UNIVERSITY of RWANDA

COLLEGE OF MEDICINE & HEALTH SCIENCES

SCHOOL OF MEDICIN &PHARMACY

CAUSES OF ADMISSION OF HIV POSITIVE PATIENTS AT UNIVERSITY TEACHING HOSPITAL OF KIGALI-MECICAL WARDS

INVESTIGATOR: Dr NIYIGENA Olivier

SUPERVISOR: Dr Leway KAILANI, Infectious disease specialist

CO-SUPERVISORS: Dr Menelas NKESHIMANA MBBS, MMED

A review submitted to The College of Medicine and Health Sciences, School of Medicine and Pharmacy in partial fulfillment of the requirements for the award of a Masters of Medicine in Internal Medicine, University of Rwanda.

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DECLARATION

I, Olivier NIYIGENA, to the best of my knowledge hereby declare and certify that the work presented in this dissertation entitled **" Causes of Admission of HIV positive Patients at University Teaching Hospital of Kigali-Medical Wards "** is entirely my own and original work and it has never been presented or submitted in whole or in part to any other university. It is submitted to the College of Medicine and Health Sciences in partial fulfillment of the academic requirements for the award of Masters of Medicine in Internal Medicine, University of Rwanda

Olivier NIYIGENA

Signature .....Date...14.1.61.19

Approved for submission by

SUPERVISORS:

Leway KAILANI, MD

Signature.....Date.....14/6/19

Menelas NKESHIMANA, MD

Signature.....Date.....

DEDICATION

To the almighty God”

To my wife” Florence DUSABIMANA”

To my dear Parents

To my dear brothers

To my Supervisors

To my Patients

This work is dedicated with great pleasure

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To God the Almighty, source of life, knowledge and wisdom.

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ABSTRACT

Background

There is limited information concerning the characteristics of HIV positive patients admitted to UTHK as well as the causes and patterns of admissions. HIV has various adverse physical and social economic effects on individual patients, their families and to the country in general.. The aim of our study was to determine the causes of admission of HIV positive patients in medical wards at UTHK, their In-hospital length of stay and their outcome

Methods

This was a prospective cohort study on HIV positive patients admitted in medical wards at UTHK between February 2018 and February 2019. Data was collected on patients' demographics, diagnosis, In-hospital length of stay and In-hospital outcome. Patients were followed up from their admission to their discharge.

Results

Among 225 participants, 52.4 % were male and the median age was 42years. The majority were in 2nd and 3rd category of Ubudehe; 39.1% and 36% respectively. The median CD4 count was 99 while the median viral load was 1146. Pulmonary TB was the most prevalent opportunistic infection (22.7%), followed by pneumonia (15.6%) and cryptococcal meningitis (10.7%). The mean In-hospital stay was 16 days for those discharged alive and 20 days for those who died in hospital. The overall mortality was 23% and 77% were discharded alive.

Conclusion

Despite the nationwide availability of ART, HIV opportunistic diseases continue to be the major cause of admissions of HIV positive patients (72.7%). Deaths related to those HIV opportunistic diseases are also substantial (77.7%).

KEYWORDS(MeSH): Causes, Admission, HIV, UTHK

ACRONYMS AND ABBREAVIATIONS

AIDS	: Acquired Immuno-Deficiency Syndrome
AML	: Acute Myeloid Leukemia
ART	: Anti Retroviral Therapy
CD4	: Cluster of Differentiation 4
CDC	: Center for Disease Control
CMHS	: College of Medicine and Health Sciences
ELISA	: Enzyme Linked Immuno-Sorbent Ass
HIV	: Human Immunodeficiency Virus
Ig G	: Immunoglobulin G
Ig M	: Immunoglobulin M
IRB	: Institutional Review Board
RBC	: Rwanda Biomedical Center
RNA	: RiboNucleic Acid
STI	: Sexually Transmitted Infection
USA	: United States of America
UTHK	: University Teaching Hospital of Kigali
WHO	: World Health Organization

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I.1. Background to the Study

I.1. Definition

In the summer of 1981, CDC reported unusual cases of pneumonia with pneumocystis jiroveci in Los Angeles in five gays who were healthy before and Kaposi's sarcoma in 26 previously healthy gays in both New York and Los Angeles. HIV virus was first isolated in a patient with lymphadenopathy in 1983 and one year later in1984 it was shown that it is the real causal agent of AIDS. [1] In Rwanda the first case of HIV was also reported in 1983.[2]

WHO's case definition of HIV infection has:

1) A positive result on a HIV antibody test confirmed by a positive result on a second, different HIV antibody test and/or ;
2) A positive virologic test confirmed by a second virological test .[3]

AIDS is a result of a chronic HIV infection. It is defined as CD4 less than 200cells/microL or the existence of any AIDS defining illness irrespective of CD4 count. When the CD4 count is less than 50 cells/microL, the word "advanced HIV infection" is used. [3]

I.2 Etiologic agent

AIDS is caused by Human Immunodeficiency Virus (HIV) which belongs to the family of human retroviruses (retroviridae) and to the subfamily of lentiviruses. There are two types of HIV; HIV-1 and HIV-2.

HIV-1 is responsible for most of the infection with HIV in the world including the USA and it has different groups including M,N,O,P. HIV-1 group M is the main cause of AIDS pandemic.

HIV-2 has groups from A to G and most of the patients with HIV-2 are found in West Africa where it was first identified in 1986. [1]

I.3 Transmission

Both HIV 1 and HIV 2 are transmitted in the same ways. These include sexual intercourse, contact with infected blood (eg: blood transfusions, shared needles), childbirth, breastfeeding. Kissing, hugging, shaking hands, sharing personal objects are not known to transmit HIV infection. [4]

The ways of acquisition of HIV infection are differently distributed worldwide. In USA male to male sexuality and use of intravenous drugs are responsible for more than half of cases. [5]

In low and middle income countries, penile-vaginal sex accounts for 70 to 80 % of HIV infection; whereas either iv-drug use or peri-natal transmission are responsible for 5 to 10% and male to male sexual intercourse occupy a smaller but increasing amount of cases. [6]

I.4 Risk factors

- Viremia of the infected person: The higher the viral load of the source, the higher the risk of transmission. [7]
- Sexual behavior: The risk of acquiring HIV infection is increased by different sexual factors; these include multiple sexual partners, non use of condom, traumatic sex with injury to the mucosa, non protected anal sex especially in a receptive partner. [8]

- Lack of circumcision: Uncircumsised males partners have a higher risk of getting HIV infection than those who are circumcised.[9]
- Sesually transmitted infections: The presence of a STI increases the risk of both transmission and acquisition of HIV infection. This risk is higher in ulcerative STIs. [7]

I.5 Epidemiology

HIV continues to be a major global public health issue, having claimed more than 35 million lives so far. In 2016, 1.0 million people died from HIV-related causes globally.

There were approximately 36.7 million people living with HIV at the end of 2016 with 1.8 million people becoming newly infected in 2016 globally. [4]

1.1 million People in the US are living with HIV, and 1 in 7 of them don't know it. In 2015, 39,513 people were diagnosed with HIV infection in the United States. Gay and bisexual men accounted for 82% (26,375) of HIV diagnoses among males and 67% of all diagnoses.

The WHO African Region is the most affected region, with 25.6 million people living with HIV in 2016. The African region also accounts for almost two thirds of the global total of new HIV infections. [4]

It is estimated that currently only 70% of people with HIV know their status. The remaining 30% – or 7.5 million people – need to access HIV testing services. In 2016, 19.5 million people living with HIV were receiving ART globally. [4]

In 2015, Rwanda had 3% estimated HIV prevalence among adults 15–49 Years. The prevalence was 4% for women and 2% for men. HIV prevalence was higher in urban areas (6%) than in rural areas (2%). The capital Kigali had 6% of HIV prevalence while south province had 3% and 2% for each of other provinces. [10]

I.6 Pathogenesis

There are many target cells of HIV virus. These include dendritic cells, macrophages and CD4+ T cells. HIV 1 is mainly transmitted via anogenital mucosa. Its envelope has a glucoprotein(GP120) that attachs to the CD4 molecule of the dendritic cells which can also be found in cervicovaginal epithelium, tonsilar and adenoidal tissue. [11]

HIV spreads by fusion of infected cells with CD4+ T cells. HIV can be found within 2 days post mucosal explosure in the regional lymph nodes, and in plasma within the following 3 days. [11]

I.7 Clinical features

Approximately 10 to 60% of patients in early stage of HIV infection are asymptomatic. [12]

The incubation period in people with acute symptomatic HIV infection varies between 2 to 4 weeks. Acute HIV infection can manifest with different symptoms including fever, adenopathy, headache, diarrhea, weight loss, sore throat, skin rash, arthralgia, myalgia, fatigue [13] [14]

As the CD4 decline there are a number of clinical conditions "non-aids defining illnesses" that can happen. Even if they can appear or get worse with AIDS-stage, a greater number of them may

present even at CD4 above 200cells/microL. These include thrush, oral hairy leukoplakia, herpes zoster, peripheral neuropathy, idiopathic thrombocytopenia purpura. [15]

If the CD4 count get lower than 200cells/microL the majority of AIDS-defining illnesses start to occur although they may appear earlier. These include:

Extrapulmonary cryptococcosis, including meningitis

Disseminated non-tuberculous mycobacterial infection

Progressive multifocal leukoencephalopathy (PML)

Candida of trachea, bronchi, or lungs

Chronic cryptosporidiosis (with diarrhea)

Chronic isosporiasis

Visceral herpes simplex infection

Cytomegalovirus (CMV) infection (retinitis or infection of organs other than liver, spleen, or lymph nodes)

Disseminated mycosis (eg, histoplasmosis, coccidiomycosis)

Recurrent non-typhoidal salmonella bacteremia

Lymphoma (cerebral or B cell non-Hodgkin) or other solid HIV-associated tumors

Invasive cervical carcinoma

Atypical disseminated leishmaniasis

Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy [3]

Few people with chronic HIV infection in the absence of ART remain asymptomatic with good CD4 count and low viral load. They are called “long-term nonprogressors”. A smaller number of them has undetectable viral load (<1copy/mL) even with ultrasensitive diagnostic testing. They are named” elite controllers” All of these patients have follow-up testing at 3 to 6 months intervals to be sure that they have not immunologically advanced. [11]

In 2008 there was a patient called Timothy Ray Brown known as" The Berlin Patient "born in Washington who was also known to have HIV since 1995 on ART. In 2006 he was diagnosed with AML. In 2007 and 2008 respectively Thimothy underwent stem cell transplantation from a donor who was homozygous for delta 32 mutation on CCR5 receptor (people with this mutation are resistant to HIV). He stopped ART after the 1st transplant and his follow up revealed that HIV was not detectable and his CD4 increased. He is considered cured. [16]

In March 2019 the anonymous patient known as" The London patient" was diagnosed with HIV infection in 2003 and had developed Hodgkin's lymphoma. In May 2016 a stem cell transplant from a donor with the CCR mutation was performed in order to treat his cancer. He stopped ART since September 2017 and now it is 18 months that he is free from HIV virus. [17]

I.8 Diagnosis

Screening tests

Antibody-only tests:

In initial screening of HIV infection, ELISA tests are used. These tests can detect antibodies (IgM & IgG) against both HIV 1&2 as early as 3 weeks following contact with the virus. They can give the results in 1 to 3 hours depending on how the test is designed in a laboratory setting. Their sensitivity and specificity is around hundred percent in diagnosing a chronic HIV infection. A positive result need to be confirmed by HIV1/HIV2 differentiation test. [18] [19]

There are also rapid diagnostic tests that can give results in a short time as 20min; these are good in a community setting or for people who rarely seek care. The sensitivity of rapid tests decreases if oral fluids are used for testing. [20]

Combination HIV antigen and antibody (fourth generation combination) tests:

These tests are able to detect both HIV antibodies and HIV P24 antigen.[21] Their sensitivity and specificity is also around 100% in chronic infection with HIV but they have an advantage of detecting acute HIV infection to the extent of 80% that antibody-only tests miss. [22]

Confirmatory tests

HIV-1/HIV-2 differentiation immunoassay:

These are used to confirm the positive result provided by a 4th generation combination test but also to differentiate between HIV-1 and HIV-2. Their sensitivity is approximately 99 to 100% and can give the result around 20min. [23]

Viral detection:

The most commonly used methods detect HIV-RNA or HIV P24 antigen

The use of viral detection as a diagnostic assay is indicated in:

- The diagnosis of a neonatal HIV infection
- The evaluation of patients with an indeterminate serological test
- The evaluation of suspected acute HIV infection in someone who may be in the window period of HIV sero-conversion.[24] [25]

I.9 Treatment

Although HIV/AIDS has no curative treatment, only after 3 years of the use of antiretroviral medications the rates of admissions and mortality by the disease have significantly reduced 60 to 80% [26]

HIV related morbidity and mortality has continued to reduce during the past ten years due to availability of antiretroviral treatment. People dying from HIV associated diseases have decreased to 43% since the year 2003 [27]

In 2015 WHO implemented a new guideline of treating everyone living with HIV infection without considering his/her CD4 count or clinical status. [28]

I.10 Prognosis

Without antiretroviral therapy (ART), people infected with HIV who have CD4 <50 cells/microL have a median survival of 12 to 18 months.[29]

Even though there is no definitive treatment for HIV, the use of antiretroviral therapy has dramatically changed its natural history to the extent that those infected with HIV in the absence of significant comorbidities if treated appropriately have a live expectancy approaching that of the general population. [30]

In Rwanda, data from 1997 to 2007 and 2008 to 2011 were analyzed in a retrospective observational cohort study about the life expectancy of HIV positive patients. It was found that from 1997 to 2007 at the age of 20 the life expectancy was 20.4 additional years. For the time between 2008 and 2011 the life expectancy has raised to 25.6 additional years. The disease burden trended down significantly especially from 1998 to 2008 [31] [32].The observed improvement in outcome was achieved from the correct identification of other issues related treatment approach such as addressing stigma to improve adherence [33]

I.2 Problem statement

Despite the fact that the government of Rwanda put much effort in HIV/AIDS prevention, free of charge access to ARVs to those who are infected and their close follow up; anecdotally an increasing number of HIV positive patients who are attending the health facilities with advanced HIV infection.

Data concerning the characteristics of HIV positive patients admitted to KUTH as well as the causes and patterns of admissions remain limited.

There is no study done yet in our setting to clarify if HIV positive patients are hospitalized because of HIV opportunistic diseases or non opportunistic conditions.

I.3. Research question

What are the causes of hospitalization of HIV positive patients at UTHK from February 2018 to February 2019?

I.4. Research Objectives

I.4.1.General Objectives

To evaluate the causes of admission of HIV positive patients at UTHK from February 2018 to February 2019

I.4.2. Specific objectives

1. To assess the prevalence of in hospital HIV opportunistic diagnosis.
2. To assess the prevalence of in hospital HIV non opportunistic diagnosis.
3. To assess in hospital outcome
4. To assess in hospital length of stay

Chap II. LITERATURE REVIEW

II.1. Empirical Review

HIV infection is present worldwide; at the end of 2016 there were 36.7 million of people who were living with it all over the world. Two thirds (25 600 000) of these people live in Africa. [4]

Between 2001 and 2008 data about reasons of hospitalization of 11645 adults living with HIV and followed in 4 different HIV clinics is the USA were gathered. It was noticed that hospitalizations for AIDS defining illness had decreased from 6.7 to 2.7 per hundred people a year but they were associated with the longest mean duration of stay of 10.5 days. Non AIDS defining infections had not significantly changed. [34]

Data regarding hospitalizations of HIV positive patients in Winnipeg Canada were obtained from the year 2003 to 2010. 307 patients were found to have had 679 hospitalizations with a mean of 2.2 hospitalizations per patient. Their age was between 18 to 72 years with a mean of 41.9 years. Male patients were 59%. There were 56 patients admitted each year 72% had a stay less than 10 days. The commonest diagnosis at admission was pneumonia (37%), followed by soft tissue infections (9.6%), then sepsis that occupied 9.4%. Among pneumonias, community acquired one occupied 55%, 42% were unclassified and 3% was nosocomial. The diagnosis of pneumonia was linked with 31% of all hospital stays. The study also found that the average cost of medical care war increased in those who had very low CD4 count (<75 cells/mm3)[35]

Between January 2007 and May 2012, in Southern Brazil, a cross-section study was carried out on patients admitted in general hospital with aim of determining the leading cause of death among HIV positive patients. Among 230 patients recruited in the study, the most causes of hospitalization were opportunistic infections mainly involving nervous system, sepsis and acute respiratory system. Overall, mortality rate was 44.8% and prolonged hospital stay was defined as cause. [36]

During the years 2000 to 2012 evaluation of hospitalization rates and causes among HIV positive patients was done in a major Israeli HIV AIDS center. Hospitalization was considered as 24 hours and above hospital stay. HIV patients have increased from 521 to 1169 from the year 2000 to 2012.It happened 1676 hospital admissions (in 557 patients) during the period of the study. The average number of admissions per hospitalized patients was 3.39. AIDS defining illnesses related

hospitalizations have reduced from 46.9% to 16.1% in contrast to HIV unrelated hospitalization that raised from 31.3% to 60.1%. Lower CD4 count and increased age at diagnosis correlated with more admissions rates (especially for AIDS defining illnesses) and mortality. AIDS defining illnesses related hospitalization keep on declining although it is still greater than that of the general population. [37]

At Enugu state university of Science and Technology teaching hospital in Nigeria; they did a 5 year (January 2006 to December 2010) review determining the admission profile and pattern of medical cases. They used medical record registers to determine mortality and morbidity data by using ICD10 coding system. In 3835 analyzed cases , the male were predominant (59.6%) , mean age of 54.3. in 604 admitted patient with infectious diseases ,503(83.3%) patients had HIV/AIDS . 19.8% of total participants died ; among those admitted with HIV/AIDS 25.2% died. In general the highest mortality rate was observed in above 70 years old group. [38]

During the period between June 2012 and October 2013 a cross sectional study was conducted in public sector district hospital of Cape Town. 1018 hospitalizations were done and HIV status was checked in 99.5%. HIV positivity was 60.1% (609 patients). 585 patients (96.1%) were put in the study. Clinical status at 90 and 180 days say checked out and elements associated with mortality independently were determined. They found that newly diagnosed TB was the most frequent primary clinical diagnosis (196 patients=3.5%).

Other bacterial infections occurred in 100 patients (17.1%). Acquired AIDS defining illnesses other than TB occupied 10.9% (64 patients). By 90 days of follow up readmission rate was 29.9(175 patients) and mortality was 13.3 (78 patients). Major cause of death was TB (37.2%) followed by other AIDS defining illnesses (24.4%). Anemia, renal failure and Aids defining illnesses other than TB were independent predictors of death. [39]

In southwest Ethiopia, at Jimma University specialized hospital a retrospective study was done in 2008. They put 610 participants in the study with the mean age of 36 years. 35.7% of admitted participants were young (21-30years). They found that the predominant reasons of admission were severe community acquired pneumonia (22.8%) , all infectious and parasitic category (16.4%), and 13.1 % were found to have chronic meningitis as well as pyogenic infections. Overall there was a mortality rate of 12.6% in medical ward. The study concluded that there was no change over 16 years in terms of outcome among admitted HIV positive patients in medical ward. [40]

Between January 2005 and December 2006, there was a prospective cohort study conducted in an ambulatory HIV care clinic in western Kenya with the aim of determining the diagnosis at admission and the outcomes of HIV positive patients attending the clinic. 495 HIV positive patients were recruited with the mean age of 38 years. Preadmission CD4 count were <100 cells/ml in 53%. 30% died at median 44 days before admission and median of 41 days after initiating combined ART, the commonest cause of death were tuberculosis (27%) and meningitis (14%). Among the survivors the median admission duration was 8 days and 6 days in the deceased people. In comparison between those who died or recently started cART with lower CD4 count and the survivors they found that the most significant association was loss of follow up. Adherence to clinic appointment and initiation of cART prior to admission were found as independent predictors of survival. The researchers concluded that even if there was a higher mortality rate observed in HIV positive patients, cART initiated prior to admission was associated with higher survival rate. [41]

In Rwanda when the first cases were reported in 1983, they presented with common opportunistic diseases including esophageal candidiasis, cryptococcal meningitis, genital herpes, kaposi's sarcoma, pulmonary and disseminated tuberculosis.[2]

Chap III. METHODOLOGY

III.1 Study type

A prospective cohort study among adults HIV positive patients admitted in UTHK, medical wards.

III.2 Study site and period

The study has been conducted in University Teaching Hospital of Kigali located in Nyarugenge district in the city of Kigali. It has been conducted during the period of twelve months from February 2018 until February 2019.

UTHK has been selected because it is located in Nyarugenge district where there is a high number of sexual workers, remember that RBC has published that one in two sexual workers has HIV infection and also MUHIMA district hospital located in Nyarugenge district does not have internal medicine department. This increases the number of HIV positive patients attending UTHK.

In addition UTHK is among the tertiary hospitals with facilities to make accurate diagnosis.

And also we have limited means with small amount of money that is why we have chosen to conduct this study in an area where a great number of HIV positive patients live and so most likely to also to have admission if needed.

IV.3 Study population

Our study has been carried out on HIV positive patients admitted to UTHK

III.4 Inclusion criteria

- ✓ Adults (≥21 years of age)
- ✓ Willing to participate in the study by signing a consent form
- ✓ Admitted to KUTH in a period between February 2018 and February 2019

III.5 Exclusion criteria

Refusal to participate in the study by not signing a consent form.

HIV negative patients admitted in medical ward/UTHK

III.6 Sample size

The sample size calculation in this study was assisted by the simplified formula provided by Yamane (1967). [42]

$$n = \frac{N}{1+N(e)^2}$$

$$n = \frac{512}{1+512(5\%)^2}$$

$$n = 224.56 \approx 225$$

Where N=Accessible total population of interest with the period of the study

e= allowed error term (e=5%)

III. 7 Description of the study

Our study looked at adults HIV positive patients admitted at UTHK medical wards from February 2018 to February 2019 who accepted to participate in the study by signing a consent form.

The researcher enrolled the patients into the research at or shortly after their admission to evaluate the complaints, and continued to follow them during their hospitalization to evaluate the duration of stay in the hospital, the diagnosis and the outcome.

III.8 Ethical consideration

The validity of the study has been assessed by Faculty of Medicine staff members who have also provided relevant advice to be observed throughout the study. Permission to carry out this study was obtained from CMHS/IRB. The purpose of this study was explained to the participant before

being included in the study. The nature of the study, its benefits to the participant has been explained in a language easily understood. A consent form was signed by each participant before inclusion. Participants are free to participate and to withdraw from the study. Data were held confidential and no data will be made public unless the participant's identification is removed.

III. 9 Plans for utilization and dissemination of results

A research report will be submitted to the University of Rwanda as a partial fulfillment of the Master of Medicine in Internal Medicine. This work will also be submitted to the hospitals as recognition to have hosted the study. It may also be presented as an oral presentation at research days. Finally, findings of this research may be submitted to international journals for academic and clinical advancements.

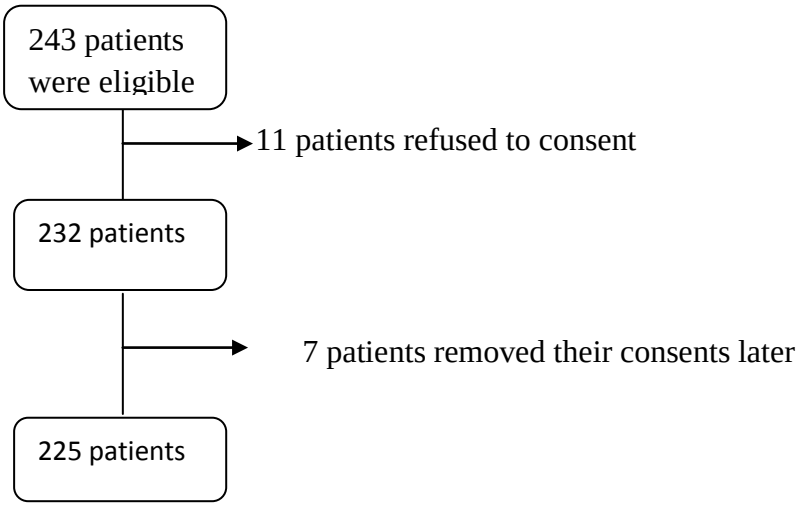
III.10 Data recording and analysis

Data collected from questionnaire for each participant were entered twice and validated in EpiData version 3.1 whereas Statistical analyses were performed with SPSS version 16. Chi-square test and multivariate logistic regression analysis was used to determine the association and correlation between variables. P-values less than 0.05 were considered to indicate a significant association between variables; then the results were presented in tables and graphs where applicable. Only participants with complete records (completed questionnaires) were included in the final analyses.

IV.RESULTS

IV.1.1. Introduction

In our study we have a total number of 243 patients eligible for the study. 11 patients of them did not consent for study participation. 7 patients changed their mind later and requested to be removed from the study.



IV.1.2. Demographic Profile of Respondents

Table 1: Association between demographic characteristics and outcome

Variables		Outcome		Total	Pvalue
		Discharged alive	Died in hospital		
Sex	Male	86(49.7%)	32(61.5%)	118(52.4%)	0.134
	Female	87(50.3%)	20(38.5%)	107(47.6%)	
Education level	None	27(15.6%)	11((21.2%)	38(16.9%)	0.122
	Primary	77(44.5%)	25(48.1%)	102(45.3%)	
	Vocational training	9(5.2%)	0(0.0%)	9(4.0%)	
	Secondary	48(27.7%)	16(30.8%)	64(28.4%)	
	University	12(6.9%)	0(0.0%)	12(5.3%)	
Ubudehe Category	category 1	45(26.0%)	11(21.2%)	56(24.9%)	0.771
	category 2	67(38.7%)	21(40.4%)	88(39.1%)	
	category 3	61(35.3%)	20(38.5%)	81(36.0%)	

Employment Status	Unemployed	72(41.6%)	14(26.9%)	86(38.2%)	**0.012***
	Self-employed(formal)	64(37.0%)	18(34.6%)	82(36.4%)	
	Self-employed(informal)	22(12.7%)	13(25.0%)	35(15.6%)	
	Public employed	11(6.4%)	5(9.6%)	16(7.1%)	
	Retired	4(2.3%)	0(0.0%)	4(1.8%)	
	Student	0(0.0%)	2(3.8%)	2(0.9%)	
Marital Status	Single	41(23.7%)	3(5.8%	44(19.6%)	**0.003***
	Married	57(32.9%)	21(40.4%)	78(34.7%)	
	Divorced or separated	44(25.4%)	23(44.2%)	67(29.8%)	
	Widow	31(17.9%)	5(9.6%)	36(16.0%)	
HIV stage	stage1	0(0.0%)	1(2.4%)	1(0.5%)	**0.001***
	stage2	9(6.2%)	1(2.4%)	10(5.3%)	
	stage3	96(65.8%)	15(35.7%)	111(59.0%)	
	stage4	41(28.1%)	25(59.5%)	66(35.1%)	
Age Category	20-40	89(51.4%)	26(50.0%)	115(51.1%)	**0.032***
	40-60	71(41.0%)	25(48.1%)	96(42.7%)	
	60-80	11(6.4%)	1(1.9%)	12(5.3%)	
	80-100	2(1.2%)	0(0.0%)	2(0.9%)	
Hb Category	2-6	10(5.8%)	4(7.7%)	14(6.2%)	**0.000***
	6-12	111(64.2%)	35(67.3%)	146(64.9%)	
	12-18	52(30.1%)	13(25.0%)	65(28.9%)	

		Outcome			
		Discharged alive	**Died in hospital**	**Total**	**Pvalue**
cd4 at current admission	1-500	114(84.4%)	32(88.9%)	146(85.4%)	*0.051*
	500-1000	15(11.1%)	1(2.8%)	16(9.4%)	
	1000-1500	6(4.4%)	3(8.3%)	9(5.3%)	
Viral load at	1-100000	113(96.6%)	30((100.0%)	14397.3%)	**0.001***
	100000-200000	2(1.7%)	0(0.0%)	2(1.4%)	

current admission	200000-300000	2(1.7%)	0(0.0%)	2(1.4%)	
Number of children	0-3	127(73.4%)	41(78.8%)	168(74.7%)	**0.003***
	3-6	43(24.9%)	8(15.4%)	51(22.7%)	
	6-9	3(1.7%)	3(5.8%)	6(2.7%)	

Source: **Primary data**, 2018

*The association is significant at 5% standard level of significance

No quantifiable socio-demographic profile of study participants, they were matched for sex, education level, ubudehe category, employment status, marital status and HIV clinical stage.

There was no significant difference in sex. Most of the participants had primary level of education (45.3%) followed by secondary level (28.4%) and 16.9% had not been at school. It is noticed that the majority of the participants were in the 2nd and 3rd ubudehe category (39.1),(36%) respectively. 38.2% were unemployed and 36.4% were self-employed with a formal activity. Most of the participants were married (34.7%) but considering the fact of living alone (single, divorced/separated, widowed); these groups occupied 65% of all participants. The clinical HIV stage 3 and 4 were most prevalent with percentages of 49.3% and 29.3% respectively.

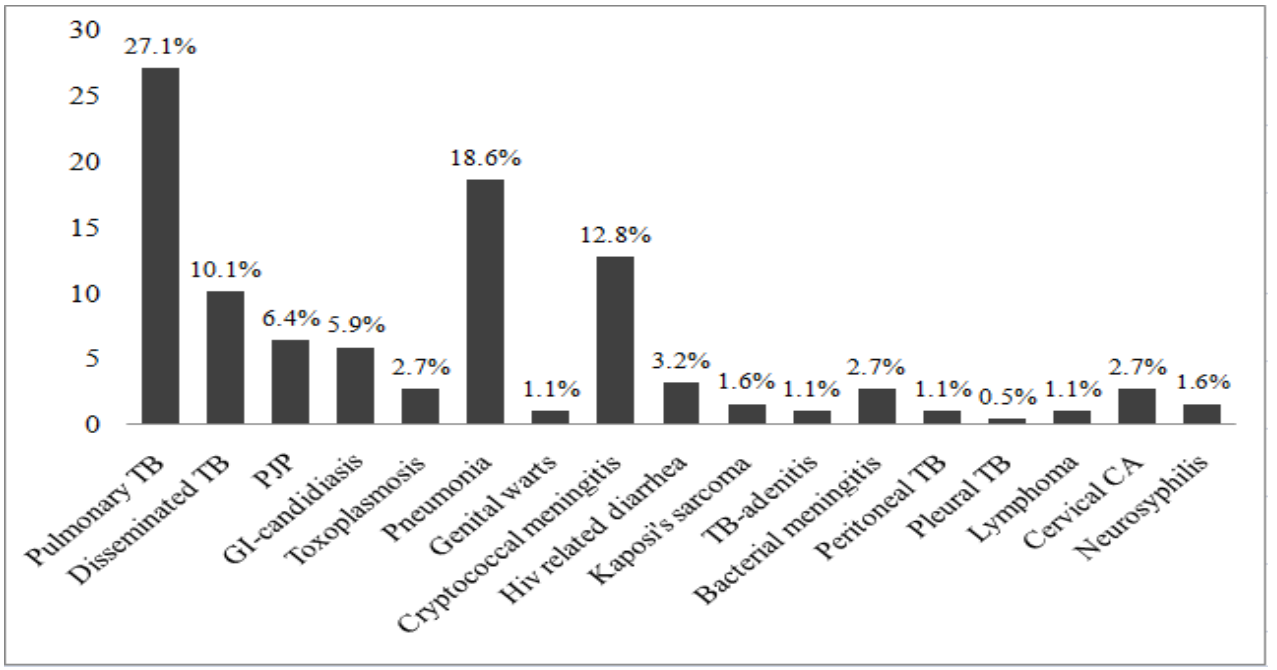
Using the Chi Square test of independence to measure the association of each variable with the outcome it was observed that employment status (P value=0.012), marital status (P value=0.003) and HIV clinical stage (P value=0.001) had association with the outcome.

Quantifiable socio-demographic profile of the study participants, they were matched for age, hemoglobin, CD4 and viral load at admission and number of children. It was observed that the mean age was 42 years and the mean hemoglobin was 10 g/dl with the mean number of children being 2.2. The median CD4 at admission was 99 with a median of viral load being 1146.

Using the Chi Square test of independence to test the association of each variable with the outcome, it was noticed that age (P value=0.032), hemoglobin (P value=0.00), viral load (P value=0.001) and number of children (P value=0.003) were associated with the outcome; hemoglobin and viral load playing the most significant role to outcome.

IV.1.3.Assessment of the prevalence of in hospital HIV opportunistic diseases

Figure 1: Prevalence of in hospital HIV opportunistic diseases

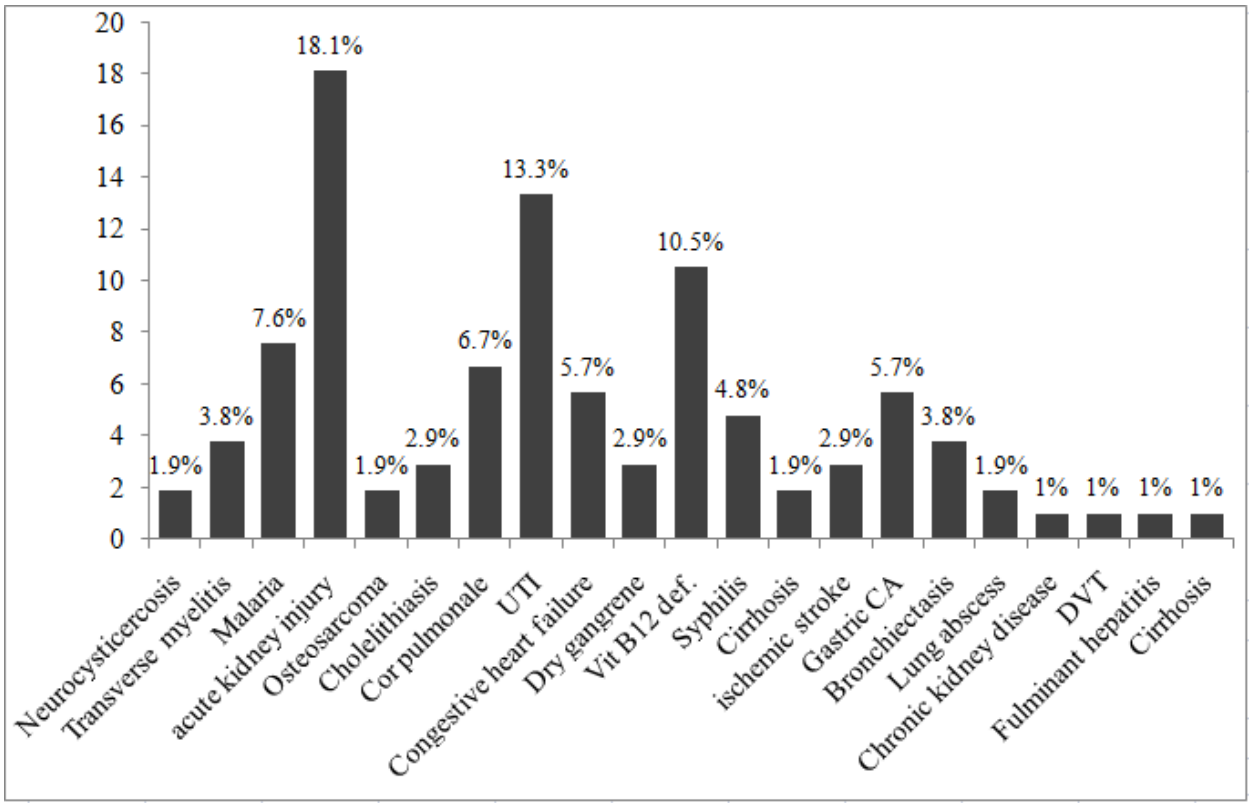


Source: **Primary data**, 2018

This figure shows different opportunistic diseases and their prevalence. It was found that pulmonary tuberculosis is the most prevalent opportunistic disease (22.7%). If the percentages of all forms of tuberculosis are added we notice that tuberculosis alone occupies a third (33.3%) of all of the opportunistic diseases. Pulmonary tuberculosis is followed by pneumonia (15.6%) and cryptococcal meningitis (10.7%).

IV.1.4.Assessment of the prevalence of in hospital HIV non opportunistic diseases

Figure 2: Prevalence of in hospital HIV non opportunistic diseases



Source: **Primary data**, 2018

This table shows different non opportunistic diseases and their prevalence. It was seen that acute kidney injury was the most prevalent (8.4%); followed by urinary tract infection (6.2%), then vitamin B12 def. (4.9%) with malaria occupying 3.6%.

IV.1.5.Assessment of in Hospital Length of Stay

Table 1: Comparison of Length of Stay between Discharged alive and Died in hospital

Outcome	N	Mean stay	Std. Deviation	Std. Error Mean
Discharged alive	173	16.2428	11.14539	.84737
Died in hospital	52	20.5000	16.76305	2.32462

Source: **Primary data**, 2018

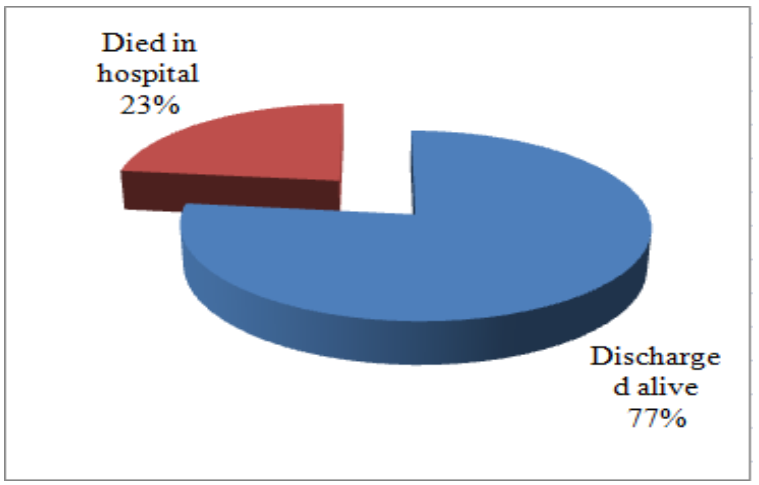
Table 2: Distribution of respondents with regard to Hospital Stay and Outcome

Days of stay	Outcome		Total
	Discharged alive	Died in hospital	
1-10	58(25.8%)	20(8.9%)	78((34.7%)
10-20	67(29.80%)	15(6.70%)	82(36.40%)
20-30	34(15.10%)	5(2.20%)	39(17.30%)
30-40	7(3.10%)	3(1.30%)	10(4.40%)
40-50	1(0.40%)	3(1.30%)	4(1.80%)
50-60	6(2.70%)	6(2.70%)	12(5.30%)
	173(76.90%)	52(23.10%)	225(100.00%)

Source: **Primary data**, 2018

This table shows the hospital length of stay and outcome cross tabulation. We notice that the mortality was higher among those who spent less days and it was decreasing with increased length of stay.

Figure 3: Assessment of in hospital outcome



Source: **Primary data**, 2018

It has been observed that 173 participants (77%) were discharged alive and 52 participants (23%) died in hospital.

IV.2. Discussion of Findings

In our study it has been observed that there is no significant difference between males and females (M:F ration=1.1); this is similar to a study done by A Akinkuotu et Al 2011 in Lilongwe on in hospital mortality rates and HIV where 50.8% of the participants were males and 49.2% were females. The similar results have been observed also in the study done by Keren Mahlab-Guri et Al called hospitalizations of HIV patients in major Israel HIV/AIDS center during the years 2000-2012 where male participants were 55.8% , whereas females were 44.2% (M:F ration=1.2)

The almost same gender proportions have been seen in the study called HIV-related medical admissions to a South African District done by Graeme Meintjes et Al where male to female ration was 0.7.

In some other studies either males or females were higher probably due to HIV distribution among those groups depending on the particular country.

In our study, the median age was 40years. This is similar to what was found in multiple other studies including the one done A Akinkuotu et Al 2011 in Lilongwe on in hospital mortality rates and HIV where the median age was 36.5; same results were found in the study called admission characteristics, diagnoses and outcomes of HIV-infected patients registered in an ambulatory HIV care program in western Kenya done by A.M. Siika et Al where the mean age was 38 years and lastly the mean age was 40 years in the study called causes of admission of AIDS patients in Southern Brazil from 2007-2012 done by Anna Caroline Guerro et Al.

These findings coincides with the ones of Rwanda Demographic Health Survey of 2014-2015 where the ages from 35-49 occupy the greatest prevalence in men and women.

It was noticed that in our study the majority of the participants were in the second and third ubudehe category, making 39.1% and 36% respectively. This reflects the usual nationwide prevalence of ubudehe categorization in which according to the ministry of local governance report of 2016 the second and third ubudehe category are the majority in the country occupying 29.8% and 53.7% respectively.(31)

In our study the married participants were 35% and the unmarried (single, divorced/separated, widowed) ones occupied 65%. This is was similar to study called causes of admission of AIDS

patients in Southern Brazil from 2007-2012 done by Anna Caroline Guerro et Al. where the married proportion was 37% and the unmarried was 66%.

These above results correlates with the findings of the RDHS 2014-2015 where 15% of the widowed and 8% of divorced/separated were HIV + compared to married ones for whom the HIV positivity was at 3% only. This indicates that HIV is more distributed in people living alone. This can be explained by the fact that they are more prone to risky behaviors (multiple sexual partners, unprotected sex, drug abuse etc).

In our study a great number of participants were in HIV clinical stage 3 and 4 respectively occupying 49.3% and 29.3%. This can be caused by poor adherence to ART or common late consultations where people present with more advanced diseases or start seeking care in traditional healers which may worsen the patients' condition leading to even poorer outcome.

We observed that in our study the median CD4 count was 99 cells and the median viral load was 1146 copies. We think that this can be explained by the probable poor adherence to ART or to increasing HIV resistance to ART among our study participants correlating with the advanced HIV clinical stage at presentation. Our study did not look on these two hypothesis and they can be other topics of future researches.

The median hemoglobin level in our study was 9.8g/dl which is which is the same as the one found in the study called HIV-related medical admissions to a South African District done by Graeme Meintjes et Al where the median hemoglobin was 9.5. We think that the reasons of low hemoglobin in our study participants are multi-factorial (HIV related, nutritional, other co-morbidities like renal, heart, GIT diseases etc). This can also be another subject of future research.

In our study we have noticed that of all the diagnosis, tuberculosis was the most common one (33.3%); followed by pneumonia (20.9%) and meningitis (12.9). These results were similar to the ones found in the study called admission characteristics ,diagnosis and outcomes of HIV infected patients registered in an ambulatory HIV care program in western Kenya done by A.M. Siika where it was observed that tuberculosis was the most prevalent diagnosis with a percentage of 27%; followed by pneumonia (15%) and meningitis (11%).

The similar results were seen in the study called HIV-related medical admissions to a South African District done by Graeme Meintjes et Al where tuberculosis was the most prevalent diagnosis (33.5%), followed by other bacterial infections then meningitis which occupied (15%).

In the above stated study done in southern Brazil tuberculosis was also the most common diagnosis among hospitalized HIV patients followed bacterial and fungal infections (PJP, candidiasis, and cryptococcosis)

According to these results, HIV opportunistic diseases occupy the majority of all diagnoses in HIV positive patients admitted despite ART.

No opportunistic diagnoses occupied 27.3% of all diagnoses in our study. This was almost similar to the findings of the study called HIV-related medical admissions to a South African District done by Graeme Meintjes et Al where non HIV related diagnosis were around 40%.

Although these diagnoses are not recognized as opportunistic diseases, for some of them HIV could have contributed to their occurrence. Eg: heart diseases, stroke, DVT, gangrene etc. This means that the proportion of HIV non related diseases might be even lower.

It has been noticed in our study that 173 participants (77%) were discharged alive and 52 participants (23%) died in the hospital.

Similar mortality results were seen in the study called HIV-related mortality at a district hospital in Botswana by Melissa et Al where the mortality among HIV positive patients was also 23%.

The same results again were remarked in the study done by Keren Mahlab-Guri et Al called hospitalizations of HIV patients in major Israel HIV/AIDS center during the years 2000-2012 where mortality rate was 20.8%.

The almost similar other results have also been seen in the study called admission characteristics, diagnosis and outcomes of HIV infected patients registered in an ambulatory HIV care program in western Kenya done by A.M. Siika where it was 30%.

In our study, HIV opportunistic diseases related mortality was predominant with a percentage of 77.7% whereas HIV non opportunistic diseases mortality was 22.3%. Among HIV opportunistic diseases related mortality, pneumonia (community acquired and PJP) occupies 25.7%, followed by tuberculosis (18%) and cryptococcal meningitis (11.5%).

Among deaths related to HIV non opportunistic diseases, cardiac diseases occupy 26.9% followed by renal diseases (17.9%).

According to these results, HIV opportunistic diseases are still a major cause morbidity and mortality in HIV positive patients admitted to hospital despite ART.

We have observed that in our study the greatest proportion (8.9%) of those who died, had spent 1-10 days, followed by the proportion (6.7%) of those who spent 10-20 days in hospital.

It is also notable that the longer the hospital stay the less the mortality; meaning that the mortality was high during the first days of hospitalization. This can indicate that probably those who died presented late in a very critical condition that it was difficult to save them.

Overall there was no significant difference in the length of hospital stay between those discharged alive and those who died in hospital; 16 days and 20 days respectively.

IV.3. study limitations

Some of the diagnoses were made based on the clinical presentation or radiological findings but without bacteriological or autopsy confirmation. Although the treating clinicians made big effort to make the proper diagnoses, the correctness/accuracy of those unconfirmed diagnoses might be different.

V. Conclusion and recommendations

V.1. conclusion

Despite the nationwide availability of ART, HIV opportunistic diseases continue to be the major cause of admissions of HIV positive patients (72.7%). Deaths related to those HIV opportunistic diseases are also substantial (77.7%).

V.2. recommendations

As it was noticed that the majority of our study participants were in the third and fourth HIV clinical stage; reasons behind advanced HIV stages in our patients were not elucidated in this study. We suspect that some of the explanations might be that their adherence to ART is poor or they have developed resistance to ART. We recommend that further studies to assess the adherence to ART and resistance among our HIV positive patients should be conducted.

As it was observed that HIV related diagnosis and mortality are still significant among our patients, we recommend that the usual HIV prevention and treatment program should be reinforced in order to decrease HIV related morbidity and mortality.

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APPENDICES

Appendix 1: INFORMED CONSENT FORM

Dear Respondents,

Informed Consent form

My name is Dr Olivier NIYIGENA, I am a student of University of Rwanda (UR), pursuing Masters in Medicine (Mmed) in Internal medicine. I am conducting a research entitled:

Causes of admission of HIV positive patients at Kigali University Teaching Hospital.

HIV is one of the diseases found worldwide and the highest prevalence is found in Africa where about two thirds of total number of infected patients worldwide is found. The aim is to determine why HIV patients are still being admitted at KUTH at a high number. We want to know if they are admitted because of HIV related diagnosis or if they are admitted because of other medical problems not related to HIV despite having HIV infection. We want also to know the time they spend in the hospital and their outcome; weather discharged or died.

Participation in this study is voluntary and you have the right to withdraw from the study at anytime. However, we hope that you will participate in this study since it will help us to know if the majority of HIV positive admissions are related to HIV itself or not. If found that they are HIV related we will see how HIV care can be improved so as to decrease HIV related admissions, and improve the overall quality of life. Whatever information you provide will be kept strictly confidential and no reference to your name or other family members will made anywhere. We do not anticipate that there would be any harmful event that would occur with the study, but for any query you refer to the research committee (researchcenter@ac.ur.rw Tel +250 788563311).

Thank you.

I ……understand the explanation by …… about the risks and benefits of this research on causes of admission of HIV positive patients at KUTH. I accept willingly to participate in the research.

Participant's signature Researcher's signature

Date:……../……/2017

Appendix 2: DATA COLLECTION FORM

I IDENTIFICATION/ Sociodemographic characteristics

1. Date…….
2. Name(abbreviation)……..Study
   Code…….
3. Contact (phone number)……..……..
4. District ……..Sector……. ……..Cell…….. …Village……..
5. Sex: ……Male ……Female
6. Age: ……..**.....**
7. Education: primary ……secondary…….university…….vocational training…….none…..
8. Income: Ubudehe category :
9. Employment:
   01=Unemployed
   02=Self-employed (formal), for example owns a shop, is a formal market vendor, etc.
   03=Self-employed (informal), for example street vendors, peanut seller, fruit seller, etc.
   04=Private or public employed
   05=Student
   06=Retired
   07=Other (Specify) 50 =Refusal 51 =Don't know
10. Marital status
    01= Single 02= married/cohabitating 03= Divorced/ Separated 04=Widow
11. How many biological, non-adopted children do you have?
    Record number:
12. What is your religion?
    01=Muslim
    02=Catholic
    03=Evangelical, protestant, or other sect of Christianity
    04=Traditional beliefs/Animist
    05= Other

II. COMPLAINTS AT ADMISSION

1. Signs and Symptoms:

Fever (temperature: ≥37.5^{0}C)	yes……No
Headache	yes……No
Cough	yes……No
Night sweats	yes……No
Weight loss	yes…….No
Dysphagia	yes…….No
Back pain	yes…….No
Meningeal signs	yes…….No
Diarrhea	yes……..No
Others	…….

III. PHYSIOLOGICAL STATE ON ARRIVAL (adapted from apache II scoring system)

BP: …… HR: …….. T: ……..

SPO2(on room air): ……RR…… ……GCS: …….

WBC: …….HB: ……PTL…….CREAT: …….

IV. DIAGNOSES AT THIS VISIT: (opportunistic/or non opportunistic)

1.……..

1……

2……

3.……

V. HIV infection

1. When were you told by a health care care provider that y
   you have HIV?
   Month ……..year…….
2. Have you ever been tested to learn what your CD4 levels are?
   Yes…. No….. Baseline CD4 (first ever performed): …

3. CD4 cells count at current admission ……
4. Most recent viral load results: ……
5. Viral load at current admission:
6. What is his/her clinical HIV stage…….
7. Have you been told by a health care provider that you need to begin antiretroviral therapy (ARVs) to treat your HIV?

   01=No 02=Yes 03=Refusal 04=Don't know
8. Have you ever taken antiretroviral (ARVs) medication to treat HIV?

   01=No 02=Yes 03=Refusal 04=Don't know
9. When did you start taking antiretroviral medication (ARVs)? Month…. Year:……
10. Are you currently taking antiretroviral medication (ARVs)?

    01=No 02=Yes 03=Refusal 04=Don't know
11. What is your current ART regimen (note to the interviewer: check the medication box if possible)

    01= First line regimen: (specify the exact drugs)

    02= Second line regimen (specify the exact drugs)

    03= Third line regimen

VI. IN HOSPITAL STAY: …….DAYS

VII. OUTCOME

1. Discharged alive ……
2. Died in the hospital…….

Appendix 3: STUDY APPROVAL

UNIVERSITY OF RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 6th /12/2017

Dr NIYIGENA Olivier
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 419 /CMHS IRB/2017

Your Project Title ***"Causes Of Admission Of HIV Positive Patients In Medical Wards At KUTH"*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
			No (Reason)	
Name of Members	**Institute**	Yes	**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS	X		
Prof Munyanshongore Cyprien	UR-CMHS		X	
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 6th December 2017, **Approval has been granted to your study.**

EMAIL: researchcenter@ur.ac.rw P.O. Box: 3286, Kigali, Rwanda WEBSITE: http://cmhs.ur.ac.rw/

Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 6th December 2017

Expiration date: The 6th December 2018

for Professor Kato J. NJUNWA
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

February 09th, 2018 **Ref.: EC/CHUK/525/2018**

Review Approval Notice

Dear Olivier Niyigena,

Your research project: ***"Causes of admission of HIV positive patients in medical wards at CHUK."***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 09/02/2018 to evaluate your protocol of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your protocol.

You are required to present the results of your study to CHUK Ethics Committee before publication.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

ETHICS COMMITTEE CHUK

Dr. Rusingiza Emanuel
The President, Ethics Committee,
University Teaching Hospital of Kigali

<<University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations>>.

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