CLINICAL AND HAEMATOLOGICAL PROFILES OF HIV INFECTED INDIVIDUALS ADMITTED TO KENYATTA NATIONAL HOSPITAL.

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DECLARATION.

This dissertation is my original work and has not been presented to any other university.

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LIST OF ABBREVIATIONS.

AIDS:	Acquired Immunodeficiency Syndrome
$CD4^+$:	T-helper/inducer lymphocytes
$CD8^+$:	T-suppressor lymphocytes
C.I.:	Confidence Interval
C.N.S.:	Central Nervous System
E.g.:	For example
ESR:	Erythrocyte sedimentation rate
G/E:	Gastroenteritis
G.I.T.:	Gastrointestinal tract
Hb:	Haemoglobin
HIV:	Human Immunodeficiency Virus
K.N.H.:	Kenyatta National Hospital
n :	Total Number of Patients
P24:	Protein 24 (Surface marker of the HIV)
P.C.P.:	Pneumocystis carinii Pnuemonia
P.T.B.:	Pulmonary Tuberculosis
Pt study:	Post mortem study
U.S.A.:	United States of America.
SD:	Standard deviation
T.B.:	Tuberculosis
WBC:	White blood cells
W.H.O.:	World Health Organisation

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To my lovely daughter **Zeinab**.

SUMMARY.

Objective: To determine the clinical stages of HIV infected patients admitted to the medical wards, and to correlate these to the haematological and immunological markers (mainly CD4, CD8 cells).

Design: A cross-sectional descriptive study.

Setting: Kenyatta National Hospital, Nairobi, Kenya. Medical wards (24,30) between January and June 1997.

Subjects: All adult medical patients who gave consent to HIV screening and turned out to be HIV positive.

Results: 317 (32.7%) of the 968 patients studied were HIV positive. 253 (79.8%) of the HIV positive patients were included in this study. 23 (9.1%), 17 (6.7%), 78 (30.9%) and 135 (53.4%) patients were found to be in stages 1,2,3 and 4 respectively.

158 (62.5%) patients had a haemoglobin of less than 10g/dl and 171 (67.6%) of the patients had a total lymphocyte count of less than 1500 cell/mm^3. 217 (85.5%) of the patients had a $CD4^+$ count of less than 380 cells/mm^3. All haematological and immunological parameters including the $CD4^+/CD8^+$ ratio were found to be declining progressively with the progression of the disease.

Conclusion: In this study the majority of the patients had developed AIDS (stage 4). The haematological and immunological parameters were generally declining with the progression of the disease.

INTRODUCTION AND LITERATURE REVIEW.

INTRODUCTION.

Since the outbreak of the AIDS pandemic in the late 1970s to early 1980s, it has become one of the major killer diseases in the world affecting especially the young age groups.

Epidemiology of HIV/AIDS

According to the WHO weekly epidemiological record, of the 1st of January 1997, 22.6 million people were estimated to be living with HIV infection or AIDS. Of these, 21.8 million were adults with 42% being women. The majority of newly infected adults are under the age of 25 years (1). By the year 2000 an estimated 30-40 million people will develop AIDS, 90% of them in developing countries (2).

By the 1st of December 1996, it was estimated that 14 million people were living with HIV/AIDS in Sub-saharan Africa, representing 63% of the world's total (1).

In Kenya, by the 18th of June 1996, the reported AIDS cases had reached 65,647 but the actual number was estimated to be 1,100,000. The HIV seroprevalence was found to be between 13-14% in urban areas and 6-7% in rural areas (3).

A study done on Nairobi prostitutes, between 1981-1985 showed a rise of HIV seroprevalence among the study population from

4% in 1981 to 61% in 1985 (4). While a 1996 report showed a prevalence of 80% among prostitutes in Nairobi (3). At the Kenyatta National Hospital (KNH) HIV seroprevalence was found to be 19% in patients admitted to the acute adult medical wards (5,6). Preliminary results from a similar study done recently in the medical wards as well showed a seroprevalence of HIV of about 40% (Dr. Gilly Arthur personal communication).

Mode of transmission of HIV

HIV has three major modes of transmission: sexual, parenteral and perinatal. There is no evidence that supports transmission through food, water, vectors or casual contact. In Africa transmission is predominantly heterosexual and this explains the equal male to female ratio.

Aetiology of HIV/AIDS

Acquired immunodeficiency syndrome (AIDS) was first described in 1981 in USA in young homosexual men who had Kaposi's sarcoma and pneumocystis carinii pneumonia. The cause of HIV/AIDS was identified two years later and was found to be a virus belonging to the retroviruses group (7). HIV is an RNA virus in the lentivirus subfamily of retroviruses.

Immunopathogenic mechanism of HIV infection

Although the hall mark of infection with HIV is progressive depletion of $CD4^+$ T Cells, a broad array of defects in the immune function of a variety of cell types also occurs. The causes of severe depletion of $CD4^+$ T cells that occurs with the disease progression are still a subject of investigation. In the early stage of infection, total $CD4^+$ T cells drop, sometimes drastically. This is often associated with a viraemia and signs and symptoms of an acute viral syndrome. As the viraemia resolves, the $CD4^+$ T cells level may rise to near normal levels (8,9). Over the ensuing clinically latent period, $CD4^+$ T cells decline at rates that vary between individuals. A variety of mechanisms have been postulated to account for this $CD4^+$ T cells depletion as follows;

1. Direct infection with cytopathicity
2. Bystander killing
3. Inability to regenerate mature cells by the bone marrow and thymus
4. Autoimmunity
5. Apoptosis due to gp 120 cross-linking of $CD4^+$
6. Superantigen effects of HIV or opportunistic pathogens (10).

In addition to the depletion of $CD4^+$ T cells there is also functional impairment of these cells (11). Autologous mixed lymphocyte reaction, T cell colony formation, expression of

IL-2 receptors and production of IL-2 are abnormal in HIV-infected individuals. $CD8^+$ T cells are also affected by HIV infection, similar to $CD4^+$ T cells. Although $CD8^+$ number gets reduced with the onset of the disease but later rises gradually until it exceeds the normal number and remains high during the clinically asymptomatic period. This rise is postulated to be due to the homeostatic mechanism of T cell, in which $CD8^+$ T cells rise as $CD4^+$ T cells reduce in number. $CD8^+$ T cell function is also altered in HIV infection. Other immunological abnormalities include: functional abnormalities of the monocyte/macrophage system, pancytopenia and myelodysplasia with polymorphonuclear leukocytes dysfunction (11), B-cell abnormalities which lead to production of large amounts of antibodies including IgA, IgG, IgD and production of large numbers of cytokines with dendritic cell abnormalities (10).

Course of infection

Following primary infection, 50-90% of individuals develop an acute clinical syndrome within 2-6 weeks which is characterized by acute onset of fever, lethargy, malaise, myalgia, headaches, retro-orbital pain, photophobia, sore throat, lymphadenopathy and maculopapular rash (7). Some patients may also develop meningoencephalitis at this stage. A high level of viraemia is indicated by elevated plasma virus and p24 titer, while viral replication occurs in peripheral

mononuclear cells. After 4-6 weeks the symptoms subside and the level of antigenaemia decreases while viral replication continues in lymphoid organs. This is followed by a long period of latency which can be up to 10 years but in most patients is around 3 years (12,13). Although parameters of viral replication are hardly detectable in peripheral blood, the immune function progressively deteriorates and the most visible sign of this is the depletion of circulating $CD4^+$ T lymphocytes and the reversal of $CD4^+/CD8^+$ ratio (13,14). This depletion of $CD4^+$ lymphocytes results in generally defective immune function characterized by occurence of frequent opportunistic infections (15).

Opportunistic infections are particularly prevalent when the $CD4^+$ T lymphocytes fall below $250/mm^3$ (16). The deterioration of the $CD4^+$ T lymphocyte levels continues until the patient dies. In one study $CD4^+$ T cell counts from dying patients were found to average $10/mm^3$ (16). Apart from $CD4^+$ T lymphocyte counts other markers of disease progression include: ß2 microglobulin and neopterin levels which are cell surface proteins that tend to increase with disease progression. The P24 antigen titers, ESR, viral burden and the presence of codon 215 mutation, can also be markers for the progression of the disease (17).

Classification and staging of HIV infections (7)

Different systems for staging HIV-1 disease have been proposed e.g. the Walter Reed classification system, the Center for Disease Control (CDC) classification system and the WHO classification system. Patients with AIDS Related Complex (ARC) are included in group IV of the CDC classification system. Definitions for AIDS Related Complex (ARC) have been proposed but most of these require AIDS type abnormalities to be shown on laboratory tests. Such definitions may not be applicable in some African countries where laboratory facilities are often lacking. Patients with AIDS and AIDS Related Complex (ARC) have similar symptoms and signs but immunological defects are less severe in AIDS Related Complex. Signs and symptoms observed in AIDS Related Complex patients include; unintentional weight loss, malaise, fatigue, lethargy, anorexia, abdominal discomfort, diarrhoea, fever, night sweats, headache, amenorrhoea, papular pruritic rash, lymphadenopathy and splenomegally. These symptoms and signs are frequently intermittent and disappear spontaneously for certain periods. By definition AIDS Related Complex (ARC) patients do not have opportunistic infections or malignancies. AIDS is at the most severe end of the clinical spectrum of HIV infection. It is characterised by the presence of opportunistic infections and tumours as a result of profound cellular immunodeficiency.

The CDC classification system is valuable for epidemiological purposes, but it is less helpful for patient management since it does not put HIV related clinical manifestations in well defined groups according to prognosis. The Walter Reed classification system, on the other hand, relies on results of lymphocytes typing and skin testing, which cannot be performed in most African countries and are difficult to interpret. Ideally it would be useful to have a staging system for HIV infection that relies only on clinical symptoms and signs and on easily diagnosable HIV-related diseases. The WHO addressed these issues and a proposal for clinical staging of HIV infection was developed. This was done after a world wide cross-sectional study (including 26 clinical centers) in which clinical conditions were correlated with laboratory markers already known to reflect disease progression (particularly $CD4^+$ T lymphocytes counts). The HIV infection clinical markers were organised into the following four prognostic categories:

1. Asymptomatic/persistent generalised lymphadenopathy (PGL).
2. Early (mild) disease
3. Intermediate (moderate) disease
4. Late (severe) disease (basically equivalent to AIDS).

In addition to this categorization, the following performance scale was incorporated into the system:

1. Asymptomatic, normal activity

2. Symptomatic, normal activity
3. Bed ridden < 50% of the day
4. Bed ridden ≥ 50% of the day.

Adult patients confirmed to be HIV positive are clinically staged (1,2,3 or 4) on the basis of the clinical findings or performance score, which ever is higher (see appendix I).

Clinical manifestations

Symptoms and signs of HIV/AIDS can be caused by the virus itself or can result from opportunistic infections and malignancies. Different infections and malignancies can occur at the same time and in the same organ (14). The clinical features are diverse and these include asymptomatic HIV positive patients, patients with generalised persistent lymphadenopathy, patients with AIDS related complex, and finally patients with full blown AIDS and associated opportunistic infections. There are many differences between the clinical presentations and the types of opportunistic infections in different parts of the world.

The frequency of clinical manifestations of HIV/AIDS in Africa in adults are as shown in the following table (12).

TABLE 1 **Frequency of clinical manifestations of HIV/AIDS in Africa (12).**

Clinical presentations	Approximate frequency
Asthenia	90%
Weight loss	80-90%
Diarrhoea	60-70%
Fever	60-70%
Cough	40-60%
Dermatosis	30-40%
Lymphadenopathy	30-40%
Dementia	10%
Kaposi's sarcoma	5-10%

other opportunistic infections for which frequencies are not given in the table due to variation in diagnostic accuracies in different reports include; TB, candidiasis, herpes zoster, herpes simplex, cryptococcal meningitis, toxoplasmosis, cryptosporidosis, chancroid and lymphogranuloma venereum (12).

A study carried out by Bhatt (18), in 1988 at Kenyatta National Hospital in 280 AIDS patients the major presenting features of AIDS were found as follows; loss of weight (86%), fever (78%), cough (60%), diarrhoea (57%), oral thrush (50%) and lymphadenopathy (48%).

In another study done by Amayo (19) in 1987 at Kenyatta National Hospital in 50 AIDS patients, the commonest general signs and symptoms were as follows; unexplained weight loss (92%), fever (66%) and generalised lymph nodes enlargement (24%). About 56% of the patients had a haemoglobin of less than 10g/dl. The other common manifestations in the gastrointestinal system were oral thrush (66%), chronic diarrhoea (60%) and dysphagia in (50%). In the respiratory system, 46% of the patients had chronic cough and 50% had pleural effusion on chest x-ray. In the central nervous system, 36% of the cases had meningitis, and this accounted for 28% of all C.N.S. manifestations. About 10% of the patients had Kaposi's sarcoma. The commonest skin manifestation was maculopapular pruritic skin rash.

Organ specific manifestations of HIV/AIDS

Gastro-intestinal diseases

In the upper GIT, the commonest fungal infection and often part of the acute HIV syndrome is oral candidosis (20). It is also a common problem when the $CD4^+$ count falls. *Candida albicans* is the predominant species, but *C. Tropicalis, C. glabrata* and *C. krusei* occur occasionally. The common symptoms being a burning sensation in the mouth and a change in taste. Oral candidosis can be detected even in otherwise apparently healthy HIV-positive individuals with a point prevalence in such populations approaching 20%. As the $CD4^+$ count falls the prevalence increases. Other oral fungal diseases associated with HIV infection include; histoplasmosis, cryptococcosis, penicilliosis and geotrichosis. Viral diseases of the mouth in HIV infected patients are also fairly common. These include; Herpes simplex virus, Cytomegalovirus and the Human Papilloma Virus. Oral hairy leukoplakia which presents as a white patch, often corrugated or even hairy in appearance, typically on the lateral margin of the tongue, can also occur on the buccal mucosa, floor of the mouth and other parts of the oral mucosa. This disease is associated with Epstien-Barr Virus infection. It can occur at any stage of the HIV disease. The incidence is found to be 20% in asymptomatic HIV patients and the frequency increases with the decline of $CD4^+$ count (21). It

has been observed in only 0.4% of prostitutes in Nairobi, Kenya (22). Kaposi's sarcoma, non-Hodgkin's lymphoma, necrotising ulcerative periodontitis, linear gingival erythema, tuberculosis and mycobacterium avium complex are also known to occur in HIV patients (20,26).

In the lower gastrointestinal tract, diarrhoea is the major complaint in these patients. Diarrhoea lasting more than one month occurs in 40-80% of patients and is often associated with other gastrointestinal symptoms like nausea, vomiting, flatulence, and abdominal cramps (13). The causes of this diarrhoea are variable. Prospective studies in HIV infected individuals with "pathogen-negative diarrhoea" demonstrated p24 antigens in the small intestine and colon. HIV, RNA has been detected with increased TNF, IL-1 and IL-6 levels (23). These HIV patients with pathogen-free diarrhoea do have minor abnormalities of villus architecture. There is characteristically a mild villus atrophy associated with either crypt hypoplasia or hyperplasia. These minor abnormalities are unlikely to cause diarrhoea but there is a consistent increase in small intestinal permeability which in addition to the minor structural abnormalities may be caused by immunological changes produced by HIV infection of the lamina propria (24).

Enteric protozoal infection however is the commonest cause of

diarrhoea in HIV-seropositive persons and is associated with apoptosis, occasional crypt abscesses, and much more severe villus atrophy than that seen with HIV infection alone (24). Microsporidia are a frequent cause of diarrhoea occurring in 19.4% of AIDS patients and was found to be correlated with severe immunodeficiency ($CD4^+$ counts > $50/mm^3$) (24,25). Cryptosporidiosis is another common cause of diarrhoea occurring on average in about 19.6% of HIV patients (24). It is found to resolve spontaneously when $CD4^+$ T lymphocytes count is > $150/mm^3$. Other causes of diarrhoea in HIV infected patients include; Cytomegalovirus enteritis (20.1%), *Mycobacterium avium intracellulare* (9.3%), *Giardia lamblia* (4-9%), *Entamoeba histolytica* (2.6%), *Campylobacter* species (3.3%), *Salmonella* (2.1%), *Shigella* (1.9%), *Clostridium difficille* (1.8%), *Isospora belli* (1.5%) and enteric viruses (3.8%) (24).

Weight loss is a major contributor to death in HIV infected patients because colonization of the gut by protozoa and other opportunistic infections like Mycobacterium avium intracellulare and Cytomegalovirus prevent absorption of additional calories by the enteral route or through simple re-feeding (24). Other gastrointestinal complications include: pancreatitis, acalculus cholecystitis and cholangitis. Liver disease also occurs and is usuallly due to disseminated infections.

Pulmonary manifestations

The most frequent and serious pulmonary complication in people with HIV infection in Africa is Mycobacterium tuberculosis (TB) infection. In Rwanda, pulmonary TB was found in 80% of HIV positive patients (26), while in Uganda it was found in 66%, and in Kenya in 30%. A study done at the Infectious Diseases Hospital (IDH) in Nairobi, Kenya, TB prevalence was found to increase gradually with increasing HIV prevalence. The annual incidence of TB among HIV patients is 7.9%, while the case rate of TB in the 20-49 years age group was found to be 100/100,000 (27). In the USA and Spain the prevalence was found to be 1.9% and 3.1% respectively (28) while in Thailand it was found to be 52% (29). The mean $CD4^+$ count range was between 310-330/mm^3 in the USA and Spain (28,30). Accordingly, isoniazid prophylaxis is recommended when TB prevalence is > 10% and $CD4^+$ lymphocytes count is < 350/mm^3 (30). The clinical presentation of TB is not different in HIV seropositive and seronegative patients (26,31). Although HIV patients are more liable to have extrapulmonary TB.

The other major pulmonary complication is *Pneumocystis carinii* Pneumonia (PCP). Which fortunately seems to occur less frequently in Africa. No PCP was detected in two autopsy studies done in Uganda (32). In Zimbabwe is was however found in 22% of HIV infected patients who had pneumonia (33). It was also found in 24% of African patients treated in Europe

and in 37% of African origin patients in the USA (34). The chest radiograph in early P.C.P may be normal. The usual appearance is of bilateral perihilar interstitial infiltrates which may progress to diffuse confluent alveolar shadowing over a period of several days. In about 20% of cases the radiographic appearance is atypical; e.g. lobar consolidation, upper zone infiltrates mimicking tuberculosis, unilateral consolidation, and nodules and mediastinal lymphadenopathy. Primary prophylaxis to prevent a first episode of *P. Carinii* pneumonia is given to patients with $CD4^+$ count of less than $200/mm^3$ ($CD4^+$ to total lymphocyte count ratio of less than 1:5). Primary prophylaxis is also recommended in patients with any other AIDS defining diseases such as Kaposi's sarcoma irrespective of $CD4^+$ count.

Bacterial pneumonia occurs more frequently in HIV infected patients than in the general population and is especially common in HIV infected intravenous drug users. The spectrum of bacterial pathogens is similar to that of a community acquired pneumonia in the non-HIV infected population. *Streptococcus pneumoniae* and *H. Influenzae* are frequent causes. *Staphylococcus aureus* and gram negative organisms are seen in advanced disease. Chest radiographs are often atypical; in one series 47% resembled *pneumocystis carinii* pneumonia (34). There is a high rate of complications including intrapulmonary cavitations, abscess formation,

empyema and death. *Pseudomonas aerugenosa* infection in HIV-infected individuals usually present with septicaemia and acute pneumonia. It has a high mortality rate and is often associated with neutropenia or with the presence of an indwelling central venous catheter. A community acquired *P. aeroginosa* bronchopulmonary infection has been described in patients with advanced HIV disease and low $CD4^+$ counts (mean $25/mm^3$) (34).

Other infectious pulmonary complications of HIV infection include; *Mycobacterium avium intracellulare*, fungal pneumonia like *Cryptococcus neoformans*, *Aspergillus fumagatus* and *Histoplasma capsulatum*. Non infectious diseases include; Kaposi's sarcoma, lymphoma, non-specific interstitial pneumonitis and lymphoid interstitial pneumonitis (34).

In a recent study carried out in Nairobi by Gilks *et al* (35), invasive pneumococcal disease was found to be present in (17-18%) of HIV infected women. About 59% of these was due to pneumococcal pneumonia, 30% was due to sinusitis and 11% was due to occult bacteraemia. $CD4^+$ counts ranged between 302-$171/mm^3$ between the first and recurrent episodes (35).

Neurological manifestations

The nervous system is often damaged in the course of infection not only by disease processes that are secondary to immune dysfunction and its systemic manifestations but also by more fundamental effects of the retrovirus. The neurological complications of HIV infection are highly stage-specific. Disease incidence rates depend on where the individual is in the course of a systemic HIV infection. This stage specificity largely relates to the dominant influence of altered immune responses and especially to severe deficiency in cell mediated defences that characterise the late phase of systemic infection i.e AIDS. During the later stages of infection both major nervous system opportunistic infections and AIDS dementia complex develop. Likewise patients become most susceptible to the metabolic diseases that result from dysfunction of other organs and to the toxic complications of drugs prescribed to prevent or treat HIV infection and its complications. Earlier in the course of infection other neurological disorders can develop, some of which relate to autoimmune reactions. Virtually all compartments of the nervous system are vulnerable to HIV-related diseases. Based on these neuroanatomical localisation, the following classification of neurological complications of HIV infections has been proposed (36):

1. Meninges and other structures surrounding the central nervous system:
   i. Aseptic meningitis and symptomless HIV infection.
   ii. Cryptococcal meningitis
   iii. Tuberculous meningitis
   iv. HIV headache
2. Brain:
   (a) Focal;
   i. Cerebral toxoplasmosis
   ii. Progressive multifocal leukoencephalopathy
   iii. Primary central nervous system lymphoma.
   (b) Diffuse;
   i. Post infectious encephalomyelitis
   ii. AIDS dementia complex
   iii. Cytomegalovirus encephalitis
3. Spinal cord:
   i. Vascular myelopathy
4. Nerves and roots:
   i. Bacterial plexitis, focal neuropathy and polyneuropathy
   ii. Subacute and chronic demyelinating polyneuropathy
   iii. Mononeuritis multiplex, benign
   iv. Distal predominately sensory polyneuropathy
   v. Cytomegalovirus polyneuropathy

5. Muscle:
   i. Inflammatory myopathy
   ii. Non-inflammatory myopathy
   iii. Zidovudine myopathy

These neurological complications can present as follows:

1. Headache or meningitic symptoms and signs
2. Focal central nervous system symptoms or signs
3. Non-focal cerebral motor disfunction
4. Myopathy

Headache apart from being a presentation of meningitis or other central nervous system disfunction can be related to poorly understood condition sometimes referred to as "HIV headache". The focal central nervous system disorders usually are AIDS related diseases and include; cerebral toxoplasmosis, primary central nervous system lymphoma and progressive multifocal leucoencephalopathy (PML).

The non focal central nervous system diseases are of two groups. The first group comprises of disorders which cause impairment of alertness and these include toxic encephalopathies, microvascular diseases related to sepsis or disseminated intravascular coagulations, and widely disseminated microscopic infections (encephalitides), of which

cytomegalovirus infection is the most common. The second group comprises of disorders in which alertness is preserved despite cognitive decline and this include AIDS dementia complex and central nervous system HIV infection.

AIDS dementia complex has been referred to as HIV-1 associated cognitive/motor complex by the WHO. It is classified into 6 stages; from 0-4, stage 0 is normal, stage 0.5-1 is usually mild, patients usually have difficulties in concentration and mental agility and forgetfulness, motor disorder is subclinical. In more severe stages 2-4, the cognitive function declines with psycho-motor retardation and diffuse motor abnormalities with released reflexes e.g snout response. Motor impairment may progress to quadriparesis, and at this stage patients usually have vacuolar mylopathy which is noted histopathologically. In these severe cases, brain atrophy is universal with normal cerebrospinal fluid though the level of markers of immune activation is increased including ß2-microglobulin and neopterin. However, this is not pathognomonic since they accompany opportunistic infection. The AIDS dementia complex is found to be due to direct HIV infection of the brain, so the most important therapeutic measure is anti-retroviral therapy, which may only delay its onset or progression for sometime, but eventually the patient develops it at the last stage (36). Epidemiology of the different central nervous system manifestations differs in the

different parts of the world. This is because of the use of different assessment methods, and availability of diagnostic facilities. For instance, cryptococcal meningitis was found in 6-12% of the AIDS patients in Africa and toxoplasmosis in about 8% from an autopsy study done in Zaire, while in France prevalence of toxoplasmosis was found to be 38% with a mean level of $CD4^+$ count of less than $100/mm^3$ (37).

Cardiac Manifestations

The commonest cardiac problem in HIV patients is tuberculous pericardial effusion. In a study done in Tanzania (7) in 1990 on HIV positive patients it was found that 72% of the patients had a pericardial effusion. Congestive cardiomyopathy is also observed in people with HIV in developed countries (7).

Eye Manifestations (38,39)

Occular complications occur in 50-75% of adult AIDS patients. Patients present with a wide range of ophthalmological lesions. They can present with herpes zoster ophthalmicus, Kaposi's sarcoma and mollusam contagiosum in the eye lids. Non specific conjunctivitis occurs in 10% of the patients and dry eye syndrome is found in a similar proportion of patients. Conjunctival Kaposi's sarcoma affects only 1% of patients. Bacterial and fungal corneal ulcers are rare. *Herpes simplex* Keratitis can also occasionally occur.

The posterior segment of the eye can also be affected. Lesions of the retina and choroid include; Cytomegalovirus retinitis, acute retinal necrosis, toxoplasma retinochoroiditis, and syphilitic retinochoroiditis.

The most common retinal findings are cotton wool spots which occur in about 50% of patients and results from microvasculopathy. Intra-retinal haemorrhages are also found including Roth's spots. The organisms usually infecting the retina are; syphilis, toxoplasmosis, candida, varicella zoster, tuberculosis and herpes simplex. Cytomegalovirus retinitis is the most common retinal infection and tends to affect patients with $CD4^+$ counts of less than $100/mm^3$. It has been found to be more frequent in the USA than in Africa.

Skin manifestation (40,41,42,43)

All skin diseases can be manifested in HIV patients either with increased frequency or with increased severity. At the primary HIV infection 75% of patients develop skin lesions including maculoerythematous eruptions on the trunk, roseola - like or morbilliform eruption on the upper body and face, and papulosquamous eruptions of the palms and soles which resemble secondary syphilis.

Viral skin infections are common in HIV patients. Herpes simplex can cause painful chronic genital and oral ulcers which are difficult to treat. Systemic dissemination is not

uncommon. Herpes zoster can be multidermatomal or recurrent and systemic dissemination can also occur. Other viral infections include; *Human papilloma virus, molluscum contagiosum, cytomegalovirus, Epstein-Barr virus (EBV),* and *measles.*

Bacterial infections are also common and presents as cellulitis, furuncles, impetigo or abscesses. The organisms include; *Staphylococcus aureus, streptococci, Corynebacterium diptheriae* and mycobacterial infections. Parasitic skin infections can also occur and are commonlly caused by *Pneumocystis carinii,* strongloidosis, *Acanthamoeba, Demodex folliculorum.*

Skin malignancy is well documented in AIDS patients. The most common one being Kaposi's sarcoma of the epidermic type and is one of the AIDS defining diseases. Infectious agents have been proposed as possible causes of kaposi's sarcoma. The organism mostly encountered is the *human herpes virus type 8* (HHV8). Other malignancies include lymphomas and squamous cell carcinoma. Other Skin conditions which has been linked with HIV infection is pruritic papular dermatosis (xerosis generalisata). It is a severely pruritic condition which is also refractory to antihistamine therapy. Seborrhoeic dermatitis is also noted with increasing frequency in HIV patients (40-50%). Drug eruptions are common in these patients. The drug eruption can be mild causing an itchy

papular reaction or severe causing toxic epidermal necrolysis (TEN).

AIM AND OBJECTIVES

AIM.

The aim of this study was to determine the different clinical stages of HIV infected patients admitted to Kenyatta National Hospital medical wards and to establish their clinical presentation, haematological markers and some immunological markers.

SPECIFIC OBJECTIVES.

The specific objectives of this study were:-

1. Determination of the different clinical stages in HIV seropositive medical patients admitted to Kenyatta National Hospital using the WHO clinical criteria.

2. Determination of the haematological markers (Hb, WBCs, and platelets) in the different clinical stages of HIV positive patients.

3. Determination of $CD4^+$ T and $CD8^+$ T lymphocyte levels in HIV positive patients at the various clinical stages.

4. Comparison of the haematological markers and $CD4^+$ T, $CD8^+$ T lymphocytes in the different clinical stages.

STUDY JUSTIFICATION.

The HIV disease presents in different forms which may also vary from continent to continent. Although many studies have been carried out at Kenyatta National Hospital on HIV patients, none has looked at the different clinical stages. It was therefore felt that this study would be necessary to establish local data to aid the clinicians in patient management. The study could also answer the question of whether from clinical staging alone one can estimate the level of $CD4^+$, $CD8^+$ cells.

MATERIALS AND METHODS.

Study Design:

This was a hospital based cross-sectional descriptive study carried out at Kenyatta National Hospital on HIV infected patients in the medical wards 24 and 30.

Study population:

The study population consisted of all consecutive adult patients admitted to the medical wards 24 and 30 between January and June 1997, who consented to HIV screening and who tested positive on ELISA.

Inclusion criteria.

1. All consecutive adult HIV positive patients admitted to wards 24 and 30 during the study period.
2. Consent to HIV testing and to participation in the study.

Exclusion criteria.

1. HIV negative patients
2. Age less than 18 years
3. Non consent to HIV testing or participation in the study.

Data collection.

A full medical history and detailed medical examination was performed by the investigator on all the study subjects.

Unconscious patients were examined without medical history. The findings from the history and physical examinations were filled in a proforma (Appendix II). The clinical staging of HIV infection was determined according to WHO clinical criteria only (laboratory data was not used for staging). (Appendix I).

Laboratory investigations.:-

i. 5mls of blood in a heparinized bottle were taken from each patient for detection of HIV antibodies by a rapid Enzyme Immunosorbent Assay (ELISA) using the Biochem detect - HIV TM test kit (Biochem Immuno System Inc., Montreal, Quebec, Canada. H3m, 3A2) which has a sensitivity of 99.9% and a specificity of 98.9% (44).

Samples found positive by the above test were confirmed using a second ELISA (Recombigen^{R} HIV-1/HIV-2 EIA), (Cambridge, Biotech Limited, Gateway, Ireland) with a sensitivity of 98% and a specificity of 99% (45).

ii. From patients found HIV positive by both tests, another 2mls of blood were taken for full blood counts and CD4/CD8 counts. These were determined using a flowcytometer - FAC scan, (Becton Dickson immunocytometry systems, mountain view, California, 94039, USA) (46).

DATA MANAGEMENT AND STATISTICAL ANALYSIS:-

The data collected was entered into a computer system using the data entry module of the statistical software call SPSS (statistical package for social sciences). Descriptive statistics such as frequency distribution, the mean and the standard deviation were used for most of the variables using the same software. One way analysis of variance (ANOVA) was used to test for significant differences in means of the continuous variables considered (e.g. HB, $CD4^+$ and $CD8^+$) betweem the four HIV stages. Harvard graphics package was used for data presentation.

STUDY LIMITATIONS

The difficulties and limitations which were encountered during the study:-

1. Facilities could not allow to diagnose the specific aetiologies of some diagnoses e.g. specific causes of diarrhoea and some of the C.N.S. diseases.

2. Some of the index diagnoses in the study were not included in the WHO clinical criteria for staging e.g. glomerulonephritis (possibly HIV nephropathy) and liver disease such as hepatoma. So in these cases perfomance scale was used for the staging but it was felt that it was not an accurate measure.

3. The HIV test results used to take 24 hours after the blood samples were delivered to the laboratory. This led to the loss of a number of patients from the study (64 patients), who had been discharged from the wards before the results were back.

RESULTS.

During the study period between January and June of 1997, 1071 patients were admitted to the medical wards 24 and 30 and of these 968 patients were screened for HIV infection. 103 were excluded on the bases of the various exclusion criteria.

Out of the 968 patients who were screened, 317 (32.7%) were found to be HIV positive. Only 253 (79.8%) of the HIV positive patients were included in this analysis as the rest of the patients had incomplete clinical data. Out of the 253 patients included in the study, 105 (41.5%) were males and 148 (58.8%) were females giving a male:female ratio of 1:1.4. The age distribution ranged from 18 to 71 years. The females had a mean age of 32.46± 9.8 years and the males had a mean age of 34.33 ± 9.1 years (figure 1 shows age and sex distribution).

AGE AND SEX DISTRIBUTION OF THE STUDY POPULATION
n = 253

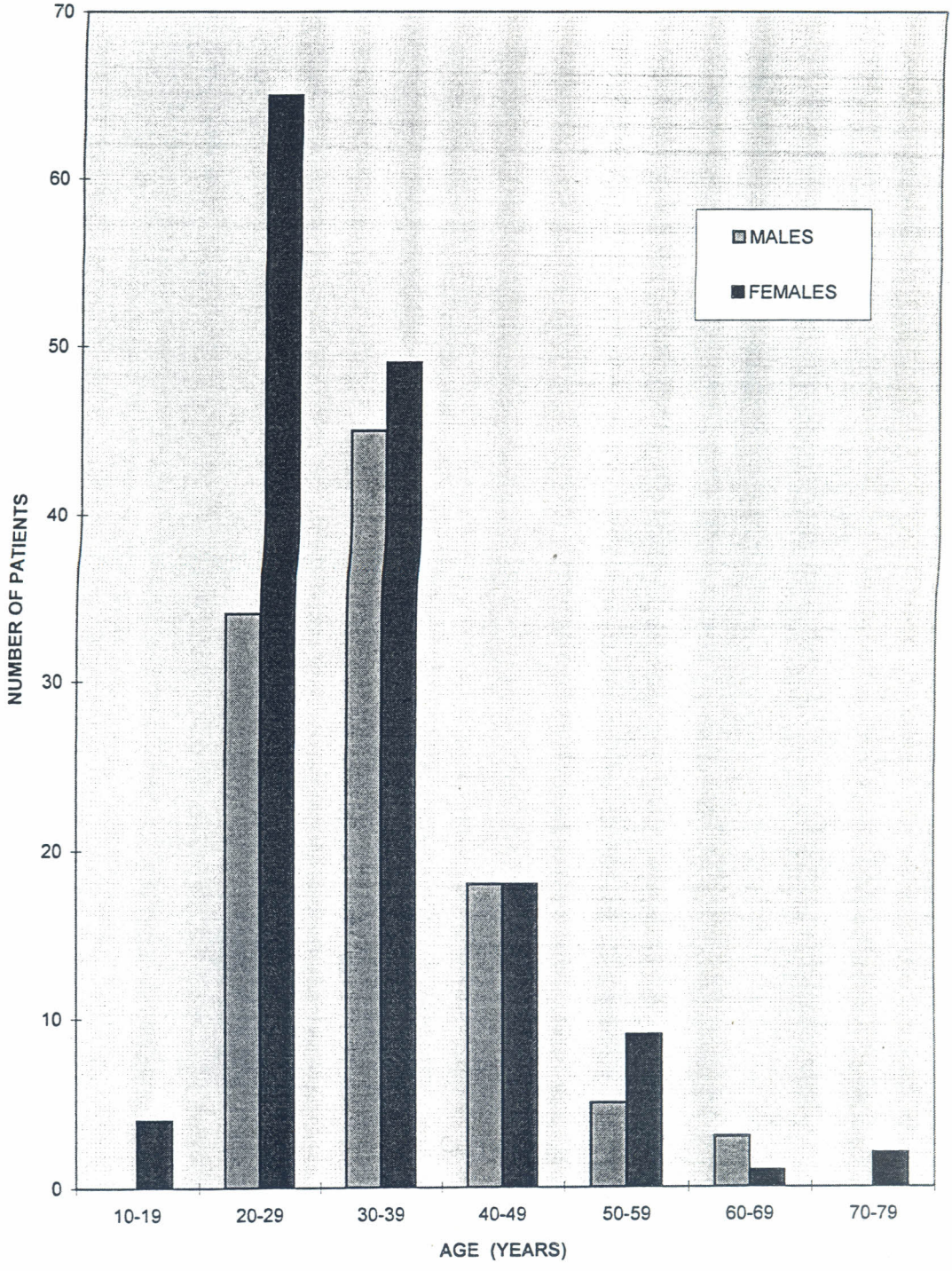

FIGURE 1

DISTRIBUTION OF CLINICAL STAGES OF HIV INFECTION IN THE STUDY POPULATION
n = 253

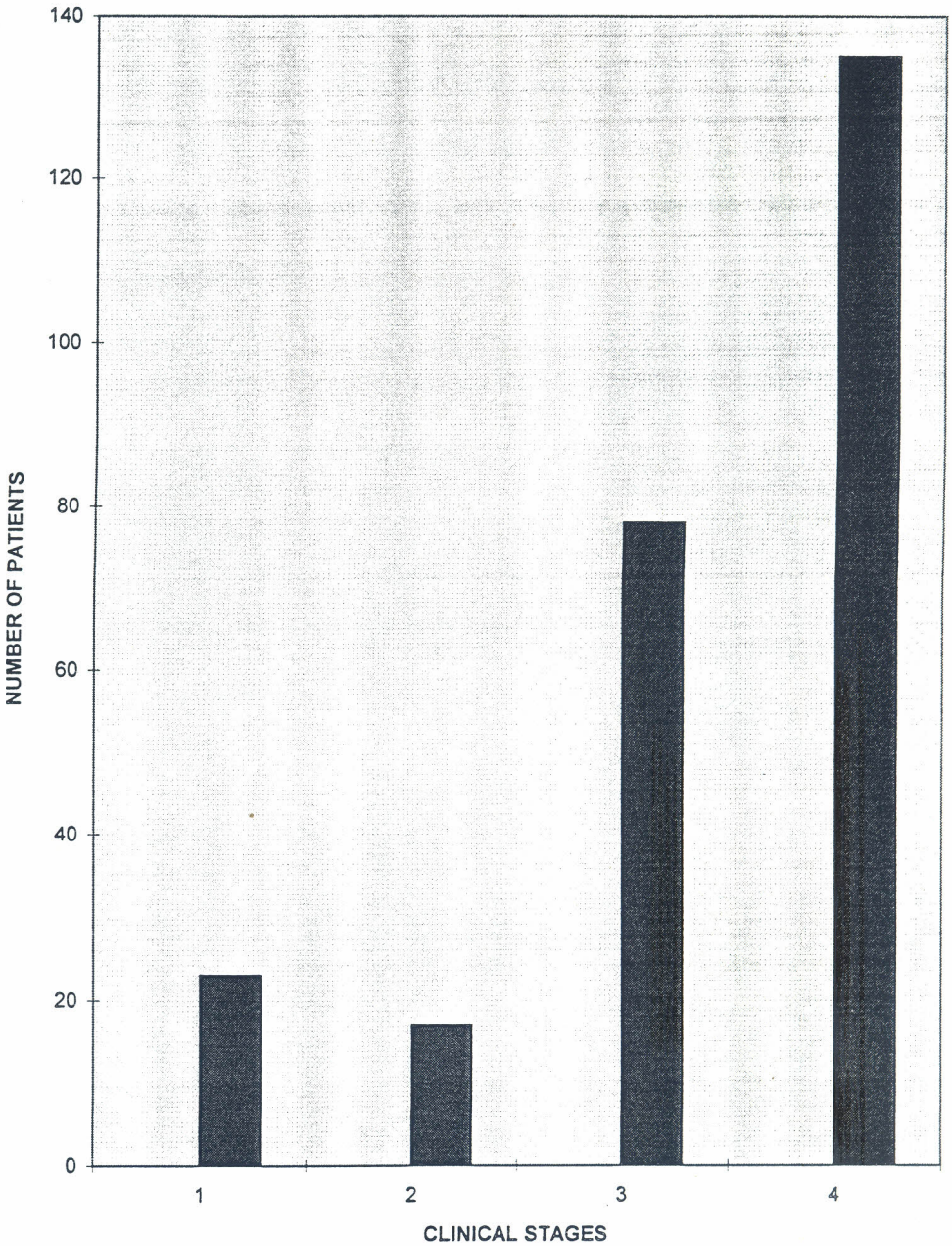

FIGURE 2

Clinical staging of HIV infection

The majority of the patients 135 (53.4%) were in stage 4 of the WHO clinical staging, which is equivalent to AIDS. In stage 3 there were 78 (30.9%) patients and this stage is also known as the AIDS related complex. Stage 1 and 2 had fewer patients 23 (9.1%) and 17 (6.7%) respectively. This is depicted in figure 2.

CLINICAL PRESENTATION:

TABLE 2: COMMON CLINICAL PRESENTATIONS OF HIV PATIENTS IN THIS STUDY.

Presentation	Percentage (%)
Fever	98
Headache	82.6
Cough	52.8
Weight loss	50
Diarrhoea	48
Oral thrush	33.2
Maculopapular rash	24.1
Kaposi's sarcoma	2.7

There was a wide spectrum of different HIV infection presentations in these patients. Most of the symptoms which were HIV related were the same as those used by the WHO for staging. HIV related diseases are not the same as opportunistic infections e.g. fever, weight loss, maculopapular rash, diarrhoea (pathogen free diarrhoea) and AIDS dementia complex are directly due to the effect of HIV and not to secondary infections. It is worth mentioning that fever was the commonest symptom (98%). The second commonest symptom was headache (82.6%) in the late stages of the disease (3,4). This was associated with mental disturbance in some of the patients (14.3%) which included changes in the mental state from mild confusion to deep coma. Signs of meningeal

irritation were noted in 17.1% in the study patients.

The third most common symptom was cough (52.8%) and 34.3% of the patients had chronic cough of more than one month. In these patients features of bilateral consolidation were noted in 34.1% of the patients and 6.7% had pleural effusion. Diarrhoea was a frequent symptom in the study population (48%). Actually 25% had chronic diarrhoea of more than one month. All those found with chronic diarrhoea were in stage 4. Oral thrush was the commonest sign (33.2%), followed by maculopapular skin rash (24.1%) and splenomegaly (13.8%). Others presented with Kaposi's sarcoma (2.7%) and some with pericardial effusion (2%).

CLINICAL DIAGNOSIS.

Most of the diagnoses were made clinically and with the help of simple investigations. Few diagnoses were based on bacteriological or pathological evidence. Wasting syndrome and AIDS dementia complex were diagnosed according to the WHO definition (appendix I).

The commonest index disease diagnosed in the study population was tuberculosis (50.6%). Pulmonary tuberculosis was found in (27.3%) of the patients, Miliary or disseminated tuberculosis in (17.8%), tuberculous meningitis (16.2%), tuberculous pleural effusion in 2% and tuberculous adenitis in 0.8% of the patients. Gastroenteritis (11.9%) included all the diarrhoeas whether chronic (83.3%) or acute (16.6%). Meningitis (14.6%) included acute pyogenic meningitis (18.9%) and chronic meningitis (81.1%). Most of the chronic meningitis cases were treated as tuberculous meningitis on clinical basis. About 10% of the patients with chronic meningitis were found to have cryptococcal meningitis as shown by a positive indian ink staining of the cerebrospinal fluid. AIDS dementia complex accounted for only 1.9% of the cases.

The other category of index diagnoses included;
malaria (2.3%), Hodgkin's lymphoma (1.6%), typhoid fever (1.6%), diabetes mellitus (0.8%), attempted suicide (0.8%), rheumatic heart disease (0.8%),

acute HIV illness (assumption) (0.4%), arthritis (0.4%), hypoglycaemia (alcohol induced) (0.4%), asthmatic attack (0.4%), hyperemesis gravidarum 0.4%, torticollis (0.4%), appendicitis (0.4%),
liver cirrhosis (0.4%), hepatocellular carcinoma (0.4%), ovarian mass (0.4%), intervetebral disc prolapse (0.4%) and renal failure (0.4%).

HAEMATOLOGICAL AND IMMUNOLOGICAL PARAMETERS:

TABLE 3 HAEMATOLOGICAL AND IMMUNOLOGICAL PARAMETERS IN THE DIFFERENT CLINICAL STAGES.

Parameter/Stage	I	II	III	IV	P VALUE
Mean Hb gm/dl (Normal=12-18)	10.8	10.6	9.2	8.6	0.009
Mean total WBC/mm^3 Normal=4000-10000	6654	7044	7276	5666	0.013
Mean total platelets x $10^3/mm^3$ Normal=140-500	228	225	221	205	0.69
Mean CD4/mm^3 Normal=380-1080	342	319	193	77	<0.001
Mean CD8 Normal=370-1010	963	1114	721	613	<0.001
Mean CD4/CD8 ratio Normal=0.6-1.6	0.51	0.33	0.28	0.11	<0.001
Mean total neutrophils Normal=2-7.9x10^9/L	4449	4278	4732	3519	0.014
Mean total lymphocytes Normal=1.5-4x10^9/L	1424	1459	1384	928	0.001

Most of the haematological parameters were found to be generally low. A high proportion 158 (62.5%) of the patients had a haemoglobin level below 10gm/dl and the haemoglobin levels declined significantly with the progression of the disease (P = 0.009). The total white blood cell count although varied widely between the stages but still showed a

trend of falling with progression of stages (P = 0.013).

The total lymphocyte counts ranged from 928-1459 showing a significant declining trend with the progression of the disease (P = 0.001). The mean neutrophil counts declined also with the progression of the disease (P = 0.014). The mean $CD8^+$ T lymphocyte counts were also found to be low but the levels showed a trend of an initial rise and then fall towards the later stages of the infection. A high proportion 217 (85.8%) of the patients had a $CD4^+$ T lymphocyte count of less than 380 cell/mm^3 which is the lowest normal value for the local population. It also showed a clear declining pattern with the progression of the disease (P < 0.001).

The mean $CD4^+/CD8^+$ ratio was lower than the normal value in all the stages and also declined progressively with the disease. About 71 (28.1%) of the patients had a platelet count of less than 140000/mm^3. Although the mean platelet count in all the stages was within normal it did not show a significant relationship to the stage progression (P = 0.69).

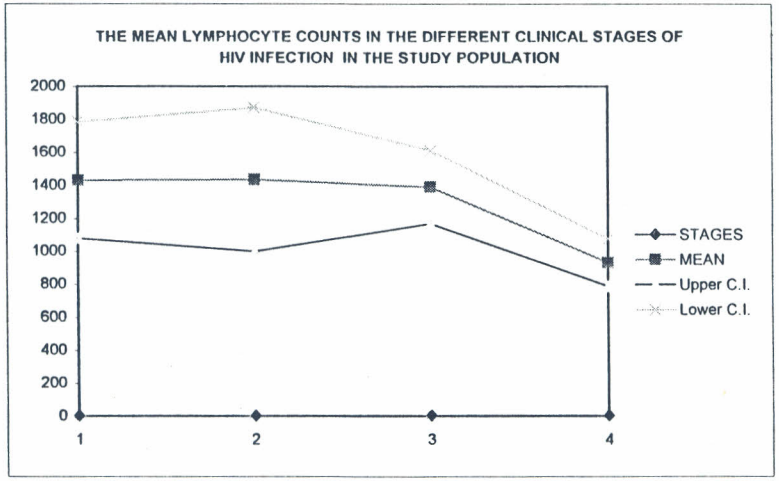

FIGURE 3 - A

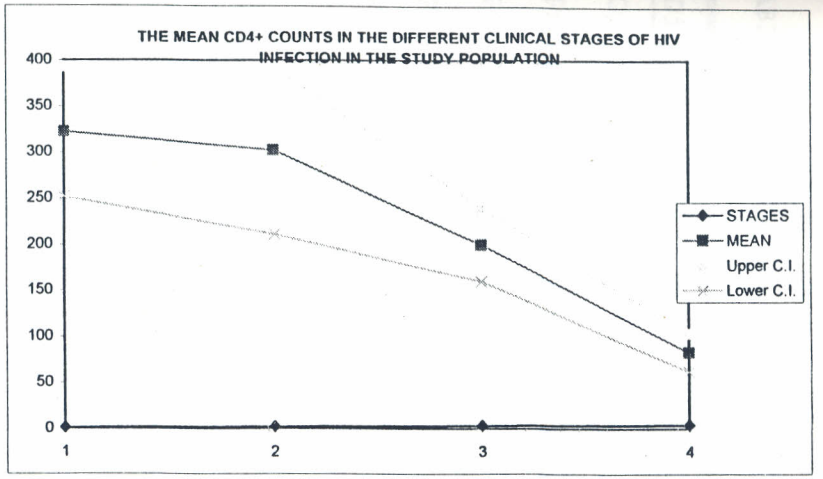

FIGURE 3 - B

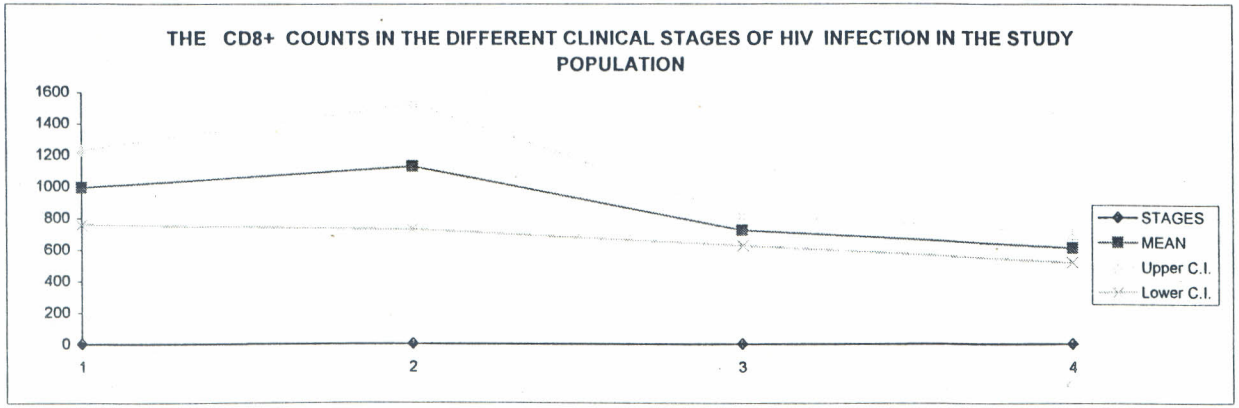

FIGURE 3 - C

FIGURES 3 - A, B, C : COMPARISON OF CD 4+, CD 8+, AND THE TOTAL LYMPHOCYTE COUNTS IN THE DIFFERENT CLINICAL STAGES OF HIV INFECTION IN THE STUDY POPULATION.

TABLE 4 CD4/CD8 BY INDEX DIAGNOSIS.

Diagnosis	Mean CD4 (±SD)	Mean CD8 (±SD)
G/E	230 (±177)	982 (±701)
Pneumonia	177 (±151)	890 (±366)
Pyogenic meningitis	176 (±163)	805 (±397)
PTB	141 (±154)	624.5 (±445)
TB. meningitis	122 (±151)	707 (±483)
Miliary TB	65 (±132)	588 (±615)
Cryptococcal meningitis	23 (±40)	218 (±122)

This table depicted the mean $CD4^+/CD8^+$ lymphocyte levels in the different index diagnoses. It is obvious that $CD4^+/CD8^+$ counts are considerably lower than the normal range. The mean $CD4^+/CD8^+$ also varied between diseases. Patients with cryptococcal meningitis recorded the lowest average $CD4^+/CD8^+$ counts. Patients with G/E on the other hand reported the highest average $CD4^+/CD8^+$ counts.

Normal CD4=380-1080/mm^3, normal CD8=370-1010/mm^3

DISCUSSION.

In this study the male to female ratio was found to be (1:1.4). This is in concurrence with previous studies showing that in Africa, HIV transmission is predominatnly heterosexual (4,7,18).

HIV infection was common in the young age group (mean age 32.4-34.3), which is the most sexually active group. This was also similar to observations in other studies done in Nairobi (4), Zaire and Zambia (54,55).

Clinical stages.

The majority of patients in this study were found to be in stage 4 of the disease which is equivalent to AIDS. This may be due to the fact that at this stage the immune system is too weak to protect the patient against micro-organisms making the patient more vulnerable to different infections which require hospitalisation and long hospital stay. The majority of patients in stage 1 and stage 2 are possibly managed as out patient and those admitted usually have a shorter hospital stay and for minor conditions which explains the lower number of aptients in these two stages.

This is the first study designed to establish the clinical stages of HIV infection in patients admitted to Kenyatta National Hospital. Previous studies have concentrated on the

prevalence of AIDS among the various study populations. In other words, these previous studies were predominantly on patients in stage IV disease (53.4%) in the current study. Other studies have indicated that of the 22.6 million who are HIV positive world wide, 37.1% had developed AIDS (1). In 1996, it was estimated that in Kenya out of the total number infected with HIV only 15.3% had developed AIDS (3). The difference in the number of patients who developed AIDS in the current study and the previous estimate might be due to the fact that the current study is hospital based.

Clinical presentations.

Patients in stage 1 and 2 presented with conditions possibly unrelated to HIV. Although some of the symptoms were similar to those in stage 3 and 4, the final diagnoses were different. Patients in stage 1,2 presented with symptoms such as fever, cough or diarrhoea but these were of acute and mild nature. Other presentations which are unrelated to HIV included; malaria, complications of diabetes mellitus and suicidal attempts.

Previous studies carried out to determine the HIV disease progression have shown that following infection, patients are usually asymptomatic and the period during which they remain so differs according to genetic factors, status of the immune system before the infection, route of infection and age at

which infection occurred (47). A small proportion (0.4%) of the patients in this study who had been managed for malaria with a negative blood film for malaria were assumed to have an acute HIV syndrome after they were tested positive for HIV, although it was not possible to do the P24 antigen, or viral culture to porve that. According to Jaffe H.W. *et al*, the prevalence of acute retroviral syndrome was low (48). In another study a 55% incidence of infectious mononucleosis like illness was reported (49). It should be noted that the symptoms and diagnoses for patients in the initial stages (1 and 2) in this study which were believed to be non-HIV related could still be associated with HIV infection although some findings such as diabetes mellitus or alcohol induced hypoglycaemia were unrelated. It is well known that a proportion of patients may develop minor constitutional symptoms months or years following a primary infection (50).

Most of the HIV related illnesses were found in stage 3 and 4. At these stages symptoms were of chronic nature and also of higher incidence in contrast to the first two stages. Stage 3 can be considered as a pre-AIDS stage where the findings included increased incidence of the constitutional symptoms of fever (21.3%) weight loss (26.6%) and cough (19%). These observation were in agreement with reports from previous workers (50).

Stage 4 disease was consistent with severe immune depletion and this was shown by the high incidence of AIDS defining diseases. A comparison of these clinical findings in this study with those in previous studies shows a marked concurrence (12,18,19). Another significant clinical observation was the appearance of oral hairy leukoplakia in (0.8%) of the patients. This was also reported to be (0.4%) in another study in Nairobi (35) and (3%) in a study done in Rwanda (26). There was a high incidence in stage 4 disease of bilateral consolidation mostly due to pulmonary TB. No cavitary lesions were noted in these patients. Abouga (31) in Abidjan, Corte de Voire, also had a similar observation.

Diagnosis.

The major cause of morbidity in these patients was tuberculosis (50.6%). This was also observed by Nunn and Gathua in a study carried out in the Infectious Diseases Hospital (IDH) Nairobi, Kenya (26). The same had been noted in Thailand where co-infection with both HIV and TB increased from 1.5% in 1990 to 45.5% in 1994 (51).

Diarrhoea was a major problem whether acute or chronic, but the causes of diarrhoea were not established due to the lack of diagnostic facilities. Even in the best centres between 15-50% of HIV patients with diarrhoea have a normal stool evaluation. These patients are often considered to have AIDS

associated enteropathy. The aetiology of which is not fully understood (50).

Haematological and immunological parameters (table 2):-

The mean haemoglobin and platelet levels fell with the progression of the disease because anaemia and thrombocytopenia are known prominent features of HIV disease. The anaemia is initially mild worsening with progression of the disease and is usually normochromic normocytic in nature (52).

The total white cell count for patients in this study did not show any special trend although at stage 4 of the disease they were slightly lower than at the other stages. The total white blood cell count and neutrophils did not have any significant correlation to fever.

The CD4 lymphocyte counts were generally low in this study. Even the mean count in stage 1 disease was less than 380/mm^3. This value was lower than the lowest normal value in the local population. The $CD4^+$ counts fell significantly with disease progression. One patient who was in stage 1 disease by clinical criteria (had a suicidal attempt) had a $CD4^+$ count of 150/mm^3. Studies done in the local population found that the $CD4^+$ levels are generally low even in normal people who are not HIV positive (Dr. Anzala, personal communication).

The $CD8_+$ lymphocytes showed a trend similar to that of $CD4^+$ cells and were particularly low in stage 3 and 4 of the disease. This was in contrast to the view that $CD8^+$ levels rise with disease progression. It has however been noted by Mark M. Fiendberg (53) that during the last stages of the disease, the homeostatic mechanisms which initially leads to arise in $CD8^+$ count as a compensation for $CD4^+$ loss breaks down for unknown reasons and ultimately leads to a reduction in the total T cells number. The $CD4^+/CD8^+$ ratio nevertheless did show a decrease with the disease progression.

Although studies carried out elsewhere established the correlation between the occurrence of opportunistic infections and levels of $CD4^+$ cells, this was not possible during the current study due to the lack of diagnostic procedures to accurately establish the nature of these opportunistic infections. This was why the investigator could only correlate $CD4^+$ level with clinical manifestations (table 4). In this study, pulmonary tuberculosis was diagnosed at a mean $CD4^+$ level of $141/mm^3$, while in other studies the mean $CD4^+$ level ranged between $310\text{-}330/mm^3$ (29,30).

Diarrhoea occurred at a mean $CD4^+$ count of $230/mm^3$, but as mentioned before the exact cause was difficult to diagnose. Other studies showed that organisms causing diarrhoea were microsporidia (19.4%) at a $CD4^+$ level of less than $50mm^3$ and

cryptosporidiosis (19.6%) at a $CD4^+$ level of less than 150/mm^3 (23,24,25). This may suggest that our patients have diarrhoea due to other opportunistic infections which occur at higher $CD4^+$ levels.

Pneumonia was observed at a mean $CD4^+$ lymphocyte level of 177/mm^3. This was similar to a study done by Gilks *et al* in Nairobi (32) where $CD4^+$ counts in patients with pneumococcal disease including pneumonia ranged between 302-177/mm^3 between the first and recurrent episodes.

Pyogenic meningitis was diagnosed presumptively (organisms rarely isolated) at a mean $CD4^+$ level of 176/mm^3, while TB meningitis was found at a mean $CD4^+$ level of 122/mm^3, and miliary TB at a mean $CD4^+$ level of 65/mm^3. This shows the declining trend of $CD4^+$ levels with disease progression. Cryptococcal meningitis although not a common finding (1.2%) occurred at a very low mean $CD4^+$ level (mean 23/mm^3) whereas in other studies it was found at a $CD4^+$ cell level of < 100/mm^3 (34).

CONCLUSIONS.

1. In this study the highest number of patients were found to be in stage 4 disease followed by stage 3, stage 1 and finally stage 2.

2. The haematological markers (Hb, platelets) were found to be declining with disease progression, while the mean total WBCs did not have a specific pattern

3. $CD4^+$ lymphocytes levels were found to be generally low but were also declining with disease progression and so did the $CD4^+/CD8^+$ ratio. $CD8^+$ T lymphocyte count did not show a specific pattern.

4. There was a good correlation between $CD4^+/CD8^+$ counts and ratio and the clinical stages. Therefore when facilities do not exist one could safely assume that those in clinical stage 3/4 of the disease will show a CD4/CD8 ratio below 0.28 in the local situation.

RECOMMENDATIONS.

1. Longitudinal follow up studies of the $CD4^+$ lymphocyte level after treating the major opportunistic infections would be useful in establishing whether the level rises after treatment of these infections.

2. It would be interesting to study viral load in relation to disease progression within our population.

3. A detailed clinical study should be carried out to determine the causes of the different clinical presentations in HIV patients such as the causes of the diarrhoea or CNS diseases and to accurately determine the common pathogens in the local population.

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APPENDIX 1.

WHO STAGING SYSTEM FOR HIV INFECTION

Clinical finding	Laboratory findings					
	A		B		C	
	Lympho-cytes >2000	$CD4^+$ >500	Lympho-cytes 1000-2000	$CD4^+$ 200-500	Lympho-cytes <1000	$CD4^+$ <200
Stage 1: Asymptomatic PGL .Performance scale 1: .Asymptomatic, normal activity	1A		1B		1C	
Stage 2: Early(mild) disease. .Weight loss <10% of body weight .Minor mucocutaneous .Manifestation, herpes zoster within the last 5 years .Recurrent upper respiratory infections, and/or .Performance scale2:Symptomatic normal activity	2A		2B		2C	
Stage 3: Intermediate(moderate) disease .Weight loss >10% of body weight .Unexplained diarrhoea > 1 month .Unexplained prolonged fever (intermittent or constant) .>1 month, oral candidiasis(thrush) .Oral hairy leukoplakia .Tuberculosis, pulmonary within the past year .Severe bacterial infections (e.g pneumonia) And/or .Performance scale 3, bed ridden <50% of day during last month	3A		3B		3C	

Clinical finding	Laboratory findings		
	A	B	C
	Lymphocyt CD4+ >2000 >500	Lymphocytes CD4+ 1000-2000 200-500	Lymphocy CD4+ <1000 <200
Stage 4: Late (severe) disease essentially AIDS: 1. HIV wasting syndrome (CDC definition)* 2. Pneumocystis carinii pneumonia 3. Toxoplasmosis of the brain 4. Cryptococcosis, extra pulmonary 5. Cryptosporidiosis with diarrhoea >1 month 6. CytomegaloVirus (CMV) disease of organs other than liver, spleen or lymph nodes 7. Herpes simplex virus infection mucocutaneous >1 month, or visceral any duration 8. Progressive multifocal leukoencephalopathy (PML) 9. Any disseminated endemic mycosis (e.g. histoplasmosis, candidiasis of the oesophagus, trachea, bronchi or lungs 10. A typical mycobacteriosis, disseminated 11. Non-typhoid salmonella, septicaemia 12. Tuberculosis, extrapulmonary 13. Lymphoma 14. Kaposi's sarcoma 15. HIV encephalopathy (CDC definition)** 16. And/or performance scale 4 Bed ridden > 50% of day during last month	4A	4B	4C

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* HIV wasting syndrome: Weight loss >10% of body weight, plus unexplained chronic diarrhoea (>1 month) or chronic weakness and unexplained prolonged fever (>1 month).

** HIV encephalopathy: Clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection that could explain the findings

APPENDIX 2.
QUESTIONNAIRE.

Title: Clinical and haematological profiles of HIV infected individuals admitted to Kenyatta National Hospital

Name.....
Age..... Sex.....
I.P. No.....

Presenting symptoms:

1. Fever.....< 1 month.....
   > 1 month.....

2. Loss of weight
   Yes ..... No.....

3. Cough.....< 1 month.....
   > 1 month.....

4. Haemoptysis Yes..... No.....

5. Dysphagia Yes..... No.....

6. Diarrhoea < 1 month.....
   > 1 month.....

7. Sores in the mouth:
   Yes..... No.....

8. Skin rash/lesions (specify).....

9. Itching: Yes..... No.....

10. Headache Yes..... No.....

11. Blurring of vision
    Yes..... No.....

12. Convulsions: Focal.....
    Generalized.....

13. Mental disturbance:
    Altered personality.....
    Altered consciousness.....

14. Neurological weakness: (specify).....

15. Sensory disturbances(specify).....

16. Others (specify).....

Past history

1. History of herpes zoster (within the last 5 years)
   Yes..... No.....

2. Pulmonary tuberculosis(during the last 1 year)
   Yes..... No.....

3. Recurrent bacterial infections(sepcify)

Signs

1. General:
   i Temperature.....
   ii. Respiratory rate.....
   iii. Pallor.....
   iv. Jaundice.....
   v. Dehydration.....
   vi. Lymphadenopathy: Yes.....No.....
   vii Oedema.....
   viii.Wasting.....

2. Respiratory:
   i. Consolidation: a. Bilateral.....
   b. Unilateral.....
   ii. Pleural effusion.....
   iii. Cavitation.....
   iv. Others (specify).....

3. Gastro-intestinal:
   i. Oral thrush.....
   ii. Hepatomegaly.....
   iii. Splenomegaly.....
   iv. Ascites.....
   v. Others(sepcify).....

4. Central nervous systems:
   i. Dementia.....
   ii. Loss of consciousness.....
   iii. Meningeal irritation.....
   iv. Focal neurological deficit:
   a. Hemipariesis.....
   b. Para pariesis.....
   c. Cranial nerves palsy.....
   d. Sensory loss(specify).....
   e. Others(specify).....

5. Skin:
   i. Maculo-papular rash.....
   ii. Herpes zoster scars.....
   iii. Ulcers (specify).....
   iv. Herpes simplex.....
   v. Kaposi's sarcoma.....
   vi. Fungal skin infection.....
   vii. Others(sepcify).....

6. Cardio vascular:
   i. Pericardial effusion.....
   ii. Congestive heart failure.....

7. Performance scale.....

8. Provisional diagnosis.....

9. Clinical stage.....

Investigation:

1. HB.....

2. W.B.C: Total.....
   Neutrophil.....
   Lymphocyte.....
   Basophils.....
   Monocytes.....
   Others(specify).....

3. Platelets.....

4. ESR.....

5. Peripheral blood film.....

6. $CD4^+$ T lymphocytes count.....

7. $CD4^+/CD8^+$ ratio.....