HIV ASSOCIATED KAPOSI'S SARCOMA: ETHNIC DIFFRENCES AMONG HIV ASSOSIATED KS PATIENTS AT KENYATTA NATIONAL HOSPITAL

BY

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A DISSERTATION SUBMITTED IN PART FULLFILMENT OF THE REQUIREMENT FOR THE AWARD OF MASTERS OF MEDICINE OF THE UNIVERSITY OF NAIROBI

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DECLARATION

THIS STUDY HAS BEEN CARRIED OUT IN PART FULFILMENT OF THE DEGREE OF MASTERS IN MEDICINE (MMED), INTERNAL MEDICINE. I CERTIFY THAT IT IS MY ORIGINAL WORK.

SIGNED……
DR. MUNGAI JOHN NJENGA, PRINCIPAL INVESTIGATOR

ABSTRACT

A study on HIV Associated Kaposi's sarcoma: Ethnic Differences among HIV associated KS patients at Kenyatta National Hospital

BACKGROUND

HIV associated Kaposi's sarcoma is common Malignancy that clinicians have to deal with frequently at KNH, both in the outpatient and inpatient set-up. The demographic background of patients with HIV associated KS attending KNH is not well documented. This study aimed to determine the patients' characteristics including age, sex, ethnic / racial background, education level as well as the districts of residence during the first 10 years of life, then 10-20 years and subsequent years.

METHODS

This was a prospective cross-sectional descriptive study carried out between May2004 and May 2005. The demographic data was obtained through face to face interviews by the principal investigator. Thorough physical examinations followed. For patients meeting the inclusion criteria, pre-test counselling for HIV testing and biopsy of KS lesion was done. 2mls of venous blood was drawn and forwarded for ELISA testing for HIV infections status using the Enzygnost kit. A biopsy or the suspected KS lesion was done under local anaesthesia for histological confirmation by a pathologist. Post-test counselling was then done before disclosing the test results to the patients, who were then referred for further specialized care.

RESULTS

90 patients were recruited for data analysis. Age information for one patient was not available while three did not give their education achievements. The males constituted 56% and female 44%. 41(46.1%) of the patients were aged 30-39 years, 28(31.5%) aged 40-49 years,13(14.6%) were aged 25-29 years while only 3(3.4%) were below 25 years. 4(4.5%) were over 50 years old. 23%,45% and 19% had achieved primary, secondary and college level education respectively. The kikuyu ethnic group formed 36.7% followed by the Luo (27.8%) Kamba (15.6%) and the Luhya (8.9%). The rest of the Kenya ethnic groups formed less than or equal to 3% each.. 4 districts (Nairobi 13%, Nyeri 11.1%, Siaya 10% and Machakos 6.7%) hosted the patients in their first 2 decades of life but thereafter majority of patients were found to reside in Nairobi district (56.7%).

CONCLUSION

There were no significant ethnic differences among patients with HIV associated KS at Kenyatta National Hospital

RECOMMEDATIONS

Future research should focus on factors contributing to the incidences of KS in both HIV positive and HIV negative Patients including any regional specific factors like prevalence of KSH

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ABBREVIATIONS

K.N.H	-	Kenyatta National Hospital
K.S.	-	Kaposi's Sarcoma
HIV	-	Human Immunodeficiency Virus
AIDS	-	Acquired Immune Deficiency Syndrome
USA	-	United States of America
GIT	-	Gastro-Intestinal Tract
KSHV	-	Kaposi's Sarcoma –associated Herpes Virus
HHVS	-	Human Herpes Virus - 8
MACS	-	Multicenter AIDS Cohort Study
NB	-	Note
CM	-	Centimetres
MLs	-	Millilitres
ELISA	-	Enzyme linked immunosorbent Assay
CDC	-	Centre for Disease Control
HBV	-	Hepatitis B Virus
HBC	-	Hepatitis C Virus
Kshs	-	Kenya Shillings

DEFINITION OF TERMS

An ethnic group or ethnicity define a group of people whose members identify with each other through a common heritage often consisting of common language, a common culture an ideology that stress common ancestry or endogamy [(1)].

PROBLEM STATEMENT

Kaposi's sarcoma is the most common malignancy associated with HIV infection, and it is known to have certain geographic, racial and ethnic distributions. This might imply that certain environmental and/or genetic factors come into play.

This study aims to determine the ethnic differences (if any) in the distribution of HIV associated K.S among patients attending KNH.

STUDY JUSTIFICATION

It is expected that the ethnic distribution of HIV-associated K.S. as seen in KNH would reflect the overall prevalence of HIV in Kenya. However, data from K.N.H cancer registry indicates that, in the year 2000, of the 994 histologically diagnosed cancers, 17 were Kaposi's sarcoma: of these 15 patients (88.2%) had names suggesting an ethnic origin of western Kenyan communities. This information is replicated in the 2002 data where 20(86.95%) out of 23 K.S. cases were of names suggesting western Kenyan Communities.

Similar results were obtained by Musibi (unpublished data) in a retrospective study of in-patients with K.S. at the Aga Khan Hospital, Nairobi, between Jan 1992 – Dec. 2000. Of the 39 patients analysed (32 males, 7 females) 17 were Luo, 7 Luhya, 3 Kisii, 3 Kalenjin, 4 Kamba and the rest were classified as others. This illustrates that 30(76.9%) out of 39 patients were from communities sharing similar/near similar geographic distribution.

This study aims to check if indeed there are ethnic differences in the distribution of HIV-associated K.S. among patients attending KNH: and hence form a basis upon which further research can be done as a follow-up.

LITERATURE REVIEW

K.S. is characterized by intense neovascularisation and spindle cells – the tumour cells of K.S. The spindle cells proliferate among characteristic slit-like spaces produced by the aberrant vascular structures. They have low mitotic index and are euploid. Fibroblasts, extravasated red cells and inflammatory cells are mixed in with the spindle cells [(2)].

Kaposi's Sarcoma is the most common tumour found in patients with HIV infection [(3)]. The original description of K.S. in 1872 was that of a rare vascular tumour characterized by multiple skin nodules appearing on the lower extremity of older men of Eastern European or Mediterranean descent. The tumour rarely involved visceral organs and generally had an indolent course. An endemic form of K.S was alter described in sub-Saharan Africa and involved younger men with cutaneous, lymphatic and visceral sites; and ad a more aggressive course. Other groups of patients likely to develop K.S are those receiving immunosuppressive therapy for organ transplants or other autoimmune diseases and of course those who have HIV/AIDS [(4)].

The recognition of Kaposi's sarcoma in gay men in USA in the early 1980's heralded the AIDS epidemic, and as many as 50% of gay individuals with AIDS developed Kaposi's sarcoma lesions [(5)]. The proportion of patients with Kaposi's sarcoma as initial manifestation of AID is approximately 11 %[(6)]. HIV –associated Kaposi's sarcoma has an aggressive clinical course, and frequently involves lymph nodes, G.I.T skin and other viscera.

Pathogenesis

A landmark in the pathogenesis of K.S was the identification by Chang and colleagues in 1994 of Kaposi's Sarcoma associated herpes virus (KSHV) or human herpes virus – 8 (HHV8) gene sequences in high Frequency in K.S tissue from patients with AIDS(7).

This virus has been identified in >90% of K.S biopsies from HIV infected and uninfected individuals but not in uninvolved tissues from the same patient or from normal controls (8-11). KSHV antigens have also been detected in blood from patients in the multicenter AIDS Cohort Study (MACs) a median of 33 to 46 months before the development of K.S. (12). The primary cell infected with KSHV believed to be a CD 19+ or CD22+ B-lymphocyte, which may serve as the carrier to transport KSHV to endothelial cells [(13)].

Epidemiology

Linked AIDS and Cancer registry data indicate that the proportion of black homosexual men who develop K.S is about ½ that of which homosexual men and there may be genetic susceptibility to K.S [14].

All forms of K.S are more common among men than women (M.F =3-4:1 in absence of Immunosuppression). However in HIV – infected individuals other than homosexuals, the K.S incidence only slightly favours men. In a retrospective study of 90 cases of K.S with particular emphasis on the familial occurrence, ethnic background and prevalence of other diseases all cases of K.S. seen at Memorial Sloan-Kettering Cancer Centre, New York, U.SA an ethnic predominance of K.S was substantiated, with most patients being immigrants from high incidence areas (54 of 77) and predominantly of Jewish and Italian heritage (52 Jewish and 17 Italian of 87) [15].

In the early 1980's the Centre for Disease Control (CDC) in Atlanta Georgia, USA observed a high frequency, 26 cases by July 1981, of K.S occurring in young homosexual men. Eight of these patients died within 24months of diagnosis. Thus was ushered in "Epidemic" K.S that is associated with AIDS [5]. HIV was assumed to be the cause of K.S for over six years until early 1990[16]. In January of that year Valerie Beral and her colleagues from CDC published a paper [17], in which they concluded "K.S. in persons with AIDS may be caused by an as yet unidentified infectious agent transmitted by sexual contact". This argument was based on the epidemiological spectrum of K.S in different AIDS risk groups and the fact that in homosexuals K.S may appear in the absence of HIV.

They reported several interesting and relevant findings concerning the incidence of K.S in the various AIDS risk groups. Forty percent of homosexual and bisexual men in 1985 and approximately 21% in 1998 had K.S. compared to approximately 1% of hemophilic AIDS patients. The next highest incidence 6% was from patients born in the Caribbean and African countries but living in the USA. There were 73 cases of K.S in transfusion recipients. K.S was most unusual in patients less than 15 years old, occurring in 1.6% of all children with AIDS (13 Cases). All but one of these USA born children with K.S were children of Haitian women, the other child was born in Central America and raised in the USA. They concluded that K.S was caused by an as yet an identified sexually transmitted infection.

Before the AIDS era, the two most often mentioned theories on aetiology of K.S were infectious and genetic theories. A very small number of cases with a familial distribution of

K.S were reported before the AIDS era but in none of these were sexual or mother – child relationships involved[18]. Infection with human herpes virus 8(HHV-8) has been consistently linked to Kaposi's sarcoma. In a test for HHV-8 antibodies in black South African patients with cancers, the anti-HHV-8 antibodies were more frequent among black than white blood donors; and among the 51 patients with K.S the standardized Seroprevalence of anti HHV-8 antibodies was 83% significantly higher than the prevalence among those without Kaposi's Sarcoma, 32% ($p<0.001$) [19]. The increased incidence of HIV associated K.S has been documented in several sub-Saharan African countries where the prevalence of HIV is high. In a study to determine the association between HIV-1 infection and cancer in the black population of Johannesburg and Soweto, South Africa, there was a strong association between HIV infection and K.S, with 27 of 33 cases being HIV seropositive, OR =61.8(95% CI 19.7-194.2) [20]. The existence of racial, ethnic and social economic factors in the transmission of HHV-8 in HIV infected patients is being established. HHV-8 the casual agent of K.S was associated with black race, Hispanic ethnic background, a lower level of education, as well as infection with syphilis, HIV, HBV or HCV, in the HIV epidemiology research study group [21]. The risk of HIV infection, and hence K.S, is closely associated with the behavioural risks among different communities. Some of the risks include homosexuality, intravenous drug use, heterosexuality as well as bisexuality. Homosexuality and or bisexuality are the major risks in the USA, where KS occurred in 21% of these risk groups.

In Italy where the intravenous drug users' account for about 70% of all AIDS cases registered, the analysis of risk factors showed that 53% of the KS cases were in homosexual men and 27% in intravenous drug users, while only 4% of KS cases were seen in heterosexuals [22]. This might not apply in the African situation where HIV transmission is predominantly heterosexual, and Kaposi's sarcoma makes up to 25 to 50 percent of soft-tissue sarcomas in children in eastern and southern Africa [23]. The causal agent for K.S, the HHV-8 shows different geographic infection rates that parallel the incidence of K.S. Lower rates occur in USA, many parts of Europe and Asia, and the highest rates in Central Africa (Uganda, Zambia) and South Africa. Its mode of transmission, predominantly sexual, in particular homosexuality, in developed countries, differs significantly from that in African countries, where infections even occur in childhood and heterosexual, maternal-infant and some other non-sexual person – person forms predominate [24].

The risk of Kaposi's sarcoma is linked to antibody status for HHV-8 but other factors do contribute. In a case-control study of Kaposi's sarcoma in HIV seronegative adults presenting at hospitals in Kampala, Uganda, Ziegler J.et al found that sex, tribal groups and household income were independent risk factors for K.S [(25)]. The seroprevalence of HHV-8 decreases with increasing levels of education and is lower in South African whites than in blacks, suggesting that factors associated with poverty may be important determinants of transmission, and hence of HIV associated K.S [(26)].

The geographical and racial distribution of K.S may be related to the regional prevalence of different strains of HHV-8. Phylogenic analysis of human herpesvirus-8 in South Africa, based on ORF 75 gene, identified a unique HHV-8 subgroup; termed N which accounts for 20% of the circulating strains [(27)] and studies to determine the degree of genetic divergence, distribution and pathogenic potential are ongoing. Similar trend has been noted in Zambia where a distinct strain of HHV-8 designated, Z, has been identified in HIV – negative childhood K.S that has shown markedly increased occurrence with HIV/AIDS epidemic. This strain of HHV-8 has been noted to have geographical variation, and may result in virulence differences and possibly has different transmission patterns [(28)].

Kaposi's sarcoma, one of the AIDS defining illnesses and it diagnosis contributes to the prognostic evaluation of HIV/AIDS patient. K.S in the lungs is most life threatening while involvement of the lymph nodes leads to a particularly poor prognosis as the disease rapidly spreads to other organs [(29-30)]. Early targeted diagnosis of K.S in HIV patients, taking the geographic and racial distribution into account may allow timely treatment, both of the tumour itself as well as use of highly active antiretroviral therapy which has been shown to result in complete resolution of K.S lesions in some cases [(31)]. HIV infection, and the resultant AIDS constitute significant proportion of the disease burden in Kenya. The adult HIV prevalence had increased to 13.5% by the year 2000; with urban areas prevalence estimated to be 17 -18% and 12-13% in rural areas. These estimated HIV prevalence ranged from 3% in North Eastern province, 10% in Coast, 11% in Rift valley, 12% in Western, 13% in Central, 16% for Nairobi and Eastern provinces to a high of 22% in Nyanza province.

Various HIV surveillance centres reported varying prevalence, with Busia, Chulaimbo, Kisumu, Mbale, Meru, Nakuru and Thika reporting prevalence of ≥20%. Nairobi, Nyeri, Tiwi, Mombasa, Kisii, Kakamega and Kitui reported prevalence of between 10- 19% while 3

centres, namely Kaplong, Mosoriot and Njambini reported prevalence of between 4-9% [32]. Thus it is to be expected that the ethnic distribution of HIV- associated K.S as seen in KNH would reflect the overall prevalence of HIV in Kenya. However data from KNH cancer registry indicates that, in the year 2000, of the 994 histologically diagnosed cancers, 17 were Kaposi's Sarcoma; of these 15 patients (88.2%) had names suggesting an ethnic origin of western Kenyan communities. This information is replicated in the 2002 data were 20 (86.95%) out of 23 K.S cases were of names suggesting western Kenyan communities.

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OBJECTIVES

The main Objective,

Describe the demographic details of patients with Human Immunodeficiency Virus associated Kaposi's Sarcoma attending Kenyatta National Hospital.

Specific Objectives

(i) Establish the human immunodeficiency virus infection status of histologically diagnosed Kaposi's sarcoma patients.

(ii) Determine the demographic details of the patients specifically the age, race/tribe, sex, education level and district of origin and residence in the first 10 years the next 10 years and thereafter.

STUDY DESIGN

This was a cross sectional descriptive study.

STUDY POPULATION

HIV-associated kaposi's sarcoma patients who were either admitted at Kenyatta National Hospital or attending hemato-oncology, dermatology and ENT clinics with diagnosis of K.S.

STUDY PERIOD

The study was carried out over a period of nine months between June 2004 and February 2005 both months inclusive.

INCLUSION CRITERIA

Patients with histological diagnosis of K.S. and who are infected by Human immunodeficiency virus.

EXCLUSION CRITERIA

1. Refusal to give consent for either HIV testing or for histological biopsy.
2. Patients using immunosuppressive medication
3. Patients of multi-ethnic/multi-racial parentage.

SAMPLE SELECTION

All consecutive patients fulfilling the inclusion criteria.

SAMPLE SIZE CALCULATION

This being a descriptive study, the sample size to meet the desired objective was calculated using the formula shown below.

$$n = \frac{(z_{1-\alpha/2})^2 P(1 - P)}{d^2}$$

Where
n = normal sample size
Z = normal standard deviation = 1.96
P = estimated risk of HIV associated Kaposi's sarcoma = 11%
d = desired accuracy = 0.05 (5%)

n, the minimum sample size = 77 patients

The minimum sample size was 77,

A sample size of 90 patients was taken to increase the power this being a descriptive study.

MATERIALS AND METHODS

. The principal Investigator liaised with the primary physicians in various hospital wards and clinics to identify patients with suspected K.S. lesions. Detailed explanation about the study and what it entails, including the invasive procedures and the use to which the information would be put to, was availed in a language which the patient understood – English or Kiswahili or both. An informed written consent was obtained, after which the patient's demographic data - names, age, sex, tribe/race, contact address/or residence and education level was entered into the proforma form. This information was obtained by interviewing the patients. All consecutive patients meeting inclusion criteria were enrolled. Information on prior diagnosis of KS and testing of HIV status was also obtained and recorded where evidence was available- Laboratory evidence of positive HIV infection and histology report positive for KS lesion. A thorough physical examination was done and any evidence of K.S. lesions recorded in the proforma form, i.e. site of the lesion(s) size of the largest lesion (cm) and the site of biopsy (the safest site). For patients who had no evidence of previous HIV testing with positive results, Pre-test counselling was done (appendix 5) after which 2 millilitres of venous blood was drawn into a plain well-labelled bottle for HIV antibody testing by ELISA (standard KNH procedure - Enzygnost kit for HIV I/II and antigens which also caters for the window period). A tissue biopsy was then taken under local anaesthesia,(for those with no previous histological evidence of KS). The specimen was immediately preserved in 10% formalin, clearly labelled and delivered to the pathologist for histological diagnosis. The standard KNH haematoxyline/eosin staining technique was used - (appendix 4).

The results of both the HIV test and tissue biopsy was availed to the patient after post-test counselling, and patient referred for further care to oncology clinic The results of HIV test and tissue biopsy was then entered into the proforma for Data analysis.

DATA ANALYSIS

The data collected was then captured in SPSS package, coded and analyzed. The analysis was done using the descriptive statistic and cross tabulations. The study finding ware then analyzed into percentages and frequencies upon which interpretations and conclusions were made. These were subsequently presentation in frequencies table, graphs and pie chart.

ETHICAL CONSIDERATIONS

I. Participation was on voluntary basis.
II. The information collected shall not be used for any other purpose than scientific/ medical and to write the thesis.
III. The study proceeded following ethical approval from the KNH ethics and research committee.
IV. Although the study involved invasive procedures, these were necessary for making a diagnosis, and optimal care was taken avoid unnecessary harm.
V. Patients benefited from the diagnosis of Kaposi's sarcoma and the standard treatment available at KNH was offered to them.

RESULTS

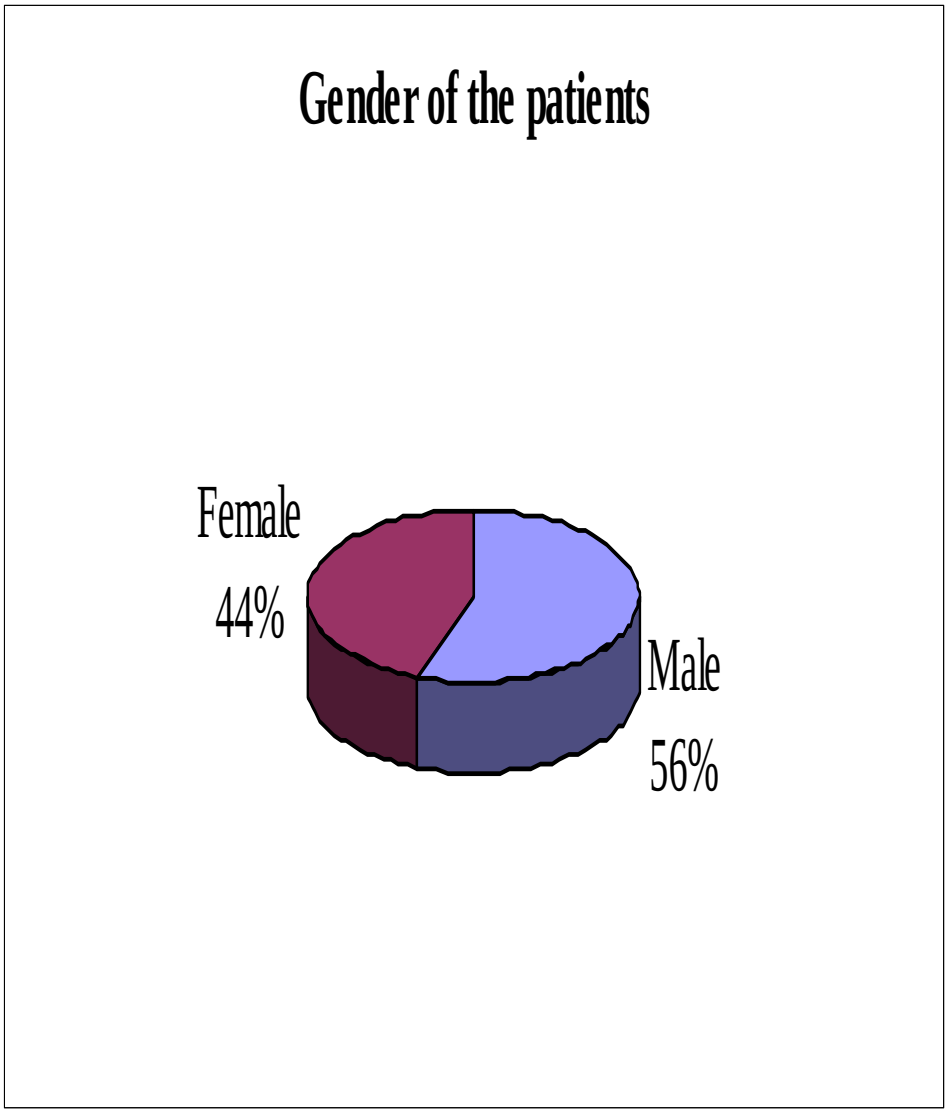
Data of 90 patients suffering from HIV –associated Kaposi's sarcoma who were either admitted at Kenyatta National Hospital or attending hemato-oncology, dermatology and ENT clinics with diagnosis of K.S was obtained using the laboratory test results and physical examinations. The questionnaire method of data collection which was administered was used to capture the details of each patient.

Demographic details of the respondents

Gender

Male patients were the majority at 56%, while the female patients were 44% as shown on the chart below.

Figure 1: Gender of the respondents



Age

Majority of the patients were aged between 30 -39 years as portrayed by 41.1%.
Followed by those who were in their 40s. Cumulatively, 64% were below 40 years of age and a minority (3.4% and 4.5%) was less than 25 years and more than 50 years old respectively. (Table 1 below). One elderly looking male patient was not aware of his actual age hence 89 patients were analysed for age .

Table 1: Age of the respondents

Years	**Frequency**	**Valid Percent**	**Cumulative Percent**
<25 years	3	3.4	3.4
25-29 years	13	14.6	18.0
30-39 years	41	46.1	64.0
40-49 years	28	31.5	95.5
> 50 years	4	4.5	100.0
Total	**89**	**100.0**	

Education level of the respondents

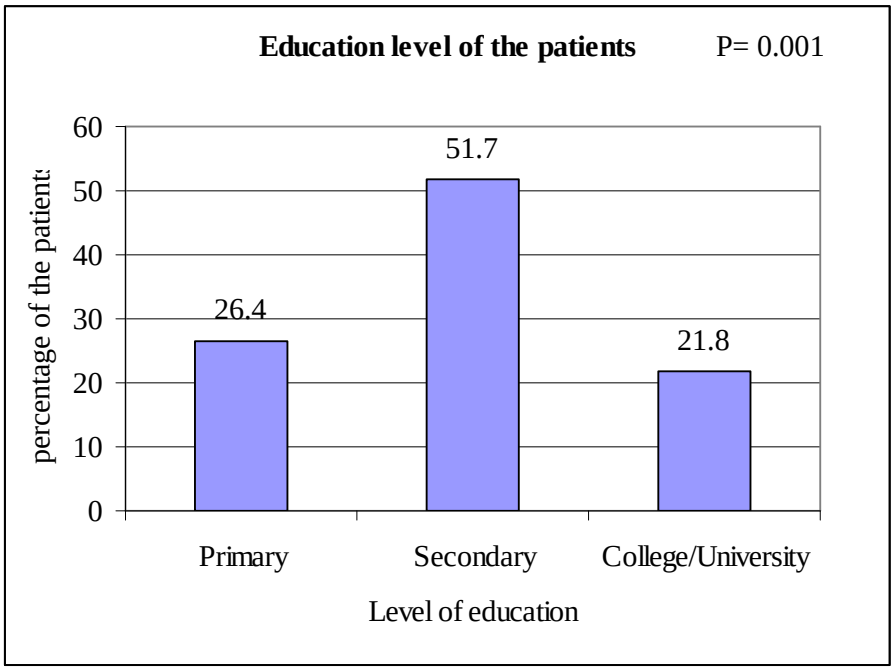
Majority (51.7%) of the patients had secondary level of education, followed by basic primary level (26.4%), while only a few as (21.8%) had managed to attain college/university education. Three of the respondents did not give the education level.

Table 2 and figure 2 illustrated the distribution of the patients in various education levels.

Table 2: Education level

Level	Frequency	Valid Percent
Primary	23	26.4
Secondary	45	51.7
College/University	19	21.8
Total	**87**	**100.0**

Figure 2: Education level of the patients



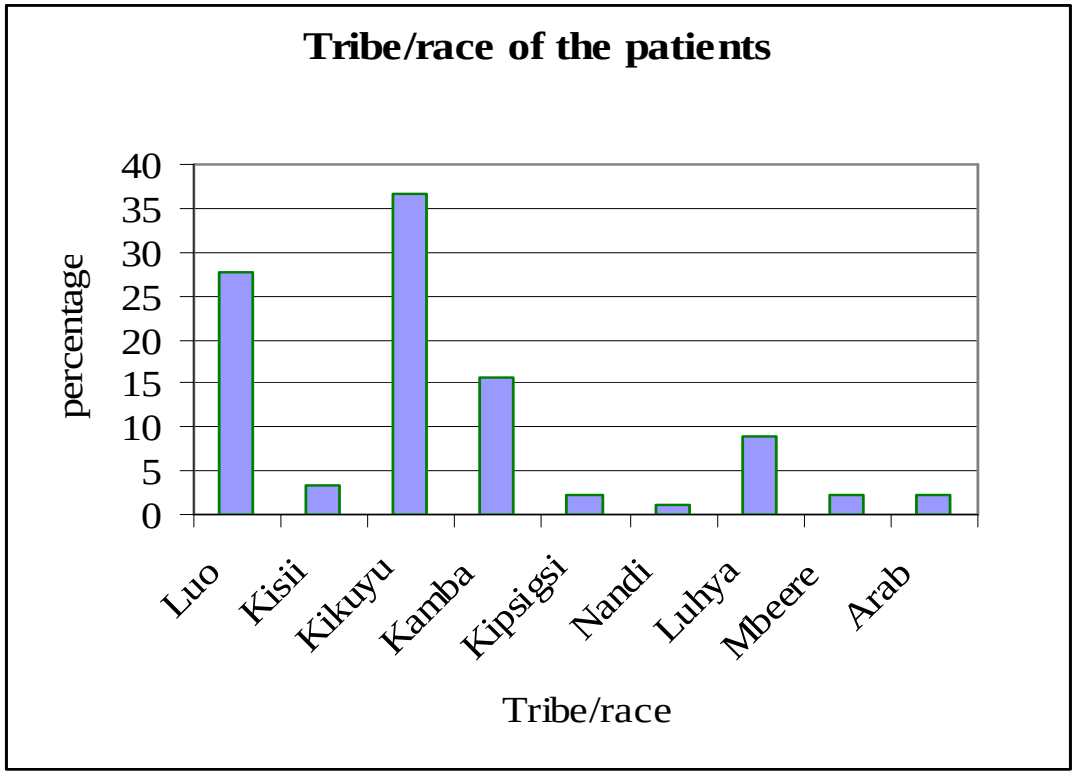
Ethnicity

The Kikuyu ethnic group had the highest number of patients (36.7%), followed by the Luo (27.8%), the Kamba (15.6%),the Luhya (8.9%) , the Kisii (3%), the Arabs (2%),the Kipsigis (2%), the Mbeere (2%), and the Nandi (1.1%).(shown in table 3 and fig 3 below).

Table 3: The ethnicity of the patient

Ethnic group	Frequency	Percent
Kikuyu	33	36.7
Luo	25	27.8
Kamba	14	15.6
Luhya	8	8.9
Kisii	3	3.3
Mbeere	2	2.2
Kipsigis	2	2.2
Arab	2	2.2
Nandi	1	1.1
Total	**90**	**100.0**

Figure 3: Ethnic distribution of HIV associated K.S in study subjects.



District of residence most of the time: 1st 10 years

About 13.3% of the patients were residents of Nairobi District in their first one year up to ten years of age, followed by 11.1% whose area of residence at that age was in Nyeri district and them rest of the patients lived in those district which are majority occupied by the members of their community/tribe. Table 6 illustrates the distribution of the respondents to the various districts from 1st decade of life.

Table 4: District of residence most of the time: 1st 10 years

District	Frequency	Percent
Nairobi	12	13.3
Nyeri	10	11.1
Siaya	9	10.0
Machakos	6	6.7
Kiambu	4	4.4
Kisumu	3	3.3
Narok	3	3.3
Makueni	3	3.3
Bondo	3	3.3
Vihiga	3	3.3
Murang'a	3	3.3
Migori	3	3.3
Busia	3	3.3
Kisii	2	2.2
Nakuru	2	2.2
Kilifi	2	2.2
Rachuonyo	2	2.2
Kirinyaga	2	2.2
Kakamega	2	2.2
Homabay	2	2.2
Kajiado	2	2.2
Kerugoya	1	1.1
Kitui	1	1.1
Nyandarua	1	1.1
Mombasa	1	1.1
Maragua	1	1.1
Mbeere	1	1.1
Laikipia	1	1.1
Baringo	1	1.1
Nandi	1	1.1
Total	**90**	**100.0**

As illustrated in table 4 above, 13% of the patients were resident of Nairobi districts in their first ten years of age followed by Nyeri 11.1%. The rest of the patients resided in those district that are traditionally occupied by members of their ethnic group.

District of residence most of the time 10-20 years

The district of residence most of the time in the 2nd decade of their Lives (14.4%) of patients resided in Nyeri district, followed by Siaya (10%), Nairobi (7.8%), Machakos (6.7%) and the other districts registered fewer numbers ranging from 1.1% to 3.3%. Table 5 illustrates the number of respondents per district in their 2nd decade of life.

District of residence most of the time: 2nd 10 years

Table 5: District of residence most of the time: 2nd 10 years

District	Frequency	Percent
Nyeri	13	14.4
Siaya	9	10.0
Nairobi	7	7.8
Machakos	6	6.7
Kiambu	4	4.4
Kisii	3	3.3
Narok	3	3.3
Makueni	3	3.3
Bondo	3	3.3
Vihiga	3	3.3
Murang'a	3	3.3
Migori	3	3.3
Busia	3	3.3
Mombasa	3	3.3
Kisumu	2	2.2
Nakuru	2	2.2
Kilifi	2	2.2
Rachuonyo	2	2.2
Kirinyaga	2	2.2
Kakamega	2	2.2
Homabay	2	2.2
Kajiado	2	2.2
Kerugoya	1	1.1
Kitui	1	1.1
Nyandarua	1	1.1
Maragua	1	1.1
Mbeere	1	1.1
Laikipia	1	1.1
Baringo	1	1.1
Nandi	1	1.1
Total	**90**	**100.0**

District of residence most of the time at the age of 20 years and above

Nairobi as a district accommodated majority or 56.7% of the sampled patients at the age of 20 years and above, followed by Nyeri district with 10% resident rate and other districts hosted between 1% and 4% of the sampled patients. Table 8 an fig 4 illustrate the distribution of the respondents, according to district of residence, from age 20yrs and above

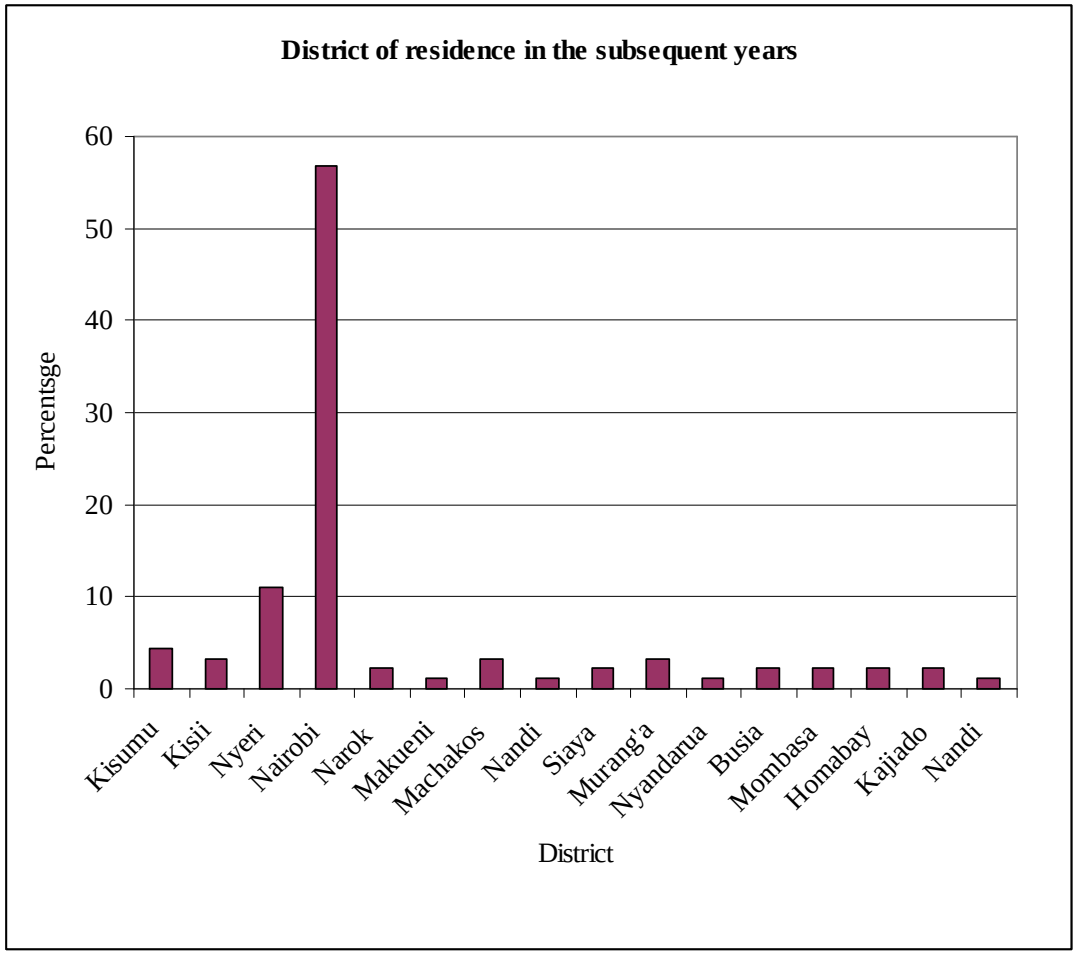
District of residence most of the time at the age of 20 years and above

56.7% of the study subject resided within Nairobi district at the age of 20 years and above, followed by Nyeri 10% and other district hosting between 1 and 4 %. (Table 6 and fig. 4 below).

Table 6: District of patient's residence in the subsequent years

District	Frequency	Percent
Nairobi	51	56.7
Nyeri	10	11.1
Kisumu	4	4.4
Kisii	3	3.3
Machakos	3	3.3
Murang'a	3	3.3
Narok	2	2.2
Siaya	2	2.2
Busia	2	2.2
Mombasa	2	2.2
Homabay	2	2.2
Kajiado	2	2.2
Makueni	1	1.1
Nandi	1	1.1
Nyandarua	1	1.1
Nandi	1	1.1
Total	**90**	**100.0**

Figure 4: District of patients' residence in the subsequent years: as from 20 years of age



DISCUSSION

Gender

This study showed that, male patients were the majority 56% compared to 44% females, M:F 1.3:1.

The Male: Female ratio for K.S in absence of HIV infection is 3-4:1 but in immunosuppression the sex ratio only slightly favour men. Therefore the sex ratio findings of male to female =1.3:1 is consistent with similar studies [(33)].

In a study of 604 individual with AIDS-K.S. who were antiretroviral naïve in Zimbabwe, Meditz, Amie et al [(34)], found the ratio of men to women as 3:1. the found no immunological or virologic differences between men and women. Both groups had similar CD4 positive lymphocytes count and peripheral blood KSHV loads even after age adjustment.

Its is not clearly known why HIV associated Kaposi's sarcoma is commoner in males and further study to evaluate gender specific factors such as female sex hormones in HIV associated K.S. patients may shed more light.

Age

K.S. is most unusual in patients less than 15 years old. Beral V., Peterman TA et al [(16)] found in a study of K.S among patients with AIDS found KS is only 1.6% of the patient age 15yrs and below. My finding of 3.4% in patients aged less than 25 years is therefore similar.

The age distribution of HIV patient with K.S , our study, is in keeping with HIV distribution in the Kenyan population. The National AIDS and STD control programs (NASCOP) - Kenya[(32)] reports more than 75% of AIDS cases occurring in adults aged 20-45yrs, with peak ages being 25-29yrs for females and 30-34yrs for males, and about 10% being children aged 5yrs and below.

Thus the peak age distribution of patients with HIV associated K.S. is similar to the age distribution of AIDS patients in Kenya (Kenya Ministry of Health, 2001) AIDS in Kenya.

Background, Projections, Impact, Interventions and Policy, 6th Ed; National AIDS and STD control).

In a study on the link between cancer and HIV diagnosis, Meredith Shiels found only small differences in the ages diagnosis of Kaposi's sarcoma even after controlling different in population structures [35]: likely due to HIV induced lose of immune control of infection with oncogenic viruses. The CD4+ cell count level, access to health care, social economic status or prevalence of KSHV do not adequately explain the early diagnosis of K.S. in HIV positive women (33years vs. 38 years) in study of HIV associated K.S by Meditz et al in Zimbabwe, [34] and further studies are recommended.

Ethnicity

According to Kenya fact book, 15th edition [32] in the 1989 national population census, the Kikuyu accounted for 20.78%, Luhya 14.38%, Luo 12.38% and Kamba 11.42% of national population. The ethnic data was not captured in the 1999 national census and also in the patients' admission data of Kenyatta National Hospital. The higher percentage of patients who are Kikuyu (36.7%) may be due to Kenyatta National Hospital being situated in Nairobi: with the majority of Kikuyu occupying the neighbouring districts (Nairobi and Central provinces).

In a study of possible contributions of genetic susceptibility to HIV associated K.S, Harry E. Prince et al, found significantly increased frequencies of HLA-Aw23 and HLA-Bw49 antigens in Caucasian AIDS-K.S group; as were HLA-DR5 and HLAbw44 antigens [36].

In the study of influence of HLA alleles on shedding of KS associated herpes virus in saliva in an African population Khaled R, alkharsah et al [37] found that 2 HLA-A alleles, A* 6801 and A*4301 as well as 1HLA- DRB1 allele group DRB1*04 were associated with shedding of KSHV in saliva. Could similar HLA allele be involved in transmission of KSHV and hence occurrence of KS among the various ethnic groups involved in this study at KNH? Future studies on genetic contribution to KS occurrence in Kenya are recommended.

Districts of residence

In the first 20 years of their life patients resided in their respective districts of birth e.g.: Nairobi 13% of the patients , Nyeri 11.1%, Siaya 10% and Machakos 6.7% this is the age bracket when sexual activity and possibly KSHV transmission through sexual activity is likely to be minimal. As the patients attained the age for college education or career, significant migration is noted e.g. Nairobi contributes 56.7% of the study patients from 13%, while Siaya and Machakos contributes only 2.2% and 3.3% respectively –as a result of out-migration. Nyeri district maintains a fairly stable figure of 11.1%-14.4%. One may hypothesize that migration to Nairobi played a significant role in the transmission of HIV and KSHV, except for Nyeri district. Increased sexual activity may also be a contributory factor as the patients attain sexual maturity. KSHV antigens have been detected in blood from patients a median of 33-46 months before the development of KS.[12] In the study of seroprevalence and transmission of Kaposi's sarcoma –associated herpes virus (KSHV/HHV8), among 215 Ugandan children, adolescents and young adults, Mayama, et.al[(38)] found that infections with KSHV occurred during early childhood and reached adult levels (approximately 50%) before the age of puberty. In their study KSHV antibodies were independently associated with hepatitis B infection. The investigators found that as opposed to sexual mode of transmission of KSHV in Northern Europe and U.S.A, transmission of KSHV in Uganda occurs largely before puberty and follows a horizontal mode. Whether the sexual or horizontal mode of KSHV transmission dominates among my study patients at KNH, or Kenya in general, would be an interesting study subject and may determine the best method for prevention of KSHV transmission, hence KS –whether childhood vaccination or HIV prevention measures in adolescents and young adults would be of any use.

CONCLUSION

There ware no significant ethnic differences among patients with HIV- associated K.S at Kenyatta National Hospital

RECOMMENDATIONS

Apart from demographics, future researches should also focus on factors contributing to incidences of Kaposi's sarcoma in both HIV positive and HIV negative patients at KNH.

Future researches should consider having information on the ethnic or racial population distribution at regional levels. This is because some regions are inhabited by many people of the same tribe hence the results will be biased

LIMITATION OF THE STUDY AND FUTURE RESEARCH GAPS

The study limited itself to demographics of K.S incidences in HIV positive patients only at KNH in Nairobi region and ignored other surrounding hospitals in different regions of the country. Information on the ethnic or racial population distribution at regional level (NAIROBI) and KNH was not available.

Since the study was limited to KNH in Nairobi region, a similar and a comprehensive study should be carried out throughout the country so as to come up with the demographics of HIV related Kaposi's sarcoma in the country which will help the researchers to draw qualitative inferences on ethnic or regional risks of K.S. in HIV patients.

Future research should consider having information on the ethnic or racial population distribution at regional levels. This is because some regions are inhabited by many people of the same tribe hence the results will be biased.

Apart from demographics, future research should also focus on factors contributing to incidences of Kaposi's sarcoma in both HIV positive and HIV negative patients at KNH.

APPENDIX 1 (A) ENGLISH VERSION

Study to determine the ethnic distribution of Kaposi's Sarcoma among HIV-infected patients in K.N.H.

Sample patient information sheet and consent explanation form

This statement is to inform you about a study we intend to do on Kaposi's Sarcoma in patients who are infected by AIDS virus. We want to find out how this cancer is distributed amongst various ethnic groups in our country being treated at K.N.H. and the factors that cause this, which can be influenced to prevent the development of K.S. in AIDS patients. There is some evidence of ethnic variation in distribution of this cancer among various communities.

In this study we will talk with you about testing you for AIDS infection (Voluntary Testing and Counselling, VCT). We will also do some minor operation on you called biopsy, which involves taking a small piece of your skin for laboratory examination to confirm whether it is cancerous. Proper care will be taken during any operation or withdrawal of blood for AIDS testing if you have not been tested already. This operation will be done under local anaesthesia and there will be some minor discomfort.

You will also be required to tell us your tribe and where you have lived before and where you are staying currently. Participation in this study is voluntary and there is no penalty for refusal to take part. You will still get the treatment even if you decline to take part and you are allowed to change your mind even after giving the consent. Participation may be beneficial to you because we will try to answer most of your questions concerning Kaposi's sarcoma and HIV. We shall advise you also offer you the standard treatment options and follow-up at the K.N.H. (if required). Your participation in this study may require you to attend the clinic more frequently than usual.

All information gathered is private and confidential and shall be used only for purposes of the study.

Read about this carefully and think about it. If you still feel that you should participate in the study, sign the consent form attached.

APPENDIX 1 (B) (KISWAHILI VERSION)

Maandishi yafuatayo yanakujulisha juu ya utafiti kuhusu ugonjwa wa saratani ya Kaposi's Sarcoma, katika wagonjwa walio na virusi vya ukimwi. Tunataka kujua vile ugonjwa huu wa Kaposi's Sarcoma ulivyo katika watu wa makabila mbali mbali wanaotibiwa katika hospitali kuu ya Kenyatta.

Katika utafiti huu, tutaongea na wewe juu ya upimaji wa virusi vya ukimwi (VCT) na pia kutakuwa na upasuaji mdogo, kama vile, kukata sehemu ndogo ya ngozi ili ipelekwe laboratory ipimwe kama iko na saratani. Pia tutapeleka damu kiasi kidogo ipimwe virusi vya ukimwi ukiwa ujawahi kupimwa mbeleni. Utaratibu ufaavyo utafuatwa katika upasuaji wowote utakavyofanywa.

Utaulizwa kabila lako na pahali ambapo umeishi kwa muda mrefu maishani mwako. Kujiandikisha katika utafiti huu ni kwa hiari yako mwenyewe na hakuna mtu yeyote atakayekunyima tiba yoyote au akuadhibu kwa namna yoyote ukikataa kujiandikisha. Unaweza kukataa kuendelea kuhusika katika utafiti huu wakati wowote, hata hivyo utapata matibabu yote unavyohitaji.

Unaweza kunufaika kutokana na utafiti huu kwa sababu tutajaribu kujibu maswali yako yote kuhusu saratani hii ya Kaposi's Sarcoma na virusi vya ukimwi. Pia utaambiwa kuhusu matibabu yafaayo na ukihitaji, kule unaweza kupata usaidizi.

Majibu yote yako itawekwa salama (yatakuwa ya siri) na haitatolewa kwa mtu mwingine yeyote, ila tu kutumiwa katika utafiti huu.

Soma maandishi haya yote kwa utaratibu. Ukikubali kujiandikisha katika utafiti huu, weka sahihi/jina katika karatasi la kujiandikisha (consent form) lifuatalo.

APPENDIX 2:

Consent form

I, _____ consent to participate in this study. The nature and purpose of this study have been fully explained to me by Dr. _____
I therefore give my informed consent.

Name _____
Date _____
Sign _____
Witness:
Sign/Names _____

Mimi _____, nemeelezwa kwa ukamilifu kuhusu utafiti huu, na nimekubali kwa hiari yangu. Nimemruhusu daktari _____ kufanya utafiti huu, na utabibu wowote unaohitajika.

Jina _____
Tarehe _____
Sahihi _____
Msahidi:
Sahihi/Jina _____
Tarehe _____

APPENDIX 3

Proforma Form

Name of Investigator _____

Name of patient _____ Consent given: Yes/No

IP/OP NO. _____ (Attach consent form)

Age _____

Sex _____

Education Level Primary ☐ Secondary ☐ ollege/University ☐
(Tick one)

Tribe/race (as said by the patient) _____

Address - Posting _____

District of origin/birth _____

District of residence most of the time: 1st 10 years _____

2nd 10 years _____

Subsequent years _____

Physical Examination

	K.S. Lesion	Size (~ in cm) of largest
	Yes/No	
Face + Neck/Neck		
Oral Cavity		
Upper limbs - Right		
Left		
Trunk		
Lower Limbs (including soles of feet): - Right		
- Left		
Site of biopsy:		
Date:		

HIV status (positive or negative) _____

Histological report: _____

APPENDIX 4

Haematoxylene and Eosin staining

1. Bring section down to water (Dewax with Xyline hydrate by descending order of alcohols to 50% of alcohol, rinse in water adequately - 2 changes).
2. Stain using haemotoxyline stain for 10-15 minutes, wash in tap water, blue using Scottish water.
3. Differentiate with 1% acid alcohol
4. Rinse in water
5. Counterstain with Eosin stain for 5 minutes. Rinse in water.
6. Dehydrate (using ascending order of alcohols).
7. De-alcoholize using xyline (2-3 changes).
8. Mount immediately using DPX.
9. Let dry, then examine.

APPENDIX 5

Pre-test counselling

The following information will be provided to the patient before testing for HIV infection

(i) What is HIV and what do we mean by word AIDS or UKIMWI (Kiswahili).

(ii) Why should one be tested for HIV infection?

(iii) What are the implications of testing positive or negative for HIV?

(iv) That the patient will not be denied appropriate medical care for declining to consent for HIV test.

APPENDIX 6

Budgeting

			Kshs.
1.	Protocol preparation + presentation	-	20,000.00
2.	Tissue biopsy + Histology = 90 pts @ 1000	-	90,000.00
3.	HIV testing-ELISA = 90 pts @ 450	-	40,500.00
4.	Stationery	-	10,000.00
5.	Result presentation + Write up	-	20,000.00
	Total Kshs.	-	**180,500.00**

Source:

1. Principal Investigator

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