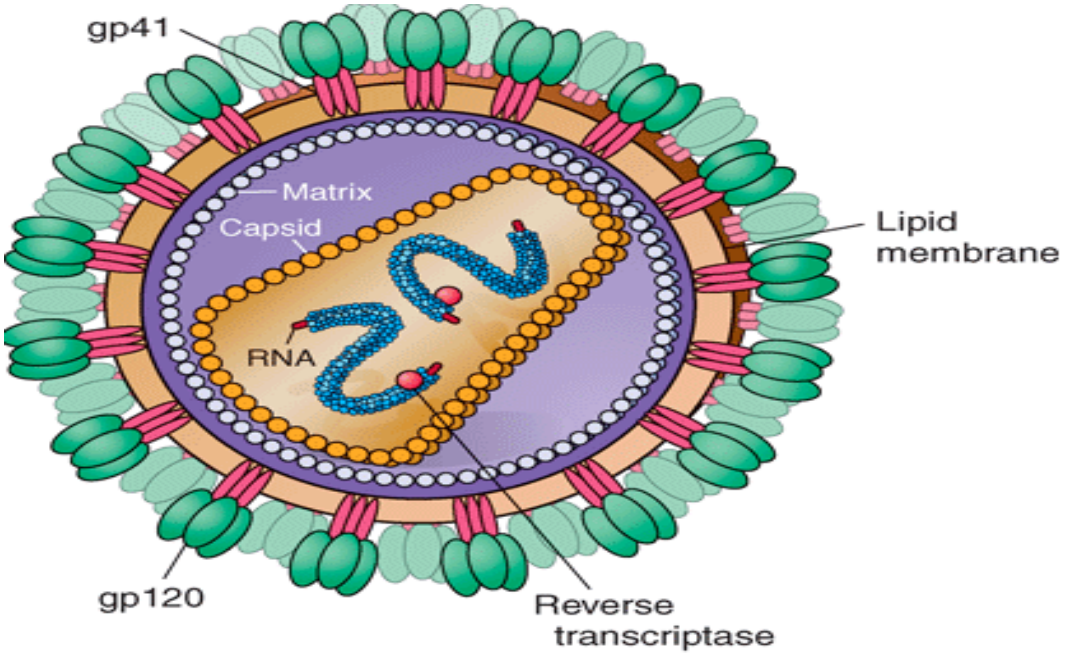


B

MAJOR ANTIGENS OF HIV

A. Envelope antigens - 1.spike antigen –gp120

2.transmembrane pedicle Ag-gp41

B. Shell antigen - Nucleocapsid protein p18

C. core antigens

1.principal core antigen p24

2.other core antigens-p15,p55

D. Polymembrane antigens- p31,p51,p66

GENE	FUNCTION
gag	Core of virion (incuding p24 antigen).
pol	Protease, reverse transcriptase and integrase enzymes.
Env	Envelope glycoproteins.
tat, rev, nef, vif, vpr, vpu	Regulates viral gene replication and host cell modification to enhance viral growth.

GROUPS

- 4 groups - group M (major), group O (outlier),group N and group P.
- Group M is further subclassified into subtypes. Includes 9 subtypes : A, B, C, D, F, G, H, J and K.
- Sometimes patients are infected with more than one subtype which recombine to give rise to CRFs (circulating recombinant forms). Examples include , CRF01_AE and CRF02_AG.
- Subtype A and F are further sub classified into sub – sub – types such as A1, A2 and F1, F2.
- The geographic distribution of these different strains is widely distributed. A, B, C, D, G and CRF01-AE, CRF-AG are by far the common strains globally. While subtype C is the most prevalent strain.
- There are numerous implications to this genetic diversity such as :

1. Wide diversity (subtypes, circulating recombinant forms),
2. Continuous viral evolution,
3. Different rates of disease progression,
4. Varied response to therapy,
5. Development of resistance,
6. Inability to develop vaccine against wide range of strains.

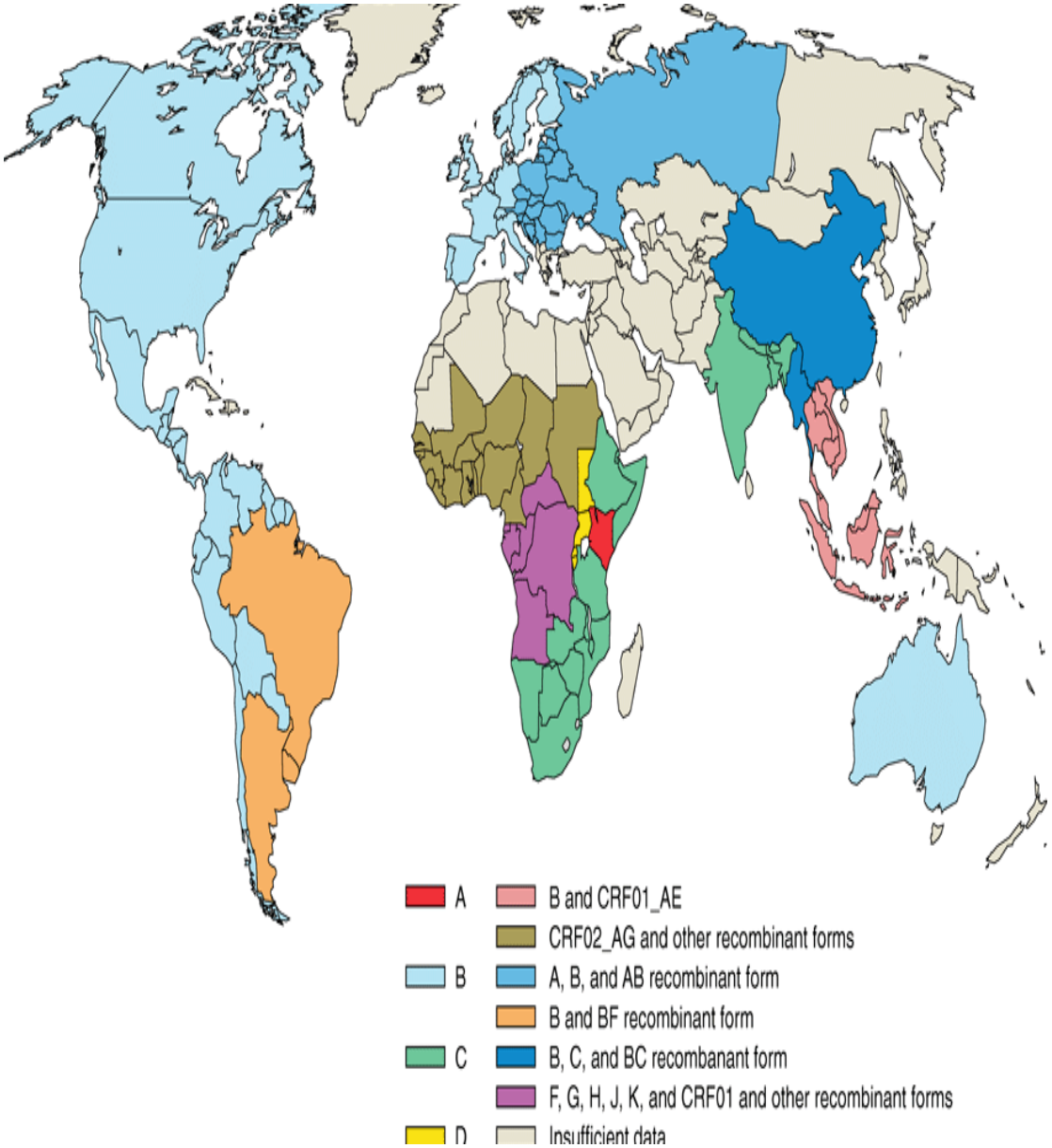
GEOGRAPHIC DISTRIBUTION OF HIV &SUBTYPES

1.	Sub-Saharan Africa	Subtype C (most common) Subtype B and G, CRFO2_AG.
2.	India	Subtype C.
3.	China	Subtypes B, C and BC recombinant forms.
3.	Southeast Asia	CRF01_AE.
4.	North America and some parts of South America	Subtype B.
5.	Australia	Subtype B.
6.	Western Europe	Subtype B.
7.	Eastern Europe	Subtype A,B and AB recombinant forms.

New emerging strains:

Thai B. Indian C.	southern China*
CRF03_AB	Former soviet union
CRF14_BG	Spain* Portugal*
BF recombinant forms	South America
CRF35_AD	Afghanistan and Iran*

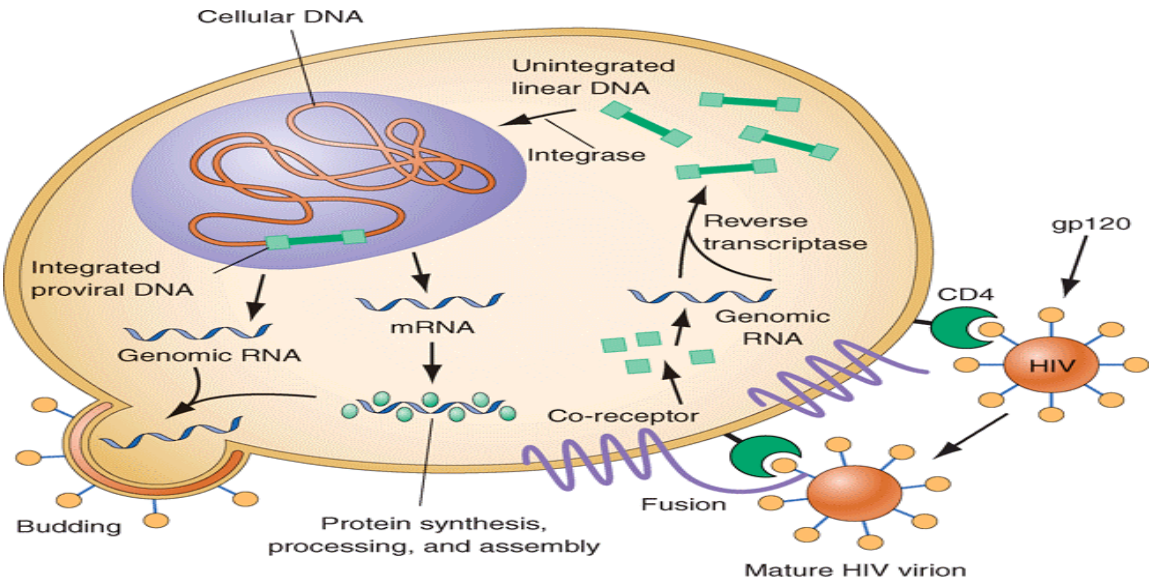
GEOGRAPHIC DISTRIBUTION OF HIV &SUBTYPES



REPLICATION CYCLE

HIV virus enters into the body through blood or tissues of infected person. After entering the virus binds with host cell (CD4 lymphocyte) through using the envelope antigens gp120 and gp41.Binding of HIV to the host cell can also mediated through the HIV coreceptors CXCR4 (for Tcell trophic HIV strains) and CCR5(for macrophage trophic strains).

After the fusion of HIV with the host cell membrane HIV genome is uncoated and internalised into the cell. Then virus reverse transcriptase mediates the transcription of HIV RNA into double strandard DNA which is incorporated into the host cell genome which leads to formation of proviruses.

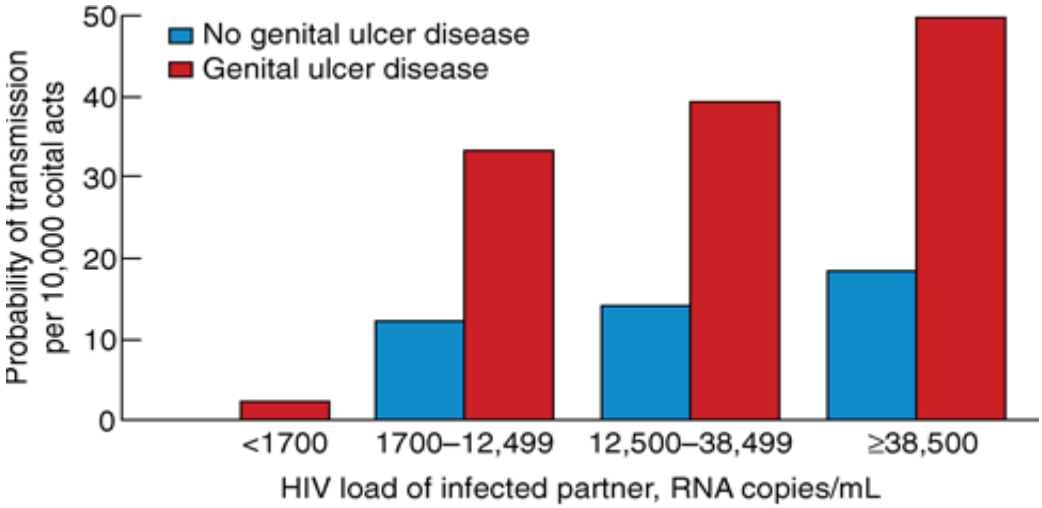


TRANSMISSION OF HIV

HIV can be transmitted through sexual, blood and blood products and maternal-fetal transmission.

SEXUAL TRANSMISSION

- Can through homosexual or heterosexual route.
- Male to female transmission rate is higher than female to male transmission rate .Increased risk of heterosexual transmission in presence of genital ulcer.



- Unprotected receptive anal intercourse increased the rate of transmission because of the thin fragile rectal mucous membrane.
- Uncircumcised males are more prone to develop HIV infection because of the foreskin contains plenty of langerhan cells , CD4 T cells and macrophages which are the targets in AIDS

TRANSMISSION BY BLOOD AND BLOOD PRODUCTS

The first case of HIV infection transmitted by blood products was reported in 1982. HIV virus can be transmitted through transfusion of contaminated white blood cells, platelets and clotting factors.

Transfusion of hyperimmune gammaglobulin , hepatitisB Ig, HepB vaccine and Rh Ig will not transmit infection. Any skin piercing including injection ,ear pricking, tatto and acupuncture can also transmit the infection.

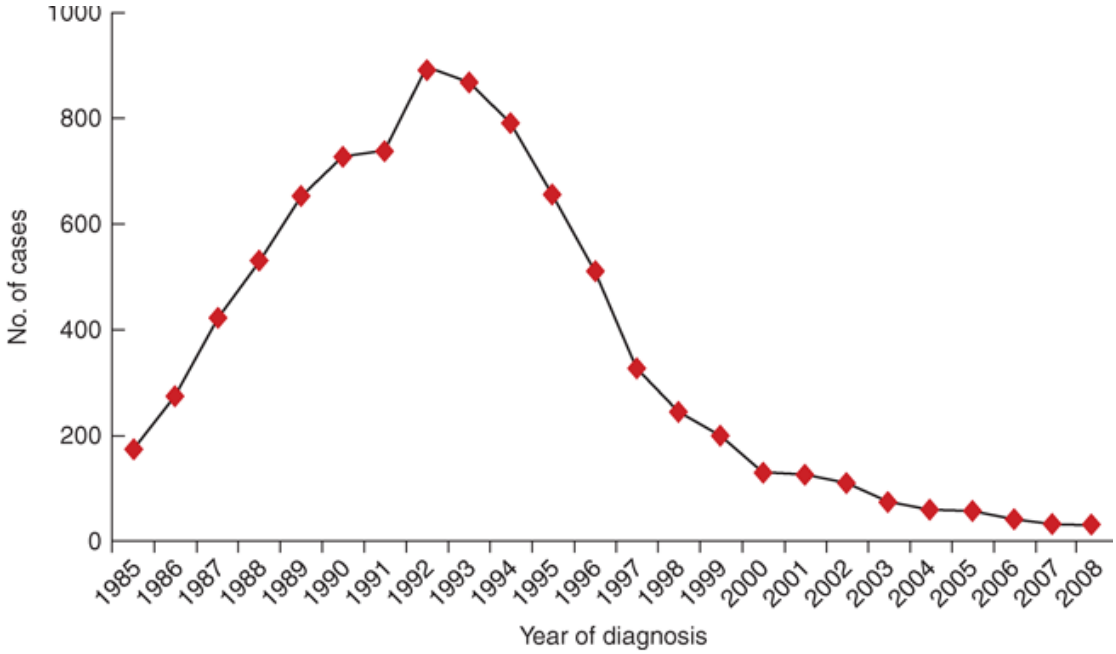
MOTHER TO FETUS/INFANT TRANSMISSION

- Maternal to fetus transmission occurs during pregnancy, during delivery and by breast feeding.
- Low maternal CD4 count is associated with the high rate of transmission.

- Prolonged second stage of labour also increase risk of HIV transmission.

Without ART to the mother in the antenatal period, risk of mother to fetus transmission is around 10% to 25% in industrialised countries, 20% to 25% in developing countries.With prophylactic ART, rate of transmission decreases by 5%.

Graph showing the number of perinatally acquired cases in children



TRANSMISSION BY OTHER BODY FLUIDS

- Saliva contains many antiviral factors such as IgA , IgG And IGM mucins , thrombospondin 1, secretory lecukocyte protease inhibitor(SLPI) which inhibits the replication of HIV and increases the clearance by the host.

- Exposure to body fluids such as sweat, urine and tears will not transmit the HIV infection.

MODES OF HIV TRANSMISSION

SEXUAL ROUTE	87%
MOTHER TO CHILD	5%
BLOOD AND BLOOD PRODUCTS	2%
INJECTION DRUG USE	2%
UNKNOWN	4%

CLINICAL FEATURES OF HIV INFECTION

AIDS (Acquired immuno deficiency syndrome) is a fatal illness characterised by multisystem involvement and development of various opportunistic infections leading to death.

Clinical manifestation of HIV infection have been classified into 3 broad categories

1. Acute HIV syndrome.
2. Asymptomatic stage.
3. Symptomatic disease.

ACUTE HIV SYNDROME

Around 50% to 70% of the individuals will develop acute HIV infection after 3 to 6 weeks of primary infection. Most common manifestations include fever, pharyngitis, headache, nausea, vomiting and diarrhoea. Symptoms will persist for several weeks and gradually subside. Neurology and dermatologic manifestations also occur in acute HIV syndrome

Systemic symptoms:

Cutaneous manifestations 1.Mucocutaneous ulcer

2.Erythematous maculopapular rash

Fever	Pharyngitis
Myalgia	Arthralgia

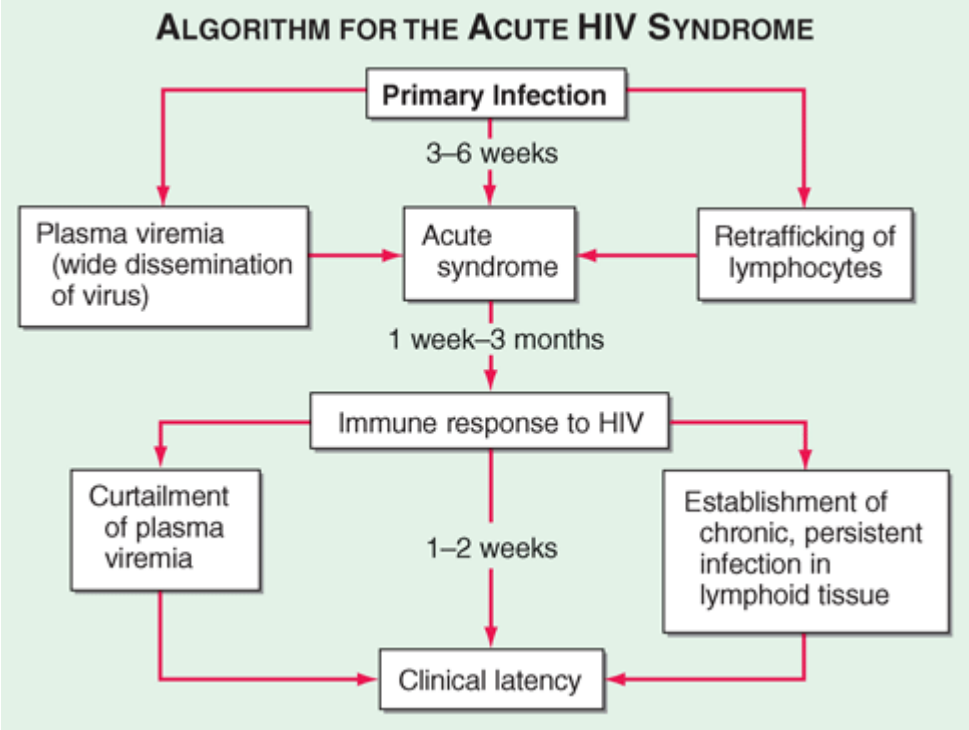
Weight loss	Nausea
Vomiting	Diarrhea
Headache	Retro orbital pain
Lymphadenopathy	

Neurological manifestations:

Encephalitis	Aseptic meningitis
Acute transverse myelitis	Peripheral neuropathy
Acute demyelinating Encephalomyelitis	

Approximately around 10% of HIV patients will have fulminant course even after the disappearance of signs and symptoms.

If antiretroviral therapy (ART) is initiated during the acute HIV infection, small percentage of patients may revert to a negative ELISA test. But after discontinuation of the treatment rapidly they will reseroconvert to positive test.



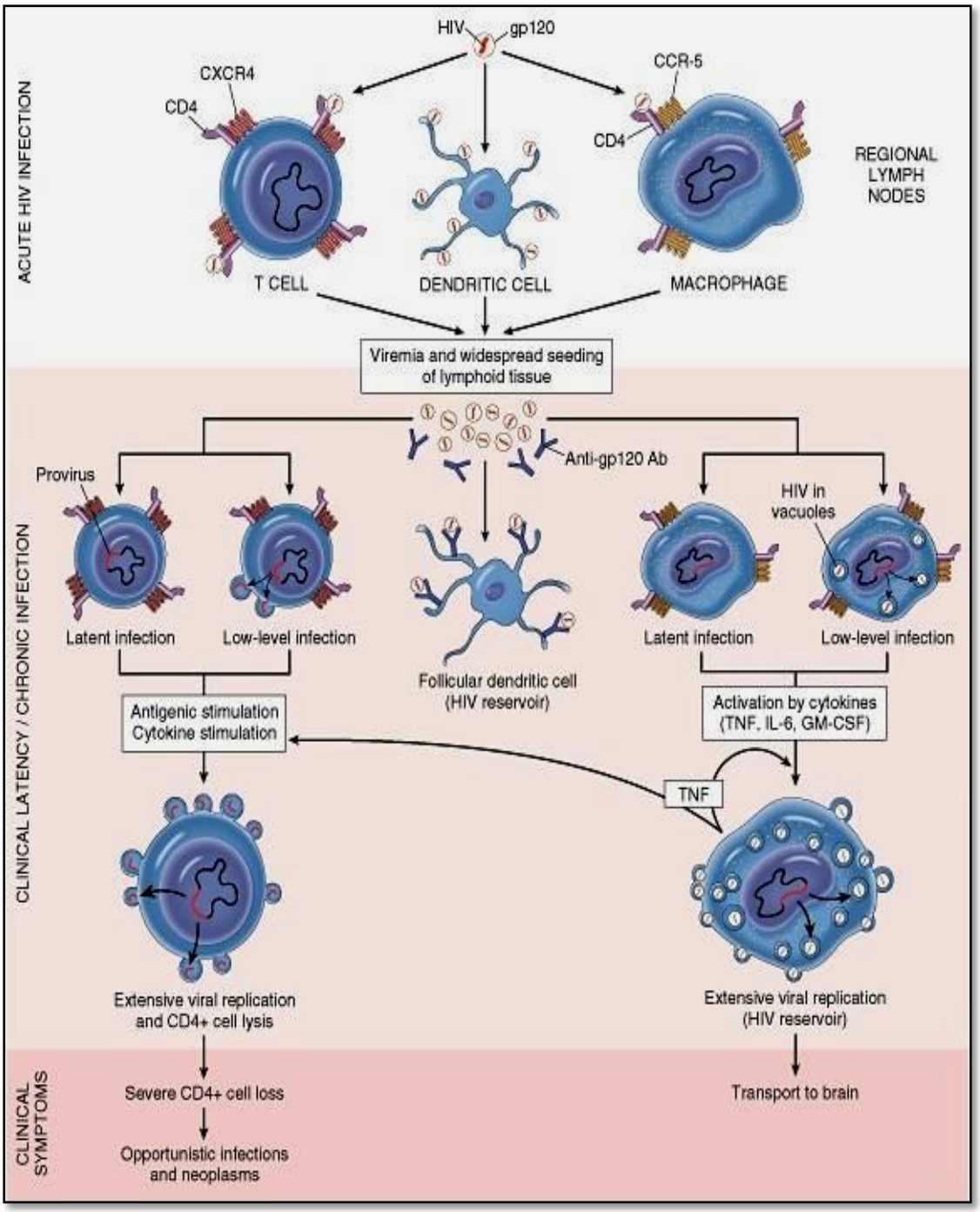
ASYMPTOMATIC STAGE

During the asymptomatic stage antibodies to HIV is present in the serum but no signs and symptomps of the disease. Duration of the asymptomatic stage varies from months to years. During this period rate of fall of CD4 count is 50/microlitre/year.

SYMPTOMATIC DISEASE

During the course of illness, signs and symptoms appear at any stage of illness. Symptoms depends upon the rate of fall of CD4 count. As the CD4 count decreases, opportunistic infection increases leading to fatal complications.

NATURAL HISTORY OF THE DISEASE IN HIV INFECTION



DISEASES OF KIDNEY & GENITOURINARY SYSTEM

Diseases of genitourinary system are due to direct consequences of HIV infection or due to neoplasm or opportunistic infections or drug toxicities.. Renal biopsy is diagnostic of HIVAN.

Drug causing renal toxicities in HIV infection are Amphotericin, pentamidine, adefovir, cidofovir and foscarnet. Renal stones are caused by Indinavir in 10% of cases. Condylomata lata a form of secondary syphilis most common in HIV patients.

"HIV-associated nephropathy (HIVAN), acute kidney injury (AKI), and chronic kidney disease (CKD) are important complications of HIV infection and may become important as patients live longer duration in the era of combined antiretroviral therapy (ART)"

Cross-sectional studies described a 4% to 17% prevalence of reduced kidney function in diverse HIV-infected populations . A recent large European cohort study examining CKD in HIV-infected patients found a prevalence of CKD around 4%. CKD and decline in renal function have been reported in association with older age, female gender, hepatitis B and C infections, diabetes, hypertension.

NEPHROPATHY ASSOCIATED WITH HIV INFECTION

HIVAN.

“Classic HIVAN was a syndrome causing focal sclerosing glomerulopathy with severe proteinuria, renal failure, and rapid progression to ESRD. It became the most common cause of ESRD in HIV-1–seropositive patients. HIVAN primarily occurs in patients of African descent , suggesting a genetic predisposition to the disease. Duffy antigen/ receptor for chemokines has controversially discussed as a candidate gene involved in the development of HIVAN . The estimated prevalence of HIVAN has around 3.5% in clinical studies to 12% in autopsy studies. Because HIVAN typically occurs late in the course of HIV-1 infection , risk factors for the development of HIVAN include a CD4 cell count 200 cells/mm3 and a high viral burden”.

“Clinical features of this syndrome include advanced renal failure and proteinuria (the protein level is often—but not necessarily—at a nephrotic level [13 g/day]), a lack of peripheral edema despite the severe loss of protein, and, frequently, enlarged kidneys visible on renal ultrasound”

Renal biopsy is the only means to establish the diagnosis of HIVAN. Characteristic histological findings include collapsing focal and segmental glomerulosclerosis, tubular epithelial atrophy with microcystic dilatation of the tubules , and lymphocytic interstitial infiltration. Viral infection of renal cells seems to play an important role in the pathogenesis of HIVAN.

RESPIRATORY SYSTEM INVOLVEMENT

HIV patients have six fold increase in incidence of pneumococcal pneumonia. Pneumocysti carini pneumonia occurs in patients with CD4 count <200/microlitre. Classical chest xray finding is dense perihilar infiltrate which is unusual in HIV patients.

Mycobacterium avium complex infection is seen in patients with CD4 count<50/microlitre. Fungal infections can also cause pneumoniain HIV patients. Two forms of Idiopathic pneumonia(Lymphoid interstitial pneumonia &Nonspecific interstitial pneumonia) have been recognized and are seen in 1% of adult HIV patients. It occurs due to polyclonal activation of lymphocytes. The disease is usually self limited.

Sinus infection is also common in HIV patients . Maxillary sinus is most commonly involved. Common organisms causing sinusitis in HIV infection are H.influenza and Staph aureus. Fungal infection like mucormycosis in HIV infection progresses very slowly and responds to amphotericinB

DISEASE OF OROPHARYNX AND GIT

Gastrointestinal manifestations in HIV infections are most commonly due to secondary infections , Kaposi sarcomas, and lymphomas. And they occur in patients with CD 4 count <300 /micro litre. Most common oral infections include candidiasis. Oesophagitis in HIV is due to Candida, CMV, HSV

Infections. HSV ulcers are usually multiple while CMV ulcer is usually solitary. Achlorhydria is also common in HIV infection but other gastric problems are rare.

Diarrheal illness in HIV is caused by bacterial infections like Salmonella, Shigella and Campylobacter spp, fungal infections like Penicillosis , Histoplasmosis, Coccididomycosis, and Parasitic infections such as Cryptosporidia, Microspora &Isospora belli.

CMV colitis was one of the common manifestations in pre ART era, but after the introduction of ART its incidence have been decreased. Patients with gastro intestinal manifestations should be screened for ophthalmic evaluation for CMV retinitis.

Few patients with HIV develop chronic gasteroenteritis.. Rectal lesions due to reactivation of herpes simplex are also more common in HIV infection.

RHEUMATOLOGIC & IMMUNOLOGICAL DISEASES :

Anaphylaxis in HIV is usually rare due to ART except Abacavir which can cause fatal allergic reactions. HLA B-57 strongly associated with allergic reactions due to abacavir.. In Sjogren's syndrome CD4 T cell infiltrates are more prominent.

Another type of arthritis also called as painful articular syndrome which involves the large joints and affects . In very few patients some rare clinical manifestations like leucocytoclastic vasculitis, CNS angiitis and polymyositis have been reported.

HEPATOBILIARY MANIFESTATIONS.

HCV infection is more common and 10 fold increase of death in HIV infection when compared to general population.Granulomatous hepatitis is one of the worst complication seen in HIV patients and the causative organisms are mycobacterium avium complex and fungal infections.

Hepatic mass also caused by tuberculosis,pertussis,hepatitis or fungal infections like C.immitis and H.capsulatum may be seen and in HIV patients.Nucleoside reverse transcriptors also cause hepatitis which is fulminant in some patients.Indinavir can also cause hyperbilirubinemia. Pentamidine and didanosine are the important causes of pancreatitis in HIV patients.

DISEASES OF ENDOCRINE SYSTEM AND METABOLIC DISORDERS

HIV lipodystrophy is a common metabolic problem in patients receiving Antiretro viral therapy and develops in 30-75% of patients.

Characteristic features of lipodystrophy are

- Increased total cholesterol,
- Increased triglycerides,
- Increased apolipoprotein B,
- Hyperinsulinemia,
- Hyperglycemia and
- Fat redistribution -truncal obesity&peripheral wasting.

Next to lipodystrophy the other common metabolic abnormality in HIV patients is hyponatremia .The important causes include SIADH due to pulmonary and CNS lesion,due to adrenal gland involvement by HIV infection itself and by CMV,cryptococcosis and histoplasmosis and due to drug toxicity by Antiretroviral therapy.

Thyroid gland is most common gland involved in HIV infection and the most common abnormality is subclinical hypothyroidism.Grave's disease can also occur 9 to 48 months after initiation of HAART.

Around 50% of HIV patients develops hypogonadism and erectile dysfunction.Testicular dysfunction can also be due to ganciclovir therapy. Avascular necrosis of hip and shoulder,osteoporosis have also been developed in HIV infection.

DISEASE OF HEMATOPOIETIC SYSTEM

Hematolgical abnormalities seen in HIV infection include anemia,leukopenia,thrombocytopenia which may be due to HIV infection, nutritional, drug induced, secondary infections and neoplasms.Zidovudine and dapsone are two drugs most commonly associated with anemia.

In some patients generalised lymphadenopathy may be the first presentation.Monoclonal gammapathy of unknown significance(MGUS) have been reported in 3% of HIV infection.

Thrombocytopenia in HIV infection may be due to associated HCV infection, cirrhosis and thrombotic thrombocytopenic purpura. Incidence of venous thromboembolism in HIV infection is 1% per year. Causes of bone marrow suppression in HIV patients include infections like mycobacterium , fungus, parvovirus B19 and lymphomas and drugs like zidovudine, dapsone, ganciclovir , interferon alpha, trimethoprim sulfmethoxazole , pyrimethamine and foscarnet

OCULAR MANIFESTATIONS

Ocular manifestations occur in 50% of patients in late stage of HIV infection.Cotton wool spots are the most common fundus finding and these are due to retinal ischemia.CMV retinitis is one of the dangerous ophthalmic complication of HIV infection and occurs in patients with CD4 count <100/microlitre.So all patients with CD4 count <100/microlitre ophthalmic screening for CMV retinitis should be done

"Acute retinal necrosis syndrome or progressive outer retinal necrosis is a rapidly progressing bilateral necrotizing retinitis and the patient may present with keratitis and iritis.It is most often associated with HSV or varicella infection.Syphilitic uveitis and kaposi sarcoma of eyelids and conjunctiva are rarely seen in HIV infection".

NEUROLOGICAL MANIFESTATIONS

Neurological problems in HIV infection is due to direct consequence of the virus or secondary to opportunistic infections like toxoplasmosis ,cryptococcosis,CMV infection or mycobacterial infection.

Cryptococci neoformans is the most common cause of meningitis in HIV infection cccurs in patients with CD4 count less than

100/microlitre.Diagnosis is confirmed by identification of organism in CSF by Indian ink examination.

Behavioral problems include apathy, irritability, and lack of initiative, with progression to a vegetative state in some instances. Some patients develop a state of agitation or mild mania. These changes usually occur without significant changes in level of alertness. This is in contrast to the finding of somnolence in patients with dementia due to toxic/metabolic encephalopathies

The precise cause of HIV-associated dementia remains unclear,although the condition is thought to be a result of a combination of direct effects of HIV on the CNS and associated immune activation.

Multinucleated giant cells, macrophages, and microglial cells appear to be the main cell types harbouring virus in the CNS. Histologically the major changes are seen in the subcortical areas of the brain and include pallor and gliosis, multinucleated giant cell encephalitis, and vacuolar myelopathy. Less commonly, diffuse or focal spongiform changes occur in the white matter. Areas of the brain involved in motor, language, and judgment are most severely affected.

“Seizures may be initial manifestion in some patients with HIV infection. The seizure threshold is often lower in patients with advanced HIV infection due to the presence of electrolyte abnormalities”

Causes of Seizures in Patients with HIV Infection

❖ HIV encephalopathy
❖ Cerebral toxoplasmosis
❖ Cryptococcal meningitis
❖ Primary central nervous system lymphoma
❖ Progressive multifocal leukoencephalopathy

“Spinal cord disease is seen in 20% of patients with HIV infection.Three main types of spinal cord disease are vacuolar myelopathy, pure sensory ataxia,&paresthesia/dysesthesia. Other neurological manifestations present in HIV infection are progressive multifocal leukoencephalopathy, primary CNS lymphoma,kaposi sarcoma,aseptic meningitis, peripheral neuropathy(AIDP&CIDP) and myopathy”.

IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME

" In some patients following inititation of ART , paradoxical worsening of preexisting , untreated or partially treated opportunistic infections occur due to Type 4 hypersensitive reactions. This is known as immune reconstitution inflammatory syndrome (IRIS). Signs and symptoms may appear at any time from two weeks to two years after initiation of ART and the symptoms include fever, localised lymphadenitis, pulmonary infiltrates, uveitis, sarcoidosis, grave's disease and raised ICT. It can be fatal in few patients and steroids can be used in treatment of IRIS".

CHARACTERISTICS OF IRIS

- Paradoxical worsening of the clinical condition following initiation of ART.
- Occurs weeks to months following initiation of ART.
- Most common in patients starting therapy with CD4 count <50/microlitre
- Frequently seen in patients with tuberculosis.
- Can be fatal.

OPPORTUNISTIC INFECTIONS IN HIV INFECTION IN RELATION TO CD4 COUNT

CD4 Count < 500 / microlitre :

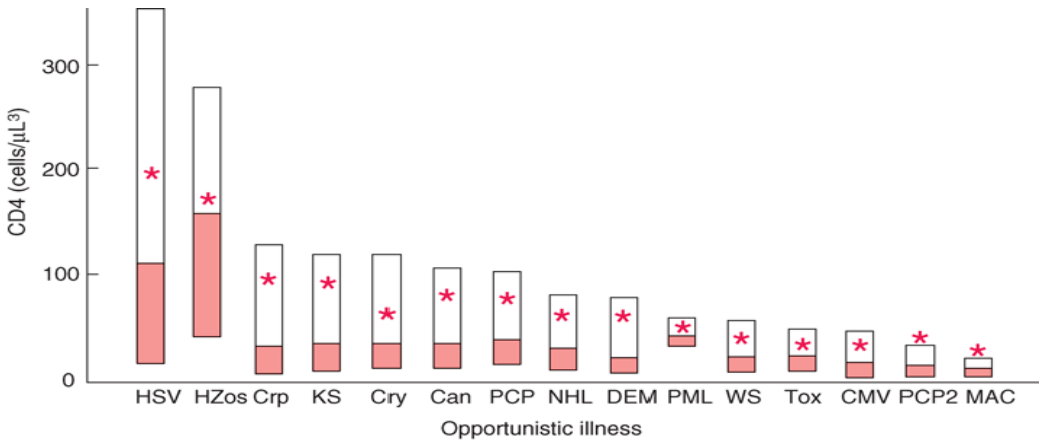
- Bacterial infections like TB, Herpes simplex
- Herpes Zoster, Vaginal Candidiasis
- Hairy leukoplakia, Kaposi sarcoma”

CD4 Count <200 / microlitre :

- Pneumocystosis,Toxoplasmosis
- Coccidiomycosis,Cryptosporidiosis
-

“CD4 Count < 50 / microlitre :

- Disseminated MAC infection, Histoplasmosis
- CMV Retinitis, CNS Lymphoma”



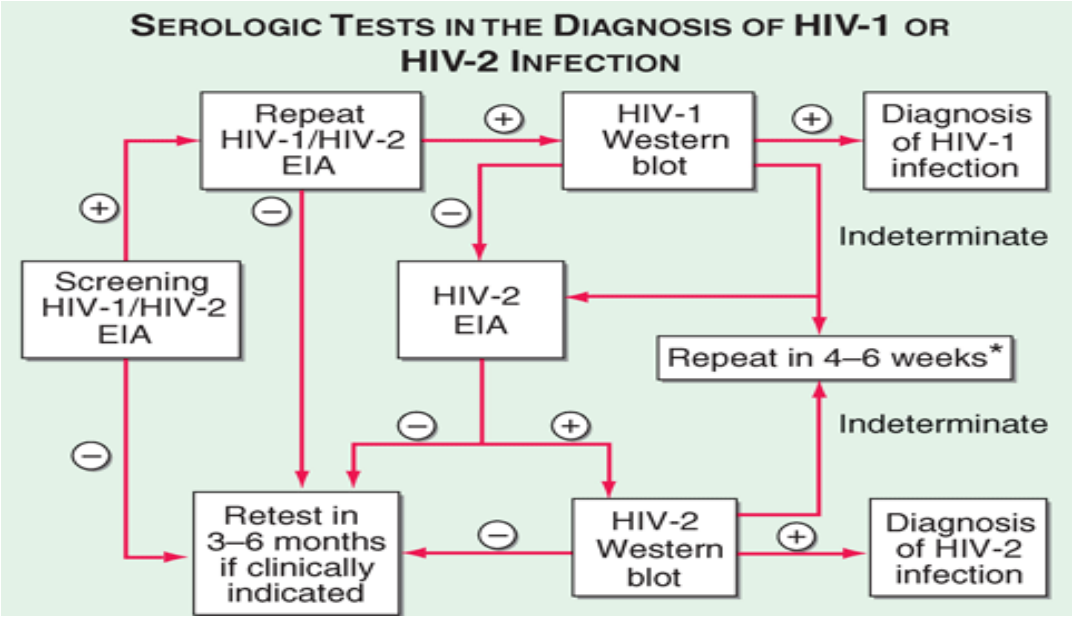
LABORATORY DIAGNOSIS OF HIV INFECTION

"Diagnosis of HIV infection based on demonstration of antibodies to virus or direct demonstration of HIV or one of its components .Antibodies to HIV in the blood appears generally 3-12 weeks of infection" .

ELISA(ENZYME LINKED IMMUNOSORBENT ASSAY) TEST

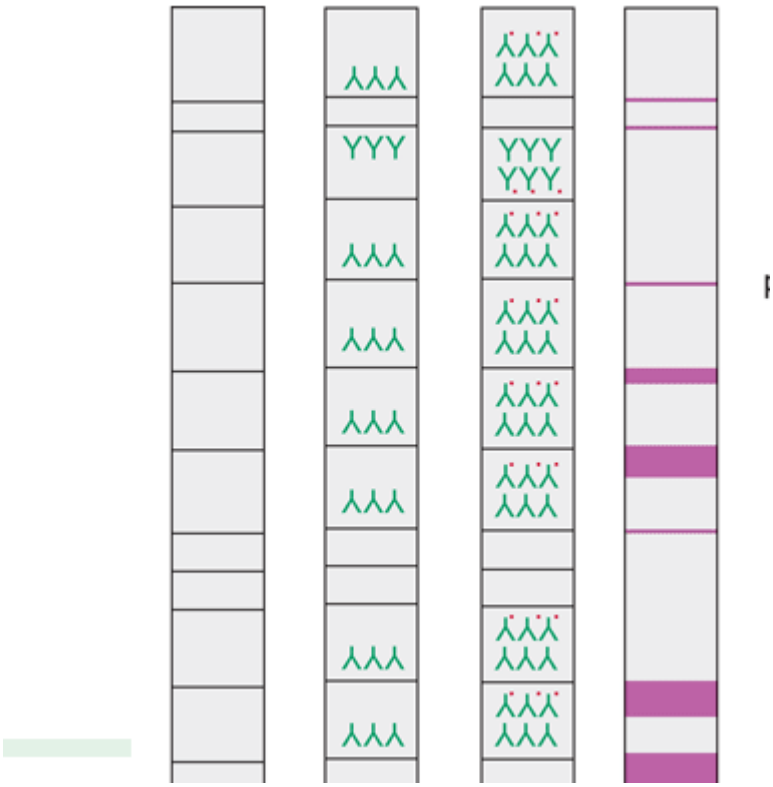
It is the best screening test for HIV infection. This test is also known as enzyme immunoassay. Results of this test is graded as positive(highly reactive), intermediate (partially reactive) and negative (nonreactive).

If results are intermediate it should be repeated within 4-6 wks ELISA test is positive usually within 22 days of infection.



WESTERN BLOT TEST

Western blot based on detection of specific antibody to viral core protein p24 and envelope glycoprotein p41. Results of this test is also graded as positive(highly reactive),intermediate (partially reactive) and negative (nonreactive). If results are intermediate it should be repeated within 4-6 weeks



WESTERN BLOT TEST

TESTS FOR MONITORING OF PATIENTS WITH HIV INFECTION

1.CD4 T cell count

2.HIV RNA estimation

3.Complete blood count

4.HIV resistance testing

5.Co-receptor tropism arrays.

6.Beta2 microglobulin

INITIAL EVALUATION OF PATIENT WITH HIV INFECTION

- History&Physical examination
- Complete hemogram
- Liver and renal function tests
- Blood sugar&Lipid profile
- CD4 count
- HIV RNA level
- Screening for Hepatitis A,B&C,syphilis&tuberculosis
- Pretest counseling

INDICATIONS FOR INITIATION FOR ANTIRETROVIRAL THERAPY

1.Acute infection syndrome

2. Chronic infection

A. Symptomatic disease (including HIV-associated nephropathy)

B. Asymptomatic disease 1. CD4+ T cell count <500/

2. Pregnancy

3. Postexposure prophylaxis.

POSTEXPOSURE PROPHYLAXIS

Postexposure prophylaxis is a necessary secondary preventive measure in health care workers and and those who are exposed to risk of HIV infection. Post exposure prophylaxis should be initiated as soon as possible within the first few hours and not later than 72hours of exposure.Two NRTI'S used for 4 weeks for less severe exposure and two NRTI'S plus other group of drugs.

MONITORING THE EFFICACY OF ART :

- "Clinical improvement – gain in weight, decrease in occurrence & severity of HIV related infections
- Increase in total lymphocyte count
- Improvement in biological markers of HIV – CD4 count & RNA"

PREVENTIVE MEASURES IN HIV INFECTION :

Health Education regarding safe sex practice,avoidance of IV drug abuse and tattooing is most important measure in preventing HIV transmission.All blood donors should be screened for HIV infection to prevent blood borne infections.

Avoiding unnecessary injections and use of sterilised disposable needle & syringes are also an effective measures in preventing HIV transmission.

Pregnant women with HIV infection should be advised to avoid pregnancy to reduce the mother to fetus transmission.

CLASSIFICATION OF ANTI RETROVIRAL DRUGS

NUCLEOSIDE OR NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS

DRUGS	DOSE	COMMON SIDE EFFECTS
ZIDOVUDINE	200mg tds or 300 mg bd	Anaemia, neutropenia, lactic acidosis, cardio toxicity
DIDANOSINE	200mg bd	Peripheral neuropathy, pancreatitis,

		hepatitis.
ZALCITABINE	0.75mg tds	Peripheral neuropathy, aphthous ulcers, hepatitis.
STAVUDINE	40mg bd	Peripheral neuropathy, pancreatitis, hepatitis.
LAMIVUDINE	150mg bd	Rash and peripheral neuropathy
EMTRICITABINE	200 qid	Skin discoloration and hepato toxicity.
ABACAVIR	300 bd	Rash, fever.
TENOFOVIR	300 qid	Gastrointestinal distress. Renal toxicity.

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

DRUGS	DOSE	COMMON SIDE EFFECTS
NEVIRAPINE	200mg od	Skin rash, hepatotoxicity.
DELAVIRIDINE	400 mg tds	Skin rash, hepatotoxicity
EFAVIRENZ	600 mg	Skin rash, neurological disturbances

	od	
EDRAVIRINE	200 mg bd	Skin rash.
RILIPIVIRINE	25 mg qid	Dizzinesss,nausea,vomiting, neurological disturbances

PROTEASE INHIBITORS

DRUGS	DOSE	COMMON SIDE EFFECTS
SAQUINAVIR	1000mg bd	GI disturbances, dyslipidemia, PR and QT interval prolongation
RITONAVIR	600 mg bd	GI disturbances, dyslipidemia, hepatitis
INDINAVIR	800 mg tds	Dyslipidemia, renal stones.
NELFINAVIR	750 mg tds	GI disturbances, dyslipidemia,
AMBRANAVIR	1200 mg bd	GI disturbances, dyslipidemia, renal stones.
LOPINAVIR	400mg /100mg bd	GI disturbances, dyslipidemia, PR and QT interval prolongation
ATAZANAVIR	400 mg qid	GI disturbances, dyslipidemia, PR and QT interval prolongation, skin rash.
TIPRANAVIR	500 mg bd	GI disturbances, dyslipidemia, skin rash, hepatitis, intracranial hemorrhage

DARUNAVIR	600 mg bd	GI disturbances, dyslipidemia, skin rash, hepatitis.

ENTRY INHIBITORS

DRUGS	DOSE	COMMON SIDE EFFECTS
ENFUVIRTIDE	90 mg sc bd	Skin rash, local injection reaction, bacterial pneumonia
MARAVIROC	150 to 600 mg bd	Hepatotoxicity, skin rash, gastro intestinal disturbances, musculoskeletal symptoms.

INTEGRASE INHIBITORS

DRUGS	DOSE	COMMON SIDE EFFECTS
RALTEGAVIR	400mg bd	GI disturbances, muscle weakness, rhabdomyolysis.
ELVITEGRAVIR	Under trial	Under trial.

RENAL ABNORMALITIES IN HIV PATIENTS

“HIV infection is the one of the leading cause of acquired renal disease throught the world. Renal abnormalities are one of the most common cause of death in HIV patients.HIV -1 infection is associated with glomerular and tubule interstitial disease, and patients with HIV infection are likely to risk for nephro

toxicity from antiretroviral therapy as well as from other medications. Co infections with the other pathogens, in particular hepatitis B and hepatitis C viruses, can complicate the clinical picture. Acute kidney injury and interstitial nephritis, due to medications and opportunistic infection, are not uncommon. As patients with HIV infection live longer period with ART, patients experiencing the complex, interacting effects of HIV itself, ART and the worldwide diseases of development, including atherosclerosis, metabolic syndrome, type 2 diabetes and end stage renal disease are most common renal complications in HIV patients include asymptomatic micro albuminuria, Acute kidney injury, Glomerulardiseases,vascularnephropathy,tubulointerstitialnephritis,fluid and electrolyte abnormalities and chronic kidney disease".

ACUTE RENAL FAILURE

Acute renal failure has been reported in 20% of hospitalized HIV patients. The most common causes include prerenal azotaemia or acute tubular necrosis due to infection, diarrheal diseases, septicaemia ,bleeding, hypoalbuminaemia or nephrotoxins. Other least common causes include tubulo interstitial nephritis and crystal nephropathy. The main pathogenesis of prerenal azotaemia is due to true or effective depletion of intravascular volume. True volume depletion is mainly because of gastrointestinal fluid loss associated with diarrhea and / or vomiting. These patients are likely prone for disordered renal regulation of salt and water balance leading onto further intravascular volume depletion.

Insensible fluid losses associated with pulmonary disorders i.e lung fluid loss due to pneumonia and prolonged fever also results in decreasing intravascular volume. sepsis due to bacterial and fungal organisms is the leading cause of haemodynamic ARF in HIV patients. The main mechanism of prerenal azotaemia in sepsis is due to combination of endotoxin associated systemic vasodilatation , arterial hypotension, capillary leakage, and renal arteriolar vasoconstriction associated with vasopressor drug therapy. Other causes of prerenala zotaemia in HIV patients include hepatorenal syndrome severe pancreatitis caused by various infections and drugs, and congestive cardiomyopathy. Medication induced ATN is the most common cause of ARF in hospitalized HIV patients. Because of their attenuated volume depleted state, these pateints are at higher risk of drug induced ATN. Pentamidine and Amphotericin B are the other drugs which can cause ATN in HIV patients. Amphotericin B infusion acutely decreases renal blood flow and induces ischemic injury by the way of afferent arteriolar vasoconstriction. It also directly disrupts renal tubular membranes in a dose dependent manner.

ACUTE TUBULOINTERSTITIAL NEPHRITIS

ATIN classically presents with triad of fever, rash and eosinophilia. The development of this classical triad is extremely variable and more often due to both the class of drugs and the host response to the offending medication. Urine analysis helps in the diagnosis of ATIN by showing low grade proteinuria, renal

tubular cells, erythrocytes, and leukocytes and cast. Eosinophiluria, which is sometimes present in patients with ATIN, but it is not specific for the disease. Gallium scanning is also useful to provide more information in the evaluation of suspected ATIN. Gallium uptake persists for 48 to 72 hours, but it is not specific for the diagnosis of ATIN, but appears relatively sensitive. Gold standard diagnosis for ATIN is renal biopsy. Biopsy specimen shows either patchy or diffuse infiltration of the interstitium with lymphocytes, plasma cells and eosinophils. Medications causing ATIN in HIV infected patients

1.beta-lactam antibiotics

2.sulfonamides

3.Histamine receptor blockers

4.quinolones

5.allopurinol

6.phenytoin

7.NSAID

CRYSTAL INDUCED NEPHROPATHY

“Deposition of insoluble crystals at kidney results in nephropathy in HIV infected patients. Intratubular crystal precipitation causes severe ARF. spontaneous chemotheraphy induced lysis of tumour cells is associated with release of intracellular purines that are converted to uric acid in systemic

circulation. These crystals are precipated in tubular lumen of the distal nephron causing intrarenal obstruction. Intravascular depletion and also acidic urine increases the risk of crystal deposition. Medications like sulphadiazine, acyclovir, indinavir and foscarnet causes intrarenal crystal deposition. Acidic urine causes further increases precipitation of these drugs in the kidney. Hypoalbuminaemia also results in higher plasma and urine free concentration of sulphonamides. Urine analysis results in characteristic needle shaped or rosette formation. Renal ultrasound studies reveal sulpha based uroliths and other calculous material sludging in the renal calices".

"ETIOLOGY OF HIV ASSOCIATED CRYSTAL NEPHROPATHY

CRYSTAL TYPE	**RISK FACTORS**
Uric acid	Volume depletion Acid urine (pH <5.5
Sulfadiazine	Volume depletion Acid urine (pH <5.5) Renal insufficiency
Acyclovir	Volume depletion Renal insufficiency

	Rapid intravenous infusion
Indinavir	Volume depletion Alkaline urine (pH>5)
Foscarnet	Volume depletion Renal insufficiency Rapid intravenous infusion”

GLOMERULAR DISORDERS

Glomerular disorder of HIV infection is a collapsing glomerulopathy. Previously it was explained as focal segmental glomerulosclerosis and then it is called as HIV associated glomerulopathy. HIV associated glomerulopathy explains all the pathological process in glomeruli associated with HIV infection.

ETIOLOGY AND PATHOGENESIS

HIV associated Collapsing glomerulopathy occurs in acute and chronic infection. In chronic cases, there will be high Viral RNA level with low CD4 t-lymphocyte count. In chronic and latent infection glomerular and tubular cells are affected. Accessory HIV proteins damage the renal cells, it was

experimentally done in transgenic mouse. It seems to that variation in MYH9 risk haplotype contributes to the risk for focal segmental glomerulosclerosis and collapsing glomerulopathy. MYH9 genetic variation is associated with Apolipoprotein L1, which is a constituent of HDL

CLINICAL MANIFESTATIONS

Edema, Proteinuria and Renal insufficiency, Reduced GFR. Imaging studies proved the increased kidney size. Increased echogenicity, but this is an unusual feature correlated with diabetic nephropathy and amyloid nephropathy. Renal biopsy is needed to confirm the disease.

PATHOLOGY

"On histological examination, HIV associated collapsing glomerulopathy is indistinguishable from Idiopathic collapsing glomerulopathy and is a pan-nephropathy with pathologic changes in glomeruli, tubules and interstitium. Both condition manifest tubuloreticular inclusions within dilated endosomal compartments within dilated endosomal compartments within glomerular endothelial cells, that is the marker for cytokine injury. In patients with hypertensive nephrosclerosis or interstitial nephritis, there will be glomerulomegaly and post adaptive FSGS caused by the glomerular hyperperfusion and hyperfiltration".

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

"Renal biopsy shows the classical changes of HIV associated collapsing glomerulopathy. Low CD4 count and Nephrotic proteinuria indicates HIV associated collapsing glomerulopathy. Plasma HIV RNA of less than 400copies/ml indicates another disease is more likely. Other diagnosis include the Diabetic nephropathy, hypertensive nephrosclerosis, HIV related immune complex glomerulonephritis".

HIV ASSOCIATED IMMUNE COMPLEX GLOMERULONEPHRITIS

"In European and asian descends the common glomerular pathology associated with HIV is Immune complex glomerulonephritis (ICGN). It is also seen in African descends. Major pathogenesis is not clear but it is believed that the disease is due to HIV antigen, but in some cases the immune complex shown to include HIV antigen and some are due to the general polyclonal B cell expansion that accompanies HIV disease. The patients present with hematuria and proteinuria thus it is clinically indistinguishable from HIV associated collapsing glomerulopathy. Histologically glomeruli shows diffuse or focal proliferative glomerulonephritis with endocapillaryproliferation.immune deposits are characterized by IgG and IgM or byIgG,IgM and IgA often with C3. They are similar to lupus nephritis but the serology for lupus is negative. The long term outcome of HIV associated ICGN has not been well defined but in general it is believed to be relatively benign in most of the cases, there are

few studies of therapy, presumably, control of HIV infection and conservative measures to control blood pressure and proteinuria are indicated".

ELECTROLYTE DISTURBANSES IN HIV INFECTED PATIENTS:

SODIUM BALANCE :

Sodium is actively pumped out of cells by the Na,K+ -ATPase pump. Sodium around 85%- 90% is extracellular and ECF volume is a reflection of total body sodium content. Normally there is always balance occurs between sodium loss and sodium gain, If it fails edema and hypovolemic state occurs due to sodium excess and sodium deficit.Change in Na concentration usually reflect disturbed water haemostasis.

HYPONATREMIA

Hyponatremia is a common finding among HIV-infected persons, with a reported prevalence of 30-60% in hospitilized patients. It is associated with increased mortality in HIV-infected patients. In a study of 96 consecutive patients with acquired immune deficiency syndrome (AIDS) or AIDS-related complex(ARC) conducted in department of medicine, long island Jewish medical centre, New Hyde Park 11042,31.3% patients had hyponatremia. The

probability of 50% survival after diagnosis of HIV infection in the hyponatremic group was 11.5 months as compared to 39 months for those without hyponatremia, p less than0.001.

The etiology and treatment of hyponatremia may differ according to the timing of its presentation. Volume depletion caused by diarrhoea or vomiting is the usual cause of hyponatremia present at the time of hospital admission. The management includes correction of the volume depletion and also the treatment of the underlying. In contrast, the syndrome of inappropriate antidiuretic hormone(SIADH) is the likely culprit among patient who develop hyponatremia during hospitalization .SIADH is associated with common pulmonary and intracranial diseases such as pneumocystis jiroveci pneumonia, toxoplosmosis and tuberculosis.

POTASSIUM BALANCE:

It is major intracellular cation. Normal serum K+ level is 3.5-5.0 mmol/L,but intracellular level is 150 mmol/L so ECF contain <2 % of total body potassium level. The ratio of ICF to ECF K+ level is 38:1.This is responsible for the development of resting membrane potential and essential for neuromuscular function.

HYPOKALEMIA:

It is defined as plasma K+ level less than 3.5 mmol/L. Hypokalemia causes intracellular acidification , which result in increased acid excretion and new HCO_3- production. It occurs due to increased HCO_3- reabsorption in PCT & increased H^+ secretion distally. This is the reason for occurrence of metabolic alkalosis in patients with hypokalemia

Clinical findings:

Presents with fatigue,muscle cramps in mild cases. Constipation, ileus , flaccid paralysis , tetany, hypercapnea , hyporeflexia and rhabdomyolysis seen in severe hypokalemia.

HYPERKALEMIA :

Plasma K^+ level more than 5.0 mmol/L.It is due to either potassium release from cells or decreased renal loss. Clinical features depends upon the ratio of ICF to ECF K^+ concentration. Both hyperkalemia and hypokalemia are common among HIV infected patients, Hypokalemia occurs due to vomiting and diarrhoea after GI infection. Amphotericin causes tubular dysfunction causing diarrhoea. Drug induced hyperkalemia occurs in patients receiving either high dose trimethoprim-sulfamethoxazole or iv pentamidine. Kidney disease in HIV patients either acute or chronic may contribute to potassium retention. Other electrolyte disturbances were hypocalcemia, hypercalcemia, hypouricemia, hyperuricemia, lactic acidosis and hypophospotemia.

MATERIALS AND METHODS

STUDY POPULATION: This study was conducted among 200 HIV positive patients coming to ART centre, Govt.Rajaji Hospital, Madurai during the period of February 2016 to July 2016. The study group will be divided into two groups: Group A ART naive patients and Group B HIV patients on ART

INCLUSION CRITERIA:

All patients aged greater than 18 attending ART OPD, diagnosed with HIV infection irrespective of Anti Retroviral Therapy

EXCLUSION CRITERIA:

Patient with Diabetes mellitus
Endocrine disorder
Known Chronic kidney disease
Obstructive uropathy
Pregnancy

ANTICIPATED OUTCOME: High prevalence of Renal and Electrolyte disturbances in HIV infected patients.

DATA COLLECTION:

A previously designed proforma will be used to collect the demographic and clinical details of the patients. Two hundred patients will be selected randomly. All the patients will undergo detailed clinical evaluation, appropriate investigations. History will be taken on details of unprotected sexual intercourse , blood transfusion, IV drug abuse, repeated

respiratory infections, fever , recurrent diarrhoea and unexplained weight loss. Presence of lymphadenopathy, oral ulcers, splenomegaly and peripheral neuropathy will be noted. Blood urea, serum creatinine, blood glucose, Serum electrolytes , CD4 count, urine routine and 24 hour urine protein will be estimated..The study group will be divided into two groups: Group A ART naive patients and Group B HIV patients on ART.

LABORATORY INVESTIGATIONS: "CD4+ count, Blood sugar, Blood Urea, Serum Creatinine, Serum sodium, Serum potassium, serum chloride, urine routine and 24 hour urine protein".

DESIGN OF STUDY: cross sectional study

PERIOD OF STUDY: February 2016 To July 2016 (6 months)

COLLABORATING DEPARTMENTS:

- Department Of Biochemistry
- ART CENTRE

ETHICAL CLEARANCE: Applied for

CONSENT: Individual written and informed consent.

ANALYSIS:STATISTICAL ANALYSIS.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: SELF

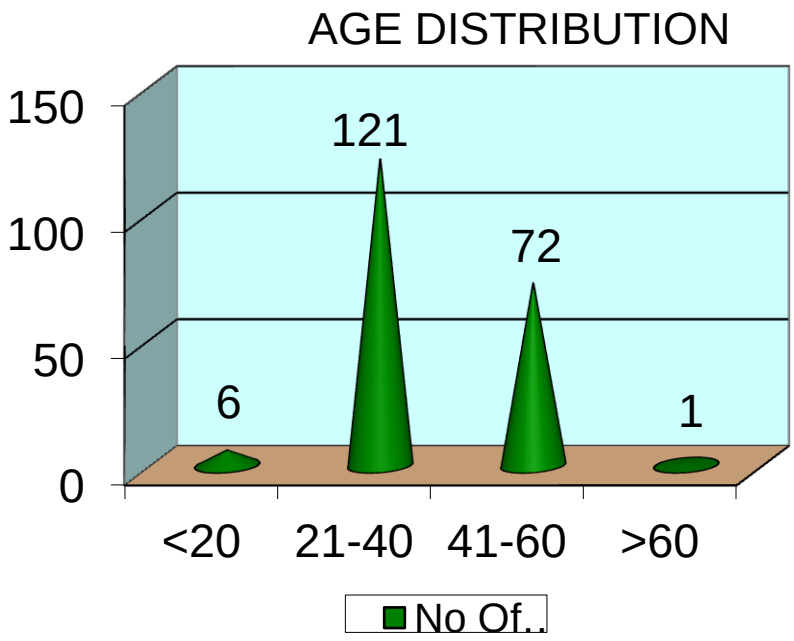
PARTICIPANTS: All patients with HIV infection, attending ART OPD of Government Rajaji Hospital, Madurai from February 2016 to July 2016 will be included in this study

OBSERVATION AND RESULTS

Table 1 Age distribution of the study population (n=200)

Age	No Of Patients
<20	6
21-40	121
41-60	72
>60	1
Total	200
Mean	37.075
SD	10.71

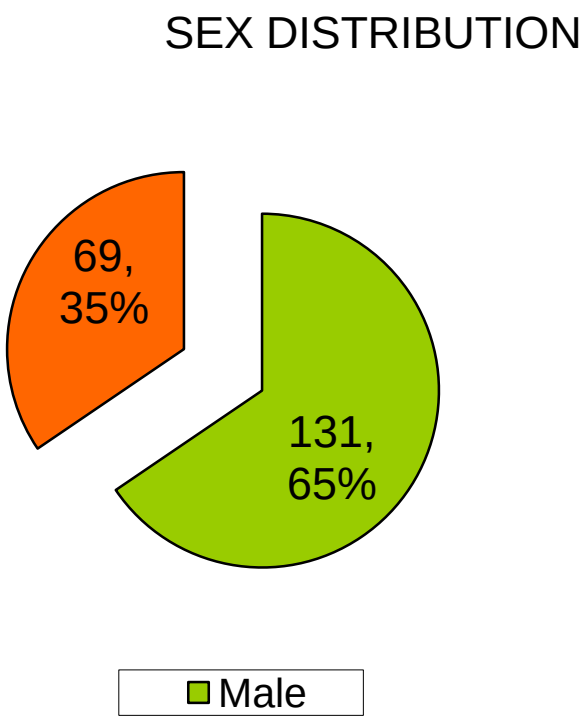
Comments: “About 60% of study population were in the age group of 21-40 years and 36% of study populalation were in the age group of 41-60 years’



Comment: Most of study population were in the age group of 21 to 60years.

SEX DISTRUBUTION

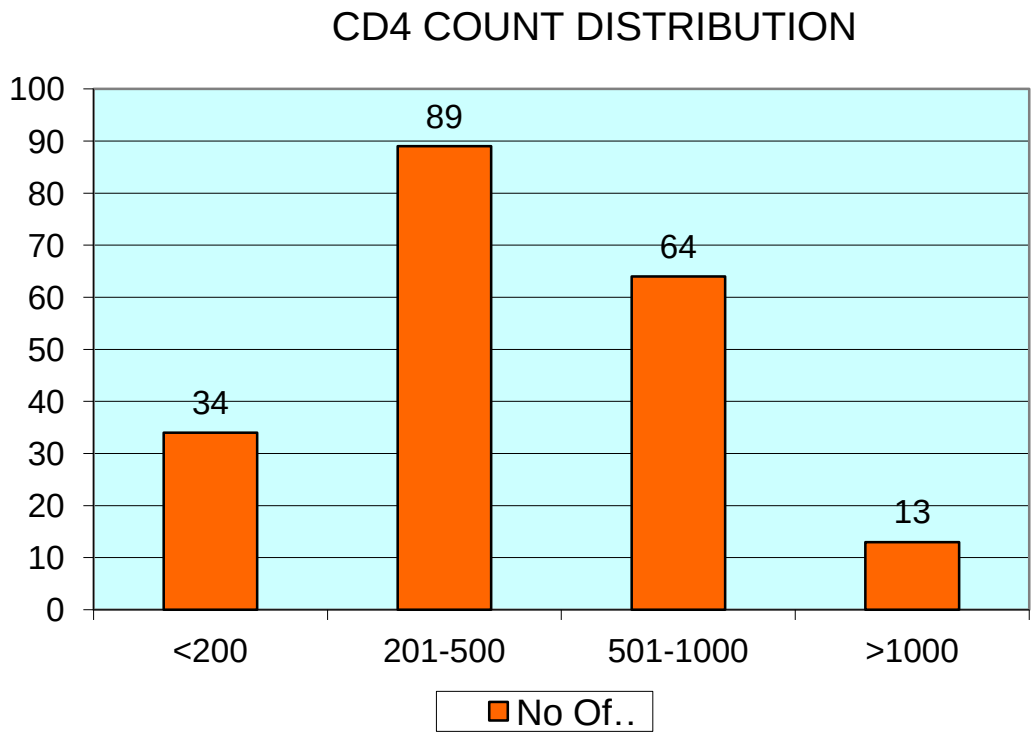
Sex	No Of Patients
Male	131
Female	69
Total	200



Comments: Males are slightly higher than in the study population

CD4 COUNT DISTRIBUTION

CD4 COUNT	No Of Patients
<200	34
201-500	89
501-1000	64
>1000	13
Total	200
Mean	480.89
SD	319.871

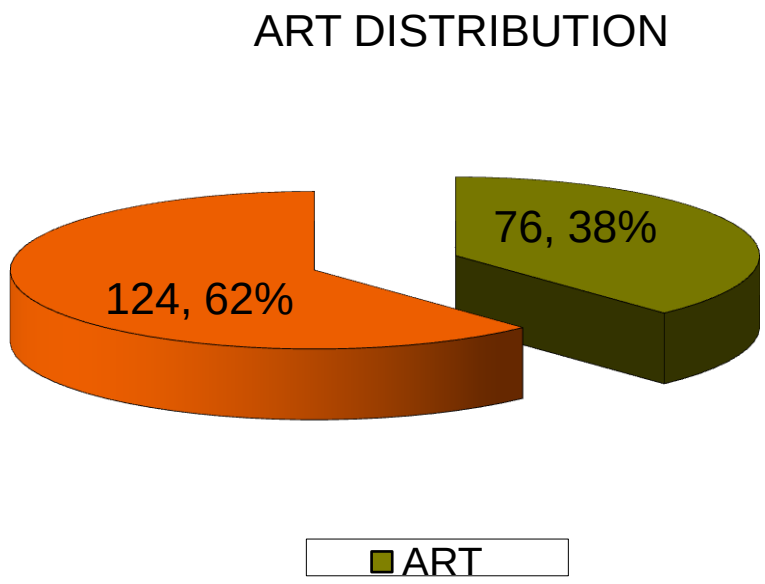


Comments : Around 45% patients have CD4 count between 200-500 and 32% patients have CD4 count 501-1000.

ART DISTRIBUTION

	No Of Patients
ART	76
ART NAÏVE	124
Total	200

	Male	Female	Total
ART	45	31	76
Nil	86	38	124
Total	131	69	200

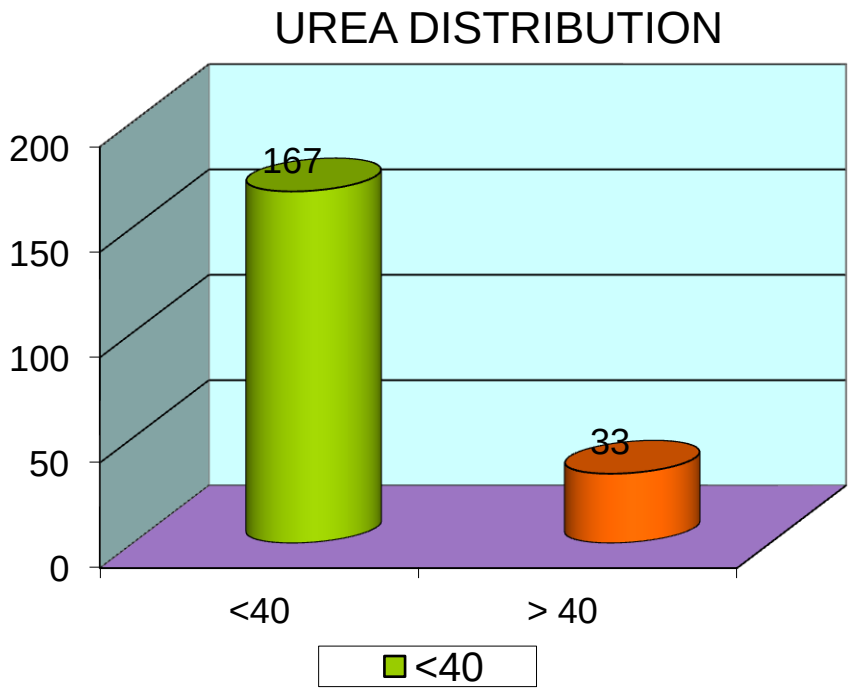


Comments -38% were on ART , 62% were ART naive.

UREA DISTRIBUTION

UREA	No Of Patients	Mean
<40	167	24.21
> 40	33	62.66
Total	200	
Mean	30.140	
SD	15.372	

Mean urea level in the study population was found to be 30.140 ; with a standard deviation of 15.372



	UREA	
ART STATUS	Mean	SD
ON ART	27.26	12.659
ART NAIVE	31.90	16.623
P VALUE	0.038 Sig	

Comments:

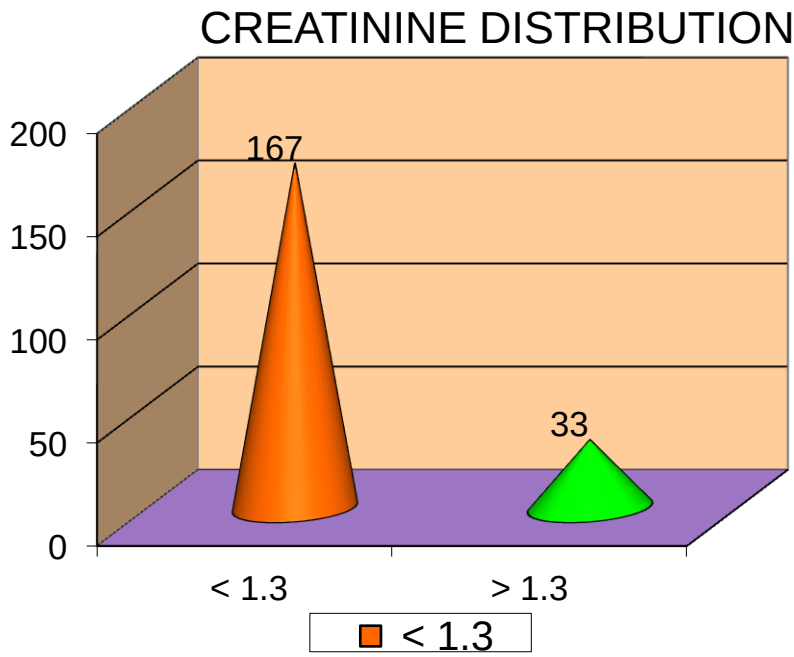
Elevated urea levels were found in 16.5% of study population. Among them elevated urea more in ART NAÏVE patients than patients taking ART. .p value of <0.038 statistically significant; indicates ‘renal abnormalities are higher in ART NAÏVE patients than patients on ART’.

CREATINE DISTRIBUTION

CREATININE	No Of Patients	Mean
≤ 1.3	167	0.92
> 1.3	33	2.22
Total	200	
Mean	1.109	
SD	0.618	

Comments :

Around 33 (16.5) patients were found to be having elevated serum creatinine >1.3 . Mean serum creatinine in the study population is 1.109 with a standard deviation of 0.618.



	CREATININE	
ART STATUS	Mean	SD
ON ART	1.00	0.328
ART NAIVE	1.18	0.735
P VALUE	0.047 sig	

Comments :

Mean creatinine in patients taking ART was 1.00 . Mean creatinine in ART naive patients was 1.18. p value 0.047 statistically significant**;** indicates renal abnormalities are higher in ART NAÏVE patients than patients on ART'.

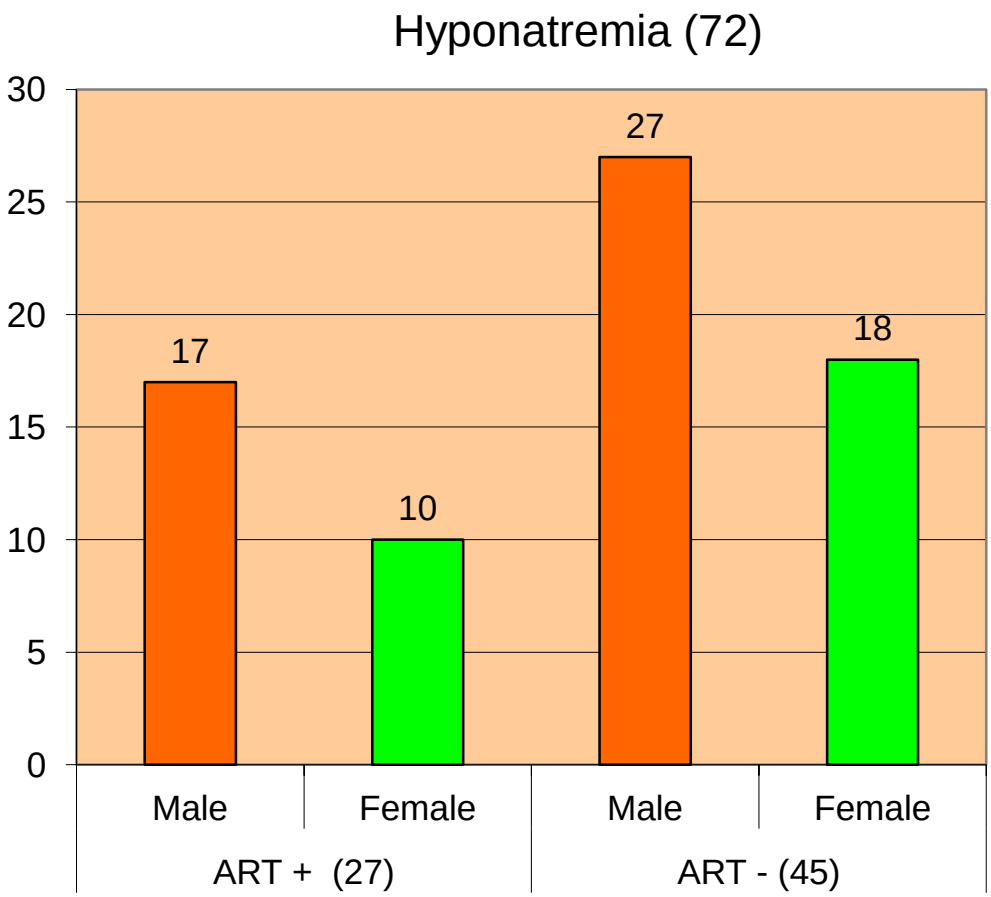
SODIUM DISTRUBUTION:

Na+	No Of Patients	Mean
<135	72	126.9
135-145	127	138.8
>145	1	147
Total	200	
Mean	133.7	
SD	7.199	

Comments: Around 72 (36%) patients were found to be having hyponatremia . Mean serum sodium in the study population is 133.7 with a standard deviation of 7.199

	ART + (27)		ART - (45)	
	Male	Female	Male	Female
Hyponatremia (72)	17	10	27	18

Comments : Among them 27 patients(37.5%)on ART and 45 patients(62.5%) were ART NAÏVE..



Comments :

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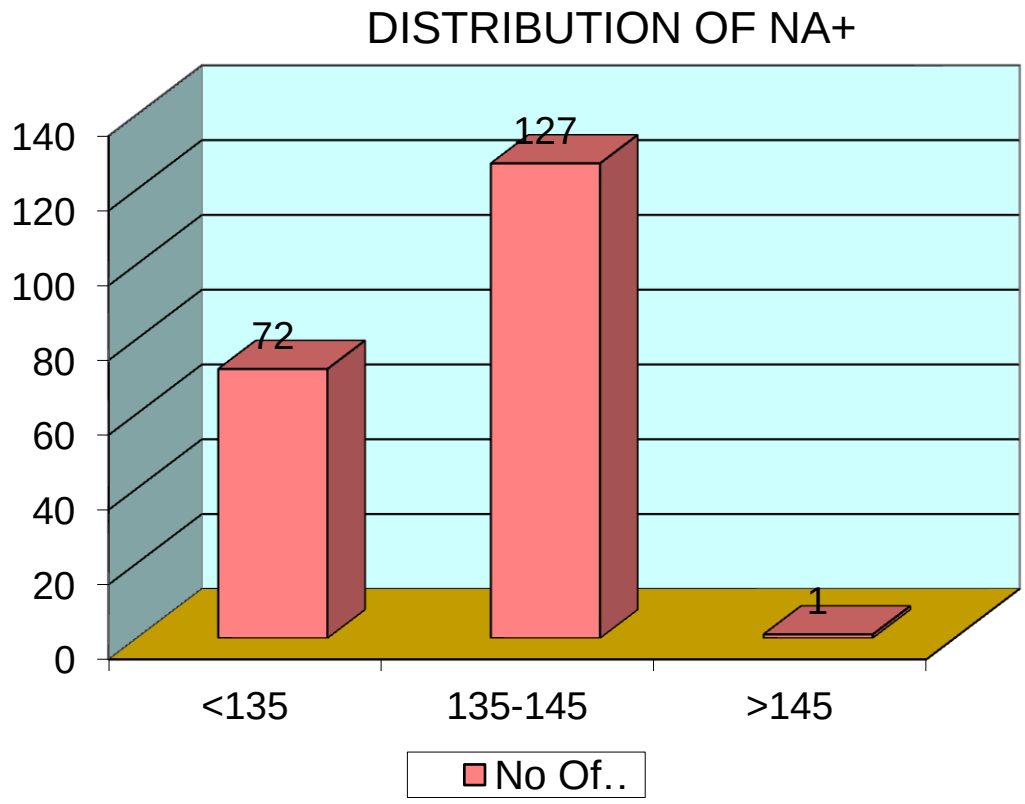


	Na +	
ART STATUS	Mean	SD
ON ART	135.13	6.109
ART NAIVE	132.82	7.685
P VALUE	0.027 sig	

Comments:

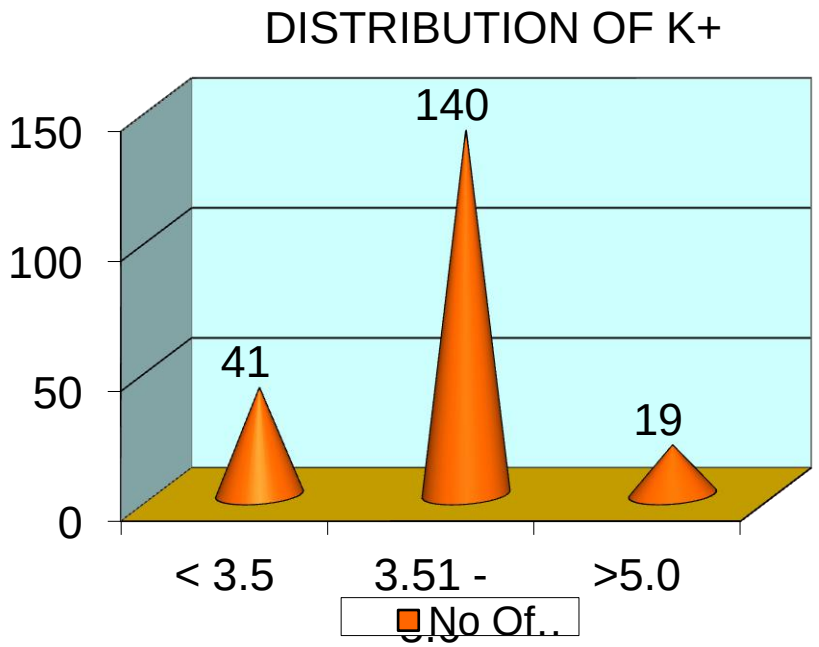
Serum sodium level found to be decreased in more ART naïve patients than those on ART, p value was< 0.027, statistically significant ,indicate Na+ level was significantly lower in ART NAÏVE patients compared to patients on ART.

DISTRUBUTION OF POTASSIUM

K+	No Of Patients	Mean
< 3.5	41	3.06
3.51 - 5.0	140	4.09
>5.0	19	5.55
Total	200	
Mean	3.892	
SD	0.894	

Comments :

Around 41 (20.5%) patients were found to be having hypokalemia . Mean serum potassium in the study population is 3.892 with a standard deviation of 0.894

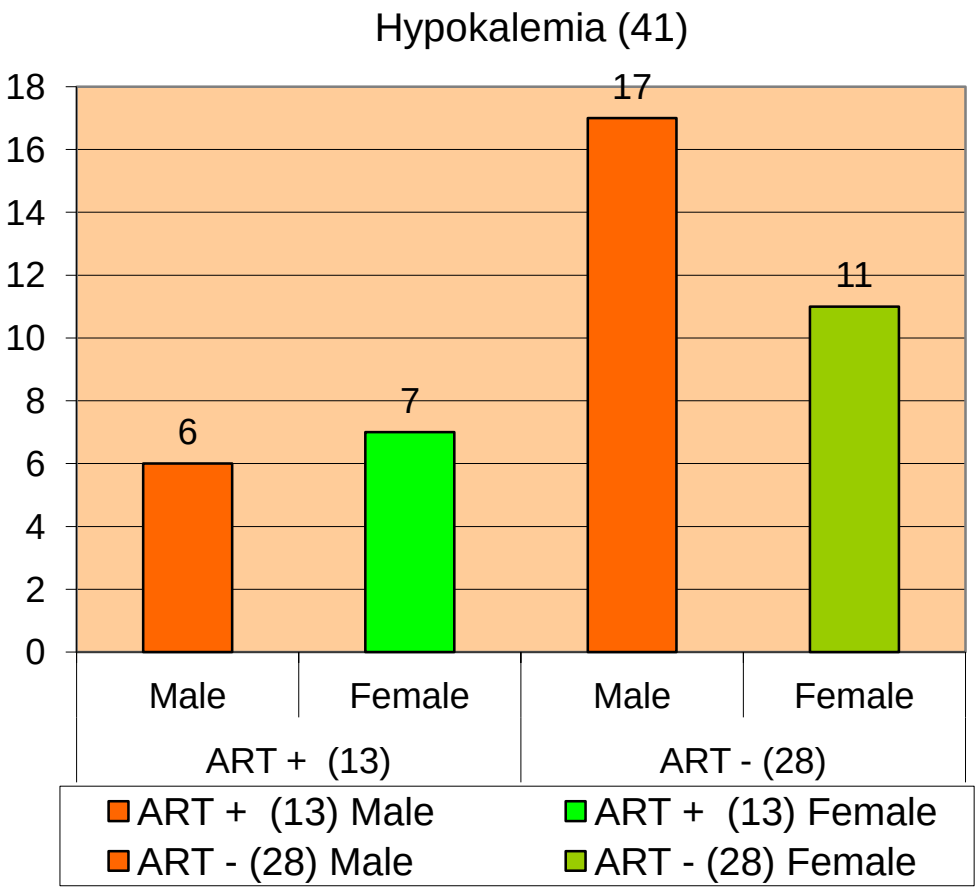


Comments :

Serum Potassium level decreased in 41 patients(20.5%) of study population, among them 13 patients (31.7%) on ART and 28 patients(68.3%) were ART NAÏVE.

	ART + (13)		ART - (28)	
	Male	Female	Male	Female
Hypokalemia (41)	6	7	17	11

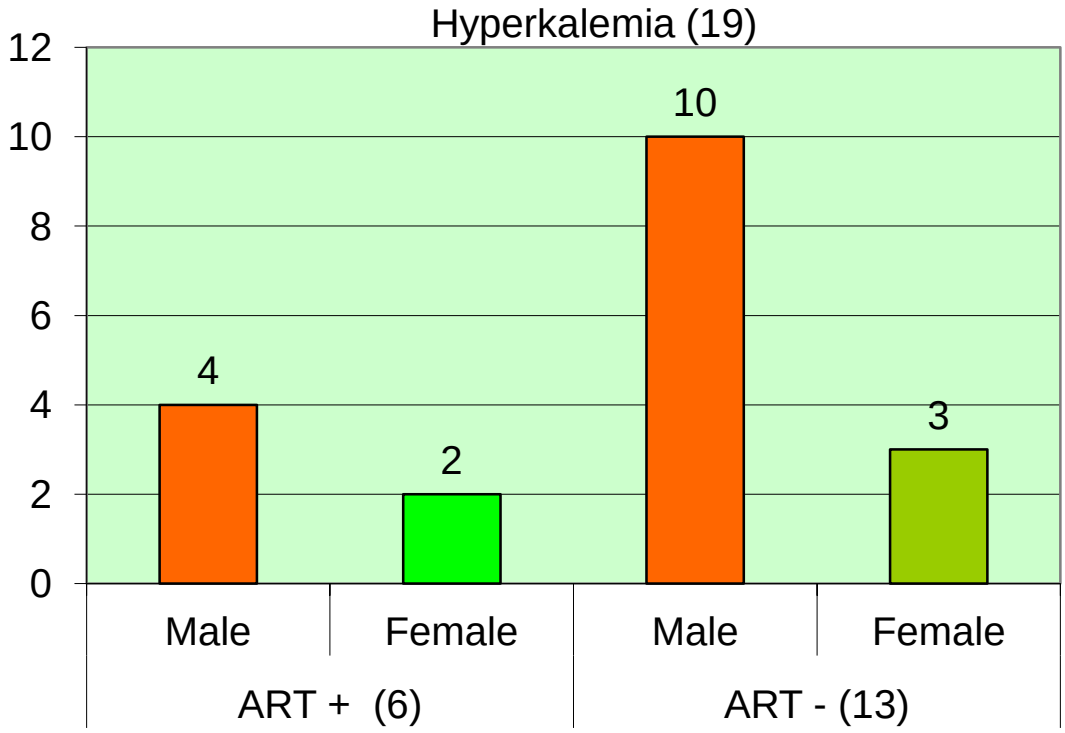
Comments : Serum Potassium level decreased in 41 patients(20.5%) of study population, among them 13 patients (31.7%) on ART and 28 patients(68.3%) were ART NAÏVE.



Comments : Serum Potassium level decreased in 41 patients(20.5%) of study population, among them 13 patients (31.7%) on ART and 28 patients(68.3%) were ART NAÏVE.

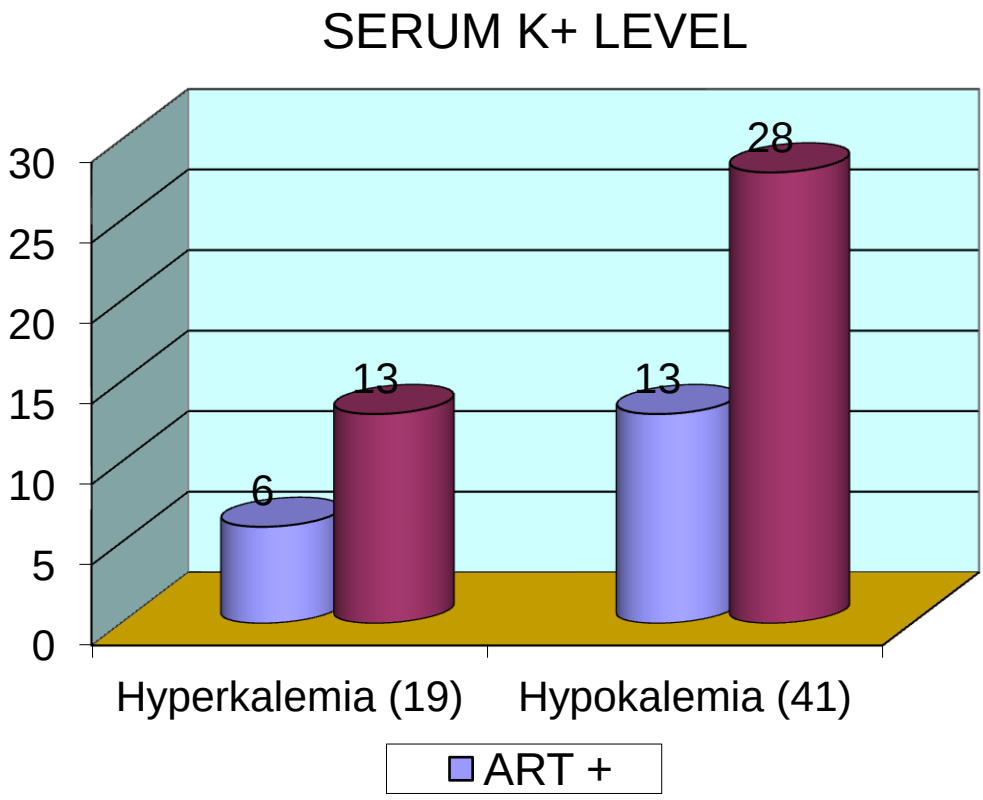
	ART + (13)		ART - (6)	
	Male	Female	Male	Female
Hyperkalemia (19)	10	3	4	2

Comments：Serum Potassium level increased in 19 patients(9.5%) of study population, among them 13 patients(68.4%)on ART and 6 patients(31.6%) were ART NAÏVE.



Comments :

Serum Potassium level incresed in 19 patients(9.5%) of study population, among them 13 patients(68.4%)on ART and 6 patients(31.6%) were ART NAÏVE. Serum Potassium level found to be increased in more ART patients than those on ART NAÏVE.

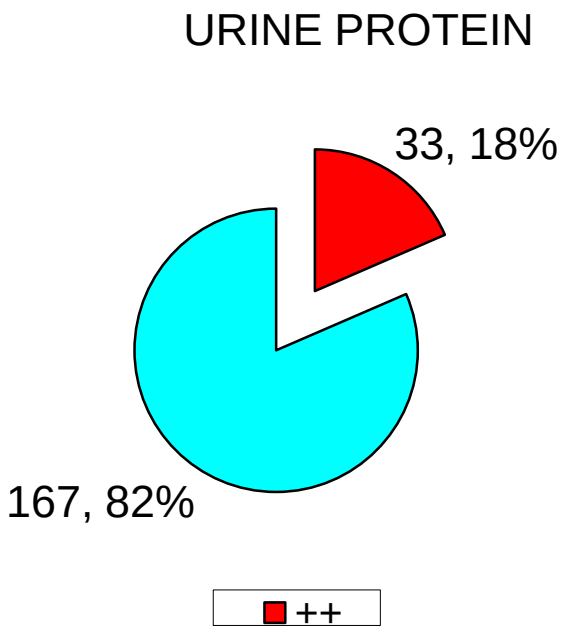


	K +	
ART STATUS	Mean	SD
ON ART	4.09	0.844
ART NAIVE	3.77	0.906
P VALUE	0.015 sig	

Comments: Serum Potassium level found to be decreased in more ART naïve patients than those on ART, p value was< 0.015, statistically significant ,indicate K+ level was significantly lower in ART NAÏVE patients compared to patients on ART.

URINE PROTEIN	No Of Patients
++	37
NIL	163
Total	200

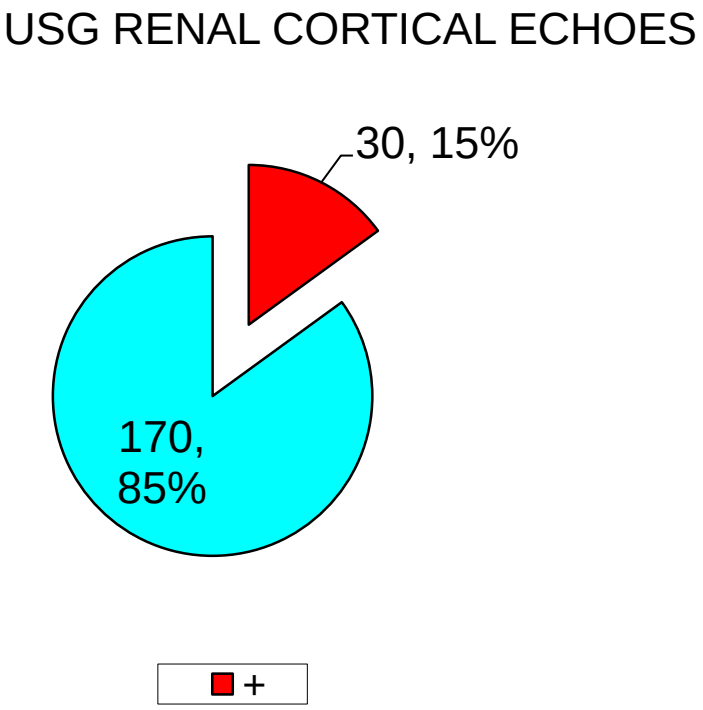
	ART + (9)		ART - (24)	
	Male	Female	Male	Female
Protenuria (33)	6	3	18	6



Comments : Proteinuria present in 33 patients (16.5%) of study population, among them 9 patients (27%) on ART and 24 patients (73%) were ART NAÏVE. Significant proteinuria was higher in ART NAÏVE patiens and lower in patient taking ART.

USG Renal cortical echoes :

USG- ↑ renal cortical echoes	No Of Patients
+	30
NIL	170
Total	200



Comments :

USG abdomen shows increased cortical echoes in 30 patients (15%) of study population, among them 7 patients (23%) on ART and 23 patients (77%) were ART NAÏVE. Renal cortical echoes were higher in ART NAÏVE patiens and low occurence in patient taking ART.

CD4 CORRELATION COEFFICIENT;

	CORRELATION coefficient	
CD4 COUNT VS UREA	0.04	Very Low
CD4 COUNT VS CREATININE	-0.01	Neg
CD4 COUNT VS Na+	0.128	Low
CD4 COUNT VS k+	0.071	Very Low

Comments :

In this study, there is very low correlation coefficient between CD4 counts and urea. There is negative correlation coefficient between CD4 counts and creatinine. The correlation coefficient is low between CD4 count and Na^+ ,K^+ levels.

DISCUSSION

Renal and electrolyte abnormalities are more common in HIV infection .This study was conducted in 200 HIV patients selected randomly irrespective of their ART status who attending ART clinic, Government Rajaji Hospital, Madurai. The study population were divided into 2 groups according to ART status. Group A ART naive patients and Group B HIV patients on ART. .About 60% of study population were in the age group of 21-40 years and 36% of study population were in the age group of 41-60 years.

Around 62% of study population were ART NAIVE and 38% were on ART. Gender distribution is of around 65% male and 35% female. Blood urea ,serum creatinine, Urine protein ,Serum sodium. Serum potassium and USG abdomen were performed in study populations.

Blood urea level was raised in 33 patients (16.5%) of study population, among them 9 patients (27%)on ART and 24 patients (73%) were ART NAÏVE. Blood urea level raised in ART naïve patients, p value was 0.038, statistically significant , indicate urea level was higher in ART NAÏVE patients and lower in patient taking ART.

Serum creatinine level was raised in 33 patients (16.5%) of study population, among them 9 patients (27%) on ART and 24 patients (73%) were ART NAÏVE. Serum creatinine level raised in ART naïve patients, p value was 0.047, statistically significant, indicate cretinine level was higher in ART NAÏVE patients and lower in patient taking ART.

Proteinuria present in 33 patients (16.5%) of study population, among them 9 patients (27%) on ART and 24 patients (73%) were ART NAÏVE. Significant proteinuria was higher in ART NAÏVE patiens and lower in patient taking ART.

USG abdomen shows increased cortical echoes in 30 patients (15%) of study population, among them 7 patients (23%) on ART and 23 patients (77%) were ART NAÏVE. For all the patients, cortico medullary differentiation was maintained. Renal cortical echoes were higher in ART NAÏVE patiens and low occurence in patient taking ART.

Review literature shows that Renal involvement found to be common in HIV infected patients.A low occurrence of renal involvement found in patients taking ART'.HIV nephropathy in US population shows heavy proteinuria and they found to develop progressive renal disease. So HIV patients are to be monitored for proteinuria. It helps to know about 1)Triggering factor

2)Progression of renal involvement 3)To minimize renal complication. HIV infected patients with oppurtinstic infectios were more prone for renal and electrolyte disturbances.

Review literature shows renal complications affects particular group of people that there will be a host response or genetic component linked with the disease incidence. The genetic predisposition in the pathogenesis of HIV nephropathy were cytokines such as

1)TGF – B

2)IL – 8

3)Monocytic chemotactic protein 1

4)RANTES

5)IFN. The above cytokines levels were found to be elevated in HIV patients with nephropathy. Over all study shows there is increased renal disturbances in ART NAÏVE patients than patients on ART suggest some renoprotective effect of ART and indicates decreased incidence of oppurtinistic infections.

Serum sodium level decresed in 72 patients(36%) of study population, among them 27 patients(37.5%)on ART and 45 patients(62.5%) were ART NAÏVE. Serum sodium level found to be decreased in more ART naïve patients than

those on ART, p value was< 0.027, statistically significant ,indicate Na+ level was significantly lower in ART NAÏVE patients compared to patients on ART.

Serum Potassium level decresed in 41 patients(20.5%) of study population, among them 13 patients(31.7%)on ART and 28 patients(68.3%) were ART NAÏVE. Serum Potassium level found to be decreased in more ART naïve patients than those on ART, p value was< 0.015, statistically significant ,indicate K+ level was significantly lower in ART NAÏVE patients compared to patients on ART

Serum Potassium level increased in 19 patients(9.5%) of study population, among them 13 patients(68.4%) on ART and 6 patients (31.6%) were ART NAÏVE. Serum Potassium level found to be increased in more ART patients than those on ART NAIVE, Probably due to drug intake such as Co-Trimoxazole, etc,.

Hyponatremia, hypokalemia and hyperkalemia are common electrolyte disturbances in HIV. I described here higher incidence of electrolyte disturbances in ART naive patients than patients taking ART. Numerous factors contributing this. Among 200 patients 72 patients had hyponatremia.The percentage of hyponatremia is 36%.

The incidence of hyponatremia may be due to

1.Volume depletion due to diarrhea and vomiting

2.The syndrome of inappropriate antidiuretic hormone

3.Persistent release of antidiuretic hormone release from infections.

In persistent vomiting and diarrhea cause hypoosmolar hyponatremia , but in SIADH there is euvolemic.

Hypokalemia occur due to gastrointestinal infections causing vomiting and diarrhea. “ Tenofovir has associated with proximal tubular dysfunction results in salt wasting state, including life threatening hypokalemia”.

SUMMARY:

HIV infection is most commonly associated with renal and electrolyte abnormalities. This study was conducted in 200 HIV patients irrespective of their ART status, and the study population were divided into 2 groups. Group A ART NAIVE patients and Group B patients taking ART. About 60% of study population were in the age group of 21-40 years and 36% of study population were in the age group of 41-60 year.

Around 62% of study population were ART NAÏVE remaining 38% of study population were taking ART. In the study group, 65% were males and 35% were females. Blood urea, Serum creatinine, Serum sodium , Serum Potassium, Urine protein and USG abdomen were done in all patients.

Elevated urea and creatinine levels were found in 16.5% of study population. Among them elevated renal parameters more in ART NAÏVE patients than patients taking ART. Since means are compared student t test used in this study. p value <0.038 and < 0.047 statistically significant indicates renal abnormalities are higher in ART NAÏVE patients than patients on ART.

Proteinuria present in 15% of the study population, which is more among ART NAÏVE patients. USG abdomen study shows increased renal cortical echoes in

15% of the study population. Cortico medullary differentiation maintained in all patients. It excludes chronic kidney disease.

Hyponatremia found in 36% of study population. Among them hyponatremia more in ART NAÏVE patients than patients taking ART. ‘p value <0.027 statistically significant indicates hyponatremia are higher in ART NAÏVE patients than patients on ART’

Hypokalemia found in 20.5% of study population. Among them hypokalemia more in ART NAÏVE patients than patients taking ART. ‘p value <0.015 statistically significant indicates hypokalemia are higher in ART NAÏVE patients than patients on ART’.

Hyperkalemia found in 9.5% of study population. Among them hyperkalemia less in ART NAÏVE patients than patients taking ART. In this study, there is very low correlation coefficient between CD4 counts and urea. There is negative correlation coefficient between CD4 counts and creatinine. The correlation coefficient is low between CD4 count and Na^+ ,K^+ levels

CONCLUSION :

- Renal involvement was seems to be common in Indian patients with HIV. Elevated Blood urea, serum creatinine and proteinuria could be an early marker of HIV associated renal lesions and screening for their presence may be beneficial.
- A low occurrence of renal involvement found in patients already on ART suggests some renoprotective effect of ART
- Hyponatremia, hypokalemia and hyperkalemia are common electrolyte disorders in HIV infected patients. Among them hyponatremia and hypokalemia incidence more in ART NAIVE patients than patient on ART.
- This indicates decreased incidence of electrolyte disturbances on patients on ART may be due to less oppurtunistic infections in them.
- The present findings need to be confirmed with further studies with larger sample size and prolonged period of follow up.

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PROFORMA

Name:

Age / Sex:

IP / OP no:

Occupation:

Presenting complaints:

Past History:

H/o , unprotected sexual intercourse, blood transfusion, tattoing, iv drug use,

H/o CLD, DM, HT, CKD, CVD, DRUG INTAKE, THYROID DISORDERS , EPILEPSY , HEPATITIS.

Personal history

alcoholic/ non alcoholic

smoker/ nonsmoker

Clinical Examination:

Consciousness

Orientation

Afebrile /Febrile

Pallor/no pallor

Cyanosis/ No cyanosis

Clubbing/No clubbing

Pedal edema / no pedal edema

Height :

Weight :

VITALS

Temperature

Pulse rate

Blood pressure

Respiratory rate

Oxygen saturation

SYSTEMIC EXAMINATION

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM

ABDOMEN

CNS

Diagnosis

MASTER CHART

S.No.	ART No.	AGE	SEX	CD4 COUNT	ON ART	UREA	CREATININE	Na+	K+	URINE PROTEIN	USG- ↑ renal cortical echoes
1	18588	23	M	497	-	20	0.9	126	3.5	+	-
2	18566	47	M	1121	-	32	0.7	135	3.5	+	-
3	18587	38	F	763	-	16	1.2	122	4	+	-
4	18595	31	F	532	-	22	0.8	122	4.5	-	-
5	18597	44	M	1389	-	21	1	136	3.9	-	-
6	9909	25	M	180	+	46	1.4	144	3.7	+	+
7	18599	46	M	158	-	18	1.1	137	5.2	-	-
8	18629	55	M	458	-	24	0.6	120	4	-	-
9	18023	44	M	480	-	58	1.6	142	3.7	+	+
10	18639	23	F	572	-	30	0.9	125	4.1	+	-
11	18657	24	M	180	-	21	1	140	4.1	+	-
12	18690	30	M	576	-	26	1.2	136	4.2	-	-
13	18478	26	F	566	-	58	2.2	138	5.1	-	+
14	18456	34	M	132	-	28	1.1	120	4	-	-
15	18464	45	F	745	-	22	0.9	139	4.8	+	-
16	18485	28	F	640	-	21	1.2	135	3.5	-	-
17	18490	53	m	129	-	42	1.6	137	2.2	+	-
18	18495	40	F	745	-	40	0.9	132	2.1	-	-
19	18488	44	M	430	-	28	1.1	140	2.2	-	-
20	18525	44	F	1023	-	36	0.9	138	3	+	-
21	18533	48	M	656	-	32	1	122	5.2	-	-
22	18536	19	M	487	-	28	1.1	136	5	+	-
23	18539	25	F	563	-	30	0.7	140	2.2	-	-
24	18825	44	M	1023	-	52	1.7	136	4	+	+
25	9962	28	M	322	+	28	1.2	128	5	-	-
26	9963	69	F	97	+	24	0.9	145	5.6	-	-
27	9965	56	M	269	+	20	0.6	128	3.8	-	-
28	9969	26	M	312	+	18	1	130	3.5	+	-
29	9913	16	M	107	+	46	1.5	136	3.7	-	+
30	9974	37	F	155	+	16	0.7	137	3.2	-	-
31	9973	40	M	206	+	24	0.7	130	3.5	-	-
32	9967	35	M	396	+	58	1.9	135	3.7	+	+
33	9976	22	F	501	+	20	0.9	134	4	-	-
34	9977	29	M	287	+	26	1	128	5	-	-
35	9978	55	F	107	+	29	1.2	135	2.8	-	-
36	9980	27	M	325	+	38	1.1	137	5.6	+	-
37	18544	46	F	734	-	52	1.7	140	3.7	+	+
38	9981	35	F	256	+	30	1	138	3.5	-	-
39	9982	28	M	513	+	28	0.7	132	3.6	-	-
40	18566	31	F	532	-	60	1.8	144	4	-	+

41	9983	27	M	654	+	21	0.9	134	4.5	-	-
42	9940	45	M	89	+	18	0.6	124	5.5	-	-
43	9943	41	F	84	+	20	0.8	135	3.1	-	-
44	9945	29	F	442	+	16	1	130	5	-	-
45	9950	39	F	165	+	18	0.6	136	3.6	-	-
46	9952	43	M	72	+	24	1.2	142	4.2	-	-
47	18635	29	M	424	-	115	7.1	135	4.1	-	+
48	9953	56	F	295	+	26	0.8	140	5.6	-	-
49	9955	33	M	366	+	29	0.9	126	5	-	-
50	9956	21	F	74	+	19	0.7	145	2.7	-	-
51	9957	53	M	374	+	23	1.1	128	3.5	+	-
52	9959	19	M	378	+	22	1	135	3.9	+	-
53	9948	35	F	232	+	48	1.4	137	5.8	-	+
54	9960	39	M	407	+	25	1.2	140	3.5	-	-
55	18686	23	M	615	-	70	2	135	5.2	+	+
56	9961	25	F	458	+	27	0.7	130	4.2	-	-
57	18830	38	M	567	-	28	0.6	120	4.5	-	-
58	18840	35	M	566	-	32	0.7	126	4.1	-	-
59	18915	45	F	145	-	36	0.8	124	5	+	-
60	9949	22	M	240	+	67	1.7	135	3.5	-	+
61	18921	42	F	560	-	30	0.7	120	4.5	-	-
62	18924	18	M	1120	-	26	1.2	137	2.1	+	-
63	18938	36	M	364	-	22	1.1	126	3.5	-	-
64	9902	35	F	779	+	20	0.8	138	5.6	-	-
65	18703	36	M	1166	-	41	1.6	140	4.3	+	-
66	9904	35	F	522	+	18	1	135	3.4	-	-
67	9906	27	M	448	+	21	0.8	145	3	-	-
68	18706	24	M	743	-	31	0.6	132	3.7	-	-
69	18707	25	M	316	+	17	0.9	137	3.9	+	-
70	18709	45	F	302	-	19	1	120	4	+	-
71	18715	40	M	56	-	20	1.2	122	4.3	-	-
72	18722	21	F	1308	-	55	1.7	139	4.1	-	+
73	18727	50	M	474	-	24	1.1	122	4.3	-	-
74	18764	45	F	546	-	26	0.7	126	3.6	-	-
75	18798	25	F	516	-	32	1.2	135	2.2	-	-
76	18816	44	M	700	-	31	0.6	124	3.5	+	-
77	18828	37	M	586	-	19	0.8	139	4	-	-
78	10012	30	F	85	+	20	1	122	3.6	-	-
79	10013	26	F	352	+	21	0.7	128	4.1	-	-
80	10015	31	M	136	+	18	1.1	140	2.8	-	-
81	10016	30	F	401	+	23	0.9	136	3.4	-	-
82	18889	26	M	563	-	67	1.8	136	4.2	+	+
83	10017	42	F	430	+	17	0.7	142	3.7	-	-
84	18029	46	M	707	-	19	1.2	137	2.2	-	-
85	18035	55	M	740	-	23	1.1	130	4.3	-	-

86	18045	59	M	130	-	31	1	135	3.8	-	-
87	18047	42	M	866	-	30	0.7	138	4.4	-	-
88	18051	58	M	475	-	28	0.9	143	3.9	-	-
89	18930	40	F	179	-	65	1.9	137	5.1	+	+
90	18065	23	F	205	-	34	1.2	135	2.2	-	-
91	18077	33	M	442	-	32	1	120	3.5	-	-
92	18079	15	M	140	-	26	0.8	138	3.4	-	-
93	18304	52	M	640	-	61	1.9	140	3.8	+	+
94	18080	47	F	250	-	22	0.6	122	3	-	-
95	18092	43	M	951	-	20	0.7	132	4	+	-
96	18094	30	F	857	-	16	1.1	120	5.3	-	-
97	18098	33	F	831	-	18	1	136	4.5	+	-
98	9984	45	M	346	+	32	0.6	128	3.5	-	-
99	18812	35	M	1528	-	50	1.7	137	4.2	-	+
100	9985	52	F	81	+	28	1.2	140	5.1	-	-
101	9986	38	M	411	+	24	0.9	135	4.1	+	-
102	9989	49	M	356	+	16	0.6	132	4.4	-	-
103	9990	23	M	398	+	32	0.8	142	4.5	-	-
104	9992	31	M	435	+	20	1	130	5	-	-
105	9994	46	M	439	+	21	1.1	136	4.2	-	-
106	9995	25	F	437	+	22	1	126	3.5	-	-
107	9996	28	M	255	+	20	1.2	135	4	-	-
108	9997	52	M	314	+	18	0.8	145	5.2	-	-
109	9998	25	F	232	+	16	0.7	126	5	-	-
110	9999	38	F	242	+	21	1.1	137	3.8	-	-
111	9951	43	M	214	+	53	1.8	142	2.8	-	+
112	10001	37	F	345	+	20	0.6	145	3.5	-	-
113	10002	52	M	636	+	24	0.8	139	5.3	-	-
114	18328	42	M	320	-	60	1.8	137	3.2	+	+
115	10006	29	M	479	+	26	1.1	135	4	-	-
116	10007	40	M	975	+	28	1.2	140	5.4	-	-
117	10008	35	F	356	+	30	1	128	4.2	-	-
118	10011	41	M	140	+	31	0.6	142	4.1	-	-
119	18294	22	M	446	-	24	0.9	122	4.2	-	-
120	18299	33	M	78	-	26	1.2	120	3.6	-	-
121	18304	52	M	320	-	28	0.6	136	3.7	-	-
122	18306	53	M	340	-	22	1	140	4	-	-
123	18360	22	M	141	-	62	4.1	135	3.5	+	+
124	18312	35	F	1528	-	24	0.7	120	3.9	-	-
125	18319	46	M	456	-	30	1.1	128	4.8	-	-
126	18323	37	F	234	-	18	0.8	137	3	-	-
127	18327	57	M	556	-	26	1.2	122	4.5	-	-
128	18336	25	M	410	-	16	1	126	4.9	-	-
129	9991	57	F	435	+	55	1.7	137	4	+	+
130	18337	26	M	370	-	30	1.2	139	2.2	-	-

131	18344	45	F	146	-	18	0.8	140	2.1	-	-
132	18350	27	M	520	-	19	1.2	124	3.7	-	-
133	18352	38	M	198	-	16	0.6	122	5	-	-
134	18363	32	M	175	-	21	1.1	137	2.1	-	-
135	18364	57	M	483	-	26	0.7	126	4.6	-	-
136	18365	40	M	505	-	28	1	138	5	-	-
137	18366	49	M	419	-	24	1	140	3.8	-	-
138	18397	26	M	443	-	60	2.1	135	3.5	+	+
139	18374	48	M	430	-	30	0.8	140	2.2	-	-
140	18390	47	F	489	-	27	1	120	3.7	-	-
141	18398	45	F	288	-	18	1.1	139	2.2	-	-
142	18400	33	M	240	-	28	0.6	142	4.1	-	-
143	18427	50	M	435	-	16	1.2	138	4.5	-	-
144	18952	32	F	382	-	65	2.2	137	4.5	-	+
145	12600	43	M	832	-	20	1	135	2.4	-	-
146	93	27	F	84	-	30	0.6	120	5	-	-
147	1183	23	M	410	-	33	1	139	4.2	-	-
148	486	24	F	449	-	24	0.9	120	3.6	-	-
149	875	27	M	921	-	30	0.7	140	4	-	-
150	18218	36	F	198	-	26	0.8	135	3.9	-	-
151	18221	45	M	254	-	18	1	136	4.3	-	-
152	18227	40	F	230	-	16	1.1	141	4	-	-
153	18238	32	F	551	-	16	1	120	4.5	-	-
154	18240	40	M	338	-	30	0.8	124	3.5	-	-
155	18253	52	M	516	-	18	0.6	135	4.1	-	-
156	18264	36	M	587	-	19	0.7	141	4	-	-
157	18265	29	F	2588	-	20	1.1	142	2	-	-
158	18147	45	M	441	-	55	1.8	141	3.6	-	+
159	18269	30	F	725	-	29	1.2	120	3.5	-	-
160	18151	56	M	921	-	88	3	141	4	-	-
161	18272	45	M	600	-	32	0.7	147	2.2	-	-
162	18275	38	F	694	-	33	1	120	4.1	-	-
163	18276	48	M	608	-	23	0.8	139	2.1	-	-
164	18277	58	F	524	+	34	1	136	5.7	-	-
165	18291	48	M	474	-	25	1.2	135	5	-	-
166	18183	29	M	329	-	33	1.1	120	4.9	-	-
167	18205	35	M	440	-	63	1.8	136	4.7	-	+
168	18132	35	M	286	-	20	1.2	124	3.5	-	-
169	18135	21	M	666	-	18	1	135	2.2	-	-
170	18142	35	F	614	-	24	0.8	122	4.5	-	-
171	18148	33	M	1087	-	26	0.7	142	4	-	-
172	18152	45	F	1116	-	30	0.6	140	2.4	-	-
173	10000	39	M	255	+	82	2.1	140	5.1	-	+
174	18157	30	M	422	-	31	1	136	4.8	-	-
175	18226	39	M	1193	-	54	1.7	139	5	-	+

176	18160	24	M	627	-	34	1.1	138	3.8	-	-
177	18161	35	M	542	-	28	0.8	141	2.1	-	-
178	18187	42	M	555	-	18	1.2	132	3.6	-	-
179	18188	40	M	918	-	22	0.9	137	3.8	-	-
180	18196	28	M	622	-	20	1.1	138	2.2	-	-
181	18209	42	M	670	-	16	1	134	4	-	-
182	18214	50	M	670	-	18	1.2	135	4.2	-	-
183	18215	29	M	401	-	20	0.8	135	4.5	-	-
184	18270	52	M	632	-	58	1.8	139	2.1	-	+
185	9921	57	M	498	+	24	0.9	132	3.5	-	-
186	9922	30	F	108	+	18	1.2	137	3.2	-	-
187	9924	38	F	175	+	26	1	122	3.5	-	-
188	9925	36	F	207	+	29	0.7	124	3.6	-	-
189	9927	29	M	547	+	20	0.6	135	3	-	-
190	9929	28	M	723	+	30	1.1	138	3.7	-	-
191	9930	27	M	301	+	18	0.8	128	3.9	-	-
192	9931	40	M	321	+	34	0.9	139	4	+	-
193	9934	22	M	520	+	16	1	140	3.2	-	-
194	9935	17	M	883	+	20	1.2	134	5.8	-	-
195	9936	35	M	402	+	20	0.7	145	5	-	-
196	9937	56	M	139	+	32	0.6	124	4.2	-	-
197	10014	36	F	315	+	59	1.8	135	3.5	-	+
198	9938	35	F	139	+	20	1.2	145	3.8	+	-
199	9939	50	M	333	+	24	1	139	3	-	-
200	18277	31	M	474	-	60	2	140	2.4	-	+

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Period of Study	:	2014-2017
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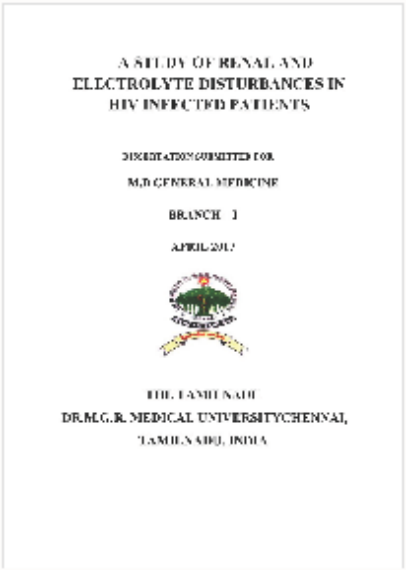

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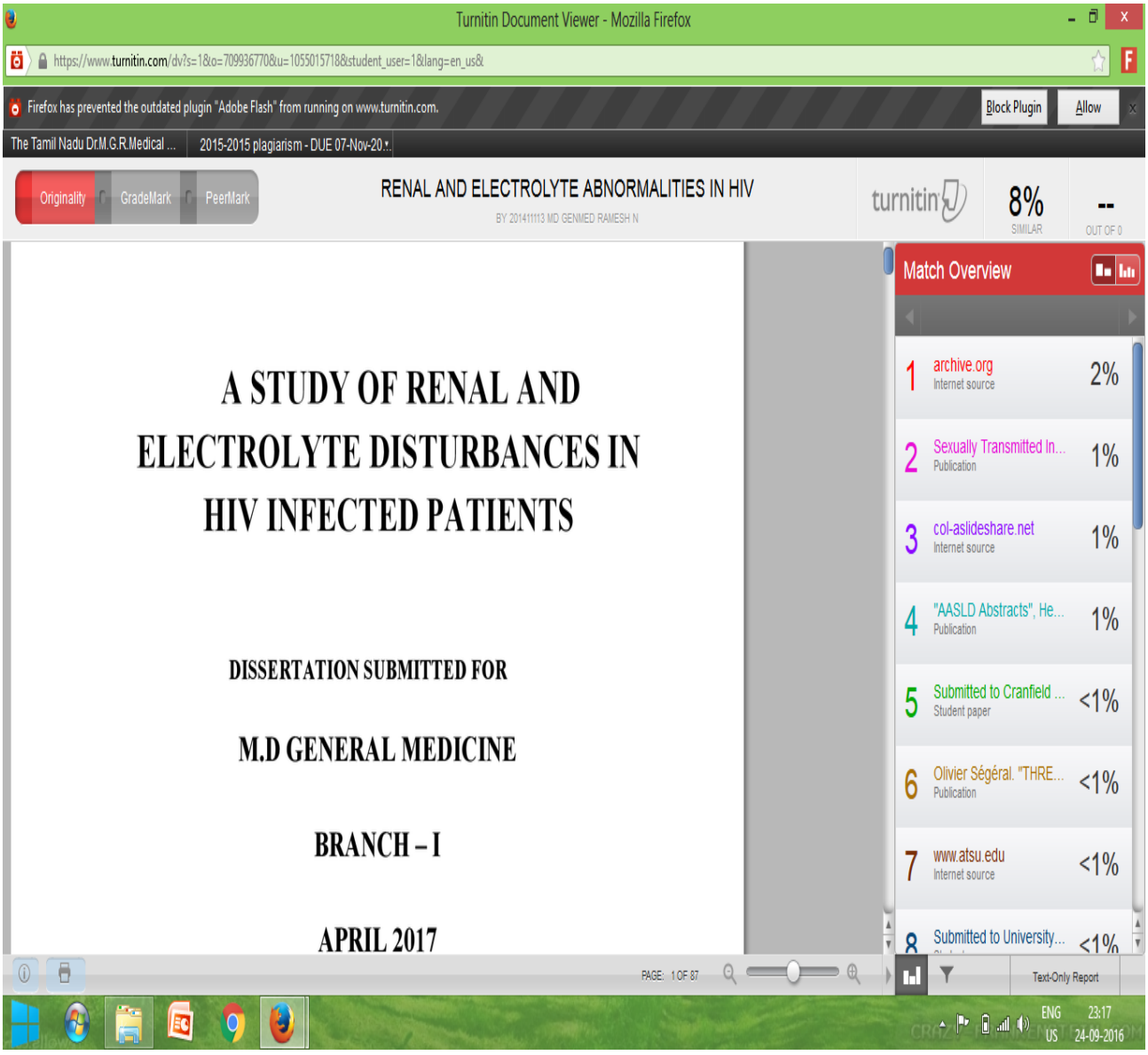
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