A Dissertation on

TO STUDY THE PREVALENCE OF RENAL INVOLVEMENT IN PATIENTS RECEIVING TENOFOVIR CONTAINING ANTI RETROVIRAL THERAPY
CROSS SECTIONAL STUDY

Submitted in partial fulfillment of Requirements for

M.D.DEGREE EXAMINATION

BRANCH -1 (GENERAL MEDICINE)

Reg.No.201911020

INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

CHENNAI-600 003.

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY,CHENNAI

MAY 2022

CERTIFICATE- I

This is to certify that the dissertation entitled **TO STUDY THE PREVALENCE OF RENAL INVOLVEMENT IN PATIENTS RECEIVING TENOFOVIR CONTAINING ANTI RETROVIRAL THERAPY** is a bonafide work done by **Dr. SOWMYA .S** Post Graduate , **Reg.no.201911020** Institute of Internal Medicine, Madras Medical College, Chennai-3, during May 2021 to October 2021 in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I General Medicine, under our guidance and supervision, during the academic year 2019 - 2022.

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I solemnly declare that the dissertation entitled **TO STUDY THE PREVALENCE OF RENAL INVOLVEMENT IN PATIENTS RECEIVING TENOFOVIR CONTAINING ANTI RETROVIRAL THERAPY** is done by me at Madras Medical College, Chennai-3 during May 2021 to October 2021 under the guidance and supervision of **Prof. Dr. S. USHA LAKSHMI.,M.D** to be submitted to The Tamilnadu Dr M.G.R Medical University towards the partial fulfillment of requirements for the award of M.D DEGREE IN GENERAL MEDICINE BRANCH-I.

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ACKNOWLEDGEMENT

I express my sincere thanks to The Dean, **Prof. Dr. E.THERANIRAJAN, MD., DCH., MRCPCH (UK)., FRCPCH(UK).,** Rajiv Gandhi government general hospital for permitting me to use the facilities of Madras Medical College and Rajiv Gandhi government general Hospital to conduct this study.

I will ever remain in gratitude to my chief **Dr.S.USHA LAKSHMI**,**M.D.,** Prof of Medicine, not only for guiding me throughout the study, but also for being my mentor and source of inspiration during the period of my post graduate training.

I express my sincere thanks to Our professor and Head of the Department of Medicine **Prof Dr.C.HARIHARAN**, **M.D.,** I owe a lot and sincerely thank them.

My family and friends have stood by me during my times of need.

Their help and support have been valuable to the study.

I would grossly fail in my duty if I fail to mention here of my patients who have ungrudgingly borne the pain and discomfort of investigations. I cannot but pray for their speedy recovery and place this study as a tribute to them and to the numerous others likely affected.

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INTRODUCTION

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,

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 has AIDS by definition, regardless of the presence or absence of symptoms or opportunistic diseases.

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 Program 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. 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 reduction in global HIV incidence likely reflect natural trends in the pandemic as well as the results of prevention programs resulting in behavior change.

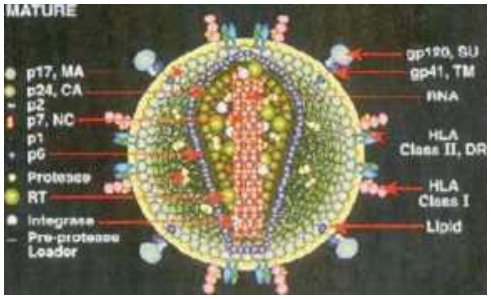
HIV prevalence in India is~3.6% amounting between 2 and 3.1 million people. On an average it comes to 2.5 million. The prevalence for adult female is 0.29% and for males 0.43%. Prevalence high in age group 15- 49 years.Among IDU's it is as high as 8.71% while it is 5.69% and 5.38% among MSM and FSW respectively. In AndhraPradesh Karnataka, Maharasthra and Tamilnadu

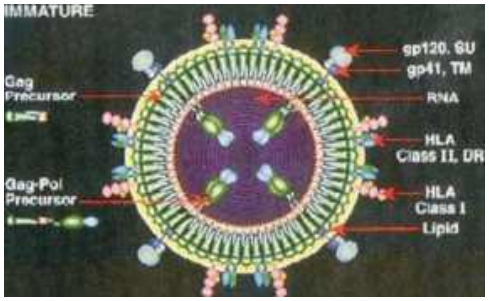
HIV is transmitted mainly through heterosexual route and is largely linked to commercial sex work. Indeed, according to selected surveys more than half of sex workers have become infected with HIV.

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 gpl20 and the transmembrane gp41

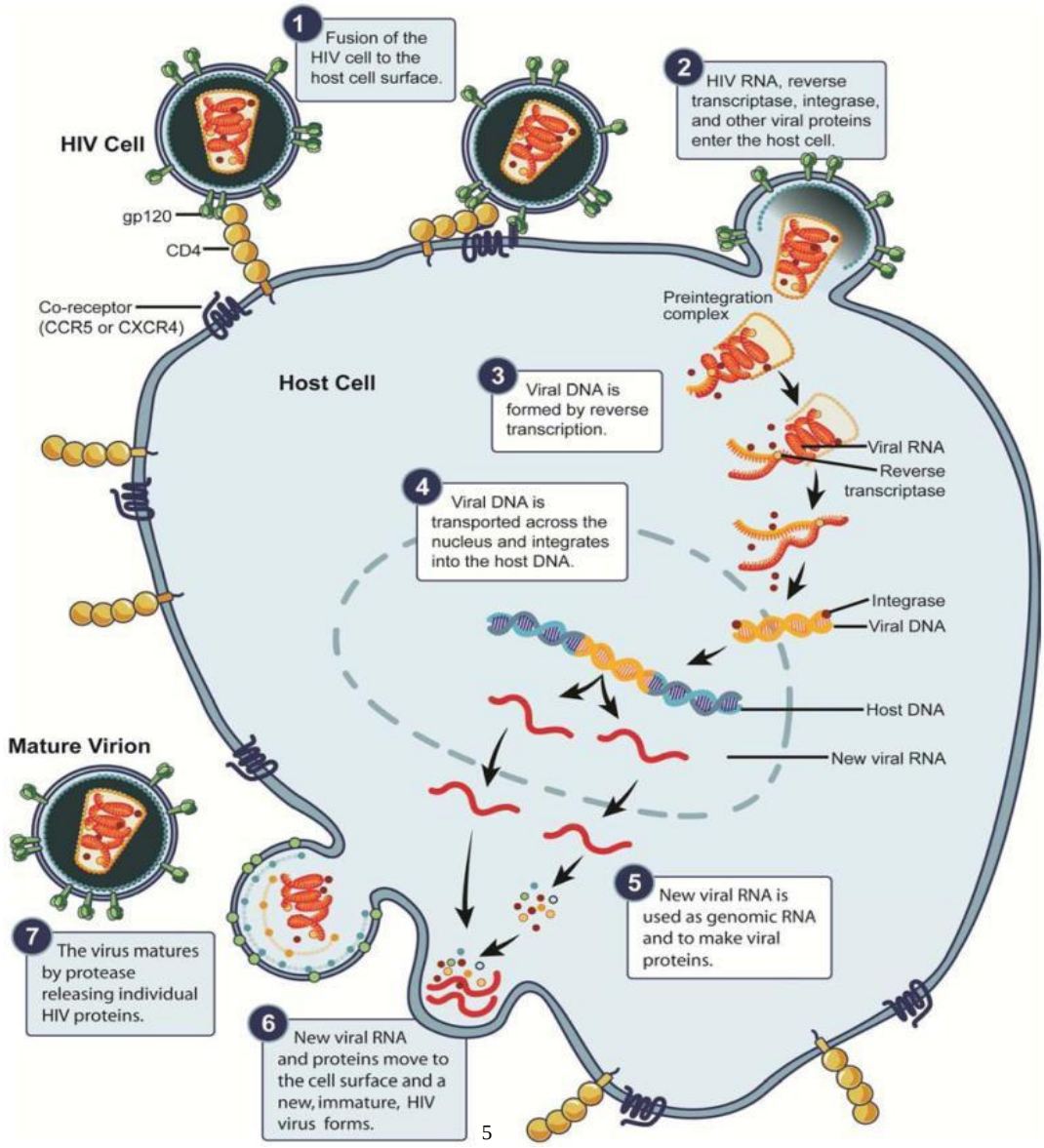
ETIOLOGIC AGENT





Gag Proteins and Precursor (p55)
Capsid Structural Protein (CA, p24) o Matrix Protein (MA, myristylated, p17) J RNA Binding Protein (P9) o RNA Binding Protein (proline-rich, p7) o Other Gag Proteins (P6, p2,p1).
Viral Encoded Enzymes
Polymerase (p61,p55)
Reverse Transcriptase ■ Rnase H o Protease (p10) o Integrase (p32)
Envelope Proteins
Surface Glycoprotein (gpi20)
Transmembrane Glycoprotein (gp41)
Accessory and Regulatory Proteins
Tat
Rev o Nef o Vif (Viral Infectivity Factor)
Vpr o Vpu o Vpx o Tev
Nucleic Acids
HIV RNA

HIV REPLICATION



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TRANSMISSION

HIV is transmitted 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 infection 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.

REVIEW OF

LITERATURE

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. A typical initial HIV regimen includes 3 HIV medications from a minimum of 2 drug classes. Although this treatment is not curative, it can provide longer lives for patients and reduce HIV transmission. This reduction of transmission has become a popular use of antiretroviral therapy for HIV-positive individuals and are with an HIV-negative partner.

The 1980s saw the devastation of the newly emerging and deadly disease of acquired immunodeficiency syndrome or AIDS. The identification of the retrovirus - now known as human immunodeficiency virus (HIV) - as the causative pathogen in the mid-1980s was the key milestone in the control of this disease. The discovery of the multi-step replicative life cycle of HIV in human CD4+ T-cells led to the identification of potential drug targets to halt or slow the replicative process. This resulted in unprecedented scientific progress in the drug discovery and drug development process.

US FDA Approved Antiretroviral Agents (listed in chronological order by year of drug approval) and Their Targets in the HIV Life Cycle

Drug Class	CCR5 Antagonist	Fusion Inhibitor	NRTI	NNRTI	INSTI	PI
FDA Approved Drugs	Maraviroc	Enfuvirtide	Zidovudine Didanosine Zalcitabine Stavudine Lamivudine Abacavir Tenofovir Emtricitabine	Nevirapine Delavirdine Efavirenz Etravirine rlipivirine	Raltegravir Elvitegarvir[1] Dolutegravir	Saquinavir Indinavir Ritonavir Nelfinavir Amprenavir Lopinavir[2] Fosamprenavir Atazanavir Tipranavir Darunavir

Abbreviations – NRTI = nucleos(t)ide reverse transcriptase inhibitor, NNRTI = non-nucleoside reverse transcriptase inhibitor, INSTI = integrase strand transfer inhibitor, PI = protease inhibitorAntiretroviral Drugs Used in the Treatment of HIV Infection

Drug	Toxicity
Zidovudine (AZT)	Anemia, granulocytopenia, myopathy, lactic acidosis, hepatomegalywith steatosis, headache, nausea
Didanosine (ddl)	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, abnormaldreams, depression
Etravirine	Rash, headache, dizziness, nausea, diarrhea
Saquinavir mesylate	Diarrhea, nausea, headaches, hyperglycemia, fat redistribution, lipidabnormalities
Fortovase	Diarrhea, nausea, abdominal pain, headaches, hyperglycemia, fatredistribution, lipid abnormalities
Ritonavir	Nausea, abdominal pain, hyperglycemia, fat redistribution, lipid abnormalities, may alter levels of many other drugs, includingsaquinavir
Indinavir sulfate	Nephrolithiasis, indirect hyperbilirubinemia, hyperglycemia, fatredistribution, 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

INTRODUCTION TO TENOFOVIR

TENOFOVIR disoproxil fumarate (TDF), a nucleotide reverse-transcriptase inhibitor in the developed and developing countries, is effective in the treatment of HIV and HBV infection and prevention of mother-to-child transmission, and, in combination with emtricitabine, as pre- and post-exposure prophylaxis in populations at high risk for HIV infection. However, prolonged exposure to TDF has been shown to cause declines of estimated glomerular filtration rate (eGFR) and reduction of bone mineral density (BMD), which have raised concerns about the long-term successful management of HIV infection with ART. After oral administration, TDF is converted to the active acyclic nucleotides (TENOFOVIR, TFV), which was filtered by the glomeruli and completely reabsorbed by the proximal renal tubules. It is primarily transported from basolateral circulation into proximal renal tubular cells via the organic anion transporter 1 (OAT-1), and then excreted into the tubular lumen by the multidrug resistance transporter 2 (MRP-2) and MRP-4.Increased accumulation of TDF in the renal tubular cells causes mitochondrial dysfunction and proximal tubular injury (proximal tubulopathy). It can cause renal failure.

Tenofovir disoproxil fumarate (tenofovir DF) is an oral prodrug of tenofovir, a nucleotide (nucleoside monophosphate) analogue with activity against retroviruses, including HIV-1, HIV-2 and hepadnaviruses. Following absorption, tenofovir DF is rapidly converted to tenofovir, which is metabolised intracellularly to its active anabolite tenofovir diphosphate, which is a competitive inhibitor of HIV-1 reverse transcriptase and terminates the growing DNA chain. Tenofovir exerts antiviral effects in a variety of cell types, including resting cells.

Tenofovir exhibits longer serum (17 hours) and intracellular (≥60 hours) half-lives than those of nucleoside analogues, which supports a flexible once-daily administration schedule. The pharmacokinetics of tenofovir are dose-proportional and similar in healthy volunteers and HIV-infected individuals. The oral bioavailability of tenofovir is enhanced by administration with a high-fat meal, but is similar at steady state when administered with or without a typical meal.

Tenofovir is not a substrate, inducer or inhibitor of human cytochrome P450 enzymes in vitro in vivo. Tenofovir DF has been studied with 15 other antiretroviral and other concomitant medications frequently used in the HIV-1-infected population. With the exception of didanosine and atazanavir, which require dosage modifications, no clinically significant drug interactions have been observed with tenofovir DF.

The recommended oral dosage of tenofovir DF in adults is 300 mg/day. Tenofovir is eliminated by renal elimination, including tubular secretion; dose-interval adjustments are necessary for tenofovir DF in patients with significant renal impairment. No dosage adjustment of tenofovir DF is necessary in patients with liver disease.

Coadminstration with other drugs that are eliminated by tubular secretion, such as cidofovir, acyclovir, valacyclovir, ganciclovir, valaganciclovir, and probenecid, may increase serum concentrations of either tenofovir or the coadministered drug Tenofovir DF is active against some nucleoside-resistant strains of HIV. However, cross-resistance is associated with multiple thymidine analogue mutations that include 41L or 210W. The signature mutation is the K65R mutation, which causes variable loss in susceptibility to tenofovir DF, didanosine, and abacavir.

TDF can cause renal proximal tubular dysfunction and also reduces estimated glomerular filtration rate more than other NRTIs. To date,

TDF-associated renal dysfunction is generally regarded as mild and tolerable and one meta-analysis published in 2010 recommended that TDF use should not be restricted even when regular monitoring of renal function and serum phosphate levels is impractical. But it is notable that low body weight is one of the risk factors for TFV nephrotoxicity and that Asians are generally of smaller body stature and have a lower median body weight than Whites and Blacks, who mostly comprise the cohorts of studies published to date.

This report reviews recent literature on TFV nephrotoxicity among PLHIV especially focusing on Asians who might be susceptible to TFV nephrotoxicity due to their smaller body stature and discusses implications for clinical care and future directions. Although tenofovir alafenamide (TAF), a new prodrug of TFV, which is safer for kidney than TDF, has been licensed and is available in some resource rich countries the main focus of this review will be on TDF-associated nephrotoxicity, since TDF has been and will be used by the vast majority of PLHIV especially in low and middle income countries including many Asian countries.

There are a number of other potential uses for tenofovir DF aside from long-term antiretroviral therapy of HIV-infected patients. Tenofovir DF is an attractive drug for use in postexposure prophylaxis regimens, given its convenience and tolerability. Data from monkey studies support the use of tenofovir DF for postexposure prophylaxis.

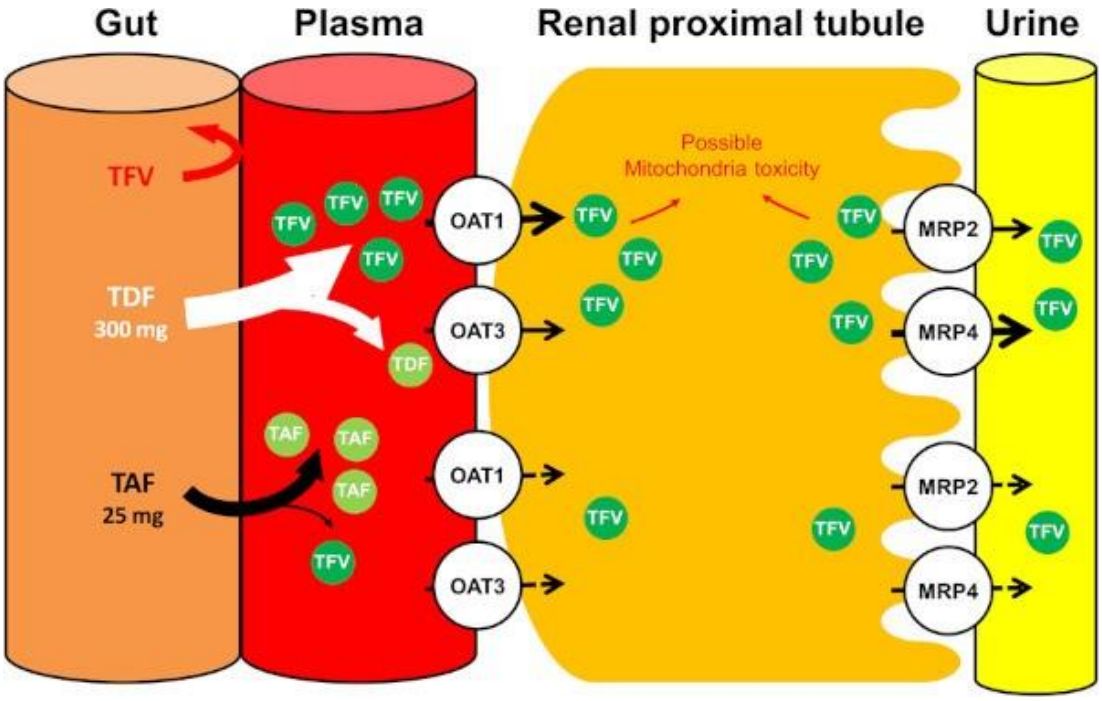
Monkeys who were inoculated with simian immunodeficiency virus (SIV) and then given tenofovir up to 24 h after inoculation remained healthy and free of detectable SIV, whereas those who did not receive the drug died quickly of SIV infection.

Similarly, it may be a promising agent for use in pregnant women to prevent perinatal transmission. Single-dose therapy with nevirapine prevents transmission to infants, but this comes at the cost of the development of NNRTI resistance in a substantial proportion of the women who take it. Resistance to tenofovir DF is slower to develop, compared with NNRTI resistance, and it may leave more options for future therapy if resistance does occur. Tenofovir DF has also been proposed as an ideal agent for "preexposure prophylaxis," the use of antiretroviral therapy (preferably for short periods of time) in individuals determined to be at risk of acquiring HIV infection on the basis high-risk behavior.

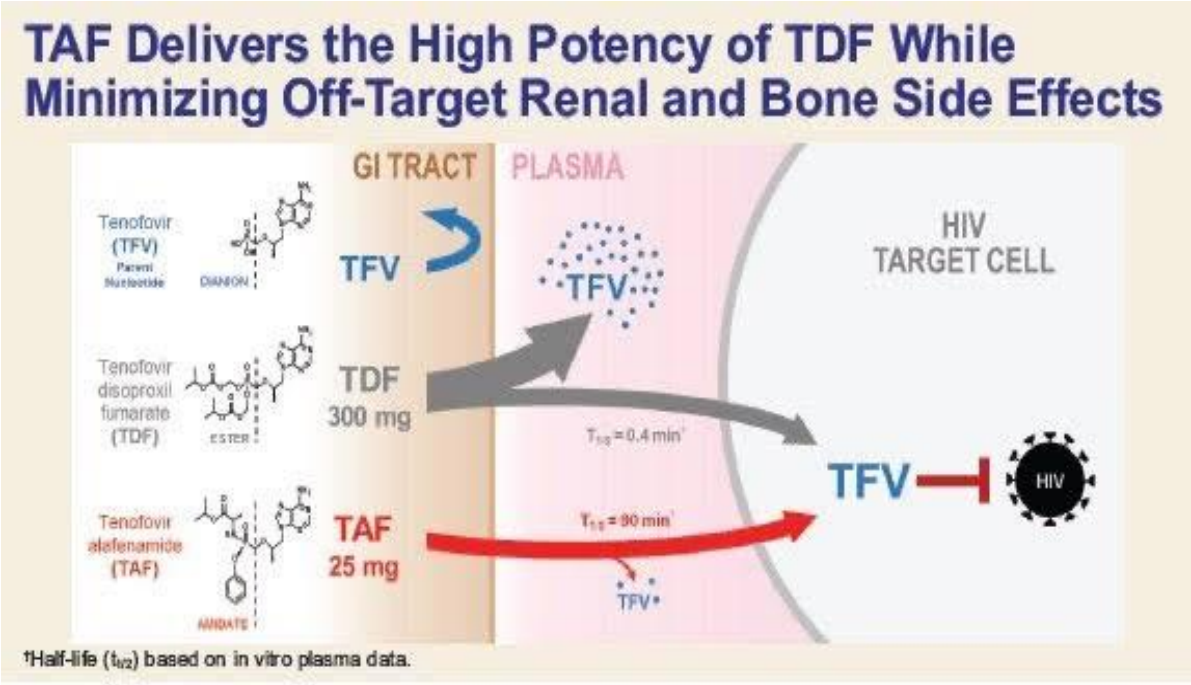
MECHANISM OF TENOFOVIR NEPHROTOXICITY

Compared with abacavir (ABC) or other NRTIs, TDF is highly potent with a high genetic barrier. TDF was first licensed for use in 2001 and soon after, a series of cases which developed tubulopathy such as Fanconi syndrome or acute tubular necrosis, or acute renal failure have been reported . TFV, a metabolite of TDF, is excreted through glomerular filtration and via active tubular secretion at the proximal tubules of the kidney . TDF-associated tubulopathy is considered to be a result of accumulation of TFV, which causes mitochondria toxicity in tubular cells through inhibition of mitochondrial DNA polymerase-γ. Renal biopsy of cases, which presented with TFV tubulopathy showed mitochondrial enlargement, depletion, and dysmorphic changes in proximal tubular cells . The use of TDF is

also associated with increased bone turnover and bone demineralization, and although the mechanism is not fully understood, renal phosphate loss due to proximal tubulopathy is considered to be a primary cause.



Excretion of tenofovir at the proximal tubular cells of the kidney and mechanism of tenofovir nephrotoxicity. Tenofovir (TFV), which is a metabolite from tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF), is excreted through glomerular filtration and enters kidney tubular cells through the basolateral membrane and is transported mainly by organic anion transporter (OAT) 1 and, to a lesser extent, OAT 3 . TFV is excreted into the urine at the apical membrane by 2 transporters on the luminal membrane; multidrug resistance protein (MRP) 4 and MRP 2 . TFV cannot be absorbed from the gut. TDF is rapidly metabolized to TFV in the plasma, whereas TAF is stable in the plasma and largely metabolized to TFV within target cells, resulting in lower plasma TFV levels.



- 91% lower plasma TFV levels minimize renal and bone effects while maintaining high potency for suppressing HIV

Accumulation of TFV within proximal tubular cells leads to mitochondrial injury and tissue hypoxia, but with TAF, likelihood of tubular injury is less . TAF itself is not a substrate for OAT- 1 or OAT-3.

A post-marketing report for Australia, Europe and US in 2007 showed that cases, which developed tubulopathy or acute renal failure were rare; among 10,343 patients, acute and chronic renal failure was reported in 0.3% and Fanconi syndrome in < 0.1%. Also other renal events, such as nephrogenic diabetes insipidus, nephritis, and proteinuria were reported in ≤ 0.1%of patients (8). In tenofovir-induced nephrotoxicity, tubulopathy is considered to precede the decline in GFR (31,32). In 2010, a meta-analysis, which analyzed 17 randomized trials and cohort studies on renal safety of TDF in PLHIV (17) was published and it concluded that, although TDF use was associated with a statistically significant

loss of renal function (mean difference compared with control subjects in calculated creatinine clearance, 3.92 mL/ min, 95% CI: 2.13-5.70 mL/min), the clinical magnitude of this effect was modest and they do not support the need to restrict TDF use in jurisdictions where regular monitoring of renal function and serum phosphate levels is impractical. However, it is notable that only one study from Asia (33) was included in this meta-analysis and that this study from Japan showed largest decrement in eGFR in TDF users compared to other NRTI users among 17 studies (mean difference: -17 mL/min (95% CI: -31.35, -2.65))

USES OF VARIOUS MARKERS FOR TENOFOVIR ASSOCIATED RENAL FAILURE

Because tenofovir tubulopathy precedes actual decrement in GFR, renal tubular markers are considered to be more sensitive than creatinine based eGFR. Among the renal tubular markers, urinary β2 microglobulin (β2M) has been most studied . β2M has been shown to be a sensitive marker for TFV nephrotoxicity , and can predict TDF-related GFR decrement in PLHIV who initiate TDF containing antiretroviral therapy . Whether new tubular markers, such as kidney injury molecule 1 (KIM-1), liver type fatty acid binding protein (L-FABP), and neutrophil gelatinase-associated lipocalin (NGAL) are useful in diagnosing or predicting TDF-related GFR decrement remains to be elucidated.Many antiretroviral agents increase serum creatinine by inhibiting excretion of creatinine at the renal tubule, which can complicate interpretation of eGFR decrement shortly after initiation of TDF containing ART . Dolutegravir, an integrase inhibitor, which is a component of preferred ART regimen in many treatment guidelines including the WHO guidelines, is one such agent . Measurement of urinary tubular markers,

such as β2M, might help distinguishing causes of eGFR decrement, which is due to inhibition of creatinine clearance by antiretroviral agents or due to TFV nephrotoxicity, although evidence is limited.

VARIOUS FORMS OF RENAL INVOLVEMENT IN HIV

1. **Acute renal failure and fluid & electrolyte disorders**
    i. Acute renal failure
    ii. Disorders of osmolality
    iii. Potassium disorders
    iv. Acid-base disorders
2. **Glomerular renal disease**
3. **HIV associated nephropathy**
    i. Other renal lesions
    ii. End stage renal disease

Acute renal failure and fluid and electrolyte disorders Acute renal failure

Causes Prerenal:

1. Volume depletion - Diarrhoea
    I. Bleeding
    II. Decreased intake
    III. NS AID'S
2. Sepsis
3. Early obstructive uropathy

Renal:

1. **Acute tubular Necrosis:**

-Ischemia / hypoperfusion

-Sepsis/endotoxemia -Radiocontrast exposure

-Nephrotoxic antibiotics

Amphotericin B, Aminoglycosides Pentamidine Foscarnet Acyclovir Cidofovir Tenofovir

2. **Acute interstitial nephritis**

-Sulfamethoxazole

-Dapsone

-NSAIDs

-Rifampin

3. **Glomerular disease**

-HIVAN

-HCV - MPGN (Mesangio proliferative glomerulo nephritis)

-other primary glomerulo nephropathies

4. **Infiltrative lesions**

-Kaposi 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

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. 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, amphotericin B, tenofovir,

adefovir and cidofovir, NSAIDs, rifampicin, 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.

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, havealso 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 Kaposi sarcoma 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.

Disorders of Osmolality:

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

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 duringhospitalization.

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 hypoosmolality lending strong support for this being the mechanism underlying the hyponatremia.

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.

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 trimethoprim - 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 .

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 Stool base losses from diarrhea 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/1.

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 .

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.

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

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 proteinuria, 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% Hypoalbuminemia disproportionate to the degree of proteinuria.

Normal or large kidneys with increased echogenicity on diagnostic ultrasound. 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.

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 CD4 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 CD4 lymphocytes, further depressing the immune system.

8. HIV is a potent stimulator of transforming growth factor -3 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 mesangial 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,issue 1,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 lgmor more of protein / day .

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.

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%)

(d) 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) ,
- Steroid treatment
- ACE inhibitors (ACE-Is),

(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.

(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 HI VAN; 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 .

(e) 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

CD4 count <200 cells /micro litre.

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.

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 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 – *a* 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 uremic syndrome Tumour invasion of the kidneys

End-Stage Renal Disease (ESRD)

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

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.

CD4 counts	Survival
> 200 cells /pl	33.4 months
< 200 cells <pl	7.7 months

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

Hemodialysis:

Most common modality for HIV patients Disadvantage includes

- Risk of infections from temporary catheters and grafts
- Risk to dialysis providers of blood and needle stick exposure

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 dialysate or ultrafiltrate.

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 antiretioviral agents in patients with membrane associated leukopenias.
- Higher average hematocrit
- Lower risk of transmitting HIV infection.

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

AIM OF THE STUDY

AIMS AND OBJECTIVES

TO STUDY THE PREVALENCE OF RENAL INVOLVEMENT IN PATIENTS RECEIVING TENOFOVIR CONTAINING ANTI RETROVIRAL THERAPY

MATERIALS AND METHODS

MATERIALS AND METHODS

Setting	:	Hospitalised HIV positive patients at RGGGH chennai
Design of the study	:	Cross sectional study
Period of study	:	10.4.2021 - 30.10.2021
Sample size	:	75
Ethical committee approval	:	obtained
Consent	:	Informed consent was obtained
Financial support	:	Nil

Selection and Details of Study Subjects

75 HIV patients hospitalised during 10.4.2021- 30.10.2021 at RGGGH chennai were included as study subjects.

Inclusion criteria

1. Age greater than 18 years
2. HIV positive patients on tenofovir

Exclusion Criteria

1. Patients with pre-existing hypertension , diabetes mellitus and on nephrotoxic drugs were excluded from the study .
2. Age less than 18 years
3. Patients who are known case of renal failure at the time of initiation of TENOFOVIR based ART. (tenofovir disoproxil fumarate)

The total number of cases screened were 200 of which 125 cases were excluded from

the study. After exclusion of these patients, the total number of patients who were taken up for study was 75.

75 patients were grouped into patients with elevated renal parameters (Sr.Creatinine >1.3 mg/dL) , without elevated renal parameters with normal electrolytes and with proximal tubular dysfunction only identified by low levels of serum phosphate and serum bicarbonate. All the patients in the study were on tenofovir disoproxil fumarate 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, urine routine examination, serum phosphorus , serum calcium , serum Uric acid , serum bicarbonate and ultrasonography of abdomen for kidney size and for other abdominal organ pathology.

The collected data was analysed , Chi square test was used for test of significance. The data was compared with previous literatures.

RESULTS
AND
OBSERVATIONS

RESULTS AND OBSERVATIONS

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0.(Armonk, NY: IBM Corp).To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference in the multivariate analysis the one way ANOVA with Tukey's Post-Hoc test was used.To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value .05 is considered as significant level.

Table 1: Group distribution

Group distribution		
	Frequency	Percent
PTD	9	12.0
CKD	9	12.0
WRF	57	76.0
Total	75	100.0

PTD- proximal tubular dysfunction

CKD- chronic kidney disease

WRF- without renal failure

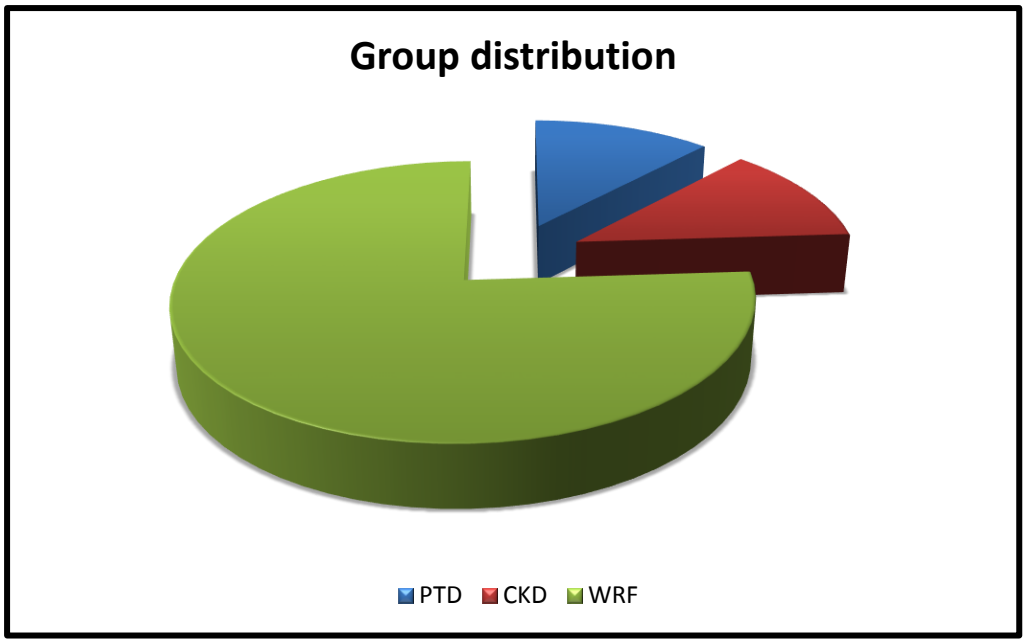


Figure 1

The above table shows Group distribution were PTD is 12.0%, CKD is 12.0%, WRF is 76.0%.

Table 2: Age distribution

Age distribution		
	Frequency	Percent
21 - 30 yrs	6	8.0
31 - 40 yrs	16	21.3
41 - 50 yrs	28	37.3
51 - 60 yrs	13	17.3
Above 60 yrs	12	16.0
Total	75	100.0
Mean ± SD = 46 ± 12 yrs		

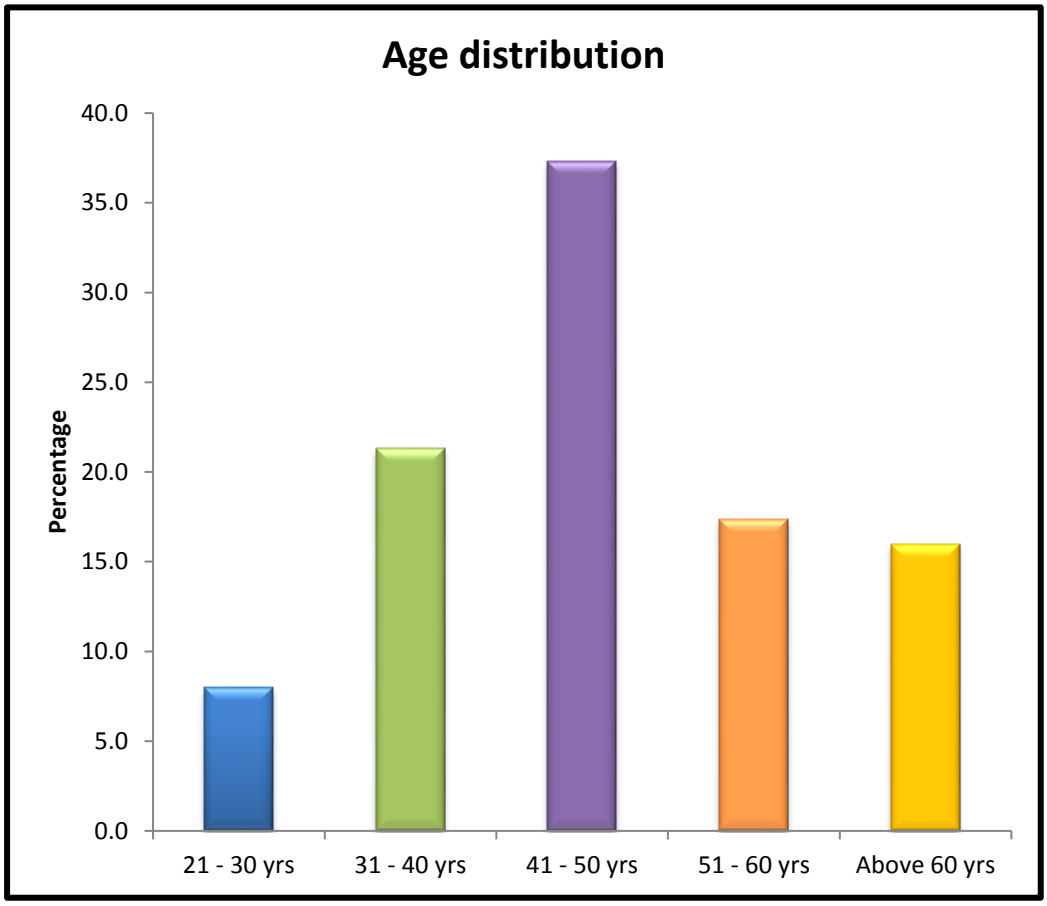


Figure 2 The above table shows Age distribution were 21-30 years is 8.0%, 31-40 years is 21.3%, 41-50 years is 37.3%, 51-60 years is 17.3%, >60 years is 16.0%.

Table 3: Gender distribution

Gender distribution		
	Frequency	Percent
Female	35	46.7
Male	40	53.3
Total	75	100.0

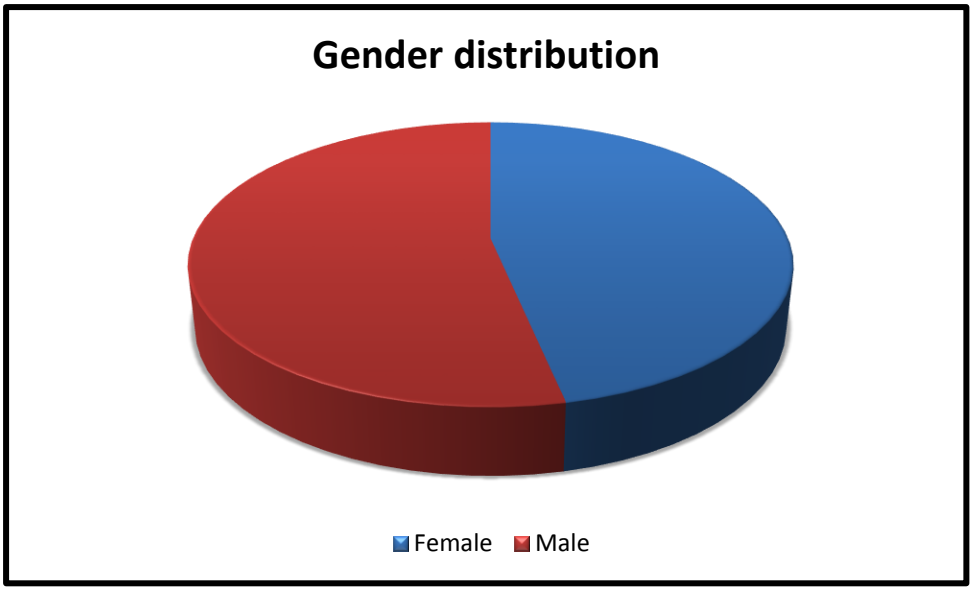


Figure 3

The above table shows Gender distribution were Female is 46.7%, Male is 53.3%.

Table 4: Comparison of Gender between the Groups by Fisher's exact test

			Groups			Total	□ 2 - value	p-value
			PTD	CKD	WRF			
Gender	Female	Count	4	4	27	35	0.047	0.977 #
		%	44.4%	44.4%	47.4%	46.7%		
	Male	Count	5	5	30	40		
		%	55.6%	55.6%	52.6%	53.3%		
Total		Count	9	9	57	75		
		%	100.0%	100.0%	100.0%	100.0%		
# No Statistical Significance at p > 0.05 level								

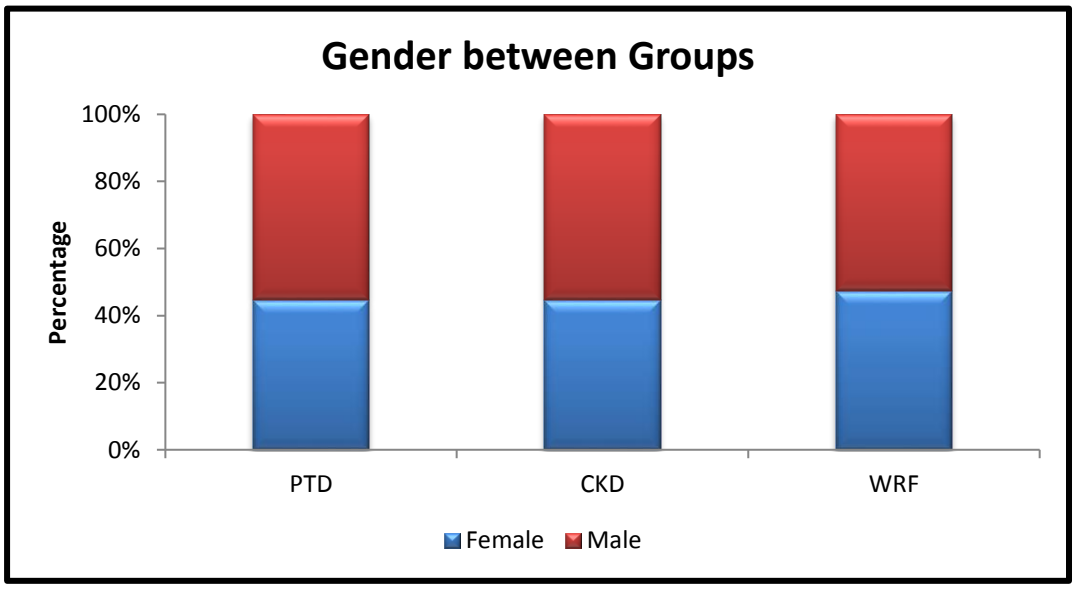


Figure 4

The above table shows comparison of Gender between Groups by Fisher's exact test were □2=0.047, p=0.977>0.05 which shows no statistical significance between Gender and Groups.

Table 5: Comparison of Age between the Groups by Fisher's exact test

			Groups			Total	□ 2 - value	p-value
			PTD	CKD	WRF			
Age	21 - 30 yrs	Count	5	1	0	6	40.458	0.0005 **
		%	55.6%	11.1%	0.0%	8.0%		
	31 - 40 yrs	Count	2	0	14	16		
		%	22.2%	0.0%	24.6%	21.3%		
	41 - 50 yrs	Count	2	3	23	28		
		%	22.2%	33.3%	40.4%	37.3%		
	51 - 60 yrs	Count	0	4	9	13		
		%	0.0%	44.4%	15.8%	17.3%		
	Above 60 yrs	Count	0	1	11	12		
		%	0.0%	11.1%	19.3%	16.0%		
Total		Count	9	9	57	75		
		%	100.0%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level								

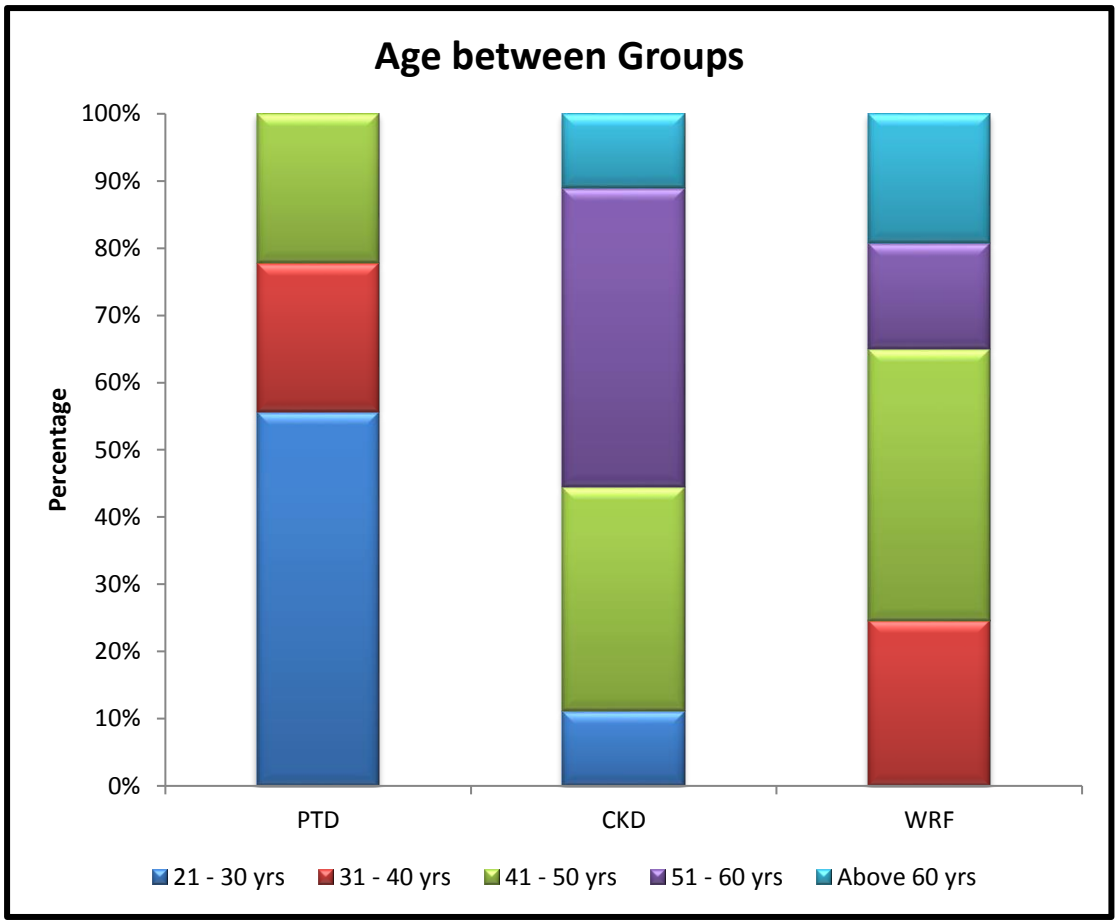


Figure 5

The above table shows comparison of Age between Groups by Fisher's exact test were $\chi^2=40.458$, $p=0.0005<0.01$ which shows highly statistical significance between Age and Groups.

Table 6: Comparison of Age between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Age	PTD	9	32.11	9.45	8.989	0.0003 **
	CKD	9	52.22	10.72		
	WRF	57	47.05	11.15		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Age	PTD	CKD	-20.1111*	5.1512	.001 **	-32.439	-7.784
		WRF	-14.9415*	3.9195	.001 **	-24.321	-5.562
	CKD	WRF	5.1696	3.9195	.389 #	-4.210	14.549
** Highly Significant at p < 0.01 and # No Statistical Significance at p > 0.05							

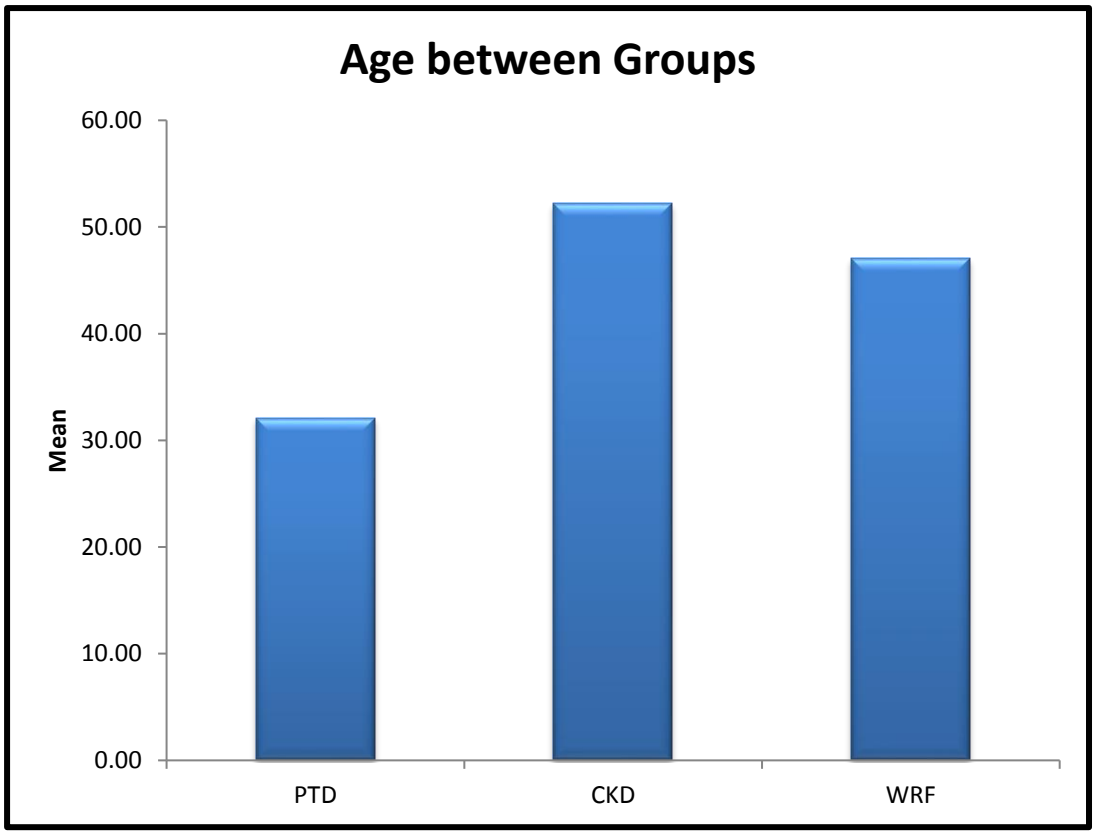


Figure 6

The above table shows the comparison of Age between Groups by using Oneway ANOVA were F-value=8.989, p-value=0.0003<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 and No Statistical Significance at p > 0.05 between Groups.

Table 7: Comparison of Duration between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Duration	PTD	9	2.89	1.27	2.514	0.088 #
	CKD	9	4.67	2.24		
	WRF	57	3.70	1.65		
# No Statistical Significance at p > 0.05 level						

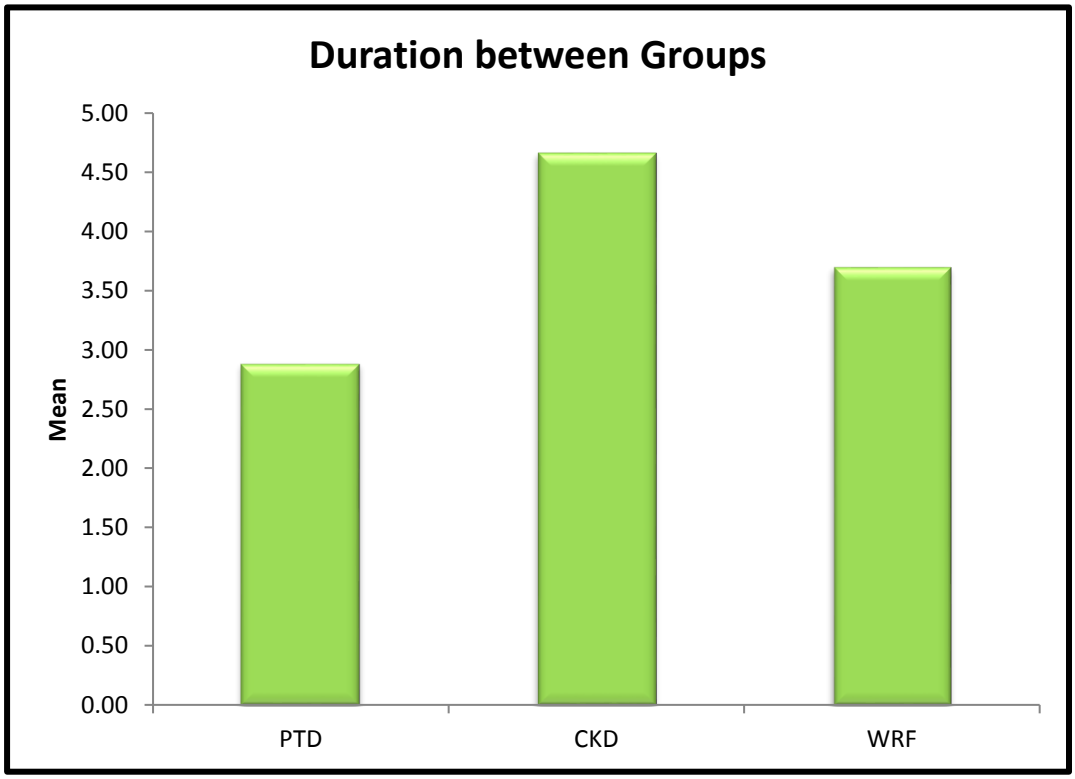


Figure 7

The above table shows the comparison of Duration between Groups by using Oneway ANOVA were F-value=2.514, p-value=0.088>0.05, which shows statistical significance difference at p >0.05 level.

Table 8: Comparison of CD 4 count between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
CD 4 count	PTD	9	243.22	69.13	24.601	0.0005 **
	CKD	9	382.44	64.42		
	WRF	57	469.93	99.13		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
CD 4 count	PTD	CKD	-139.2222*	43.8041	.006 **	-244.051	-34.394
		WRF	-226.7076*	33.3299	.0005 **	-306.470	-146.945
	CKD	WRF	-87.4854*	33.3299	.028 *	-167.248	-7.723
** Highly Statistical Significance at p < 0.01 and * Significant at p < 0.05							

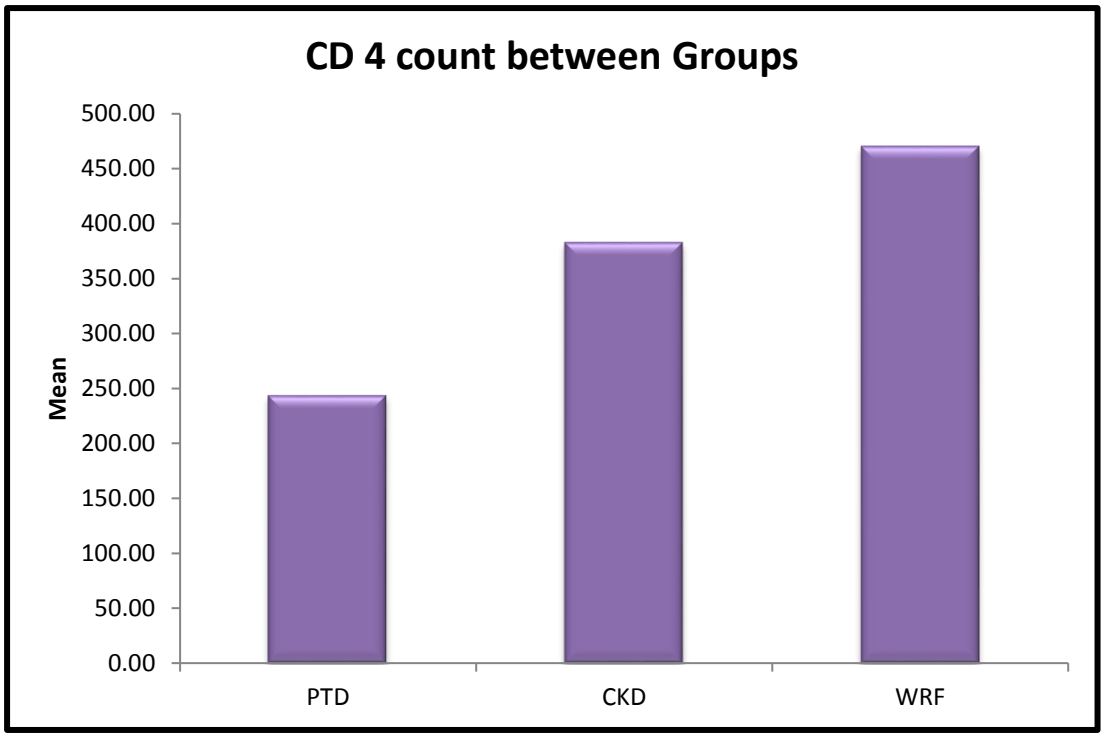


Figure 8

The above table shows the comparison of CD 4 count between Groups by using Oneway ANOVA were F-value=24.601, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level, Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 and Statistical Significance at p < 0.05 between Groups.

Table 9: Comparison of Urea between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Urea	PTD	9	35.56	5.64	168.287	0.0005 **
	CKD	9	66.33	13.12		
	WRF	57	26.16	4.39		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Urea	PTD	CKD	-30.7778*	2.8920	.0005 **	-37.699	-23.857
		WRF	9.3977*	2.2005	.0005 **	4.132	14.664
	CKD	WRF	40.1754*	2.2005	.0005 **	34.909	45.441
** Highly Statistical Significance at p < 0.01 level							

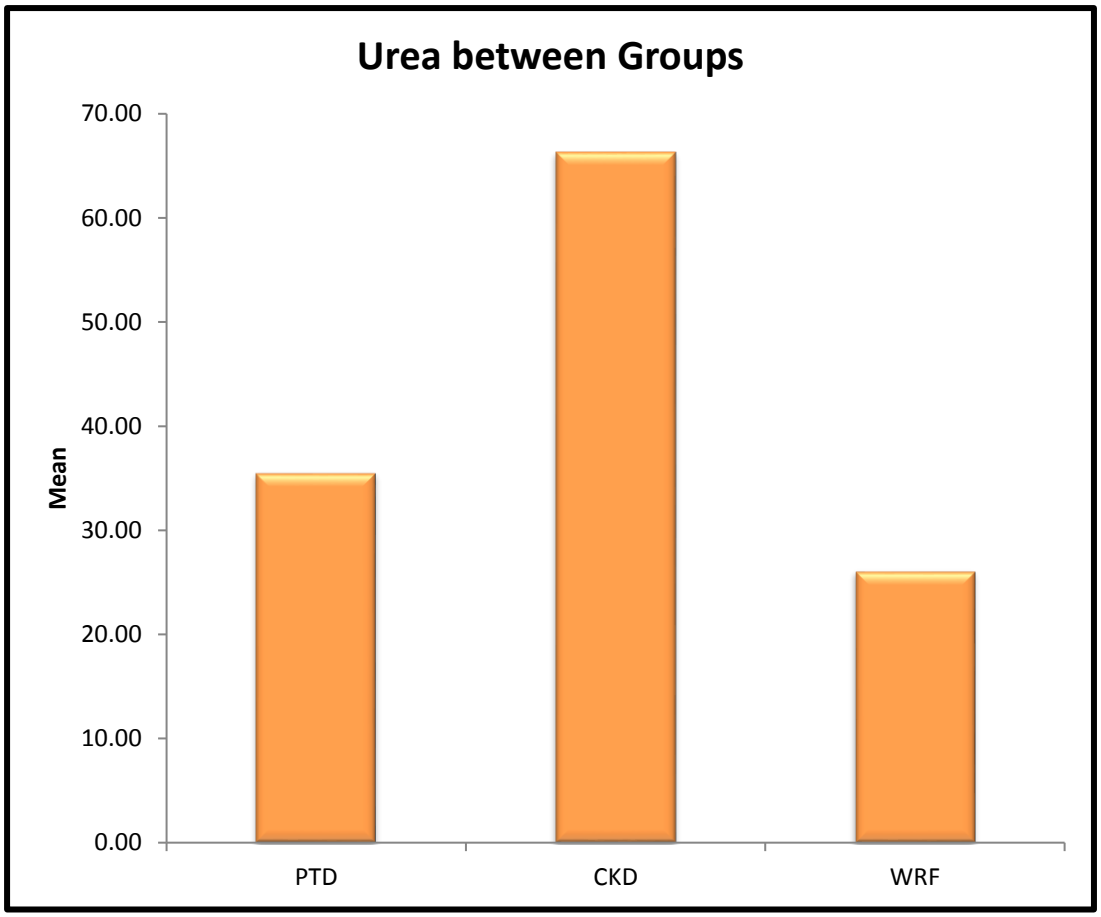


Figure 9

The above table shows the comparison of Urea between Groups by using Oneway ANOVA were F-value=168.287, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.

Table 10: Comparison of Creatinine between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Creatinine	PTD	9	1.04	0.20	299.429	0.0005 **
	CKD	9	3.21	0.79		
	WRF	57	0.70	0.10		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Creatinine	PTD	CKD	-2.1667*	.1350	.0005 **	-2.490	-1.844
		WRF	.3462*	.1027	.003 **	.100	.592
	CKD	WRF	2.5129*	.1027	.0005 **	2.267	2.759
** Highly Statistical Significance at p < 0.01 level							

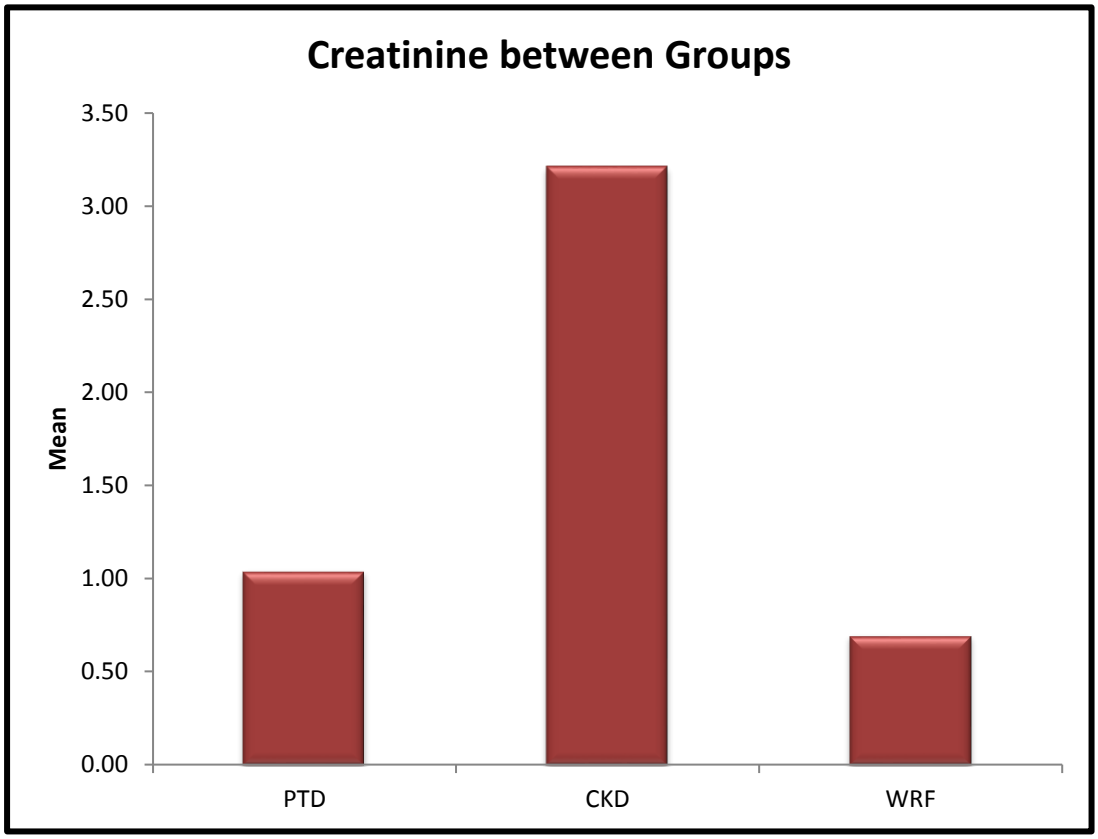


Figure 10

The above table shows the comparison of Creatinine between Groups by using Oneway ANOVA were F-value=299.429, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.

Table 11: Comparison of Sodium between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Sodium	PTD	9	129.44	3.40	48.164	0.0005 **
	CKD	9	134.00	5.22		
	WRF	57	138.26	1.88		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Sodium	PTD	CKD	-4.5556*	1.2513	.001 **	-7.550	-1.561
		WRF	-8.8187*	.9521	.0005 **	-11.097	-6.540
	CKD	WRF	-4.2632*	.9521	.0005 **	-6.542	-1.985
** Highly Statistical Significance at p < 0.01 level							

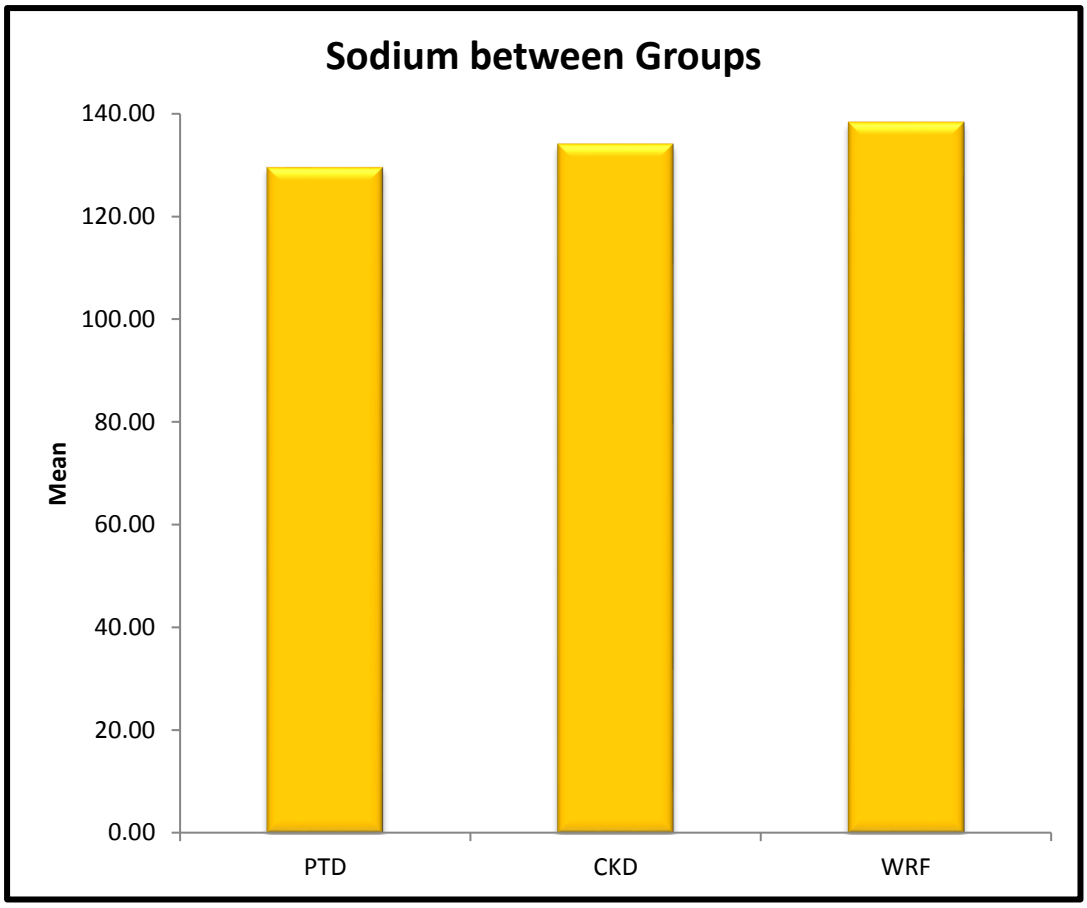


Figure 11

The above table shows the comparison of Sodium between Groups by using Oneway ANOVA were F-value=48.164, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.

Table 12: Comparison of Potassium between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Potassium	PTD	9	2.87	0.19	56.251	0.0005 **
	CKD	9	4.42	0.99		
	WRF	57	4.00	0.00		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Potassium	PTD	CKD	-1.5556*	.1579	.0005 **	-1.933	-1.178
		WRF	-1.1333*	.1201	.0005 **	-1.421	-.846
	CKD	WRF	.4222*	.1201	.002 **	.135	.710
** Highly Statistical Significance at p < 0.01 level							

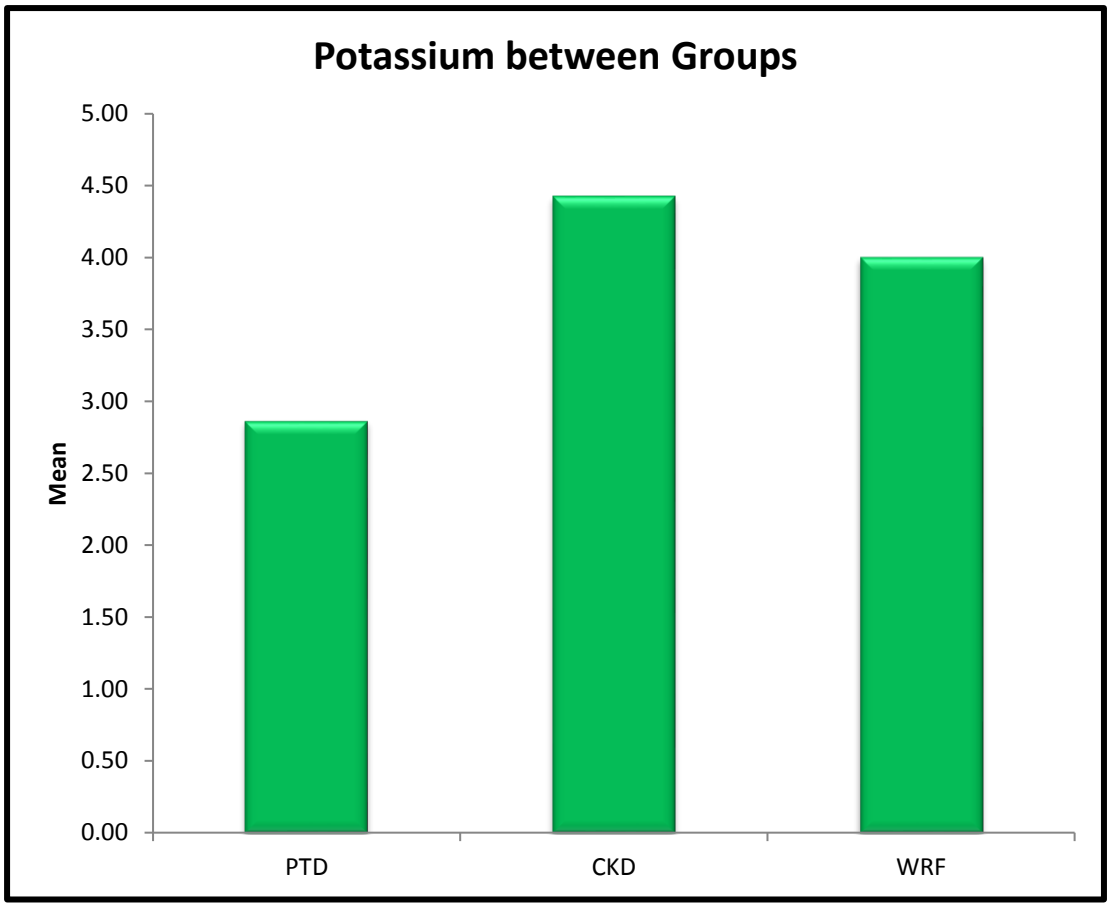


Figure 12

The above table shows the comparison of Potassium between Groups by using Oneway ANOVA were F-value=56.251, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.

Table 13: Comparison of Bicarbonate between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Bicarbonate	PTD	9	15.44	1.13	840.992	0.0005 **
	CKD	9	15.44	1.74		
	WRF	57	23.93	0.37		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Bicarbonate	PTD	CKD	0.0000	.3607	1.000 #	-.863	.863
		WRF	-8.4854*	.2745	.0005 **	-9.142	-7.829
	CKD	WRF	-8.4854*	.2745	.0005 **	-9.142	-7.829
** Highly Significant at p < 0.01 and # No Statistical Significance at p > 0.05							

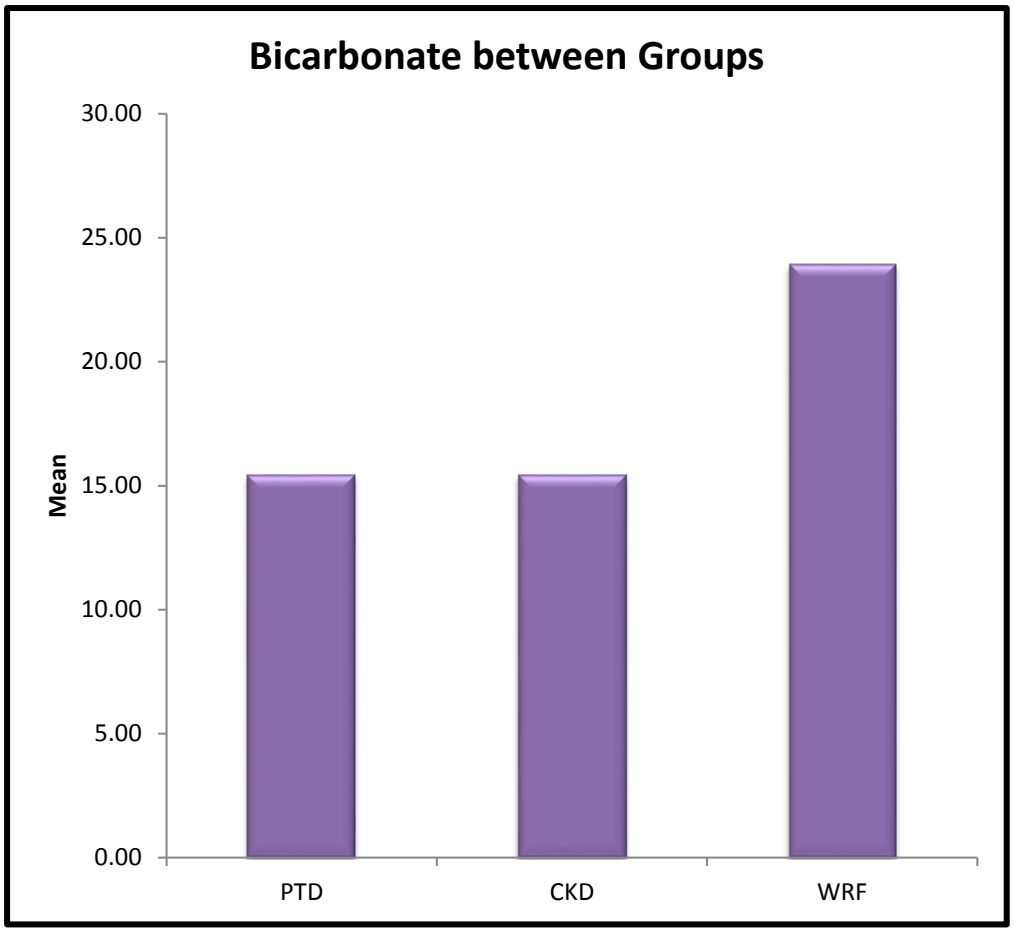


Figure 13

The above table shows the comparison of Bicarbonate between Groups by using Oneway ANOVA were F-value=840.992, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 and No Statistical Significance at p > 0.05 between Groups.

Table 14: Comparison of Calcium between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Calcium	PTD	9	6.61	0.65	370.588	0.0005 **
	CKD	9	6.94	0.63		
	WRF	57	9.00	0.00		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Calcium	PTD	CKD	-.3333	.1428	.058 #	-.675	.009
		WRF	-2.3889*	.1087	.0005 **	-2.649	-2.129
	CKD	WRF	-2.0556*	.1087	.0005 **	-2.316	-1.795
** Highly Significant at p < 0.01 and # No Statistical Significance at p > 0.05							

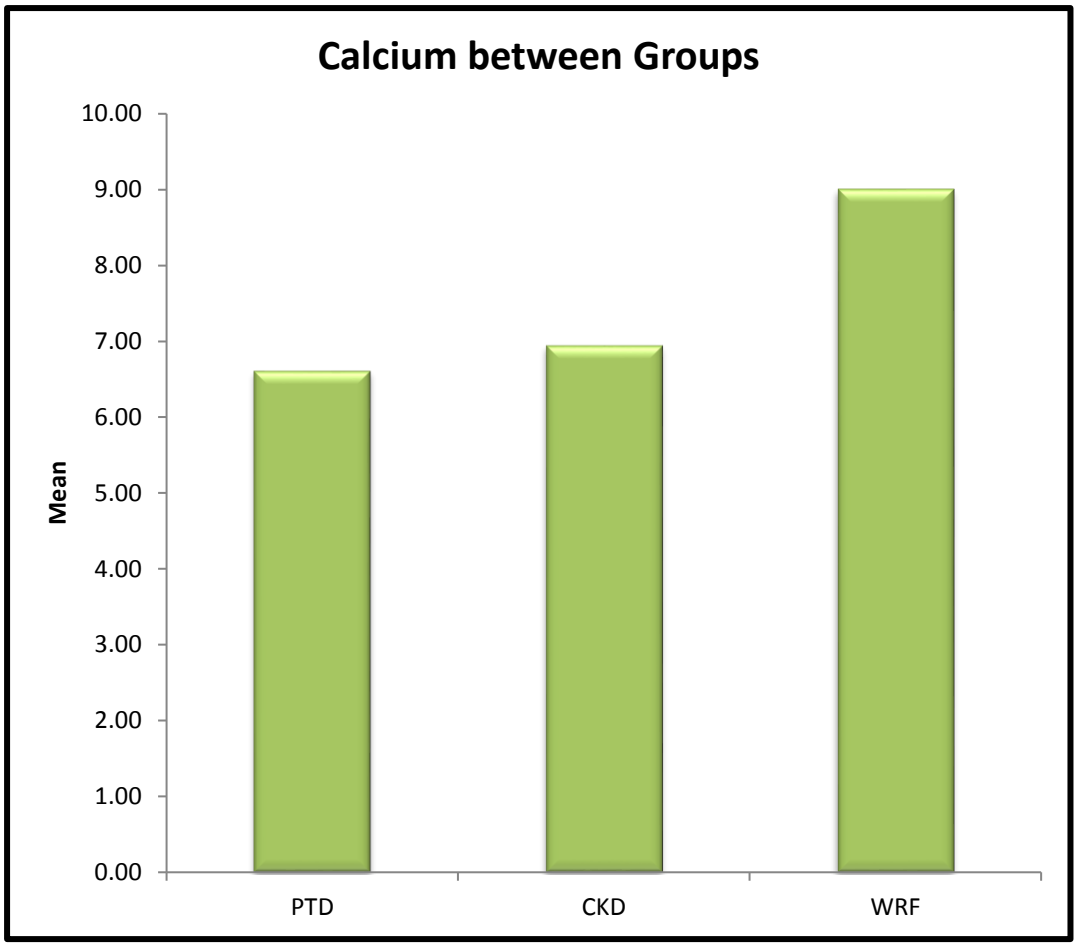


Figure 14

The above table shows the comparison of Calcium between Groups by using Oneway ANOVA were F-value=370.588, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 and No Statistical Significance at p > 0.05 between Groups.

Table 15: Comparison of Phosphorous between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Phosphorous	PTD	9	2.16	0.63	158.769	0.0005 **
	CKD	9	3.89	0.60		
	WRF	57	4.00	0.00		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Phosphorous	PTD	CKD	-1.7333*	.1364	.0005 **	-2.060	-1.407
		WRF	-1.8444*	.1038	.0005 **	-2.093	-1.596
	CKD	WRF	-.1111	.1038	.535 #	-.360	.137
** Highly Significant at p < 0.01 and # No Statistical Significance at p > 0.05							

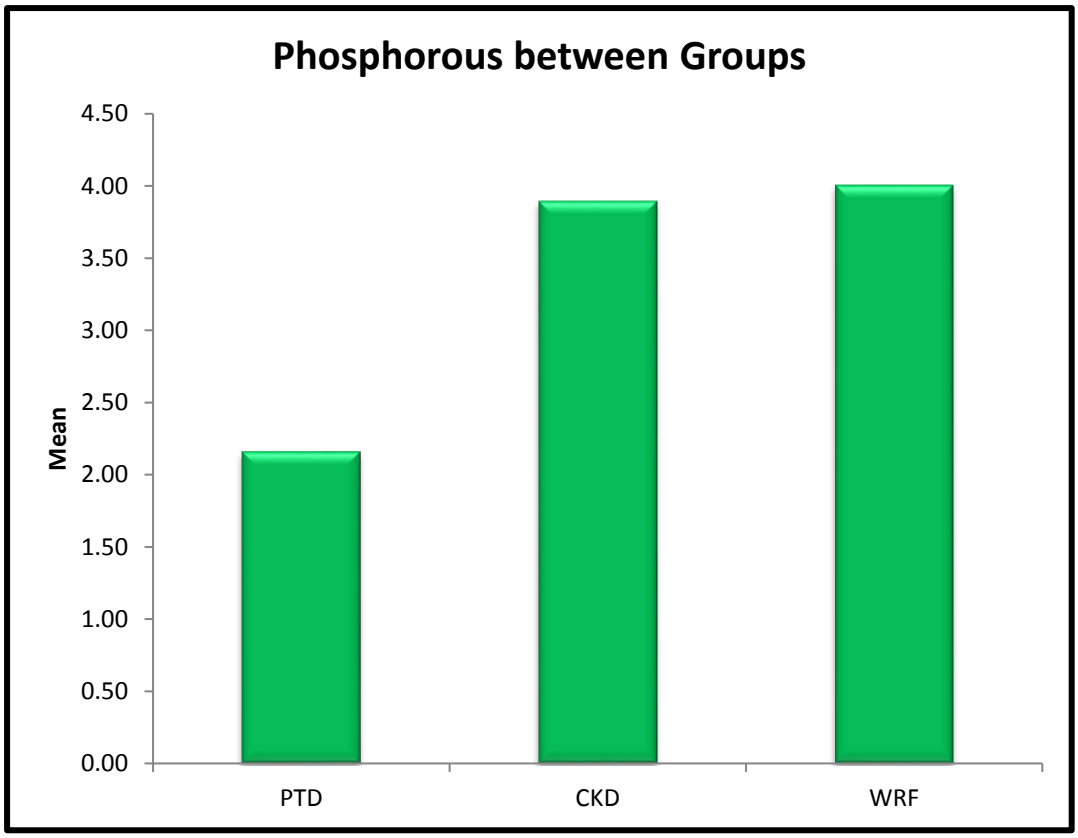


Figure 15

The above table shows the comparison of Phosphorous between Groups by using Oneway ANOVA were F-value=158.769, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 and No Statistical Significance at p > 0.05 between Groups.

Table 16: Comparison of Uric acid between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Uric acid	PTD	9	2.33	0.61	105.6	0.0005 **
	CKD	9	4.00	0.75		
	WRF	57	4.00	0.00		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Uric acid	PTD	CKD	-1.6667*	.1521	.0005 **	-2.031	-1.303
		WRF	-1.6667*	.1158	.0005 **	-1.944	-1.390
	CKD	WRF	0.0000	.1158	1.000 #	-.277	.277
** Highly Significant at p < 0.01 and # No Statistical Significance at p > 0.05							

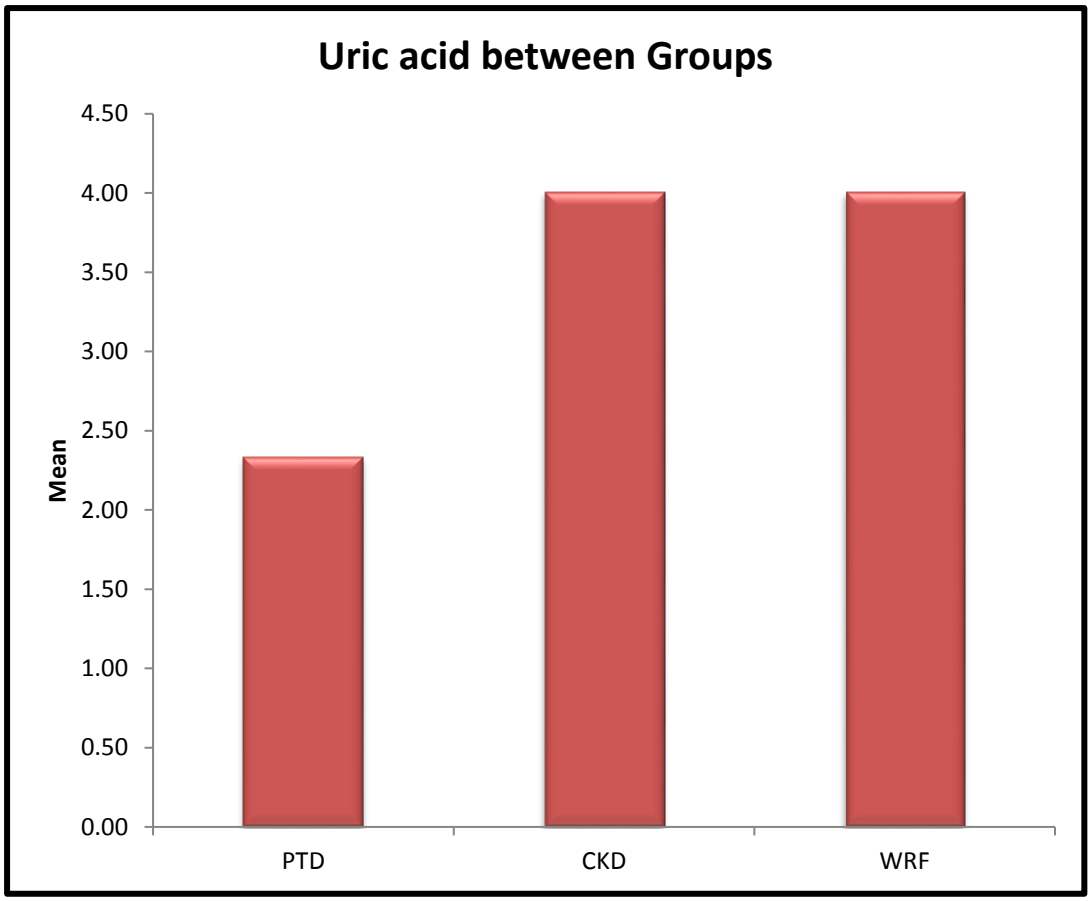


Figure 16

The above table shows the comparison of Uric acid between Groups by using Oneway ANOVA were F-value=105.6, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 and No Statistical Significance at p > 0.05 between Groups.

Table 17: Comparison of Urine PCR between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Urine PCR	PTD	9	0.89	0.29	312.341	0.0005 **
	CKD	9	1.27	0.28		
	WRF	57	0.20	0.00		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Urine pcr	PTD	CKD	-.3778*	.0631	.0005 **	-.529	-.227
		WRF	.6889*	.0480	.0005 **	.574	.804
	CKD	WRF	1.0667*	.0480	.0005 **	.952	1.182
** Highly Statistical Significance at p < 0.01 level							

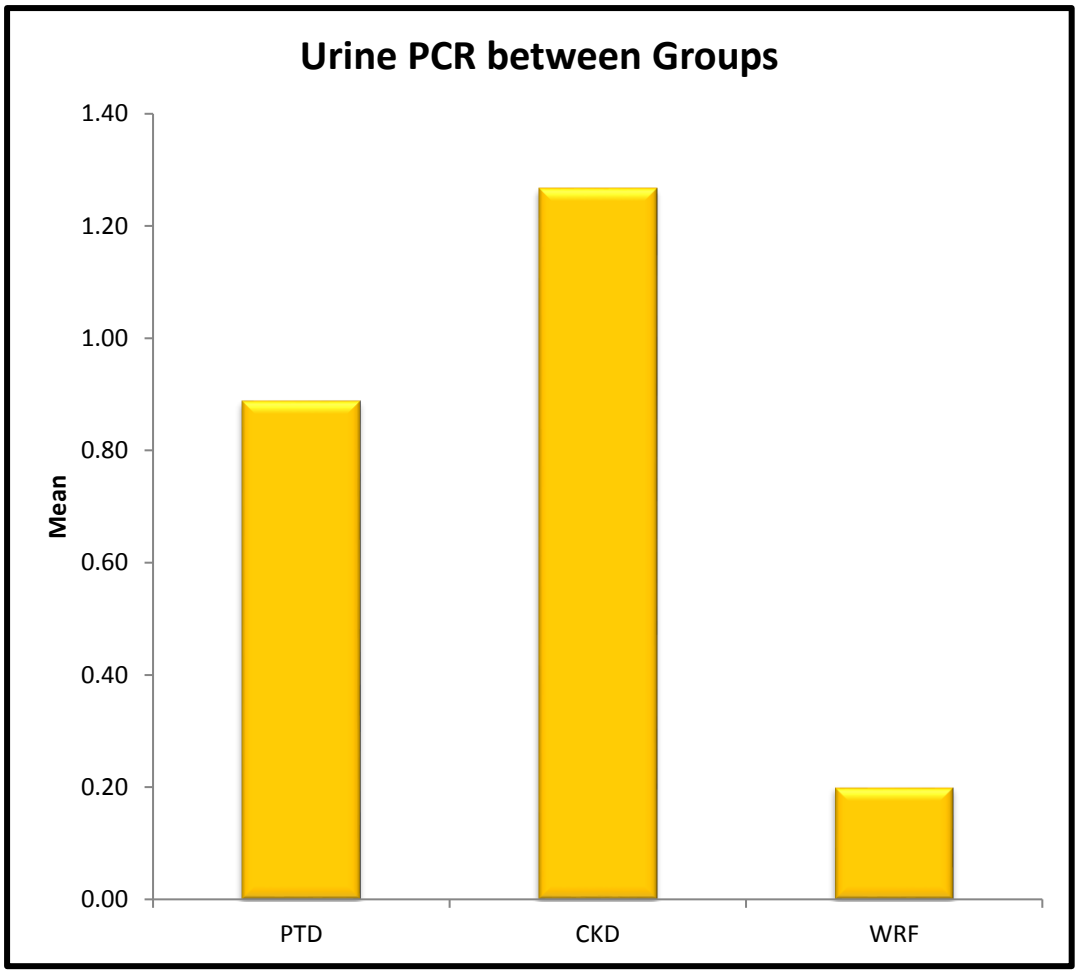


Figure 17

The above table shows the comparison of Urine PCR between Groups by using Oneway ANOVA were F-value=312.341, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.

Table 18: Comparison of Urine albumin between the Groups by Oneway ANOVA test

Variable	Groups	N	Mean	SD	F-value	p-value
Urine albumin	PTD	9	0.56	0.88	55.125	0.0005 **
	CKD	9	1.11	0.33		
	WRF	57	0.00	0.00		
** Highly Statistical Significant at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
(I) Groups			MD (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Urine albumin	PTD	CKD	-.556*	.148	.001 **	-.91	-.20
		WRF	.556*	.113	.0005 **	.29	.83
	CKD	WRF	1.111*	.113	.0005 **	.84	1.38
** Highly Statistical Significance at p < 0.01 level							

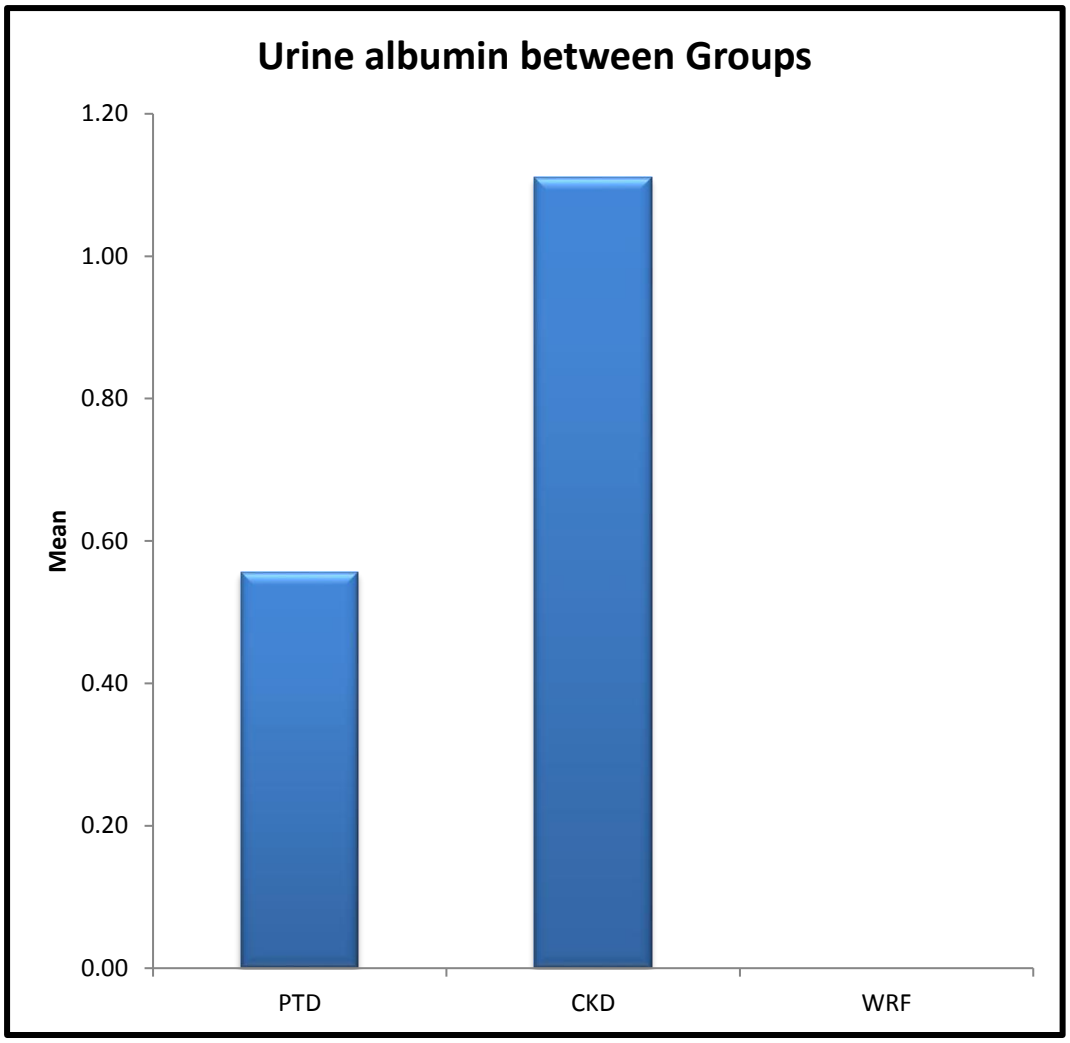


Figure 18

The above table shows the comparison of Urine albumin between Groups by using Oneway ANOVA were F-value=55.125, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.

SUMMARY

SUMMARY

- The Group distribution were PTD is 12.0%, CKD is 12.0%, WRF is 76.0%.
- The Age distribution were 21-30 years is 8.0%, 31-40 years is 21.3%, 41-50 years is 37.3%, 51-60 years is 17.3%, >60 years is 16.0%.
- The Gender distribution were Female is 46.7%, Male is 53.3%.
- The Gender between Groups by Fisher's exact test were χ^2=0.047, p=0.977>0.05 which shows no statistical significance between Gender and Groups.
- The Age between Groups by Fisher's exact test were χ^2=40.458, p=0.0005<0.01 which shows highly statistical significance between Age and Groups.
- The Age between Groups by using Oneway ANOVA were F-value=8.989, p-value=0.0003<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 and No Statistical Significance at p > 0.05 between Groups.
- The Duration between Groups by using Oneway ANOVA were F-value=2.514, p-value =0.088>0.05, which shows statistical significance difference at p >0.05 level.

  The CD 4 count between Groups by using Oneway ANOVA were F-value=24.601, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level, Followed by Post Hoc Tests – Tukey HSD - Multiple Comparisons table shows Highly Significant at p <0.01 and Statistical Significance at p < 0.05 between Groups.
- The Urea between Groups by using Oneway ANOVA were F-value=168.287, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows

Highly Significant at p < 0.01 between Groups.

- The Creatinine between Groups by using Oneway ANOVA were F-value=299.429, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.
- The Sodium between Groups by using Oneway ANOVA were F-value=48.164, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups. The Potassium between Groups by using Oneway ANOVA were F-value=56.251, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p < 0.01 between Groups.
- The Bicarbonate between Groups by using Oneway ANOVA were F-value=840.992, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p <

  0.01 and No Statistical Significance at p > 0.05 between Groups.
- The Calcium between Groups by using Oneway ANOVA were F-value=370.588, p-value=0.0005<0.01, which shows highly statistical significance difference at p <0.01 level. Followed by Post Hoc Tests - Tukey HSD - Multiple Comparisons table shows Highly Significant at p <

  0.01 and No Statistical Significance at p > 0.05 between Groups.

CONCLUSION

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- The Group distribution were PTD is 12.0%, CKD is 12.0%, WRF is76.0%.
- The Age distribution were 21-30 years is 8.0%, 31-40 years is 21.3%, 41-50 years is 37.3%, 51-60 years is 17.3%, >60 years is 16.0%.
- The Gender distribution were Female is 46.7%, Male is 53.3%.
- The Gender between Groups by Fisher's exact test were □2=0.047, p=0.977>0.05 which shows no statistical significance between Gender and Groups.

LIMITATION

LIMITATIONS

In our study only small number of patients (75) were involved and since it was a cross sectional study , the causal relationship could not be identified using a cross sectional analysis.

Renal biopsy could not be done because of ethical problems.

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BIBILIOGRAPHY

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ANNEXURES

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
PTD	-Proximal tubular dysfunction
HIV	-Human Immunodeficiency Virus
HIV AN	-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

Name :

Age / Sex : IP. No :

Address :

Occupation:

ART regimen:

Duration:

Socioeconomic Status :

CD4 count - CD4 %:

Height: Weight:

Blood Pressure –

CLINICAL DETAILS:

INVESTIGATIONS:

Urine - Spot Protein / Creatinine Ratio:

Urine - Albumin: Dep: Sugar :

Sr.Urea:

Sr. Creatinine

Sr. Electrolytes - Na:

K: HC03:

Calcium:

Phosphorous:

Uric acid:

USG. Abdomen & Pelvis:

PATIENT CONSENT FORM

Study Detail : To study the prevalence of renal involvement in patients recieving tenofovir containing antiretroviral therapy

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Patient may check (√) these boxes

- I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.
- I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.
- I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as

required under the law. I agree not to restrict the use of any data or results that arise from this study.

- I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.
- I hereby consent to participate in this study.
- I hereby give permission to undergo detailed clinical examination and blood investigations as required.

Signature of investigator Signature/Thumb impression of participant

Patient name and address

நோயாளிகள் ஆலோசனைபடிவம்:

ஆய்வுவிவரம்:

" டெனோஃபோவரைப் பெறும் நோயாளிகளில்

சிறுநீரக செயலிழப்பு பரவல் அறிய ஆய்வு"

ஆய்வுமையம்: ராஜீவ்காந்திஅரசுபொதுமருத்துவமனை, சென்னை.

நோயாளியின்பெயர்:

நோயாளியின்வயது: அடையாளஎண்:

நோயாளிஇந்தபெட்டிகளைசரிபார்க்கலாம் (check):

மேற்கண்ட ஆய்விற்கான நடைமுறையின் நோக்கத்தை நான் புரிந்து கொண்டேன் என்பதை உறுதிப்படுத்துகிறேன். கேள்வி கேட்க எனக்கு வாய்ப்பு உள்ளது, எனது முழு திருப்திக்கும் எனது எல்லா கேள்விகளுக்கும் சந்தேகங்களுக்கும் பதில் அளிக்கப்பட்டுள்ளது.

ஆய்வில் எனது பங்கேற்பு தன்னார்வமானது என்பதையும், எனது சட்ட உரிமைகள் பாதிக்கப்படாமல், காரணமின்றி எந்த நேரத்திலும் திரும்பப்பெற எனக்கு சுதந்திரம் உள்ளது என்பதையும் நான் புரிந்து கொள்கிறேன்.

மருத்துவ ஆய்வின் ஸ்பான்சர், ஸ்பான்சர் சார்பாக பணிபுரியும் மற்றவர்கள், நெறிமுறைக்குழு மற்றும் ஒழுங்குமுறை அதிகாரிகள் எனது சுகாதார பதிவுகளைப் பார்க்க எனது அனுமதி தேவையில்லை என்பதை நான் புரிந்து கொள்கிறேன், தற்போதைய ஆய்வு மற்றும் மேற்கொண்டுள்ள எந்தவொரு ஆராய்ச்சியையும் பொறுத்தவரை அதனுடன், நான் ஆய்வில் இருந்து விலகினாலும் இந்த அணுகலை ஒப்புக்கொள்கிறேன். எவ்வாறாயினும், சட்டத்தின் கீழ் தேவைப்படாவிட்டால், மூன்றாம் தரப்பினருக்கு வெளியிடப்பட்ட அல்லது வெளியிடப்பட்ட எந்தவொரு

தகவலிலும் எனது அடையாளம் வெளிப்படுத்தப்படாது என்பதை நான் புரிந்து கொள்கிறேன். இந்த ஆய்வில் எழும் எந்தவொரு தரவு அல்லது முடிவுகளின் பயன்பாட்டை கட்டுப்படுத்த வேண்டாம் என்று நான் ஒப்புக் கொள்கிறேன்.

மேற்கண்ட ஆய்வில் பங்கேற்கவும், ஆய்வின் போது கொடுக்கப்பட்ட அறிவுறுத்தல்களுக்கு இணங்கவும், ஆய்வுக்குழுவுடன் உண்மையுடன் ஒத்துழைக்கவும், எனது உடல் நலம் அல்லது நல்வாழ்வில் ஏதேனும் சரிவு ஏற்பட்டால் அல்லது எதிர்பாராத அல்லது அசாதாரணமான ஏதேனும் ஏற்பட்டால் உடனடியாக ஆய்வு ஊழியர்களுக்கு அறிவிக்கவும் ஒப்புக்கொள்கிறேன். அறிகுறிகள். இந்த ஆய்வில் பங்கேற்க நான் இதன் மூலம் ஒப்புக்கொள்கிறேன்.

தேவைக்கேற்ப விரிவான மருத்துவ பரிசோதனை மற்றும் இரத்த விசாரணைகளை மேற்கொள்ள நான் இதன் மூலம் அனுமதி அளிக்கிறேன்.

ம்: நோயாளியின்கையொப்பம் / கட்டைவிரல்எண்ணம்:

ஆய்வுஆய்வாளர்பெயர்: நோயாளியின்பெயர் மற்றும் முகவரி:

INFORMATION TO PARTICIPANTS

Investigator: DR.SOWMYA.S

Study centre: Rajiv Gandhi Government General Hospital and Madras Medical College,Park Town,Chennai 03.

STUDY TITLE: “To study the prevalence of renal involvement in patients receiving Tenofovir containing Anti retroviral therapy”

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria.

Rights and confidentiality:

The participation in this study is purely voluntary. You have every right not to participate in this study. All the data collected in this regard from you will be kept discretely and your name will not be revealed at any circumstances.

To whom you may contact?

If you have any doubts and clarification required you can call the doctor SOWMYA.S

at the 9840533229 mobile number at any time. Signature / Thumb Impression of Patient

Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013/RR-16
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
DR.SOWMYA S,
Post Graduate, MD (General Medicine),
Institute of Internal Medicine,
Madras Medical College,
Chennai – 600003.

Dear DR. SOWMYA S,

The Institutional Ethics Committee has considered your request and approved your study titled **"TO STUDY THE PREVALENCE OF RENAL INVOLVEMENT IN PATIENTS RECEIVING TENOFOVIR CONTAINING ANTI RETROVIRAL THERAPY"- NO.09042021.** The following members of Ethics Committee were present in the meeting held on **07.04.2021** conducted at Madras Medical College, Chennai 3.

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

We approve the proposal to be conducted in its presented form.

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

Member Secretary, Ethics Committee

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

Curiginal

Document Information

Analyzed document	DR.SOWMYA.S M.D FINAL YEAR THESIS copy.docx (D122076516)
Submitted	2021-12-12T09:45:00.0000000
Submitted by	Dr.Sowmya. S
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Similarity	2%
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Sources included in the report

SA	**New mutations into HIV edited.docx** Document New mutations into HIV edited.docx (D75239726)	5
SA	**HIV-29-03-20 plag.docx** Document HIV-29-03-20 plag.docx (D66815053)	2
W	URL: https://www.worldwidejournals.com/global-journal-for-research-analysis-GJRA/recent_issues_pdf/2021/May/evaluation-of-performance-of-lung-ultrasound-lus-in-paediatric-pneumonia_May_2021_4825906161_3601334.pdf Fetched: 2021-12-12T09:45:03.2630000	2
W	URL: https://docplayer.net/216690421-Original-research-paper.html Fetched: 2021-12-12T09:45:02.0930000	4

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **TO STUDY THE PREVALENCE OF RENAL INVOLVEMENT IN PATIENTS RECEIVING TENOFOVIR CONTAINING ANTI RETROVIRAL THERAPY** of the candidate Dr. SOWMYA.S with registration Number 201911020 for the award of MASTERS DEGREE in the branch of GENERAL MEDICINE personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 2% percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

Place:Chennai

Date:

MASTER CHART

MASTER CHART

Age	Sex	ART REG	Duration	CD 4 count	Urea	Creatinine	Sodium	Potassium	Bicarbonate	Calcium	Phosphorous	Uric acid	Urine protein creat..	Urine albumin	Usg abdomen
25	Female	Tle	4	154	44	1.3	126	2.8	15	6	1.5	1.5	1.2	2+	Normal
45	Male	Tle	5	200	36	1.2	127	2.9	15	6	1.5	1.5	1	2+	Normal
30	Female	Tle	2	185	40	1.1	124	2.6	14	6	1.4	2.5	1	1+	Normal
21	Female	Tle	3	250	40	1.2	130	3	15	6.5	2	2	1	0	Normal
35	Male	Tle	3	250	30	1	130	3	16	6.5	2	2	1	0	Normal
45	M	Tle	2	250	30	1	135	3	18	6.5	2.5	3	0.5	0	Normal
25	M	Tle	2	240	30	1	130	2.5	15	8	2.5	2.5	1	0	Normal
40	F	Tle	4	260	40	1	130	3	15	7	3	3	0.3	0	Normal
23	M	Tle	1	400	30	0.6	133	3	16	7	3	3	1	0	Normal
50	F	Tle	10	350	60	2.5	135	4.5	19	7	4.5	4	1.2	2+	B/l contracted kidney
55	M	Tle	5	356	70	4	137	4.7	14	7.5	4	5	1.6	1+	B/l contracted kidney
60	M	Tle	3	400	66	3.5	130	5	14	7	4	4	1.5	1+	B/l contracted kidney
66	M	Tle	4	456	75	3.5	142	5.6	15	7	4	4	1	1+	B/l contracted kidney

30	F	Tle	3	350	35	1.5	130	2.8	14	6	2.5	2.5	1	1+	B/l contracted kidney
57	F	Tle	6	250	80	4	136	5.7	14	7	4	5	1.5	1+	B/l contracted kidney
45	M	Tle	4	400	75	3	140	4.5	16	7	4.5	4	1	1+	B/l contracted kidney
60	F	Tle	3	450	68	3.5	128	3.5	16	6	3.5	3.5	1.6	1+	B/l contracted kidney
47	M	Tle	4	430	68	3.4	128	3.5	17	8	4	4	1	1+	B/l contracted kidney
45	M	Tle	1	350	20	0.5	135	4	22	9	4	4	0.2	0	Normal
42	M	Tle	2	460	21	0.5	135	4	22	9	4	4	0.2	0	Normal
43	F	Tle	3	450	25	0.6	135	4	24	9	4	4	0.2	0	Normal
53	F	Tle	4	600	23	0.6	135	4	24	9	4	4	0.2	0	Normal
35	M	Tle	5	800	21	0.6	135	4	24	9	4	4	0.2	0	Normal
35	F	Tle	6	700	21	0.6	136	4	24	9	4	4	0.2	0	Normal
34	M	Tle	1	410	21	0.7	136	4	24	9	4	4	0.2	0	Normal
42	F	Tle	2	420	25	0.8	136	4	24	9	4	4	0.2	0	Normal
43	M	Tle	3	415	24	0.8	136	4	24	9	4	4	0.2	0	Normal
41	F	Tle	4	456	26	0.8	136	4	24	9	4	4	0.2	0	Normal
43	M	Tle	5	425	26	0.8	136	4	24	9	4	4	0.2	0	Normal
33	F	Tle	5	415	25	0.8	136	4	24	9	4	4	0.2	0	Normal
32	M	Tle	6	418	28	0.7	136	4	24	9	4	4	0.2	0	Normal

31	M	Tle	6	450	29	0.7	136	4	24	9	4	4	0.2	0	Normal
34	M	Tle	7	426	27	0.7	136	4	24	9	4	4	0.2	0	Normal
42	F	Tle	7	521	24	0.7	136	4	24	9	4	4	0.2	0	Normal
46	F	Tle	1	521	24	0.7	136	4	24	9	4	4	0.2	0	Normal
48	M	Tle	3	550	25	0.8	138	4	24	9	4	4	0.2	0	Normal
55	M	Tle	1	526	28	0.9	138	4	24	9	4	4	0.2	0	Normal
56	M	Tle	3	562	29	0.7	138	4	24	9	4	4	0.2	0	Normal
54	M	Tle	4	582	30	0.8	138	4	24	9	4	4	0.2	0	Normal
53	M	Tle	4	547	31	0.8	138	4	24	9	4	4	0.2	0	Normal
43	M	Tle	5	459	32	0.7	138	4	24	9	4	4	0.2	0	Normal
33	F	Tle	5	487	34	0.8	138	4	24	9	4	4	0.2	0	Normal
32	F	Tle	6	415	34	0.8	138	4	24	9	4	4	0.2	0	Normal
34	F	Tle	6	423	34	0.8	138	4	24	9	4	4	0.2	0	Normal
45	M	Tle	6	426	35	0.5	138	4	24	9	4	4	0.2	0	Normal
46	M	Tle	4	425	35	0.7	138	4	24	9	4	4	0.2	0	Normal
65	F	Tle	4	458	35	0.7	138	4	24	9	4	4	0.2	0	Normal
63	M	Tle	4	475	36	0.8	138	4	24	9	4	4	0.2	0	Normal
32	F	Tle	3	478	20	0.7	140	4	24	9	4	4	0.2	0	Normal
57	M	Tle	4	418	21	0.7	140	4	24	9	4	4	0.2	0	Normal
34	F	Tle	2	452	21	0.7	140	4	24	9	4	4	0.2	0	Normal
45	M	Tle	4	452	21	0.7	140	4	24	9	4	4	0.2	0	Normal
46	F	Tle	4	415	23	0.7	140	4	24	9	4	4	0.2	0	Normal
45	M	Tle	3	415	23	0.8	140	4	24	9	4	4	0.2	0	Normal
43	M	Tle	4	415	25	0.6	140	4	24	9	4	4	0.2	0	Normal
42	F	Tle	4	478	25	0.6	140	4	24	9	4	4	0.2	0	Normal
41	F	Tle	3	548	26	0.6	140	4	24	9	4	4	0.2	0	Normal

38	F	Tle	4	547	26	0.8	140	4	24	9	4	4	0.2	0	Normal
39	M	Tle	3	569	25	0.7	140	4	24	9	4	4	0.2	0	Normal
76	F	Tle	2	521	25	0.7	140	4	24	9	4	4	0.2	0	Normal
65	M	Tle	1	523	28	0.6	140	4	24	9	4	4	0.2	0	Normal
64	M	Tle	1	651	24	0.6	140	4	24	9	4	4	0.2	0	Normal
63	M	Tle	1	547	24	0.6	140	4	24	9	4	4	0.2	0	Normal
63	F	Tle	1	587	25	0.6	140	4	24	9	4	4	0.2	0	Normal
62	F	Tle	2	519	21	0.6	140	4	24	9	4	4	0.2	0	Normal
64	M	Tle	6	591	21	0.6	140	4	24	9	4	4	0.2	0	Normal
64	F	Tle	5	482	28	0.6	140	4	24	9	4	4	0.2	0	Normal
43	F	Tle	4	362	25	0.6	140	4	24	9	4	4	0.2	0	Normal
42	M	Tle	3	348	24	0.5	140	4	24	9	4	4	0.2	0	Normal
54	F	Tle	4	348	24	0.7	140	4	24	9	4	4	0.2	0	Normal
54	M	Tle	4	347	21	0.8	140	4	24	9	4	4	0.2	0	Normal
43	F	Tle	3	340	28	0.8	140	4	24	9	4	4	0.2	0	Normal
54	F	Tle	3	321	29	0.8	140	4	24	9	4	4	0.2	0	Normal
43	M	Tle	5	250	30	0.8	140	4	24	9	4	4	0.2	0	Normal
65	F	Tle	5	290	30	0.9	140	4	24	9	4	4	0.2	0	Normal