Clinical outcome of HIV patients who commence antiretroviral therapy at different CD4 levels

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A research report submitted to the faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of Master of Science in Medicine (Pharmacotherapy)

Declaration

I, Khutjo Peter Mothapo declare that this research report is my own work. It is being submitted for the degree of MSc (Med) Pharmacotherapy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other institution.

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Acknowledgements

I would like to thank the following:

My supervisor Ms Shirona Naidoo, thank you very much for your dedication. I have learned a lot under your guidance.

The management at the intuitions where the study was conducted for allowing me access to data.

Prof Schoemann for data analysis.

I would also want to thank my mother, Dike, Naledi, Tebogo and Jackie for proof reading.

This is dedicated to my son, Matidi Neo Mothapo

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ABSTRACT

Background: The decision of when to start treatment in an HIV-infected individual has always been problematic as far as CD4 count is concerned.

Aims: To determine the clinical outcome of patients who commence HAART at different CD4 cell count levels.

Method: Retrospective analysis of records of a cohort of patients who are received ART at workplace wellness clinics in three mines in Limpopo province from January 2003 to December 2009. Patients were divided into three groups based on their baseline, group A (CD4 <100), group B (CD4 101-200) and group C (CD4 201-250)

Each patient's data was analyzed one year after his/her commencement.

Results: The percentage of patients who died in group A (16%) differs significantly from the percentage of patients who died in group B (4%) (Fisher exact test p= 0.038) and also differ significantly from the percentage of patients who died in group C (0%) (Fisher exact test p= 0.011). The percentages of patients who developed TB in the three groups are 8%, 8% and 2.9% respectively. When compared statistically, these percentages do not differ significantly (Fisher exact test p=0.059).The percentages of patients with severe bacterial pneumonia in the three groups (2%, 2% and 0% respectively) do not differ significantly (Fisher exact test p=0,276).The percentage of hospital admissions for patients in group A (18%) differ significantly from the percentage in group B (6%) and the percentage in group C (6%) (Fisher exact test p= 0.05). The percentage of patients with weight loss of more than 10% of baseline value in group A (24%) differ significantly from the percentage in group B (4%) (Fisher exact test p= 0.003) and also differ significantly to from the percentage in group C (0%) (Fisher exact test p= 0.001). The percentage of patients with undetectable viral load in group B (89%) is significantly different from the percentage in group A (69%) (Fisher exact test p= 0.03) and is also significantly different from the percentage in group C (61%) (Fisher exact test p= 0.008).The change in mean CD4 cell count was found to be statistically significant within each group (paired t test, p<0.0001), but the mean changes between the three groups (132,141 and 172) respectively, do not differ significantly (ANOVA test).

Conclusion: Patients with baseline CD4 cell count of less than 100 have a poor clinical outcome when compared to patients with baseline CD4 cell count of more than 100. Efforts must be made to identify patients early before CD4 cell count fall to below 100 and preferably initiate HAART when CD4 cell count is above 200.

INTRODUCTION

Statistics of HIV and AIDS

Since its discovery in the early nineteen eighties, Human Immunodeficiency Virus (HIV) has caused an epidemic of unequalled proportion. Its spread is exponential and seems unrelenting. It has had a substantial effect on the lives of the people, i.e. destroying communities and families and leaving children orphaned. Because it is more prevalent among the ages of 15 to 49 years, grandparents have to take the role of the deceased parents and in instances where grandparents are deceased it results in child-headed households. More and more government resources are now being directed to curb the spread of HIV and to treat the infected and help the affected (Statistics South Africa 2009).

The South African population is estimated at around 49 million, 52% of which is female. The estimated overall HIV prevalence rate of the whole population is approximately 10.6%. The total number of people living with HIV is estimated at approximately 5.21 million. An estimated 17% of people aged 15 to 49 years are HIV positive. This is high as compared to the United States of America (USA) and Eastern Europe where the prevalence is around 2% .In South Africa, the prevalence is spread along the racial line. The prevalence in Africans is 13.6%, Coloureds at 1.7%, Indians at 0.3%, and Whites at 0.3% (Centers for Disease Control and prevention 2007, Statistics South Africa 2009, UNAID 2008 and Human Sciences Research Council 2008). Perhaps this vast difference between racial groups may be due to underreporting.

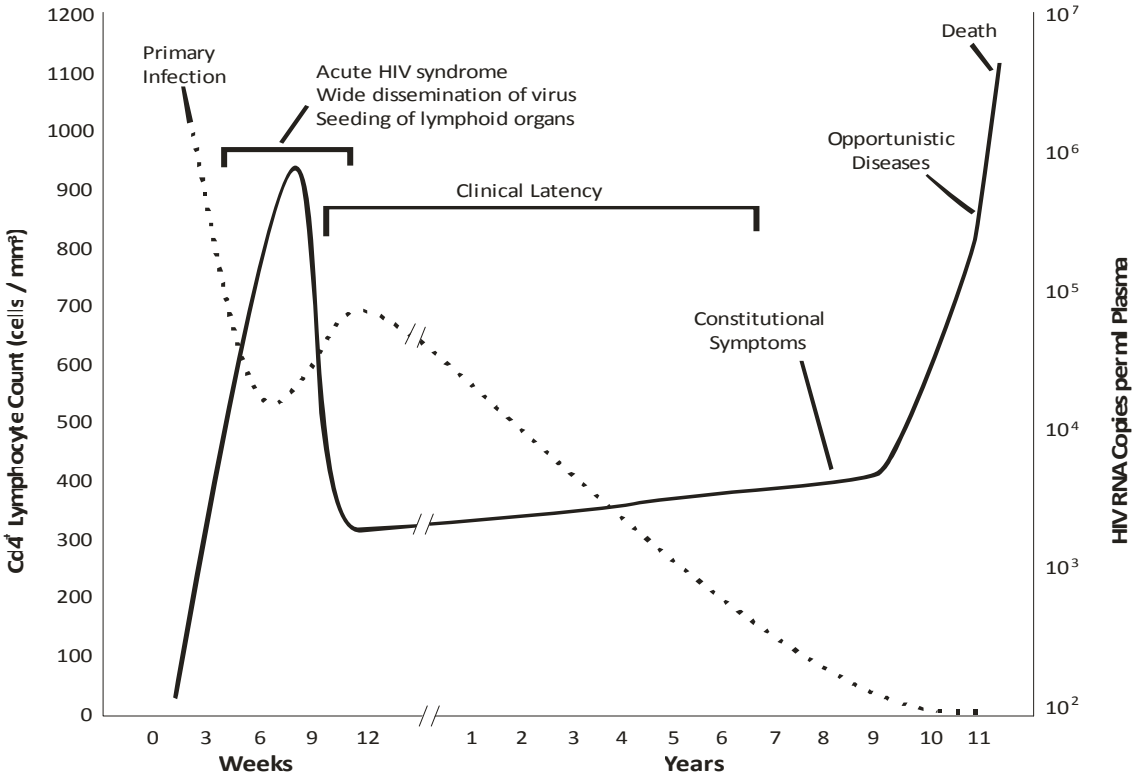
The rate of new HIV infections has fallen in several countries, but globally these favourable trends are at least partially offset by an increase in new infections in other countries, especially in the Sub-Saharan African region. This region remains the most heavily affected by HIV, accounting for 67% of all people living with HIV and 57% of AIDS deaths in 2007 (UNAID 2008). This is one of the poorest regions in the world and due to reluctance of the government and cost of antiretroviral drugs, access to treatment is inadequate.

Clinical features of HIV and AIDS

Immediately after infection, the virus is harboured in the gut-associated lymphoid tissue (GALT), the lymphatic tissue of the small bowel. The early phase of infection is characterised by viral amplification in GALT which results in peak viremia and a rapid decline in CD4 count. This occurs two to six weeks after the infection and is often associated with “acute retroviral syndrome” characterised by flu-like

symptoms. After this acute infection CD4 increases again, almost reaching the normal level and the viremia decreases. The infected person is now asymptomatic and this may persist for about ten years. Although the infected person is without symptoms, the CD4 count gradually decreases due to continuous HIV replication. The symptomatic phase starts when the CD4 count decreases to a level where the immune system is unable to cope with the infection (Brencheley et al., 2004).

Figure 1: Natural history of HIV infection in an average patient without antiretroviral therapy from the time of transmission to death at 10-11 years (Bartlett F 2008).



HIV infection can generally be broken down into four distinct stages: primary infection, clinically asymptomatic stage, symptomatic HIV infection and progression from HIV to AIDS. In resource-poor communities, medical facilities are sometimes poorly equipped and it is not possible to use CD4 and viral load test results to determine the right time to begin antiretroviral treatment. The World Health Organization (WHO) has, therefore, developed a staging system for HIV disease based on clinical symptoms which may be used to guide medical decision making (WHO 2006).

Table 1 outlines the WHO clinical staging of HIV/AIDS for adults and adolescents with confirmed HIV infection (WHO 2006).

Clinical stage	Associated conditions
1	Asymptomatic Persistent generalized lymphadenopathy
2	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
3	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)
4	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 septicemia (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

Progressive loss of CD4 cells is the cardinal manifestation of the effect of HIV. CD4 cell count has therefore been used as an indicator of the severity of the infection and has been shown to be an independent risk factor for progression to AIDS and death. CD4 cell percentages below 15 are independent predictors of mortality in AIDS-free patients starting HAART, including those with CD4 count between 200 and 350. CD4 percentage should be considered for inclusion in the guidelines used to determine when to start therapy (Moore et al., 2006). However, most adults' HAART guidelines use absolute CD4 count rather than the percentage count.

HAART has changed the course of HIV infection from a rapidly fatal to a chronic manageable disease. HAART reduces the amount of virus in the blood, ideally to below a detectable limit of the assay. This allows gradual recovery of the immune system and consequently results in the reduction of HIV-related illnesses therefore leading to reduced morbidity and mortality (Mzileni et al., 2008 and Wilson et al., 2008).

Treatment initiation

The decision of when to start treatment in an HIV-infected individual has always been problematic as far as the CD4 count is concerned. Treatment should be initiated at an early point in the individual's course of disease, prior to a time when CD4 cell loss is such that there is substantial risk of clinical progression. On the other hand, there is an inconvenience that comes with taking life-long treatment with possible fatal toxic effects.

Of the NNRTI's, efavirenz is associated with neuropsychiatric side effects which range from nightmares to acute psychosis and also possible foetal defects should a woman fall pregnant. Nevirapine is associated with hepatotoxicity which occurs more frequently in women with a baseline CD4 cell count above 250. The NRTI are associated with peripheral neuropathy, anaemia and lactic acidosis which is potentially fatal. The protease inhibitors predominantly cause lipodystrophy which is characterised by abnormal fat redistribution with peripheral wasting and central obesity (Montessori et al., 2004). These side effects may interfere with activities of daily living, negatively affecting the quality of life and also becoming a major obstacle to adherence. A study by Mutimura et al., 2007, in Rwanda showed that body fat alterations negatively affect psychological and social domains of the quality of life and may result in stigmatization and marginalization.

HAART has a positive impact on the quality of life but baseline characteristics like low CD4 cell count and more advanced HIV disease stages are predictors of decreased quality of life once on HAART (Wouters at al., 2009 and Lui et al., 2006).

Thus, there is a need for clinicians to balance the risk of delaying treatment (potentially placing the patient at risk of serious illness and death from AIDS) with the inconvenience of taking life-long treatment and possible long-term adverse effects of antiretroviral drugs.

On the basis of evidence that clinical progression rates were low while the CD4 cell count remained above 200 but increased rapidly at lower levels, most early treatment guidelines recommended that HAART be delayed until CD4 cell count had fallen to below 200 (Hammer., et al 2008).

Table 2: The South African antiretroviral treatment guidelines 2004 (Department of Health 2004).

Adults and adolescents - including pregnant women
CD4 count < 200cell/mm^3 – irrespective of stage OR -WHO stage IV AIDS-defining illness, irrespective of CD4 count AND -Patient expresses willingness and readiness to take ART adherently

Recently, most guidelines (DHHS-USA Department of Health and Human Services, IAS-USA-International AIDS Society) have recommended initiation of HAART at CD4 of 350 and below. This was supported by data from cohort studies which showed that immune suppression (indicated by low CD4 counts) at the start of therapy worsens the prognosis (Thompson et al., 2010 and Department of Health and Human Services (DHHS) 2007).

There is however evidence that support starting HAART in AIDS-free treatment naïve patients with CD4 cell count of more than 350. The implication is that we may see guidelines changing the CD4 count threshold of initiating HAART to 450 in the near future. Data analysis from over 45000 patients, who were followed up in cohort studies in Europe and North America, suggests that deferring the start of HAART in AIDS-free HIV-1-infected patients until CD4 cell counts are in the range 251 to 350 leads to increased rates of combined endpoint of AIDS or death as compared to starting HAART when CD4 cell count is in the range of 351 to 450 (Sterne J, 2009). Also, patients with baseline CD4 cell counts more than 350 return to nearly normal CD4 cell counts after six years, but for patients with lower baseline CD4, the increase in CD4 cell plateaus at a lower level despite virological suppression (Moore et al., 2007). Patients who fail to exhibit a marked increase in the CD4 cell count despite achieving complete suppression of the viral load are referred to as “immunological nonresponders” and make up to 30% of all HIV- infected patients who are on long-term HAART. These patients have an increased risk of AIDS and death. They are a challenge to the treating physician because although several treatment modalities like protease inhibitors and CCR5 receptor antagonists (Maraviroc) have

been suggested and investigated, unfortunately no consensus has been reached yet on the most efficacious treatment. (Gazzola et al., 2009 and Taiwo B, 2009)

Despite the vast evidence that the threshold of starting HAART should at least be 350, the new guidelines for South African public service still use CD4 cell count of 200 as the threshold of starting HAART. The threshold is increased to 350 only for pregnant women and patients infected with TB.

Table 3: The South African antiretroviral treatment guidelines 2010 (Department of Health South Africa 2010).

Eligible to start ART
CD4 count < 200cell/mm^3 – irrespective of clinical stage OR -CD4 count < 350cell/mm^3 -In patients with TB/HIV -In pregnant women OR -WHO stage IV irrespective of CD4 count OR -MDR/XDR TB irrespective of CD4 count
Require fast track (i.e. ART initiation within 2 weeks of being eligible)
Pregnant women eligible for life long ART OR Patients with very low CD4 count (<100) OR Stage IV, CD4 count not yet available OR - MDR/XDR TB

Increasing the CD4 cell count threshold for initiating HAART in pregnant women and TB patients to 350 indicates that the government is aware of the international guidelines and the clinical evidence supporting them and acknowledges the need to increase the threshold to 350 in all HIV-positive patients. However, financial constraints continue to be a limiting factor. The national budget for HIV/AIDS and TB for 2010/ 2011 financial year is R6.5 billion which is 33.1% of the total health budget. This has been increased by 33% from the previous year. Health Minister Dr Aaron Motswaledi said that the massive demand of antiretroviral drugs will collapse the fiscus if not stopped by reducing the rate of infection by 50% by 2011 (Budget review, 2010). Increasing the CD4 cell count threshold for initiating HAART to 350 will not only increase the budget for antiretroviral drugs, but infrastructure will need to be developed to cater for the increasing number of patients and the need for both medical and administrative personnel will also increase. All these expenses will put even more strain on the health budget. It is due to these financial difficulties that South Africa, like many other developing countries opts for treatment guidelines where fewer patients are considered eligible.

The benefits of increasing HAART CD4 cell count initiation threshold to 350 are more cost-effective in the long-term. The rate of opportunistic infections decreases when HAART is started early decreasing the rate and the cost of hospitalization. The mortality will decrease, thus maintaining the country's work force and reducing the number of child-headed households. The number of people dependent on social grants will also decrease (Walensky et al., 2009 and Badri et al., 2006).

There are two reasons to increase the CD4 cell count threshold of starting HAART in pregnant HIV-positive women from 200 to 350. Firstly, it is to protect the mother from disease progression and secondly it is to protect the fetus and the subsequent infant from contracting HIV. In HIV-positive women, CD4 declines faster after pregnancy. The comparative immunological advantage possessed by fertile women is subsequently lost as a result of their pregnancy (van der Paal et al., 2007). Mother –to-child-transmission (MTCT) is the primary means by which newborns worldwide acquire HIV infection. Transmission occurs during three major time points during pregnancy and the postpartum period: in utero, intrapartum and during breastfeeding.

Strategies to reduce MTCT focus on these periods of exposure and include maternal and infant use of antiretroviral drugs, caesarean section before onset of labour or rapture of membranes when indicated and complete avoidance of breastfeeding. In the United States and other developed countries, a

combination of these interventions decreased the risk of mother-to –child transmission to less than 2% (Anderson et al., 2009 and Sturt et al 2010).

For sub-Saharan Africa, a study conducted by Torpey et al in 2010 in Zambia, showed that in cases where the mother and infant received antiretroviral treatment, the transmission rate was 6.5% whereas it was 20.9% when there was no intervention given to the mother or the baby. In cases where a single dose of nevirapine was given the transmission rate was 8.5% while it was 6.8% with zidovudine plus single dose nevirapine. HAART was associated with observed transmission rates of 5.0%. Whereas these estimates were not significantly different from one another, they were all significantly lower than no intervention. However in the Kesho Bora study there was a significant difference in MTCT at 12 months between breastfeeding women who initiated AZT/3TC/LPV-r starting between 28 and 36 weeks and those receiving a short course regimen (RR 0.58, 95% CI: 0.34-0.97) (deVincenzi, 2009). MTCT also decreased significantly when AZT/3TC/NVP was compared with a short-course regimen at seven months in a feeding intervention study (RR 0.15, 95% CI: 0.04-0.62) (Bae et al., 2008) and at 12 months in a population where either exclusive breastfeeding or replacement feeding was encouraged (RR 0.14, CI: 0.04-0.47) (Ekouevi et al., 2008). In the Mma Bana study (a randomized controlled trial in a breastfeeding population) there was no difference in MTCT at six months between the AZT/3TC/LPV-r and AZT, 3TC, and abacavir (ABC) arms (RR 0.17, 95% CI: 0.02-1.44). Both regimens also showed 92-95% efficacy in virologic suppression at delivery and during the breastfeeding period (Shapiro et al., 2009).

This clinical evidence proves that antiretroviral drugs are effective in the prevention of mother-to child transmission of HIV and that triple therapy is superior to mono or double therapy. HAART is the best option for the mother, the fetus and the subsequent infant because it offers the best chance to attain virological suppression which is essential to halt maternal disease progression, decrease the risk of in utero and intrapartum transmission and also decrease the risk of post-partum transmission through breast milk.

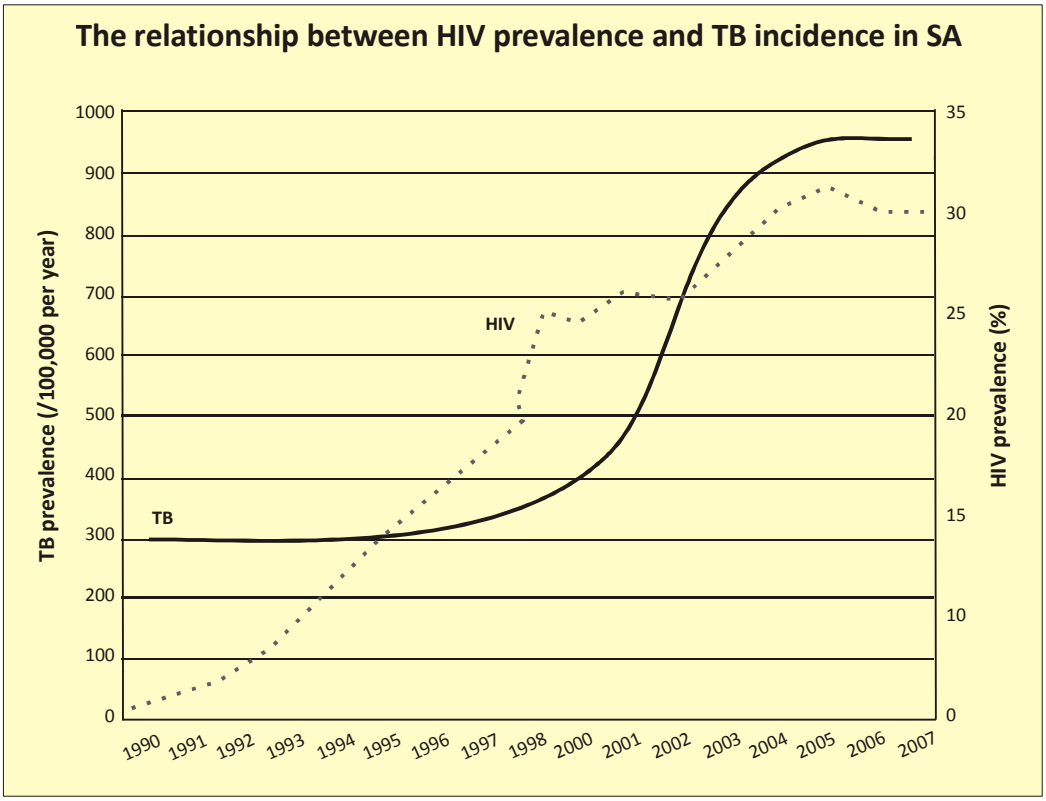
The threshold for initiating HAART in HIV-infected individuals who contract tuberculosis (TB), multi-drug resistant (MDR) TB and extensively drug-resistant (XDR) TB has also been increased from 200 to 350 because TB accelerates the course of HIV-induced disease. It does this by activating viral replication and accentuating the decline in CD4 cell count (Goldfeld et al., 2007). Also, Mugusi et al., 2009, observed in a study of 887 sputum smear positive PTB patients between the ages of 18 and 65

years receiving standard 8 months anti-TB treatment in Dar es Salaam Tanzania, that the mortality rate among HIV-infected TB patients was high despite the use of effective anti-TB therapy. Most deaths occur after successful completion of therapy, an indication that patients die from causes other than TB. HIV infection was the strongest independent predictor of mortality in this cohort. The mortality rate was also observed to be extraordinarily high in patients with MDR and XDR TB (Gandhi et al., 2009). Hence the new guidelines recommend that these patients should be fast-tracked, that is HAART should be started within two weeks of being eligible.

Initiation of HAART during TB therapy reduces mortality by 56%. The interval between the completion of TB therapy and initiation of HAART is important as a considerable number of deaths occur during this time. There is no difference in levels of viral suppression between patients who initiate HAART during TB therapy and patients who initiate HAART after completion of TB therapy and the rates of adverse events are the same in the two groups (Karim, 2010).

The incidence of TB is increased in HIV-positive patients. Among individuals with latent Mycobacterial infection, the lifetime risk of developing active TB is approximately 10% in non-HIV-infected people. In those with HIV infection the risk is increased to around 10% per year. HIV alters the clinical presentation of TB and compromise the response to anti-TB treatment. The proportion of smear–negative TB and extrapulmonary TB is higher among HIV co-infected TB patients. (Wilson., et al 2008).

Figure 2: The link between HIV prevalence and TB incidence in South Africa (Department of health 2010).



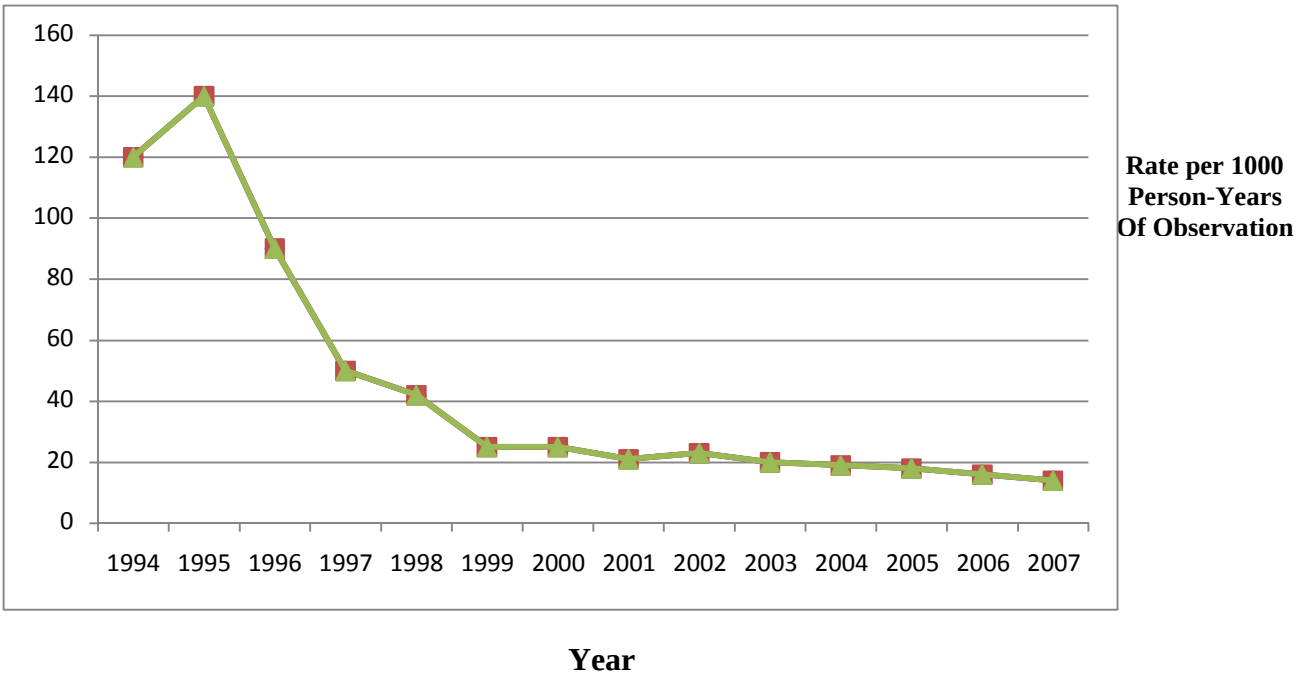
It is estimated that around 70% of new adult cases of TB in South Africa are co-infected with HIV. TB preventative therapy is therefore essential in HIV-positive patients. It involves the administration of one or more anti-TB drugs to individuals with latent TB in order to prevent progression to active disease. It is essential to exclude active TB prior to starting preventive therapy in order to avoid giving one or two anti-TB drugs to patients with TB disease who require a full treatment regimen. Patients are screened for signs and symptoms of active TB: current cough, fever, loss of weight and drenching night sweats. If one or more of these are present, the patient is considered a TB suspect and is not eligible for preventive therapy until active disease is excluded by sputum smear microscopy and TB culture. Isoniazid 5mg/kg/day (maximum 300mg/day) given for a duration of 6 months is the regimen used in South African public sector institutions. Patients should be monitored for the development of peripheral neuropathy and hepatitis when they are put on this regimen (Department of Health South Africa 2010).

HAART reduces the risk of developing TB by 64% in HIV-infected patients, but when combined with TB preventative therapy the risk is reduced by 89% (Golub et al., 2009). It is therefore crucial to implement TB preventative therapy in the HIV wellness clinics.

Delaying or deferring the initiation of HAART until the CD4 cell count is low predisposes the patients to the development of Immune Reconstitution Inflammatory Syndrome (IRIS). A paradoxical worsening of the patient's clinical condition after the initiation of HAART characterizes the syndrome. Potential mechanisms for the syndrome include a partial recovery of the immune system or exuberant host immunological response that leads to enhanced cell-mediated response to live or dead organisms or shed antigen. This may present as either unmasking of latent infection, recurrence of symptoms and signs of previously identified and treated infection or exacerbation of symptoms of a condition that is being currently treated. Mycobacterium tuberculosis is the most frequently implicated infectious pathogen. It presents with high fever, massively enlarged lymph nodes, massive pleural effusion, worsening of pulmonary infiltrates on chest x-ray and extra-pulmonary TB. Mortality and morbidity of TB IRIS is high with the mortality of 9.5% observed in one study (Manosuthi et al., 2006, Lawn et al., 2007and Murdoch et al., 2007).

HAART not only reduces the incidence of TB but also reduces the incidence of other opportunistic infections.

Figure 3: Incidences of first AIDS-defining opportunistic infection, according to year, among all patients in care, HIV Outpatient Study, 1994–2007 (Brooks 2009)



During the first four years of HAART a uniform decline in opportunistic infections occur even in patients who had low CD4 cell counts at the initiation of HAART as long as viral load remained undetectable. An increase occurs later in patients with immunological and virological failure but also in patients with only virological failure (De Beaudrop P et al 2010). The overall rate of the new episode of major opportunistic infections is 8% in the first year of HAART. The first few months of HAART are a crucial period, particularly in patients with advanced disease where PCP and cryptococcosis are still common. Approximately 80% of opportunistic infections develop within the first three months of HAART and subsequently decline over time. Of note is that 15% develop within the first two weeks of HAART before any detectable increase in the CD4 cell count. This may be explained by the improvement in immune function that results from the precipitous decline in plasma HIV and a switch from type2 to type1 cytokines profiled in the T-lymphocyte stimulation assay that occur in the early period of treatment (Manosuthi et al., 2007)

The incidence bacterial community acquired pneumonia is high in HIV-infected patients than in people without HIV. Streptococcus pneumonia is the most common pathogen and is isolated in about 60% of cases (Madeddu et al., 2008). The clinical outcomes measured by time to clinical stability, length of stay and mortality among community acquired pneumonia hospitalised HIV-infected patients are similar to those without HIV infection in both developed and developing countries (Malinis, 2009). But Sogaard et al, 2009, observed that the first hospitalisation for pneumonia among HIV- infected individuals was associated with elevated risk of death up to more than a year later. The use of HAART decreases this risk, independent of CD4 cell count.

Cryptococcal meningitis is one of the most important HIV-related opportunistic infections especially in the developing world. In countries with high HIV/AIDS prevalence it is the most common cause of meningitis overall, more frequent than Streptococcus pneumonia, Neisseria meningitidis and TB meningitis. Its incidence ranges from 0.04 to 12% per year among persons with HIV and it is the cause of death in as many as 20 to 30% of patients with AIDS (Park et al., 2009 and Makadzange et al., 2010). A combination of antifungal is more superior to mono- therapy in the treatment of cryptococcal meningitis. Amphotericin B combined with flucytosine is the recommended regimen, but due to unavailability of flucytosine in some parts of the world, especially Sub-Saharan Africa, a combination of amphotericin B and fluconazole is the alternative regimen (Jarvis et al., 2010).

The optimum time to initiate HAART in HIV-infected patients with serious opportunistic infections has until recently been undefined. Initiation of early HAART is associated with the risk of immune reconstitution inflammatory syndrome (IRIS), complex drug interactions and a high pill burden but deferral risks advancing immunosuppresion and mortality. It has been demonstrated in patients with a range of fungal and bacterial infections that early HAART initiation (median, 12 days after diagnosis of infection) resulted in fewer adverse events or deaths related to AIDS progression compared with initiation of HAART after acute infection treatment (median, 45 days after diagnosis of infection). Unlike other opportunistic infections early (<72hours) HAART initiation after diagnosis of cryptococcal meningitis is associated with poor outcome, 3-year mortality of 88% compared to 54% in patients who defer ART until after 10 weeks of fluconazole (Meintjes et al., 2010 and Makadzange et al., 2010).

After successful treatment of an acute infection, patients with cryptococcal meningitis should get secondary prophylaxis if their CD4 cell count is below 200. Fluconazole is the most common drug used. Without secondary prophylaxis at least 50 to 60% of patients will have disease relapse. Failed prescription, dispensing, referral for or adherences to secondary prophylaxis are reasons for the large number of relapses (Jarvis, 2010).

Despite the fact that South African Department of Health started implementing free HIV/AIDS Plan in 2004, with a rapid scale-up of HAART, in the public sector with the purpose of providing access to care and treatment for 80% of people living with HIV by 2011(Basset et al., 2009 and Wang B et al., 2009), patients still present with advanced disease. Heterosexual males were more at risk of being late presenters as compared to females. The lower proportion of females being late presenters can be attributed to a higher uptake of Voluntary Counselling and Testing (VCT) as part of routine health care during pregnancy. Furthermore, females get tested soon after their spouses test HIV positive, thereby being tested much earlier than their male counterparts who generally get tested on developing symptoms. Higher age groups, especially those above 45 years, are associated with late presentation (Mojumdar et al., 2010). Homosexual men, intravenous drug use and living alone were independently associated with early presentation. These groups have higher risk awareness than patients in stable partnerships, leading to more frequent testing and earlier diagnosis (Wolbers et al., 2008).

Despite late presentation, patients with advanced disease can still get improvement in their virological, immunological and clinical status. Demographic factors such as gender, baseline CD4 and baseline viral load are not related to achieving early virologic success. Patients with baseline CD4 cell count of less than 50cell/mm^3 have a similar virologic response when compared to those with CD4 cell count of more than 50cell/mm^3. In the severely immunocompromised (median baseline CD4 cell count of 6cell/$mm^{3)}$ 71% of patients achieved undetectable plasma HIV RNA after 48weeks of HAART compared to 75% in a group of patients with mean baseline CD4 cell count of 139cell/mm^3 (Manosuthi et al.,2007).

However, long-term virologic success is predicted by the potency of HAART, adherence to treatment, baseline viremia, baseline CD4 cell count and rapid reduction of viremia in response to treatment. Early immunological recovery is not dependent on baseline CD4 cell count. Severely immunocompromised patients with a median baseline CD4 cell count of 5cell/mm^3 showed an increase of 151cell/mm^3 by 48weeks (Manosuthi et al., 2007 and Kilaru et al., 2006). This is even better than the expected increase of approximately 100cell/mm^3 per 12months of initiating HAART (Wilson et al., 2008). However, Moore R et al., 2007, showed that long-term (6 years) increase is achieved in patients with different baseline CD4 cell count, but only patients with baseline CD4 cell count of more than 350cell/mm^3 returned to nearly normal levels and patients with baseline CD4 cell counts of less than 350 the increase plateaus at a lower level.

Since HAART is provided free of charge in South African public sector hospitals and clinics adherence becomes the next critical step for successful treatment of HIV and AIDS. The highest levels of antiretroviral therapy adherence are associated with higher rates of maintained virological suppression, lower risk of virological failure and decreased rate of disease progression. For sustained viral suppression, adherence rate of more than 95% is required. Patients with an adherence rate of less than 95% are more likely to develop virological failure (Gross, 2006). However since HAART is a lifetime treatment, maintaining an almost full adherence level over such a long term poses a significant challenge for both patient and health-care providers (Wang et al., 2007).

Different factors contribute to poor or non-adherence in different communities and populations. In the workplace, active promotion of HIV testing may have extended HAART to individuals who, without provider initiation, would not have spontaneously sought care. Provider-initiated testing makes

HAART available to individuals less motivated to seek care, thus patients may need additional adherence support especially addressing uncertainty about the health benefit of HAART (Dahab et al., 2010). Traditional medicine use appeared to affect adherence negatively. Patients are advised by both health-care providers and traditional healers not to "mix" HAART and traditional medicine and this leads to ART interruptions. Given that traditional medicine use is common in most Sub-Saharan African settings, a deeper understanding and clarification to providers on how to counsel patients while on HAART is critical. Doubt about the existence of HIV disease, own HIV-infected status or both inhibit adherence. About 19% of patients were uncertain or did not believe that HIV existed, while 24% were uncertain or did not believe that they were HIV-infected. This is despite having received at least three intensive counselling sessions on HIV and HAART prior to starting treatment. This highlighted the need to find effective ways to support adherence to HAART even if the individual does not accept biomedical concepts of HIV disease (Dahab et al., 2008)

Transport costs and the user fee, including costs associated with travelling from remote areas to clinics or the registration fees needed in private facilities in Uganda and Tanzania limit adherence. Long waiting times may discourage patients from going to clinics. In Botswana patients report that they spend four or more hours at the clinics, the longest waiting time being twelve hours. Expansion of treatment access points of care to communities to diminish travelling time and waiting time may have a positive impact on adherence. Hunger is also a problem especially during the initial stages of treatment when the body needs extra nutrition as it regains strength and weight. Some patients can only take their HAART once a day as that is the only time they have food (Hardon et al., 2007, Charurat et al., 2010).

Stigma is another problem and results in patients losing their jobs, being abandoned, and badly treated by their partners after disclosure and being isolated from their communities. Others do not disclose their HIV status, and thus do not receive the social support they need and cannot take their drugs on time (Hardon et al., 2007).

In low-income settings, drug side-effects and alcohol were thought to contribute to poor adherence. Having social support, a strong belief in the value of treatment and the ability to fit HAART into daily routine were reported as facilitators of adherence (Dahab et al. 2008). Wang et al., 2007 showed that non-adherence among patients with no reminder tools were greater than those who employed some reminder method.

The use of adherence measures, including incorporating refill-based method into clinical practice may allow for the early identification of patients destined to virological failure because of poor adherence (Gross, 2006).

Although longer pre-HAART waiting time predicts better treatment outcome (Dahab et al 2010), this results in higher rates in loss to care and deaths before starting HAART. In an HIV clinic in Durban, the mean time from initial CD4 count to first HAART training was 3.6 months and patients had to undergo three training sessions a month apart before HAART could be started. This resulted in 16.4% HAART-eligible not returning for their follow-ups and of these, 34% died before or within 2 months after their first HAART training. Also, nearly half of newly diagnosed HIV-infected persons had pre-treatment loss to care as defined by not following up for CD4 count results. Factors associated with higher rates of pre-treatment loss to care were: living more than 10km from the health centre, unemployment, a history of TB treatment and referral for HIV testing by a health care provider as opposed to self-referral (Basset et al., 2009 and Losina et al., 2010).

METHODOLOGY

Study design

This is an observational study. It is a retrospective analysis of records of a cohort of patients who are receiving HAART at workplace wellness clinics in three mines in Limpopo province from January 2003 to December 2009.

Study population and site

Records of adult HIV patients enrolled at workplace wellness clinics of three mines in Limpopo province. These clinics are situated within a radius of 150km of the city of Polokwane and have been providing HAART since January 2003. The clinics are monitored by and use treatment guidelines from the Aurum Institute of South Africa (Maraisane M 2007). Patients are referred from primary health care centre after undergoing voluntary counseling and testing. Upon referral the medical practitioner enrolls the patient into the wellness programme by completing a "core record" form. This form is used to compile patients' information including demographics (name, gender, identity number, address and home language) and medical history (including smoking and alcohol consumption, previous TB preventive prophylaxis and any previous HIV-related conditions). A physical examination is conducted to check for HIV-related conditions or any other medical conditions. Blood is then taken for confirmatory HIV ELISA test and CD4 count and the patient is given a review date which is usually within a week's time.

Patients with positive HIV-ELISA test and CD4 cell count of 250 and below or a WHO stage 4 disease are started on treatment provided they are willing to start and TB has been excluded on history, physical examination and chest x-ray (patients signs and symptoms of TB, a clinical examination suggestive of TB or abnormal chest x-ray are investigated for TB by sputum smear and culture).

Before starting HAART, blood for baseline viral load is taken and an "HAART assessment" form is completed. This form contain the following details: name of the patient; baseline CD4 cell count; WHO stage; whether consent form for treatment is signed; history of previous HAART; conditions which are contraindications to specific antiretroviral drugs; conditions where certain antiretroviral drugs should be used cautiously and possible drug interactions between antiretroviral drugs and the patient's current medications.

HAART-naïve patients receive first line therapy which consists of two nucleoside reverse transcriptase inhibitors (NRTI) and one non-nucleoside reverse transcriptase inhibitor (NNRTI). Patients are then followed-up at 2weeks, 6 weeks, 12 weeks and 24 weeks from the date of HAART initiation. The subsequent follow-ups are at 6 month intervals. At each visit a medical practitioner completes a "visit" form which takes history of hospitalization or diagnosis of TB since the last visit. History of current symptoms and adherence to treatment is also taken. Physical examination including vital signs (height, weight, blood pressure, pulse rate, respiratory rate and temperature) is performed. Chest x-ray is done if indicated by history and physical examination. A clinical assessment is then made and any new WHO stage 3 or 4 disease documented on the "physical exam" form and treated. Blood is taken to check full blood count, liver transaminases, urea and electrolyte at every visit while blood for CD4 count and viral load is taken at 6 week, 24 week and the subsequent 6 month visit.

Inclusion criteria

Male and female HIV-positive patients older than 18 years on regimen 1 treatment (Maraisane M 2007).Patients were all treatment naïve and have initiated HAART from January 2003 to December 2009. Patient must have completed one year of uninterrupted HAART since initiation of treatment.

Exclusion criteria

Patient on treatment regimen 2 (Maraisane M 2007) were excluded because this regimen contain protease inhibitors which have a different pharmacological properties to NRTI and NNRTI. Patients with WHO stage 4 diseases at baseline were excluded from the study because compared to other WHO stages; stage 4 disease has a relatively poor prognosis despite HAART. This would bring bias by a confounding effect. Patients who has defaulted treatment were excluded. Adherence was assessed by patients collecting treatment monthly and patients who skipped at least one month were excluded. Patients who were not naïve to HAART were excluded because of possible resistance to antiretroviral drugs that may have been acquired.

Outcome

1. CD4 count
2. Viral load
3. Frequency of hospital admissions.
4. Weight loss greater than 10% of baseline body weight.
5. Development of TB.
6. Development of severe bacterial pneumonia i.e. Pneumonia which need admission and antibiotics.
7. Development of meningitis.
8. Mortality

Sampling and data collection

From January 2003 to December 2009 327 patients were started on HAART and their records were retrieved from filling rooms. For the study, patients were divided into three groups based on their baseline CD4 cell count. Patients in group A had CD4 cell count of less than 100, in group B had CD4 cell count of 101 to 200 and in group C had CD4 cell count of 201 to 250. Of the 327 patients' records, 50 qualified for inclusion in the first group, 50 qualified for inclusion in the second group and 35 qualified for inclusion in the third group. A data collection sheet (annexure 1) was used to collect data from the records

Ethical consideration

Mine management gave permission for data to be collected and analyzed for this study. Patients' names were not used only file numbers were used on the data collection sheets. The study protocol was approved by the research ethics committee of the faculty of health sciences of the University of the Witwatersrand. Data protection procedures were strictly followed and patient identifiers were available only to the principal investigator. Ethical principles of confidentiality and respect for privacy were observed at all times and data was used solely for the purpose of this research project.

Data analysis

Each patient's data was analyzed one year after his/her commencement of HAART. Data capturing verified and validation checks conducted. Patients were categorized into the following three groups based on their baseline CD4 cell count: Group A (CD4 cell count of less than 100) Group B (CD4 cell

count of 100 to 200) and Group C (CD4 cell count of 201 to 250). The clinical outcomes of all groups compared.

Progressive loss of CD4 cells is the main manifestation of the effect of HIV. This compromise the immune system and consequently the body become susceptible to opportunistic infections and hence AIDS. HAART halts viral replication resulting in immune recovery. A good response to HAART is considered to be an increase in CD4 cell count by 100cells/µl in the first year or an increase in CD4 cell count by 15cells/µl per month and suppression of the virus to undetectable level (Moore D 2006, Moore D2007, and Wilson D 2008). Analysis of CD4 cell count and viral load one year after initiation of HAART serve as a marker of immunological and virological response to HAART. CD4 cell count and viral load at one year post HAART initiation were compared to the baseline values. . CD4 cell count and viral load at one year post-HAART initiation were compared to the baseline values.

Respiratory conditions, especially TB and pneumonia are the most common manifestations of HIV and contribute markedly to morbidity and mortality. The incidence of TB is increased 3 to 12 folds by HIV (CDC 2009 and Bartlett J 2009). Decline in the incidence of TB and pneumonia is a positive response to HAART. Details of development of severe pneumonia (diagnosed by history, clinical examination and chest x-ray) and TB (diagnosed by sputum smear or culture) were obtained from the “visit forms”.

Meningitis is the most fatal and most debilitating of the opportunistic infections. HAART decrease the incidence of meningitis (Park B 2009and Makadzange A 2010).data of development of meningitis (diagnosed by cerebro-spinal fluid microscopy or culture, India ink or cryptococcal antigen) was also obtained from the “visit” forms.

Initiation of HAART is associated with weight gain of at least 5.0kg in the first 6 months of HAART (Bizuwork T 20007) and weight loss of more than 10% of baseline body weight is classified as a stage 3 disease. When interpreted together with other outcome measures, continued weight loss despite HAART indicates deterioration in the patient’s condition. Weight at one year after ART initiation is compared to that at baseline and assessed if there has been a decrease of more than 10%.

Development of opportunistic infections often leads to hospital admissions. Diseases assessed in this study are classified as WHO stage 3 and 4. However some of the WHO stage 2 and even stage 1

diseases may lead to hospitalization contributing considerably to HIV morbidity. Assessment of hospitalization due to HIV-related conditions is a useful marker of morbidity. Frequency of hospital admissions is obtained from “visit forms”.

Information about death was obtained from the wellness and primary health care files and also death certificates for patients who died at other institutions

This study focus on the clinical outcome of patients and although quality of life evaluations may provide a wider perspective of a patient’s health status by exploring patients’ perceptions of their health, disabilities and capabilities, the clinical outcome measures in this study does provide information about the health-related quality of life.

Under the guidance of a research statistician, statistical analyses were performed on SAS Release 9.2 and p values less or equal to 0.05 were considered to be significant.

To test the relationship between categorical variables i.e. weight loss greater than 10% of baseline body weight, hospital admissions, development of TB, development of severe bacteria pneumonia, development of meningitis and mortality the Pearson chi-square test is used. The chi-square test was also used for the viral load as it is classified as either less than 50copies or less than 400copies. The chi-square test functions by contingency tables where the frequencies of each categorical variable are computed. A measure of association is then calculated. The chi-square test requires that the expected frequencies are not very small. The reason for this assumption is that the chi-square inherently tests the underlying probabilities in each cell, and when the expected cell frequencies fall, these probabilities cannot be estimated with sufficient precision. To avoid making incorrect inferences from the chi-square test, the general rule is that an expected frequency less than 5 in a cell is too small to use. It should be noted that the chi-square test is quite sensitive to the sample size. If the sample size is too small, the chi-square test value is overestimated; if it is too large, the chi-square test value is underestimated. To overcome this problem we use the following measures of association: Phi–square coefficient, Cramer’s V and Contingency Coefficient. The Phi–square coefficient is used when the variables under consideration have two possible values. When this is true, the data matrix will always have a simple 2x2 design. The Contingency Coefficient is used when there are three or more values for each variable, as long as there are an equal number of possible values leading to the construction of a data matrix that

has an equal number of rows and columns e.g. 3x3 table. Cramer's V is used when the number of possible values for the two variables is unequal, yielding a different number of rows and columns in the data matrix e.g. 2x3 table.

Although the Pearson chi-square is the most commonly used chi-square test, there are other chi-square test and the SAS will always give the values of these tests. The Continuity adjusted chi-square testis similar to the Pearson chi-square except that it is adjusted for continuity of the chi-square distribution, the Mantel-Haenszel chi-square which is useful when there is a linear association between the raw variable and the column variable and the Likelihood ratio chi-square which calculate the maximum likelihood of the sample data based on an assumed distribution model.

When the sample sizes are small the chi-square test is inappropriate. The Fisher’s exact test which is the appropriate test even when some variables have zero frequencies was then performed.

To test the relationship between continuous variables ie baseline mean CD4 cell count and the increase in mean CD4 cell count in one year, the t test was used. The t test was used to compare the two samples means. It becomes unreliable in case of more than two samples. The ANOVA test (which is the appropriate test) was used to compare the three sample means simultaneously.

RESULTS AND DISCUSSION

Hospital Admissions

The FREQ Procedure

Table 4: The FREQ Procedure for hospital admission for group A

			Cumulative	Cumulative
Group A	Frequency	Percent	Frequency	Percent
NO	41	82.00	41	82.00
YES	9	18.00	50	100.00
Frequency Missing = 85				

Table 5: The FREQ Procedure for hospital admission for group B

			Cumulative	Cumulative
Group B	Frequency	Percent	Frequency	Percent
NO	47	94.00	47	94.00
YES	3	6.00	50	100.00
Frequency Missing = 85				

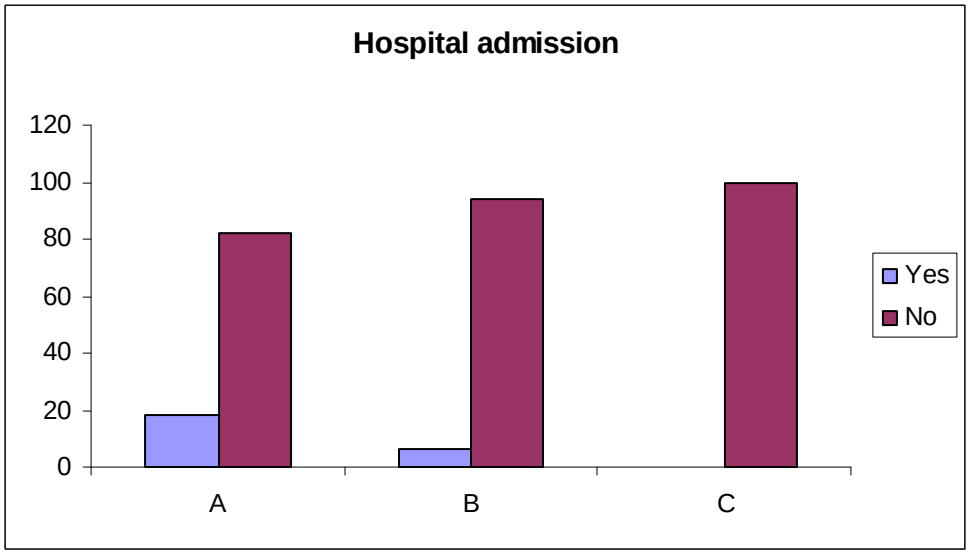
Table 6: The FREQ Procedure for hospital admission for group C

			Cumulative	Cumulative
Group C	Frequency	Percent	Frequency	Percent
NO	33	94.29	33	94.29
YES	2	5.71	35	100.00

Table 7: Comparison of hospital admission percentages between groups A, B and C

	CD4 count		
Admitted	A < 100	B 100 - 200	C 201 - 250
Yes	9 (18%)	3 (6%)	2 (6%)
No	41 (82%)	47 (94%)	33 (94%)
Total	50 (100%)	50 (100%)	35 (100%)

Figure 4: Frequency of hospital admission



Of the 50 patients in group A 9 were admitted to hospital for HIV-related conditions in their first 12months of HAART, in group B 3 of the 50 patients were admitted to hospital for HIV-related conditions in their first 12 months of HAART and in group C 2 of the 35 patients were admitted to hospital for HIV-related conditions in their first 12 months of HAART. The percentage of hospital admissions for patients in group A (18%) differ significantly from the percentage in group B (6%) and the percentage in group C (6%) (Fisher exact test p= 0.05). No difference in hospital admissions was observed between group B and group C.

As HAART is now available and widely accessible, most HIV-infected persons are surviving and experiencing longer life expectancies. Hospitalizations have become an important outcome measure and are an important component of excess health care costs among this population. Hence, data on

the rates of hospitalizations are useful for both health care planning and the development of strategies to improve the health of HIV patients. Factors associated with a reduced risk of hospitalization include CD4 counts >350 cells per cubic millimeter and HAART use among patients with a CD4 count <350 cells per cubic millimeter (Crum-Cianflone N 2010). However (Parkes R 2006) observed no difference in the need for hospitalization when the pre-HAART period was compared with the first 3months of HAART in a study of 500 patients initiating HAART with a median CD4 cell count of 97cellsμ/l Patients were not stratified according CD4 cell count.

Weight loss

The FREQ Procedure

Table 8: The FREQ Procedure for weight loss for group A

			Cumulative	Cumulative
Group A	Frequency	Percent	Frequency	Percent
NO	38	76.00	38	76.00
YES	12	24.00	50	100.00
Frequency Missing = 85				

Table 9: The FREQ Procedure for weight loss for group B

			Cumulative	Cumulative
Group B	Frequency	Percent	Frequency	Percent
NO	48	96.00	48	96.00
YES	2	4.00	50	100.00
Frequency Missing = 85				

Table 10: The FREQ Procedure for weight loss for group C

			Cumulative	Cumulative
Group C	Frequency	Percent	Frequency	Percent
NO	35	100.00	35	100.00
Frequency Missing = 100				

Table 11: Comparison of weight loss frequencies between groups A, B and C

Weight loss	Group A	Group B	Group C	Total
No	38 76.00	48 96.00	35 100.00	121
Yes	12 24.00	2 4.00	0 0.00	14
Total	50	50	35	135

Table 12: Statistics for Table 11

Statistics	DF	Value	Prob
Chi-square	2	16.2255	0.0003
Likelihood Ratio Chi-Square	2	18.0469	0.0001
Mantel-Haenszel Chi-Square	1	0.0253	0.8736
Phi Coefficient		0.3467	
Contingency coefficient		0.3276	
Cramer's V		0.3467	

Fisher's Exact Test	
Table Probability (P)	3.900E-05
Pr<= P	1.732E-04
Sample Size = 135	
Sample Size = 135	

Table 13: Comparison of weight loss frequencies between group A and B

Weight loss	Group A	Group B	Total
No	38 76.00	48 96.00	86
Yes	12 24.00	2 4.00	14
Total	50	50	100

Table 14: Statistics for Table 13

Statistics	DF	Value	Prob
Chi-square	1	8.3056	0.0040
Likelihood Ratio Chi-Square	1	9.0903	0.0026
Continuity Adj. Chi-Square	1	6.7276	0.0095
Mantel-Haenszel Chi-Square	1	8.2226	0.0041
Phi Coefficient		0.2882	
Contingency coefficient		0.2769	
Cramer's V		0.2882	

Fisher's Exact Test	
Cell (1, 1) Frequency (F)	48
Left-sided Pr <= F	0.9996
Right -Sided Pr >= F	0.0038
Table probability (P)	0.0034
Two-sided Pr <= P	0.0076

Sample Size = 100

Table 15: Comparison of weight loss frequencies between groups A and C

Weight loss	Group A	Group C	Total
No	38 76.00	35 100.00	73
Yes	12 24.00	0 0.00	12
Total	50	35	85

Table 16: Statistics for Table 15

Statistics	DF	Value	Prob
Chi-square	1	9.7808	0.0018
Likelihood Ratio Chi-Square	1	14.0979	0.0002
Continuity Adj-Chi-Square	1	7.9015	0.0049
Mantel-Haenszel Chi-Square	1	9.6658	0.0019
Phi Coefficient		-0.3392	
Contingency coefficient		0.3212	
Cramer's V		-0.3392	

Fisher's Exact Test	
Cell (1, 1) Frequency (F)	38
Left-sided Pr <= F	9.227E-04
Right -Sided Pr >= F	1.0000
Table probability (P)	9.227E-04
Two-sided Pr <= P	0.0011
Sample Size = 85	

Table 17: Comparison of weight loss frequencies between groups B and C

Weight loss	Group B	Group C	Total
No	48 96.00	35 100.00	83
Yes	2 4.00	0 0.00	2
Total	50	35	100

Table 18: Statistics for Table 17

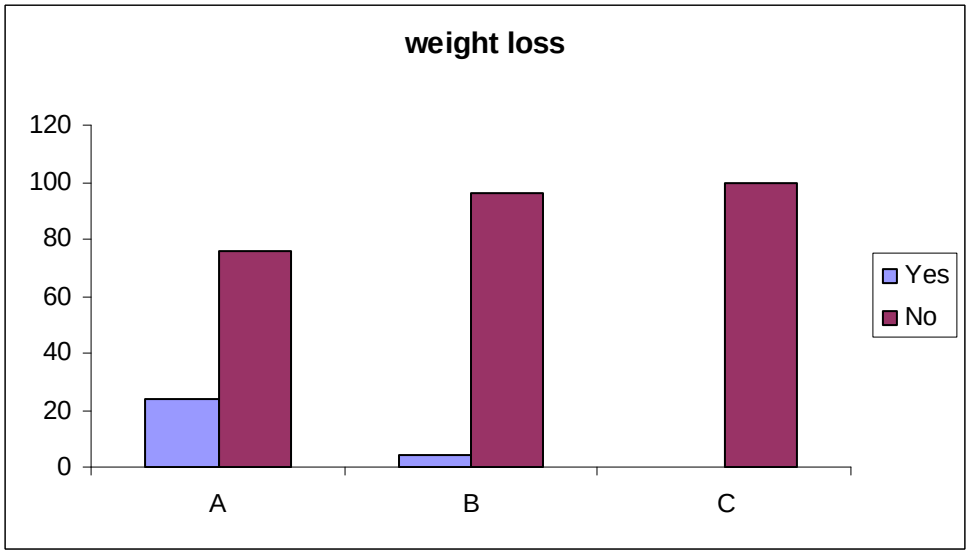
Statistics	DF	Value	Prob
Chi-square	1	1.4337	0.2312
Likelihood Ratio Chi-Square	1	2.1562	0.1420
Continuity Adj. Chi-Square	1	0.2213	0.6381
Mantel-Haenszel Chi-Square	1	1.4169	0.2339
Phi Coefficient		-0.1299	
Contingency coefficient		0.1288	
Cramer's V		-0.1299	

Fisher's Exact Test	
Cell (1, 1) Frequency (F)	48
Left-sided Pr <= F	0.3431
Right -Sided Pr >= F	1.0000
Table probability (P)	0.3431
Two-sided Pr <= P	0.5098
Sample Size = 85	

Table 19: Comparison of weight loss percentages between groups A, B and C

	CD4 count		
Weight loss	A < 100	B 100 - 200	C 201 - 250
Yes	12 (24%)	2 (4%)	0 (0%)
No	38 (76%)	48 (96%)	35 (100%)
Total	50 (100%)	50 (100%)	35 (100%)

Figure 5: Frequency of weight loss >10% of baseline body weight



After 12months of HAART, out of the 50 patients in group A 12 had weight loss more than 10% of their baseline body weight, in group B 2 of the 50 patients had weight loss of more than 10% their baseline body weight and in group C none of the 35 patients had weight loss of more than 10% of baseline body weight. The percentage of patients with weight loss of more than 10% of baseline value in group A (24%) differ significantly from the percentage in group B (4%) (Fisher exact test p= 0.003) and also differ significantly to from the percentage in group C (0%) (Fisher exact test p= 0.001).

In the study of the effectiveness of HAART in South Africa, (Fairall L 2008) observed an increase in body weight of 602g with each month of HAART but there was no correlation between weight gain and baseline CD4 cell count.

In an audit of how patients get on to HAART in Malawi and the weight gain they experience in the first six months, there was an observed gradual increase in weight with the mean gain of 6.0kg in men and 5.0kg in women. There was a slight increase in weight gain in patients with WHO clinical stage 3and 4 compared to those with stage 1 and 2 (Bizuwork T 2007). Even in this study no correlation was made between weight gain and baseline CD4 cell count. Despite the observed weight gain stipulated above, unintentional weight loss of 5% or greater still occur despite control of HIV infection (Tang A 2005).

Weight loss contributes significantly not only to morbidity and mortality of HIV and AIDS but also to stigmatization. Weight gain is therefore not only clinically important but is also crucial psychosocial aspect of the patient. Many factors contribute to weight loss in HIV infection and more than one factor is commonly present. Decreased intake due to anorexia, painful swallowing due to oropharyngeal or oesophageal disease, increased metabolic rate common in the early course of infection and malabsorption are some of the common causes of weight loss (Wilson D 2008).

Development of TB

The FREQ Procedure

Table 20: The FREQ Procedure for development of TB for group A

			Cumulative	Cumulative
Group A	Frequency	Percent	Frequency	Percent
NO	46	92.00	46	92.00
YES	4	8.00	50	100.00
Frequency Missing = 85				

Table 21: The FREQ Procedure for development of TB for group B

			Cumulative	Cumulative
Group B	Frequency	Percent	Frequency	Percent
NO	46	92.00	46	92.00
YES	4	8.00	50	100.00
Frequency Missing = 85				

Table 22: The FREQ Procedure for development of TB for group C

			Cumulative	Cumulative
Group C	Frequency	Percent	Frequency	Percent
NO	34	97.14	34	97.14
YES	1	2.86	35	100.00

Table 23: Comparison of frequencies of development of TB in group A, B and C

Development of TB	Group A	Group B	Group C	Total
No	46 92.00	46 92.00	34 97.14	126
Yes	4 8.00	4 8.00	1 2.86	9
Total	50	50	35	135

Table 24: Statistics for table 23

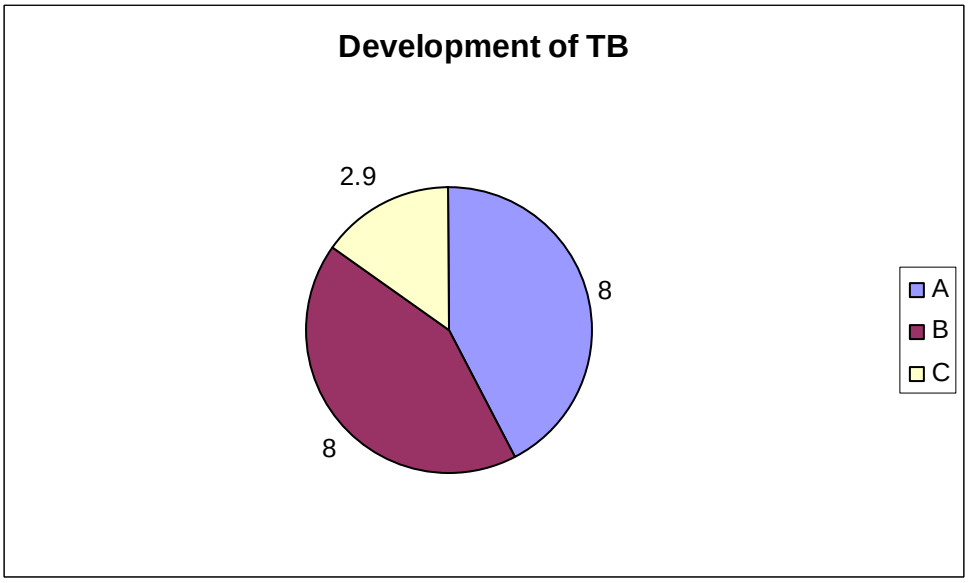
Statistics	DF	Value	Prob
Chi-square	2	1.1020	0.5764
Likelihood Ratio Chi-Square	2	1.2954	0.5233
Mantel-Haenszel Chi-Square	1	0.7657	0.3815
Phi Coefficient		0.0904	
Contingency coefficient		0.0900	
Cramer's V		0.0904	

Fisher's Exact Test	
Table Probability (P)	0.0594
Pr<= P	0.7477
Sample Size = 135	

Table 25: Comparison of development of TB percentages between groups A, B and C

Developed TB	CD4 count		
	A < 100	B 100 - 200	C 201 - 250
Yes	4 (8%)	4 (8%)	1 (2.9%)
No	46 (92%)	46 (92%)	34 (97.1%)
Total	50 (100%)	50 (100%)	35 (100%)

Figure 6: Frequency of development of TB



In group A out of the 50 patients 4 developed TB, in group B also out of the 50 patients 4 developed TB and in group C out of the 35 patients only 1 developed TB. The percentages of patients who developed TB in the three groups are 8%, 8% and 2.9% respectively. When compared statistically, these percentages do not differ significantly (Fisher exact test p=0.059).

Although the risk of developing TB is increased ten-folds in HIV patients compared to the general population (Wilson D et al 2008),TB can occur at any stage of CD4 cell depletion (Ngowi B 2008).This is not strange as TB does occur even in immuno-competent individuals.

Diagnosis of TB HIV-infected patients can sometimes be difficult because TB is mainly diagnosed by microscopic identification of Mycobacterium tuberculosis bacilli on sputum sample or by culture. However, due to alteration of the normal immune response to Mycobacterium tuberculosis in persons with HIV transfer of bacilli into respiratory secretions is markedly reduced. Thus HIV increases the proportion of smear-negative TB (Mendelson M 2007). Also the value of chest x-ray in helping with the diagnosis of TB is limited in HIV-infected patients. Although no chest x-ray pattern is absolutely typical of TB, upper lobe infiltrations and cavitations which occur frequently in TB patients are not commonly found in TB patients who are co-infected with HIV. Changes in chest x-ray in TB patients who are co-infected with HIV reflect the degree of immunocompromise. In early HIV disease (mild immunocompromise), the appearance is often classical with cavitation and upper lobe infiltrate while in late HIV disease (severe immunocompromise) the appearance is often of interstitial and no cavitation (van Cleeff M 2005).

Development of severe bacterial pneumonia

The FREQ Procedure

Table 26: The FREQ Procedure for development of severe bacterial pneumonia for group A

			Cumulative	Cumulative
Group A	Frequency	Percent	Frequency	Percent
NO	49	98.00	49	98.00
YES	1	2.00	50	100.00
Frequency Missing = 85				

Table 27: The FREQ Procedure for development of severe bacterial pneumonia for group B

			Cumulative	Cumulative
Group B	Frequency	Percent	Frequency	Percent
NO	49	98.00	49	98.00
YES	1	2.00	50	100.00
Frequency Missing = 85				

Table 28: The FREQ Procedure for development of severe bacterial pneumonia for group C

			Cumulative	Cumulative
Group C	Frequency	Percent	Frequency	Percent
NO	35	100.00	35	100.00
Frequency Missing = 100				

Table 29: Comparison of frequencies of development of severe bacterial pneumonia in group A, B and C

Development of severe bacterial pneumonia	Group A	Group B	Group C	Total
No	49 98.00	49 98.00	35 100.00	133
Yes	1 2.00	1 2.00	0 0.00	2
Total	50	50	35	135

Table 30: Statistics for Table 29

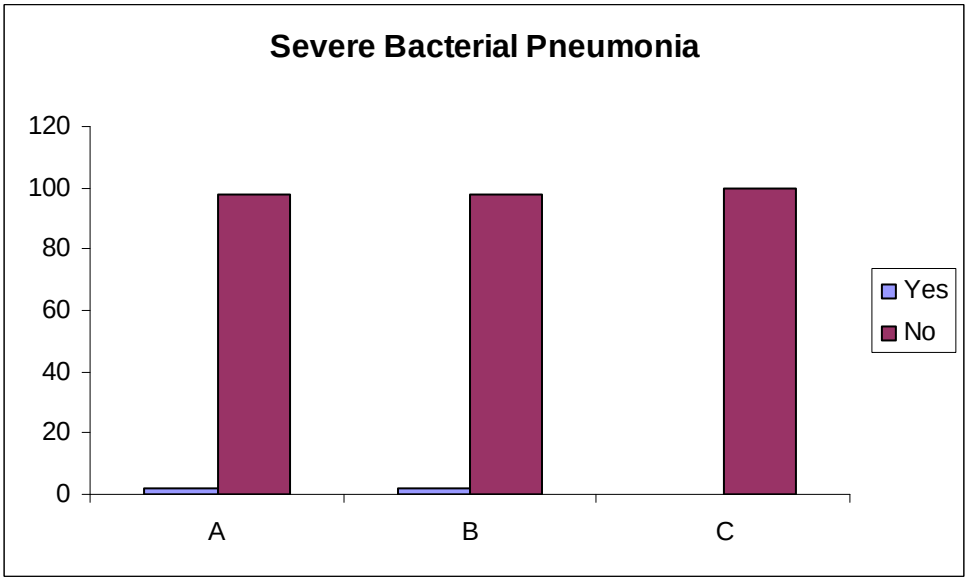
Statistics	DF	Value	Prob
Chi-square	2	0.7105	0.7010
Likelihood Ratio Chi-Square	2	0.2109	0.5458
Mantel-Haenszel Chi-Square	1	0.4937	0.4823
Phi Coefficient		0.0725	
Contingency coefficient		0.0724	
Cramer's V		0.0725	

Fisher's Exact Test	
Table Probability (P)	0.2764
Pr<= P	1.0000
Sample Size = 135	

Table 31: Comparison of development of severe bacterial pneumonia percentages between groups A, B and C

Severe Bacterial Pneumonia	CD4 count		
	A < 100	B 100 - 200	C 201 - 250
Yes	1 (2%)	1 (2%)	0 (0%)
No	49 (98%)	49 (98%)	35 (100%)
Total	50 (100%)	50 (100%)	35 (100%)

Figure 7: Frequency of development of severe bacterial pneumonia



The percentages of patients with severe bacterial pneumonia in the three groups (2%, 2% and 0% respectively) do not differ significantly (Fisher exact test p=0,276). The spectrum of pulmonary disease in HIV-infected patients has changed because of widespread use of HAART but bacterial pneumonia continues to be a matter of concern. HAART has significantly reduced the incidence of bacterial pneumonia and the incidence declines as the immunological status of the patient improves.

Baseline CD4 cell count of more than 200 with decreased risk of pneumonia (Saindou M). But Curran A et al 2008 noted that bacterial pneumonia is the most common admission in HIV-infected patients and Streptococcus pneumonia is the main cause and that the rates of invasive disease in advanced HIV infection is 100 times that of HIV-uninfected individuals. It was also noted that HAART and pneumococcal vaccination did not have a significant influence on bacteraemia rate, in-hospital complications or mortality. No study was found where the incidence of post-HAART pneumonia was compared in patients with different baseline CD4 cell counts.

Development of meningitis

The FREQ Procedure

Table 32: The FREQ Procedure for development of meningitis for group A

			Cumulative	Cumulative
Group A	Frequency	Percent	Frequency	Percent
NO	50	100.00	50	100.00
Frequency Missing = 85				

Table 33: The FREQ Procedure for development of meningitis for group B

			Cumulative	Cumulative
Group B	Frequency	Percent	Frequency	Percent
NO	50	100.00	50	100.00
Frequency Missing = 85				

Table 34: The FREQ Procedure for development of meningitis for group C

			Cumulative	Cumulative
Group C	Frequency	Percent	Frequency	Percent
NO	35	100.00	35	100.00
Frequency Missing = 100				

Table 35: Comparison of development of meningitis percentages between groups A, B and C

Bacterial or cryptococcal meningitis	CD4 count		
	A < 100	B 100 - 200	C 201 - 250
Yes	0 (0%)	0 (0%)	0 (0%)
No	50 (100%)	50 (100%)	35 (100%)
Total	50 (100%)	50 (100%)	35 (100%)

No patient in the three groups developed meningitis.

Cryptococcal meningitis is the commonest cause of adult meningitis in HIV patients. It accounts for 63% of cases and the incidence range from 0.04 to 12% per year. This might be due the small sample size in this study (135), the fact the incidence of meningitis is low even in HIV infected individuals (0.04 to 12% per year) (Park B et al 2009) and also HAART has been shown to decrease in incidence of meningitis.

Mortality

The FREQ Procedure

Table 36: The FREQ Procedure for mortality for group A

			Cumulative	Cumulative
Group A	Frequency	Percent	Frequency	Percent
NO	42	84.00	42	84.00
YES	8	16.00	50	100.00
Frequency Missing = 85				

Table 37: The FREQ Procedure for mortality for group B

			Cumulative	Cumulative
Group B	Frequency	Percent	Frequency	Percent
NO	48	96.00	48	96.00
YES	2	4.00	50	100.00
Frequency Missing = 85				

Table 38: The FREQ Procedure for mortality for group C

			Cumulative	Cumulative
Group C	Frequency	Percent	Frequency	Percent
NO	35	100.00	35	100.00
Frequency Missing = 100				

Table 39: Comparison of frequencies of mortality in group A, B and C

Mortality	Group A	Group B	Group C	Total
No	42 84.00	48 96.00	35 100.00	125
Yes	8 16.00	2 4.00	0 0.00	10
Total	50	50	35	135

Table 40: Statistics for table 39

Statistics	DF	Value	Prob
Chi-square	2	9.0288	0.0110
Likelihood Ratio Chi-Square	2	10.5327	0.0052
Mantel-Haenszel Chi-Square	1	0.1372	0.7111
Phi Coefficient		0.2586	
Contingency coefficient		0.2504	
Cramer's V		0.2586	

Fisher's Exact Test	
Table Probability (P)	0.0017
Pr<= P	0.0144
Sample Size = 135	

Table 41: Comparison of frequencies of mortality in group A and B

Mortality	Group A	Group B	Total
No	42 84.00	48 96.00	90
Yes	2 16.00	8 4.00	10
Total	50	50	100

Table 42: Statistics for table 41

Statistics	DF	Value	Prob
Chi-square	1	4.0000	0.0455
Likelihood Ratio Chi-Square	1	4.2552	0.0391
Continuity Adj-Chi-Square	1	2.7778	0.0956
Mantel-Haenszel Chi-Square	1	3.9600	0.0466
Phi Coefficient		0.2000	
Contingency coefficient		0.1961	
Cramer's V		0.2000	

Fisher's Exact Test	
Cell (1, 1) Frequency (F)	48
Left-sided Pr <= F	0.9922
Right -Sided Pr >= F	0.0458 0
Table probability (P)	0.0380
Two-sided Pr <= P	0.0916
Sample Size = 100	

Table 43: Comparison of frequencies of mortality in group A and C

Mortality	Group A	Group C	Total
No	42 84.00	35 100.00	77
Yes	8 16.00	0 0.00	8
Total	50	35	85

Table 44: Statistics for table 43

Statistics	DF	Value	Prob
Chi-square	1	6.1818	0.0129
Likelihood Ratio Chi-Square	1	9.0666	0.0026
Continuity Adj-Chi-Square	1	4.4476	0.0349
Mantel-Haenszel Chi-Square	1	6.1091	0.0134
Phi Coefficient		-0.2697	
Contingency coefficient		0.2604	
Cramer's V		-0.2697	

Fisher's Exact Test	
Cell (1, 1) Frequency (F)	42
Left-sided Pr <= F	0.0112
Right -Sided Pr >= F	1.0000
Table probability (P)	0.0112
Two-sided Pr <= P	0.0186

Sample Size = 85

Table 45: Comparison of frequencies of mortality in group B and C

Mortality	Group B	Group C	Total
No	48 96.00	35 100.00	83
Yes	2 4.00	0 0.00	2
Total	50	35	85

Table 46: Statistics for table 45

Statistics	DF	Value	Prob
Chi-square	1	1.4337	0.2312
Likelihood Ratio Chi-Square	1	2.1562	0.1420
Continuity Adj-Chi-Square	1	0.2213	0.6381
Mantel-Haenszel Chi-Square	1	1.4169	0.2339
Phi Coefficient		-0.1299	
Contingency coefficient		0.1288	
Cramer's V		-0.1299	

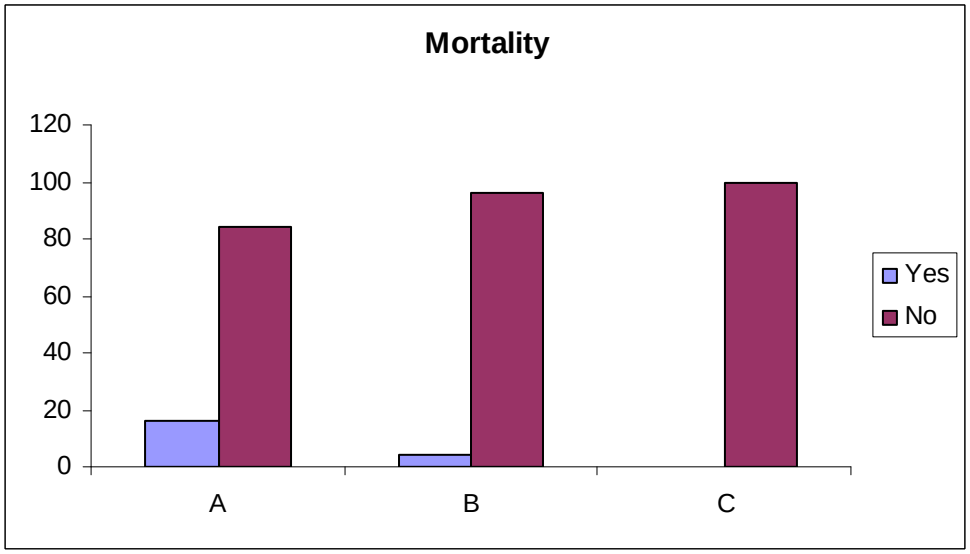
Fisher's Exact Test	
Cell (1, 1) Frequency (F)	48
Left-sided Pr <= F	0.3431
Right -Sided Pr >= F	1.0000
Table probability (P)	0.3431
Two-sided Pr <= P	0.5098

Sample Size = 85

Table 47: Comparison of mortality percentages between groups A, B and C

Mortality	CD4 count		
	A < 100	B 100 - 200	C 201 - 250
Yes	8 (16%)	2 (4%)	0 (0%)
No	42 (84%)	48 (96%)	35 (100%)
Total	50 (100%)	50 (100%)	35 (100%)

Figure 8: Mortality rate



Within 12months of HAART 8 patients died in group A, 2 patients died in group B and no patient died in group C. The percentage of patients who died in group A (16%) differs significantly from the percentage of patients who died in group B (4%) (Fisher exact test p= 0.038) and also differ significantly from the percentage of patients who died in group C (0%) (Fisher exact test p= 0.011). Although the percentage of patients who died in group B (4%) does not statistically differ significantly from the percentage of patients who died in group C (0%), clinically two deaths significantly from no death because the primary aim of HAART is to preserve life. (Madec Y 2007) stratified 1735 patients starting HAART with a median CD4 cell count of 20 and observed that mortality rate at 2 years increased as CD4 cell count at HAART at initiation decreased (mortality

rate of 4.4, 4.5, 7.5 and 24.7% in patients with CD4 cell count of more than 100, 51 to 100, 21 to 50 and less than 20 cell/µl respectively $p<10^{-4}$). In sub-Saharan Africa between 8 to 26% of patients die in the first year of HAART. Mortality is strongly associated with CD4 cell count of less than 50 cell/µl and WHO clinical stage 4 disease. Hazard ratio for association between CD4 cell count of less than 50 cell/µl (versus Cd4 cell count of more than 50 cell/µl) and mortality rate was observed to be 2.5 (95% CI, 1.9- 3.2) (Lawn S 2008).

Change in CD4 cell count

Table 48: The means procedure of CD4 count at baseline

Variable	Label	N	Mean	Median	Std Dev	Minimum	Maximum
Group A	Group A	50	48.26	49.00	27.24	1.00	94.00
Group B	Group B	50	155.34	160.00	25.18	103.00	198.00
Group C	Group C	35	230.97	237.00	17.14	201.00	250.00

Table 49: The means procedure of CD4 count after 1 year of HAART

Variable	Label	N	Mean	Median	Std Dev	Minimum	Maximum
Group A	Group A	42	183.10	179.00	117.05	6.00	642.00
Group B	Group B	48	295.27	281.00	125.35	84.0	657.00
Group C	Group C	35	403.26	386.00	165.62	26.00	839.00

Table 50: The means procedure of increase in CD4

Variable	N	Mean	Std Dev	Pr > |t|
Group A	42	131.71	115.57	<.0001
Group B	48	140.65	126.64	<.0001
Group C	35	172.29	163.80	<.0001

Comparison of mean CD4 counts

The GLM Procedure

t Tests (LSD) for diff

Table 51: t Tests for comparison of men CD4 counts

Grouping	Mean	N	groups
Z	131.71	42	A
Z	140.65	48	B
Z	172.29	35	C

NOTE: Cell sizes are not equal.

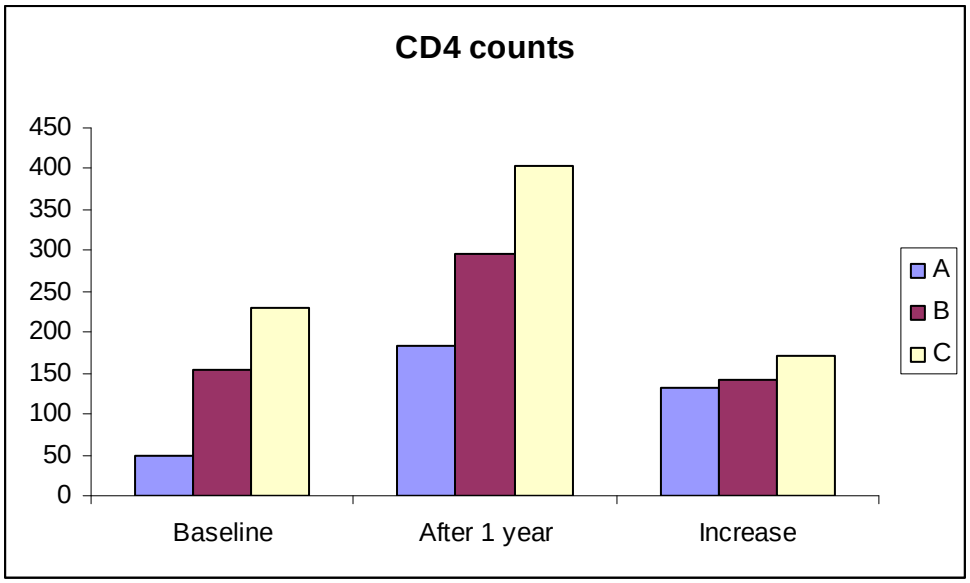
Means with the same letter are not significantly different.

Table 52: Change in the mean CD4 count from baseline to 1 year post HAART

Group*	Mean CD4 count (± SD)		
	Baseline	After 1 year	Increase
Less (n=50/42) A	48 (±27)	183 (±117)	132 (±116)
Between (n=50/48) B	155 (±25)	295 (±125)	141 (±127)
More (n=35/35) C	231 (±17)	403 (±165)	172 (±164)

* Sample sizes in brackets are at baseline and after 1 year respectively

Figure 9: Change in mean CD4 cell count



The increase in mean CD4 cell count from baseline to one year post HAART for group A, B and C were 132, 141 and 172 respectively. The change in mean CD4 cell count was found to be statistically significant within each group (paired t test, $p<0.0001$), but the mean changes between the three groups (132,141 and 172) respectively do not differ significantly (ANOVA test). This implies that the change in CD4 cell count one year after initiation of HAART is not dependent on the baseline CD4 cell count.

The increase in mean CD4 cell count in this study was found to be similar to other studies. According to (Wilson D 2008) an increase of 100 CD4 cell per year is a marker of good response to HAART. In a study conducted in Free State South Africa (Fairall L 2008) observed that each month of HAART was associated with an increase in CD4 cell count of 15.1cells/µL and then concluded that HAART provided through South African government health services is as effective as that provided in high-income countries. Moore R (2007) stratified 655 patients into three groups by baseline CD4 cell counts. The first group composed of patients with CD4 cell count of less or equal to 200, the second group composed of patients with CD4 cell count of 201 to 350 and the third group composed of patients with CD4 cell count of more than 350.The increase in CD4 cell count was similar among the three groups in the first year of HAART but by 6years the median CD4 cell count was 493cells/µL among patients with baseline CD4 count of less or equal to 200cells/µ, 508

cells/µL among those with baseline CD4 cell count of 201 to 350 and 829 cells/µL among those with baseline CD4 cell counts of more than 350 cells/µL. He then concluded that significant increase in CD4 cell count occur in all strata during the first year of HAART but there is a lower plateau in CD4 cell count for patients who initiate HAART at lower CD4 cell count. In a study of 1835 patients with a median baseline CD4 cell count of 204cells/µL, the greatest mean yearly increase in CD4 cell count of 100cells/µL was seen in the first year after starting HAART. Significant but lower yearly increase in CD4 cell count of about 50 cells/µL were seen even at 5years of after starting HAART. This study found little evidence of the plateau effect. It also found that normalization of CD4 cell count might be achievable for all HIV-infected individuals if viral suppression is maintained for significantly long period (Mocroft A 2007).

Change in viral load

The FREQ Procedure

Viral load after 1 year of HAART: Overall

Table 53: The frequency procedure for viral load suppression in the three groups after 1 year of HAART

Viral-Load	Frequency	Percent	Cumulative Frequency	Cumulative Percent
51 - 400	25	26.04	25	26.04
<=50	71	73.96	96	100.00
Frequency Missing = 39				

Viral load after 1 year of HAART: Individual groups

Table 54: The FREQ Procedure for viral load suppression for group A

Viral-Load	Frequency	Percent	Cumulative Frequency	Cumulative Percent
51 - 400	10	31.25	10	31.25
<=50	22	68.75	32	100.00
Frequency Missing = 18				

Table 55: The FREQ Procedure for viral load suppression for group B

Viral-Load	Frequency	Percent	Cumulative Frequency	Cumulative Percent
51 - 400	4	11.11	4	11.11
<=50	32	88.89	36	100.00
Frequency Missing = 14				

Table 56: The FREQ Procedure for viral load suppression for group C

Viral-Load	Frequency	Percent	Cumulative Frequency	Cumulative Percent
51 - 400	11	39.29	11	39.29
<=50	17	60.71	28	100.00
Frequency Missing = 7				

Viral load after 1 year of HAART: Group

Table 57: Comparison of frequencies of viral load suppression in group A, B and C

Viral load	Group A	Group B	Group C	Total
Viral load of 51-400	22 68.75	32 88.89	17 60.71	71
Viral load ≤ 50	10 31.25	4 11.11	11 39.29	25
Total	32	36	28	96

Table 58: Statistics for table 57

Statistics	DF	Value	Prob
Chi-square	2	7.1675	0.0278
Likelihood Ratio Chi-Square	2	7.7246	0.0210
Mantel-Haenszel Chi-Square	1	6.6935	0.0097
Phi Coefficient		0.2732	
Contingency coefficient		0.2636	
Cramer's V		0.2732	

Fisher's Exact Test	
Table Probability (P)	0.0011
Pr<= P	0.0263
Sample Size = 96	

Table 59: Comparison of frequencies of viral load suppression in group A and B

Viral load	Group A	Group B	Total
Viral load of 51-400	22 68.75	32 88.89	54
Viral load ≤ 50	10 31.25	4 11.11	14
Total	32	36	68

Table 60: Statistics for table 59

Statistics	DF	Value	Prob
Chi-square	1	4.2025	0.0404
Likelihood Ratio Chi-Square	1	4.2837	0.0385
Continuity Adj-Chi-Square	1	3.0610	0.0802
Mantel-Haenszel Chi-Square	1	4.1407	0.0419
Phi Coefficient		0.2486	
Contingency coefficient		0.2413	
Cramer's V		0.2486	

Fisher's Exact Test	
Cell (1, 1) Frequency (F)	32
Left-sided Pr <= F	0.9913
Right -Sided Pr >= F	0.0396
Table probability (P)	0.0308
Two-sided Pr <= P	0.0694

Sample Size = 68

Table 61: Comparison of frequencies of viral load suppression in group B and C

Viral load	Group B	Group C	Total
Viral load of 51-400	32 88.89	17 60.71	49
Viral load ≤ 50	4 11.11	11 39.29	15
Total	36	28	64

Table 62: Statistics for table 61

Statistics	DF	Value	Prob
Chi-square	1	6.9674	0.0083
Likelihood Ratio Chi-Square	1	7.0607	0.0079
Continuity Adj-Chi-Square	1	5.4857	0.0192
Mantel-Haenszel Chi-Square	1	6.8585	0.0088
Phi Coefficient		0.3299	
Contingency coefficient		0.3133	
Cramer's V		0.3299	

Fisher's Exact Test	
Cell (1, 1) Frequency (F)	32
Left-sided Pr <= F	0.9985
Right -Sided Pr >= F	0.0094
Table probability (P)	0.0079
Two-sided Pr <= P	0.0156

Sample Size = 64

Table 63: Comparison of frequencies of viral load suppression in group A and C

Viral load	Group A	Group C	Total
Viral load of 51-400	22 68.75	17 60.71	39
Viral load ≤ 50	10 31.25	11 39.29	21
Total	32	28	60

Table 64: Statistics for table 63

Statistics	DF	Value	Prob
Chi-square	1	0.4239	0.5150
Likelihood Ratio Chi-Square	1	0.4236	0.5152
Continuity Adj-Chi-Square	1	0.1442	0.7041
Mantel-Haenszel Chi-Square	1	0.4168	0.5185
Phi Coefficient		0.0840	
Contingency coefficient		0.0838	
Cramer's V		0.0840	

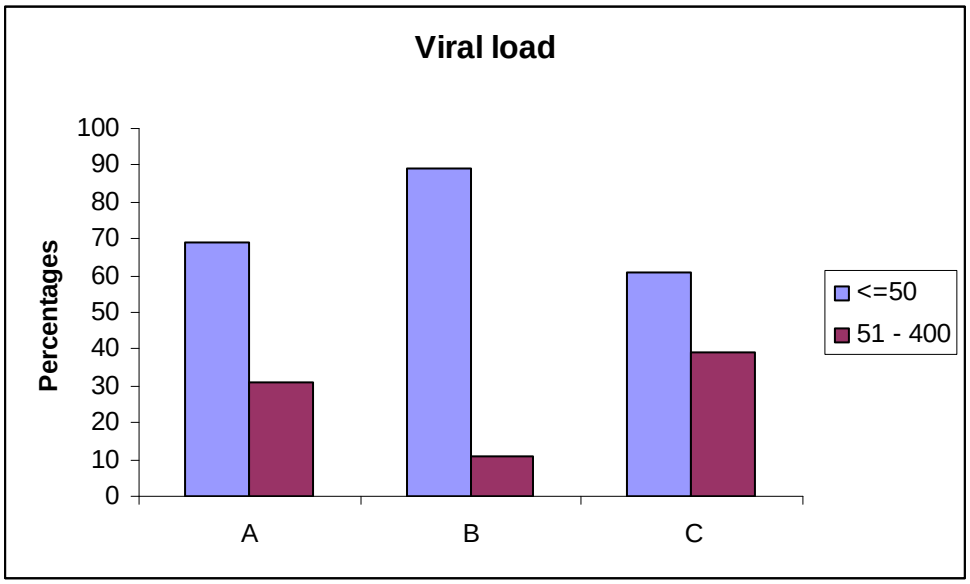
Fisher's Exact Test	
Cell (1, 1) Frequency (F)	22
Left-sided Pr <= F	0.8218
Right -Sided Pr >= F	0.3517
Table probability (P)	0.1735
Two-sided Pr <= P	0.5926

Sample Size = 60

Table 65: Comparison viral load suppression percentages between groups A, B and C

	Viral load		
Viral load	A <100	B 100 - 200	C 201 - 250
<=50	22 (69%)	32 (89%)	17 (61%)
51 - 400	10 (31%)	4 (11%)	11 (39%)
Total	32 (100%)	36 (100%)	28 (100%)

Figure 10: Change in viral load



The purpose of HAART is to suppress viral replication to such an extent where viral copies are not detected in blood thereby giving the immune system an opportunity to recover. In group A 32 (76%) patients suppressed viral replication by 12 months of ART and of those 22 (69%) attained undetectable viral load. In group B 36 (86%) patients suppressed viral replication, of those 32 (89%) attained undetectable viral load and in group C 28 (88%) patients and of those 17 (61%) attained undetectable viral load. The percentage of patients with undetectable viral load in group B (89%) is significantly different from the percentage in group A (69%) (Fisher exact test p= 0.03) and is also significantly different from the percentage in group C (61%) (Fisher exact test p= 0.008).

Poor virological outcomes are associated with low baseline CD4 cell count (Street E 2009, Palella F 2003). In contrast, a study done in China found that viral response rate is unlikely to be associated with baseline CD4 cell count (Zheng-yin L 2009).

CONCLUSION

Early (first year) clinical outcome is an important tool to assess the efficiency of the treatment program. It assesses the immediate response to treatment and assists in detecting early non-adherence to treatment and other causes of treatment failure.

The benefits of HAART are remarkable. It has changed the course of HIV infection from a rapidly fatal disease to a chronic manageable condition by reducing morbidity and mortality. The decision to initiate HAART is balanced between starting too early or too late as guided by the patient's CD4 cell count. Initiating HAART too early may unnecessarily predispose the patient to potentially fatal adverse effects while delaying HAART places the patient at risk of serious illness and death.

Patients who initiate HAART with CD4 cell count of less than 100 have a high mortality rate when compared to patients who initiate HAART with CD4 cell count of 100 to 200 and patients who initiate HAART with CD4 cell count of 201 to 250. They also continue to loose weight exceeding 10% of baseline body weight which contributes to stigmatasation and marginalisation. This may negatively affect follow-up and adherence to treatment.

There are higher rates of hospital admissions due to HIV-related illnesses despite being on HAART in patients with baseline CD4 cell counts of less than 100. This is one of the factors that contribute to high cost of health care to HIV patients thereby putting a strain on the national health budget. It also results in high rate o f absenteeism at work among HIV-infected individuals.

The rate of AIDS-defining illnesses such as meningitis, TB and pneumonia is however not increased in these patients when compared to patients with baseline CD4 cell count of more than 100 once HAART has been commenced. This indicates that other HIV-related conditions are responsible for high hospitalization rate in patients with baseline CD4 cell count of less than 100.

There was no difference in the change in mean CD4 cell count at 1 year of HAART in patients with baseline CD4 cell count of less than 100 when compared to patients with a CD4 cell count of 101 to 200 and patients with CD4 cell count of 201 to 250. This indicates that early immunological

recovery is independent of baseline CD4 cell count. However patients with baseline CD4 cell count of 101 to 200 had a higher percentage of viral suppression than patients with baseline CD4 cell count of less than 100. Viral suppression is strongly dependent on adherence to treatment which is affected among others by the presence of co-morbid conditions. Adherence in this study was assessed by monthly collection of treatment at the clinics and no pill count was being performed. Patients were not stratified according to the presence or absence of co-morbid conditions.

Patients with baseline CD4 cell count of less than 100 have a poor clinical outcome when compared when compared with patients with patients with baseline CD4 cell count of more than 100.

RECOMMENDATIONS

Efforts must be made to identify patients early before CD4 cell count fall to below 100 and preferably initiate HAART when CD4 cell count is above 200.

Most recent guidelines (DHHS-USA Department of Health and Human Services, IAS-USA-International AIDS Society) recommend initiation of HAART at CD4 of 350 and below. This is supported bydata from prospective observational cohorts and clinical trials which demonstrate worse clinical outcomes among patients who begin receiving HAART at CD4 cell counts less than 350 or who have symptomatic HIV disease (Thompson M et al 2010 and Department of Health and Human Services (DHHS) 2007).

LIMITATIONS

Adherence in this study was assessed by monthly collection of treatment at the clinics and no pill count was being performed.

Patients were not stratified according to the presence or absence of co-morbid conditions.

Clinical staging before initiation HAART was not taken into account except that only patients with stage 4 disease were excluded.

Patients who did not have a record of results at the end of one year of initiation of HAART were excluded

Annexure: 1

Patient's file number	Hospital admissions	Weight loss > 10% of baseline body weight	Development of TB	Severe bacterial pneumonia	Bacterial or cryptococcal meningitis	Mortality	CD4 Count Baseline	CD 4 Count After 1 year of HAART	Viral Load Baseline	Viral Load After 1 year HAART
1.										
2.										
3.										
4.										
5.										
6.										
7.										
8.										
9.										
10.										

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