

**SAINT PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE**



**IMPAIRED RENAL FUNCTION AND ASSOCIATED FACTORS  
AMONG HIV INFECTED INDIVIDUALS WHO ARE ON  
FOLLOW-UP IN TWO TERTIARY HOSPITALS' ART CLINIC,  
Addis Ababa, Ethiopia.**

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**ADDIS ABABA, ETHIOPIA**

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## **ABSTRACT**

**Background:** It has been 4 decades since Human Immune deficiency Virus (HIV) has become a global issue of public health importance; a lot has changed about the disease since then. The occurrence of renal impairment in HIV infected individuals shown to be associated with both increased morbidity and mortality of the infected individuals. Due to which, finding the common causes of renal impairment in HIV infected individuals has paramount importance.

**Objective:** The study aims to assess impaired renal function and associated factors among HIV infected individuals in ART clinic at Zewuditu memorial hospital(ZMH) and St. Paul's millennium medical college(SPHMMC), from April to August 2021.

**Methodology:** A cross sectional study was conducted to assess the association of impaired renal function and different factors among HIV infected individuals. Data was collected from medical chart of the patients in anti-retroviral therapy (ART) clinic of respective hospitals. Data collection took 2 months, July 01 2021 to August 30, 2021, among patients who were on follow up at SPHMMC and ZMH ART clinic. Descriptive and analytic data analysis were done. Data was collected using checklist, entered in EpiData version 3.01, and analyzed using SPSS version 20. Texts, tables and figures were used to present the results. Variables with a p-value of  $<0.25$  on bivariate analysis were taken to Multivariable logistic regression to see the statistical significance and at  $<0.05$  statistically significant was declared.

**Result:** The total number of samples were 405 all of them were included in the in the analysis. The magnitude of the renal dysfunction revealed from this study was 8.4% (95% Confidence Interval: 5.51 to 11.4). Multivariable logistic regression shows that being female (Adjusted Odds Ratio = 4.5; 95%CI: 1.94, 10.36), Baseline CD4 count less than 200, (AOR = 3.4; 95% CI:1.34, 8.70), history of opportunistic infection, (AOR = 2.7; 95% CI: 1.02, 7.39), were significantly associated with the impaired renal function.

**Conclusion:** The prevalence of impaired renal function was low when compared to other studies done in Ethiopia. Being female, lower CD4 count and having history of opportunistic infection were associated with impaired renal function. Health institutions involvement in early detection and prevention of opportunistic infection among patient with HIV prevent renal function impairment.

**Key words:** impaired renal function, HIV infection, ART clinic, Addis Ababa, Ethiopia.

## **ABBREVIATIONS AND ACRONYMS**

ABC-Abacavir

AIDS-Acquired Immune Deficiency Virus

AKI-Acute Kidney Injury

ARC-Annualized Rate of Change

ART-Anti Retroviral Therapy

ATV-Atazanavir

BMI-Body Mass Index

CDC-Center for Disease Control

CKD-Chronic Kidney Disease

Ddi- Didanosin

DTG-Delutogravir

D4T-Stavudin

eGFR-Estimated Glomerular Filtration Rate

ESRD-End Stage Renal Disease

FSGS-Focal Segmental Glomerular Sclerosis

GC-Gregorian Calendar

HCV-Hepatitis C Virus

HIVAN-HIV Associated Nephropathy

HIVICK-HIV Associated Immune Complex Kidney Disease

HIV-Human Immune Deficiency Virus

NVP-Nevirapin

PI-Protease Inhibitors

PLHIV-People Living With HIV

Scr-Serum Creatinine

SSA-Sub Saharan Africa

SPHMM C-Saint Paul's millennium medical college.

TDF-TenofovirDiproxilFumarate

VL-Viral Load

WHO-World Health Organization

ZMH-Zewuditu memorial hospital

3TC-Lamuvudin

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# 1. INTRODUCTION

## 1.1. Background

Renal impairment is the inability of the kidneys to perform excretory function. Which is filtering or getting rid of toxin and waste products, removal or metabolism of drugs, keeping balance of the body fluids and electrolytes, release of hormones which acts on different parts of the body. Renal impairment can be classified as acute kidney injury (AKI) and chronic kidney disease (CKD) based on the duration and reversibility of the disease. Which is usually characterized by reduced glomerular filtration rate(GFR) with or without decrease in urine output(1).

HIV infected individuals are at risk of both AKI and CKD like any other people. Moreover they are at increased risk of renal impairment compared to the general population, because of the virus, opportunistic infection and poly pharmacy they are taking(2).

A relatively high prevalence of renal dysfunction was reported throughout the world and most importantly in several African countries in ART naïve HIV positive people. Low body mass index (BMI), low CD4count, high viral load(VL) , concomitant hepatitis C virus (HCV) infection, and advanced stage of the disease were identified as risk factors for development of renal impairment in ART naïve HIV positive people in addition to the traditional risk factors for kidney diseases in the general population(3).

HIV/AIDS continues to have devastating health effects globally, with over 39 million HIV/AIDS-related deaths to date and more than 38 million people living with HIV currently. Despite great advancements in ART and worldwide progress towards implementation of treatment-as-prevention programs, approximately 2.2 million people become newly infected with HIV every year(4). Sub-Saharan Africa (SSA) is heavily affected by HIV and AIDS than any other region of the world. An estimated 22.9 million people are living with HIV in the region which accounts two thirds of the globally infected population(5).

The first description of severe proteinuria with a rapid loss of kidney function in HIV-infected patients with AIDS was published in 1984. The histopathological pattern corresponded to collapsing focal segmental glomerulosclerosis (FSGS), a condition, later known as HIV associated nephropathy (HIVAN), that usually presents. Although HIVAN is the best known

example of HIV-associated kidney disease, a large spectrum of kidney syndromes is now known to occur in HIV-infected patients,(6).Evidently due to the introduction of ART the classic HIVAN become less common while other kidney disease are concomitantly increased. It has been shown that people with high viral load, low CD4 count, and advanced disease is the major risk factor for HIVAN With introduction of ART those risk factors significantly reduced instead other risk factors become more prominent, like lifelong exposure of ART(2).

Early initiation of ART improves renal function, despite which HIV-infected patients are still at higher risk for both AKI and CKD, which are interconnected syndromes responsible for a heavy burden of mortality among HIV infected individuals(6). Since 2016 WHO recommends initiation of ART despite clinical stage and CD4 count which may further reduce the incidence of HIVAN, but the overall risk-benefit for kidney health is unknown(2).Renal impairment in HIV-infected persons manifests in a variety of ways, including AKI, HIV-associated kidney disease, co morbid CKD, and treatment-related kidney toxicity. The burden of CKD and end-stage renal disease (ESRD) remains high in the HIV- infected population(7).

## **1.2 Statement of the problem**

HIV infection is a global health problem with approximately 80% of those infected in under developed or developing countries. In the United States, approximately 1.1 million people are currently infected, of which 14.2% maybe unrecognized. It is estimated that 1.8 million people were newly infected with HIV in 2016, with SSA the most severely affected region. Data from 2015 also indicate that 82.3% of new HIV infections occurred in individuals 15–49 years, with 17% in those more than 50 years of age. Notably, 40% of those 55 and older were diagnosed late in the course of infection, with presumably greater risk of developing age-related renal disease(8).

The coexistence of kidney disease and HIV/AIDS significantly increases mortality of affected individual(9).

Just over 50% of people infected with HIV worldwide are receiving ART, with profound effects on quality of life and survival. ART improves renal survival even when started after renal disease has ensued. As a result, there is increasing prevalence of CKD, now found in 2.4–47.6% of HIV-infected patients, across variable geographic areas and Ethnicity(8). However, to the best knowledge of the investigator, studies conducted regarding renal dysfunction among HIV patients in Ethiopia are limited. This study will generate evidence on the prevalence of renal function impairment and associated factors including duration of ART, regimen of ART, age, the presence of other traditional risk factors of renal impairment, CD4, Viral Load and WHO clinical stage and the disease characteristic and demography of HIV which intern would indicate possible mitigation strategy. To the scope of the researcher, no similar study was done at the study area among people living with HIV/AIDS. Therefore, this study is aimed at assessing the prevalence and factors associated with renal dysfunction among people living with HIV and attending the ART clinic at Zewuditu Memorial Hospital and Saint Paul's Hospital Millennium Medical College

### **1.3 Significance of the study**

The findings from this study will help the followings:

Patients with the specific problem could benefit from the result of this study directly or indirectly. These patients will seek treatment and investigations as early as possible.

Zewuditu Memorial Hospital and Saint Paul's Hospital Millennium Medical College: The hospitals could use the study result as a base line for future studies and for academic purpose.

The Addis Ababa Health Bureau: The study result could help find an important direction to organize and strengthen health services in collaboration with respective health facilities.

Locally Based Governmental, and None-Governmental Organizations and Researchers: The study results could also be used as baseline information for locally based organizations and researchers working similar issue.

## **2. LITERATURE REVIEW**

Studies have shown that the prevalence of HIV associated renal disease varies according to geographical locations, For instance according to inter-continental research which was conducted on people living with HIV in 2019 the estimated prevalence of CKD in HIV population measured using CKD-EPI equation ranges from 2.5% in Europe to 7.4% in North America(10).

### **2.1 Magnitude/prevalence of renal dysfunction**

A retrospective study of HIV-infected patients conducted in Liaoning province China in 2018, 306 patients were included in this study. There were 15 female and 291 male patients. The prevalence of renal impairment among Chinese hospitalized HIV positive patients was 5.56% (17/306)(11).

A cross-sectional study done to assess the prevalence of renal dysfunction among HIV infected patients receiving Tenofovir in Kampala, Uganda in 2018 showed that the prevalence of renal dysfunction was 2.52%(n=77)(12).

According to a hospital-based cross-sectional study conducted among newly diagnosed HIV positive individuals in Northern Uganda, the prevalence of impaired renal function to be 14.4% (n=52) (eGFR<60 mL/min/1.73 m<sup>2</sup>) and of this 71.2%(n=37) was moderate renal impairment (eGFR 30–59.9 mL/min/1.73 m<sup>2</sup>) and 15 (28.8%) was severe renal impairment (eGFR<30 mL/min/1.73 m<sup>2</sup>)(13).

Another study conducted to determine Renal Dysfunction among HIV-Infected Patients Starting Antiretroviral Therapy in Mwanza, Tanzania in 2009/10 revealed a prevalence of renal dysfunction (eGFRs<90 ml/min/1.73m<sup>2</sup>)to be 63.7% (226). Overall, 38.6% (n=137) had eGFRs of 60–89 ml/min/1.73m<sup>2</sup>, and 24.5%(n=87) had eGFRs of 30–59 ml/min/1.73m<sup>2</sup>(14)

A cross sectional study done in Jima university hospital revealed that the prevalence of Renal impairment was 18.2%(15) .

### **2.2. Factors associated with renal impairment**

According to systemic scoping review which was conducted in South Africa in 2017 on HIV patients in the Era of ART which included 11 studies. Normal renal function occurred from 28.4 to 79% of the patients. Older age, a lower CD4 count, a low hemoglobin and detectable viral load were associated with renal impairment(16).

In a cross-sectional study conducted in Mwanza, Tanzania in to determine Renal Dysfunction among HIV-Infected Patients Starting Antiretroviral Therapy female gender (OR 3.0, 95% confidence interval (CI) [1.8–5.1],  $p < 0.0001$ ), Body mass index (BMI)  $< 18.5$  (OR 2.3 [1.3–4.1],  $p = 0.004$ ), CD4 Tcell  $< 200$  cells/mm<sup>3</sup> (OR 2.3 [1.1–4.8],  $p = 0.04$ ), and world health organization (WHO) clinical stage (OR 1.6 [1.2–2.3],  $p = 0.001$ ) were factors independently associated with renal dysfunction(14).

A hospital-based cross-sectional study conducted among newly diagnosed HIV positive individuals in Northern Uganda showed that Age  $> 34$  years (OR 2.8, 95%CI [1.3-5.9],  $P = 0.009$ ), CD4 cell count  $< 350$  cells/ $\mu$ l (OR 2.4, 95% CI [1.0-4.7 ],  $P = 0.039$ ), and proteinuria (OR 9.6, 95%CI [5.2-17.9 ],  $P < 0.001$ ), were significantly associated with impaired renal function(13)

#### 2.2.1. HIV associated nephropathy

Since HIVAN is a classical kidney disease which is usually mentioned with HIV. Its occurrence is less common and depends on certain population genetics, And it is diagnosed histologically in HIV patient with heavy proteinuria, A biopsy series from patients in the New York area in the pre-ART era identified HIVAN in 76.5% of renal biopsies, whereas HIVICD lesions (with nephrotic range proteinuria) were identified in ~30% of patients infected with HIV in Washington DC before the introduction of protease inhibitors(17).

A large US multicenter study performed in 2004 found that 52.8% of patients infected with HIV who underwent a renal biopsy had a diagnosis other than HIVAN, of whom 34% were treated with ART. HIVICD lesions represented 30.3% of the renal biopsy diagnoses in this series. A 2013 analysis of kidney biopsy samples taken from individuals with HIV infection included in the Johns Hopkins HIV clinical cohort found that 32.2% of patients had HIVICD and 20.9% had HIVAN A possible shift from HIVAN to HIVICD could be attributed to the widespread use of ART(18).

SSA has the largest HIV epidemic worldwide, with an estimated 25 million people infected with the virus in 2007. HIV-associated CKD is also highly prevalent in Nigeria; with one data series showing that ~40% of patients infected with HIV and not undergoing ART had proteinuria or a reduction in creatinine clearance. The prevalence of HIVICD in patients, who underwent kidney

biopsy in South Africa in 2006, was 21.2%, of whom 7.3% were treated with ART, and 27% of the patients in this biopsy series were diagnosed with HIVAN(19).

Another study from South Africa found that HIVAN was present in 83.3% of patients with kidney disease who had not been treated with although various renal pathologic diagnoses were identified in this cohort, only ~6.6% of the cases had HIVICD. Finally, a renal biopsy series was performed retrospectively from 2005–2008 and prospectively from 2008–2010 in a cohort of patients infected with HIV from Cape Town, South Africa from this cohort, 57.2% had HIVAN, 8.3% had HIVICD, and 30.2% had features of both HIVAN and HIVICD. A total of 37.5% of the patients in this series were treated with ART, of whom 40% had HIVAN and 50% had HIVICD. These results highlight the essential role of renal biopsy in discriminating between the diverse renal lesions that may be encountered in patients infected with HIV in the ART(18).

#### 2.2.2. ART related nephrotoxicity

The advent of ART has dramatically changed outcome of HIV+ patients in the last two decades reducing mortality and risk of progression to AIDS, even though important adverse side effects including nephrotoxicity arose with its use. Direct renal injury occurs with tubular dysfunction, acute interstitial nephritis and renal calculi. Indirect mechanisms of injury are due to medication dosing errors, drug–drug interactions, ART-induced rhabdomyolysis, lactic acidosis and metabolic complication(10).

In the EuroSIDA Study, which was a prospective observational pan European cohort in which more than 23,000 patients has been enrolled from 35 European country of HIV-positive persons, each additional year of TDF, atazanavir, and ritonavir-boosted lopinavir was associated with 16%, 21%, and 8% higher incidence of CKD, respectively. Similar findings were observed among individuals without baseline CKD in the Data Collection on Adverse Events of Anti-HIV drugs Study over a median follow-up of 7.2 years (20).

Recent retrospective analysis of a prospective French HIV cohort of patients starting ART with baseline eGFR>60 mL/min/ 1.73 m<sup>2</sup>, CKD incidence was 9.6 per 1000 patient-years. The incidence was highest in patients treated with boosted PI with TDF.(6)A subsequent meta-analysis of 17 studies reported faster kidney function decline (23.9 ml/min) and slightly increased risk of AKI (risk difference of 0.7%) among TDF versus non TDF users. The risk of

nephrotoxicity may be higher among TDF users with concomitant use of ritonavir-boosted protease inhibitors(20).

A hospital based prospective cross-sectional study done in Ethiopia to determine TDF related renal toxicity, showed 16 (25.4%) of whom had fall in eGFR greater than 25% relative to baseline. Only age greater than 50 years, baseline CD4 count less than 200 cells/mm<sup>3</sup>, and baseline proteinuria were significantly associated with renal dysfunction in multi-variable logistic regression. There was 8.4 ml/min/1.73m<sup>2</sup> mean change in eGFR relative to baseline at six months of the study (21).

### 2.2.3. Patterns of renal impairment in HIV infected individuals

In a prospective cross-sectional study conducted in New York with 25,114 HIV-infected patients in the post-ART era, AKI of 2.82 % and 2.66 % mortality of 5.83 % and 5.1% compared with patients without HIV was found(19).

data which was collected from treat Asia HIV observational data base Of 2547 patients eligible for this analysis, Tenofovir was being used by 703 (27.6%) at baseline. Tenofovir use, high baseline eGFR, advanced HIV disease stage, and low nadir CD4 were associated with a decrease in eGFR during follow-up. Chronic kidney disease occurred at a rate of 3.4 per 1000 patient/years. Factors associated with CKD were Tenofovir use, old age, low baseline eGFR, low nadir CD4, and protease inhibitor use(22).

According to a Greek cohort a patient profile in 2003 and 2013 two cross-sectional analyses (2003 and 2013) on data from the AMACS cohort were performed. 2,403 PLHIV were identified in 2003 and 4,910 in 2013 (1,730 contributing for both cross-sections) Serum creatinine levels seemed stable mg/dL in both years; but eGFR decreased significantly within the decade 102.8 vs. 98.8ml/min/1.73m<sup>2</sup> in 2003 and 2013, respectively and the prevalence of CKD (i.e. as eGFR < 60 ml/min/1.73m<sup>2</sup>) increased also significantly from 1.1% in 2003 to 4.9% in 2013. Significant increases were also observed in the proportion of patients with mildly reduced kidney function (i.e. with eGFR between 60 and 89 ml/min/1.73m<sup>2</sup>)(23).

Data's from west African cohort shows that three thousand, one hundred and thirty-eight patients (72% women) were followed for a median of 4.5(2.2–6.9) years. At baseline, median eGFR was 110.7(94.4–128.4) ml/min/1.73m<sup>2</sup> and 93 (3%) patients exhibited eGFR < 60 ml/min/1.73m<sup>2</sup>.

The lowest-performing progressions of eGFR during the first year of ART were observed in patients with 40-49 yr. age range, age  $\geq 50$  year and high blood pressure at ART initiation. The prevalence of CKD was 0.5% and the incidence was 1.9 cases/1000 person-years. The risk of CKD was higher in patients with high blood pressure, 40-49 yr. patients,  $\geq 50$  yr. patients and patients exposed to abacavir (ABC) or didanosine (ddI) based ART (24).

According to a retrospective cross-sectional study which was conducted at Togo, Lomé which tried to identify risk factors for renal failure There were 3118 HIV-infected patients included in that study. The median estimated filtration rate was 94.7 ml/min/1.73m<sup>2</sup>: 2.9% had an eGFR < 15 ml/min/1.73 m<sup>2</sup>. Most of patients had HIV1. In the multivariate analysis, age greater than 40 years, and female gender and hyperleukocytosis. greater than 10,000/mm<sup>3</sup> were significantly associated with renal disease (25). In the contrary on another retrospective study which was done in Nigeria assessed predictors of renal impairment among HIV infected individuals on this study data for 315 (189 females and 126 males) patients were retrieved. The mean age of the population was 39.55 $\pm$ 12.34. Seventy-eight patients (24.8%) had a reduced eGFR defined as  $\leq 60$ ml/min with more females than males (25.4% vs 23.5%) having reduced eGFR. Younger age and female sex were found to have significant associations with reduced eGFR(26).

According to retrospective cross-sectional study which has a comparative nature which was done at Black lion Hospital, out of 180 participants included in the study, 59 (32.78%) were males and the remaining 121 (67.22%) were females. Mean serum total protein was higher in patients on ART groups (5.78  $\pm$  1.39) than treatment-naïve (4.76  $\pm$  2.19). The mean serum creatinine level was not significantly different among three groups. The mean serum creatinine clearance in treatment naïve groups (111.05  $\pm$  11.33) was lower than the control groups (115.05  $\pm$  44.41) and patients on ART (114.76  $\pm$  28.54). The prevalence of renal impairment as defined by CrCl < 60 mL/min (eGFR < 60 ml/min/1.73 m<sup>2</sup>) is higher in treatment-naïve participants than those on ART and HIV-negative control groups(5).

According to the data which was collected from nutritional intervention trial Ethiopia Jimma a total of 340 HIV positive and 100 HIV negative adults were included in this study. Creatinine clearance was determined for 46 of HIV positive adults. Serum creatinine increased with increasing age, weight, height, body surface area, fat free mass and grip strength in both HIV positive and negative adults. No difference was observed in eGFR between HIV positive and

HIV negative adults. For all eGFR equations, the correlation between eGFR and 24-hr creatinine clearance was 0.45–0.53 and the accuracy within 30% of 24-hr creatinine clearance was 24–46%(27).

A cross sectional study conducted I Jimma town, in Jimma University Hospital revealed that age  $\geq 50$  years (AOR = 3.6; 95% CI 1.4, 9.6), advanced WHO stage (AOR = 2.3; 95% CI 1.1, 4.7), and CD4 count  $<200$  (AOR = 6.9; 95% CI 3.3, 14.2) were independent risk factors among HAART naive participants. Female gender (AOR = 6.6; 95 CI %1.2, 34), age  $\geq 50$  years (AOR = 12.1; 95% CI:1.7, 84) and CD4 count  $<200$  (AOR = 17; 95% CI 5.2, 58) were independent risk factors among ART experienced participants(15).

### 2.3 Proposed conceptual framework

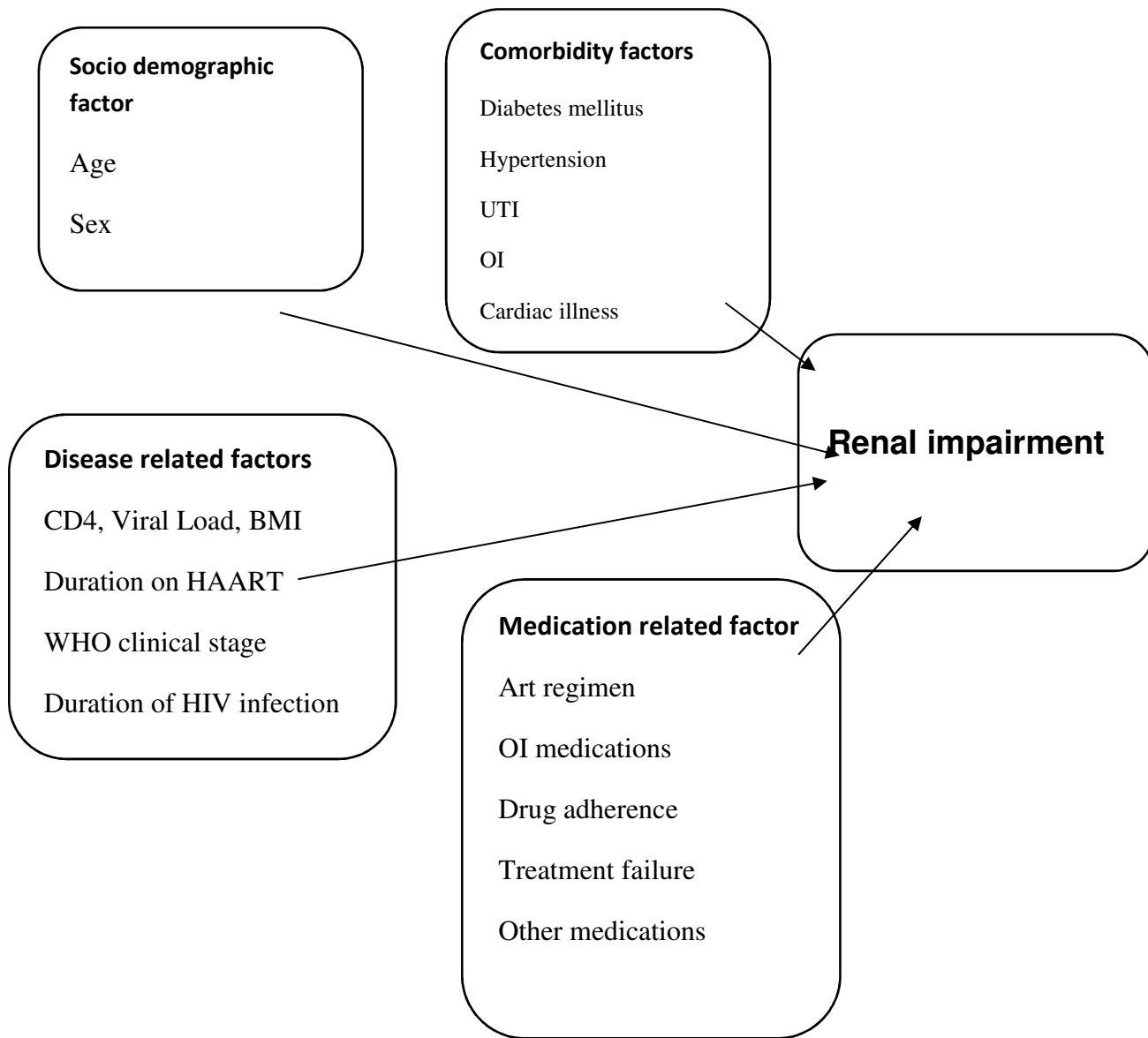


**Figure 1:** conceptual framework organized from literature review.

### **3. OBJECTIVES**

#### **3.1. General objective**

To assess renal impairment and associated factors among HIV infected individuals at SPHMMC and ZMH ART clinic, Addis Ababa, Ethiopia, 20221.

#### **3.2 Specific objective**

- To determine the prevalence of renal impairment among HIV infected individuals at SPHMMC and ZMH ART clinic
- To identify factors associated with impaired renal function among HIV infected individuals at SPHMMC and ZMH ART clinic.

## **4. METHODS AND MATERIALS**

### **4.1 Study area**

Zewuditu memorial hospital was one of the sites where the study was conducted. It is located in the capital city, AddisAbaba. It was built, owned and operated by seventh-day Adventist's church, but was nationalized during the Derg regime in about 1976. The hospital is named after empress Zewuditu the cousin and predecessor on the throne of emperor Haile Selassie. Today the Zewuditu hospital is operated by ministry of health. Zewuditu hospital is Ethiopian's leading hospital in treatment of ART and currently treats over 7000 people each month. It is also one of few governments owned dialysis center in the town. The center has 2 nephrologists and 28 other supporting staffs.

SPHMMC ART clinic was the other site this study was conducted. SPHMMC is also located in Addis Ababa, Ethiopia and its one of the largest tertiary referral hospitals in the capital under the federal ministry of health. It was built by Emperor Haile Selassie in 1961 with the aim of providing health service to those unable to afford care. It has catchment population of more than 5 million population. Medical college was added in 2007 and currently there are over 13 departments. One of them being department of internal medicine, under the department there are number of subspecialties. ART clinic is one of the several outpatient departments in SPHMMC. Saint Paul's renal unit has different centers under it like dialysis center, transplant center and outpatient department kidney disease follow up. It is the only transplant center in the country since 2016. It has also nephrology subspecialty program.

### **4.2 Study period**

This study was conducted from July 01 2021 to August 30, 2021.

### **4.2. Study design**

This study used a cross sectional study design.

### **4.3 Population**

#### **4.3.1 Source population**

The source population were all HIV infected individuals who had follow up in ART clinic at SPHMMC and ZMH.

#### 4.3.2 Study population

The study populations were all patients who had follow ups at ART clinic at SPHMMC and ZMH in the last five years and those who fulfilled the inclusion criteria.

#### 4.4.1. Inclusion criteria

All patients who had follow-ups at ART clinics of SPHMMC and ZMH in the past 5 years and those who had complete laboratory and clinical data regarding their renal status during the study period. This study included all adults aged 18 and above only.

#### 4.4.2. Exclusion criteria:

Those patients with solitary kidney, with diagnosis of obstructive uropathy at any time in their follow up period and those with incomplete investigation results, and pregnant women at the time of renal impairment assessment.

#### 4.5.1. Sample size determination

Sample size was calculated by using the single population proportion formula

$$n = Z^2 p(1-p) / d^2$$

n= required sample size

Z= confidence level at 95% (standard value of 1.96)

d= margin of error = 5%

P= estimated prevalence renal impairment of patients in ART clinic not known in Ethiopia and 50% is taken as proportion of population to give maximum sample size.

$$n = (1.96)^2 * 0.5 * 0.5 / (0.05)^2$$

$$n = 384$$

Since the study population is <10,000, there is a need to use population correction formula which is  $n = n_i * N / (N + n_i)$  where  $n_i$  = initial sample size = 368

$$N = \text{study population} = 9000$$

$$N = \text{total number of HIV infected individuals both at}$$

ZMH and SPHMMC who are follow up at follow up.

Because the source population is <10,000, the final sample size determined as follows

**n**

$$n_f = \text{-----}$$

$$[1 + n/N]$$

$$Nf=384/(1+384/9000) = 368$$

The final sample size by adding 10% contingency 405 were sampled.

#### 4.6.2 Sampling method

From 2000 patients in the ART from last year HMIS, from both SPHMMC and ZMH using systematic random sampling of the past 5 years 405 samples were selected. By dividing the total number of patients in the past 5 years (2010/405) which gives k value approximately 5. The first chart was selected by lottery method. After the first chart, the next charts were selected every 5<sup>th</sup> interval.

### 4.7. Data collection methods

#### 4.7.1. Data collection instruments and measurements

The questionnaire was adapted from different literates. The questionnaire consists of information on the socio demographic and economic status adapted from EDHS.

**Renal dysfunction:**for this study to determine renal dysfunction GFR will be calculated using the Chronic kidney Disease Epidemiology Collaboration (CKD-EPI) formula which is more accurate than the Cockcroft gault formula and modification of diet and in renal disease(MDRD) formulas. then renal dysfunction will be noted as either eGFR less than 60 ml/min/1.73m<sup>2</sup>(28).

**BMI:** Weight and height measurement will be taken from patients charts and BMI will be calculated by dividing weight in Kg for height in m<sup>2</sup>. The BMI cut of value according to WHO classification (in Kg/m<sup>2</sup>) will be <18.5 (underweight), 18.5-24.99(normal), 25-29.99(overweight),>30 (obese),>35(morbidly obese)(29).

#### 4.7.2. Data collectors

Document review was done by 10 data collectors and supervised by 2 supervisors. The principal investigator had also a supervisory role.

#### 4.7.3. Data collection procedure

The data were collected using document review by nurses and physicians working in the ART clinic.Review of medical records was used to collect the data on socio demographic and clinical Characteristics of the study participant including the outcome variable..

## 4.8 Study Variables

### 4.8.1 Dependent Variable

Renal impairment (Yes/No)

### 4.8.2. Independent Variables

**Socio demographic factors:** age,sex

**Disease related factors:**weight,presence of anemia,BMI,duration of HIV infection.history of,ARV treatment failure,ART regimen,Opportunistic infection,drug adherence,Duration of ART, Baseline CD4, Baseline Viral load ,WHO clinical staging during diagnosis

**Related Co-morbidities** (DM, HTN, CLD, Cardiac illness), presence of UTI

## 4.9 Operational definitions

**Renal function impairment:** A patient diagnosed with either CKD or AKI, deranged renal function that is characterized by raised SCr. at a point in time.

**AKI:** Increase in SCr by 50% within 7 days, or increase in SCr by 0.3 mg/dl (26.5  $\mu$ mol/l) within 2 days, or oliguria or GFR<60 ml/min/1.73 m<sup>2</sup> for <3 months, or decrease in GFR by  $\geq$ 35% or increase in SCr by >50% for <3 months and or kidney damage for less than 3 months(9).

**CKD:**GFR<60 ml/min/1.73 m<sup>2</sup> for >3 months or kidney damage for greater 3 months and bilateral shrunken on ultrasound(9).

**Hypertension:** a Patients with a value greater than 140/90 mmHg will be considered as hypertensive(29).

**systolic hypertension:** A patient with blood pressure > 140 mmHg will be considered to have systolic hypertension(29).

**Nutritional assessment:** BMI cut of value according to WHO classification (in Kg/m<sup>2</sup>) will be <18.5 (underweight), 18.5-24.99(normal), 25- 29.99(overweight),>30 (obese)(29).

**Electrolytes:**Patients' electrolytes will be reported as low, high or normal range depending on reference ranges of:

- ✓ Potassium 3.5–5.0 mEq/l
- ✓ Calcium 4.5–5.5 mEq/l

- ✓ Phosphate 0.97–1.45mEq/l
- ✓ Sodium 136-145mEq/l
- ✓ Magnesium 1.5-2.5mEq/l
- ✓ Chloride 97-107mEq/l (30).

**Diabetes mellitus:** DM is defined fasting blood sugar >125 mg/dl, OR HgA1c>6.5 %, symptoms of hyperglycemia and random blood sugar >.200 ,OR two hour oral glucose tolerance test >200mg/dl(31).

**1c:** Zidovudidn/Lamivudin/Nevirapin

**1e:**Tenofovir/Lamivudin/Efavirinez

**1j:**Tenofovir/Lamivudin/Dolutogravir

**2h:**Tenofovir/Lamivudin/lopinavir/ritonavir

**2f:**Atazanavir/ritonavir/Lamivudin/Zidovudin

**1g:**Abacavir/Lamivudin/Efavirinez

#### **4.10 Data quality control**

To ensure the quality of data, preceding data collection, and data collectors were trained for one day by the principal investigator on the objective, relevance of the study and confidentiality of information and how to collect the specific data needed for this study.

Pretest was done by taking 5% total sample size of in SPHMMC before the actual data collection to check its variability and the questionnaire were assessed for its clarity, length and completeness and the necessary correction were done accordingly. Those items that were not be clear were revised and those variables, which were not documented, were removed. The documents involved in pretest were excluded from the actual data analysis of study.

#### **4.11 Ethical consideration**

Ethical clearance was obtained from Research Ethics committee of St Paul's Hospital Millennium Medical College, and Zewuditu hospital, ART clinics and renal clinics of Zewuditu hospital and St. Pauls' millennium medical college.

The information obtained was kept confidential Throughout the data collection and other activities related to the study appropriate COVID-19 prevention protocol was followed.

#### **4.12. Methods of Data management and analysis**

The data was entered into EpiData 3.1 and was exported to IBM SPSS statistics version 20 to clean and to analyze the data. Descriptive statistics were carried to determine the proportion, mean and the standard deviation. Bi-variate and multi-variable logistic regression analyses were performed to examine the association between the explanatory variables and the outcome variable. Before analyzing binary logistic regression, variables were cross-tabulated for observed values different from 0 and expected value greater than 5 and were involved for bivariate analysis. A variable with a p-value < 0.25 in bi-variate analysis was recruited for multivariate analysis. Before multivariate analysis, possible col-linearity between the explanatory variable was tested and a VIF>5 was used to screen for col-linearity. Hosmer-Lemeshow goodness-to-fit model was used for multivariate fitness and >0.05 was a cut point to assure good fitness. In multivariate, Adjusted Odds Ratio with 95 % Confidence Interval (CI) at P value less than 0.05 was used to declare the statistical significance of associations.

## 4. RESULT

### 4.1: socio-demographic characteristics

The total number of samples were 405 all of them were included in the analysis. Majority of the study participants were females 250(61.7%). The mean age of the study participants was  $36.72 \pm 5.45$  SD. Majority 229(56.5%) of the study participants were in the age group 30 to 44. (Refer **Table 1**)

**Table 1:** Shows the socio-demographic characteristics of participants

| NO. | Variable            |                             | Frequency | Percent (%) |
|-----|---------------------|-----------------------------|-----------|-------------|
| 1.  | Gender Distribution | Male                        | 155       | 38.3        |
|     |                     | Female                      | 250       | 61.7        |
|     |                     | Total                       | 405       | 100         |
| 2   | Age distribution    | Less than 25                | 45        | 11.1        |
|     |                     | 25-29                       | 41        | 10.1        |
|     |                     | 30-34                       | 60        | 14.8        |
|     |                     | 35-39                       | 107       | 26.4        |
|     |                     | 40-44                       | 62        | 15.3        |
|     |                     | 45-49                       | 56        | 13.8        |
|     |                     | Greater than or equal to 50 | 34        | 8.4         |
|     |                     | Total                       | 405       | 100         |

## 4.2. Clinical Factors

### 4.2.1.Subsection of the Clinical factors

The majority 403 (99.5%) of the participants' BMI was in the range 18.5 to 24.99. Thirteen (3.5%) had a history of medical illnesses and 10 of these patients took medication for their medical illness. Ten of the study participants were diagnosed with Hypertension and 8 were diagnosed with DM. (Refer to **Table 2**).

**Table 2:** showing the clinical factors for impaired renal function.

| NO. | Variable                                                |                             | Frequency | Percent (%) |
|-----|---------------------------------------------------------|-----------------------------|-----------|-------------|
| 1   | BMI                                                     | Less than or equal to 18.49 | 2         | 0.5         |
|     |                                                         | 18.5-24.99                  | 403       | 99.5        |
|     |                                                         | Total                       | 405       | 100         |
| 2.  | History of medical illnesses                            | Yes                         | 13        | 3.5         |
|     |                                                         | No                          | 392       | 96.5        |
|     |                                                         | Total                       | 405       | 100         |
| 3   | On treatment(drugs) for their chronic medical condition | Yes                         | 10        | 76.9        |
|     |                                                         | No                          | 3         | 23.1        |
|     |                                                         | Total                       | 13        | 100         |
| 4   | Type of Medical illness                                 | DM                          | 8         | 1.98        |
|     |                                                         | HTN                         | 10        | 2.5         |
|     |                                                         | Cardiac illness             | 1         | 0.2         |

### 4.2.2.Subsection of the clinical factors

Regarding the duration of ART treatment 197 (48.7) were in treatment from 13 to 36 months. Majority 284 (70.1%) of the study participants have stated their ART with an initial Regimen 1E, 308(76%) of the participants were at 1<sup>st</sup> or 2<sup>nd</sup> WHO clinical stage during their initiation according to the charts reviewed. (Refer **Table 3**)

**Table 3:** shows other clinical factors related with HIV/AIDS and Impaired renal function

| NO. | Variable                             |                          | Frequency | Percent (%) |
|-----|--------------------------------------|--------------------------|-----------|-------------|
| 1   | Duration of ART treatment            | Less than or equal to 12 | 49        | 12.1        |
|     |                                      | 13-24                    | 97        | 24.0        |
|     |                                      | 25-36                    | 100       | 24.7        |
|     |                                      | 37-48                    | 75        | 18.5        |
|     |                                      | 49-60                    | 84        | 20.7        |
|     |                                      | Total                    | 405       | 100         |
| 2   | Patient's Initial Regimens           | 1E                       | 284       | 70          |
|     |                                      | 1J                       | 116       | 28.6        |
|     |                                      | 1C                       | 3         | 0.7         |
|     |                                      | Others( ATV/DTG/3Tc)     | 2         | 0.4         |
|     |                                      | Total                    | 405       | 100         |
| 3   | WHO clinical stage during initiation | Stage I and II           | 308       | 76          |
|     |                                      | Stage III and IV         | 97        | 24          |
|     |                                      | total                    | 405       | 100         |
|     | Stage during Renal insult            | Stage I                  | 376       | 92.8        |
|     |                                      | Stage II                 | 5         | 1.2         |
|     |                                      | Stage III                | 9         | 2.2         |
|     |                                      | Stage IV                 | 15        | 3.7         |
|     |                                      | total                    | 405       | 100         |
|     | Viral Load during renal insult       | Undetectable             | 363       | 89.6        |
|     |                                      | Detectable               | 30        | 7.4         |
|     |                                      | Undetermined             | 12        | 3.0         |
|     |                                      | total                    | 405       | 100         |

#### 4.2.3. Subsection of the Clinical Factors

One hundred seventy-six(43.5%) had history opportunistic infection. Majority 206 (50.9%) of the study participants had a base line CD4 count of  $\geq 200$  during Renal Insult and 294 (72.6%) of the study participants had the most recent CD4 count of  $\geq 200$ . All the participants had experienced HAART.(Refer **Table 4**)

**Table 4:** shows other clinical factors related with HIV/AIDS and Impairment Renal function

| NO. | Variable                        |             | Frequency | Percent (%) |
|-----|---------------------------------|-------------|-----------|-------------|
| 1.  | Status of HAART                 | Experienced | 405       | 100         |
|     | Base line CD4 count             | $\geq 200$  | 294       | 72.6        |
|     |                                 | <200        | 54        | 13.3        |
|     |                                 | Total       | 405       | 100         |
|     |                                 | $\geq 200$  | 294       | 72.6        |
| 2   | Last updated CD4                | $\geq 200$  | 319       | 78.8        |
|     |                                 | <200        | 73        | 18.0        |
|     |                                 | Undermined  | 13        | 3.2         |
|     | History of Treatment Failure    | yes         | 23        | 5.7         |
|     |                                 | no          | 382       | 94.3        |
|     |                                 | total       | 405       | 100         |
|     | History of poor drug adherence  | Yes         | 22        | 5.4         |
|     |                                 | No          | 383       | 94.6        |
|     |                                 | Total       | 405       | 100         |
|     | History Opportunistic infection | Yes         | 176       | 43.5        |
|     |                                 | No          | 229       | 56.5        |
|     |                                 | total       | 405       | 100         |

#### 4.3. OUTCOME VARIABLE

The magnitude of the impaired renal function revealed from this study was 8.4% (95% CI: 5.51 to 11.4). (Refer figure 2)

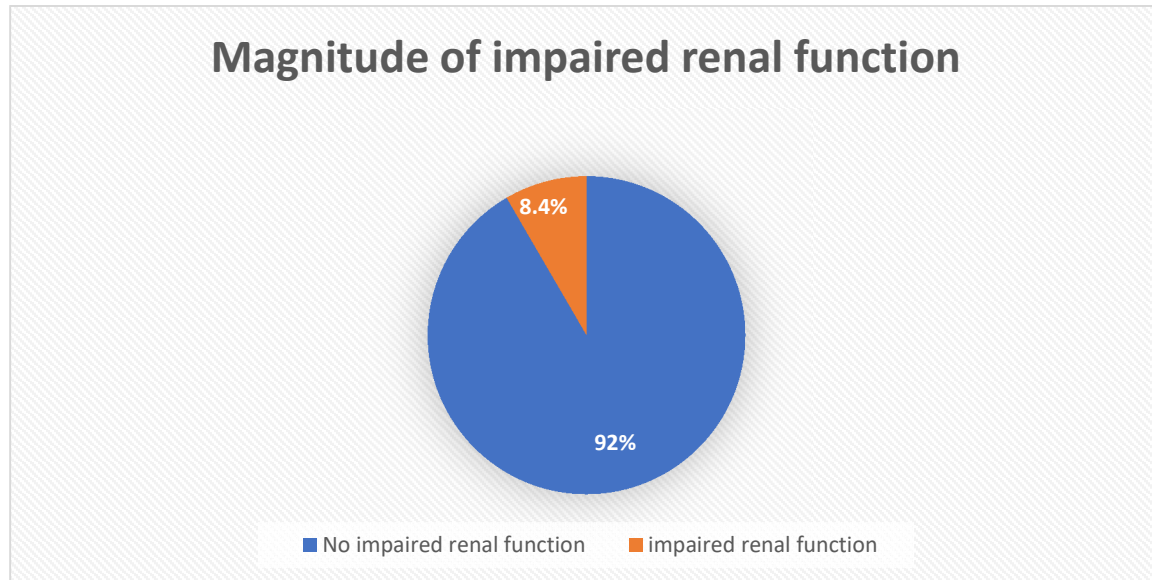


**Figure 2:** Showing the magnitude of the impaired renal function

##### 4.3.1. Subsection of the outcome variables

From the total impaired, renal function majority of the patients were AKI, 23 (67.6%). Stages of CKD indicated were at stage IIIA and IIIB. (Refer Table 5)

**Table 5:** Showing the types of impaired renal functions and stages of CKD

| NO. | Variable                  |                         | Frequency | Percent (%) |
|-----|---------------------------|-------------------------|-----------|-------------|
| 2   | Type of Renal dysfunction | AKI                     | 23        | 67.6        |
|     |                           | Deranged renal function | 7         | 20.6        |
|     |                           | CKD                     | 4         | 11.8        |
|     |                           | Total                   | 34        | 10          |
|     | Stages of CKD             | Stage IIIA              | 2         | 50          |
|     |                           | Stage IIIB              | 2         | 50          |
|     |                           | Total                   | 4         | 100         |

#### 4.4. Laboratory Results

From 34 patients with renal impairment 9(26.5%) has anemia(hgb<13) compared with 17(4%) out of 405.MCV at the time of renal impairment revealed that majority, 29(85.3%) were normal. RDW at the time of renal impairment indicated that majority, 28(82.4%) were Normal. (**Refer Table 6**)

**Table 6:** Showing the laboratory results of patients with impaired renal function

| NO. | Variable                                   |                                          | Frequency | Percent (%) |
|-----|--------------------------------------------|------------------------------------------|-----------|-------------|
| 1.  | Hemoglobin at the time of Renal Impairment | Less than 13                             | 9         | 26.5        |
|     |                                            | 13-16                                    | 25        | 73.5        |
|     |                                            | Total                                    | 34        | 100         |
| 2   | MCV at the time of renal impairment        | Normal                                   | 29        | 85.3        |
|     |                                            | Low                                      | 2         | 8.8         |
|     |                                            | High                                     | 3         | 5.9         |
|     |                                            | Total                                    | 34        | 100         |
|     | RDW at the time of renal impairment        | Normal                                   | 28        | 82.4        |
|     |                                            | High                                     | 6         | 17.6        |
|     |                                            | Total                                    | 34        | 100         |
|     | Presence of casts in the urine             | Yes                                      | 3         | 0.7         |
|     |                                            | No                                       | 31        | 97.0        |
|     | Serum creatinine                           | Creatinine greater than or equals to 1.2 | 34        | 100         |
|     | 2+ dipstick Urine protein                  | Positive                                 | 5         | 14.7        |
|     |                                            | Negative                                 | 29        | 85.3        |
|     |                                            | Total                                    | 34        | 100         |
|     |                                            | Creatinine greater than equals to 1.2    | 34        | 100         |

|  |                        |          |    |      |
|--|------------------------|----------|----|------|
|  | Ultra sound renal size | Normal   | 31 | 91.2 |
|  |                        | Shrunken | 1  | 2.9  |
|  |                        | Not done | 2  | 5.9  |
|  |                        | Total    | 34 | 100  |

#### **4.5. Bi-variable and Multi-variable Logistic Regression Analysis for Renal Impairment**

To identify the factors associated with Impaired Renal Function among patients, a logistic model was fitted with Impaired Renal Function (dichotomous) being the dependent variable and the selected independent variables. The Variables with a p-value  $> 0.25$  were excluded from the multi-variable analysis. Those variables include BMI, history of medical illness, WHO clinical stage and viral load. The variables with p-value of  $\leq 0.25$  in the bi-variable analysis were taken to multi-variable logistic regression analysis to see whether they have true association or not. Those variables include gender, age, Duration of ART treatment, Patients' initial and current regimens, History of treatment failure, history of poor treatment adherence, history of opportunistic infections and Base line CD4.

In the multi variable logistic regression, gender, patient's initial regimen, history of opportunistic infections and Base line CD4 count have p-value  $< 0.05$ , hence they were significantly associated with the impaired renal function.

The chance of female Patients with HIV having impaired renal functions was 4.48 times higher likelihood of suffering from impaired renal function when compared with their male counterparts. The chance of patients with HIV taking initial regimen of 1E and 1J had 95% less likelihood of having renal impairment when compared with patients taking other type of initial regimens. Those patients with HIV infection had opportunistic infections had 2.74 times higher chance of having impaired renal function when compared with those patients without opportunistic infections. Those patients with base line CD4 count of less than 200 had 2.74 times higher chance of having impaired renal function when compared with patients with CD4 count of greater than or equal to 200. (Refer **Table 7& Table 8**).

**Table 7: Bi-variable logistic regression for all the independent Variables**

| Explanatory Variables          | Category     | Impaired renal function |     | OR (95% CI)& P-value |         |
|--------------------------------|--------------|-------------------------|-----|----------------------|---------|
|                                |              | Yes                     | No  | COR (95% CI)         | P-value |
| Gender                         | male         | 24                      | 131 | 1                    | 0.000   |
|                                | Female       | 10                      | 240 | 4.4(2.04, 9.48)      |         |
| Age                            | < 50         | 32                      | 339 | 1                    | 0.221   |
|                                | ≥ 50         | 2                       | 32  | 1.51(0.35, 6.60)     |         |
| BMI                            | 17-18.49     | 0                       | 2   | 1                    | 0.999 * |
|                                | 18.5- 24.99  | 34                      | 369 | Very large number    |         |
| Duration of ART treatment      | ≤ 24 months  | 7                       | 139 | 1                    |         |
|                                | 25-36        | 10                      | 90  | 0.45(0.17, 1.23)     | 0.122   |
|                                | 37-48        | 7                       | 68  | 0.49 (0.17, 1.45)    | 0.197   |
|                                | 49-60        | 10                      | 74  | 0.37 (0.14, 1.02)    | 0.055   |
| Hx of medical illnesses        | No           | 21                      | 371 | Very Large number    | 0.998 * |
|                                | Yes          | 13                      | 0   | 1                    |         |
| Viral load during renal insult | undetectable | 24                      | 338 | 1                    |         |
|                                | Detectable   | 10                      | 20  | open-ended           | 0.999 * |
|                                | undetermined | 0                       | 12  | open-ended           | 0.999 * |
| WHO clinical stage             | Not advanced | 25                      | 296 | 1                    | 0.39 *  |
|                                | Advanced     | 9                       | 75  | 0.71(0.32, 1.57)     |         |
| Patients' initial regimen      | 1E           | 25                      | 259 | 1                    |         |
|                                | 1J           | 6                       | 110 | 1.77(0.71, 4.43)     | 0.223   |
|                                | Others       | 3                       | 2   | 0.06(0.01, 0.40)     | 0.003   |
| Patients' current regimen      | 1J           | 28                      | 333 | 1                    | 0.191   |
|                                | others       | 6                       | 38  | 0.53(0.21, 1.37)     |         |

|                                     |       |    |     |                  |       |
|-------------------------------------|-------|----|-----|------------------|-------|
| History of Opportunistic infections | No    | 25 | 204 | 1                | 0.007 |
|                                     | Yes   | 9  | 167 | 1.94(, 4.18)     |       |
| History of poor drug adherence      | No    | 30 | 353 | 1                | 0.100 |
|                                     | Yes   | 4  | 18  | 2.61(0.83, 8.22) |       |
| History of treatment failure        | No    | 30 | 352 | 1                | 0.120 |
|                                     | Yes   | 4  | 19  | 0.41(0.13, 1.27) |       |
| Base line CD4                       | < 200 | 8  | 178 | 3.0(1.32, 6.79)  | 0.009 |
|                                     | ≥ 200 | 26 | 193 | 1                |       |

\*Variables removed from multi-variable logistic regression, due to their p-values is greater than 0.25.

**Table 8:**Multi-variable Logistic Regression Analysis for variables of P-value of ≤0.25.

| Explanatory Variables     | Category    | Impaired renal function |     | OR (95% CI)& P-value |         |                  |         |
|---------------------------|-------------|-------------------------|-----|----------------------|---------|------------------|---------|
|                           |             | Yes                     | No  | COR (95% CI)         | P-value | AOR (95% CI)     | P-Value |
| Gender                    | male        | 24                      | 131 | 1                    | 0.000   | 1                | 0.000   |
|                           | Female      | 10                      | 240 | 4.4(2.04, 9.48)      |         | 4.48(1.94,10.34) |         |
| Age                       | < 50        | 32                      | 339 | 1                    | 0.221   | 1                |         |
|                           | ≥ 50        | 2                       | 32  | 1.51(0.35, 6.60)     |         | 1.28(0.25, 6.53) |         |
| Duration of ART treatment | ≤ 24 months | 7                       | 139 | 1                    |         | 1                |         |
|                           | 25-36       | 10                      | 90  | 0.45(0.17, 1.23)     | 0.122   | 0.44(0.12, 1.62) |         |
|                           | 37-48       | 7                       | 68  | 0.49 (0.17, 1.45)    | 0.197   | 0.41(0.10, 1.79) |         |
|                           | 49-60       | 10                      | 74  | 0.37 (0.14, 1.02)    | 0.055   | 0.35(0.09, 1.34) |         |
| Patients' initial regimen | 1E          | 25                      | 259 | 1                    |         | 1                |         |
|                           | 1J          | 6                       | 110 | 1.77(0.71, 4.43)     | 0.223   | 0.94(0.25, 3.52) |         |
|                           | Others      | 3                       | 2   | 0.06(0.01, 0.40)     | 0.003   | 0.05(0.01, 0.48) | 0.01    |
| Patients' current         | 1J          | 28                      | 333 | 1                    |         | 1                |         |

|                                     |        |    |     |                  |       |                  |       |
|-------------------------------------|--------|----|-----|------------------|-------|------------------|-------|
| regimen                             | others | 6  | 38  | 0.53(0.21, 1.37) | 0.191 | 0.67(0.18, 2.55) |       |
| History of Opportunistic infections | No     | 25 | 204 | 1                | 0.007 | 1                | 0.043 |
|                                     | Yes    | 9  | 167 | 1.94(, 4.18)     |       | 2.74(1.02, 739)  |       |
| History of poor drug adherence      | No     | 30 | 353 | 1                | 0.100 | 1                |       |
|                                     | Yes    | 4  | 18  | 2.61(0.83, 8.22) |       | 0.38(0.10, 1.49) |       |
| History of treatment failure        | No     | 30 | 352 | 1                | 0.120 | 1                |       |
|                                     | Yes    | 4  | 19  | 0.41(0.13, 1.27) |       | 0.30(0.06,1.43)  |       |
| Base line CD4                       | < 200  | 8  | 178 | 3.0(1.32, 6.79)  | 0.009 | 3.42(1.34, 8.70) | 0.01  |
|                                     | ≥ 200  | 26 | 193 | 1                |       | 1                |       |

## 5. DISCUSSION

The overall prevalence of renal function impairment This study was in line with a cross sectional study done among Chinese hospitalized HIV positive patients that showed the prevalence was 5.56% ((11))

The result of this study was lower when compared with a study done in Uganda, revealed that a hospital-based cross-sectional study conducted among newly diagnosed HIV positive individuals in Northern Uganda, the prevalence of impaired renal function to be 14.4%(13) and it was also lower with the another study conducted to determine Renal Dysfunction among HIV-Infected Patients Starting ART in Mwanza, Tanzania which revealed a prevalence of renal dysfunction was 63.7%.This could be attributed to in our study all the patients included were ART experienced .This supports the idea that Test and treat approach has a paramount importance in reducing renal impairment (14).

This prevalence impaired renal function in this study was higher when compared with a cross-sectional study done to assess the prevalence of renal dysfunction among HIV infected patients receiving Tenofovir in Kampala, Uganda in 2018 showed that the prevalence of renal dysfunction which was 2.52% which is probably this study included only those who are on proven effective Tenofovir based regimen(12).Variation in the population, sample size, the definition used to classify impaired renal function could be attributed to these differences.

There were different factors associated with the renal function impairment in this study. These factors include gender, Patients initial regimen, History of Opportunistic infections, Base line CD4. A lower CD4 count(< 200 ) were shown to be associated with renal function impairment in a study done in South Africa (16). Another cross sectional study conducted, Tanzania in to determine Renal Dysfunction among HIV-Infected Patients Starting Antiretroviral Therapy CD4 count (<200 cells/mm<sup>3</sup>) was factors independently associated with renal dysfunction(14). another hospital based prospective cross-sectional study done in Ethiopia revealed that baseline CD4 count less than 200 cells/mm<sup>3</sup>(21).

A cross sectional study, conducted in Tanzania to determine Renal Dysfunction among HIV-Infected Patients Starting ART were female gender, was a factor independently associated with renal dysfunction(14). Another retrospective cross sectional study which was conducted at Togo, Lomé which tried to identify risk factors for renal failure, female gender was significantly

associated impaired renal function (25). This might be due to the higher proportion women make up the majority of total number people living with HIV/AIDS in Ethiopia and in this study.

In this study, there was association of presence of opportunistic infections with renal function impairment among patients with HIV, which was supported by an established evidence that renal function impairment is associated with the presence of opportunistic infections done in United states of America(32) and United kingdom(33). This could be, because the opportunistic infections directly affecting the renal function or it facilitated the damage imposed by the HIV infection on the renal function.

## **6. STRENGTH AND LIMITATION OF THE STUDY**

### **Strength:**

It was relatively quick and inexpensive to conduct. Since this study used cross sectional study design, which was important to identify multiple exposures to an outcome variable at the same time.

Multi-center study would make it more representative.

Used larger sample size.

### **Limitation**

It used a secondary data, some of the variables were not recorded then I have forced to remove some variables from the questionnaire and then from analysis.

## 7. CONCLUSION

The finding of this study clearly indicated that there is a relatively low prevalence of impaired renal function among patients with HIV in the two tertiary hospitals art clinic who are on ART, in Addis Ababa as compared with other studies done in Ethiopian and other SSA studies. Impaired renal function was significantly associated with female gender, taking initial regimens other than TDF/3TC/EFV and TDF/3TC/DTG, having opportunistic infection and having CD4 count of less than 200. Based on this and previous many studies this risk of having renal impairment lower on those who are on ART which contains TDF as its backbone, even if the drug has been incriminated for its renal toxicity along with protease inhibitors in earlier days, this study in addition to other recent studies showed the prevalence of Renal dysfunction is much lower with those patients who are taking TDF containing regimen. And test and treat approach has a positive impact regarding renal outcome.

## **8. RECOMMENDATIONS**

**For health Institutions:** Routine investigation of CD4 count could help to understand the level of CD4 count. Specially determining base line CD4 count as per the national guideline. It also important that health institutions involvement in early detection and prevention of opportunistic infection among patient with HIV prevent renal function impairment. Initial assessment basic investigation like renal function test, Complete Blood count, serum electrolyte, urinalysis, and abdominal ultrasound has to be practiced.

**For Individual Patients:** The patients, especially females, are expected to practice regular follow up their CD4 count, seek treatment for the opportunistic infections.

## 9. REFERENCES

1. Kulohoma BW. H3Africa: crucial importance of knowledge on human demographic history in strategies for data exploitation—an analysis of the Luhya in Webuye, Kenya population from the 1000 Genomes Project. Wellcome Open Research. 2018;3.
2. Swanepoel CR, Atta MG, D'Agati VD, Estrella MM, Fogo AB, Naicker S, et al. Kidney disease in the setting of HIV infection: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney international*. 2018;93(3):545-59.
3. Yilma D, Abdissa A, Kæstel P, Tesfaye M, Olsen MF, Girma T, et al. Renal function in Ethiopian HIV-positive adults on antiretroviral treatment with and without tenofovir. *BMC Infectious Diseases*. 2020;20(1):1-11.
4. Pandey A, Galvani AP. The global burden of HIV and prospects for control. *The Lancet HIV*. 2019;6(12):e809-e11.
5. Eneyew K, Seifu D, Amogne W, Menon M. Assessment of renal function among HIV-Infected patients on combination antiretroviral therapy at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. *Technology and Investment*. 2016;7(3):107-22.
6. Campos P, Ortiz A, Soto K. HIV and kidney diseases: 35 years of history and consequences. *Clinical kidney journal*. 2016:sfw104.
7. Wyatt CM. Kidney disease and HIV infection. *Topics in antiviral medicine*. 2017;25(1):13.
8. Hou J, Nast CC. Changing concepts of HIV infection and renal disease. *Current opinion in nephrology and hypertension*. 2018;27(3):144-52.
9. Barry R, James MT. Guidelines for Classification of Acute Kidney Diseases and Disorders. *Nephron*. 2015;131(4):221-6.
10. Alfano G, Cappelli G, Fontana F, Di Lullo L, Di Iorio B, Bellasi A, et al. Kidney disease in HIV infection. *Journal of clinical medicine*. 2019;8(8):1254.
11. Sun C, Wen Y, Liu S, Cui W, Zhou Y, Deng B, et al. Prevalence of renal impairment among HIV positive patients hospitalized in the first hospital of China medical university. *INTERNATIONAL JOURNAL OF CLINICAL AND EXPERIMENTAL MEDICINE*. 2018;11(8):8622-7.
12. Nyende L, Kalyesubula R, Sekasanvu E, Byakika-Kibwika P. Prevalence of renal dysfunction among HIV infected patients receiving Tenofovir at Mulago: a cross-sectional study. *BMC nephrology*. 2020;21(1):1-6.
13. Odongo P, Wanyama R, Obol JH, Apiyo P, Byakika-Kibwika P. Impaired renal function and associated risk factors in newly diagnosed HIV-infected adults in Gulu Hospital, Northern Uganda. *BMC nephrology*. 2015;16(1):1-7.
14. Mwemezi O, Ruggajo P, Mngumi J, Furia FF. Renal Dysfunction among HIV-Infected Patients on Antiretroviral Therapy in Dar es Salaam, Tanzania: A Cross-Sectional Study. *International Journal of Nephrology*. 2020;2020.
15. Mekuria Y, Yilma D, Mekonnen Z, Kassa T, Gedefaw L. Renal function impairment and associated factors among HAART Naïve and experienced adult HIV positive individuals in Southwest Ethiopia: a comparative cross sectional study. *PloS one*. 2016;11(8):e0161180.
16. Assaram S, Magula NP, Kinoo SM, Mashamba-Thompson TP. Renal manifestations of HIV during the antiretroviral era in South Africa: a systematic scoping review. *Systematic reviews*. 2017;6(1):1-11.
17. Gupta SK, Eustace JA, Winston JA, Boydston II, Ahuja TS, Rodriguez RA, et al. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2005;40(11):1559-85.
18. Nobakht E, Cohen SD, Rosenberg AZ, Kimmel PL. HIV-associated immune complex kidney disease. *Nature Reviews Nephrology*. 2016;12(5):291-300.

19. Wearne N, Okpechi IG. HIV-associated renal disease-an overview. *Clinical nephrology*. 2016;86(7):41.
20. Jotwani V, Atta MG, Estrella MM. Kidney disease in HIV: moving beyond HIV-associated nephropathy. *Journal of the American Society of Nephrology*. 2017;28(11):3142-54.
21. Yazie TS, Orjino TA, Degu WA. Reduced kidney function in tenofovir disoproxil fumarate based regimen and associated factors: a hospital based prospective observational study in Ethiopian patients. *International journal of nephrology*. 2019;2019.
22. Joshi K, Boettiger D, Kerr S, Nishijima T, Van Nguyen K, Ly PS, et al. Changes in renal function with long-term exposure to antiretroviral therapy in HIV-infected adults in Asia. *Pharmacoepidemiology and drug safety*. 2018;27(11):1209-16.
23. Pantazis N, Chini M, Antoniadou A, Sambatakou H, Skoutelis A, Gargalianos P, et al. The HIV patient profile in 2013 and 2003: Results from the Greek AMACS cohort. *Plos one*. 2018;13(9):e0203601.
24. Kaboré NF, Poda A, Zoungrana J, Da O, Ciaffi L, Semdé A, et al. Chronic kidney disease and HIV in the era of antiretroviral treatment: findings from a 10-year cohort study in a west African setting. *BMC nephrology*. 2019;20(1):1-10.
25. Amekoudi EYM, Sabi KA, Dolaama B, Tona KG, Noto-Kadou-Kaza B, Kola E, et al. Risk Factors of Renal Failure in HIV Patients at Initiation of ARV Treatment: Retrospective Study of 3118 Patients Followed in Infectious Diseases Department at Lomé University Hospital. *Open Journal of Nephrology*. 2019;9(03):55.
26. Ogiator MO, Ojobi JE, Asor P. Predictors of Renal Dysfunction Among Patients With Human Immunodeficiency Virus Seen at Benue State University Teaching Hospital, Makurdi, Nigeria.
27. Yilma D, Abdissa A, Kæstel P, Tesfaye M, Olsen MF, Girma T, et al. Serum creatinine and estimated glomerular filtration rates in HIV positive and negative adults in Ethiopia. *PloS one*. 2019;14(2):e0211630.
28. Seape T, Gounden V, van Deventer HE, Candy GP, George JA. Cystatin C-and creatinine-based equations in the assessment of renal function in HIV-positive patients prior to commencing highly active antiretroviral therapy. *Annals of clinical biochemistry*. 2016;53(1):58-66.
29. Kent S, Fusco F, Gray A, Jebb SA, Cairns BJ, Mihaylova B. Body mass index and healthcare costs: a systematic literature review of individual participant data studies. *Obesity Reviews*. 2017;18(8):869-79.
30. Hoorn E, Tuut M, Hoorntje S, van Saase J, Zietse R, Geers A. Dutch guideline for the management of electrolyte disorders-2012 revision. *Neth J Med*. 2013;71(3):153-65.
31. Association AD. 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes—2020. *Diabetes care*. 2020;43(Supplement 1):S98-S110.
32. Li Y, Shlipak MG, Grunfeld C, Choi AI. Incidence and risk factors for acute kidney injury in HIV Infection. *American journal of nephrology*. 2012;35(4):327-34.
33. Roe J, Campbell LJ, Ibrahim F, Hendry BM, Post FA. HIV care and the incidence of acute renal failure. *Clinical Infectious Diseases*. 2008;47(2):242-9.

## 10.ANNEXES

### Annex 1: Questionnaire

#### PART 1: SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS.

| S. No | Questions                        | Options                                                                                                   | Remark |
|-------|----------------------------------|-----------------------------------------------------------------------------------------------------------|--------|
| 101   | Card Number:                     |                                                                                                           |        |
| 102   | Sex                              | A. Male<br>B. Female                                                                                      |        |
| 103   | What is your age?                | _____                                                                                                     |        |
| 104   | What is your religion?           | A. Orthodox<br>B. Catholic<br>C. Protestant<br>D. Muslim<br>E. Others(specify) _____                      |        |
| 105   | What is your Marital Status?     | A. Never married<br>B. Married<br>C. Living together<br>D. Divorced/separated<br>E. Widowed               |        |
| 106   | Where is your residence?         | A. Urban<br>B. Rural                                                                                      |        |
| 107   | What is your Ethnicity?          | A. Oromo<br>B. Amhara<br>C. Harari<br>D. Tigre<br>E. Gurage<br>F. Others(specify) _____                   |        |
| 108   | What is your educational status? | A. Unable to read and write<br>B. Able to read and write<br>C. Primary school<br>D. Secondary/preparatory |        |

|            |                          |                                                                                      |  |
|------------|--------------------------|--------------------------------------------------------------------------------------|--|
|            |                          | E. Diploma and above                                                                 |  |
| <b>109</b> | What is your occupation? | A. Jobless<br>B. Self-employee<br>C. Government employee<br>D. Others(specify) _____ |  |
|            |                          |                                                                                      |  |

## Part II: clinical factors

| No. | Questions                                                      | Options                                                               | Remark |
|-----|----------------------------------------------------------------|-----------------------------------------------------------------------|--------|
| 1.  | BMI(Wt./H <sup>2</sup> ):                                      | _1.<br><br>2_____                                                     |        |
| 2.  |                                                                |                                                                       |        |
| 3.  | Previous hx of chronic medical illness                         | 1. DM<br>2. HTN<br>3. Cardiac illness<br>4. liver disease<br>5. other |        |
| 4.  | Previous use of medication for their chronic medical condition | 1. Yes<br>2. No                                                       |        |
| 5.  | How long since the diagnosis of HIV                            | _____ years                                                           |        |
| 6.  | What is the regimen of your drug                               | _____                                                                 |        |
| 7.  | Any history of OI                                              | 1. Yes<br>2. No                                                       |        |
| 8.  | History of AIDS defining illness prior to initiation of ART?   | 1. Yes<br>2. No                                                       |        |

|     |                              |                                |  |
|-----|------------------------------|--------------------------------|--|
| 9.  | Drug adherence to ART        | _____                          |  |
| 10. | History of treatment failure | 1. Yes<br>2. No                |  |
| 3.  | Who stage                    | 1. Advanced<br>2. Non-advanced |  |
| 4.  | CD4 count                    | 1. $\geq 200$<br>2. $< 200$    |  |
| 5.  | Status of HAART              | 1. Naïve<br>2. Experienced     |  |

### Part III. Laboratory results

Laboratory measurements: please circle the result

| No | Biochemical indices                         | Result                                          | Base line | 2 <sup>nd</sup><br>After<br>3months | 3 <sup>rd</sup> After 6months | 2 <sup>nd</sup> |
|----|---------------------------------------------|-------------------------------------------------|-----------|-------------------------------------|-------------------------------|-----------------|
| 1  | Hemoglobin                                  | 1. 11-12.9mg/dl<br>2. 8-10.9mg/dl<br>3. <8mg/dl |           |                                     |                               |                 |
| 2. | MCV                                         | 1. 80-100fl<br>2. <80fl<br>3. >100fl            |           |                                     |                               |                 |
| 3. | RDW                                         | 1. 11-14<br>2. >14<br>3. 3. <11                 |           |                                     |                               |                 |
| 4. | calcium                                     |                                                 |           |                                     |                               |                 |
| 5. | PTH                                         |                                                 |           |                                     |                               |                 |
| 6. | Phosphorus                                  |                                                 |           |                                     |                               |                 |
| 7. | Serum iron                                  |                                                 |           |                                     |                               |                 |
| 8. | Urine analysis presence or absence of casts |                                                 |           |                                     |                               |                 |
| 9. | 24-hour urine protein                       |                                                 |           |                                     |                               |                 |

|     |                                            |  |                                        |  |  |  |
|-----|--------------------------------------------|--|----------------------------------------|--|--|--|
| 10. | CD4                                        |  |                                        |  |  |  |
| 11. | Viral load                                 |  |                                        |  |  |  |
| 12. | Urine protein                              |  |                                        |  |  |  |
| 13  | RFT (calculate GFR if deranged Creatinine) |  | (Please fill in the laboratory result) |  |  |  |
| 14. | Ultrasound renal size                      |  |                                        |  |  |  |

## **ASSURANCE OF INVESTIGATOR**

I the undersigned resident agree to accept all responsibilities for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per te

rms and conditions of the Research and Publication Directorate and /or Department of Public Health of St. Paul's Hospital Millennium Medical College.

Name of the Resident: \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

## **APPROVAL OF ADVISORS**

Name of Public Health Advisor: \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Name of Clinical Advisor: \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_