# COMPARISON OF CLINICAL CHARACTERISTICS AND ONE YEAR OUTCOMES AMONG HIV POSITIVE AND HIV NEGATIVE PATIENTS ON MAINTENANCE HAEMODIALYSIS AT THE KENYATTA NATIONAL HOSPITAL AND NAIROBI HOSPITAL RENAL UNITS

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# ABBREVIATIONS

| | |
|---|---|
| ACR | Albumin: Creatinine ratio |
| AIDS | Acquired Immune Deficiency Syndrome |
| ART | Antiretroviral Therapy |
| AV | Arteriovenous |
| CKD | Chronic Kidney Disease |
| CMV | Cytomegalovirus |
| eGFR | Estimated Glomerular Filtration Rate |
| ESKD | End Stage Kidney Disease |
| GN | Glomerulonephritis |
| HAART | Highly Active Antiretroviral Therapy |
| HIV | Human Immunodeficiency Virus |
| HIVAN | HIV-Associated Nephropathy |
| KAIS | Kenya AIDS Indicator Survey |
| KDIGO | Kidney Disease Improving Global Outcomes |
| KDOQI | Kidney Disease Outcomes Quality Initiative |
| KENPHIA | Kenya Population HIV Impact Assessment Report |
| KNH | Kenyatta National Hospital |
| TDF | Tenofovir Disoproxil Fumarate |
| TMA | Thrombotic Microangiopathy |
| UNAIDS | United Nations Programme on HIV and AIDS |
| VA | Vascular Access |

# ABSTRACT

***Background***

HIV remains a leading cause of mortality in Kenya. Additionally, prevalence of chronic kidney disease (CKD) is on the rise both globally and locally. HIV is a known risk factor for chronic kidney disease, and with greater life expectancy among HIV positive patients, the number of patients with both HIV and chronic kidney disease is predicted to rise. Little is known about the outcomes including mortality rates of HIV positive patients on haemodialysis compared to their HIV negative counterparts in our region. Further, there is a paucity of local published data regarding the prevalence of HIV among patients undergoing maintenance haemodialysis.

***Aims***

This study's aim was to determine the documented prevalence of HIV among patients on haemodialysis at the Kenyatta National Hospital and Nairobi Hospital Renal Units between 1st January 2010 and 31st December 2019. It further compared selected clinical characteristics, one year mortality and loss to follow up rates among HIV positive patients on haemodialysis during this period compared to their HIV negative counterparts.

***Methods***

This was a retrospective cohort study, involving chart review of patients on maintenance haemodialysis at the Kenyatta National Hospital and Nairobi Hospital Renal Units between 1st January 2010 and 31st December 2019. Outcomes (mortality, loss to follow up) at one year since initiation of haemodialysis in the Units were compared between HIV positive patients on haemodialysis versus HIV negative patients matched by age, sex, year of dialysis initiation and dialysis centre. Rates of documented vascular access-related infection were also compared.

***Statistical analysis***

Sociodemographic variables were presented as means (± standard deviation) for continuous variables and proportions for categorical variables. Chi square test was used to compare proportion of haemodialysis patients with the outcomes of interest (mortality, loss to follow up at one year), comparing HIV positive patients with their HIV negative counterparts. Time to mortality or loss to follow up for each group was derived from Kaplan-Meier plots. Statistical significance was defined at a p value of less than 0.05.

***Results***

HIV prevalence among 565 patients on maintenance haemodialysis between 2010 and 2019 at the two centres was 11.9%. Male:female ratio was 1.9:1, with a mean age of 50.0 [±12.7] years and 50.2[±13.3] years among HIV positive and HIV negative patients respectively. All 67 HIV positive and 201 HIV negative patients (1:3 ratio) matched by age, sex, year of dialysis initiation and dialysis centre were included in the final analysis. Median duration on haemodialysis was significantly shorter among HIV positive patients at 15 months [IQR 5-36] compared to 24 months [IQR 12-36] among HIV negative patients. HIV positive patients were less likely to utilize an arteriovenous fistula for dialysis (OR 0.4[95% CI: 0.2-0.9], p=0.019), had a twofold higher risk of vascular access-related infections (OR 2.0[95% CI: 1.1-3.6]. p=0.03), and a 5.6 fold higher risk of tuberculosis compared to HIV negative patients (OR 5.6[95% CI: 1.0-29.9], p=0.039). Mean haemoglobin, serum calcium and albumin levels were also significantly lower among HIV positive patients compared to their HIV negative counterparts (mean haemoglobin 7.7g/dl [±1.1] versus 8.4g/dl [±1.4] respectively, p=0.001; mean serum calcium 1.8mmol/l [±0.3] versus 2.0mmol/l [±0.3] respectively, p<0.001; mean albumin 31.0g/l [±5.1] versus 33.0 [±5.5] respectively, p=0.007). HIV positive patients were also five times more likely to have received a blood transfusion (OR 5.4[95% CI: 2.4-12.5], p<0.001). There was a trend towards higher mortality at one year among HIV positive patients (22.4%) compared to HIV negative patients (13.4%), p=0.053. Time to mortality at one year was significantly shorter among HIV positive patients (log rank p value from the Kaplan Meier estimates=0.038). HIV positive patients were also twice as likely to be lost to follow up (OR 2.9 [95% CI: 1.1-7.9], p=0.034).

***Conclusion***

Prevalence of HIV among patients on maintenance haemodialysis is higher than in the general population at 11.9%. There is a higher risk of vascular access-related infections, tuberculosis, lower haemoglobin, lower albumin and lower serum calcium levels among HIV positive patients on maintenance haemodialysis compared to HIV negative patients. There was a trend towards higher mortality at one year among HIV positive patients, who also had a significantly shorter time to mortality, as well as higher rates of loss to follow up compared to HIV negative patients.

***Recommendations***

Closer follow up of HIV positive patients on maintenance haemodialysis, with optimization in the management of anaemia and hypocalcemia in this subgroup of patients. Further studies are required to determine factors underlying the lower uptake of arteriovenous fistulae, higher rates of loss to follow up, and the significantly shorter time to mortality among HIV positive patients.

# 1. INTRODUCTION

Kenya has the fifth largest number of people living with HIV globally(1), with HIV and its complications remaining one of the leading causes of mortality in the country(2). HIV is also an important cause of kidney disease, especially in Sub Saharan Africa which carries the highest burden of HIV globally. Chronic kidney disease (CKD) is defined by the Kidney Disease Improving Global Outcomes (KDIGO-2012) as abnormal kidney function or structure, present for three or more months, and that have implications for health. Abnormalities include one or more of: decreased estimated glomerular filtration rate (eGFR) <60ml/min per 1.73m$^2$, albumin:creatinine ratio (ACR) ≥ 30mg/g (≥3 mg/mmol), abnormalities detected by histology, imaging or on urine sediment, or a history of having received a kidney transplant(3).

The prevalence of CKD is on the rise globally, driven by an increase in risk factors like diabetes mellitus, hypertension, as well as HIV(4). Kenya has an estimated 4 million Kenyans living with CKD(5). Among these, about 10,000 patients have end stage kidney disease, a condition requiring renal replacement therapy that is offered as either peritoneal dialysis, haemodialysis or kidney transplantation. Haemodialysis is the most popular modality used in Kenya. By 2017 there were an estimated 2,300 patients on haemodialysis countrywide(6), a number that in 2020 now stands at over 4,300 (*source: Kenya Renal Association Registry, personal communication*). Estimates from other Sub Saharan countries show that about 10% of patients on haemodialysis are HIV positive(7–9). These numbers are also likely to rise with the increasing longevity seen among HIV positive patients on adequate antiretroviral therapy.

Studies on their outcomes including mortality, loss to follow up and vascular access outcomes that have been carried out globally have given conflicting results. Whereas studies in more developed countries such as France and South Africa report no difference in outcomes when comparing HIV positive versus negative patients on haemodialysis(10,11), significantly higher one year mortality rates among HIV positive patients have recently been documented in Cameroon(12). The outcomes among Kenyan HIV positive patients on haemodialysis compared to their HIV negative counterparts are unknown.

# 2. LITERATURE REVIEW

## 2.1 EPIDEMIOLOGY

Since the first reports of AIDS among homosexual males in the US in the 1980s, HIV has managed to transform its narrative from a death sentence to a chronic condition with good life expectancy(13). This is as a result of the introduction of effective antiretroviral therapy. In Sub Saharan Africa however, the burden of disease continues to take up significant portions of resource allocation to health.

Globally, by 2018 an estimated 37.9 million people were living with HIV/AIDS according to a 2019 United Nations Programme on HIV and AIDS (UNAIDS) report(14). Since the peak in 1994, new infections have reduced by 40% globally, with a worldwide annual incidence of 1.5 million cases. AIDS-related mortality globally has also declined by more than half, from 1.7 million in 2004 to 770,000 in 2018(14).

In Kenya, the latest Kenya Population HIV Impact Assessment report (KENPHIA 2018) puts the current national prevalence of HIV in adults at 4.9%(1). This shows a steady decline over the years, from 7.1% according to the 2007 Kenya AIDS Indicator Survey [KAIS](15), to 5.6% from the 2012 KAIS report(16). KENPHIA 2018 puts the number of patients living with HIV in Kenya at 1.3million (95% CI: 1.2 to 1.4 million), with 36,000 new infections annually (incidence rate of 0.14% in 2018, compared to 0.5% in the 2012 KAIS report).

Kenya adopted the test and treat strategy in 2016, where all patients found to be HIV positive are started on life saving antiretroviral therapy, as opposed to only those with low CD4 counts as was the case previously. Among the patients who know their HIV status, 96% were on antiretroviral therapy by 2018, and among all the adult patients on antiretroviral treatment, viral suppression rates in Kenya approach 90.6%(1).

HIV/AIDS however continues to be a top cause of both morbidity and mortality in Kenya. According to the Global Burden of Disease report, despite a more than 50% reduction in deaths caused by HIV/AIDS, it still remains the number one cause of mortality in the country, a position it has maintained in both the 2007 and 2017 report(2).

Chronic kidney disease (CKD) is also progressively becoming more common worldwide, driven by rising cases of risk factors including non communicable diseases such as diabetes mellitus and hypertension(4). Infectious diseases such as HIV, hepatitis B and C also have significant contributions, as well as exposure to heavy metals and various environmental toxins. It is also being increasingly recognized that in many patients an underlying risk factor

may not be clearly elicited, giving rise to the entity known as Chronic Kidney Disease of Unknown Origin (CKDu)(17).

According to the Global Burden of Disease (1997 – 2017) report, prevalence of CKD worldwide was 9.1%, representing 697.5 million people living with chronic kidney disease. This is a 29.3% increase in prevalence over the period between 1997 and 2017(4). Worryingly, the burden is concentrated in countries in the lowest socioeconomic status quintiles, with those in Sub Saharan Africa having a higher burden than expected for their level of development. Alarmingly, mortality from CKD over the same period shot up by 41%, with 1.2million deaths related to all stages of CKD in 2017(4).

Availability of renal replacement therapy strategies for management of end stage kidney disease unfortunately continues to lag behind the rise in cases, especially in countries classified as low and middle income. By 2015, there were 2.5 million patients receiving renal replacement therapy, a number expected to double by 2030(18). Unfortunately, renal replacement facilities are in short supply in many countries, with estimated premature mortality of more than 2 million patients due to lack of access to these facilities(18).

In Sub Saharan Africa, a 2014 systematic review that included 90 studies showed a CKD prevalence of 13.9% in the region, higher than the global prevalence of 9.1%(19). The prevalence ranged from 2% in Ivory Coast to as high as 30% in Zimbabwe, pointing to the vast heterogeneity in the region. Like elsewhere, hypertension and diabetes mellitus are important risk factors, but infectious diseases like HIV, with 22 million people living with the condition in Sub Saharan Africa, are also important risk factors for CKD in the region(19).

In South Africa for example, a retrospective study of 294 kidney biopsy results for Black patients with nephrotic syndrome found that HIV-associated nephropathy was the predominant histologic finding among those with secondary causes of glomerular diseases, at 42.8%(20). Further, in a population-based study covering countries in East, South and West Africa (the AWI Gen study published in 2019), the risk factors for kidney damage in over 10,000 participants were diabetes (RR 2.22; 95% CI 1.76-2.78), hypertension (RR 1.97; 95% CI 1.68-2.30, **HIV** (RR 1.65; 95% CI 1.36-1.99) and older age (RR 1.04; 95% CI 1.03-1.05)(21).

In Kenya, the same population-based collaborative study that included sites in Nairobi puts the prevalence of chronic kidney disease(as defined by reduced eGFR <60ml/min/1.73m2, or ACR> 3mg/mmol, or both) at 13.4%(21). In this study, one of the major factors associated

with CKD was HIV infection, which was associated with an almost two fold increased risk of CKD (RR 1.97;95% CI:1.60-2.42) . This points towards the growing burden of HIV as a risk factor for CKD, due to both direct nephrotoxic effects of HIV and its treatment, as well as increased survival of HIV positive patients.

Further, how common is chronic kidney disease among patients with HIV? A study by Wools-Kaloustian et al conducted among 373 antiretroviral treatment-naive outpatients in Western Kenya found a CKD prevalence of 11.5%, as defined by a creatinine clearance of <60ml/min(22). Among ambulant HIV positive patients on highly active antiretroviral therapy at the Kenyatta National Hospital Comprehensive Care Clinic, Kairu et al found a much higher overall prevalence of CKD, at 88%. CKD in this study was defined as either eGFR<60ml/min, or urine albumin:creatinine ratio >30mg/g, or both(23). It is important to note that this study included patients with other risk factors for CKD (eg. co-morbid hypertension or diabetes), who were excluded in the study by Wools-Kaloustian et al.

Among patients with chronic kidney disease who develop end stage kidney disease, various life-sustaining therapies are available including peritoneal dialysis, haemodialysis and kidney transplantation. Haemodialysis is the most commonly used modality worldwide, with more than 2.7 million patients on haemodialysis globally in 2010, a number expected to more than double by 2030(18). Treatment of end stage kidney disease is cost-intensive, using up to 2-3% of annual healthcare budgets in developed countries, despite the fact that those receiving these treatments make up less than 0.03% of the total population(24).

In Kenya, the Ministry of Health estimates that about 4 million Kenyans have chronic kidney disease. Among these, about 10,000 are in end stage kidney disease, out of whom only a paltry 10% are able to access dialysis services(5). According to the Kenya Renal Association, the number of patients on maintenance haemodialysis in the country has increased eight times from about 300 patients in 2006, to approximately 2,400 patients by 2018(6,25).

The number of dialysis units has also gone up in the country, thanks to the Government's Managed Equipment Services scheme announced in 2013 that saw a rapid expansion of dialysis units across all the 47 counties. From the initial dialysis unit set up at the Kenyatta National Hospital in 1984, the country currently has 51 public hospital-based dialysis units across the entire country, 89 units in private hospitals, and 11 units in faith-based healthcare facilities(26). Another major reform in the country was the introduction of a benefit package covering dialysis sessions in 2015 by the country's National Health Insurance Fund(27).

Unlike the situation previously in South Africa where access to haemodialysis was limited in patients who had HIV/AIDS due to dialysis rationing(28), Kenyans living with HIV/AIDS and have end stage kidney disease are able to fully access haemodialysis services. With HIV having emerged as a risk factor for end stage kidney disease, the prevalence of HIV among patients on haemodialysis has been documented in various countries. In Cameroon for example, the seroprevalence of HIV among chronic haemodialysis patients was reported at between 10 to 13.5%(7,8). According to The South African Renal Registry 2016 Report, 10.6% of all patients on the various forms of renal replacement therapy are HIV positive(9), and a study among those specifically on chronic haemodialysis reported a HIV seroprevalence rate of 9.75%(11).

With a significant proportion of patients on haemodialysis being HIV positive in Sub Saharan Africa, several studies globally have looked at outcomes among this subset of patients compared to their HIV negative counterparts. The results of these studies in the various regions have often been conflicting, even in the post-ART era. Some studies in France and South Africa have reported no difference in outcomes between HIV positive and negative patients(10,11), while in Cameroon the one year survival rate among HIV positive patients was significantly lower(12). The situation in Kenya is unknown.

## 2.2 HIV AND THE KIDNEY- PATHOPHYSIOLOGY

The mechanisms underlying renal disease among patients with HIV are both varied and complex. They can however be summarized into one of four major pathways: direct effects of HIV infection, effects of systemic immune responses, effects of opportunistic superinfections resulting from immunosuppression, and drug-related effects on the kidney.

- **HIV-associated nephropathy (HIVAN)**

Probably the most commonly known renal complication of HIV infection, HIVAN was first described by researchers in the US in 1984(29). Years later, it is now thought that HIVAN is a result of renal tubular epithelial cell infection with HIV. Several viral proteins including Vpr and Nef have been implicated in the pathophysiology. HIV has been shown to localize within podocytes, with resultant podocytopathy.

- **Immune-mediated kidney disease in HIV**

In patients with HIV, immune-mediated renal disease may involve either deposition of circulating immune complexes within glomerular tufts, or in situ deposition of antibodies directed against glomerular antigens. The final common pathway leads to activation of complement, with resultant immune mediated kidney disease including lupus-like glomerulonephritis, HIV-associated IgA nephropathy and membranoproliferative glomerulonephritis(30).

- **Drug-induced tubular and interstitial renal injury**

Nephrotoxic effects of antiretroviral agents have long been documented, with Tenofovir diosproxil fumarate (TDF) commonly implicated. TDF accumulates within proximal renal tubular cells via uptake by organic anion transporters 1 and 2. Mechanisms of TDF-induced nephrotoxicity include proximal renal tubular damage as a result of mitochondrial toxicity, that may lead to acute kidney injury and Fanconi's syndrome, while distal tubular injury may present as nephrogenic diabetes insipidus.

- **Thrombotic microangiopathy (TMA)**

Cytopathic effects of HIV on endothelial cells may lead to endothelial cell injury, with subsequent activation of platelets leading to thrombosis, a consumptive coagulopathy and multiorgan dysfunction.

**Table 1. Spectrum of kidney diseases associated with HIV infection**(30,31)

| | |
|---|---|
| ***1. Acute kidney injury***<br>• Prerenal azotemia<br>• Acute tubular necrosis<br>• Rhabdomyolysis | ***6. Infiltrative lesions of the kidney***<br>• Kaposi's sarcoma<br>• Lymphoma<br><br>***7. Arterionephrosclerosis*** |
| ***2. HIV immune-complex kidney disease***<br>• Lupus-like GN<br>• IgA nephropathy<br>• Postinfectious GN<br>• Mesangial proliferative GN<br>• Membranoproliferative GN<br>• Cryoglobulinemic GN | ***8. Opportunistic infections affecting kidney parenchyma***<br>• Viral – CMV, Parvovirus, Herpes simplex<br>• Fungal- Cryptococcus, Candida<br>• Mycobacterial<br>• Mycoplasma<br>• Microsporidia<br>• Bacterial pyelonephritis |
| ***3. HIV-associated nephropathy*** | ***9. Thrombotic microangiopathies*** |
| ***4. Antiretroviral therapy-associated***<br>• TDF-induced nephrotoxicity<br>• Crystal nephropathy<br>• Tubulointerstitial nephritis<br><br>***5. Tubulointerstitial nephritis***<br>• Immune reconstitution syndrome | ***10. Urinary tract obstruction***<br>• Intrinsic ureteral obstruction- blood clots, fungus balls<br>• Extrinsic ureteral obstruction- retroperitoneal fibrosis, lymphadenopathy<br>• Bladder outlet obstruction |

## 2.3 OUTCOMES AMONG HIV POSITIVE PATIENTS ON HAEMODIALYSIS

Survival of AIDS patients on maintenance haemodialysis in the pre-ART era was dismal. In a case series published in 1987 by Rao et al in the US, median survival on dialysis of 31 AIDS patients with end stage renal disease was a paltry 1.4 months. Out of the 31 patients, only 2 were alive after 5 months(32), underlying the poor prognosis of these patients.

Despite significant improved survival among HIV positive patients with the advent of effective combined antiretroviral therapy, it has been variously postulated that these improvements may not be seen in HIV positive patients on haemodialysis. One reason may be due to inadequate understanding of antiretroviral drug pharmacokinetics in patients with ESKD on dialysis, with the possibility that these patients may have subtherapeutic ART drug levels(33).

Further, these patients may be at increased risk of fatal opportunistic infections as a result of the double immunosuppression from both the HIV infection as well as the uremic milieu. In addition, dialyzer membranes themselves may possibly worsen the immunosuppressive effects of HIV infection via activation of cytokines that are pro-inflammatory such as Tumor Necrosis Factor, Interleukin 1 and Interleukin 6, which have been shown to increase replication of HIV in vitro(34). This effect on proinflammatory cytokines has been documented with use of cuprophan as well as polysulfone dialyzer membranes(35).

Depending on geographical location and due to differences in healthcare access and sociodemographic parameters, there have been stark differences in reported outcomes among HIV positive patients with end stage kidney disease undergoing haemodialysis. Several studies have shown no difference in mortality when comparing HIV positive ESKD patients to HIV negative patients, while some show poorer prognosis and higher risk of death, even with the advent of HAART. This section outlines both sets of outcomes, with a look at the systemic differences in sociodemographics and healthcare access in the various regions.

In one of the first prospective cohort studies in the post-HAART era carried out in France between 2002 and 2004, global prevalence of HIV among over 27,000 haemodialysis patients was 0.59% (the French Dialysis in HIV/AIDS cohort ). Their one and two year survival rates over the period between 2002 and 2004 was compared with 584 HIV negative age-, sex- and ethnicity-matched patients in the DOPPS II (French Dialysis Outcomes and Practice Patterns Study II) database. Survival rates were 93.8 % ( ± 1.9) at 1 year, and 89.4% ( ± 2.4%) at 2 years, and were not statistically significantly different between the two cohorts(10).

Risk factors significantly associated with mortality in this cohort included low CD4 count, high viral load, history of opportunistic infection, and lack of treatment with HAART. The documented causes of death among the HIV positive patients were infections (31%), sudden death (18%), malignancy (13%) and unknown (22%). It is important to note some salient sociodemographic and clinical features of the patients captured in this French cohort of patients: only 65% were Black, 86% were on ART, and these patients were less likely to have Hepatitis C virus coinfection or be intravenous drug users(10).

In the US, data from the large United States Renal Data System looked at the trends in 1 year survival rates of 6,166 HIV infected patients on haemodialysis over the period 1990 to 1999. Survival rates of these patients (89% of whom were Black) markedly improved from 56% to 74% over this period(33), partly attributed to improved ART coverage and prompt treatment of opportunistic infections. This study however did not have a comparator group of HIV

negative patients on haemodialysis, though the authors go on to conclude that the survival rates of their patients were lower compared to HIV negative patients in other cohorts(33).

Closer home in Sub Saharan Africa, survival data in these patients is again conflicting. In South Africa, a country with a reasonably vibrant economy and better socioeconomic status than many African countries, Fabian et al compared vascular and infection-related morbidity and mortality of black HIV positive patients on chronic haemodialysis to age-, sex- and ethnicity matched HIV negative counterparts(11). It is interesting to note that prior to 2008, HIV positive patients were excluded from dialysis in public hospitals in South Africa on the basis of their HIV status alone, a policy that was revised in 2008. Their study was restricted to patients with medical insurance, who have unlimited access to haemodialysis.

In this study, prevalence of HIV among 2,010 patients on chronic haemodialysis during the defined period was 9.75%. Survival of both HIV positive (n=48) and HIV negative patients (n=96) at 1 year was excellent and not statistically different, at 100% for HIV positive and 99% for HIV negative patients. There were however statistically significant differences in morbidity outcomes, with HIV positive patients recording higher rates of vascular access-related infections and tuberculosis. HIV positive patients also had lower levels of haemoglobin and albumin(11).

The excellent survival outcomes in this study may however not be generalizable to the majority of low and middle income black Africans who may not have access to healthcare insurance and unlimited access to haemodialysis services.

In West Africa, the survival narrative among HIV positive patients with end stage kidney disease is rather different. Halle, Ashuntantang and colleagues in Cameroon compared one year survival rates among 57 HIV positive patients on chronic haemodialysis to HIV negative counterparts between 2007 and 2015. The two groups were matched by age, sex, dialysis unit, comorbid conditions and year of initiation of dialysis. One year survival rates were significantly lower among the HIV positive patients compared to their HIV negative counterparts (61.4% vs 78.9%, p = 0.042)(12). The main causes of death in the HIV positive patients were sepsis and tuberculosis, with lack of ART treatment independently associated with mortality.

This study showed that HIV positive patients on haemodialysis in this African setting were at a two fold higher risk of mortality compared to their HIV negative counterparts (HR 2.05; 95% CI 1.03-4.08). This is despite free access to combined antiretroviral therapy and

haemodialysis access. It is important to note though that despite access to HAART the levels of severe immunosuppression were quite high (46% had CD4 cell count <200 cells/$mm^3$; median CD4 cell count was 212 cells/$mm^3$), predisposing these patients to infectious complications.

Outcomes among HIV positive patients on maintenance haemodialysis in Kenya have not been documented.

## 2.4 VASCULAR ACCESS-RELATED INFECTIOUS COMPLICATIONS

Haemodialysis requires use of a vascular access, which may be in the form of an arteriovenous graft, arteriovenous fistula, or central venous catheter (tunnelled or non-tunelled). Use of an arteriovenous fistula is the preferred modality, although this may not always be feasible. Complications associated with these various forms of vascular access include infection, access failure, thrombosis and stenosis.

In a meta-analysis involving over two hundred studies comparing complication rates between the different types of vascular access, rates of access failure, infection and mortality were lowest with AV fistulae, followed by AV grafts, and highest with central venous catheters(36). As such, the 2019 KDOQI (Kidney Disease Outcomes Quality Initiative)guidelines on vascular access recommend use of AV fistulae or grafts over long-term central venous catheters (37). Similarly, in patients with HIV, AV fistulae may be associated with better patency rates and lower infection rates compared to AV grafts(38).

Vascular access-related infection is associated with significant morbidity and mortality among patients with end stage kidney disease. With the concomitant immunosuppression among patients with HIV, the risk of vascular access-related infection has been postulated to be higher. Several studies have however found conflicting results. Mokrzycki et al found no difference in rates of tunnelled catheter-related infections between 40 HIV positive patients and 41 HIV-negative controls(39).

Similarly, in a prospective cohort study in the US involving 33 HIV positive patients and 55 age-, sex- and access date matched controls, there was no difference in rates of catheter-related bacteremia over a 6.5 year period (52% and 49% respectively, p=0.83)(40). However in the same study, HIV positive patients were more likely to have infections with polymicrobial organisms, and were also more likely to be admitted for management of catheter-related bacteremia compared to their HIV negative counterparts.

In South Africa, Nuria et al compared prevalence of catheter-related infection among HIV positive patients on maintenance haemodialysis versus HIV negative patients. They found no statistically significant differences in infection rates among the two groups, especially if CD4 count was more than 200cells/µl, and viral load was undetectable among those who were HIV positive. However, HIV patients took a longer time to recover from infection (54% HIV negative versus 10% HIV positive patients had adequate control of their infection within a week of treatment).(41)

There have also been several studies reporting increased risk of vascular access-related infections among HIV positive patients. In a retrospective cohort study comparing vascular access complications among HIV positive versus HIV negative patients on haemodialysis, Mitchell et al found lower rates of infection-free graft survival at 1 year among HIV positive patient with AV grafts compared to HIV negative patients using the same type of access (17% versus 62%). Rates of other complications including graft thrombosis were also higher in HIV positive patients using AV grafts (HR for graft thrombosis 3.22, 95% CI, 1.66-10.32, P = 0.002). AV fistula use was associated with similar cumulative vascular access survival in both groups(42).

An older study by Curi et al showed higher prosthetic AV graft infection rates among HIV positive patients on chronic haemodialysis (30% versus 7% for HIV negative patients, p=0.04). There were however no differences in vascular access-related infections among HIV positive versus negative patients using AV fistulae. Interestingly, low CD4 counts less than 200cells/µl were not associated with development of infection(43).

In general then, several studies highlighted above seem to suggest that HIV infection per se may not necessarily result in a higher risk of vascular access-related infection. It may however be associated with increased risk of infection with polymicrobial organisms and longer times to recovery once treatment is began. Type of vascular access in both HIV positive and negative patients is also an important consideration, with the risk of vascular access-related infections highest in those using tunnelled central venous catheters. This may have an important implication in countries such as Kenya, where a recent study by Kabinga et al showed that majority of long term haemodialysis patients are still using tunnelled central venous catheters (40% versus 14.5% using AV fistulae)(44).

## 2.5 ANAEMIA AND HYPOALBUMINEMIA

Anaemia, defined as a haemoglobin level lower than 13g/dl in males and lower than 12g/dl in females, occurs in upto 53% of patients with end stage kidney disease(45). Among South African patients on maintenance haemodialysis, Fabian *et al* compared haemoglobin levels among HIV positive versus HIV negative patients. Among 48 HIV positive patients and 96 HIV negative patients, mean haemoglobin level in was statistically significantly lower among those with HIV, at 9.5g/dl and 10.6g/dl respectively ($p<0.01$)(11). Anaemia was however not associated with mortality in this study. Halle *et al* also found similar results in Cameroon, with mean haemoglobin levels lower among HIV positive patients on haemodialysis (7.12±1.70g/dl) compared to those who were HIV negative (7.86±1.98 g/dl respectively, $p=0.045$)(12).

HIV could exacerbate anaemia severity in chronic kidney disease via direct negative effect on erythropoiesis, opportunistic infections or effect of antiretroviral medications such as zidovudine(46). Anaemia negatively affects quality of life, and is also independently associated with cardiovascular mortality, cardiac failure and left ventricular hypertrophy among patients with chronic kidney disease(47,48).

Similarly, hypoalbuminemia (serum albumin levels less than 40g/l) has been shown to be a powerful predictor of mortality among patients on maintenance haemodialysis(49). Serum albumin has been used as an indicator of both underlying inflammation and nutritional status among patients with chronic kidney disease. Hypoalbuminemia both at the initiation of haemodialysis as well as during the course of maintenance haemodialysis have both been associated with elevated risk of death in these patients(49).

Among HIV positive patients with end stage kidney disease on peritoneal dialysis, Ndlovu *et al* in South Africa reported higher rates of hypoalbuminemia among HIV positive patients compared to their HIV negative counterparts (mean difference 4.24g/L 95% [CI 2.02-6.46], $p<0.001$)(50). In this study, baseline serum albumin <25g/l was independently associated with mortality.

# 3. STUDY JUSTIFICATION

Since the advent of effective antiretroviral therapy, survival among HIV positive patients has substantially improved. Kenya has a double burden of large numbers of patients with HIV, as well as growing numbers of patients with chronic kidney disease. A significant proportion of these patients with chronic kidney disease require renal replacement therapy services such as haemodialysis. To the best of our knowledge, outcomes among patients on maintenance haemodialysis in Kenya, particularly comparing HIV positive versus HIV negative patients have not been documented.

Whereas data from more developed countries studies shows no difference in outcomes such as mortality in these patients, the situation in developing countries which have a larger burden of HIV and less developed infrastructure may not be the same. Cameroon for example recently reported higher mortality rates among HIV positive patients compared to HIV negative patients on haemodialysis.

The situation in Kenya, which has the world's fifth largest number of patients living with HIV remains unknown. From our literature search, the current prevalence of HIV among haemodialysis patients in the country is also undocumented, which would be important so as to be able to quantify the total burden of HIV-associated disease.

## 3.1 PROBLEM STATEMENT

There is a high burden of both HIV and chronic kidney disease in Kenya. Outcomes including mortality of HIV positive patients on haemodialysis as compared to their HIV negative counterparts remains unknown.

# 4. RESEARCH QUESTION

Is there a difference in one year mortality rate, loss to follow up, documented vascular access-related infections, anaemia and hypoalbuminemia among HIV positive patients on haemodialysis at the Kenyatta National Hospital and Nairobi Hospital Renal Units compared to HIV negative patients on haemodialysis?

# 5. STUDY OBJECTIVES

## 5.1 BROAD OBJECTIVE

To determine the prevalence of HIV among haemodialysis patients over the last ten years, and compare the mortality rate at one year, loss to follow up and documented clinical parameters among HIV positive patients on haemodialysis compared to their HIV negative counterparts.

## 5.2 SPECIFIC OBJECTIVES

i. To determine the documented prevalence of HIV among patients dialyzing at the Kenyatta National Hospital and Nairobi Hospital over the period between 2010 and 2019.

ii. To document the average duration on maintenance haemodialysis prior to mortality or loss to follow up, comparing HIV positive and HIV negative patients.

iii. To compare documented clinical parameters of HIV positive versus HIV negative patients on haemodialysis (types of vascular access, prevalence of vascular access-related infections, haemoglobin levels, blood transfusions received, albumin levels and major infections eg. tuberculosis, sepsis) over the one year period since initiation of haemodialysis.

iv. To compare outcomes (mortality, loss to follow up) at one year since initiation of dialysis, comparing HIV positive versus HIV negative patients matched by age, sex, year of haemodialysis initiation and dialysis centre.

# 6. METHODOLOGY

## 6.1 STUDY DESIGN

This was a retrospective cohort study.

## 6.2 STUDY SITES

The study was carried out at the Kenyatta National Hospital and Nairobi Hospital Renal Units. Kenyatta National Hospital (KNH) is the largest teaching and referral hospital in East and Central Africa, with a bed capacity of 1800. The Renal Unit has been in operation since 1984, and offers haemodialysis, peritoneal dialysis and kidney transplantation services.

It has 5 specialist Physician/Nephrologists, and is also the training site for the East African Kidney Institute's Clinical Nephrology Fellowship for subspecialty training in the East African region. It currently offers haemodialysis services to about 180 patients with end stage kidney disease. About 20 haemodialysis machines currently serve three shifts of patients per day, with each dialysis session lasting four hours on average.

The Nairobi Hospital Renal Unit is a private unit that offers haemodialysis services to about 100 patients with end stage kidney disease. It has 17 haemodialysis machines serving two shifts of outpatients per day, one shift coming in the morning and another in the afternoon. Each dialysis session lasts four hours on average.

## 6.3 STUDY POPULATION

The study population was patients on maintenance haemodialysis at the Kenyatta National Hospital and Nairobi Hospital Renal Units in the period between 2010 and 2019.

### 6.3.1 INCLUSION CRITERIA

1. Patients with end stage kidney disease on maintenance haemodialysis for at least three months (this confirms end stage kidney disease rather than an acute kidney injury that required haemodialysis for less than three months) over the period between 2010 and 2019.
2. Have documented HIV results.
3. Comparator group were patients with end stage kidney disease on maintenance haemodialysis between 2010 and 2019, documented to be HIV negative, and matched to the HIV positive patients by age, sex, year of haemodialysis initiation and dialysis centre.
4. Age greater than 18 years.

### 6.3.2 EXCLUSION CRITERIA

1. Patients on haemodialysis for acute kidney injury

2. Pregnant patients

## 6.4 SAMPLE SIZE

This study compared 1-year mortality between HIV positive and HIV negative patients. Sample size was calculated as follows:

$$n_1 = \frac{\left(Z_{1-\propto/2} + Z_{1-\beta}\right)^2 \bar{p}\bar{q}(r+1)}{r(p_1 - p_2)^2}$$

$$n_2 = rn_1$$

Where:

$n_1$ – number of cases

$n_2$ – number of controls

$Z_{1-\propto/2}$ – standard normal at 95% confidence interval = 1.96

$Z_{1-\beta}$ – standard normal at 80% power = 0.84

$p_1$ – Outcome of interest in the comparison group - mortality in HIV negative CKD patients = 21.1% (Halle et al, 2018).

$p_2$ - Outcome of interest in the study group – mortality in the HIV positive CKD patients= 38.6% (Halle et al, 2018).

*r* – Ratio of cases to controls

$\bar{p} = \frac{p_1 + rp_2}{r+1}$ and $\bar{q} = 1 - \bar{p}$

When substituted in the formula

If,

r =2: Cases (HIV positive) = 76 and Controls (HIV negative) = 152

r =3: Cases (HIV positive) = **65** and Controls (HIV negative) = **195** (**Total = 260 patients**)

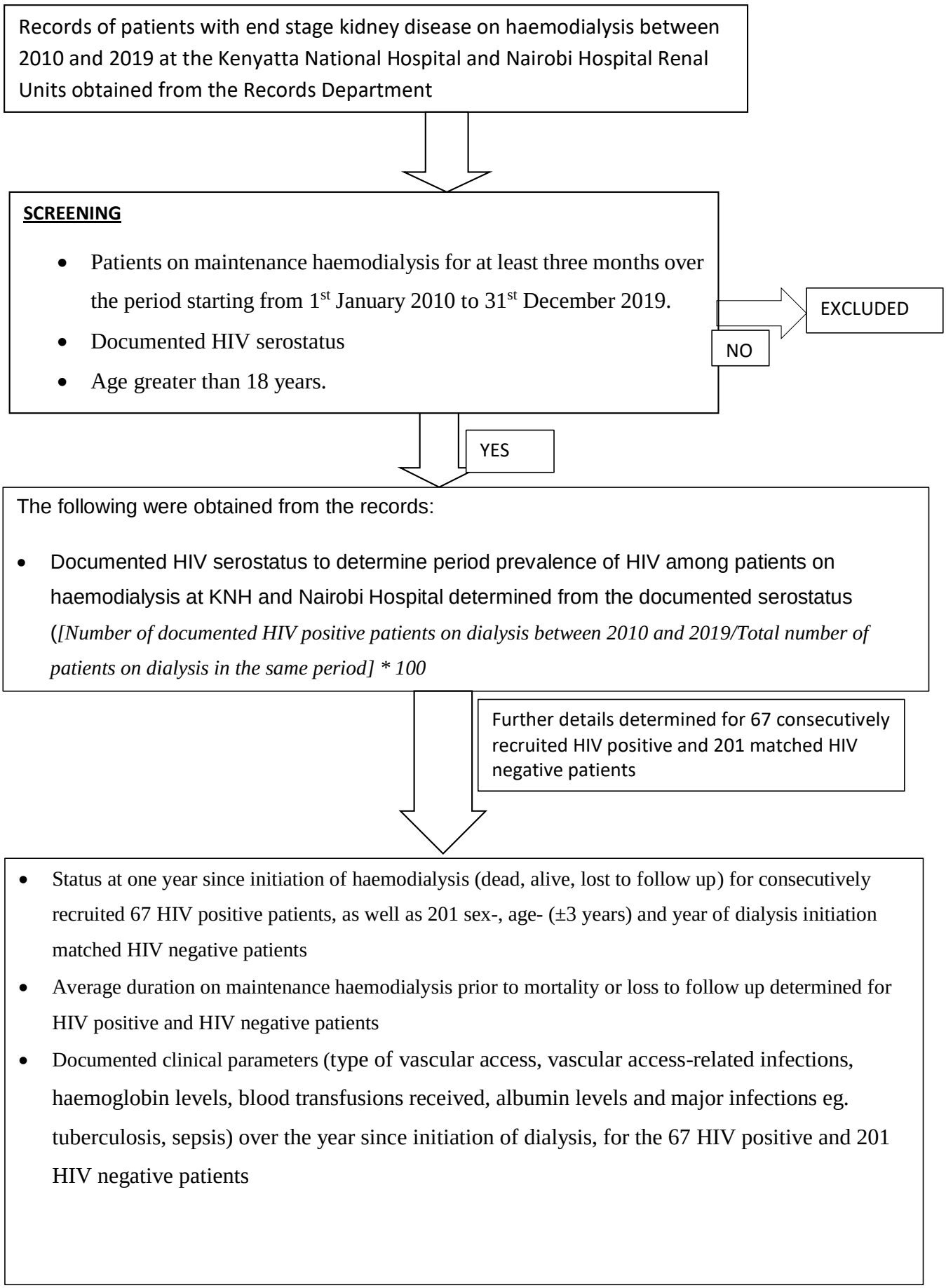
r =4: Cases (HIV positive) = 60 and Controls (HIV negative) = 238

A total of **268** patients were finally sampled for the study, with **67** HIV positive matched with **201** HIV negative CKD patients (**1:3** ratio), recruited over the ten year period between 2010 and 2019. This met the minimum sample size requirement of **260** patients (65 HIV positive and 195 HIV negative patients).

## 6.5 SAMPLING METHOD

Patients meeting the inclusion criteria in each arm were consecutively recruited into the study.

## 6.6 SCREENING AND RECRUITMENT FLOW CHART



## 6.7 DATA COLLECTION

- **Screening**

The haemodialysis registers in the Renal Units at Kenyatta National Hospital and Nairobi Hospital were used to obtain a list of all patients who were on haemodialysis in the units between 1st January 2010 and 31st December 2019. The records of these patients were then obtained from the Kenyatta National Hospital and Nairobi Hospital Renal Units records departments. Records of patients who met the study inclusion criteria were then included in subsequent data collection.

- **Data collection to meet the HIV prevalence objective**

Documented HIV status was captured for all patients dialyzing in the two units over the period between 1st January 2010 and 31st December 2019. This was used to determine the period prevalence of HIV among dialysis patients.

- **Data collection to meet the objective of comparing outcomes and clinical parameters of HIV positive and HIV negative dialysis patients**

Patient records for the first 67 consecutively recruited documented HIV positive dialysis patients were retrieved and the following data extracted: sociodemographic characteristics, clinical presentation, laboratory parameters captured, type of vascular access used and any documented vascular access-related complications. Status at one year since date of initiation of dialysis was extracted from the patient records and documented as either dead, lost to follow up, or still alive on dialysis. Duration on maintenance haemodialysis prior to either mortality or loss to follow up was also captured.

Similar data was extracted from records of 201 age-, sex-, year of dialysis initiation and dialysis centre- matched patients (in a 1: 3 ratio ie 1 HIV positive patient matched to 3 HIV negative patients).

# 7.DEFINITION OF STUDY VARIABLES

**a. <u>Dependent variable</u>**

**Outcomes:** Patient status one year from the date of initiation of haemodialysis. This was defined as either ***Dead*** (documented loss of life from any cause within the first year of haemodialysis initiation), ***Alive*** (still on active haemodialysis at one year since date of initiation of haemodialysis), ***Lost to follow up*** (status unknown/ not documented yet not on haemodialysis at one year since initiation of haemodialysis) or ***Transferred out*** (documented to have opted to seek haemodialysis services at another facility.

**b. <u>Independent variables</u>**

- **HIV positive:** Patient with end stage kidney disease on maintenance haemodialysis for at least three months and documented to be HIV positive.

- **HIV negative:**Patient with end stage kidney disease on maintenance haemodialysis for at least three months and documented to be HIV negative.

- **Vascular access-related infection**(37)- Was defined as documented:
  i. **Exit site infection**: Redness, induration, tenderness ≤2cm from catheter exit site, or drainage of pus from the exit site.
  ii. **Tunnel infection**: Tenderness, redness and/or induration that extends along the length of the subcutaneous tunnel, or
  iii. **Catheter related blood stream infection**: Clinical manifestations (fever, chills and/or hypotension) and at least one positive blood culture from the dialysis circuit or peripheral vein and no other apparent source.

- **Anaemia:** Haemoglobin level <12g/dl in males and <11g/dl in females.
- **Hypoalbuminemia:** Serum albumin level <35g/L.
- **Major infections**: Included documented tuberculosis diagnosed on the basis of chest x-ray, sputum microscopy or Gene-expert testing, documented sepsis, or documented pneumonia.

# 8. DATA MANAGEMENT

## 8.1 Data acquisition

The instrument used for data acquisition was the study questionnaire (**Appendix I**). At the end of data collection, questionnaires were coded, entered and managed in Microsoft Access database.

## 8.2 Data privacy

Standards to protect personal information were ensured. No subject identifiers were included in the data collection instruments, with only a unique serial number entered in the study questionnaire and sample labels.

## 8.3 Data storage

The Principal Investigator verified the filled data forms for completeness. The data forms were then kept in a secure lockable cabinet only accessible by the PI and the statistician. The data was entered electronically using the Statistical Package for Social Sciences (SPSS) version 17.0, (SPSS Inc.,Chicago, IL,USA). Upon data entry completion, cleaning and verification of correctness of entered data was carried out on the hard copy forms that were then safely stored in a lockable cabinet. The electronic files were backed up in three compact discs and stored offsite.

## 8.4 Statistical analysis

- **Descriptive statistics**

  Quantitative variables eg age were summarized using means and standard deviations, or medians and interquartile ranges for skewed variables. Histograms were used for graphical summaries.

  Qualitative variables eg. marital status, level of education were summarized using proportions and graphically using barplots.

- **Inferential statistics**

  Level of significance for all tests (two-sided) was set at 0.05, with 95% confidence intervals reported.

  Prevalence of HIV was calculated as number of documented HIV positive patients on dialysis between 2010 and 2019/Total number of patients on dialysis in the same period] * 100, expressed as a percentage.

Mean duration on maintenance haemodialysis was calculated as total number of months on haemodialysis in each group of patients/number of patients on maintenance haemodialysis in each group. T test was used to determine if the mean duration on maintenance haemodialysis in the HIV positive patients differed from that in the HIV negative patients.

Chi square test of association, or Fischer's exact test for small numbers, was used to compare proportion of patients with major infections (tuberculosis, sepsis) and vascular access related infections among those who were HIV positive versus those who were HIV negative. For continuous variables such as haemoglobin, albumin and calcium levels, T test was used to compare means between the two groups.

Chi square test was also used to determine whether the proportion of patients with the outcomes of interest (mortality, loss to follow up) among patients with HIV on dialysis differed from that among HIV negative patients on dialysis.

Time to mortality or loss to follow up was derived from Kaplan Meier curves.

# 9. PROTECTION OF HUMAN PARTICIPANTS

This Human Subjects Research met the definition of 'Clinical Research'.

**a. Human subjects involvement and characteristics of study population**

This was a retrospective cohort study and data was collected from chart reviews. Chart records were retrieved for patients who met the following eligibility criteria: Age ≥18 years, end stage kidney disease on maintenance haemodialysis for at least three months over the period between 2010 and 2019, and documented to be HIV positive. Comparator group were patients with end stage kidney disease on maintenance haemodialysis between 2010 and 2019, documented to be HIV negative, and matched to the HIV positive patients by age, sex, year of haemodialysis initiation and dialysis centre.

**b. Research site**

The study was conducted at the Kenyatta National Hospital and Nairobi Hospital Renal Units Records Departments. The study was undertaken after ethical approval had been obtained from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee

(KNH/UoN ERC). Authorization to conduct the study was also sought from the respective hospital administration units.

**c. Sources of material**

Research data for this study was obtained using a pre-designed proforma (Appendix 1). All the data was obtained only for the purpose of research. The pre-designed study proforma collected data on sociodemographic variables, medical and drug history, outcomes at one year since initiation of dialysis, and vascular access-related complications.

**d. Linkages to subjects**

Confidentiality of all participant data was maintained at all times. All data was coded and stored in a locked cabinet, with only the principal investigator and data manager able to access these files. Data entered into the digital database was stripped of all patient identifiers, and used only participants' study code number. This data was password-encrypted.

**e. Potential risks**

There were no foreseeable risks involved in this retrospective cohort study that mainly entailed chart reviews.

**f. Potential benefits and importance of the knowledge gained**

The study has enhanced knowledge on whether specific outcomes are either better, worse or not different among patients with co-morbid chronic kidney disease and HIV compared to those without HIV. The study also served as an audit of outcomes among maintenance haemodialysis patients at the KNH and Nairobi Hospital Renal Units over the past 10 years.

# 10. STUDY PLAN

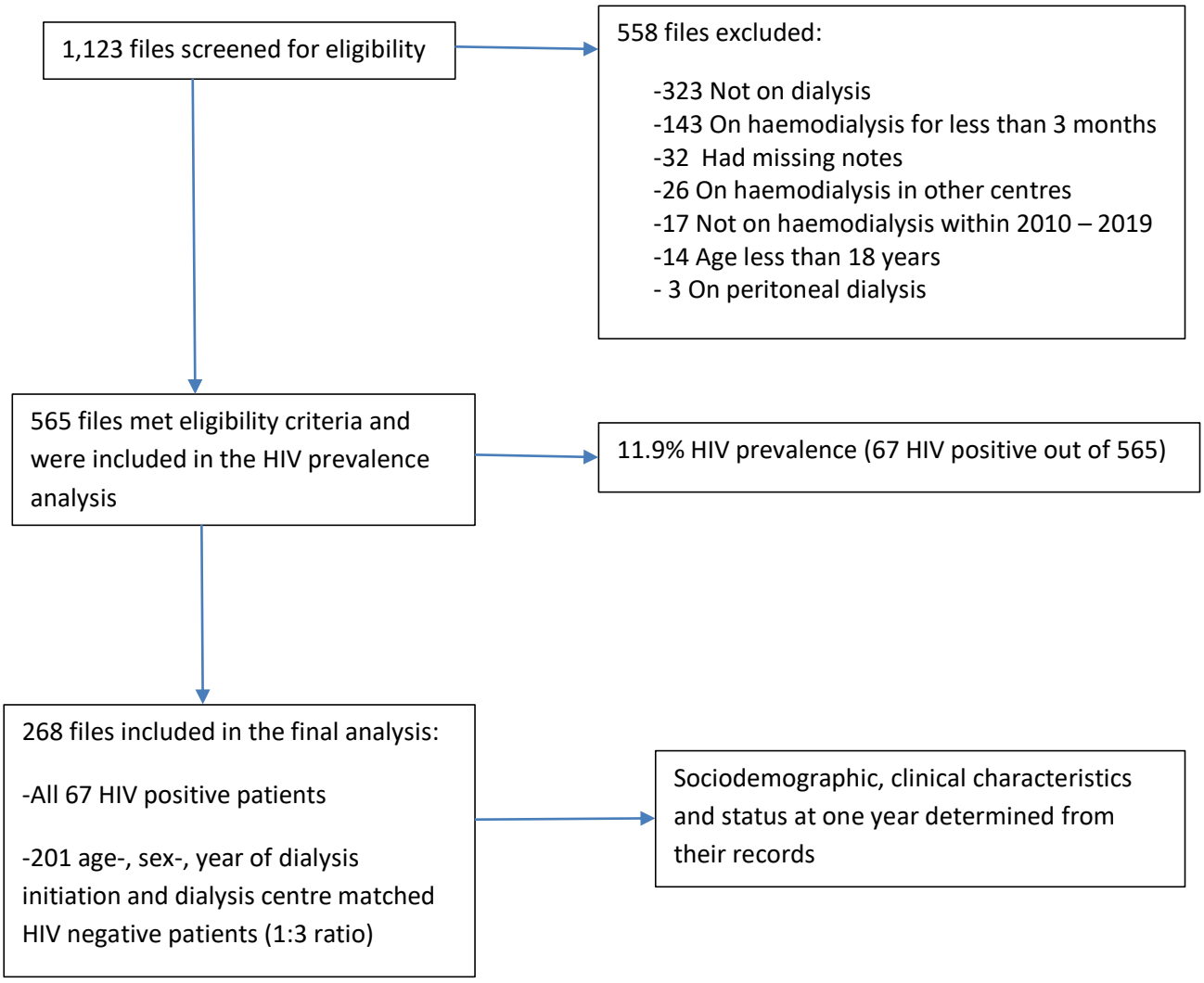
**Table 2. Study plan**

| | |
|---|---|
| Proposal write up | Jan-March 2021 |
| Proposal presentation | March 2021 |
| Ethics approval | August 2021 |
| Data collection | Aug- October 2021 |
| Data analysis | October-November 2021 |
| Results presentation | December 2021 |

# 11. RESULTS

1,123 files were screened for eligibility, with 558 excluded for various reasons as outlined in the flow chart below. 565 files met inclusion criteria, and were used to determine HIV prevalence. All 67 HIV positive patients and 201 age-, sex-, year of dialysis initiation and dialysis centre matched HIV negative patients were then included in the final analysis. The study flow chart is shown below.

**Figure 2. Study Flow Chart**



## 11.1 SOCIODEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS

**Table 3. Sociodemographic Characteristics of HIV Positive and HIV Negative Patients on Maintenance Haemodialysis**

| Variable | HIV positive (n=67) | HIV negative (n=201) | P value |
|---|---|---|---|
| **Gender** | | | |
| Male | 44 (65.7) | 132 (65.7) | 1.000 |
| Female | 23 (34.3) | 69 (34.3) | |
| **Mean age in years (SD)** | 50.0 (12.7) | 50.2 (13.3) | 0.911 |
| Min-Max | 19-79 | 18-79 | |
| **Marital status** | | | |
| Single | 17 (25.4) | 48 (23.9) | 0.974 |
| Married | 49 (73.1) | 146 (72.6) | |
| Separated | 0 | 2 (1.0) | |
| Widowed | 1 (1.5) | 5 (2.5) | |
| **Level of education** | | | |
| None | 0 | 1 (0.5) | 0.258 |
| Primary | 23 (34.3) | 53 (26.4) | |
| Secondary | 26 (38.8) | 69 (34.3) | |
| College/University | 18 (26.9) | 78 (38.8) | |
| **Occupation** | | | |
| Student | 2 (3.0) | 8 (4.0) | 0.893 |
| Unemployed | 8 (11.9) | 31 (15.4) | |
| Employed | 25 (37.3) | 80 (39.8) | |
| Self employed | 23 (34.3) | 57 (28.4) | |
| Retired | 9 (13.4) | 12 (12.4) | |
| **Health insurance** | | | |
| NHIF | 52 (77.6) | 162 (80.6) | 0.862 |
| Others | 8 (11.9) | 20 (10.0) | |
| None | 7(10.4) | 19(9.5) | |
| **Hospital** | | | |
| KNH | 45 (67.2) | 116 (57.7) | 0.171 |
| Nairobi | 22 (32.8) | 85 (42.3) | |

Study participants were matched by age, sex, year of initiation on dialysis and dialysis centre. Mean age of our study participants was 50.0 years (±12.7) and 50.2 years (±13.3) for HIV positive and HIV negative patients respectively (p=1.00). There was a male preponderance, with a male:female ratio of 1.9:1. As demonstrated in Table 3 above the HIV positive and HIV negative study participants were closely matched sociodemographically.

## 11.2 PREVALENCE OF HIV AMONG PATIENTS ON MAINTENANCE HAEMODIALYSIS

The prevalence of HIV among patients on maintenance haemodialysis was 11.9% (95% CI 9.2-14.5%). Majority of the patients (86.6%) were on antiretroviral therapy.

**Table 4: Prevalence of HIV-infection**

| Variable | Frequency (%) | 95% CI |
|---|---|---|
| **HIV status** | | |
| Positive | 67 (11.9) | 9.2 – 14.5 |
| Negative | 498 (89.1) | 85.5 – 90.8 |

## 11.3 CLINICAL CHARACTERISTICS OF HIV POSITIVE AND HIV NEGATIVE PATIENTS ON MAINTENANCE HAEMODIALYSIS

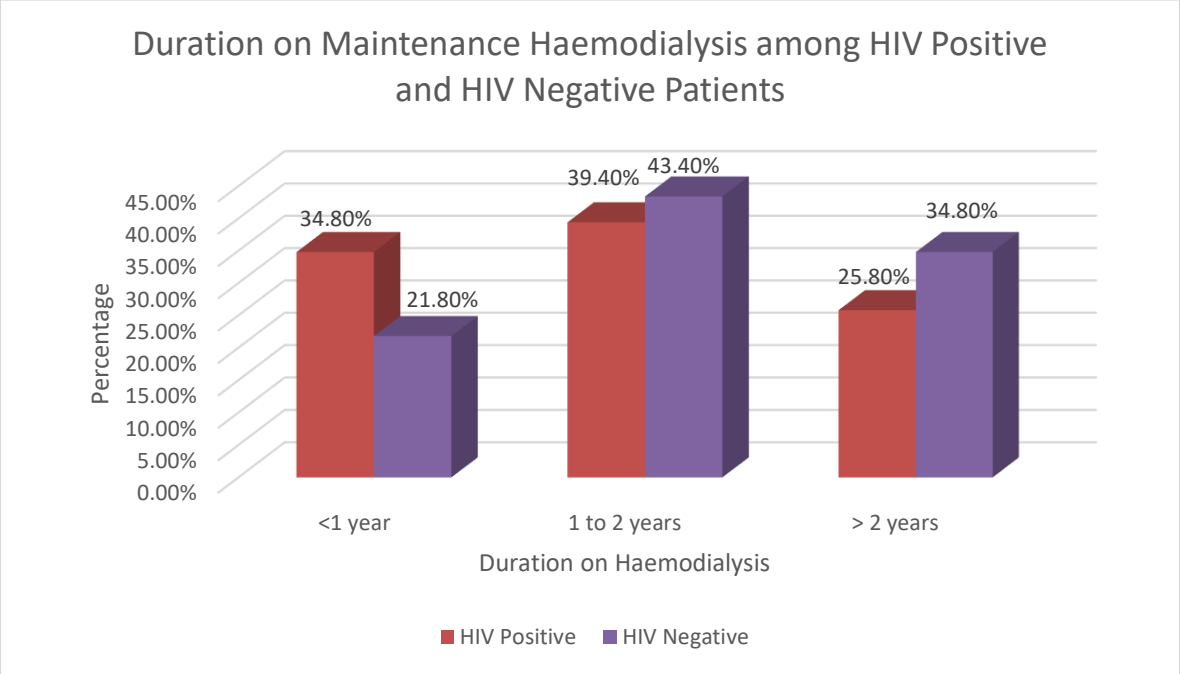
### 11.3.1 Duration on Haemodialysis

The duration on maintenance haemodialysis among HIV positive and HIV negative patients is summarized in Table 5 and Figure 3 below. The HIV positive patients were less likely to have dialyzed for more than two years compared to HIV negative patients (OR 0.5 [95% CI: 0.2-1.0], p=0.038).

**Table 5. Duration on Maintenance Haemodialysis among HIV Positive and HIV Negative Patients**

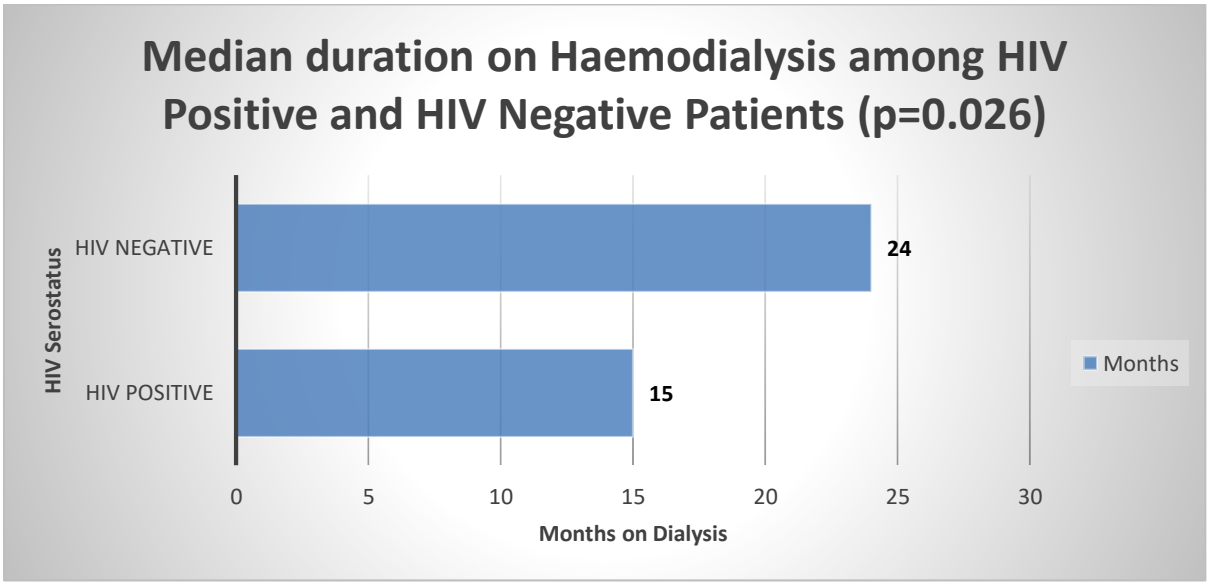
| | HIV Positive | HIV Negative | OR (95% CI) | P value |
|---|---|---|---|---|
| **Duration of dialysis** | | | | |
| < 1 year | 23(34.8) | 43(21.8) | 1.0 | |
| 1 to 2 years | 26(39.4) | 86(43.4) | 0.6(0.3-1.1) | 0.095 |
| >2 years | 17(25.8) | 69(34.8) | 0.5(0.2-1.0) | **0.038** |

**Figure 3. Duration on Maintenance Haemodialysis among HIV Positive and HIV Negative patients**




HIV positive patients had a statistically significant shorter median duration on haemodialysis of 15 months (IQR 5-36) compared to HIV negative patients at 24 months (IQR 12-36 months), p=0.026 (see Figure 4 below).

**Figure 4. Median duration on Haemodialysis among HIV Positive and HIV Negative Patients on Maintenance Haemodialysis**



### 11.3.2 Vascular access profile and complications among HIV Positive and HIV Negative patients on Maintenance Haemodialysis

Most patients were dialyzing via tunnelled cuffed dialysis catheters (62.1% and 52.5% of HIV positive and HIV negative patients respectively, p=0.175). HIV positive patients were however less likely to dialyze via an arteriovenous fistula compared to their HIV negative counterparts (OR 0.4 [95% CI: 0.2-0.9]). HIV positive patients were also more likely to use their vascular access for a shorter median duration (11months versus 12 months among HIV positive and negative patients respectively, p= 0.042).

HIV positive patients had a two fold higher risk of vascular access-related infections compared to HIV negative patients (OR 2.0 [95% CI: 1.1-3.6], p=0.030). These results are summarized in Figure 5 and Table 6 below.

**Figure 5. Types of vascular access among HIV Positive and HIV Negative patients on Maintenance Haemodialysis**

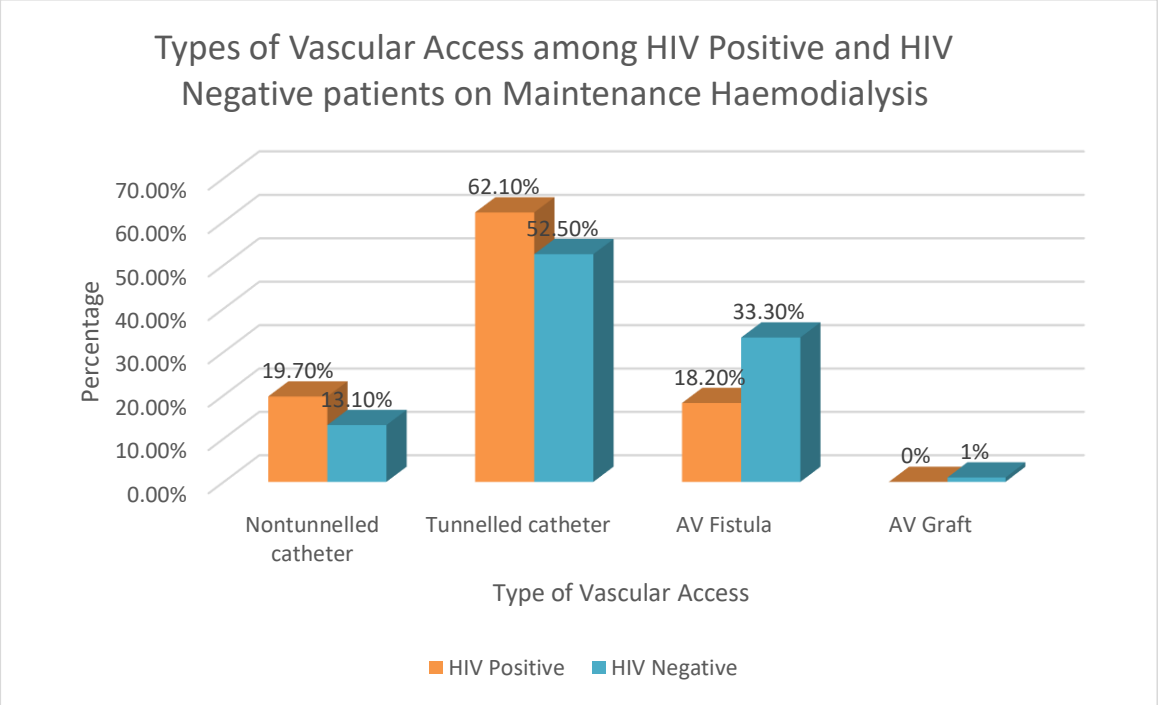


**Table 6. Vascular access profile and vascular access-related infections among HIV Positive and HIV Negative patients on Maintenance Haemodialysis**

| Variable | HIV positive | HIV negative | OR (95% CI) | P value |
|---|---|---|---|---|
| **Current vascular access (VA)** | | | | |
| Haemodialysis catheter | | | | |
| • Nontunnelled | 13 (19.7) | 26 (13.1) | 1.6 (0.8-3.4) | 0.193 |
| • Tunnelled cuffed | 41 (62.1) | 104 (52.5) | 1.5 (0.8-2.6) | 0.175 |
| Arteriovenous fistula | 12 (18.2) | 66 (33.3) | 0.4 (0.2-0.9) | **0.019** |
| Arteriovenous graft | 0 | 2 (1.0) | - | 1.000 |
| **Duration of VA (months).** | | | | |
| Median (IQR) | 11 (3-12) | 12 (6-18) | - | **0.042** |
| **VA-related infection** | | | | |
| Yes | 22 (32.8) | 40 (19.9) | 2.0 (1.1-3.6) | **0.030** |
| No | 45 (67.2) | 161 (80.1) | 1.0 | |

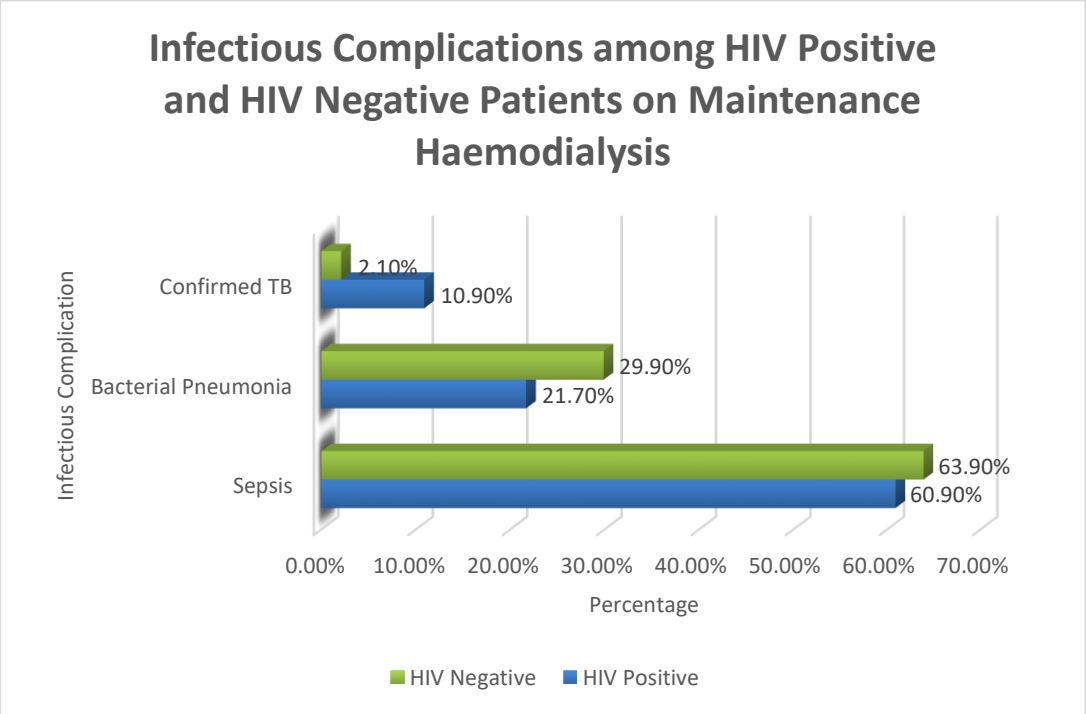
### 11.3.3 Other Infectious Complications among HIV Positive and HIV Negative patients on Maintenance Haemodialysis

HIV positive patients were 2.7 times more likely to have had a history of major infection compared to HIV negative patients (OR 2.7 [95% CI: 1.5-4.8], p=0.001). Sepsis was the most common documented major infection, occurring in 60.9% of HIV positive and 63.9% of HIV negative patients, but this difference was not statistically significant(p=0.565). HIV positive patients were however 5.6 times more likely to have documented tuberculosis compared to HIV negative patients (OR 5.6 [95% CI: 1.0-29.9], p=0.039).

**Table 7. Infectious Complications among HIV Positive and HIV Negative Patients on Maintenance Haemodialysis**

| Variable | HIV Positive | HIV Negative | OR (95% CI) | P value |
|---|---|---|---|---|
| **History of major infection** | | | | |
| Yes | 48 (71.6) | 98 (48.8) | 2.7 (1.5-4.8) | **0.001** |
| No | 19 (28.4) | 103 (51.2) | 1.0 | |
| **Type of infection** | | | | |
| TB | 5 (10.9) | 2 (2.1) | 5.6 (1.0-29.9) | **0.039** |
| Sepsis | 28 (60.9) | 62 (63.9) | 0.8 (0.4-1.6) | 0.565 |
| Bacterial pneumonia | 10 (21.7) | 29 (29.9) | 0.6 (0.3-1.4) | 0.261 |
| Others | 3 (6.5) | 4 (4.1) | 1.6 (0.3-7.6) | 0.681 |

**Figure 6. Infectious complications among HIV Positive and HIV Negative Patients on Maintenance Haemodialysis**




## 11.3.4 Blood transfusion history and Hemoglobin levels among HIV Positive and HIV Negative patients on Maintenance Haemodialysis

Mean haemoglobin levels were significantly lower among HIV positive patients compared to their HIV negative counterparts (mean haemoglobin 7.7 [±1.1]g/dl versus 8.4 [±1.4]g/dl respectively, $p<0.001$). HIV Positive patients were five times more likely to have received a blood transfusion compared to HIV negative patients ( OR 5.4 [95% CI: 2.4-12.5], $p<0.001$). They also had a higher mean number of units of blood transfused compared to HIV negative patients (2.4 [±0.9] units versus 2.0 [±0.9]units in HIV positive and negative patients respectively, $p=0.037$).

**Table 8. Blood transfusion history and Hemoglobin levels among HIV Positive and HIV Negative patients on Maintenance Haemodialysis**

| Variable | HIV Positive (n=67) | HIV Negative (n=201) | OR (95% CI) | P value |
|---|---|---|---|---|
| **Hemoglobin (g/dl)**<br>Mean (SD)<br>Min-Max | <br>7.7(1.1)<br>4.8-11.8 | <br>8.4(1.4)<br>5.0-12.7 | <br>- | <br>**0.001** |
| **Ever received blood transfusion**<br>Yes<br>No | <br>60 (89.6)<br>7(10.4) | <br>123 (61.2)<br>78 (38.8) | <br>5.4 (2.4-12.5)<br>1.0 | <br>**<0.001** |
| **Number of blood transfusions**<br>Mean (SD)<br>Min- Max | <br>2.4 (0.9)<br>1-5 | <br>2.0 (0.9)<br>1-4 | <br>- | <br>**0.037** |

### 11.3.5 Calcium, phosphate, PTH and albumin levels among HIV Positive and HIV Negative patients on Maintenance Haemodialysis

HIV positive patients had significantly lower mean serum calcium levels compared to HIV negative patients (1.8 mmol/l [±0.3] versus 2.0 mmol/l [±0.3] respectively. Mean serum albumin levels were also significantly lower among HIV positive patients in comparison to HIV negative patients (31.0 [±5.1]g/l versus 33.0 [±5.5]g/l respectively. There was no statistically significant difference in mean phosphate and parathyroid hormone levels between the two groups as shown in Table 9 below.

**Table 9. Calcium, phosphate, PTH and Albumin profile among HIV Positive and HIV Negative patients on Maintenance Haemodialysis**

| Variable | HIV Positive | HIV Negative | OR (95% CI) | P value |
|---|---|---|---|---|
| **Calcium (mmol/l)**<br>Mean (SD)<br>Min-Max | n=67<br>1.8 (0.3)<br>1.1- 2.6 | n=189<br>2.0(0.3)<br>1.3-3.5 | <br>- | <**0.001** |
| **Corrected Calcium (mmol/l)**<br>Mean (SD)<br>Min-Max | n=67<br>2.0 (0.3)<br>1.2-3.0 | n=184<br>2.1(0.3)<br>1.3-3.5 | <br>- | **0.001** |
| **Phosphate (mmol/l)**<br>Mean (SD)<br>Min-Max | n=67<br>1.8(0.8)<br>0.6-4.2 | n=186<br>1.7(0.7)<br>0.4-3.8 | <br>- | 0.067 |
| **PTH (ng/ml)**<br>Mean (SD)<br>Median (IQR)<br>Min-max | n=11<br>612.0 (527.7)<br>479 (329-691)<br>34- 1696 | n=37<br>445.0 (442.5)<br>329 (140-607)<br>22.7-1647 | <br>- | <br>0.283<br>0.280 |
| **Albumin (g/l)**<br>Mean (SD)<br>Min-Max | n=67<br>31.0 (5.1)<br>17-42 | n=189<br>33.0 (5.5)<br>15-44 | <br>- | **0.007** |

## 11.4 ONE YEAR OUTCOMES AMONG HIV POSITIVE AND HIV NEGATIVE PATIENTS ON MAINTENANCE HAEMODIALYSIS

One year mortality among HIV positive patients was 22.4% compared to 13.4% among HIV negative patients (p=0.053). HIV positive patients were 2.9 times more likely to be lost to follow up compared to their HIV negative counterparts (OR 2.9 [95% CI: 1.0-4.1], p=0.034). Time to mortality was significantly shorter among HIV positive patients compared to HIV negative patients as depicted in the Kaplan Meier curves below (log rank p value= 0.038).

**Table 10. One year outcomes among HIV Positive and HIV Negative patients on Maintenance Haemodialysis**

| Variable | HIV positive | HIV negative | OR (95% CI) | P value |
|---|---|---|---|---|
| **Outcome at 1 year** | | | | |
| Alive | 43 (64.2) | 157 (78.1) | 1.0 | |
| Dead | 15 (22.4) | 27 (13.4) | 2.0 (1.0-4.1) | 0.053 |
| Loss to follow up | 8 (11.9) | 10 (5.0) | 2.9 (1.1-7.9) | **0.034** |
| Transfer out | 1 (1.5) | 7 (3.5) | 0.5 (0.1-4.4) | 0.548 |

**Figure 7. Kaplan Meier curve for Time to Mortality at one year (Log rank p value= 0.038)**

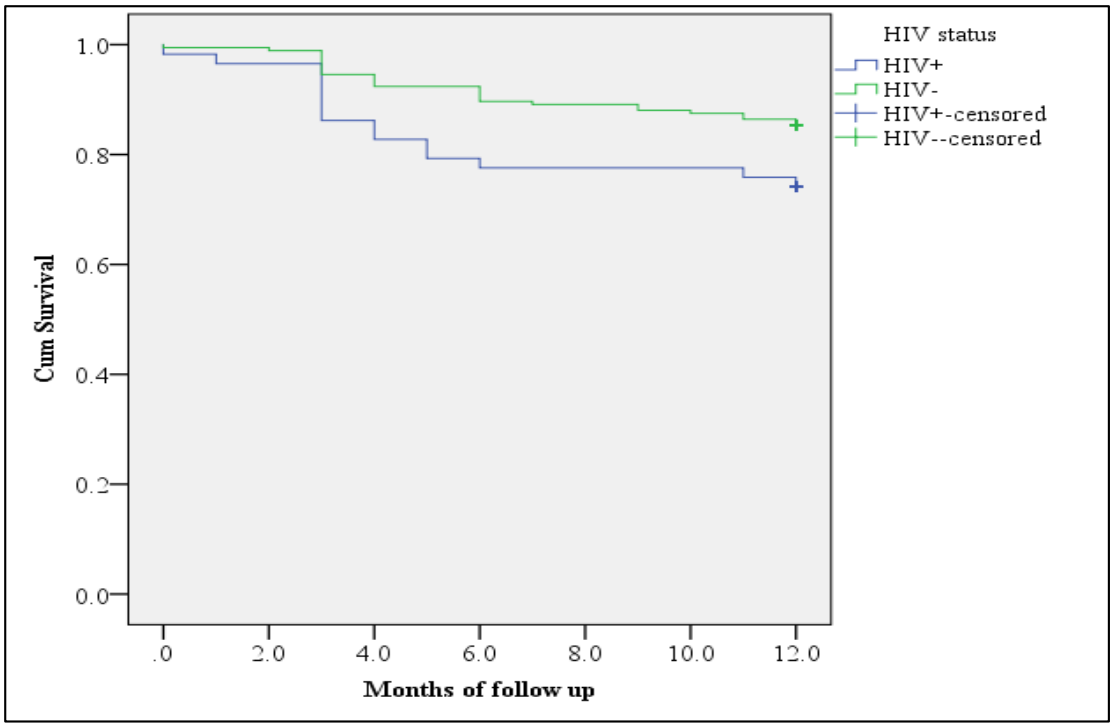
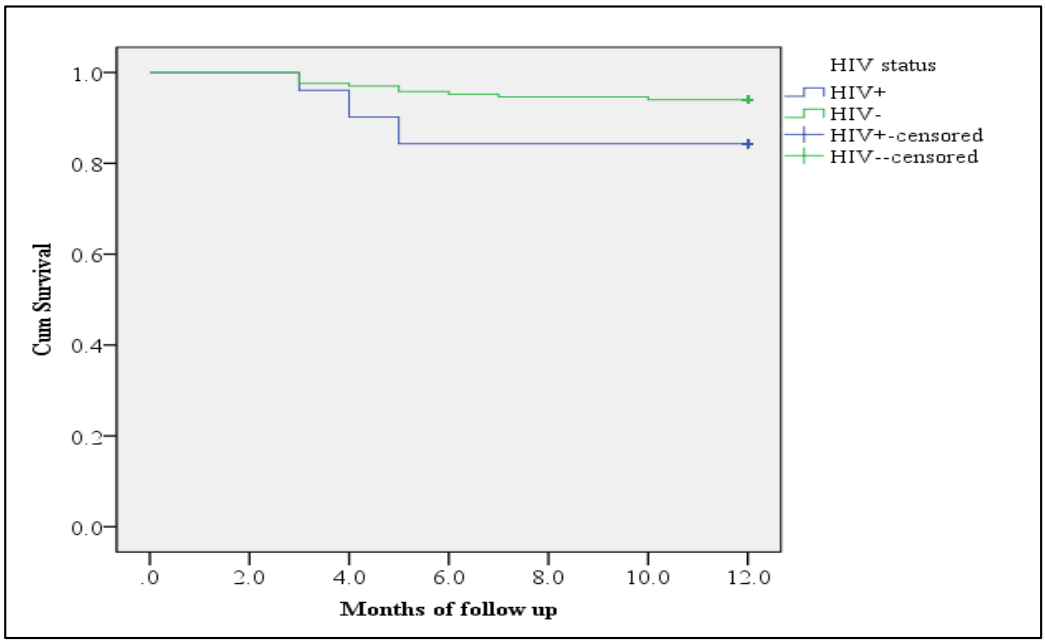


**Figure 8. Kaplan Meier curve for Time to loss to follow up at one year among HIV Positive and HIV Negative patients on Maintenance Haemodialysis (Log rank p value=0.026)**



# 12. DISCUSSION

HIV continues to be a leading infectious cause of chronic kidney disease in deveoping countries. Whereas studies comparing one year outcomes among HIV positive and HIV negative dialysis patients in developed countries have shown no difference between the two groups, the situation in developing countries may not be the same, as demonstrated in Cameroon(12). This study thus set out to elucidate the prevalence of HIV among patients on maintenance haemodialysis at two of the largest dialysis centres in Nairobi, Kenya, as well as determine one year outcomes comparing HIV positive and HIV negative patients, matched by age, sex, year of dialysis initiation and dialysis centre.

The prevalence of HIV among patients on maintenance dialysis at the two centres was 11.9%. This is comparable to studies carried out in South Africa (HIV seroprevalence rate of 9.75%)(11) and Cameroon (HIV seroprevalence between 10 and 13.5% among patients on maintenance haemodialysis)(7,8). These HIV seroprevalence rates are however much higher compared to rates in developed countries such as France (prevalence rate of 0.36%)(51) and Japan (prevalence rate of 0.024%)(52). The higher prevalence in developing countries likely reflects the higher burden of HIV in Sub Saharan Africa.

Additionally, the prevalence of HIV among the dialysis patients in this study was found to be more than double that in the Kenyan general population, with a prevalence rate of 4.9%(1). HIV positive patients have previously been shown to have a higher risk of end stage kidney disease compared to the general population. Rasch *et al* demonstrated a threefold higher risk of requiring chronic renal replacement therapy among HIV positive patients compared to age- and sex-matched controls in a large population-based study carried out in Denmark(53). This increased risk of end stage kidney disease in HIV positive patients is likely a result of the deleterious effects of HIV infection itself as well as antiretroviral therapy on the kidney(30,31)**.**

Mean age of patients on maintenance haemodialysis in this study was 50.0 (±12.7) years among HIV positive patients and 50.2 (±13.3) years among age-matched HIV negative patients. This is slightly higher than the mean age among dialysis patients in Cameroon (46.0±11.4 years)(12), but lower than that of dialysis patients in developed countries such as Switzerland (mean age 55.0±16 years)(54). It has been shown that end stage kidney disease requiring dialysis tends to occur at an earlier age in developing countries(55), possibly driven by late diagnosis of chronic kidney disease hence pre-empting strategies to delay progression of CKD.

There was a male predominance noted among study participants, with a male:female ratio of 1.9:1. This is comparable to other studies carried out locally, with Odhiambo *et al* reporting a male:female ratio of 1.6:1(56) among dialysis patients, and Nadeem et al finding a male:female ratio of 2.5:1 among patients with chronic kidney disease attending renal clinics at the Kenyatta National Hospital(57). The male predominance among dialysis patients may be a reflection of the larger numbers of male patients with chronic kidney disease eventually progressing to end stage kidney disease. Male gender has also been associated with more rapid progression of chronic kidney disease, possibly mediated by sex hormone-related effects on glomerular haemodynamics, mesangial proliferation, and cytokine release(58).

Most study participants had insurance cover under the National Hospital Insurance Fund (NHIF). NHIF began to cover the cost of two dialysis sessions per patient per week in the year 2016, leading to increased uptake of this cover among dialysis patients in the country. Study participants not covered by NHIF were mostly foreign nationals with other private insurance medical covers.

Median duration on maintenance haemodialysis in our study was significantly shorter among HIV positive patients compared to HIV negative patients. This probably reflects the higher loss to follow up and mortality rates in this group of patients as discussed in greater detail in the section on outcomes.

**Vascular access profile**

Most patients in both arms of this study were utilizing tunnelled, cuffed catheters for dialysis, at 62.1% of HIV positive patients. This is comparable to the findings by Shosi et al, who found that 65.2% of patients on maintenance haemodialysis at KNH were using tunnelled, cuffed catheters(59).

Use of arteriovenous fistula was documented in 18.2% of HIV positive and 33.3% of HIV negative patients, with HIV positive patients less likely to utilize an AV fistula compared to their HIV negative counterparts. This is similar to findings by Halle et al in Cameroon, where only 8.8% of HIV positive patients utilized an AV fistula for dialysis, compared to 21.1% of HIV negative patients, although this difference did not reach statistical significance in their study($p=0.06$)(12).

It is unclear whether this lower rate of uptake of AV fistula among HIV positive patients is due to physician inertia in referral for AV fistula creation, patient inertia, or the higher rates of artherosclerotic peripheral vascular disease documented among HIV positive patients(60),

that may preclude successful AV fistula fashioning. Presence of peripheral vascular disease has been shown to be associated with a lower likelihood of having an AV fistula (aOR 0.55, 95% CI:0.38-0.79)(61). The lower uptake among HIV positive patients requires further studies to determine the underlying factors, since AV fistulae remain the vascular access of choice among HIV positive patients, with comparable outcomes to HIV negative patients(62,63).

HIV positive patients in this study had a twofold higher risk of vascular access-related infections compared to their HIV negative counterparts. Similar findings were reported by Nicastri et al, who found a five to ten fold higher risk of vascular access-related infections among HIV positive patients (64). Mokrzycki et al however found no difference in catheter-related infections among HIV positive compared to HIV negative patients, although HIV positive patients had higher rates of gram negative bacteria and fungal infections(39). Mitchell et al also found similar rates of vascular access-related infections among HIV positive and HIV negative patients, but HIV positive patients had a higher risk of infection with polymicrobial organisms, as well as higher risk of hospitalization for the same(40). Higher risk of vascular access-related infections among HIV positive patients may possibly be driven by the higher rates of immunosuppression, concomitant intravenous drug abuse, and use of vascular access other than AV fistulae in this group of patients(65).

Overall, the documented rates of vascular access-related infections in our set up are worryingly high, with more than two-thirds of patients having had at least one episode of VA-related infection. This warrants further studies probing the use of aseptic techniques during catheter insertion, during connection to the dialysis machines, as well as determination of patients' knowledge on self-care of the dialysis catheters.

**Other Infectious Complications**

HIV positive patients in this study were more than two times as likely as their HIV negative counterparts to have had a history of major infection. The most common major infectious complication documented was sepsis, occurring in more than half of all patients with documented major infection. There was however no statistically significant difference in rates of sepsis between the two groups. Dialysis patients have been shown to be at increased risk of sepsis, with the most common foci being vascular access catheters and lower respiratory tract infections(66). Reasons for increased sepsis rates in dialysis patients include immunosuppression secondary to uremia, presence of comorbid conditions such as diabetes mellitus, as well as presence of indwelling dialysis catheters(67).

Presumed bacterial pneumonia is also a significant infectious complication in these patients, occurring in about a fifth of patients, with no statistically significant difference between the two groups. Rates of pneumonia in dialysis patients are higher than in the general population due to similar reasons as listed above, with dialysis patients at 14 to 16 fold higher risk of pneumonia-associated mortality compared to the general population(68). With pneumonia occurring in one out of five patients in our study, this warrants close monitoring, early diagnosis and prompt treatment of pneumonia in both HIV positive and HIV negative dialysis patients in our set up.

HIV positive patients were more than five times likely to have documented tuberculosis compared to their HIV negative counterparts. It has previously been established that patients on maintenance haemodialysis are at increased risk of tuberculosis, with the first report published in 1974(69). Since then multiple population-based studies have shown that patients on maintenance haemodialysis are at 6.9 to 25.3 higher relative risk of developing TB compared to the general population(70–72). The reasons for this increased risk of TB in dialysis patients are multifactorial, including uremia-associated immunosuppression with impaired lymphocyte, neutrophil and monocyte function, as well as malnutrition, Vitamin D deficiency and hyperparathyroidism that all contribute to impaired immunity(73–76). Additionally, nosocomial transmission of tuberculosis within dialysis centres both from infected healthcare workers and patients can occur(77).

With the additional immunosuppression by HIV, dialysis patients with HIV are at an even greater risk of TB compared to their HIV negative counterparts, as demonstrated in our study. Similar findings were reported among South African dialysis patients by Fabian *et al,* with HIV positive patients having an eight-fold higher incidence of TB compared to HIV negative patients on maintenance haemodialysis(11). It would thus be prudent to closely monitor and have a higher index of suspicion and screening for TB among HIV positive dialysis patients, who may not demonstrate the classical signs and symptoms of tuberculosis(78).

**Anaemia and blood transfusion history**

HIV positive patients in this study were more likely to have received a blood transfusion compared with HIV negative patients, with a statistically significant higher mean number of units transfused. HIV positive patients also had significantly lower mean haemoglobin levels compared to their HIV negative counterparts (7.7g/dl versus 8.4g/dl respectively). HIV

positive patients on dialysis have previously been reported to have lower haemoglobin levels compared to their HIV negative patients in studies from South Africa (haemoglobin levels of 9.5 g/dl versus 10.6g/dl respectively, $p<0.01$)(11) and Cameroon (haemoglobin levels of 7.12g/dl versus 7.86g/dl respectively, $p=0.045$)(12), which may necessitate use of more blood transfusions in this group of patients.

The lower levels of haemoglobin among HIV positive patients on dialysis may be a consequence of the additional effects of HIV on suppression of erythropoiesis, negative effects of opportunistic infections on the bone marrow, as well as adverse effects of various antiretroviral agents such as zidovudine(46). The lower haemoglobin levels may thus lead to higher rates of blood transfusion among HIV positive patients as demonstrated in our study. This has implications for future renal transplantation outcomes among these patients as blood transfusion may increase the risk of sensitization to HLA antigens, which has been associated with poorer graft outcomes(79). As they are at risk of more blood transfusions compared to their HIV negative counterparts, strategies to optimize use of iron and erythropoiesis stimulating agents among HIV positive patients on dialysis should be pursued.

**Calcium, phosphate, PTH and albumin levels**

HIV positive patients had significantly lower mean serum calcium and albumin levels compared to HIV negative patients. There was however no difference between the two groups in mean serum phosphate and parathyroid hormone levels. Among dialysis patients in Cameroon, Halle et al found no difference in serum calcium and phosphate levels between HIV positive and HIV negative patients(12).

HIV positive patients have however been shown to have higher risk of hypocalcemia compared to healthy controls(80). Reasons for this include a higher prevalence of Vitamin D deficiency among HIV positive patients, hypoalbuminemia, as well as due to Fanconi's syndrome associated with antiretroviral medications such as Tenofovir(81,82). Additionally, HIV positive patients may have altered parathyroid gland function, with resultant impaired release of parathyroid hormone(83). This may be due to the fact that parathyroid gland cells express a CD4-like moiety, potentially making the gland a target of infection by the human immunodeficiency virus(84).

Lower albumin levels among HIV positive patients on maintenance haemodialysis compared to HIV negative patients have also been reported among South African patients. In a study by

Fabian et al, South African HIV positive patients on maintenance haemodialysis had significantly lower serum albumin levels when compared to HIV negative patients (mean serum albumin 32.5g/dl [±5.7] versus 34.8[±4.7] respectively, p=0.015)(11). Reasons for lower albumin levels in these patients include malnutrition as a consequence of reduced protein intake, as well as inflammation, since albumin is a negative acute phase protein(85). HIV-associated nephropathy may also be associated with additional urinary loss of albumin. Hypoalbuminemia has been associated with higher mortality among haemodialysis patients, with each 10g/l (or 1g/dl) decrease in serum albumin associated with a 47% higher risk of mortality among these patients(86).

**One year outcomes among HIV Positive and HIV Negative Patients on Maintenance Haemodialysis**

In the censored analysis, time to mortality among HIV positive patients on maintenance haemodialysis was significantly shorter compared to HIV negative patients (log rank p value=0.038). There was a trend towards higher mortality rate at one year among HIV positive patients (22.4%) compared to HIV negative patients (13.4%), p=0.053. One year mortality rate among HIV positive dialysis patients in Cameroon was found to be higher compared to HIV negative patients in a study by Halle *et al* (mortality rate of 38.6% versus 21.1% among HIV positive and negative patients respectively, p=0.042)(12). There have been other studies, mostly in higher income countries, that have previously reported no difference in survival among HIV positive and HIV negative patients on maintenance haemodialysis. Comparable survival rates in the two groups have been reported in France (10) and South Africa(11).

Mortality rate among HIV positive patients in our study (22.4%) is lower compared to HIV positive patients on dialysis in Cameroon (38.6%)(12), but higher compared to HIV positive patients in France (6.2%)(10), and comparable to HIV positive patients in Iran (25%)(87). Lower mortality rate in our patients compared to Cameroonian patients may be partly explained by the relatively high levels of antiretroviral coverage at 86% in our study.

Among French HIV positive dialysis patients, low mortality rates may be explained by the fact that most of the patients (86%) were on HAART, with majority achieving viral suppression (54%), and having relatively higher CD4 counts (mean CD4 334 cells/$mm^3$)(10).

This is in contrast to HIV positive patients in Cameroon where mean CD4 count was 212 cells/$mm^3$, with 46% of patients having CD4 counts less than 200cells/$mm^3$(12).

Factors that have been associated with higher mortality rates among HIV positive dialysis patients compared to HIV negative patients include lack of treatment with HAART, lower CD4 counts, higher viral load, history of opportunistic infection, intravenous drug use, hypoalbuminemia and African American race(10,12,88). Additionally, it may be a more arduous task to achieve viral suppression among HIV positive patients on haemodialysis due to the possibility of altered ARV drug pharmacokinetics as a result of dialytic removal of these drugs, leading to subtherapeutic drug levels(46). This may in addition predispose these patients to drug resistant strains of HIV. HIV positive dialysis patients are also at higher risk of infectious complications that may increase risk of mortality, such as tuberculosis as seen in this study, due to the synergistic immunosuppressive effects of both HIV and uremia on cell-mediated immune responses. It has also been previously reported that dialyzer membranes may activate proinflammatory cytokines leading to increased replication of HIV(34,35).

HIV positive patients in this study had a more than twofold higher risk of loss to follow up compared to HIV negative patients. Loss to follow up was shown to be a significant impediment to successful haemodialysis among Tanzanian patients, driven mainly by lack of finances in low to middle income country settings(89). Loss to follow up is also an obstacle to adequate care among HIV positive patients, with rates reported at between 17% to 29% at two years in low and middle income countries, necessitating strategies to re-engage patients in care(90). Further studies to explore the reasons underlying loss to follow up in these patients will be prudent, as loss to follow up among HIV positive patients has been associated with higher rates of mortality, morbidity and hospitalization(91).

# 13. CONCLUSION

Prevalence of HIV among patients on maintenance haemodialysis in this study was higher than that in the general Kenyan population. HIV positive patients had worse clinical parameters, including lower mean levels of haemoglobin, serum calcium and albumin compared to HIV negative patients. Additionally, HIV positive patients had a higher risk of infectious complications and significantly shorter time to mortality. These findings may possibly be driven by higher rates of malnutrition and inflammation among these patients, as well as the additive deleterious effects of uremia and HIV on cell-mediated immunity and bone marrow suppression. Further studies in this population are warranted to elucidate the underlying reasons for these poorer outcomes, as well as strategies to mitigate against the same.

# 14.STUDY LIMITATIONS AND MITIGATION MEASURES

i. Presence of known confounding variables that may affect the outcome of interest and differ between the two study groups (age, sex, year of dialysis initiation, dialysis centre) – this was mitigated by matching the HIV positive patients and their HIV negative counterparts by age, sex, year of dialysis initiation and dialysis centre.

ii. Missing/incomplete data- Only data that was available was included in the analysis.

# 15.RECOMMENDATIONS

1. Closer follow up of HIV positive patients on haemodialysis by both the Nephrology and Infectious Disease teams to improve outcomes and retention rates.

2. Optimize pharmacologic management of anaemia among HIV positive patients on maintenance haemodialysis to reduce the attendant risks of recurrent blood transfusions.

3. Need for closer monitoring and screening for tuberculosis among HIV positive patients on maintenance haemodialysis.

4. Further studies to determine the factors underlying the lower uptake of arteriovenous fistulae among HIV positive patients.

5. Follow up studies to determine the causes of higher rates of hypocalcemia among HIV positive patients on maintenance haemodialysis.

6. Further determination of the drivers of poorer outcomes among HIV positive patients, including studies profiling the pharmacokinetics of antiretroviral medications among HIV positive patients on maintenance haemodialysis.

# 16. STUDY BUDGET

| 17. Components | Unit of Measure | Duration/ Number | Unit Cost(Kshs) | Total Cost(Kshs) |
|---|---|---|---|---|
| Personnel | | | | |
| **Research Assistant** | | **3 for 3 months** | **30,000.00** | **270,000.00** |
| **Training of Assistants** | | **2 days** | **3,000.00** | **24,000.00** |
| **Statistician** | | **1** | **40,000.00** | **40,000.00** |
| **Data Entry Clerk** | | **1** | **20,000.00** | **20,000.00** |
| **Transcribing Fee** | **-** | **-** | **-** | **-** |
| Printing | | | | |
| **Consent Form** | **-** | **-** | **-** | **-** |
| **Assent Form** | **-** | **-** | **-** | **-** |
| **Questionnaires** | **6 pages** | **1** | **10.00** | **60.00** |
| **Interview Guide** | **-** | **-** | **-** | **-** |
| **Final Report** | **100 pages** | **1** | **10.00** | **1,000.00** |
| Photocopying | | | | |
| **Consent Form** | **-** | **-** | **-** | **-** |
| **Assent Form** | **-** | **-** | **-** | **-** |
| **Questionnaires** | **6 pages each** | **300** | **5.00** | **9,000.00** |
| **Interview Guide** | **-** | **-** | **-** | **-** |
| **Final Report** | **6 copies** | **100 pages** | **5.00** | **3,000.00** |
| **Final Report Binding** | **6 copies** | **100 pages** | **250.00** | **1,500.00** |
| Diagnostic Services N/A | | | | |
| Other costs | | | | |
| **Stationery** | | **9** | **100.00** | **900.00** |
| **ERC Fees** | | **1** | **5,000.00** | **5,000.00** |
| **Records Access Fee** | | **1** | **1,000.00** | **1,000.00** |
| **Poster Printing** | **1** | **1** | **2,500.00** | **2,500.00** |
| | | | | |
| **Total** | | | | **377,960.00** |

# 18. REFERENCES


1. KENPHIA-2018-PREL-REP-2020-HR3-final.pdf [Internet]. [cited 2020 Apr 28]. Available from: http://www.health.go.ke/wp-content/uploads/2020/02/KENPHIA-2018-PREL-REP-2020-HR3-final.pdf

2. Kenya [Internet]. Institute for Health Metrics and Evaluation. 2015 [cited 2020 Apr 28]. Available from: http://www.healthdata.org/kenya

3. Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. Kidney Int. 2014 Jan 1;85(1):49–61.

4. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2020 Feb 29;395(10225):709–33.

5. Government steps up fight against kidney diseases – MINISTRY OF HEALTH [Internet]. [cited 2020 Apr 29]. Available from: http://www.health.go.ke/government-steps-up-fight-against-kidney-diseases/

6. Yang C-W, Harris DCH, Luyckx VA, Nangaku M, Hou FF, Garcia Garcia G, et al. Global case studies for chronic kidney disease/end-stage kidney disease care. Kidney Int Suppl. 2020 Mar;10(1):e24–48.

7. Patrice HM, Namme LH, Elvis T, Vanessa T, François KF, Gloria A, et al. Prevalence of Hepatitis B surface antigen and anti-HIV antibodies among patients on maintenance haemodialysis in Douala, Cameroon. Health Sci Dis [Internet]. 2013 Aug 30 [cited 2020 Apr 30];14(3). Available from: http://hsd-fmsb.org/index.php/hsd/article/view/207

8. Luma HN, Halle MP, Eloumou SAFB, Azingala F, Kamdem F, Donfack-Sontsa O, et al. Seroprevalence of human immunodeficiency virus, hepatitis B and C viruses among haemodialysis patients in two newly opened centres in Cameroon. Pan Afr Med J [Internet]. 2017 Jul 31;27. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5622837/

9. Davids MR, Jardine T, Marais N, Jacobs JC. South African Renal Registry Annual Report 2016. Afr J Nephrol. 2018 Nov 27;21(1):61–72.

10. Tourret J, Tostivint I, Montcel ST du, Bragg-Gresham J, Karie S, Vigneau C, et al. Outcome and Prognosis Factors in HIV-Infected Hemodialysis Patients. Clin J Am Soc Nephrol. 2006 Nov 1;1(6):1241–7.

11. Fabian J, Maher HA, Clark C, Naicker S, Becker P, Venter WDF. Morbidity and mortality of black HIV-positive patients with end-stage kidney disease receiving chronic haemodialysis in South Africa. SAMJ South Afr Med J. 2015 Feb;105(2):110–4.

12. Halle MP, Edjomo AM, Fouda H, Djantio H, Essomba N, Ashuntantang GE. Survival of HIV infected patients on maintenance hemodialysis in Cameroon: a comparative study. BMC Nephrol. 2018 Jul 5;19(1):166.

13. Wandeler G, Johnson LF, Egger M. Trends in life expectancy of HIV-positive adults on ART across the globe: comparisons with general population. Curr Opin HIV AIDS. 2016 Sep;11(5):492–500.

14. UNAIDS_FactSheet_en.pdf [Internet]. [cited 2020 Apr 28]. Available from: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

15. KAIS_2007_Final.pdf [Internet]. [cited 2020 Apr 28]. Available from: http://guidelines.health.go.ke:8000/media/KAIS_2007_Final.pdf

16. KAIS-2012.pdf [Internet]. [cited 2020 Apr 28]. Available from: https://nacc.or.ke/wp-content/uploads/2015/10/KAIS-2012.pdf

17. Caplin B, Yang C-W, Anand S, Levin A, Madero M, Saran R, et al. The International Society of Nephrology's International Consortium of Collaborators on Chronic Kidney Disease of Unknown Etiology: report of the working group on approaches to population-level detection strategies and recommendations for a minimum dataset. Kidney Int. 2019 Jan 1;95(1):4–10.

18. Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. The Lancet. 2015 May 16;385(9981):1975–82.

19. Stanifer JW, Jing B, Tolan S, Helmke N, Mukerjee R, Naicker S, et al. The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Glob Health. 2014 Mar 1;2(3):e174–81.

20. Okpechi IG, Rayner BL, Swanepoel CR. Nephrotic syndrome in adult black South Africans: HIV-associated nephropathy as the main culprit. J Natl Med Assoc. 2010 Dec;102(12):1193–7.

21. George JA, Brandenburg J-T, Fabian J, Crowther NJ, Agongo G, Alberts M, et al. Kidney damage and associated risk factors in rural and urban sub-Saharan Africa (AWI-Gen): a cross-sectional population study. Lancet Glob Health. 2019 Dec 1;7(12):e1632–43.

22. Wools-Kaloustian K, Gupta SK, Muloma E, Owino-Ong'or W, Sidle J, Aubrey RW, et al. Renal disease in an antiretroviral-naïve HIV-infected outpatient population in Western Kenya. Nephrol Dial Transplant. 2007 Aug 1;22(8):2208–12.

23. Kairu BN. Prevalence Of Chronic Kidney Disease Among Ambulatory Human Immunodeficiency Virus/acquired Immunodeficiency Syndrome Patients On Antiretroviral Therapy At The Kenyatta National Hospital [Internet]. 2015 [cited 2020 Apr 29]. Available from: https://www.semanticscholar.org/paper/Prevalence-Of-Chronic-Kidney-Disease-Among-Human-On-Kairu/81444dee64eadce656b2f0025fd4826abed5f646

24. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. Kidney Int. 2011 Dec 2;80(12):1258–70.

25. More diagnosed with kidney diseases as NHIF pay-outs rise - Daily Nation [Internet]. [cited 2020 Apr 29]. Available from: https://www.nation.co.ke/news/1056-5028696-q3o59r/index.html

26. World Kidney Day 2019 – MINISTRY OF HEALTH [Internet]. [cited 2020 Apr 29]. Available from: http://www.health.go.ke/world-kidney-day-2019/

27. Barasa E, Rogo K, Mwaura N, Chuma J. Kenya National Hospital Insurance Fund Reforms: Implications and Lessons for Universal Health Coverage. Health Syst Reform. 2018 Oct 2;4(4):346–61.

28. Moosa MR, Kidd M. The dangers of rationing dialysis treatment: The dilemma facing a developing country. Kidney Int. 2006 Sep 2;70(6):1107–14.

29. Rao TKS, Filippone EJ, Nicastri AD, Landesman SH, Frank E, Chen CK, et al. Associated Focal and Segmental Glomerulosclerosis in the Acquired Immunodeficiency Syndrome. N Engl J Med. 1984 Mar 15;310(11):669–73.

30. Cohen SD, Kopp JB, Kimmel PL. Kidney Diseases Associated with Human Immunodeficiency Virus Infection. N Engl J Med. 2017 Dec 14;377(24):2363–74.

31. Wyatt CM, Morgello S, Katz-Malamed R, Wei C, Klotman ME, Klotman PE, et al. The spectrum of kidney disease in patients with AIDS in the era of antiretroviral therapy. Kidney Int. 2009 Feb;75(4):428–34.

32. Rao TKS, Friedman EA, Nicastri AD. The Types of Renal Disease in the Acquired Immunodeficiency Syndrome. N Engl J Med. 1987 Apr 23;316(17):1062–8.

33. Ahuja TS, Grady J, Khan S. Changing Trends in the Survival of Dialysis Patients with Human Immunodeficiency Virus in the United States. J Am Soc Nephrol. 2002 Jul 1;13(7):1889–93.

34. Kedzierska K, Crowe SM. Cytokines and HIV-1: interactions and clinical implications. Antivir Chem Chemother. 2001 May;12(3):133–50.

35. Singh NP, Bansal R, Thakur A, Kohli R, Bansal RC, Agarwal SK. Effect of membrane composition on cytokine production and clinical symptoms during hemodialysis: a crossover study. Ren Fail. 2003 May;25(3):419–30.

36. Almasri J, Alsawas M, Mainou M, Mustafa RA, Wang Z, Woo K, et al. Outcomes of vascular access for hemodialysis: A systematic review and meta-analysis. J Vasc Surg. 2016 Jul 1;64(1):236–43.

37. Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update. Am J Kidney Dis. 2020 Apr 1;75(4):S1–164.

38. Lucas GM, Ross MJ, Stock PG, Shlipak MG, Wyatt CM, Gupta SK, et al. Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected With HIV: 2014 Update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis. 2014 Nov 1;59(9):e96–138.

39. Mokrzycki MH, Schröppel B, von Gersdorff G, Rush H, Zdunek MP, Feingold R. Tunneled-cuffed catheter associated infections in hemodialysis patients who are seropositive for the human immunodeficiency virus. J Am Soc Nephrol JASN. 2000 Nov;11(11):2122–7.

40. Mitchell D, Krishnasami Z, Allon M. Catheter-related bacteraemia in haemodialysis patients with HIV infection. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2006 Nov;21(11):3185–8.

41. Avila-Danguillecourt N, Moodley AA, Makinga P. Prevalence and outcomes of central venous catheter-related bacteraemia in HIV-infected versus non-HIV-infected patients undergoing haemodialysis treatment for end-stage kidney disease. South Afr J HIV Med [Internet]. 2018 Nov 22;19(1). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6295969/

42. Mitchell D, Krishnasami Z, Young CJ, Allon M. Arteriovenous access outcomes in haemodialysis patients with HIV infection. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2007 Feb;22(2):465–70.

43. Curi MA, Pappas PJ, Silva MB, Patel S, Padberg FT, Jamil Z, et al. Hemodialysis access: Influence of the human immunodeficiency virus on patency and infection rates. J Vasc Surg. 1999 Apr 1;29(4):608–16.

44. Kabinga SK, Kayima JK, McLigeyo SO, Ndungu JN. Hemodialysis vascular accesses in patients on chronic hemodialysis at the Kenyatta National Hospital in Kenya. J Vasc Access. 2019 Nov 1;20(6):697–700.

45. Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. PloS One. 2014;9(1):e84943.

46. Mandayam S, Ahuja TS. Dialyzing a Patient with Human Immunodeficiency Virus Infection: What a Nephrologist Needs to Know. Am J Nephrol. 2004;24(5):511–21.

47. Astor BC, Arnett DK, Brown A, Coresh J. Association of kidney function and hemoglobin with left ventricular morphology among African Americans: the Atherosclerosis Risk in Communities (ARIC) study. Am J Kidney Dis Off J Natl Kidney Found. 2004 May;43(5):836–45.

48. McClellan WM, Flanders WD, Langston RD, Jurkovitz C, Presley R. Anemia and renal insufficiency are independent risk factors for death among patients with congestive heart failure admitted to community hospitals: a population-based study. J Am Soc Nephrol JASN. 2002 Jul;13(7):1928–36.

49. Owen WF, Lew NL, Liu Y, Lowrie EG, Lazarus JM. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med. 1993 Sep 30;329(14):1001–6.

50. Ndlovu KCZ, Chikobvu P, Mofokeng T, Gounden V, Assounga A. Serum albumin and mortality in patients with HIV and end-stage renal failure on peritoneal dialysis. PLOS ONE. 2019 Jun 10;14(6):e0218156.

51. Poignet JL, Desassis JF, Chanton N, Litchinko MB, Zins B, Kolko A, et al. [Prevalence of HIV infection in dialysis patients: results of a national multicenter study]. Nephrologie. 1999;20(3):159–63.

52. Yanagisawa N, Ajisawa A, Imamura A, Suganuma A, Tsuchiya K, Nitta K, et al. Prevalence of HIV infection among patients receiving chronic dialysis therapy in Japan : a nationwide study based on a questionnaire survey. Nihon Toseki Igakkai Zasshi. 2014;47(10):623–8.

53. Rasch MG, Helleberg M, Feldt-Rasmussen B, Kronborg G, Larsen CS, Pedersen C, et al. Increased risk of dialysis and end-stage renal disease among HIV patients in Denmark compared with the background population. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2014 Jun;29(6):1232–8.

54. Lehmann PR, Ambühl M, Corleto D, Klaghofer R, Ambühl PM. Epidemiologic trends in chronic renal replacement therapy over forty years: A Swiss dialysis experience. BMC Nephrol. 2012 Jul 2;13(1):52.

55. Jha V, Chugh K. Dialysis in developing countries: Priorities and obstacles. Nephrology. 1996;2(2):65–71.

56. Odhiambo JO, Otieno FA, Twahir A. Dialysis outcomes and practice patterns among chronic kidney disease patients receiving hemodialysis at a private dialysis centre in Nairobi, Kenya between May 2016 and July 2016. 2018 [cited 2021 Oct 26]; Available from: http://erepository.uonbi.ac.ke/handle/11295/106472

57. Sheikh NI. Cardiovascular risk factors associated with chronic renal insufficiency in black patients as seen at the Kenyatta National Hospital [Internet] [Thesis]. University of Nairobi.; 2003 [cited 2021 Dec 6]. Available from: http://erepository.uonbi.ac.ke/handle/11295/24971

58. Silbiger SR, Neugarten J. The impact of gender on the progression of chronic renal disease. Am J Kidney Dis. 1995 Apr 1;25(4):515–33.

59. Shosi RA. The adequacy of hemodialysis in end stage renal disease at Kenyatta National Hospital [Internet] [Thesis]. University of Nairobi, CHS, Kenya; 2003 [cited 2021 Oct 27]. Available from: http://erepository.uonbi.ac.ke/handle/11295/6342

60. Beckman JA, Duncan MS, Alcorn CW, So-Armah K, Butt AA, Goetz MB, et al. Association of HIV infection and risk of peripheral artery disease. Circulation. 2018 Jul 17;138(3):255–65.

61. Allon M, Ornt DB, Schwab SJ, Rasmussen C, Delmez JA, Greene T, et al. Factors associated with the prevalence of arteriovenous fistulas in hemodialysis patients in the HEMO Study. Kidney Int. 2000 Nov;58(5):2178–85.

62. Mitchell D, Krishnasami Z, Young C, Allon M. Arteriovenous access outcomes in haemodialysis patients with HIV infection. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2007;

63. Dicken QG, Cheng TW, Farber A, Levin SR, Jones DW, Malas MB, et al. Patients with human immunodeficiency virus infection do not have inferior outcomes after dialysis access creation. J Vasc Surg. 2020 Dec 1;72(6):2113–9.

64. Nicastri E, Petrosillo N, Viale P, Ippolito G. Catheter-related bloodstream infections in HIV-infected patients. Ann N Y Acad Sci. 2001 Nov;946:274–90.

65. Castro CEF, Madariaga MG. Vascular access-related infections in HIV patients undergoing hemodialysis: case description and literature review. Braz J Infect Dis. 2008 Dec;12:531–5.

66. Abou Dagher G, Harmouche E, Jabbour E, Bachir R, Zebian D, Bou Chebl R. Sepsis in hemodialysis patients. BMC Emerg Med. 2015 Oct 14;15(1):30.

67. Sarnak MJ, Jaber BL. Mortality caused by sepsis in patients with end-stage renal disease compared with the general population. Kidney Int. 2000 Oct 1;58(4):1758–64.

68. Sarnak MJ, Jaber BL. Pulmonary infectious mortality among patients with end-stage renal disease. Chest. 2001 Dec;120(6):1883–7.

69. Pradhan RP, Katz LA, Nidus BD, Matalon R, Eisinger RP. Tuberculosis in Dialyzed Patients. JAMA. 1974 Aug 12;229(7):798–800.

70. Ahmed AT, Karter AJ. Tuberculosis in California dialysis patients. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 2004 Mar;8(3):341–5.

71. Chou KJ, Fang HC, Bai KJ, Hwang SJ, Yang WC, Chung HM. Tuberculosis in maintenance dialysis patients. Nephron. 2001 Jun;88(2):138–43.

72. Chia S, Karim M, Elwood RK, FitzGerald JM. Risk of tuberculosis in dialysis patients: a population-based study. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis. 1998 Dec;2(12):989–91.

73. Girndt M, Sester U, Sester M, Kaul H, Köhler H. Impaired cellular immune function in patients with end-stage renal failure. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 1999 Dec;14(12):2807–10.

74. Lim WH, Kireta S, Leedham E, Russ GR, Coates PT. Uremia impairs monocyte and monocyte-derived dendritic cell function in hemodialysis patients. Kidney Int. 2007 Nov;72(9):1138–48.

75. Chan TY. Vitamin D deficiency and susceptibility to tuberculosis. Calcif Tissue Int. 2000 Jun;66(6):476–8.

76. Tzanno-Martins C, Futata E, Jorgetti V, Duarte AJ. Restoration of impaired T-cell proliferation after parathyroidectomy in hemodialysis patients. Nephron. 2000 Mar;84(3):224–7.

77. Centers for Disease Control and Prevention (CDC). Tuberculosis transmission in a renal dialysis center--Nevada, 2003. MMWR Morb Mortal Wkly Rep. 2004 Sep 24;53(37):873–5.

78. Segall L, Covic A. Diagnosis of Tuberculosis in Dialysis Patients: Current Strategy. Clin J Am Soc Nephrol. 2010 Jun 1;5(6):1114–22.

79. Obrador GT, Macdougall IC. Effect of Red Cell Transfusions on Future Kidney Transplantation. Clin J Am Soc Nephrol. 2013 May 7;8(5):852–60.

80. Kiran NA, Kanth MR, Satyannarayana V a. R, Kumar PSG. Serum calcium and phosphorus levels in patients of HIV positive under the treatment. Int J Clin Biochem Res. 2020 Jun 15;7(2):164–7.

81. Sandhu S, Desai A, Batra M, Girdhar R, Chatterjee K, Kemp EH, et al. Severe Symptomatic Hypocalcemia from HIV Related Hypoparathyroidism. Case Rep Endocrinol. 2018 Sep 25;2018:8270936.

82. Quimby D, Brito MO. Fanconi syndrome associated with use of tenofovir in HIV-infected patients: a case report and review of the literature. AIDS Read. 2005 Jul;15(7):357–64.

83. Hellman P, Albert J, Gidlund M, Klareskog L, Rastad J, Akerström G, et al. Impaired parathyroid hormone release in human immunodeficiency virus infection. AIDS Res Hum Retroviruses. 1994 Apr;10(4):391–4.

84. Hellman P, Karlsson-Parra A, Klareskog L, Ridefelt P, Bjerneroth G, Rastad J, et al. Expression and function of a CD4-like molecule in parathyroid tissue. Surgery. 1996 Dec;120(6):985–92.

85. Kaysen GA. Serum albumin concentration in dialysis patients: Why does it remain resistant to therapy? Kidney Int. 2003 Nov;64:S92–8.

86. de Mutsert R, Grootendorst DC, Indemans F, Boeschoten EW, Krediet RT, Dekker FW, et al. Association between serum albumin and mortality in dialysis patients is partly explained by inflammation, and not by malnutrition. J Ren Nutr Off J Counc Ren Nutr Natl Kidney Found. 2009 Mar;19(2):127–35.

87. Soleymanian T, Raman S, Shannaq FN, Richardson R, Jassal SV, Bargman J, et al. Survival and morbidity of HIV patients on hemodialysis and peritoneal dialysis: one center's experience and review of the literature. Int Urol Nephrol. 2006;38(2):331–8.

88. Rodriguez RA, Mendelson M, O'Hare AM, Hsu LC, Schoenfeld P. Determinants of Survival among HIV-Infected Chronic Dialysis Patients. J Am Soc Nephrol. 2003 May 1;14(5):1307–13.

89. Meremo AJ, Ngilangwa DP, Mwashambwa MY, Masalu MB, Kapinga J, Tagalile R, et al. Challenges and outcomes of haemodialysis among patients presenting with kidney diseases in Dodoma, Tanzania. BMC Nephrol. 2017 Jul 4;18(1):212.

90. Alizadeh F, Mfitumuhoza G, Stephens J, Habimaana C, Myles K, Baganizi M, et al. Identifying and Reengaging Patients Lost to Follow-Up in Rural Africa: The "Horizontal" Hospital-Based Approach in Uganda. Glob Health Sci Pract. 2019 Mar 22;7(1):103–15.

91. Birhanu MY, Leshargie CT, Alebel A, Wagnew F, Siferih M, Gebre T, et al. Incidence and predictors of loss to follow-up among HIV-positive adults in northwest Ethiopia: a retrospective cohort study. Trop Med Health. 2020 Sep 14;48(1):78.

# 19. APPENDICES

## 18.1 APPENDIX I: STUDY PROFORMA

**Study Title: Comparison of one year outcomes and clinical characteristics among HIV Positive and HIV Negative patients on Maintenance Haemodialysis at the Kenyatta National Hospital and Nairobi Hospital Renal Units**

***Screening demographics***

***Date*** ☐☐ ☐☐ ☐☐

**Screening ID** ☐☐☐☐☐ **Participant ID** ☐☐☐☐☐

| **I. Screening Demographics** | | | | |
|---|---|---|---|---|
| 1. | Gender Male ☐ Female ☐ | | | |
| 2. | Age ☐☐ *ears* | | | |
| 3. | Marital status<br>a. Single ☐<br>b. Married ☐<br>c. Separated ☐<br>d. Divorced ☐ | | | |
| 4. | Level of education | | | |
| | None | Primary | Secondary | College/University |
| 5. | Occupation | | | |
| | Student | Unemployed | Employed | Self employed |
| | | | | |
| 8. | Do you have health insurance?<br>Yes _____ NHIF_____<br>Other _____<br>No_____ | | | |
| | | | | |
| | **Completed by:** _____in*itials/date)* | | | |

***Date*** ☐☐ ☐☐ ☐☐

**Screening ID** ☐☐ ☐☐☐ **Participant ID** ☐☐☐☐☐

| **Inclusion criteria** | |
|---|---|
| 1 | Is the participant ≥18 years of age? Yes ☐ No ☐ |
| 2 | Is the participant documented HIV positive?* ☐ Yes ☐ No |
| 3 | Did the patient initiate haemodialysis at the Kenyatta National Hospital or Nariobi Hospital in the period between 1st January 2010 and 31st December 2019? ☐ Yes ☐ No |
| ***For the comparator group HIV status should be negative** | |
| **Exclusion criteria** *question 7 & 8 need to be answered in the negative for eligibility* | |
| 7 | If female- is the patient pregnant? Yes ☐ No ☐ |
| 8 | Based on the information from item 1-7, is the participant eligible or not? Eligible ☐ Not eligible ☐ |
| | **Completed by:_____ (***initials/date***)** |

***Date*** ☐☐ ☐☐ ☐☐

**Screening ID** ☐☐☐☐☐ **Participant ID** ☐☐☐☐☐

| **Part 1: To determine period prevalence of HIV among all on haemodialysis between 1/1/2010 & 31/12/2019** | |
|---|---|
| 1. | Date of initiation of Haemodialysis at the Kenyatta National Hospital / Nairobi Hospital<br>☐☐ ☐☐ ☐☐<br>*dd mm yy* |
| 2. | Documented serostatus for:<br>a. HIV Positive ☐ Negative ☐<br>Date test was done ☐☐ ☐☐ ☐☐<br>*dd mm yy*<br>b. Hepatitis B Positive ☐ Negative ☐<br>Date test was done ☐☐ ☐☐ ☐☐<br>*dd mm yy*<br>c. Hepatitis C Positive Negative<br>Date test was done ☐☐ ☐☐ ☐☐<br>*dd mm yy* |
| 3. | Cause of Chronic Kidney Disease if documented<br>a. Hypertension ☐<br>b. Diabetes mellitus ☐<br>c. Pregnancy-related ☐<br>d. SLE ☐<br>*e.* Glomerulonephritis ☐<br>State type if histology documented_____<br>*f.* HIV ☐<br>*g.* Polycystic kidney disease ☐<br>*h.* Obstructive Uropathy (eg Ca prostate) ☐<br>*i.* Missing ☐<br>Other (Please state) _____ |

**Part 2: For the 65 HIV positive consecutively recruited HIV positive and 195 matched HIV negative patients- Clinical parameters and duration on haemodialysis**

| **2a. Medical history** | |
|---|---|
| 1. | If HIV positive what is the documented:<br>a. Last CD4 count _____cells/mm3<br>b. Last Viral Load _____copies/ml<br>c. ART regimen _____<br>Duration on this regimen_____ |

| | |
|---|---|
| | d. Any previous ART regimen_____<br>Duration on this regimen _____<br><br>Reason for treatment switch_____<br><br>e. Any documented opportunistic infection? Yes ☐ No ☐<br>If yes, state which one_____ |
| 2. | Has the patient ever received a blood transfusion?<br>Yes ☐ No ☐<br><br>If yes, number of blood transfusions_____ |
| 3. | Any history of major infection?<br>Yes ☐ No ☐<br><br>If yes, which one?<br>Tuberculosis ☐ (Diagnosis via CXR ☐ /Sputum AAFBs ☐ /Geneexpert ☐<br>Sepsis ☐<br>Other, please state_____ |

| **2b: Haemodialysis details** | |
|---|---|
| 1. | Type of vascular access (current)<br>a. Nontunnelled (temporary) haemodialysis catheter<br>Yes ☐ No ☐<br><br>Duration _____(months/years)<br><br>b. Tunnelled cuffed (permanent) haemodialysis catheter<br>Yes ☐ No ☐<br>Duration_____<br><br>c. Arteriovenous fistula<br>Yes ☐ No ☐<br>Location: Brachiocephalic Yes No<br>Radiocephalic Yes No<br>Other (State) _____<br>Duration_____<br><br>d. Arteriovenous graft<br>Yes ☐ No ☐<br>Duration_____ |
| 2. | Any previous vascular access? Yes ☐ No ☐ |

If Yes, document the type, duration and reason for halting use of the vascular access.

| Previous type of Vascular Access | Dates Used/Duration | Reason why vascular access was no longer used |
|---|---|---|
| | | |
| | | |
| | | |

3. Any documented vascular access complications? Yes ☐ No ☐

If Yes, which one?

a. Vascular access-related infection ☐
b. Thrombosis ☐
c. Stenosis ☐
d. Other ☐

If other please state _____

If vascular access-related infection, which one?

a. Exit site infection ☐
b. Tunnel infection ☐
c. CRBSI ☐

4 Any documented dialysis-related complications? Yes ☐ No ☐

If Yes, please document which one _____

5 Total duration on haemodialysis at the Centre (from haemodialysis initiation to mortality/loss to follow up or transfer out) _____months

**Part 3. Documented drug history**

1. Any documented medications for Anaemia (Erythropoeitin, Iron)? Yes ☐ No ☐

If Yes, please state the name of the medication, dose and duration on the treatment:

| Drug name | Dose | Duration on treatment |
|---|---|---|
| | | |
| | | |
| | | |
| | | |

**Part 4. Documented laboratory parameters**

| | |
|---|---|
| 1 | Please document the average reading for the following parameters (one reading per quarter of the year under review):<br>a. Haemoglobin _____g/dl<br>b. Serum calcium_____mmol/l<br>c. Serum phosphate_____mmol/l<br>d. Albumin _____g/l<br>e. PTH_____ng/ml |

**Part 5. Outcomes at 1 year**

| | |
|---|---|
| 1. | Date 1 year from initiation of dialysis<br>dd mm yy<br>☐☐ ☐☐ ☐☐ |
| 2. | Status at 1 year from initiation of dialysis<br>a. Alive Yes ☐ No ☐<br>b. Dead Yes ☐ No ☐<br><br>If Yes, please record date mortality occurred ☐☐ ☐☐ ☐☐ dd mm yy )<br><br>If Yes, please state cause of death if documented_____<br>c. Lost to follow up Yes ☐ No ☐<br>If yes, loss to follow up after what duration on dialysis_____<br><br>d. Transferred to another dialysis centre Yes ☐ No ☐<br><br>If yes, reason for transfer _____<br><br>If yes, new dialysis centre_____ |
| | |

## 18.2 APPENDIX II: ETHICAL APPROVAL- KNH/UON ERC

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COLLEGE OF HEALTH SCIENCES
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Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/286

16th August , 2021

Dr. Mary Nigandi Kubo
(Clinical Nephrology Fellow)
East African Kidney Institute
School of Medicine
College of Health Sciences
University of Nairobi

APPROVED
16 AUG 2021

Dear Dr. Kubo

**RESEARCH PROPOSAL: COMPARISON OF ONE YEAR OUTCOMES AND CLINICAL CHARACTERISTICS AMONG HIV POSITIVE AND HIV NEGATIVE PATIENTS ON MAINTENANCE HAEMODIALYSIS AT THE KENYATTA NATIONAL HOSPITAL AND NAIROBI HOSPITAL RENAL UNITS (P203/03/2021)**

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 16th August 2021 – 15th August 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal).
vii. Submission of an executive summary report within 90 days upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

**PROF. M.L CHINDIA**
**SECRETARY, KNH- UoN ERC**

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Director, East African Kidney Institute, UoN
Supervisors: Prof. Seth Oumah McLigeyo, Dept.of Clinical Medicine & Therapeutics, UoN
Prof. Joshua K. Kayima, Dept.of Clinical Medicine & Therapeutics, UoN
Dr. Benjamin M. Wambugu, Consultant Physician & Nephrologist, KNH
Dr. Khalida B. Soki, Consultant Physician & Nephrologist, Kenya Renal Association

## 18.3 ETHICAL APPROVAL- NAIROBI HOSPITAL ERC

THE NAIROBI HOSPITAL

Our Ref. TNH/ADMIN/CEO/DMSR/26/05/21

26 May 2021

Dr. Mary Nigandi Kubo
Nephrology Fellow
East African Kidney Institute
University of Nairobi

Dear Dr. Kubo,

RE: **OUTCOME OF MAINTENANCE HAEMODIALYSIS AMONG HIV POSITIVE AND HIV NEGATIVE PATIENTS AT THE KENYATTA NATIONAL HOSPITAL AND THE NAIROBI HOSPITAL RENAL UNIT- (TNH-ERC/DMSR/PR/011/21)**

Reference is made to your request to carry out the above study at The Nairobi Hospital. We are pleased to advise that approval has been granted.

In line with the Research Projects Policy, you will be required to submit quarterly update reports of the study to the Committee. You are also required to submit a copy of the final findings for the Committee's records.

Do note that information/data collected and potential findings shall not be in conflict with the Hospital's Confidentiality Clause which states that **"You will not without consent of the Association disclose any of its secrets or other confidential matters to anyone who is not authorized to receive them".**

Please note that this approval is valid for the period May 2021 to May 2022 and if an extension is required, an application to that effect should be made within 30 days of the expiry of this approval.

Yours sincerely,
For: The Nairobi Hospital

James Nyamongo
CHIEF EXECUTIVE OFFICER

c.c. Chairman, TNH-Ethics & Research Committee
Director, Medical Services & Research
Director, Nursing Services
Charge Nurse, Renal Unit

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