
# A STUDY ON PREVALENCE AND RISK FACTORS OF RENAL DYSFUNCTION AMONG HOSPITALIZED HIV INFECTED ADULT PATIENTS AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA

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# DECLARATION

I declare that this dissertation is my own work. It is being submitted for the Master's degree in Internal Medicine at the University of Zambia, Lusaka. It has not been submitted before for any degree or examination at this or any other University.

**Signed…….**

**Student**

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**Supervisor**

**Signed.....**

**Head of Department**

## ABSTRACT

**Background-** Despite the highest disease burden of HIV, Sub-Saharan Africa has limited data on HIV related kidney disease in the region. Kidney disease is a recognised complication in HIV infected patients, presenting with either can be acute renal failure (ARF) or chronic kidney disease (CKD). This study investigated the prevalence and factors associated with renal dysfunction among hospitalised HIV infected patients at the University Teaching Hospital (UTH), Lusaka.

**Methodology**- This was a cross sectional study that was conducted at the University Teaching Hospital Lusaka, Zambia. Enrolment of all eligible participants started from August 2010 to October, 2010. Inclusion criteria were hospitalised patients aged 16years and above who consented to the study. Qualified HIV counselors were used to counsel the patients. After obtaining demographic information, study participants were screened for HIV upon their consenting for the test. A full clinical history and examination was done by study physician to determine the factors associated with renal dysfunction.

**Results-** Of the 300 recruited hospitalised patients in this cross sectional study, 154(51%) were males. In HIV infected patients mean SD was 35.6(9.5) and 44.1(20.0) in uninfected HIV infected subjects. Our study observed a significantly higher prevalence of renal dysfunction among hospitalised HIV infected patients (42%) compared to (27%) among uninfected HIV patients p=0.006 and 2fold increased likelihood of developing kidney dysfunction; 1.96(1.21-3.17). WHO stage III was associated with renal dysfunction in HIV infected patients. Tenofovir a first line antiretroviral drug in Zambia wasn't associated with renal dysfunction. Mean arterial pressure (MAP) <65mmHg was not associated with kidney disease in multivariable analysis.

**Conclusion-**Renal dysfunction is significantly higher among hospitalised HIV infected compared to uninfected patients

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# GLOSSARY

**ACEI** Angiotensin Converting Enzyme Inhibitor

**ADQI** Acute Dialysis Quality Initiative

**AIDS** Acquired Immune Deficiency Syndrome

**AKI** Acute Kidney Injury

**ALT** Alanine aminotransferase

**ATN** Acute Tubular Necrosis

**ARF** Acute Renal Failure

**ART** Anti Retroviral Therapy

**ARB** Angiotensin Receptor Blocker

**AST** Aspartate aminotransferase

**AZT** Zidovudine

**CKD** Chronic Kidney Disease

**CVA** Cerebrovascular accident

**DBP** Diastolic Blood Pressure

**DM** Diabetes Mellitus

**ESKD** End Stage Kidney Disease

**FBS** Fasting blood sugar

**GFR** Glomerular Filtration Rate

**HAART** Highly Active Antiretroviral Treatment

**HB** Hemoglobin

**HIVAN** HIV Associated Nephropathy

**HTN** Hypertension

| | |
|---|---|
| **MAP** | Mean Arterial Pressure |
| **MOD** | Multiple Organ Dysfunction |
| **MOH** | Ministry of Health |
| **NSAIDS** | Non Steroid Anti Inflammatory Drugs |
| **OI** | Opportunistic Infections |
| **OR** | Odds Ratio |
| **PCP** | Pneumocystis Carinii Pneumonia |
| **PTID** | Patient Information Identification Number |
| **RBS** | Random blood sugar |
| **RIFLE** | Risk Injury Failure Loss and End stage |
| **RRT** | Renal Replacement Therapy |
| **SD** | Standard Deviation |
| **SBP** | Systolic Blood Pressure |
| **UTH** | University Teaching Hospital |
| **UPCR** | Urine Protein Creatinine Ratio |
| **UTI** | Urinary Tract Infection |
| **WHO** | World Health Organization |
| **WBC** | White Blood Count |

# CHAPTER 1

## 1.0 INTRODUCTION

Renal disease disproportionately affects patients living with HIV. Although Sub-Saharan Africa endures over 60% of the world's burden of HIV disease, there is limited data in the region on HIV related kidney disease, with most available data coming from the developed countries [1, 2]. Kidney disease is a recognised complication in HIV infected patients whose presentation can be acute renal failure (ARF) or chronic kidney disease (CKD) [3].

The few outpatient renal screening studies that have been done in Sub-Saharan Africa describe varying prevalence ranging between 6% to almost 50%. Screening outpatient studies in South Africa reported 6% and 5.5% renal dysfunction, 33.5% in Zambia and 48.5% in Uganda [4]. In hospitalised HIV infected patients, prevalence is up to 10 times higher and carries high mortality. This can be explained by differences in criterion employed in defining kidney dysfunction, study designs used and the subject population studied.

Prevalence and risk factors of renal dysfunction among hospitalised HIV infected patients remains unknown in developing countries like Zambia. In 2009, a prevalence of renal dysfunction of 33.5% among HIV infected outpatients commencing Highly Active Antiretroviral Treatment (HAART) in Lusaka, Zambia was found. It is estimated that more than 574 000 HIV infected patients may well have renal disease [5]. Zambia like most Sub-Saharan countries has limited facilities offering renal replacement therapy (RRT) with only one public Haemodialysis Unit with limited machines. The study thus investigated the prevalence and factors associated with renal dysfunction among hospitalised HIV infected and uninfected patients at the University Teaching Hospital (UTH), Lusaka.

# CHAPTER 2

## 2.0 LITERATURE REVIEW

HIV infected patients are affected by a spectrum of renal diseases that include ARF, electrolyte imbalances and acid base disorders, glomerular diseases, CKD and side effects that come with HIV treatment [3].

## 2.1 Prevalence and incidence

Incidence and prevalence of renal dysfunction varies in developed countries and is a major complication in HAART naïve and HAART experienced hospitalised HIV infected patients [4]. The Incidence of ARF in developed countries is between 5% and 20%. For example, a London study found an incidence of 5.7% in new HIV care patients and the risk of developing ARF was 10 times higher during the first three months of HIV care whereas a New York study showed increased incidence from 2.9% to 6%. The likelihood of developing kidney dysfunction was three times more likely among HIV infected than in HIV negative patients [6, 38].

Lopez *et al.* found prevalence of 47% renal dysfunction in hospitalised HIV infected patients in Portugal. The overall mortality was 43% and was higher among patients with ARF and 95% died within the first month of hospitalization [7]. Wyatt *et al*. in New York found renal dysfunction common among hospitalized HIV infected patients in both pre-HAART and post HAART patients and rare among HIV infected out patients [8, 20]. CKD prevalence among HIV infected patients in developed countries ranges between 5.5% and 8.7% and higher in those of African ethnicity [6].

In Sub-Saharan Africa, prevalence of renal dysfunction shows varying trends as well. Muloma *et al.* in an outpatient screening study among 219 antiretroviral naive patients attending an HIV clinic in Kenya found one in four HIV patients had kidney dysfunction. In Uganda, 48.5% participants attending HIV clinic had renal insufficiency [4, 9]. In Nigeria, prevalence for CKD ranges from 8-12% among hospitalised HIV infected patients [10] and 26% in Cote d'Ivoire (4). The definition criterion for renal dysfunction in these studies was based on Glomerular Filtration Rate and proteinuria.

In Zambia, Mulenga *et al.* found 33.4% renal insufficiency at initiation of HAART with increased mortality in a cohort study of outpatient HIV naive patients in eighteen primary public health care facilities in Lusaka [5].

## 2.2 Risk factors of renal dysfunction among HIV infected patients

There are various risk factors predisposing HIV infected patients to developing renal dysfunction. This development happens by and large due to the same reasons as in non HIV infected. However, certain factors are exclusive to HIV and the incidence is higher in HIV patients [11]. The causes of renal disease in HIV patients can be community or hospital acquired but hospitalised patients have a higher risk of developing renal dysfunction (up to ten times more common) with worse outcomes[3].

Volume depleting conditions are a major cause of pre renal failure in HIV patients due to chronic gastroenteritis among HIV infected patients [12, 23, 26]. Hypotension causes reduced mean arterial pressure (MAP) leading to Acute Tubular Necrosis (ATN) [4, 30, 38]. The causes of reduced MAP among hospitalised HIV infected patients include gastroenteritis, sepsis with shock and dehydration. Disordered renal regulations of salt and water balance such as adrenal insufficiency and tubular dysfunction are also contributory to volume depletion conditions and hypotension among HIV infected patients [12, 13]. Gastroenteritis is caused by opportunistic infections, malabsorption and drug treatments for HIV and related opportunistic infections. Opportunistic infections (OIs) causing chronic diarrhoea are cryptosporidiosis, isospora belli, microsporidiosis, mycobacterium avium complex (MAC) and malignancies affecting the gastrointestinal tract [13, 14].

Infections are a leading cause of severe renal dysfunction in studies among HIV infected patients. AIDS leads to impaired immunity in HIV infected patients [11]. Rao and Freidman observed sepsis induced renal dysfunction in half of the hospitalised patients [15]. Among ninety seven critically ill hospitalised HIV-infected in Portugal, 47.4% had renal dysfunction and sepsis was the leading cause. In multivariable analysis, age > 60years, severity of illness and hepatitis C were independent predictors of renal dysfunction [7].

In a London study, the common infections in early setting ARF were AIDS defining illnesses such as cryptoccocal meningitis, pneumocystis carinii pneumonia (PCP) and toxoplasmosis. Bacterial infections were associated with late onset ARF [16]. In other studies, sepsis was associated with 52% renal dysfunction, the majority of which were AIDs associated infections. The common sites of infections were the central nervous system (meningitis, encephalitis, pneumonias, lung abscesses, gastroenteritis, pancreatitis, cholangitis and other skin infections. The most isolated organisms were Cryptococcus neoformans, Pneumocystis carinii jiroveci, Cytomegalovirus, Herpes simplex virus, Mycobacterium tuberculosis, and Mycobacterium avium complex and Staphylococcus aureus [14]. In other studies, non infective diseases such as liver diseases were a major cause of renal dysfunction in hospitalised HIV positive patients [14, 17, 20].

Medications prescribed to HIV patients may also cause renal dysfunction [8, 20, 26]. Some of these medications include HAART, medications for treatment or prophylaxis of OIs and herbal medications. For example, tenofovir disoproxil fumerate is a first line antiretroviral drug in Zambia and has been linked to renal dysfunction though the incidence is very low [5, 18] (MOH guidelines 2007). Amphotericin B is used for treatment of cryptococcus neoformans which is the most common cause of meningitis at UTH [19]. Trimethoprim/Sulfamethoxazole, a drug used for pneumocystis carinii pneumonia prophylaxis among HIV patients with CD4 count below 350cells/$mm^3$ and treatment, can cause renal dysfunction [18].

HIV patients with CD4 counts below 200cells/$mm^3$ are more predisposed to development of renal dysfunction. In Franceschini study, sixty nine episodes of renal dysfunction occurred among 39 patients with CD4 counts <200cell/$mm^3$ compared to forty renal dysfunctions episodes among 30 patients with CD4 counts 200cells/$mm^3$ [14, 20-26].

Patients with higher viral load are significantly at risk of developing renal dysfunction among hospitalised patients [14, 26]. Franceschini *et al.* found increased renal dysfunction among hospitalised patients, HIV RNA >10,000copies/ml (mean log10 HIV RNA 4.2 1.3 versus 3.4 1.3, respectively, $p< 0.00001$). WHO stages III and IV of the disease have also been associated with renal dysfunction among HIV infected patients in Zambia [5].

Malnutrition, age, and severity of HIV disease were common risk factors in hospitalised HIV patients with kidney dysfunction in a Nigerian study [10, 26]. Anaemia is also associated with renal dysfunction among HIV infected patients and contributes significantly to morbidity and mortality [5, 10, 26].

## 2.3 Mortality and renal dysfunction in hospitalised HIV infected patients

Mortality rates are high in HIV patients with renal disease. They range from 25% to 80% depending on the cause of kidney injury and co-morbidities in the patient [20].

Although reversible with RRT, development of renal dysfunction carries high mortality in HIV infected patients compared to non-HIV infected patients [3]. Of the 700 patients admitted with ARF at the Johannesburg Hospital, almost 20% had HIV and mortality was 20% among the HIV infected patients [4, 26]. At the University Teaching Hospital Haemodialysis Unit in Lusaka, mortality was 34.4% among 58 hospitalised HIV infected patients with renal dysfunction in the first half of the 2009 (unpublished UTH audit 2009).

In other studies, established CKD at HAART initiation was associated with higher mortality independent of HIV related risk factors for death. HIV infected patients with kidney dysfunction were twice likely to die compared to those with normal kidneys [4, 39].

Development of ARF is a strong predictor of in-hospital mortality in HIV infected patients. Moreover, CKD in HIV infected is also associated with development of ARF and in-hospital mortality [17].

## 2.4 Definition of renal dysfunction

### 2.4.1 Acute Renal Failure definition

Despite some advances in treatment and understanding pathogenesis of ARF, definition has been a subject with controversy, confusion and lack of consensus. Lack of standard definition has also resulted in varying reported incidences and mortality. There are more than 30 ARF definitions in literature that have been used today. To establish a uniform definition, Acute Dialysis Quality Initiative (ADQI) was formed and represents efforts of a workgroup seeking to develop a consensus definition and evidence based statement in the field of ARF [27]. ADQI identified a definition and classification of ARF called RIFLE criteria. RIFLE defines three levels of severity of ARF based on changes in serum creatinine or urine output from baseline condition. A RIFLE criterion is a new system of classification from an evidence appraisal and expert opinion.

**'RIFLE'** stands for:

**Ri**sk is 1.5x increases in serum creatinine from normal or GFR decrease by 25% or urine output less than 0.5ml/kg per hour for 6 hours. **I**njury is 2 x increases in serum creatinine from normal, or GFR decrease by 50% or urine output less than 0.5ml/kg per hour for 12hours.

**F**ailure 3x serum creatinine increase from normal or GFR decrease by 75% or urine output less than 0.5ml/kg per hour for 24hours.

**L**oss and **E**nd stage are outcome parameters.

Concerns on RIFLE criterion were on use of small changes in serum creatinine and urine output. Others pointed that 50% increment in creatinine was conservative and that smaller changes in creatinine were important. Despite this, RIFLE has been used in over 100 000 studies in nephrology and critical care literature [28, 29].

### 2.4.2 Definition of CKD

According to National Kidney Foundation, CKD is evidence of kidney damage that persists for ≥ 3months. Severity of damage is graded according to renal function on basis of GFR or creatinine clearance into five stages [21].

**CKD stage 1** is kidney damage with normal or increased GFR above 90ml/min/1.73m$^2$.

**CKD stage 2** is kidney damage with mild or reduced GFR ranging 60-89ml/min/1.73m$^2$

**CKD stage 3** is kidney damage with moderate GFR ranging 30-59ml/min/1.73m$^2$

**CKD stage 4** is kidney damage with severe GFR ranging 15-29ml/min/1.73m$^2$

**CKD stage 5** is ESKD with GFR below 15ml/min/1.73m$^2$ and in need of permanent renal replacement therapy in form of dialysis [21].

# CHAPTER 3

## 3.0 STUDY JUSTIFICATION

Prevalence and factors associated with renal dysfunction among Hospitalised HIV infected patients in UTH and the rest of Zambia is unknown. Renal dysfunction also seems to be high among hospitalised HIV infected patients at the University Teaching Hospital and is a major cause of morbidity and mortality. The factors may be worse in HIV infected than HIV-negative patients. There has been no study in Zambia that has investigated the prevalence and factors associated with renal dysfunction among hospitalized HIV infected patients. ARF is reversible if diagnosis and intervention is early enough. Treatment of ARF is temporal and cheaper whereas treatment of CKD is long term and more expensive worldwide. Also progression of CKD to ESKD can also be delayed with early diagnosis and intervention.

The information generated would shed light on the burden of renal dysfunction among HIV patients in Zambia and be helpful for policy makers and clinicians to formulate guidelines for prevention, treatment and intervention of renal dysfunction. This will reduce the number of patients developing renal dysfunction and in long run reduce mortality, morbidity and costs associated with renal dysfunction. Therefore the study will add knowledge to the field of medicine in Zambia.

## 3.1 Research Hypothesis

Our research hypothesis was that HIV infected patients have a higher prevalence of renal dysfunction than non-HIV infected patients.

## 3.2 GENERAL OBJECTIVE

To investigate prevalence of renal dysfunction and the associated factors in hospitalized HIV infected and uninfected patients in UTH.

### 3.2.1 Specific Objectives

- To determine the proportion of renal dysfunction in hospitalized HIV and non-HIV infected patients in UTH admission wards and Adult filter Clinic.
- To determine the factors associated with renal dysfunction among hospitalized HIV infected and HIV-negative patients.
- To compare the prevalence of renal dysfunction in hospitalized HIV and non-HIV infected patients.

# CHAPTER 4

## 4.0 STUDY DESIGNS AND METHODS

This was a cross sectional study that was conducted at the University Teaching Hospital, Lusaka, Zambia. Enrolment of all eligible participants took place from August, 2010 to October, 2010. All eligible hospitalised patients at AFC and Phase V medical admission wards were recruited to the study after consenting. Selection of participants was by convenient sampling of every consecutive patient that was admitted from Monday to Saturday in the day time. A maximum of ten hospitalised patients were enrolled to the study in a day. Using a data collection sheet, information on age, race, gender, and marital status was obtained. Patients' data was obtained within 48hours of hospitalisation to the admission wards. Study participants were screened for HIV upon their consenting for the test. Qualified HIV counselors were used to counsel consenting patients before an HIV test. A full clinical history and clinical examination was done by study physician who then assessed risk factors for renal dysfunction as well as clinical presentation (see appendix).

### 4.1 Inclusion Criteria

- Hospitalized patients admitted to the University Teaching Hospital medical admission wards (Adult filter clinic and phase V) who agreed to participate in the study were recruited

- Aged 16years and above

### 4.2 Sample size

Using a prevalence of 20% of renal dysfunction among hospitalized HIV infected patients and 8% among non HIV infected, sample size was calculated using the Pocock's formula. A minimum sample size of 141 HIV positive and 141 uninfected patients was adequate to detect a difference at 0.05 significant levels

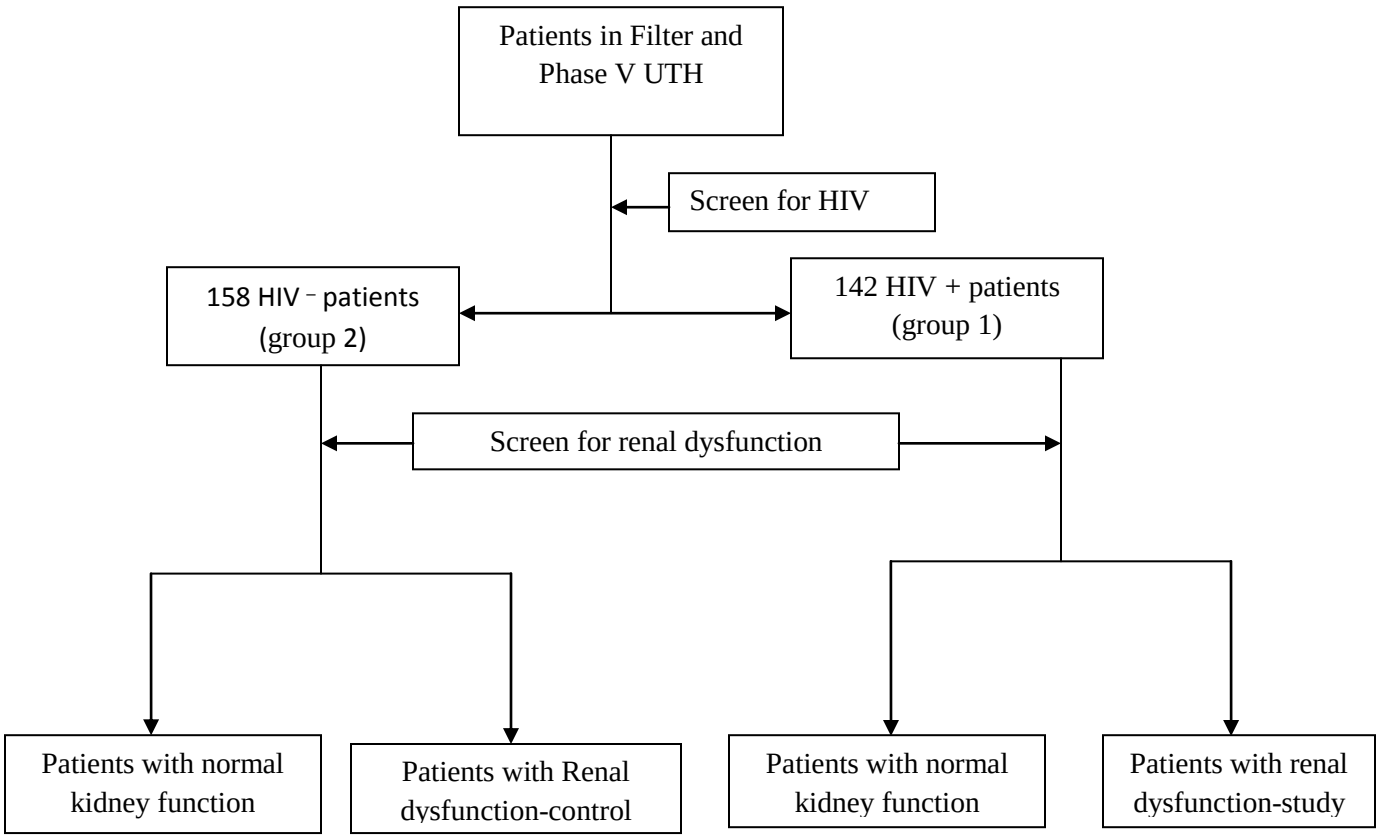
$$N = \frac{[P_1 (100-P_1) + P_2 (100-P_2)]}{(P_1-P_2)^2 \times f(\alpha, ß)}$$

$$N = \frac{20(100-20) + 8(100-8)}{12^2 \times 7.85 = 127}$$

**$P_1$=** prevalence in Hospitalized HIV infected patients

**$P_2$=** prevalence in non-HIV

**Figure 1 Participants flow chart**



## 4.3 Ethical consideration

The protocol for this study was approved by the UNZA Biomedical Research Ethics Committee, ethics clearance certificate number 026-04-10. An informed and signed consent was obtained from the patients or next of kin. Details about the benefits or harm related to the study were explained to the participant or next of kin. Additionally, issues of confidentiality and procedures were explained as well. Study participants were assured of confidentiality.

## 4.4 Procedures

### 4.4.1 Biochemistry and hematology

Blood and urine samples assessing renal function were collected soon after patient assessment and hospitalisation. Creatinine samples were collected in heparinised tubes while urine samples in plain bottles. EDTA containing tubes were used to collect Complete Blood Counts (CBC) and CD4 counts. An Olympus AU 400 analyzer was used for determination of biochemistry parameters. A PENTRA 80 and XT-2000 was used to determine CBC and Fax caliber to determine CD4 counts.

### 4.4.2 Serum Creatinine

Serum creatinine was measured using the modified Jaffe method. In alkaline solution, creatinine forms a yellow orange complex with picrate and this colour intensity is directly proportional to the creatinine concentration. This was measured spectrophotometrically at 510nm. The normal range is 60-120micromole/l.

### 4.4.3 Serum albumin

Serum albumin was measured by a colorimetric assay using an end point method. Albumin binds with bromocresol green (ionic dye stuff) at a pH value of 4.1 to form a blue-green complex. The colour intensity of the blue-green colour is directly proportional to the albumin concentration and this was determined spectrophotometrically at 510nm. Normal values are 34– 48g/l.

### 4.4.4 Serum urea

Urea was measured by the decrease in NADH absorbance per unit time. Urea is hydrolyzed by urease to produce carbon dioxide and ammonia. The produced ammonia combines with 2-oxogluterate and NADH yielding glutamate and $NAD^+$.

### 4.4.5 Random Blood sugar

An Accu-chek active 2001 glucometer was used to measure the random blood sugar during patient assessment. Patients' history of diabetes mellitus was noted in those already diagnosed with diabetes mellitus.

### 4.4.6 Blood pressure measurement

Blood pressure (BP) measurement was recorded non-invasively in the arm at the brachial area. MAP was calculated as diastolic blood pressure plus one third pulse pressure. Patient's history of hypertension as well as duration was noted in those already diagnosed with hypertensive disease.

## 4.5 Study definitions

### 4.5.1 Renal dysfunction

For the purpose of this study renal dysfunction was defined as rise of serum creatinine 1.5x upper limit of normal i.e. ≥ 180micromole/l with or without decrement in urine output. (Zambia Laboratory Services/UTH normal values for creatinine is 60-120micromole/l)

### 4.5.2 Sepsis and MOD

Sepsis was defined according to the ACCP/SCCM Consensus Conference as a focus of infection with two or more of the following parameters:

- temperature >38 $^oC$ or <36 $^oC$
- heart rate >90beats /min
- respiratory rate >20breaths/min

- White cell count >1200mm$^3$ or <4000/ mm$^3$

Patients with more than two dysfunctional organs were considered to have multi-organ dysfunction (MOD).

## 4.6 Variables

The following were explanatory variables for this study:

### 4.6.1 Independent variables

- Sex
- Sepsis( as defined above)
- Age
- Herbal medications
- diarrhoea
- Drugs (NSAIDs, Septrin, Tenofovir, Amphotericin, ACEI/ARB, others)
- WHO stage of HIV ( I,II,III,IV)
- CD4 count

  <200cells/ mm$^3$

  200-350cells/ mm$^3$

  >350cells/ mm$^3$
- Hypertension ( ≥ 140/90mmHg)
- Diabetes Mellitus (Fasting of 7.8mmol/l or RBS of 11.1mmol/l)

### 4.6.2 Dependant variable

- Renal dysfunction as defined above was the dependant variable.

## 4.7 Statistical analyses

Data was collected onto a hard copy data entry sheet. Each participant had a patient identification (PTID) number. The data from the hard copy entry sheet was then transferred to a data entry programme on ***epi info*** version 3.5.1.dataset computer.

All statistical analysis was performed using ***epi info*** version 3.5.1 dataset. We used frequency tables to describe both categorical and quantitative variables. For continuous variables, means and percentages were used to discuss participants and the student t-test was used to test for significance. For categorical variables, frequencies, proportions and percentages were used to discuss participants and chi-square test was used to assess association between the variables. A step wise multivariable logistic regression was used to determine the independent factors associated with renal dysfunction among hospitalised HIV infected and non-HIV infected patients. We began with albumin <35g/dl, amphotericin B, anemia, CD4 count, diarrhoea, any HAART, tenofovir based regimen, MAP below 65mmhg, NSAIDS, septrin, vomiting and WHO stage III/IV. Variables with highest p values ($p>0.5$) were eliminated in step wise manner. A p value of less than 0.05 was taken as statistically significant.

# CHAPTER 5

## 5.0 RESULTS

### 5.1 Social-demographic characteristics of the participants

Patient demographics and clinical findings are shown in table 1 and described briefly here. Of the 300 recruited hospitalised patients in this cross sectional study, 154(51%) were males. Because continuous variables other than age had a non-Gaussian distribution, intergroup differences in medians of the variables were compared using Kruskal-Wallis test for non parametric distributions. Patients age ranged from 16 to 91years with mean of 40.1(standard deviation of 16.4); in HIV infected patients mean SD was 35.6(9.5) and 44.1(20.0) in HIV-negative subjects. Of the entire group, 204(68%) were married, 11(3.7%) divorced, 54(8%) single and 31(10.3) widowed. only 2(0.7%) patients were non-black.

### 5.2 Clinical characteristics of HIV and non-HIV infected subjects

There was significant hypertension among the HIV negative patients compared to HIV positive patients. Of the total 41(14%) hypertensive patients, 35(22%) were HIV negative and 6(4%) were HIV positive patients; $p<0.001$. Systolic blood pressure and diastolic blood pressure were significantly higher ($p<0.001$) among the HIV-negative patients. The mean duration of hypertension was 6 and 5 years among the HIV-negative and positive patients respectively.

Regarding nephrotoxic drugs, there was significant use of septrin among HIV infected patients compared to HIV negative $p< 0.001$. ACEI/ARB and NSAIDs were used significantly in HIV uninfected patients $p <0.001$. Septrin is used as a prophylactic drug for OI in HIV infected patients. Among the HIV-negative on NSAIDS, 29(50%) were on ASA, 21(36%) on brufen and the 8(13%) on diclofenac sodium. Of the total 29patients with heart failure, 18(62%) were on 75mg ASA (aspirin) as an anti-platelets drug. Only 3 of 300 (1%) were using herbal medications prior to admission.

Significantly more HIV positive hospitalised patients experienced vomiting and diarrhoea compared to the non HIV infected patients with $p=0.006$ and 0.003 for vomiting and diarrhoea

respectively. All the 12 HIV negative patients had acute diarrhoea of less than 14days. Among the 27 HIV positive, 10 had chronic diarrhoea lasting more than 14days**.**

**Table 1 Baseline characteristics of HIV positive and HIV negative subjects**

| | **Total (n=300)** | **HIV+ (n=142)** | **HIV- (n=158)** | **p-value** |
|---|---|---|---|---|
| **Age, mean (SD)** | 40.1 (16.4) | 35.6 (9.5) | 44.1 (20) | 0.005 |
| **Male** | 154 (51) | 80 (56) | 74 (47) | 0.10 |
| **Diarrhea** | 39 (13) | 27 (19) | 12 (8) | 0.003 |
| **Vomiting** | 49 (16) | 32 (23) | 17(11) | 0.006 |
| **Anuria** | 13 (4) | 6 (4) | 7 (4) | 0.93 |
| **Diabetes** | 20 (7) | 4 (3) | 16 (10) | 0.01 |
| **Hypertension** | 41 (14) | 6 (4) | 35 (22) | <0.001 |
| **SBP mean (SD)** | 113 (30) | 105(17) | 120(36) | <0.001 |
| **DBP mean SD** | 71 (19) | 66(13) | 75(22) | <0.001 |
| **Pulse mean (SD)** | 95(12) | 97(12) | 93(12) | 0.0038 |
| **Temperature mean (SD)** | 37(1) | 37(1) | 37(1) | 0.02 |
| **MAP <65mmHg** | 32(10.7) | 21(14.8) | 11(7) | 0.028 |
| **Nephrotoxic drugs** | | | | |
| **NSAIDs** | 86(29) | 28(20) | 58(37) | <0.001 |
| **ACEI/ARB** | 54(18) | 2(1.4) | 52(33) | <0.001 |
| **Septrin** | 111 (37) | 110 (78) | 1 (0.6) | < 0.001 |
| **Tenofovir** | 51(17) | 51(35.9) | 0 | <0.001 |
| **Amphotericin B** | 6(2) | 6(4.2) | 0 | 0.009 |
| **Heart failure** | 29(9.7) | 1(0.7) | 28(17.7) | <0.001 |
| **CVA** | 19(6.3) | 2(1.4) | 17(10.8) | <0.001 |
| **Sepsis** | 91(30.3 | 62(43.7) | 29(18.4) | <0.001 |
| **Malignancy** | 16(5.3) | 10(7) | 6(3.8) | 0.212 |
| **Anemia <8g/dl** | 102(34) | 57(40) | 45(28) | 0.033 |
| **Creatinine >180 micromole/l** | 103 (34) | 60 (42) | 43 (27) | 0.006 |

* Variables expressed as SD otherwise in %

Sepsis was significantly higher among the HIV infected patients compared to HIV-negative patients (p<0.001). The causes of sepsis among the HIV positive patients were meningitis 27(43%), pneumonias 21(34%), encephalitis 9 (14%) and others 5 (8%).

Of the total 29 sepsis HIV-negative patients, 11(38%) had pneumonia, 5(17%) meningitis, 4(13%) encephalitis and 9(31%) others. Included among other sepsis causes were patients with infected ulcers, Urinary Tract Infections (UTI) with systemic inflammatory response syndrome (SIRS).

## 5.3 Laboratory characteristics of participants

The laboratory characteristics of participants are described briefly below (table 2);

There were no differences in ALT (p=0.06) and AST (p=0.77) measurements among the two groups. The mean hemoglobin was significantly lower in the HIV positive group compared to the HIV-negative group <0.001.

**Table 2 Laboratory characteristics of HIV positive and HIV negative subjects.**

| | **Total N=300** | **HIV+ N=142** | **HIV- N=158** | **P value** |
|---|---|---|---|---|
| **WBC** | 8(5) | 7(4) | 9(6) | 0.006 |
| **PLT** | 247(145) | 248(142) | 245(148) | 0.84 |
| **ALT** | 58(135) | 46(54) | 68(179) | 0.12 |
| **AST** | 106(312) | 72(79) | 138(422) | 0.05 |
| **Albumin** | 35(7) | 35(6) | 35(7) | 0.90 |
| **Urea** | 14(16) | 15(15) | 13(17) | 0.03 |
| **Hb** | 9.6(4) | 9(3) | 10(4) | <0.001 |
| **UPCR** | | | | |
| **1-2.9999** | 83(29.6%) | 49(36%) | 34(23.3%) | 0.02 |
| **= or > 3** | 35(12.5%) | 14(10.4%) | 21(14.4%) | 0.02 |

*All parameters SD except UPCR

## 5.4 Prevalence of renal dysfunction among HIV positives and HIV-negative participants

Renal dysfunction was more common in HIV+ patients with an unadjusted odds ratio of 1.96 (1.21-3.17), see Table1). Age adjusted OR for renal dysfunction in HIV positive versus HIV negative using 2 variable logistic regressions was 1.99 (1.20-3.28). Among the HIV infected, 42% had renal dysfunction compared to 27% among non HIV infected p= 0.006. Among the HIV positives 33(41.3%) were males and 43.5 were females. While in non HIV positives, 26 (35.1%) were males and 17(20.2%) females.

## 5.5 Factors associated with renal dysfunction among Hospitalised HIV positive patients

The characteristics associated with renal dysfunction among hospitalised HIV infected patients are briefly described here and shown in table 3.

WHO stage III was an associated factor for development of renal dysfunction compared to WHO stage IV (OR 2.3; 1.16-5.00, 95%CI). WHO stage 1V disease had a lower odds (OR 0.42; 0.20-0.86, 95%CI). Of the total 142 HIV positive patients, 2(1.4%) were in stage 1, 86(60%) in stage 111 and 54(38%) in stage 1V of HIV infection. Of the 54 WHO stage 4 disease, 18(33%) had Extra pulmonary tuberculosis (EPTB), 8(14.8%) confirmed cryptococcal meningitis, 9(16.6%) KS, 3(5.5%) PCP, 2(3.7%) cryptosporidiosis, 2(3.7%) suspected HIV Associated Nephropathy (HIVAN) with the remaining 12(22%) having other stage 4 disease conditions.

Tenofovir was not associated with renal dysfunction among hospitalised patients (1.03; 0.45-2.37, 95%CI). Other drugs not associated with renal dysfunction were amphotericin B (OR 1.49; 0.26-8.39, 95% CI) and septrin (OR 1.09; 0.49-2.42, 95% CI). Of the 61patients on HAART, 85.2% were on tenofovir based regimen, 9.8% on AZT (zidovudine) based regimen and 4.9% on stavudine based regimen.

**Table 3 Factors associated with renal dysfunction among HIV positive participants**

| | Renal dysfunction N=60 | No renal dysfunction N=82 | OR (95% CI) |
|---|---|---|---|
| **HTN** | 2(3.3) | 4(4.9) | 1.48(0.26-8.39) |
| **DM** | 2(3.3) | 2(2.4) | 1.37(0.19-10.08) |
| **Diarrhoea** | 16(26.7) | 11(13.4) | 2.35(0.99-5.52) |
| **Vomiting** | 24(40) | 8(9.8) | 6.17(2.52-15.08) |
| **Nephrotoxic Drugs** | | | |
| **NSAIDS** | 12(20) | 16(19.5) | 1.03(0.45-2.37) |
| **Tenofovir** | 23(38) | 28(34) | 1.19(0.59-2.39) |
| **Amphotericin** | 2(3.3) | 4(4.9) | 1.49(0.26-8.39) |
| **Septrin** | 47(78.3) | 63(76.8) | 1.09(0.49-2.42) |
| **CD4 defined as** | | | * |
| **>350cell/ml** | 5(81) | 10(15) | 1.0 |
| **200-350** | 5(8) | 12(15) | 0.68(0.14-3.07) |
| **<200cells/ml** | 50(83) | 62(76) | 1.29(0.40-4.19) |
| **WHO** | | | |
| **III** | 43(72) | 43(53) | 1.0 |
| **IV** | 16(27) | 38(46) | 0.42(0.20-0.86) |
| **Sepsis** | 23(38.3) | 39(47.6) | 0.68(0.34-1.35) |
| **Malignancy** | 2(3.3) | 8(9.8) | 0.32(0.06-1.55) |
| **MAP < 65** | 14(23.3) | 7(8.5) | 3.26(1.22-8.67) |
| **Anaemia†** | 26(43) | 31(37.8) | 1.26(0.64-2.47) |

†Anaemia defined as Hb < 8 g/dl

## 5.6 Factors associated with renal dysfunction among HIV-negative patients

The factors for kidney dysfunction in hospitalised HIV-negative patients are shown in table 4 and briefly described below.

Hypertensive was a significant factor for the development of kidney dysfunction among the non-HIV disease patients (OR 4.15; 1.87-9.19, 95% CI).

Usage of ACEI/ARBs was a significant factor for the development of renal dysfunction among HIV-negative hospitalised patients (OR 2.03; 0.61-6.67, 95%CI). Of the total 54 patients on ACE/ARBs, the distribution was enalapril 90.1%, captopril 5.5% and Losartan 3.7%.

**Table 4 Factors associated with renal dysfunction among HIV negative participants**

| | Renal dysfunction | No renal dysfunction | OR (95% CI) |
|---|---|---|---|
| **HTN** | 18(42) | 17(15) | 4.15(1.87-9.19) |
| **DM** | 5(11.6) | 11(9.6) | 1.24(0.37-3.82) |
| **Diarrhoea** | 5(11.6) | 7(6) | 2.03(0.61-6.77) |
| **Vomiting** | 9(21) | 8(7) | 3.54((1.27-9.89) |
| **Nephrotoxic Drugs** | | | |
| **NSAIDS** | 16(37) | 42(36) | 1.03(0.49-2.13) |
| **ACEI/ARB** | 22(51) | 30(26) | 2.97(1.43-6.15) |
| **Septrin** | 00 | 1(0.9 | Undefined |
| **Sepsis** | 6(14) | 23(20.0) | 0.64(0.24-1.72) |
| **Heart Failure** | 9(21) | 19(16.5) | 0.80(0.24-2.61) |
| **CVA** | 4(9.3) | 13(11.3) | 1.24(0.38-4.04) |
| **Malignancy** | 00 | 6(5.2) | 1.54(0.44-5.70) |
| **Anemia(Hb<8g/dl)** | 29(25) | 16(37.2) | 1.75(0.83-3.71) |
| **MAP<65mmHg** | 4(9.3) | 7(6.1) | 1.54(0.44-5.70) |

## 5.7 Factors associated with renal dysfunction in HIV positive multivariable logistic regression.

We performed multivariable stepwise logistic modeling to identify factors independently associated with renal dysfunction among hospitalised patients among the HIV positive patients. We began with the following variables: albumin<35g/dl, amphotericin B, and anemia (defined as Hb <8g/dl), CD4 count, diarrhoea, any HAART, tenofovir based regimen, MAP<65mmHg, NSAIDS, septrin, vomiting and WHO stages 111 and IV. Results for multivariable regression are shown in table 5 and described below;

Vomiting was associated with renal dysfunction among hospitalised HIV disease patients in both univariable and multivariable analysis (OR 7.77; 2.46-24.53 95%CI).

MAP below 65mmHg was not an independent factor for renal dysfunction among hospitalised HIV infected patients. WHO stage III was independently associated with renal dysfunction among hospitalised HIV infected patients (OR 0.17; 0.05-0.53, 95%CI).

**Table 5 Factors associated with renal dysfunction in HIV+ multivariable logistic regression**

| Term | Odds Ratio | 95%CI |
|---|---|---|
| **AGE** | 1.02 | (0.97-1.06) |
| **Amphoterin B** | 3.60 | (0.43-30.19) |
| **CD4 <200** | 0.46 | (0.09-30.19) |
| **CD4 200-350** | 0.52 | (0.14-1.98) |
| **CD4 >350** | 1 | |
| **Diarrhoea** | 0.48 | (0.12-1.91) |
| **Tenofovir** | 2.13 | (0.39 -11.39) |
| **MAP<65mmHg** | 2.50 | (0.73-8.58) |
| **NSAIDS** | 1.94 | (0.69-5.46) |
| **Sepsis** | 0.26 | (0.09- 0.70) |
| **Vomiting** | 7.77 | (2.46-24.53) |
| **WHO Stage III** | 1 | |
| **WHO Stage IV** | 0.18 | (0.06-0.53) |
| **Any HAART** | 0.49 | (0.09-2.55) |

* OR for age is the increasing odd per year of life. In a stepwise fashion we eliminated the variable with the highest p value, if the $p > 0.5$. The logistic regression results for the remaining variables are shown above.

## 5.8 Factors associated with renal dysfunction in uninfected HIV participants multivariable logistic regression

Multivariable stepwise logistic modeling to identify factors independently associated with renal dysfunction among hospitalised patients among the HIV-negative patients was done. We began with the following variables: age, ACEI/ARBs, albumin<35g/dl, anemia (HB<8g/dl), diarrhoea, DM, heart failure, HTN, MAP<65mmHg, NSAIDS, sepsis and vomiting. Results for multivariable logistic regression are shown in table 6

Vomiting was an independent risk factor for renal dysfunction among HIV negative patients (OR 4.43; 1.40-16.66, 95%CI

Hypertension was a significant independently risk factor for renal dysfunction among hospitalised HIV negative patients (4.75; 1.59-14, 95%CI).

**Table 6 Factors associated with renal dysfunction in uninfected HIV participants' multivariable logistic regression**

| Term | Odds Ratio | 95%CI |
|---|---|---|
| **Age** | 0.98 | (0.96-1.00) |
| **ACEI/ARB** | 2.65 | (1.01-7.00) |
| **Albumin <35 g/dl** | 2.97 | (1.25-7.05) |
| **Anaemia** | 1.93 | (0.78-4.78) |
| **HTN** | 4.75 | (1.59-14.20) |
| **Sepsis** | 1.75 | (0.52-5.88) |
| **Vomiting** | 4.83 | (1.40-16.66) |

* OR for age is the increasing odd per year of life. OR for albumin is the decreasing odd of renal failure per g/dl increase in albumin. In a stepwise fashion we eliminated the variable with the highest p value, if the p > 0.5. The logistic regression results for the remaining variables are shown in Table 6

## 5.9 Laboratory findings of participants with renal dysfunction

The laboratory characteristics of HIV positive participants are shown in table 7.1 and described briefly below;

There were no significant differences in hemoglobin among the HIV positive patients and HIV-negative with renal dysfunction compared to those without renal dysfunction p=0.490.

**Table 7.1 Laboratory findings in HIV positive patients with and without renal dysfunction**

| | **Total HIV + 142** | **Renal dysfunction N=60** | **No renal dysfunction N=82** | **p-value** |
|---|---|---|---|---|
| **Albumin** | 34(32-37) | 34(32-36) | 34(31-37) | 0.914 |
| **ALT** | 46(54-89) | 41(23-71) | 24(14-40) | 0.004 |
| **AST** | 43(27-84) | 47(34-93) | 37(23-67) | 0.025 |
| **Hb** | 6(4-16) | 8.3(6-11.5) | 9(6-11.7) | 0.490 |
| **Platelet** | 233(144-342) | 194(110-298) | 249(162-397) | 0.024 |
| **WBC** | 7(4.3-8.6) | 6(4.6-8.7) | 6.9(4-9) | 0.970 |
| **Urea** | 6.7(5-23) | 26.5(18.5-35) | 5(4-6) | <0.001 |
| **Creatinine** | 107(79-266) | 296(189-665 | 81(66-96) | <0.001 |

*Kruskal-Wallis test used to compare nonparametric variables

*Medians and interquartile ranges used

**Table 7.2 Laboratory findings of HIV-negative participants with renal dysfunction.**

| | Total HIV – N=158 | Renal dysfunction N=43 | No renal dysfunction N=115 | p-value |
|---|---|---|---|---|
| **Albumin** | 34(29-40) | 36(25-38) | 36(30-42) | 0.003 |
| **ALT** | 34(29-40) | 28(17-83) | 22(14-40) | 0.061 |
| **AST** | 34(21-75) | 34(19-84) | 34(22-68) | 0.766 |
| **Hb** | 11.1(7-13) | 11(7-12) | 11(7-13) | 0.402 |
| **Platelet** | 229(133-345) | 189(128-279) | 250(141-371) | 0.059 |
| **WBC** | 7.6(5-11) | 8(6-11) | 7(5-12) | 0.226 |
| **Urea** | 6(4-16) | 29(23-48) | 4(3-6) | <0.001 |
| **Creatinine** | 105(77-183) | 476(189-1426) | 91(74-111) | <0.001 |

*Medians and interquartile ranges used

# CHAPTER 6

## 6.0 DISCUSSION

This study was carried out to determine prevalence and risk factors contributing to kidney dysfunction in hospitalised HIV positive and HIV negative patients. Our case definition of kidney dysfunction was at least 1.5 fold increase in serum Creatinine from normal (>180micromol/l).

Prevalence of renal dysfunction from our study was 42% among hospitalised HIV positive infected patients compared to 27% among non HIV infected patients. This is similar to Lopez *at al.* study that found 47% among critically ill hospitalised patients. The subject populations in Lopez's study were critically ill and hence the slight increase in total number of renal dysfunction cases. Additionally, UTH is the only tertiary referral hospital for all renal and non-renal disease. Franceschini *et al.* also found increased renal dysfunction among hospitalised HIV in both pre-HAART (2.9 vs. 1.0 adjusted OR 4.62; 95Cl) and post HAART error (6 vs. 2.72 adjusted OR 2.82; 95CL) [7, 14]. In a few in-patient studies in Africa, renal dysfunction ranged from 17% to almost 30% in HIV positive patients [4, 26]. The difference is that the African studies recruited patients with surgical and obstetric conditions as well.

Mean arterial pressure appeared to be a risk factor for renal dysfunction but when adjusting for other co-variables it was found to be statistically not significant unlike previous studies done in Europe and Africa. This may be explained by the small sample size recruited in our study. Valerie et al found 38% renal dysfunction due to volume depleting conditions among hospitalised HIV positive patients. The causes of low mean arterial pressure included sepsis with shock, chronic gastroenteritis and adrenal insufficiency [11, 12, 30].

WHO stage III was a risk factor for renal dysfunction in our study unlike previous studies that found both stages III and IV as contributory risk factors [5]. Other studies found WHO stage IV renal protective similar to our study [31]. Patients with renal failure come in WHO stage III presenting with chronic diarrheal diseases. Only when the causative agents for diarrhoea are known that they are classified as stage IV.

Tenofovir was not associated with renal dysfunction among hospitalised HIV infected patients in our study. This is in keeping with many other studies. Izzedine et al study found no differences in tenofovir based regimen compared to non-tenofovir based regimen [8]. Mauss *et al.* 2005 found renal impairment among patients taking tenofovir compared with patients not receiving tenofovir. Patients on tenofovir had higher proteinuria while their GFR remained the same. Cohort and case control studies found that renal failure associated with Tenofovir was not more common than with other ARV regimens [31-33]. Renal dysfunction due to tenofovir depends on a complex interaction on genetic, environmental and pharmacological factors which may explain the protective effect.

In our study, a CD4 count below 200 cells was not associated with renal dysfunction among hospitalised HIV infected patients unlike previous studies. In other studies, a low CD4 count was a predictor of renal dysfunction and likelihood of kidney dysfunction increased with CD4count <100 cells/mm. In a London study, patients with CD4 counts <50 cell/mm had a 10 fold risk of developing kidney dysfunction compared to 1.6 fold risk among those with CD4 counts between 200 to 350 cells[ 34,35]. In our study, HIV infected patients with CD4 counts ranges 200cells, <100 cells and < 50cells were not compared unlike previous studies. Limited sample size of HIV hospitalised patients in our study may as well explain the difference.

Sepsis in this study was not associated with renal dysfunction unlike previous studies [7]. Previous studies demonstrated 52% renal dysfunction dues to sepsis resulting from sepsis induced arterial hypotension and a reduced MAP. The AIDS defining illnesses were not the common causes of sepsis induced renal dysfunction in our study. Under diagnosis due to limited laboratory backup may explain the differences in our study.

Hypertension was a significant risk factor for renal dysfunction among hospitalised HIV-negative patients similar to other studies in Europe and Africa [10]. The likelihood of developing renal dysfunction among hypertensive patients was almost five fold after adjusting for other co-variable. Hypertension is both a cause and complication of renal dysfunction and determines prognosis. Primary kidney disease is responsible for almost 4% hypertension in the general populations [36-37].

Vomiting was associated with kidney disease in both HIV positive and HIV negative patients. Vomiting and nausea are common clinical presentation of kidney disease. This is similar to the Nigerian study that found vomiting a common presentation of renal dysfunction among HIV infected patients [10].

## 6.1 Study limitations

The severity of co-morbidities using APACHE score were not determined among both HIV positive and HIV negative patients in this study due to non availability of laboratory reagents and limitation of the funding.

Renal biopsies among patients with renal dysfunction were not done for histological confirmation. More than 10% nephrotic proteinuria found in both HIV-negative and HIV positive patients merited kidney biopsy. Biopsy was also necessary in determining the proportion of CKD in hospitalised patients.

As patients in our study were critically ill and bedridden, we were unable to measure their body mass index using weight and heights to quantify their nutritional status. The later has been associated with renal disease in previous studies.

# CHAPTER 7

## 7.0 CONCLUSION

In conclusion, prevalence of renal dysfunction among hospitalized HIV infected patients was higher compared to uninfected HIV patients, in keeping with previous studies.

WHO stage III and vomiting were associated with renal dysfunction among HIV infected patients in line with previous studies. In HIV negatives, hypertension was a risk factor for renal dysfunction. Tenofovir was not associated with kidney disease in our study.

In view of the high prevalence of renal dysfunction among hospitalised HIV infected patients, it is recommended that baseline creatinine and UPCR be done on all patients and CrCl be used in the initiation of HAART. Kidney biopsies should be done on all patients for histopathological diagnosis and confirmation. A longitudinal study should be done in future looking at outcome of these patients with kidney disease in a resource limited country like Zambia.

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# APPENDICES

# APPENDIX 1

**Informed Consent Form**

(With translations for non-English writing or speaking participants)

Title: Prevalence and risk factors of renal dysfunction among Hospitalised HIV-infected patients at the University Teaching Hospital, Lusaka

**Site:** Phase V admission and Adult Filter

Hello,

My name is Dr Justor Banda a medical Doctor in Department of Medicine at the University Teaching Hospital and doing a research study for my Masters.

**Introduction**

You are invited to consider participating in this research study. Your participation is voluntary and can withdraw from the study at anytime without problems in future. It is important that you read and fully understand information on this leaflet as it will help you in making the decision. If unable to understand, an interpreter will be provided to help you go through the leaflet.

**Purpose of the study**

The human body has kidneys performing different functions that include removing waste products. The kidneys are a common complication in hospitalised patients and the risk is higher in HIV infected than non-HIV patients. It is a major cause of mortality and morbidity at the University Teaching Hospital. HIV, opportunistic infections and their treatment contribute to kidney damage in Hospitalised HIV infected patients.

**Procedures of the study**

If you agree to participate in the study, information about your sex and age will be obtained. A qualified HIV counselor will counsel you before an HIV test. A physician will examine and collect history assessing renal dysfunction. Samples of blood and other tests relevant to your illness will be drawn for testing renal dysfunction and other co morbidities.

**Possible risk factors are as follows:**

Blood collection may cause pain at site of puncture.

Air emboli and infection are very rare complications that can occur after vein puncture. Qualified personnel will collect the blood samples to prevent such complications.

**Benefits of the study**

Benefits are that participants in this study will be screened for kidney dysfunction and the findings will help in laying intervention strategies for kidney disease.

**Financial arrangements**

You will not be paid for participating in the study. There are no costs for any related study procedures.

**Confidentiality**

All information obtained during the course of this study will be kept strictly confidential. Your records will be given unique identification numbers and the initial identification details won't be used. All physical records will be kept in a locked locker with access limited to the research team. Electronic data will be password protected.

**Source of Information**

If you have any questions, concerns and clarifications, please contact the following:

Dr Justor Banda, Department of Internal Medicine/Bag RW1X, Lusaka phone +260977819656 or Chairperson, UNZA Biomedical Research Ethics Committee, P.O. Box 50110, Lusaka

Phone +2601256067

I.....having read and clearly understood the above written information, consent to taking part in this research study.

Participants signature or thumb print Date_____

Witness Date_____

# APPENDIX 2

## DATA COLLECTION SHEET

Identification no____ ____ ____

Date____ ____ _____

**TITLE:** Prevalence and Risk factors for renal dysfunction among Hospitalised HIV infected adult patients at University the Teaching Hospital, Lusaka

1. **DEMOGRAPHIC DATA**
    a. Age ____ ____
    b. Sex □male □ female
    c. Marital status □ single □married □divorced □widowed
    d. Race □Black □non-Black
2. **HISTORY**
    a. Diarrhoea □Y/□N, Duration □< 14 days, □> 14days, Frequency/day.....
    b. Vomiting □Y/□N, Duration □ <14 days, □> 14days, Frequency/day.....
    c. Passing urine □Y / □N, if not passing then duration of not passing urine.....
    d. Hypertension□ Y/ □N, duration of hypertension.....
    e. Diabetes □Y/□N, duration of Diabetes.....
    f. History of Kidney diseases □Y/□N.....
    g. Herbal medications □Y/□N, name of medication(s).....
    h. Nephrotoxic drugs
        i. □Brufen □ASA □Indocid □diclofenac □Naproxen □Other NSAIDS.....
        ii. □Enalapril □captopril □Losartan □other ACEI or ARBs.....
        iii. Tenofovir □Y/ □N

iv. Septrin □Y/ □N
v. Amphotericin B □Y/ □N
vi. Others.....

3. HIV status □positive □negative
4. If on HAART type of regimen patient is on.....
5. **CLINICAL EXAMINATION**
    a. BP_____/ _____
    b. Pulse.....
    c. Temp.....
    d. Pedal oedema □Y/□N
    e. Reduced skin tugor □Y/ □N
    f. Pulmonary oedema □Y/ □N
    g. Mental state- □oriented □confused □inappropriate words □incomprehensible sounds □no verbal response
    h. Uraemic frost □Y/□N
    i. Uraemic pericarditis □Y/□N
    j. Acidotic breathing □Y/□N
    k. Pallor □Y/□N
    l. Sepsis- □pneumonia □meningitis □encephalitis □other site of infection.....
    m. WHO stage □ I, □II, □III, □IV and diagnosis qualifying patient for WHO stage.....
6. **LABORATORY RESULTS**
    a. Hb.....
    b. WBC.....
    c. Platelets.....
    d. AST.....
    e. ALT.....
    f. Albumin.....
    g. Urine protein.....
    h. Urine creatinine.....

i. Creatinine.....
j. Urea.....
k. $CD4^{+}$count.....
l. RBS.....

# APPENDIX 3

## THE UNIVERSITY OF ZAMBIA

### BIOMEDICAL RESEARCH ETHICS COMMITTEE

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Lusaka, Zambia

**Assurance No. FWA00000338**
**IRB00001131 of IORG0000774**

27 July, 2010
Our Ref: 026-04-10

Dr Justor Banda
Department of Internal Medicine
Private Bag RW1X
LUSAKA, ZAMBIA

Dear Dr Banda,

**RE:** SUBMITTED RESEARCH PROPOSAL: **"PREVEVALENCE AND RISK FACTORS OF RENAL DYSFUNCTION AMONG HOSPITALISED ADULT PATIENTS AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA"**

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 22 April, 2010 where changes/clarifications were recommended. We would like to acknowledge receipt of the corrected version with clarifications. The proposal is now approved.

**CONDITIONS:**

- This approval is based strictly on your submitted proposal. Should there be need for you to modify or change the study design or methodology, you will need to seek clearance from the Research Ethics Committee.
- If you have need for further clarification please consult this office. Please note that it is mandatory that you submit a detailed progress report of your study to this Committee every six months and a final copy of your report at the end of the study.
- Any serious adverse events must be reported at once to this Committee.
- Please note that when your approval expires you may need to request for renewal. The request should be accompanied by a Progress Report (Progress Report Forms can be obtained from the Secretariat).
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

Mrs Mercy Mbewe
**A/CHAIRPERSON**

**Date of approval**: 27 July, 2010 **Date of expiry**: 26 July, 2011