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MORBIDITY AND CD4+ CELL COUNTS AT INITIAL PRESENTATION OF A COHORT OF HAART-NAIVE, HIV POSITIVE KENYAN PATIENTS: IMPLICATIONS TO INITIATING HAART

A. E. O. OTEDO, C. F. OTIENO, C. OKAL, D. OTHERO, G.O. OYOO and E. O. OMONGE

ABSTRACT

***Background*: Sub-Saharan Africa with under 10% of the world's total population accounts for 60-70% of all HIV/AIDS cases. While these patients require HAART to manage the disease, HAART is not universally available. Majority of the patients are in resource-constrained settings, have multiple co- morbidities/infections, opportunistic infections, present late for treatment and are in the advanced stages of the HIV/A±IDS infection.**

***Objective*: To describe the CD4+ cell counts, opportunistic infections and laboratory parameters of a cohort of HIV positive, HAART-naïve patients at first presentation.**

***Design*: Cross sectional, prospective, descriptive, consecutive entry study.**

***Setting*: Kisumu District Hospital wards (medical, surgical) and medical outpatient clinic, Nairobi Rheumatology Clinic, Nairobi West Hospital and the Mater Hospital between January 2001 and December 2008.**

***Main outcome measures:* Socio-demographic parameters, opportunistic infections, CD4+ cell counts and complete blood count, biochemistry, HBsAg markers and anti-HCV serostatus.**

***Results*: Eight hundred and thirty four (350 males and 484 females) patients were screened. Three hundred and seventy (94 males and 276 females) patients were excluded. Four hundred and sixty four (256 males and 208 females) patients were finally included in the study. The mean age was 37.2 ±10.6 years, range (12-78). The M: F ratio was 1.2:1. The mean CD4+ cell count was 106.5 ± 125.2 cells/μl manifesting severe immnosuppression. Fifteen (3.2%), 19(4.1%), 43(9.3%) and 387(83.5%) had CD4+ cell counts of > 500, 350-499, 200-349 and < 200 cells/μl respectively. The mean white blood cell count was 8.63 ± 8.8 × 10^3/ml (4.8-10.8 × 10^3/μl). Over half (51.3%) patients had leucopaenia, white cell count < 4.8 × 10^3/μl, 35 (7.5%) had leucocytosis and the rest 191 (41.2%) patients had normal white blood cell counts. The mean haemoglobin level was 7.16 ± 5.01 g/dl (12-18 g/dl) and 154 (33.2%) had haemoglobin level < 5g/dl manifesting severe anaemia. The patients had multiple co-morbidities and 248 (53.4%) had ≥ 2 co-morbidities.**

***Conclusion*: The patients presented with severe immunosuppression evidenced by low CD4+ cell counts, anaemia and multiple co-morbidities. Majority presented late at which point the cost of management is high and outcomes are likely to be poor. They required HAART and prompt management of the co-morbidities to mitigate morbidity and reduce mortality. It would be prudent to study treatment outcomes and their determinants overtime in patients with severe HIV disease. Also, requiring study is how long such patients with severe HIV disease who commence HAART would last on first line treatment before requirement of alternative treatment.**

INTRODUCTION

Today, over 38 million people are living with HIV/AIDS infection globally, with five million new infections acquired annually (1,2). Sub-Saharan Africa, with under 10% of the world's total population accounts for 60-70% of HIV/ AIDS cases worldwide. In Botswana, about 45% of pregnant women are infected. Kenya has an estimated national prevalence of 6.8% and approximately 1.1 million people living with AIDS (PLWAs) and still experiencing devastating effects of HIV/AIDS epidemic (3, 4). These patients require highly active anti-retroviral therapy (HAART) to manage the disease. It is noteworthy that Sub-Saharan Africa has a population of 25.4 million people living with HIV/AIDS, 3.1 million new HIV/AIDS infection annually and experiences 2.3 million HIV/AIDS related deaths annually (5).

First diagnosed about 30 years ago, HIV/AIDS presents with multiple opportunistic infections and other co-morbidities especially in the advanced stages where HAART had not been initiated. Most patients in resource-constrained setting present late to patient support centres / comprehensive care clinics (PSCs/CCCs) because of stigma, poor socio- economic status, inaccessibility to care in PSCs/CCCs for a variety of reasons. Lately the government has rolled out free HAART access in various parts of the country as a public health intervention programme.

Few studies have been done locally to show the morbidity pattern and CD4+ cell count at initial presentation to the clinics. Indeed the management of opportunistic infections has a bearing on the choice of HAART and outcomes.

This study presents a cohort of HAART naïve, HIV positive patients whose clinical and laboratory parameters were analysed at the initial presentation to the clinics. This was at a time when there were few CCCS/PSCS countrywide. The patients were funding their own care, the ARTS and the medications for managing co-morbidities.

MATERIALS AND METHODS

Eight hundred and thirty four patients (350 males and 484 females) were examined and screened.
Three hundred and seventy (94 males and 276 females) were excluded due to incomplete data and as a result, only 464 (256 males and 208 females) were included in the study. Informed, signed consent was obtained from each patient, (< 18 years old or in coma, signed by parent(s) or guardian). The ethics and standards committee of Kisumu District Hospital and hospital administration of the other hospitals, approved the study. A standard questionnaire was run for each study subject and it included: bio-data, symptoms and signs. Each patient underwent a thorough clinical examination by the clinicians. A DTC (diagnostic testing and counselling) was done to each previously undiagnosed patient and post-test counselling was sustained for all patients. Twenty patients presented for care with a known HIV positive sero-status from a referral voluntary counselling and testing (VCT) centre. Under aseptic technique, blood was drawn from the cubital fossa and used to determine complete blood count, CD4+ cell count, and ELISA test for HIV and hepatitis B surface antigen (HBsAg), AST, ALT and anti-HCV antibodies. A clinical diagnosis was made for each patient who was then investigated and managed appropriately as an out- or in-patient. The CD4+ cell count was determined using fluorescent activated cell sorter (FACS) flow cytometry method with a sensitivity of 1-2000 cells/μl (FACS count machine from Baxton, Dickson). Appropriate investigations (Laboratory, radiology) were undertaken to further evaluate/confirm the diagnosis (Table 1). Complete blood count was done using the Coulter counter machine. The liver function tests were analysed using the technicon RA 1000 machine (Technicon RA systems No. sm-0034 D91 and sm4-0137, D 91, 1996). The results were expressed as mean ± SD, histograms and tables.

Intervention: The patients were seen for routine clinical care in the hospitals where the study was conducted. The opportunistic infections and other co-morbidities were managed appropriately. HAART was promptly initiated (within 7-29 days) in all the included patients.

Twenty eight patients (17 females, 11 males) could not start HAART promptly due to the severe co-morbidities they had which had to be managed (10 had severe anaemia of haemoglobin < 5g/dl which required blood transfusion, 13 had hepatitis B virus infection and non-viral causes of elevation

of transaminases-AST and ALT and five had cryptococcous meningitis and were in coma). The patients survived and were subsequently followed up by the authors (MDs) as out patients. Follow up CD4+ cell counts were done every three to four months on average to assess response to HAART. The patients who had CD4+ cell counts < 100 cells/ μl were followed up every month or as need arose.

Patients who could not afford HAART were referred to alternative HIV-CARE clinics available.

ARTs - Stavudine/ Lamivudine/ Nevirapine or Efavirenz.
- Fixed dose combination-EMTRI 30/40 or Triomune 30/40

RESULTS

Eight hundred and thirty four (350 males and 484 females) were evaluated for the study. Three hundred and sixty six (90 males and 276 females) were excluded due to incomplete data (HIV positive but no data on CD4+ cell count and haematological parameters). Four hundred and sixty four (256 males and 208 females) patients were included. The male: female ratio was 1.2:1. The mean age was 37.2 ± 10.6 years (range 12-78). The mean CD4+ cell count was low, 106.5 ± 125.2 cells/ μl, range of (0.4-1022 cells/ μl). Fifteen (3.2%), 19(4.1%) and 43(9.3%) patients had CD4+ cell counts > 500, 350-499 and 200-349 cells/ μl respectively. Three hundred and eighty seven (83.4%) patients had CD4+ cell count of < 200 cells/ μl manifesting severe immunosuppression.

Two hundred and thirty eight (51.3%) patients had leucopenia with low white cell count < 4.8 × 103/ ml, 191 (41.2%) had normal white cell count of 4.8-10.8 × 10^3/ml and 35 (7.5%) had leucocytosis (white cell count > 10.8 × 10^3/ml). Mean haemoglobin level was 7.16 ± 5.01 g/dl. Eighteen (3.9%) patients, 50(10.8%) patients, 109(23.5%) patients, 127 (27.3%) patients and 160 (34.5%) patients had haemoglobin levels of > 10.6g/dl, 9.5-10.5 g/dl, 8.0-9.4 g/dl, 6.5-7.9g/dl and < 6.5g/dl respectively

Thus, 160 (34.5%) patients had severe anaemia with haemoglobin < 6.5g/dl. The patients who were excluded: declined HIV test (30), had stigma about the disease (17), needed more counselling time (51), or tested positive for HIV (271) and referred to other centres offering government funded, free access to HAART, OI management drugs and other aspects of HIV care (Kenyatta National Hospital, Mission Hospitals, PGH Kisumu).

Figure 1

Enrollment flow chart of the patients in the study

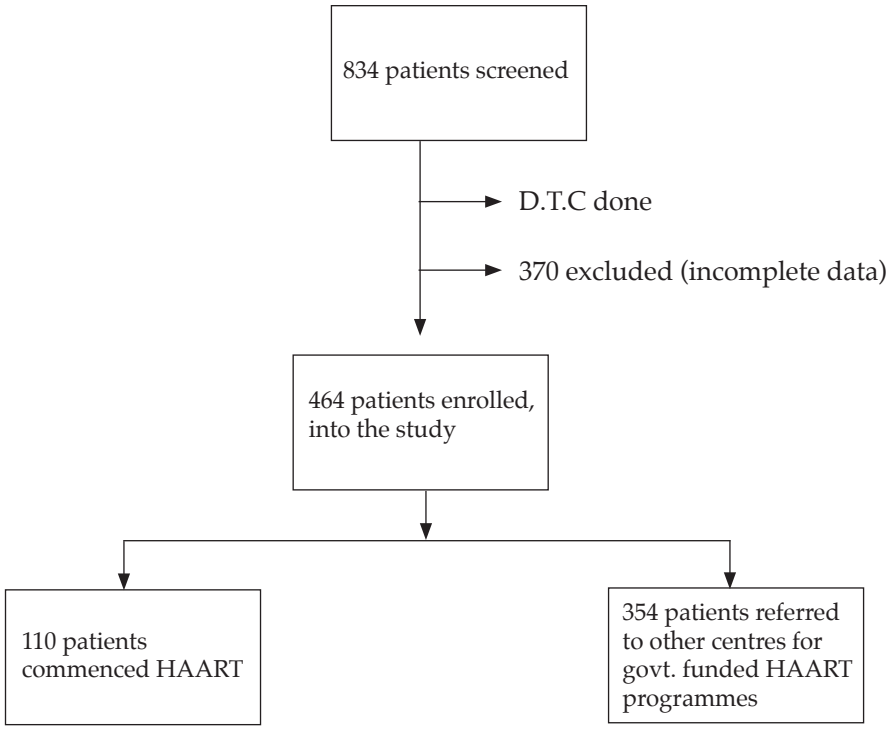


Table 1
Patients recruitment during the study period.

Year of Study	No. of patients recruited.
2001	52
2002	120
2003	257
2004	267
2005	124
2006	10
2007	4
Total	464

Table 2
Baseline characteristics: Demographic and laboratory profile of the 464 study patients.

Characteristic	Mean ± SD/Proportion
M:F ratio	256:208 (1.2:1)
Mean age (years)	37.2 ± 10.6 (12-78)
Mean CD4+ cell count (350-1600 cells/μl)	106.5 ± 125.2 (0.4-1022)
HIV infection	***All patients***
CDC *clinical staging*	
A.	23 (5%)
B.	27 (5.8%)
C.	414(89.2%)
***CD4+ cell count clusters (350-1600cells/μl)**	
> 500	15 (3.2%)
350-499	19 (4.1%)
200-349	43 (9.3%)
< 200	387 (83.4%)
Haematology	
Mean haemoglobin-(HB)-(10.6-17.0 g/dl)	7.16 ± 5.01 (2.9-13)
HB > 10.6	18 (3.9%)
HB 9.5-10.5	50 (10.8%)
HB 8.0-9.4	109 (23.5%)
HB 6.5-7.9	127 (27.3%)
HB< 6.5	160 (34.5%)
White blood cell count (4.8-10.8 X10^3/μl)	
Mean white cell count	8.63 ± 8.8 (2.3-20.1 X 10^3/μl)
> 10.8	35 (7.5%)
4.8-10.8	191(41.2%)
< 4.8	238(51.3%)
***Biochemistry* (Mean ± SD)**	

ALT (5-37 IU/L)	123.2 ± 20.1
AST (5-40 IU/L)	101.7 ± 23.7
Hepatitis serology	
HBsAg positive	119(25.6%)
Anti-HCV positive	Nil
History of HAART	
HAART naïve	ALL patients recruited
HAART regimen commenced	None-354 (76.3%)*, triomune 30/40-60 (13.0%), Combivir/Efavirenz 34(7.3%),d4T/ddi/efavirenz 16(3.4%)
	*Reffered to other centres offering HAART
Data are Mean ± SD, or number of patients (%)	HAART

*CDC-Centres For Disease Control. Source, Morb. Mort. Week. Rep. 42 (No. RR-17), Dec. 18. 1992 (A-asymptomatic PGL, B-Symptomatic, not A or C conditions, C-AIDS defining illness. HB-haemoglobin-Anaemia classification, WHO/ACTG-anaemia grades REF: (20). Combivir(AZT+3TC),ALT-alanine transaminase, AST-aspartate transaminase.

Figure 2

The age group distribution of patients with HIV who were seen at first presentation to the clinic

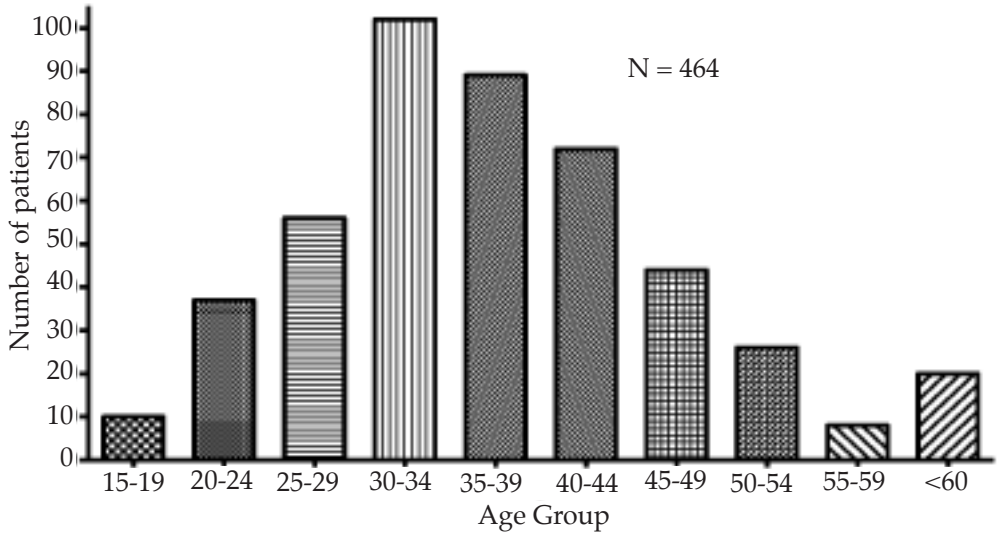


Figure 3

Age group gender based distribution of patients with HIV who were seen at first presentation to the clinic

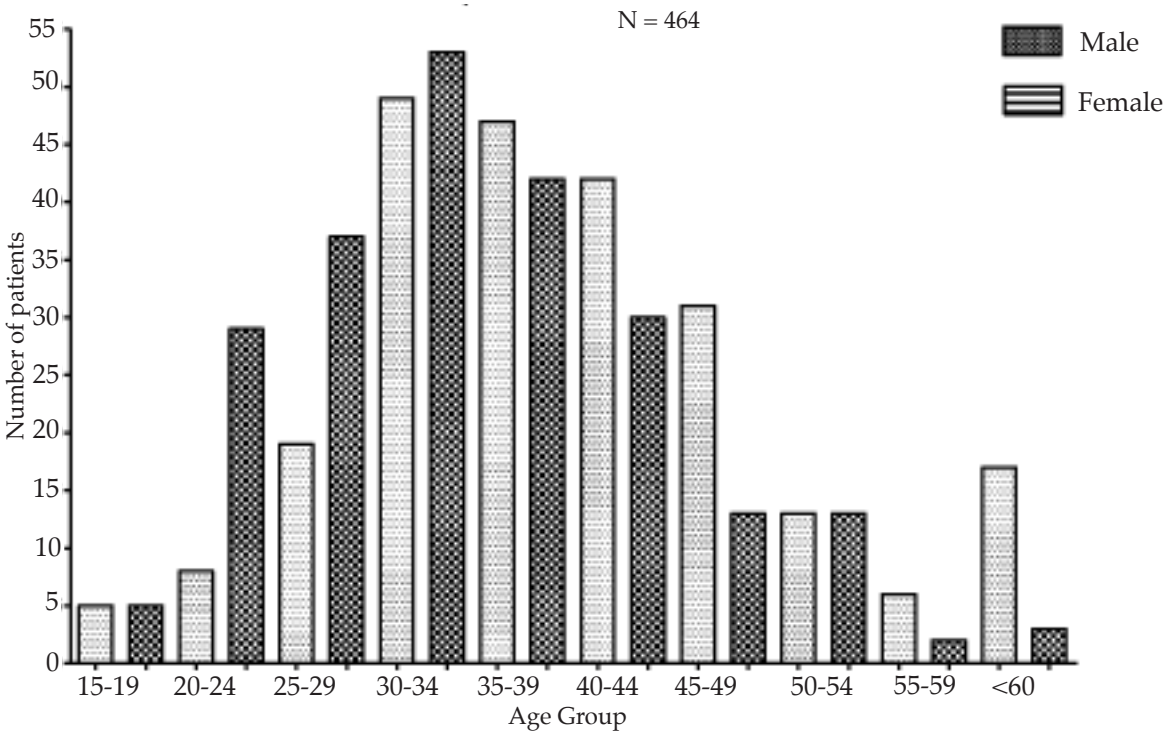


Table 3

Morbidity pattern and mode of diagnosis in cohort of the 464 HIV positive HAART naïve study patients.

Disease/condition	Freq.	Mode of diagnosis
Herpes zoster virus (HZV)	21	Clinical
Tuberculosis (Pulmonary and extrapulmonary)	37	Sputum (Z-N staining), lymph node biopsy, chest x-ray
Cryptococcus Meningitis	124	CSF-Indian ink staining
Chronic Diarrhoea (cryptosporidium,giardia)	15	Stool-M/C/S, modified Z-N staining
Vasculitis	8	Clinical, venogram,C-T scan
Hepatitis B virus (HBV)	119	HBsAg serology (ELISA method)
Oral Candidiasis	50	Clinical
Pneumocystis jiroveci pneumonia (PJP)	27	Clinical, LDH (lactate dehydrogenase), chest X-ray
Deep venous thrombosis-Lower limbs	5	Doppler ultrasound
Cholecystitis/Cholangitis	78	Clinical, ultrasound of abdomen
Anaemia	396	Clinical, complete blood count
Pyomyositis	8	Surgical incision/drainage, pus culture,sensitivity.
Kaposi's Sarcoma	16	Biopsy and histology
Bacterial Pneumonia	12	Clinical, Chest X-ray

Sepsis *	5	Clinical, complete blood count.
Bacterial Meningitis	8	CSF-M/C/S/biochemistry
Neuropathy	3	Clinical
Parotitis	3	Parotid gland biopsy and histology
Non Hodgkin's lymphoma	14	Lymph node biopsy and histology
Toxoplasmosis	4	C-T scan head/brain, Toxoplasma antibodies
Psoriasis	4	Clinical
Hepatocellular carcinoma	12	Clinical,ultrasound,histology,α-fetoproteins
Sexually transmitted infections	10	Urine-M/C/S, clinical,pus swab-culture
Renal dysfunction	4	24 hour urinary protein,urea, electrolytes,creatinine

Sepsis-the patients had peritonitis, fallopian tube abscess, anal fissure, puerperal sepsis, and septic oral sores with attendant leucocytosis. It is noted that 248(53.6%) patients had two or more co-morbidities.

M/C/S - Microscopy, culture and sensitivity; CSF - Cerebrospinal fluid

Table 4

Demographic and laboratory profile of the patients who had > 2 co-morbidities.

Parameter	Value
M:F	131: 117 (N=248)
Mean Age (years)	38.4 ± 11.5 (12-78)
CD4+ cell counts	
Mean CD4+ cell count (350-1600 ells/μl)	107 ± 127 (0.4-885)
≥ 500	6(2.4%)
350-499	5(2.0%)
200-349	20(8.1%)
< 200	217(87.5%)
Haemoglobin categories (normal-10.6-17 g/dl)	
Mean haemoglobin	7.5 ± 3.13 (1-16.5)
> 10.6	None
9.5-10.5	70(28.3%) patients
8- 9.4	31(12.5%) patients
6.5- 7.9	40(16.1%) patients
< 6.5	107(43.1%) patients
Mean White blood cell count (X 10^9/L)	8.4 ± 4.97 (0.5-24.2)
Mean Neutrophil count(45-70%)	63.6 ± 18.4 (40-79.8)

Anaemia classification WHO/ACTG –anaemia grades REF (20).

Table 5
Co-Morbidities.

Co-Morbodity	No. of patients	Co-Morbidity	No. of patients
Meninigitis/Sepsis	3	Cholecystitis/Kaposi's sarcoma	2
Herpeszoster/anal fissure/oral candidiasis	4	Cholecystitis/Oral candidiasis/ pneumonia	1
PTB/vasculitis	3	HBV/Psoriasis1	
PJP/vasculitis/gastroenteritis	5	HBV/pneumonia	5
HBV/PJP/fallopian tubal abscess	1	HBV/Vasculitis	1
HBV/gastroenteritis	6	HBV/Hepatoma	4
DVT/pyomyoisitis	2	HBV/Oral candidiasis	7
Pyomyositis/Oral candidiasis	3		
HBV/KS/Oral candidiasis	3	HBV/Genital ulcer disease	6
PTB/Oral candidiasis	5	HBV/meningitis-bacterial	2
PTB/cryptococcus		HBV/Cholecystitis	1
Bacterial meningitis/gastroenteritis	4	HBV/Cholecystitis/Oral candidiasis	1
PTB/PJP	2	HBV/Peritonitis	1
Pneumonia/Oral candidiasis	42	HBV/seborrhoea/PJP	1
Herpes zoster virus/Oral thrush	3	HBV/cryptococcus	1
PTB/HBV	9	Hepatoma/Oral candidiasis	1
PTB/AIDS dementia complex	1	HBV/Herpes zoster virus	1
PJP/HBV	2	HBV/Taenia corporis	5
Toxoplasmosis/cryptococcus	1	Non Hodgkin's lymphoma/oral thrush/pneumonia	3
PJP/Oral candidiasis	1	Hodgkin's lymphoma/ oral candidiasis/anaemia	10
HBV/Kaposi's sarcoma	3	Burkitt's lymphoma/anaemia	2
Cryptococcus/KS/Oral candidiasis	2		
Cryptococcus/PJP	1		
Cholecystitis/PTB	4		
Cholecystitis/PJP	9		
Cholecystitis/cryptosporidium	4		
Cholecystitis/Oral candidiasis	12		
Cholecystitis/gastroenteritis	4		
Cholecytitis/Herpes zoster virus infection	11		

HBV - Hepatitis B Virus
HCV - Hepatitis C Virus
KS - Keposi's Sarcoma
PJP - Pneumocycstis Jirovecic Pneumonia
PCB - Pulmonary Tuberculosis

Figure 4

Distribution of CD4 count at presentation among 248 HIV positive patients seen in the medical outpatient clinic

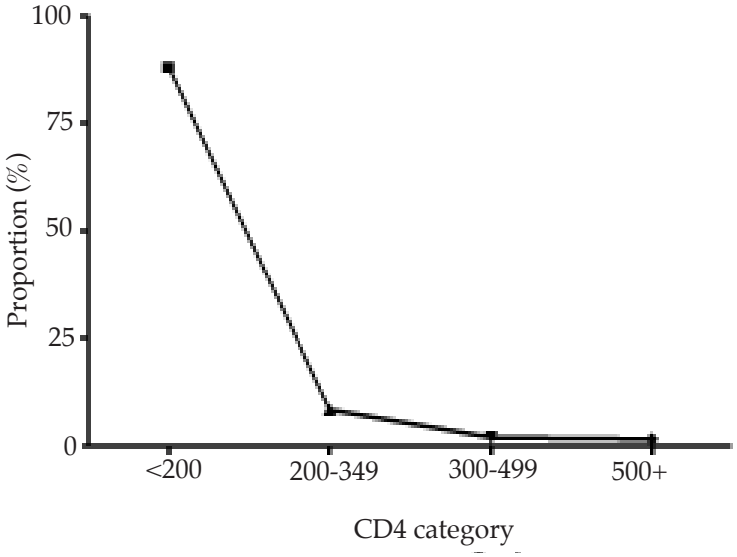
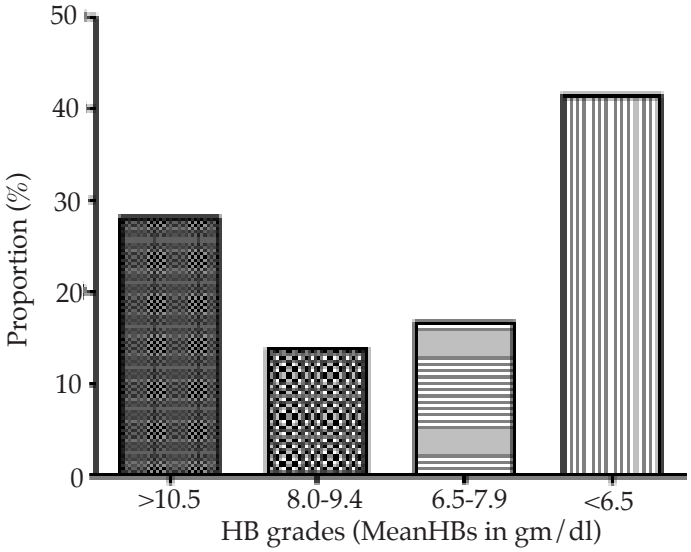


Figure 5

Distribution of haemoglobin (HB) levels among 248 HIV positive patients seen at the medical outpatient clinics



DISCUSSION

HIV remains a major health burden in the third world, more so, the sub-Saharan Africa, that has the highest burden of the disease (5). HAART is proven to lead to suppression of HIV viral load to undetectable levels (<50 copies/μl), an increase in CD4+ cell count and a dramatic decrease of opportunistic infections (5).

As depicted in the study, patients presented late to the various clinics with severe immunosuppression with a mean CD4+ cell count of 106.5 ± 125.2 cells/μl. Indeed, more than four out of five (83.4%) the study patients had CD4+ cell counts < 200 cells/μl, hence had severe immunosuppression. These patients had multiple co-morbidities where more than half 248 (53.6%) had ≥2 co-morbidities. These patients required immediate treatment for opportunistic diseases/ co-morbid conditions and HAART initiation to avert further clinical deterioration. Progress in effecting earlier diagnosis and initiating HAART remains an important public health goal but has been insufficient globally (6-8). In this Cohort, only 34(7.3%) patients had CD4+ cell counts > 350 cells/μl (the threshold below which HAART should be initiated).

The majority 430 (92.7%) patients had CD4+ cell counts < 350 cells/μl. These were patients with multiple co-morbidities, Table 5.

Most opportunistic infections occur at lower CD4+ cell counts, < 350 cells/μl but we must remain cognisant of the fact that opportunistic infections also occur at higher CD4+ cell counts because of qualitative dysfunction and must be looked for and managed appropriately (9-11). Lately, Centres for Disease Control (CDC) has recommended HIV screening and testing in routine clinical care between the ages 13-65 years, in a Diagnostic Testing and Counselling (DTC)strategy. This would facilitate early detection of HIV disease, initiation of ARTs and maintenance of immune function or achievement of immune preservation before patients deteriorate (6-11). The reality is that many individuals may harbour undiagnosed HIV infection for long. Indeed studies have shown that increased screening is highly cost-effective, leads to early diagnosis of HIV infection which benefits both the individual by timely HAART initiation and the public by decreased HIV transmission either through behavioural changes and/or ART therapy (10, 11).

Worth mentioning are AIDS- associated malignances and non- infectious conditions (Non- Hodgkin's lymphoma, Kaposi's sarcoma, Progressive multifocal leucoencephalopathy, hepatocellular carcinoma, cholangitis/cholecystitis, deep venous thrombosis) which are poorly managed because most comprehensive care clinics do not have adequate diagnostic capacity and expertise in treatment in many centres outside cities except a few selected centres locally in this country. The patients therefore are expected to purchase these expensive co-therapies even though ARTs are provided free of charge. More often than expected, patients with HIV/AIDS who are allergic to sulphonamides and have toxoplasmosis are expected to buy the expensive alternative treatments. Studies have shown that appropriate combined cytotoxic therapy for Kaposi's sarcoma and non-Hodgkin's lymphoma and HAART leads to adequate disease remission (12).

Suffice to note that pulmonary Kaposi's sarcoma, progressive multifocal leucoencephalopathy and some non- Hodgkin's lymphomas remain an ominous diagnosis and difficult to treat even in the HAART era and have a median survival between 6-18 months (12-14). HAART has been shown to reduce the rates of Kaposi's sarcoma and non Hodgkin's lymphoma and not other cancers (13, 14). Thus, such co-morbidities in the study patients should not be a condemnation to mortality if and when managed appropriately and timely.

Cryptococcus meningitis, a major killer in HIV/AIDS patients is a critical and challenging co-morbidity. While few HIV care clinics have the right antifungal medications especially fluconazole, they do not always have amphotericin B and other alternatives for reasons of cost and expertise and facilities to monitor treatment.

Pneumocystis Jiroveci pneumonia, toxoplasmosis, deep venous thrombosis, vasculitis and cholangitis/cholecystitis receive neither adequate diagnostic work up nor optimal therapy in the majority of patients because the cost is beyond reach of many of the patients like those included in this study.

In advanced HIV/AIDS disease, like the study patients in our cohort, protein S and factor VIII become progressively abnormal and are associated with vascular morbidities. Rising HIV- I viral load and declining CD4+ cell counts lead to increased factor VIII and decreased protein S activity leading to a hypercoagulable state (15). Therefore, it is not surprising that DVT occurs more frequently in the HIV-infected people than the un-infected population.

In the developed world, liver diseases are leading causes of non-AIDS deaths in HIV positive patients.

The risk factors for liver-related deaths in HIV positive patients include lower CD4+ cell count, hepatitis C virus (HCV) infection, active hepatitis B virus (HBV) infection, intravenous drug abuse and older age (16). HBV/HIV and HCV/HIV co-infections have been demonstrated in the local population (17, 18). The HIV care clinics must evaluate liver conditions and offer appropriate management in view of the prolonged life HIV patients anticipate while on HAART and the prevalence of HBV infection in Kenya. Indeed, ARTs and certain co-medications for example, anti-tuberculosis drugs, enhance the risk for liver damage. Tuberculosis is very common in HIV infected patients with severe immunosuppresion. Tuberculosis, both pulmonary and extra pulmonary Tuberculosis (TB) is a prevalent opportunistic infection. T.B infection is associated with higher HIV viral load. There is growing evidence in new case-control studies that aggressively treating both HIV and T.B is beneficial (19). Indeed T.B infection is a major cause of death in HIV-infected patients worldwide and there is need for prompt anti-retroviral therapy in HIV-infected patients diagnosed with TB

(20). This study presents the magnitude of challenge in treating TB in severely immunocompromised HIV infected patients, especially in public health settings which use nevirapine based HAART combinations. Lately efavirenz has been made available in public health ART programe.

The prevalence of anaemia in this cohort was high at 396(85.3%) patients having haemoglobin level < 9.4 g/dl and 160 (35.3%) patients had haemoglobin < 6.5. g/dl. Only 22 (4.7%) patients had haemoglobin > 10.6 g/dl. Anaemia in HIV is a poor prognostic marker of disease progression or death, independent of CD4+ cell counts and HIV viral load (21). Anaemia also delays the initiation of HAART especially when use of AZT is intended as part of first line combination therapy. Anaemia also impacts negatively on the quality of life of patients. Moderate to severe forms of anaemia may require blood transfusion before HAART initiation to avoid delay of treatment. This is especially so when there is pancytopaenia at the time when the patient presents to the clinic. HAART is effective in reducing the risk of anaemia and enabling low haemoglobin to recover although clinical trials data indicate that differences in the effects of HAART on anaemia exists between AZT-and d4T- based regimens (21,22).

Prevention of anaemia in patients with HIV/AIDS should be the mainstay of management. As studies have identified that patients with CD4+ cell counts < 200 cells/mm^3 and opportunistic diseases are at an increased risk, intervention with HAART along current treatment guidelines, that is, HAART before CD4+ cells fall below 250 cells/mm^3, should reduce the risk of an individual developing anaemia (23).

A study in Spain demonstrated that earlier HAART initiation may reduce risk of progression of HIV infection to AIDS and that the best time to initiate HAART in asymptomatic HIV- infected patients appears to be before CD4+ cell counts falls below 350 cells/μl (23). Indeed, the HAART drugs are now better and there are more comfortable treatment regimens.

Over half, 238(51.3%) patients had leucopaenia of < 4.8 × 103cml (4.8-10.3 × 103/ml), with an associated neutropaenia and lymphocytopaenia. It has been noted that worsening parameters of HIV/AIDS disease (low CD4+ cell count, high HIV viral load and presence of opportunistic infections) are associated with increasing occurrence of neutropaenia and more severe bacterial infections especially in women (21,22). A CD4+ cell count of < 200 cells/μl is associated with the increased risk of neutropaenia by 82% and an HIV-RNA load of >100,000 copies/ml increases the risk by 47% (22). However, in this study, HIV viral loads were not done because of high cost. CD4+ cell count and HIV- RNA are significant independent risk factors for developing neutropaenia.

HAART without zidovudine has been noted to significantly decrease the risk of developing neutropaenia. Zidovudine is associated with the development of anaemia and neutropaenia (22, 24).

CD4+ cell counts do not rigidly define susceptibility to an opportunistic infection. Rather, there is a continuum of risk that decreases as the CD4+ cell count increases: the published thresholds are merely guidelines to direct clinicians. In the studies done, allowing the CD4+ cell count to fall to 250 cells/μl permitted some of the patients to fall too far into the susceptible range and some may have had high viral loads to reduce immunologic function further (24). The traditional thresholds of CD4+ cell counts remain valuable, reliable indicators, but they represent a biologic spectrum of risk, not an absolute indicator. Thus, opportunistic infections can occur after initiation of HAART, but they usually occur when CD4+ cell counts are still low or they occur rarely at a " higher than expected" CD4+ cell counts (25).

In conclusion, many patients with HIV infection presented in advanced stage of the disease, severely immune-suppressed with opportunistic infections and several other co-morbidities. Two hundred and seventeen (87.5%) of the patients who had ≥ 2 co-morbidities had CD4+ cell counts < 200 cells/μl. They received inadequate diagnostic work-up and access to comprehensive therapy because of cost. These issues complicate access to HAART and jeopardise patient outcomes in spite of the genuine efforts. We recognise that the exhaustive patient work- up was curtailed by costs and the opportunistic infections and co-morbidities may have been under-diagnosed or not fully defined. Severe HIV disease will therefore remain a major challenge to public health interventions of HIV management in resource-constrained settings for some time to come. Even when one accesses HAART, the severe opportunistic infections and severe co-morbidities of HIV infections increases mortality escpecially when not correctly identified

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