RETROSPECTIVE ASSESSMENT OF THE OPPORTUNISTIC INFECTIONS AMONG HIV/AIDS PATIENTS ATTENDING MBARARA REGIONAL REFERRAL HOSPITAL.

BY

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DECLARATION

I, Mwandah Daniel Chans, a final year pharmacy student declare to the best of my knowledge that the contents of this dissertation are from my personal findings. This report has not been duplicated by anybody or submitted to any academic institution for any award.

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DEDICATION

I would like to dedicate this dissertation to the Almighty Father in heaven for the everlasting unconditional love and all the support I have gained throughout my studies.

I also dedicate my work to all those who have supported me during my challenging academic course and to the School Of Pharmacy of KIU-Western Campus and hope to add to the knowledge in the school.

I would finally dedicate this dissertation to my beloved nephews Jeremiah , Raheem ,Isaac and Timothy as an encouragement to read pharmacy.

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TABLE OF CONTENTS

KAMPALA INTERNATIONAL UNIVERSITY
WESTERN CAMPUS
LIBRARY
P. O. BOX 71
BUSHENYI

KAMPALA INTERNATIONAL UNIVERSITY
WESTERN CAMPUS
LIBRARY
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BUSHENYI

LIST OF FIGURES

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BUSHENYI

List of Acronyms

ABC.....Abstinence, Being faithful, Condom use

AEDs.....AIDS defining events

ART.....antiretroviral therapy

ARV.....antiretroviral

CDC.....centre for disease control

HAART.....highly active antiretroviral therapy

HIV.....human immune deficiency virus

INH.....isoniazid

IRIS.....immune recombinant inflammatory syndrome

IUCD.....intrauterine contraceptive device

MRRH.....Mbarara regional referral hospital

NRTIs.....nucleoside reverse transcriptase inhibitors

NNRTIs.....non nucleoside reverse transcriptase inhibitors

OIs.....opportunistic infections

PCP.....*pneumocystis jiroveci* pneumonia

PCR.....polymerase chain reaction

PML.....Progressive Multifocal Leukoencephalopathy

PMTC.....prevention of mother to child transmission

STI.....Sexually Transmitted Infection

WHO..... World Health Organization

ABSTRACT

BACKGROUND

People with advanced HIV/AIDS are vulnerable to infections and malignancies that are called opportunistic infections because they have a weakened immune system. Opportunistic infections continue to cause morbidity and mortality in patients with Human Immune Deficiency Virus (HIV)-1 infection. Some OIs only affect women or affect women more than men.Potent combination antiretroviral therapy (ART) has reduced the incidence of OIs for certain patients with access to care. However, certain patients in the developed and developing world do not have access to care and have OIs.

OBJECTIVE

To assess the occurrence of opportunistic infections among HIV/AIDS patients attending Mbarara Regional Referral Hospital.

METHODS

A retrospective study covering the period of February 2011 to December 2011. Slovin's formula of sample size determination was used. The population size was 15,000 people, the calculated sample size was 390 people, However this sample size was small and thus was increased to a 1500 and every 10^{th} file was selected.

RESULTS

65% females, 35% were males, married (55%), divorced (7%), 22% single, 16% widowed; 20% for WHO stage1, 5% for stage2, 4% for stage3, 8% for stage4. 39% had diarrhea, 28% missing OI, 7% had cryptococcosis, 6% had oral candidiasis, 5% tuberculosis and vaginal candidiasis, 4% herpes zoster, while 3% had herpes simplex, 2% had genital warts and 1% had esophageal candidiasis. Metronidazole and ciprofloxacin were most used drugs, others were nystatin suspension, fluconazole, amphotericin, acyclovir were represented by 5% of the total treatment, 3% represented nystatin pessaries, DOTS and vitamin B complex, 2% for clotrimazole cream and amitryptiline and 1% podophyllum resin. 72% of patients were on HAART, 27% on PreART and 1% on truvada.

CONCLUSION

The highest percentage of patients with OIs were from WHO clinical stage one and this could me an important indicator to avoid these OIs by careful monitoring of patients in this stage. The drugs most commonly used for the OIs were metronidazole and ciprofloxacin for diarrhea and this call for more procurement of these drugs, so that they are readily available to treat the patients, however proper diagnosis should be done to establish the exact causative agent before treatment. The female gender had the highest percentage as compared to men, similarly, Married had the highest incidence as compared to the divorced thus the married require the health education about fidelity and faithfulness as a method to prevent more problems.
The patients on HAART whose combinations contained a protease inhibitor had the lowest incidence of opportunistic infections.

CHAPTER ONE

1.0 INTRODUCTION

Infections with HIV/AIDS lead to serious health threats from diseases known as "opportunistic" infections (OIs) (WHO 2004). Opportunistic infections for this case take advantage of the weakened immune system, and can cause devastating illnesses. Opportunistic infections imply a declining immune system (Ruth Hope et al. 2007). Most life-threatening Opportunistic infections are known to be prevalent when the *CD4 count* is below 200 cells/mm^3 (Bolton-Moore C et al. 2007). OIs are the most common cause of death for people with HIV/AIDS (WHO,2010). Human immunodeficiency virus (HIV) is the causative agent for AIDS disease; the most common serotype is HIV-1 and is the infectious agent that has led to the worldwide AIDS epidemic (Hargrove JW et al. 2008). There is also an HIV-2 that is much less common and less virulent, but eventually produces clinical findings similar to HIV-1 (Schüpbach J et al. (2007). The HIV-1 type itself has a number of subtypes (A through H and O) which have differing geographic distributions but all produce AIDS similarly. HIV is a retrovirus that contains only RNA (Hallett T et al. (2008)). HIV is a sexually transmitted disease; infection is aided by Langerhans cells in mucosal epithelial surfaces which can become infected (Schüpbach J et al. (2007). Infection is also aided by the presence of other sexually transmitted diseases that can produce mucosal ulceration and inflammation (Freeman EE (2006). The CD4+ T-lymphocytes have surface receptors to which HIV can attach to promote entry into the cell (Baral S et al. (2009). The infection extends to lymphoid tissues which contain follicular dendritic cells that can become infected and provide a reservoir for continuing infection of CD4+ T-lymphocytes. HIV can also be spread via blood or blood products, most commonly with shared contaminated needles used by persons engaging in intravenous drug use. Mothers who are HIV infected can pass the virus on to their fetuses in utero or to infants via breast milk (Haas J et al.(1996).

When HIV infects a cell, it must use its reverse transcriptase enzyme to transcribe its RNA to host cell proviral DNA. It is this proviral DNA that directs the cell to produce additional HIV virions which are released (Baeten JM et al. (2007). Dual tropic HIV stains have been identified, the presence of a CCR5 mutation may explain the phenomenon of resistance to HIV infection in some cases (Clavel F. 1986). Over time, mutations in HIV may increase the ability of the virus to infect cells via these routes. Infection with cytomegalovirus may serve to enhance HIV infection

via this mechanism, because CMV encodes a chemokine receptor similar to human chemokine receptors (Nattermann J et al. (2003)). When the CD4 lymphocyte count drops below 200/microliter, then the stage of clinical AIDS has been reached. This is the point at which the characteristic opportunistic infections and neoplasms of AIDS appear (Staszewski S et al. 2003).

1.10 Background of the study

Although the overall incidence of many opportunistic infections has decreased with effective chemoprophylaxis and combination antiretroviral therapy, prompt recognition and appropriate management are imperative to decrease mortality related to these conditions. Primary care management of HIV infection includes preventing and treating opportunistic infections, monitoring antiretroviral therapy. (Peter a. Selwyn et al. 2011)

Acquired Immune Deficiency Syndrome was recognized in 1981 as a new syndrome capable of destroying the human beings (CDC 1981). The impact of this disease on human suffering, cultures, demographics, economics, and even politics has been felt in nearly every society across the globe. The sudden appearance of the epidemic among previously known rare diseases was soon recognized on the basis of its association with immune suppressant characteristics, hence forth unrecorded in human history. Different opportunistic infections typically occur at different stages of HIV infection. In early HIV disease people can develop tuberculosis, malaria, bacterial pneumonia, herpes zoster, staphylococcal skin infections and septicemia. These are diseases that people with normal immune systems can also get, but with HIV they occur at a much higher rate. It also takes longer for a person with HIV to recover than it takes for someone with a healthy immune system (United Nations Development Programme, 2005, China)

When the immune system is very weak due to advanced HIV disease or AIDS, opportunistic infections such as PCP, toxoplasmosis and cryptococcosis develop. Some infections can spread to a number of different organs, which is known as 'disseminated' or 'systemic' disease. Many of the opportunistic infections that occur at this late stage can be fatal.

Highly Active Antiretroviral Therapy (HAART) can reduce the amount of HIV in someone's body and restore their immune system. The introduction of HAART has dramatically reduced the

incidence of opportunistic infections among HIV-positive people who have received the drugs. Yet the prevention and treatment of opportunistic infections remains essential.

Around the world, millions of people living with HIV in resource-poor communities have no access to antiretroviral drugs. And even where the drugs are available, they do not entirely remove the need for preventing and treating opportunistic infections. Usually it is advisable for people with acute opportunistic infections to begin HIV treatment right away, especially if the infection is difficult to treat. However in certain cases it may be better to delay beginning HIV treatment and instead only to administer treatment for the opportunistic infection, especially if there are concerns about drug interactions or overlapping drug toxicities.

Those who have already started taking antiretrovirals may require other drugs in certain circumstances. In particular, some opportunistic infections may be unmasked shortly after starting HIV treatment as the immune system starts to recover, and these may require specific treatment. Measures to prevent and treat opportunistic infections become essential if antiretrovirals stop working because of poor adherence, drug resistance or other factors.

Providing prevention and treatment of opportunistic infections not only helps HIV-positive people to live longer, healthier lives, but can also help prevent TB and other transmissible opportunistic infections from spreading to others.(British HIV Association , 2010)

HIV-positive people can reduce their exposure to some of the microorganisms that threaten their health. They should be especially careful around uncooked meat, domestic animals, human excrement and lake or river water. However there is no practical way to reduce exposure to the microorganisms that cause candidiasis, MAC, bacterial pneumonia and other diseases because they are generally common in the environment. (Walker, A.S et al , 2010)

In 1998, an estimated 1.9 million people were living with HIV/AIDS (UNAIDS 1999). AIDS had overtaken malaria as a leading cause of death among people aged 12–49 years and was responsible for 12 per cent of all deaths. (MacAdam , 2003) reported that more than 800,000 people in Uganda had lost their lives to the HIV/AIDS epidemic, leaving behind an estimated two million orphans who had lost one or both parents.

Uganda has long basked in the praise of the international community over its swift and Progressive response to its crippling HIV/AIDS epidemic.

Back in the 1980s more than 30% of Ugandans had contracted the HIV virus. Now the national prevalence rate is around 6.4%, an achievement attributed largely to the country's rapid acknowledgment of the crisis it faced, the roll out of national prevention and treatment messages and its embrace of open discourse around causes and solutions to the virus. (Annie Kelly, 2008)

Around 130,000 Ugandans are infected with the HIV virus every year, according to the Uganda AIDS Commission. The government's new national HIV/Aids strategic plan bleakly predicts that the number of HIV positive Ugandans will rise from 1.1 million in 2006 to 1.3 million in 2012.

There have also been warnings of the impact rising numbers of HIV patients will have on Uganda's already fragile economy. The Ministry of Finance says that, increasing at its current rate, the wave of new HIV cases could see Uganda's annual gross domestic product (GDP) fall by 1.2% in the next five years.

The implications on Ugandan's health system would also be grim. According to officials at Uganda's Ministry of Health, 70% of medical admissions are HIV-related. Yet Uganda's chronic shortage of trained healthcare workers – the health ministry says the country is running at 60% capacity - means that there are already insufficient numbers of qualified professionals to distribute and administer treatment plans. While 156,000 people are receiving antiretroviral treatment, more than double that number are still not on HIV medication.

The profile of HIV and AIDs in Uganda is also changing. The most recent figures suggest that up to 65% of new HIV infections are now transmitted within marriage.

The number of "discordant couples", where one partner is HIV positive and the other negative, is also rising. This raises the need for a whole new approach to prevention and treatment, which up until now has focused largely on the ABC approach of promoting abstinence first and then fidelity and contraception.

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1.20 PROBLEM STATEMENT

People with advanced HIV/AIDS are vulnerable to infections and malignancies that are called opportunistic infections because they have a weakened immune system. Opportunistic infections continue to cause morbidity and mortality in patients with Human Immune Deficiency Virus (HIV)-1 infection. Some OIs only affect women or affect women more than men.

Potent combination antiretroviral therapy (ART) has reduced the incidence of OIs for certain patients with access to care. However, certain patients in the developed and developing world do not have access to care and have OIs. Other patients do not have a sustained response to antiretroviral agents for multiple reasons, including poor adherence, drug toxicities, drug interactions, or initial acquisition of a drug-resistant strain of HIV-1. Therefore, OIs will continue to cause substantial morbidity and mortality in patients with HIV-1 infection.

The ministry of health introduced the HIV care/ART card for use in management of HIV/AIDS patients, including the OIs; it is therefore imperative to review whether clinicians adhere to this tool of reporting data among HIV/AIDS patients.

1.30 PURPOSE OF THE STUDY

The study was done with an aim of identifying the opportunistic infections that are most common among the patients, as well as the treatments used. This will improve on the literature available on opportunistic infections and provide information on probable measures how to manage and prevent these infections. It will also provide information that will enable clinicians to adhere to the HIV care/ART card from the ministry of health.

1.4.1 BROAD OBJECTIVE

To assess the occurrence of opportunistic infections among HIV/AIDS patients attending Mbarara Regional Referral Hospital.

1.4.2 SPECIFIC OBJECTIVES

1. To assess the common opportunistic infections diagnosed among HIV/AIDS patients managed during the period of February 2011 to January 2012 in Mbarara Regional Referral Hospital.
2. To determine the WHO HIV/AIDS clinical staging at which these opportunistic infections were most common.
3. To point out the anti retro viral regimens for opportunistic infections.
4. To review the trend of opportunistic infections in HIV/AIDS patients treated with respect to marital status and gender.
5. To determine the adherence to the HIV care/ART card in reporting OIs.

1.50 JUSTIFICATION

Opportunistic infections occur at different stages of HIV/AIDS disease, the prevalence in females and males should always be known. It is also important to determine the relationship between antiretroviral therapy and the occurrence of opportunistic infections. This study is also intended to provide guidance for policy making and management of opportunistic infections in HIV/AIDS patients for example, in terms of medicine procurement and therapeutic drug monitoring. Recording of OIs and treatment is vital in treatment and improving the quality of life of HIV/AIDS patients thus determining whether they are recorded will provide information on the importance of HIV care/ART card in monitoring of these OIs. Evaluating outcomes among the HIV-infected patients starting in resource-limited settings is vital to understanding the impact of current treatment programs and guiding future strategies.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 WHO clinical staging of HIV disease in adults and adolescents (2006 revision)

In resource-poor settings, medical facilities are sometimes poorly equipped and tests to measure CD4 count and viral load are unavailable. In this case, another method to determine whether an individual should begin treatment is used. The World Health Organisation (WHO) developed a staging system for HIV disease based on clinical symptoms, which may be used to guide medical decision making.

Clinical Stage I:

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage II:

- Moderate unexplained weight loss (under 10% of presumed or measured body weight)
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular chelitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

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Clinical Stage III:

- Unexplained severe weight loss (over 10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for longer than one month
- Unexplained persistent fever (intermittent or constant for longer than one month)
- Persistent oral candidiasis

- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (below 8 g/dl), neutropenia (below 0.5 billion/l) and/or chronic thrombocytopenia (below 50 billion/l)

Clinical Stage IV:

- HIV wasting syndrome
- Pneumocystis pneumonia

- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
- Recurrent septicaemia (including non-typhoidal Salmonella)
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis

- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

Most patients who develop AIDS or severe opportunistic infections today are unaware of their HIV infection status. Since the year 2000, around 50 % of patients who presented with AIDS at the outpatient clinic were unaware of their HIV infection at the time. Another 35 % of patients had not been treated with antiretroviral drugs until AIDS was diagnosed. These patients often present late, usually in a very serious condition. AIDS remains life threatening, and a severe PCP does not become less critical because of the overall improvement in long-term survival (CDC. (2009).The acute danger remains. Therefore, every HIV clinician should be familiar with the diagnosis and therapy of OIs, even today. Although much has improved in recent years, many problems remain. There is still no adequate treatment available for diseases such as PML or cryptosporidiosis, and resistance will become an increasing problem with other infections. HAART does not always lead to immediate improvement, and may even complicate things because from 3.3 to 0.4 per 100 child-years; herpes zoster from 2.9 to 1.1 per 100 child-years; disseminated *Mycobacterium Avium* complex (MAC) from 1.8 to 0.14 per 100 child-years; and *Pneumocystis jirovecii* pneumonia (PCP) from 1.3 to 0.09 per 100 child-years (Slogrove AL et al. 2009).

During a median follow-up period of 43 months (interquartile range, 19-70 months), 2880 ADEs (AIDS defining events) were diagnosed in 2262 patients; 1146 patients died. The most common ADEs were esophageal candidiasis (in 360 patients), Pneumocystis jiroveci pneumonia (320 patients), and Kaposi sarcoma (308 patients). The greatest mortality hazard ratio was associated with non-Hodgkin's lymphoma (hazard ratio, 17.59; 95% confidence interval, 13.84-22.35) and progressive multifocal leukoencephalopathy (hazard ratio, 10.0; 95% confidence interval, 6.70-14.92). Three groups of ADEs were identified on the basis of the ranked hazard ratios with bootstrapped confidence intervals: severe (non-Hodgkin's lymphoma and progressive multifocal leukoencephalopathy [hazard ratio, 7.26; 95% confidence interval, 5.55-9.48]), moderate (cryptococcosis, cerebral toxoplasmosis, AIDS dementia complex, disseminated Mycobacterium avium complex, and rare ADEs [hazard ratio, 2.35; 95% confidence interval, 1.76-3.13]), and

mild (all other ADEs [hazard ratio, 1.47; 95% confidence interval, 108-.2.00]). (Macroft.A et al 2009.)

In another study, of the 2410 participants, 143 developed 186 Ols after initiation of potent antiretroviral therapy. Incidence of any OI decreased from 15.1 per 100 person-years in the 6 months before therapy to 7.7 in the first 3 months after starting treatment, 2.6 in the following 6 months, and 2.2 per 100 person-years between 9 and 15 months. Reductions in incidence ranged from 38% per month for Kaposi sarcoma (P<.001) to 5% per month for non-Hodgkin lymphoma (P = .31). Baseline CD4 cell count continued to predict the risk of disease progression after initiating potent therapy. Compared with CD4 cell counts above 200 x 10(6)/L, the hazard ratio for developing Ols was 2.5 (95% confidence interval [CI], 1.4-4.5) for counts between 51 and 200 x 10(6)/L and 5.8 (95% CI, 3.2-10.5) for counts below 51 x 10(6)/L at baseline. Independent of baseline CD4 cell count, a rise in CD4 cell count by 50 x 10(6)/L or more and undetectable HIV-1 RNA in plasma (<400 copies/mL) by 6 months reduced risk of subsequent events, with hazard ratios of 0.32 (95% CI, 0.20-0.52) and 0.39 (0.24-0.65), respectively. (Erard V et al (1999)

2.2 COMMON OPPORTUNISTIC INFECTIONS IN HIV DISEASE

Even after starting therapy and with effective suppression of viral load, patients with persistently low CD4 counts remain at high risk for opportunistic infections. In general, all patients remain at a relatively high risk for opportunistic infections and other AIDS-related events for the first 6 months of antiretroviral therapy (Rodríguez B. et al. (2006). Opportunistic infections and conditions include the following (added in the 1993 AIDS surveillance case definition)

Bacterial and Mycobacterial infections such as; Mycobacterium Avium Complex (MAC, MAI), Salmonellosis, Syphilis and Neuroshyphilis, Turberculosis (TB)Bacillary, angiomatosis (cat scratch disease). Fungal Infections; Aspergillosis, Candidiasis (thrush, yeast infection) Coccidioidomycosis, Cryptococcal Meningitis, Histoplasmosis. Malignancies; Kaposi's Sarcoma, Lymphoma; Systemic Non-Hodgkin's Lymphoma (NHL), Primary Central Nervous System Lymphoma. Protozoal Infections Cryptosporidiosis, Isosporiasis, Microsporidiosis, Pneumocystis Carinii Pneumonia (PCP), Toxoplasmosis. Viral Infections; Cytomegalovirus (CMV), Hepatitis, Herpes Simplex (HSV, genital herpes), Herpes Zoster (HZV, shingles)Human

Papiloma Virus (HPV, genital warts, cervical cancer), Molluscum Contagiosum, Oral Hairy Leukoplakia (OHL), Progressive Multifocal Leukoencephalopathy (PML), Neurological conditions, AIDS Dementia Complex (ADC), Peripheral Neuropathy. Other Conditions and Complications; Apthous Ulcers, Malabsorption (Center for disease control. 2009).

***Pneumocystis carinii* pneumonia (PCP),** as the condition is commonly termed (although the causative organism has been renamed *Pneumocystis jiroveci*, is the most common opportunistic infection in persons with HIV infection. *(Michael S. Gottlieb et al).* PCP is a frequent HIV associated opportunistic infection which occurred in 70%-80% of patients with AIDS prior to the widespread use of primary PCP prophylaxis and ART, which has led to a significant decline of cases. The symptoms are mainly pneumonia along with fever and respiratory symptoms such as dry cough, chest pain and dyspnoea (difficulty in breathing). Definitive diagnosis requires microscopy of bodily tissues or fluids.

Severe cases of PCP are initially treated with TMP-SMX or clindamycin and oral primaquine. Mild cases can be treated with oral TMP-SMX throughout. With both of these regimens, toxicity (notably allergic-type reactions) often requires changes in therapy.

Prevention of PCP is strongly recommended for HIV-infected persons with very weak immune systems wherever PCP is a significant health problem for HIV-infected persons, and also after their first episode of PCP. The preferred drug is usually TMP-SMX.

Pneumocystis first came to attention as a cause of interstitial pneumonia in severely malnourished and premature infants during World War II in Central and Eastern Europe. Before the 1980s, fewer than 100 cases of PCP were reported annually in the United States, occurring in patients who were immune suppressed (e.g., cancer patients receiving chemotherapy and solid-organ transplant recipients receiving immunosuppressants). In 1981, the Centers for Disease Control and Prevention reported PCP in 5 previously healthy homosexual men residing in the Los Angeles area (Safrin S. et al.; (1996)). According to the CDC, as of February 20th, 1989, 30,534 Americans had died of AIDS-associated PCP.

In some areas of the world, Pneumocystis carinii pneumonia ranks as the most common opportunistic infection in AIDS. It is less frequent in developing countries where tuberculosis

and fungal infections are more common opportunistic infections. (WHO Regional Office for South-East Asia 2011) *P jiroveci* is now one of several organisms known to cause life-threatening opportunistic infections in patients with advanced HIV infection worldwide (J A Sonnabend 2006.)

Treatment of PCP may be initiated before the workup is complete in severely ill high-risk patients. Treatment of PCP depends on the degree of illness at diagnosis, determined on the basis of the alveolar-arterial gradient. Antibiotics are primarily recommended for treatment of mild, moderate, or severe PCP. In AIDS the rate of PCP recurrence was about four times higher than the 15% threshold suggested by Walter Hughes as an indication for prophylaxis Trimethoprim-sulfamethoxazole (TMP-SMX) has been shown to be as effective as intravenous pentamidine and more effective than other alternative treatment regimens. Corticosteroids are used as adjunctive initial therapy only in patients with HIV infection who have severe PCP. Preventive measures (eg, smoking cessation and chemoprophylaxis) can play an important role in disease management (Cunha BA. 2007).

Kaposi sarcoma (Kaposi's sarcoma, KS) was described initially in 1872 by a Hungarian dermatologist, Moritz Kaposi. Kaposi sarcoma is a spindle-cell tumor thought to be derived from endothelial cell lineage. This condition carries a variable clinical course ranging from minimal mucocutaneous disease to extensive organ involvement. Kaposi sarcoma can be primarily categorized into four types: epidemic of AIDS-related, immunocompromised, classic or sporadic, and endemic (African) (DeVita V. et al. 2008).

HIV-associated Kaposi's sarcoma causes dark blue lesions, which can occur in a variety of locations including the skin, mucous membranes, gastrointestinal tract, lungs or lymph nodes. The lesions usually appear early in the course of HIV infection.

Treatment depends on the lesions' symptoms and location. For local lesions, injection therapy with vinblastine has been used with some success. Radiotherapy can also be used, especially in hard-to reach sites such as the inner mouth, eyes, face and soles of the feet. For severe widespread disease, systemic chemotherapy is the preferred treatment.

Epidemic AIDS-related Kaposi sarcoma

This entity occurs in patients with advanced HIV infection and is the most common presentation of Kaposi sarcoma. It is the most common malignancy seen in HIV-infected patients, especially where access to HAART (highly active antiretroviral therapy) is limited. AIDS-related Kaposi sarcoma is the most clinically aggressive form of Kaposi sarcoma. Seroconversion to human herpes virus 8 (HHV-8) positivity predates the development of epidemic Kaposi sarcoma by 5-10 years. The interval for development of Kaposi sarcoma is shortened in patients where HIV infection precedes seroconversion to HHV-8 positivity. The presence of decreased CD4 counts and increased HIV-1 viral loads are independent prognostic factors in the development of epidemic Kaposi sarcoma. Less than one-sixth of HIV-infected patients have CD4 count of over 500 per microliter. The disease usually develops in HIV infected patients with severe immunodeficiency (Nawar E. et al. 2005) Relative affluence may increase the risk of Kaposi sarcoma in HIV positive patients.

Candidiasis

There are two main types of candidiasis: localised disease (of the mouth and throat or of the vagina) and systemic disease (of the oesophagus, and disseminated disease). HIV-positive women commonly acquire the mouth and throat variant (usually known as thrush or OPC). It is believed to occur at least once in the lifetime of all HIV-infected patients. OPC in HIV-positive patients indicates a decline in immunodeficiency and, when ART is absent, is a sign of the onset of AIDS. However, the vaginal variant is a common occurrence among HIV-negative women.

While OPC is not a cause of death, it causes severe discomfort. The symptoms of candidiasis of the vagina include itching and possibly a thick vaginal discharge. Candidiasis of the mouth and throat can cause oral pain and make swallowing difficult, the main symptom is creamy white legions in the mouth that can be scraped away. Oesophageal (gullet) candidiasis is a more serious condition which can cause pain in the chest that increases with swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease (for example, blindness when it affects the eyes), and can be life threatening.

Localised disease may be treated at first with relatively inexpensive drugs such as nystatin, miconazole or clotrimazole. Systemic candidiasis requires treatment with systemic antifungal agents such as fluconazole, ketoconazole, itraconazole or amphotericin.

HIV-related upper digestive tract complications are well documented. Candida infection often affects the oral cavity, leading to dysphagia or odynophagia or the esophagus, manifesting as sharp or burning substernal discomfort (Carolyn chu et al).

Candidiasis is caused by infection with species of the genus *Candida,* predominantly with *Candida albicans. Candida* species are ubiquitous fungi that represent the most common fungal pathogens that affect humans. *Candida* species are true opportunistic pathogens that exploit recent technological advances to gain access to the circulation and deep tissues (L, Lewandowski D. et al. 2004). As with most fungal infections, host defects also play a significant role in the development of candidal infections. Host defense mechanisms against *Candida* infection and their associated defects that allow infection are as follows: Intact mucocutaneous barriers - Wounds, intravenous catheters, burns, ulcerationsPhagocytic cells -Granulocytopenia, Polymorphonuclear leukocytes - Chronic granulomatous disease, Monocytic cells - Myeloperoxidase deficiencyComplement -HypocomplementemiaImmunoglobulins - Hypogammaglobulinemia, Cell-mediated immunity - Chronic mucocutaneous candidiasis, diabetes mellitus, cyclosporin A, corticosteroids, HIV infection, Mucocutaneous protective bacterial florae - Broad-spectrum antibiotics (Yang YL. 2003)

In HIV-positive people, oral thrush and vaginal yeast infections can occur at any time, regardless of their CD4 cell counts. The more the immune system becomes damaged, oral thrush and vaginal yeast infections are more likely to occur and recur more frequently. HIV-positive people with damaged immune systems, usually with a CD4 cell count less than 200, are also more likely to develop candidiasis deeper in their bodies, such as in their esophagus or their lungs. As with many opportunistic infections, candidiasis will usually improve or recur less often if antiretroviral therapy significantly increases CD4 cell counts. (Tim Horn et al)

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Tuberculosis

Tuberculosis (TB) is a bacterial infection that primarily infects the lungs. Tuberculosis is the leading HIV-associated opportunistic disease in developing countries. For people who are dually infected with HIV and TB, the risk of developing active tuberculosis is 30-50 fold higher than for people infected with TB alone. And because mycobacterium can spread through the air, the increase in active TB cases among dually infected people means: more transmission of the TB bacterium, more TB carriers, more TB in the whole population.

Tuberculosis is harder to diagnose in HIV-positive people than in those who are uninfected. The diagnosis of TB is important because TB progresses faster in HIV-infected people. Also, TB in HIV-positive people is more likely to be fatal if undiagnosed or left untreated. TB occurs earlier in the course of HIV infection than many other opportunistic infections.

A proper combination of anti-TB drugs achieves both prevention and cure. Effective treatment quickly makes the individual non-contagious, which prevents further spread of the TB germ. The DOTS (directly observed treatment short course) treatment strategy recommended by WHO treats TB in HIV-infected persons as effectively as it treats those without the virus. A complete cure takes 6 to 8 months and uses a combination of antibiotics. In addition to curing the individual, it also prevents further spread of the disease to others. This is why treating infectious cases of TB has important benefits for society as a whole.

Isoniazid preventive therapy is recommended as a health-preserving measure for HIV-infected persons at risk of TB, as well as for those with latent TB infection.

Tuberculosis (TB), a multisystemic disease with myriad presentations and manifestations, is the most common cause of infectious disease–related mortality worldwide. The World Health Organization (WHO) has estimated that 2 billion people have latent TB and that globally, in 2009, the disease killed 1.7 million people. New TB treatments are being developed, and new TB vaccines are under investigation. Although TB rates are decreasing in the United States, the disease is becoming more common in many parts of the world. In addition, the prevalence of drug-resistant TB is also increasing worldwide. Co-infection with the human immunodeficiency virus (HIV) has been an important factor in the emergence and spread of resistance.

According to WHO,

Tuberculosis (TB) is second only to HIV/AIDS as the greatest killer worldwide due to a single infectious agent.
In 2010, 8.8 million people fell ill with TB and 1.4 million died from TB.
Over 95% of TB deaths occur in low- and middle-income countries, and it is among the top three causes of death for women aged 15 to 44.
In 2009, there were about 10 million orphan children as a result of TB deaths among parents.
TB is a leading killer of people living with HIV causing one quarter of all deaths.
Multi-drug resistant TB (MDR-TB) is present in virtually all countries surveyed.
The estimated number of people falling ill with tuberculosis each year is declining, although very slowly, which means that the world is on track to achieve the Millennium Development Goal to reverse the spread of TB by 2015.

The TB death rate dropped 40% between 1990 and 2010

The US Centers for Disease Control and Prevention (CDC) has been recording detailed epidemiologic information on tuberculosis (TB) since 1953. The incidence of TB has been declining since the early 20th century because of various factors, including basic infection-control practices (isolation). Beginning in 1985, a resurgence of TB was noted. The increase was observed primarily in ethnic minorities and especially in persons infected with HIV. TB control programs were revamped and strengthened across the United States.

As an AIDS (acquired immunodeficiency syndrome)-related opportunistic infection, TB is associated with HIV infections, with dual infections being frequently noted. Globally, coinfection with HIV is highest in South Africa, India, and Nigeria.

Persons with AIDS are 20-40 times more likely than immunocompetent persons to develop active TB. Correspondingly, TB is the leading cause of mortality among persons infected with HIV.

Worldwide, TB is most common in Africa, the West Pacific, and Eastern Europe. These regions are plagued with factors that contribute to the spread of TB, including the presence of limited

resources, HIV infection, and multidrug-resistant (MDR) TB. Consequently, although international public health efforts have put a huge curb on the rate of increase in TB, these regions account for the continued increase in global TB.

TB occurs in every part of the world. In 2010, the largest number of new TB cases occurred in Asia, accounting for 60% of new cases globally. However, Sub-Saharan Africa carried the greatest proportion of new cases per population with over 270 cases per 100 000 population in 2010. (WHO 2010)

In 2010, about 80% of reported TB cases occurred in 22 countries. Some countries are experiencing a major decline in cases, while cases are dropping very slowly in others. Brazil and China for example, are among the 22 countries that showed a sustained decline in TB cases over the past 20 years. China, in particular, has made dramatic progress in TB control. Between 1990 and 2010, the TB death rate in the country fell by almost 80% and the total number of people ill with TB dropped by half. (WHO 2010)

The widespread use of potent antiretroviral therapy (ART) has led to a dramatic decline in the incidence of opportunistic infections In a cohort of 2410 patients followed in seven centers in Switzerland in 1995-1997, the incidence of any OI decreased from 15.1 per 100 person-years in the 6 months before therapy to 7.7 in the first 3 months after starting treatment, 2.6 in the following 6 months, and 2.2 per 100 person-years between 9 and 15 months .In a multicenter study of more than 8500 HIV-infected patients in the United States, the rates of OIs declined from 140 per 1000 person-years of observation in 1995 to less than 20 per 1000 person-years of observation in 2007. Similar trends have been noted in resource-limited setting. (Ledergerber.B, Freedberg KA, Brooks JT, et al 2009.)

Cryptococcosis

Cryptococcosis is caused by a fungus that primarily infects the brain. It most often appears as meningitis and occasionally as pulmonary or disseminated disease. Untreated cryptococcal meningitis is fatal.

Cryptococcosis is relatively easy to diagnose. However, its treatment (either amphotericin B with or without flucytosine or in mild cases with oral fluconazole) and secondary chemoprophylaxis are often impossible in developing countries because of high cost and limited availability of the drugs required.

It is recommended that ART should be administered to those diagnosed with cryptococcal disease. In the case of cryptococcal meningitis there are risks of initiating ART as there is evidence that immune reconstitution inflammatory syndrome (IRIS) may develop. HIV progression versus the onset of IRIS are risks that must be weighed when treating HIV and cryptococcosis meningitis.

Cryptosporidiosis and isosporiasis

Cryptosporidiosis (crypto) and isosporiasis are both caused by protozoan parasites. These diseases are easily spread by contaminated food or water, or by direct contact with an infected person or animal. Both crypto and isosporiasis cause diarrhoea, nausea, vomiting and stomach cramps. In people with healthy immune systems, these symptoms do not last more than about 14 days. However, if the immune system is damaged then they can continue for a long time. Diarrhoea can interfere with the absorption of nutrients and this can lead to serious weight loss.

To confirm diagnosis of either disease, the stool is normally checked for parasites and their eggs. There is no cure for crypto, but antiretroviral therapy to restore immunity can effectively clear up the infection. For isosporiasis, TMP-SMX (trimethoprim-sulfamethoxazole) is often the preferred treatment.

Cytomegalovirus

Cytomegalovirus (CMV) is a virus that infects the whole body. Infection usually occurs in childhood yet the virus remains dormant unless the immune system is suppressed. It most commonly appears as retinitis, which causes blurred vision and can lead to blindness, and also as gastrointestinal disease. CMV can also affect other organs such as the lungs or liver, and is capable of causing fever, diarrhoea, nausea, pneumonia-like symptoms and dementia.

CMV infection may be treated with drugs such as ganciclovir, valganciclovir, cidofovir and forscarnet. Before the roll out of ARV, studies identified that up to 40% of AIDS patients aquired CMV. Access to ARV's now deter the chances of infection as immune systems can be supported. It is recommended to initiate ART following anti-CMV treatment in order to reduce the chance of a relapse.

CMV gastrointestinal disease

Esophagitis is the second most common gastrointestinal (GI) manifestation of cytomegalovirus (CMV) infection after colitis (Sandeep Mukherjee et al). CMV esophagitis has been reported in patients who have undergone transplantation, patients undergoing long-term renal dialysis, patients with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS), and patients with other debilitating diseases. Patients with HIV infection are at increased risk because their $CD4^+$ lymphocyte counts fall to less than 100 cells/μL (Wilcox CM. et al. 2004). In patients with HIV infection or AIDS, CMV infection is an opportunistic infection that signals a decline in patient immunity. CMV esophagitis has been described in only 3 patients who had been immunocompromised by conditions other than transplantation, HIV infection, or AIDS. No cases have been reported in healthy hosts (Borges MC. Et al 2009).

Herpes simplex and Herpes zoster

The usual symptoms of herpes simplex virus infection (HSV, which causes sores around the mouth and genitals) and herpes zoster virus infection (or varicella zoster virus (VZV), which causes chickenpox (varicella) and shingles (zoster)) are not life-threatening but can be extremely painful. Both viruses are also capable of causing retinitis and, less often, encephalitis (which can be life-threatening). Herpes Zoster is transmitted usually through the respiratory route, whereas Herpes Simplex Virus is transmitted through contact with secretions from an infected area.

Both herpes simplex and herpes zoster are usually diagnosed by simple examination of the affected area, and may be treated with drugs such as acyclovir, famciclovir and valacyclovir. One particular study found using acyclovir to treat herpes simplex in those living with HIV and not taking ARVs, modestly reduces the risk of HIV disease progression.

Histoplasmosis

Histoplasmosis is a fungal infection that primarily affects the lungs but may also affect other organs. Infection occurs through inhalation of fungus spores. Symptoms can include fever, fatigue, weight loss and difficulty in breathing.

Disseminated histoplasmosis infection may be diagnosed using an antigen test, and can be fatal if left untreated. Treatment usually involves amphotericin B or itraconazole.

Leishmaniasis

Leishmaniasis is transmitted by sandflies and possibly through sharing needles. The most serious of its four forms is visceral leishmaniasis (also know as kala azar) which is characterised by irregular bouts of fever, substantial weight loss, swelling of the spleen and liver and anaemia (occasionaly serious). In its more common forms, leishmaniasis can produce disfiguring lesions around the nose, mouth and throat, or skin ulcers leading to permanent scarring.

Treatment of leishmaniasis is with either a pentavalent antimony or liposomal amphotericin B in the case of visceral leishmaniasis. Sodium stibogluconate is used to treat cutaneous leishmaniasis. If left untreated, visceral leishmaniasis is usually fatal.

MAC

The germs of the mycobacterium avium complex (MAC) are related to the bactria that causes tuberculosis. MAC disease generally affects multiple organs, and symptoms include fever, night sweats, weight loss, fatigue, diarrhoea and abdominal pain. It is not believed that person-to-person transmission occurs; the MAC organisms are present throughout the environment. Infection occurs through the respiratory or gastrointestinal tract, infecting individuals with severely inhibited immune systems.

MAC should be treated using at least two antimycobacterial drugs to prevent or delay the emergence of resistance. Such drugs include clarithromycin, azithromycin, ethambutol and rifabutin.

Toxoplasmosis (toxo)

Toxoplasmosis is caused by a protozoan found in uncooked meat and cat faeces. This microbe infects the brain and can cause raised intracranial pressure, which leads to headaches and vomiting. Other symptoms include confusion, motor weakness and fever. In the absence of treatment, disease progression results in seizures, stupour and coma. Disseminated toxo is less common, but can affect the eyes and cause pneumonia.

Definitive diagnosis of toxoplasmosis requires radiographic testing (usually an MRI scan). The infection is treated with drugs such as pyrimethamine, sulfadiazine and clindamycin. Leucovorin may also be used to prevent the side-effects of pyrimethamine. Prophylaxis against toxoplasmosis is through taking Trimethoprim-Sulphamethoxazole (TMP-SMX)

Recommendations advise HIV-positive individuals to: Avoid ingestion of undercooked meat, To wash hands after any contact with soil, to avoid emptying cat litter trays, or to empty trays daily and wash hands thoroughly after every disposal.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design and method.

A retrospective study covering the period of February 2011 to December 2011 at Mbarara Regional Referral Hospital was be carried out.

3.2 Sample Collection.

The samples used were the information in files available for the patients that have been on antiretroviral therapy (ART) and were managed at the Immune suppressed clinic of Mbarara regional referral Hospital within the study period.

3.3 Sampling Technique.

The files were selected randomly for the desired duration of time from the HIV/AIDS clinics of the M.R.R.H

Slovin's formula of sample size determination was used,

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

Where n= sample size

N= population size

e= margin of error (usually 0.05 since the preferred confidence level in sampling is 95%)

The population size was 15,000 people, the calculated sample size was 390 people, However this sample size was small and thus was be increased to a 1500 and every 10^{th} file was selected.

3.4 Study Area.

The study was carried out at Mbarara Regional Referral Hospital at the Immune suppressed syndrome clinic. It is the referral hospital for the entire country and specifically for the districts of Mbarara, Bushenyi, Ntungamo, Kiruhura, Ibanda and Isingiro. The hospital also serves as the

teaching hospital of Mbarara University of Science and Technology. The hospital is located in the city of Mbarara, Mbarara District, Ankole sub-region, Western Uganda. The hospital is located within the central business district of the city. This location lies approximately 295 kilometres (183 mi), by road, southwest of Kampala, the capital of Uganda and the largest city in that country. The coordinates of Mbarara Hospital are: 0° 36' 59.00"S, 30° 39' 32.00"E (Latitude:-0.616389; Longitude: 30.658890). The Immune Suppression Syndrome (ISS) Clinic in Mbarara, Uganda, is a prototypical municipal HIV/AIDS clinic in Africa, caring for over 15,000 HIV-infected adults since it began in 1998

3.4.1 Inclusion and Exclusion Criteria.

Only available and relevant information on opportunistic infections covering the chosen period of study was used in this research, only HIV/AIDs patients registered for management in the study area were considered for the study.

3.4.2 Limitation of the Study.

It is a study that did not involve direct interactions with the patients and thus no active follow up of the cases.

Mbarara hospital has over 15,000 patients thus more time was needed to do the study as well as a bigger sample size to represent a greater proportion of this population.

Most of the OI treatment was not provided at the immune suppressed syndrome clinic (ISS) since most patients were referred to other health centers for OI treatment and were mainly attending the ISS clinic for refill of their ARVs.

Diarrhea was recorded as one of the OIs, however the cause was not specified and thus the researcher was unable to establish whether it was due to which micro organism.

A financial constraint since Mbarara is located about 80kilometers from Bushenyi and this required transportation and facilitation which limited the researcher.

The institution program of Kampala International University being tight, it was a hectic period when carrying out the research. This was so because the tight school schedule would interfere with the time of collecting data from the files.

Some data was not available in the files and this also limited the researcher.

3.4.3 Data Collection.

A checklist was be used to carry out this study, this consisted of the opportunistic infections diagnosed among HIV/AIDS patients and these were recorded in a table.

3.4.4 Ethical Considerations.

Ethical approval was be obtained from the Institutional research and ethics committee board of Kampala International University Western Campus

A letter of permission and introduction was obtained from the Dean School of Pharmacy, the study will be highly confidential and the results will be treated without disclosure of the patients' names and personal information.

A letter of permission to do the study was then obtained from the Deputy Executive Director of Mbarara regional referral hospital before the research was done.

3.4.5 Dissemination of results.

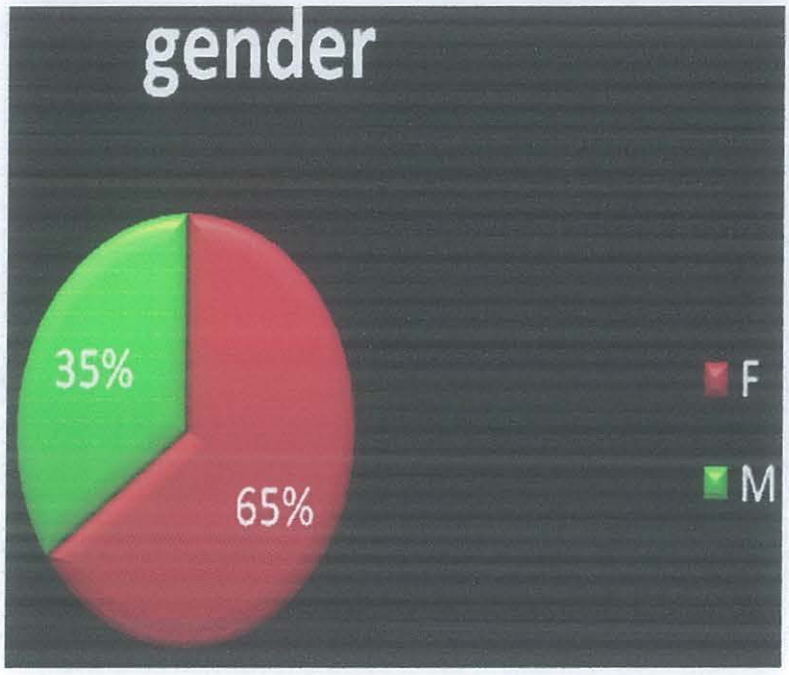
The dissemination plan includes the following;

1. Publication of working papers at Kampala International University-Western Campus.
2. Presentation of the results of the study in seminars and workshops.
3. Results will be communicated to policy makers and international donor agents.
4. Publication of articles in the national journal.

4.0 RESULTS

infections were most commonly diagnosed among HIV/AIDS patients in the study area and how they were recorded and managed. A total of 1,500 patients was reviewed.

Of the sampled patients, 65% were females, while 35% were males, indicating a higher percentage of females as compared to males.



SAMPLED PATIENTS ATTENDIND ART CLINIC IN MBARARA REGIONAL REFERRAL HOSPITAL.

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FIGURE ONE: A PIE CHART REPRESENTING THE GENDER DISTRIBUTION OF THE SAMPLED PATIENTS ATTENDIND ART CLINIC IN MBARARA REGIONAL REFERRAL HOSPITAL.

4.2 PREVALENCE OF OPPORTUNISTIC INFECTIONS

The population was sampled with a main aim of determining the opportunistic infections that occur and are recorded among patients, the results showed that 39% had diarrhea, which was the highest and followed by 28% had no OI, 7% had cryptococcosis, 6% were recorded to have oral candidiasis, 5% with vaginal candidiasis, 5% with tuberculosis and vaginal candidiasis, 4% with herpes zosta, while 3% had herpes simplex, 1% had esophageal candidiasis and skin fungal infection which were the lowest percentages.

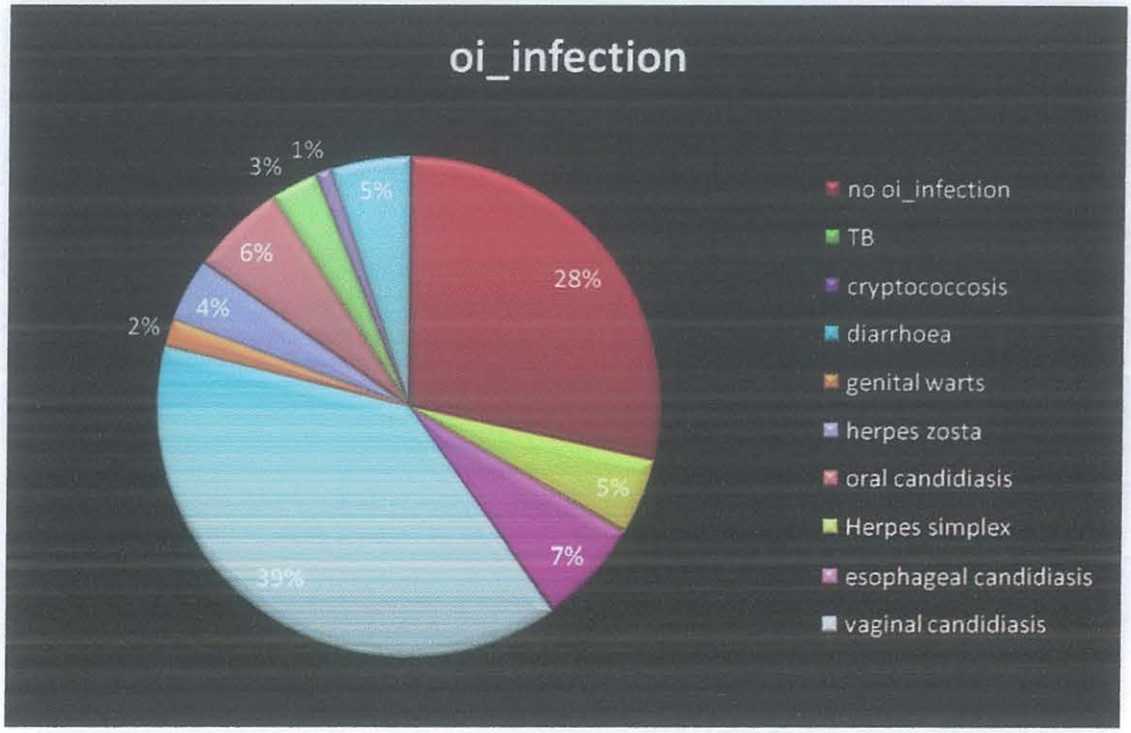

FIGURE 2: A PIECHART SHOWING THE PERCENTAGES OF THE PREVALENCE OF OIs

4.3 DRUGS USED IN TREATMENT FOR THE OPPORTUNISTIC INFECTIONS

Different drugs were used for treating the above OIs and are represented in the diagram below. Some of the drugs were not recorded due to treatment not being provided at the ART clinic, while others were being prescribed as an adjunctive treatment. 17% sampled population indicated no treatment recorded for the OI, this was the highest, 18% indicated treatment with metronidazole (for diarrhea) and 16% with ciprofloxacin; 13% showed treatment with nystatin suspension while 10% with fluconazole, both amphotericin and acyclovir were represented by 5% of the total treatment, and 3% represented nystatin pessaries, vitamin B complex and DOTS (Directly Observed Treatment Shortcourse.). Clotrimazole cream, multivitamin and amytriptiline were represented by 2% , 1% was the lowest percentage which represented podophyllin,

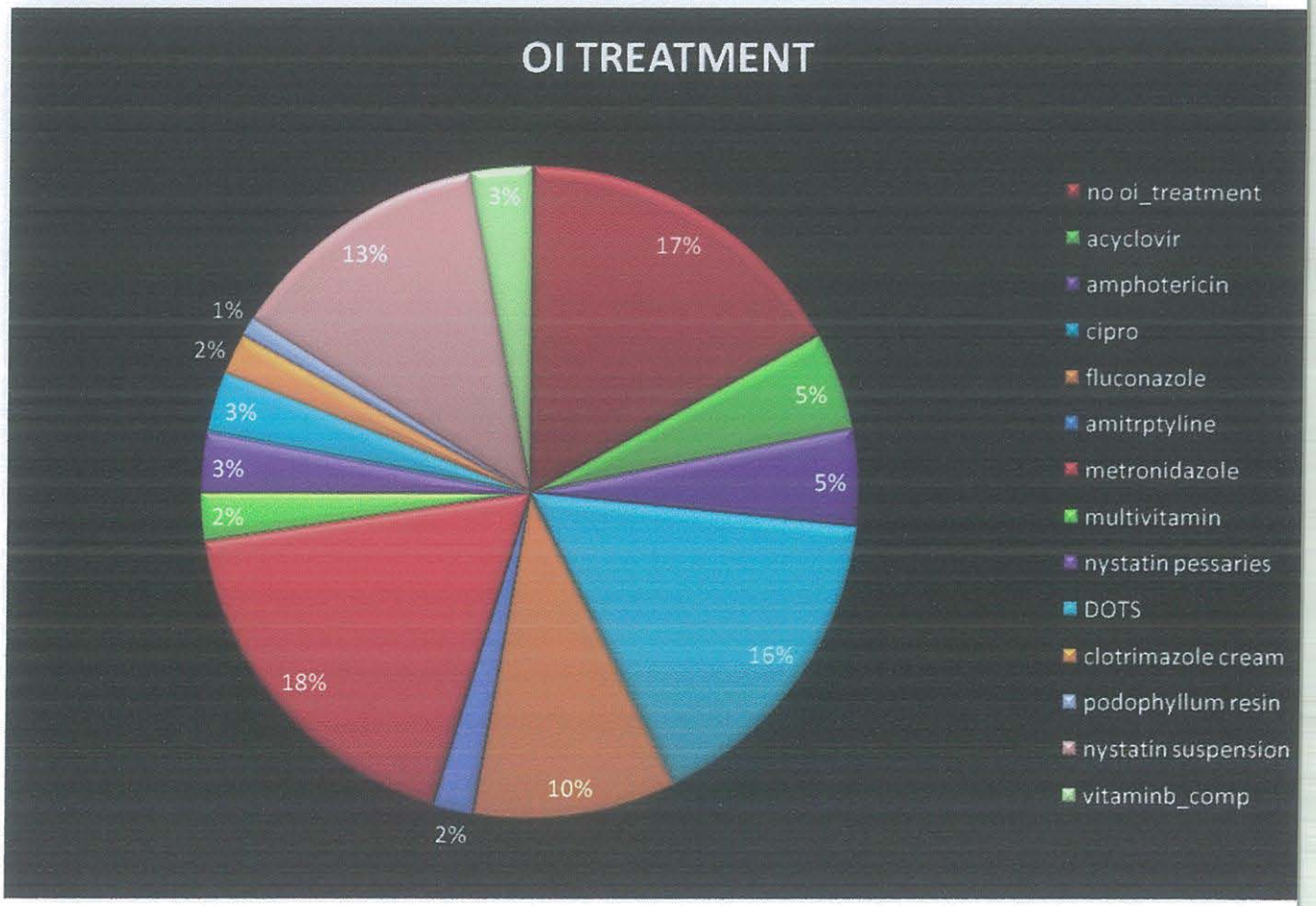

FIGURE 3: A PIE CHART REPRESENTING THE PERCENTAGES OF DRUGS USED IN THE TREATMENT OF THE RECORDED OIs.

OI TREATMENT	
no oi_treatment	17
acyclovir	5
amphotericin	5
cipro	16
fluconazole	10
amitrptyline	2
metronidazole	18
multivitamin	2
nystatin pessaries	3
DOTS	3
clotrimazole cream	2
podophyllum resin	1
nystatin suspension	13
vitaminb_comp	3
Total	100

FIGURE 4: A TABLE REPRESENTING THE PERCENTAGES OF DRUGS USED IN MANAGEMENT OF THE DIFFERENT OIs.

4.4 MARITAL STATUS

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In the reviewed cases, majority of the subjects were married (55%), followed by the single (22%), widowed (16%) and finally the divorced (7%). The single group combined those whose marital status was recorded as single, never married and separated.

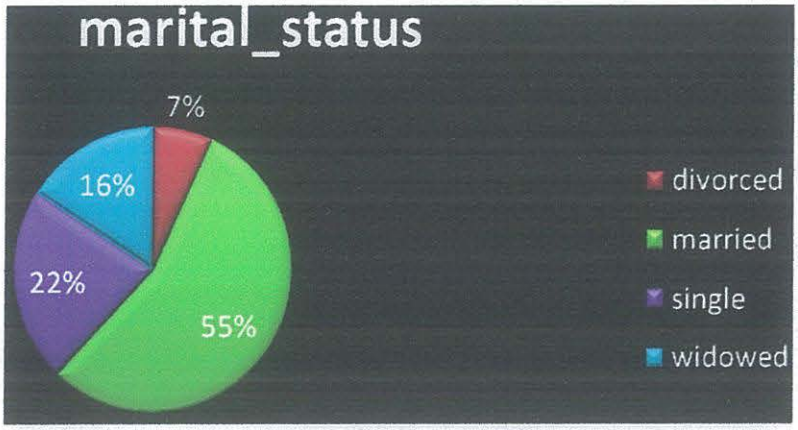

FIGURE 5: A PIECHART SHOWING THE DISTRIBUTION OF OIs ACCORDING TO MARITAL STATUS IN THE SAMPLE POPULATION.

4.5 WHO HIV/AIDS CLINICAL STAGING

HIV/AIDS patients that were retrospectively reviewed fell under a category of the World Health Organization clinical stages as; 20% for stage1, 5% for stage2, 4% for stage3, 8% for stage4, while for the remaining 63% the WHO stage was not recorded in the files.

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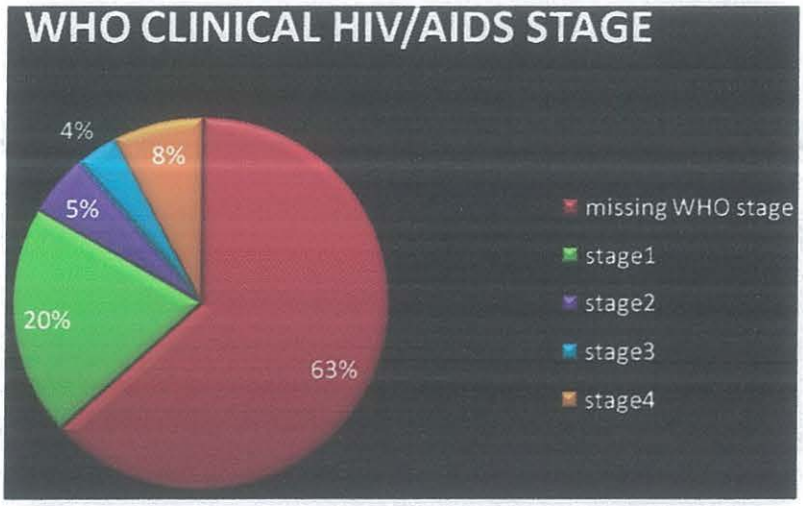

FIGURE 6: A PIECHART SHOWING THE CLINICAL HIV/AIDS staging of the patients according to the world health organization.

4.6 ANTIRETROVIRAL DRUG REGIMENS

Different patients were on different ART regimens, it was found out that all patients were on HAART, except for those who had not yet started taking anti retro viral drugs, the percentages were as follows; 27% were not yet on ART and this was the highest percentage, 21% were on efvtdf_3tc, 17% were on efvtruvada, 14% on cbv nvp, 10% on cbvefv, 4% on nvptdf_3tc, 2% on kaltruvada , while for efvd4t_3tc, kaltdf_3tc and truvada, it was 1%.

ART drug regimen	
pre ART	27
cbv nvp	14
cbvefv	10
efvd4t_3tc	1
efvtdf_3tc	21
efvtruvada	17

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kaltruvada	2
kaltdf_3tc	1
nvptdf_3tc	4
nvptruvada	2
truvada	1
Total	100

FIGURE 7: A TABLE REPRESENTING THE PERCENTAGE DISTRIBUTION OF THE ART DRUG REGIMENS OF THE PATIENTS.

It shows that 72% were on HAART which consists of cbv nvp, cbvefv, efvd4t_3tc, nvptruvada, efvtruvada, kaltruvada, kaltdf_3tc, nvptdf_3tc, efvtdf_3tc.

KEY FOR DRUG REGIMENS

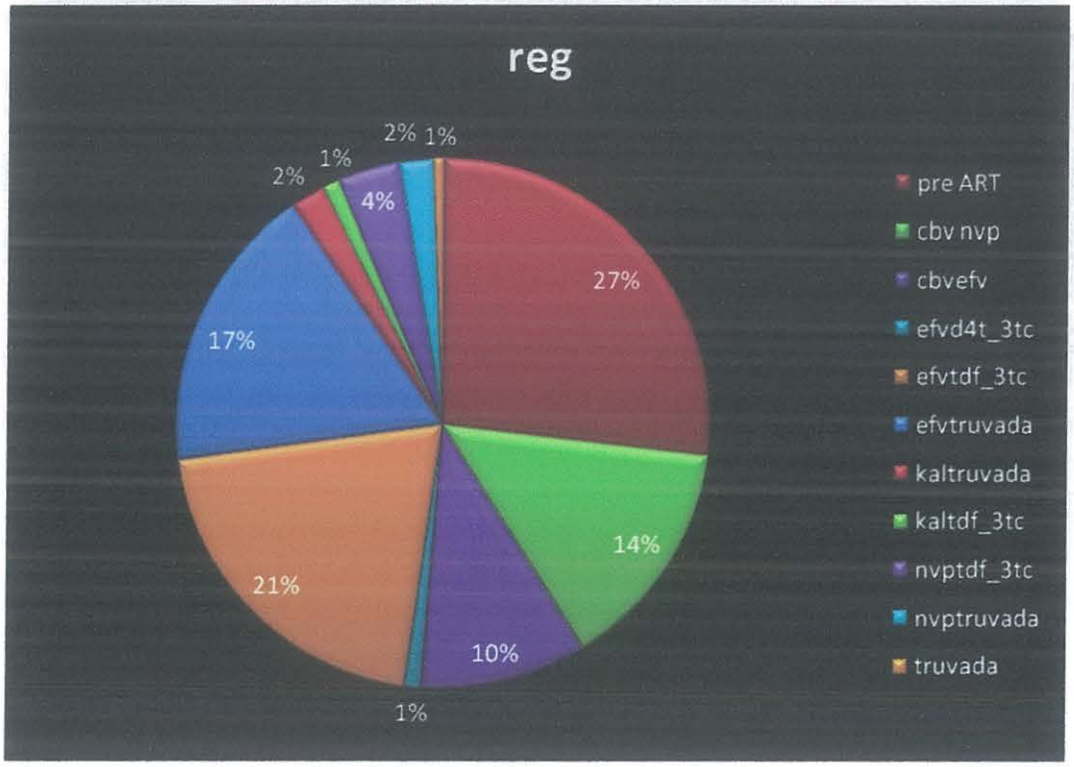
ART drug regimen	
pre ART	Not on ART
cbv nvp	Combivir/niverepine
cbvefv	Combivir/efavirenz
efvd4t_3tc	Efavirenz/tenofovir/lamivudine
efvtdf_3tc	Efavirenz/tenofovir/lamivudine
efvtruvada	Efavirenz/truvada
kaltruvada	Lopinavir/ritonavir
kaltdf_3tc	Ropinavir/ritonavir/tenofovir/lamivudine
nvptdf_3tc	Nevirapine/tenofovir/lamivudine
nvptruvada	Nevirapine/truvada
truvada	1

Total	100

Combivir= zidovudine(300mg)/Lamivudine(150mg)

Truvada= tenofovirdisoproxil(245mg)/Emitricitabine(200mg)

Kal=kaletra= Lopinavir(100mg)/Ritonavir(25mg)



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CHAPTER FIVE

5.1 DISCUSSION

The females had the highest percentage of OIs as compared to males, and this also means the percentage of HIV positive women was higher than for men. This may be due to some OIs attacking only women, such as Vaginal candiasis, and also that Women often have older partners, and men rarely have partners much older than themselves, women are also more involved in risk activities such as sex workers who will have more multiple partners. Women also tend to be more active in attending the ART clinics as compared to most men that chose to be discrete claiming to have a busy schedule and have to provide for their families. Generally women are at a greater risk of heterosexual transmission of HIV. Biologically women are twice more likely to become infected with HIV through unprotected heterosexual intercourse than men WHO (2009). Women are less likely to be able to negotiate condom use and are more likely to be subjected to non-consensual sex.

From the opportunistic infections recorded, the highest percentage was diarrhea (39%) for which the cause was not specified, this could be due to the HIV itself - a condition termed HIV enteropathy. In some cases there is impaired epithelial barrier function. Diarrhea in HIV/AIDS patients is commonly infective in origin (Wilcox CM *et al*,1996). A whole range of pathogens may give rise to diarrhea, including bacteria, virus, mycobacteria and parasites, involving the small and/or large bowel. Classical pathogens in HIV/AIDS include *Cryptosporidia*, *Isospora belli, Microsporidia* and *Mycobacterium avium-intracellulare* (MAI). Systemic infections could occur when the pathogen disseminates from the gut, as in some cases of bacterial infections (MAI, *Salmonella, Shigella, Campylobacter*). Advance in HIV treatment is changing the profile of AIDS-associated diarrhea. Highly active antiretroviral therapy (HAART) is causing a reduction of opportunistic infections as the cause of diarrhea (Sande MA *et al* 1997). Chronic diarrhea, if occurs, is more likely to be a result of the side effects of antiretrovirals themselves.

Cryptococcosis was the second most common opportunistic infection (7%), followed by vaginal candiasis and this is attributed to the weakened immune system. Infection with HIV continues to be more important risk factor for development of central nervous system cryptococcosis and is an important contributor to morbidity and mortality in HIV infected patient it is caused by

Cryptococcus neoformans. Because of effective antiretroviral treatment (ART) available, the incidence of cryptococcosis, along with other opportunistic infections, has decreased. But the decrease in new cases of cryptococcosis may have started even earlier; other data suggest a decline in incidence associated with the more frequent use of azole antifungals. Since oral and vaginal candidiasis can occur in the presence of a relatively high CD4 count, the impact of HAART on their occurrence may be less than that on oesophageal candidiasis This decline has been correlated with reduction in HIV-1 RNA levels in the plasma.

TB prevalence was found to be 5% of the total population, TB remains an important cause of illness and death in patients receiving ART in Uganda. However, both appear to decline markedly, after 6 months of ART (from a study in tororo Uganda by Moore D *et al.*) Undiagnosed tuberculosis is a challenge for tuberculosis control and new approaches are needed

Among HIV-1 infected individuals, HSV-1 and HSV-2 infections are common, with prevalences that approximate or exceed those in the general population. Preexisting antibody to HSV-1 is associated with milder or asymptomatic primary HSV-2 infection. Many HIV-1-infected persons are already infected with HSV-2 at the time of HIV-1 acquisition, and cases of primary HSV-2 infection therefore are relatively uncommon among HIV-1-infected individuals. Notably, primary genital HSV-2 occurring in an HIV-1-infected person is a marker for ongoing unsafe sexual practices. When primary infection occurs among HIV-1-infected persons with advanced immunosuppression, its course tends to be prolonged and more severe.

Primary varicella infection (chicken pox) occurs infrequently in HIV-infected adults, as more than 90% of adults in the United States possess antibodies to the virus as a result of childhood varicella infection. Given the widespread prevalence of varicella-zoster virus (VZV) infection in adults, most HIV-infected adults are at risk of developing VZV reactivation and herpes zoster.

28% of the population had no OI infection, this could be attributed to the ability of their immune systems to fight off the infections in addition to HAART, it was also observed that prophylactic treatment was available for the patients, which was mainly trimethoprim-sulphamethoxazole (septrin) or dapsone for those sensitive to septrin, this explains the absence of PCP infection.

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The OI treatment correlated with the OI infection, with the highest percentage of patients being treated with metronidazole (18%) followed by ciprofloxacin (16%). This was because of the

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diarrhea which could have been due to infections like shigella, or other common agents that cause diarrhea in HIV and upper respiratory infections that are common in HIV/AIDS, however 17% indicated no OI treatment and this could be as a result of treatment for the OI not being provided at the ART centre since patients are referred to another government health centre for the treatment.

For fungal infections, nystatin oral suspension represented 13% and could be attributed to the cost (cheap) , reduced toxicity and availability and drug-drug interactions with Anti retro Viral drugs compared to other antifungals, this was followed by Fluconazole (10%) which is very effective in treatment of oral candidiasis and cryptococcosis, however has some drug interactions with ARVs such as it increases the plasma concentrations of neverapine and ritonavir (BNF 2010), and thus used upon anticipated resistance to nystatin for the case oral candidiasis but usually preferred to Amphotericin B in treatment of cryptococcosis because of its cheaper cost, and easier method of administration (oral) compared to amphotericin which is usually given intravenously, is nephrotoxic and is quite more expensive though it has a shorter duration of treatment and no drug interactions with ARVs compared to fluconazole. Amphotericin use was thus 5% in management of severe fungal infections (cryptococcosis). Vaginal candiasis was mainly treated with nystatin pessaries due to their effectiveness and availability, clotrimazole cream was also used to treat the fungal skin infection due to its desired efficacy, wide spectrum and easy accessibility and cheap cost. For the tuberculosis the treatment used was DOTS (Directly Observed treatment Short course) due to anticipated non-compliance and in addition Vitamin B complex was also given to protect the nerves from neuritis, however pyridoxine would have been given at 10mg daily.

Herpes zoster and Herpes simplex were treated using acyclovir (5%) because its available and affordable. Other drugs that can be use for these infections such as valaciclovir, famciclovir are more expensive and very toxic as compared to acyclovir. Amitryptiline was used because of the neuropathic pain associated with shingles.

Genital warts treatment recorded was podophyllum resin (1%), other treatments such as silver nitrate were not recorded.

Mulitivitamin tablets were represented by a percentage of 2%, was given to prevent depletion of vitamins, which play a protective role in the body, and since ARVs are associated with a myriad of side effects, such as aneamia, these are important for protective purposes.

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As per the marital status, majority of the patients were married (55%) while the least was divorced (7%), the prevalence of HIV among married is as a result of infidelity, husbands who are known to be cheaters should know, that when they cheat, their wives may also do the same. Due to trust and the unprotected sex associated with marriage, the risk of infection with HIV is high.

The WHO clinical staging, stage1 was the highest with 20% and the lowest was the 4% for stage three. 63% of the stages were not recorded. Asymptomatic and Persistent generalized lymphadenopathy clinically indicate stage1 thus it was the most common as per the clinicians. This implies that stage 1 was the most highly recorded stage by the clinicians on first contact with the patients, since the WHO stage is only recorded once for each patient whether they improve or decline clinically. Those that were not recorded it could have been due to negligence of the clinicians or absence of clinical signs and symptoms of the HIV/AIDS disease as per WHO staging.

Different patients were on different ART regimens, it was found out that all patients were on HAART, except for those who had not yet started taking anti retro viral drugs and 1% that was on truvada alone, the percentages were as follows; 26% were not yet on ART and this was the highest percentage, 21% were on efvtdf_3tc, 17% were on efvtruvada, 14% on cbv nvp, 10% on cbvefv, 4% on nvptdf_3tc, 2% on kaltruvada , while for efvd4t_3tc, kaltdf_3tc and truvada, it was 1%.

From the ART combinations, it can be shown that the highest percentage was not yet ART and thus had the highest incidence of opportunistic infections, followed by those on efvtdf_3tc, the lowest percentages 2% for kal truvada and 1% for kal-tdf, cbv-tdf, efvd4t-3tc and truvada. The low prevalence of OIs is mainly due to HAART (Highly Active Anti retro viral therapy) which is known to strengthen the immune system thus reducing OIs. Also protease inhibitors are associated with the lowest incidence of OIs. This decline has been correlated with reduction in HIV-1 RNA levels in the plasma.

5.2 CONCLUSION

From this study, diarrhea was the most common opportunistic infection among the reviewed patients, this calls for proper diagnosis to establish the exact cause of the diarrhea.

The least commonly occurring OI was esophageal candiasis there was also a considerable number of cases of TB, cryptococcosis as well as oral and vaginal candidiasis; A considerable number of patients also had no OIs and this was because some of the infections were not reported in the ART care card from the ministry of health.

The drugs most commonly used for the OIs were metronidazole and ciprofloxacin for diarrhea and this calls for more procurement of these drugs, so that they are readily available to treat the patients, however proper diagnosis should be done to establish the exact causative agent before treatment.

The female gender had the highest percentage as compared to men, similarly, Married had the highest incidence as compared to the divorced thus the married require the health education about fidelity and faithfulness as a method to prevent more problems.

The patients on HAART whose combinations contained a protease inhibitor had the lowest incidence of opportunistic infections.

The highest percentage of patients with OIs were from WHO clinical stage one and this could me an important indicator to avoid these OIs by careful monitoring of patients in this stage, however some of the WHO stages were not recorded and this could have affected the percentage.

5.3 RECOMENDATIONS

A detailed prospective study that involves active interactions between patients, clinicians and the researcher should be carried out to ascertain whether the patients respond to the treatments given to them.

There are a number of things that can be done in order to reduce the burden of the epidemic among women. These include promoting and protecting women's human rights, increasing education and awareness among women and encouraging the development of new preventative technologies such as post-exposure prophylaxis and microbicides.

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The proper diagnosis of the causative organisms of diarrhea should be established before treatment, as well as the health education to the HIV/AIDS patients on how to prevent these infections.

Even though the coccidian parasites are considered AIDS-defining opportunistic pathogens according to CDC, their screening is not done even in known HIV patients in most routine laboratories at the primary care level due to the lack of knowledge, expertise and technique

Therefore, it is suggested that steps should be taken to prevent the occurrence of these diseases in AIDS patients, as often the disease may take a fulminant form. This can be done by drinking safe water and avoiding contact with contaminated soil.

The use of fluconazole is effective in prospective controlled trials to prevent cryptococcosis as well as mucosal candidiasis in advanced HIV disease. However, mortality is not reduced. Prolonged primary prophylaxis is therefore not advised, "because of the effectiveness of therapy for acute disease, the low mortality associated with mucosal candidiasis, the potential for resistant *Candida* organisms to develop, the possibility of drug interactions, and the cost of prophylaxis". As secondary prophylaxis, chronic treatment with fluconazole 100-200 mg daily may be considered in frequently recurrent esophageal candidiasis. However, recurrent oesophagitis is becoming uncommon in the era of HAART.

The treatment centers for OIs should be established at the ART centre for easy monitoring and follow up of the OIs, as this will improve on the diagnosis and recording of the infections on the HIV ART care card.

Pyridoxine 10mg/20mg daily should be recommended for prophylaxis against peripheral neuropathy in Tuberculosis treatment and this should be recorded.

HAART is highly recommended to reduce the occurrence of OIs amongst the HIV/AIDS patients, especially that consisting of a protease inhibitor such as Kaletra, however it is expensive thus requires planning by the ministry of health and sourcing for funding from the international community since these drugs are expensive.

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The use of Trimethoprim-sulphamethoxazole or dapsone for prophylaxis against PCP is very effective and thus reduces morbidity among HIV/AIDS patients, ministry and non governmental organizations should continue to supply these drugs. This also protects against toxoplasmosis.

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