PATTERN OF HEAD AND NECK MALIGNANT NEOPLASMS IN HIV-INFECTED PATIENTS MANAGED AT THE KENYATTA NATIONAL HOSPITAL

A dissertation submitted in part fulfillment of the requirements for the degree of Master of Dental Surgery in Oral & Maxillofacial Surgery by:

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DECLARATION

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TABLE OF CONTENTS

CHAPTER 1

CHAPTER 2

LIST OF FIGURES.

ABBREVIATIONS

KS	Kaposi's sarcoma
OKS	Oral Kaposi's sarcoma
NHL	Non-Hodgkin's lymphoma
SCC	Squamous cell carcinoma
HL	Hodgkin's lymphoma
BL	Burkitt's lymphoma
KNH	Kenyatta National Hospital
HPV	Human papilloma virus
UAT	Upper aerodigestive tract
WHO	World Health Organisation
CDC	Centers for Disease Control
SPSS	Statistical Package for Social Sciences

ABSTRACT

Background: **Infection with HIV is associated with profound immunosuppression and hence those afflicted face a greater risk of developing local or systemic malignant disease, the diagnosis of which is a form of surveillance for the acquired immunodeficiency syndrome (AIDS). The most commonly reported neoplasms of the head and neck region in HIV-infected patients include oral Kaposi's sarcoma/Kaposi's sarcoma (OKS/KS) and non-Hodgkin's lymphoma (NHL). There is also an increased risk of oral squamous cell carcinoma (SCC). Therfore, the pattern of occurrence of these diseases needs to be established.**

Objective: **To describe the pattern and spectrum of head and neck malignancy in HIV-infected patients.**

Setting: **Kenyatta National Hospital (KNH).**

Study Period: **From February to June 2006**

Subjects: **Both in-patients and out-patients on the medical and surgical wards; and clinics at the hospital.**

Methodology: **A descriptive cross-sectional study recruiting HIV-infected patients, above the age of 18 years with both non-neoplastic and neoplastic oral manifestations. Data were collected using a structured questionnaire and clinical examination and biopsy done for histopathology. It was analysed using the statistical package for social sciences (SPSS) soft ware version 12. Descriptive and inferential statistics were done using the T-test and χ^2-test.**

Results: **Of the 200 participants, 116 (58%) were males and the rest females with an age range of 18 to 61 years (mean=37yrs). Females were significantly younger (mean=33yrs) than males (mean 37=yrs) (T-test;2.57;P<0.05 [0.001]). The prevalence of neoplastic lesions in this study was 27%, among whom, 37 (68%) patients had OKS/KS**

followed by 9 (17%) with SCC, then 7 (13%) with NHL, and 1 (2%) with BL. There were more females than males presenting with lesions of OKS/KS and SCC, compared to NHL. The youngest patient presented with SCC at age 18yrs (mean=35.7), followed by KS at 23 yrs (mean=36.3) and NHL at 33yrs (mean=43.9). Most study participants 193 (96.5%) were in stage III/IV of the disease and the remaining 7 (3.5%) in stage II.

Conclusion: **The pattern determined in this study revealed that a younger age group of patients presented with neoplasms. In this study the most common malignant neoplasms were OKS/KS, SCC and NHL. Most of these malignant lesions became more apparent in the advanced stages of the HIV disease.**

Key Words: **HIV, Malignancy, Head and Neck region**

CHAPTER 1

1. INTRODUCTION AND LITERATURE REVIEW

The global AIDS epidemic shows no signs of abating since its first detailed clinical description in 1981(1). It is now estimated that by the end of 2004 there were about 40 million people living with the Human Immunodeficiency virus (HIV) infection in the world, among whom only 1.6 million live in high income countries, the remaining 95% of the infected individuals being resident in low income countries. At the beginning of the 21st century, HIV/AIDS was and remains the most common cause of early death in Africa and the fourth most common cause of such deaths globally (2). The global statistics make it clear that the burden remains greatest in Africa, although it is home to only 11 % of the world's population. In Africa, AIDS has single-handedly reversed gains in life expectancy and reductions in childhood mortality (3). One third of the estimated 40 million people living with HIV/AIDS are between the ages of 15-24 years. Nowhere is the HIV/AIDS crisis more profound than in sub-saharan Africa where 28.1 million people are living with HIV/AIDS. With new infections rising and the need to care for the increasing number of HIV/AIDS patients, most countries in Africa lack the economic capacity and infrastructure to handle the economic and health costs of the disease. Estimations show that heavily affected countries in sub-saharan Africa could lose more than 20% of their Growth Development Potential (GDP) by 2020. As the AIDS pandemic enters its 24th year, the number of people living with HIV infection continues to increase steadily (4).

It has been demonstrated that HIV infection and subsequent immunosuppression results in an increased risk of developing malignant disease. At the dawn of the third decade of the AIDS epidemic, it is apparent that the spectrum of neoplasia in the backdrop of underlying HIV infection and acquired immunodefiency is

highly dynamic (5). In 1996 it was seen that malignancies that were diagnosed more frequently in AIDS than in the general population included Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL), melanoma, anal carcinoma and adenocarcinoma of the liver (6).

Diverse diseases and conditions have been observed in the head and neck region since the AIDS epidemic. The number of infected patients with the HIV-infection is still increasing, especially in the heterosexual population. The presence of these diseases is an indication of the progression to AIDS and they serve as potential clinical markers of the HIV viral load. They are strongly associated with profound immunosuppression and hence are coupled with an increased propensity of developing neoplasms. Some of these manifestations appear, not only in the classification of the Centers for Disease Control (CDC), but are also used in planning for treatment and evaluating the overall prognosis. It was reported initially that 41% of patients had head and neck manifestations. As awareness has increased, however, recognition of these lesions has also increased, until it now seems that nearly 100% of patients with AIDS have both neoplastic and non-neoplastic lesions (7).

HIV-infected individuals had an overall two-fold increase in the risk of malignant disease (8). Oral malignancies associated with HIV infectiion may reflect local head and neck disease or represent systemic malignant disease. The presence of oral malignancies varies with risk factors for transmission of HIV, including unprotected sexual activity, contact with blood or blood products, and injection drug abuse; and differs geographically based on behaviour, viral cofactors, HIV therapy and genetic variation (9). Traditionally, the most common cancer in the head and neck region SCC, is overshadowed by KS and NHL in patients with HIV infection. As is the case of lung carcinoma, however, SCC has been seen in excess in HIV-infected populations (10). The prevalence tends to show variability depending upon the geographical location, ethnicity, gender, sexual practices;

and the immunological status of the patient that constitutes both the CD4 cell count and viral load of the patient.

Kaposi's Sarcoma (KS)/Oral Kaposi's sarcoma (OKS)

KS/OKS is the most prevalent AIDS-associated malignancy (11). In more than 20% of the patients with KS, the oral cavity is the initial site of presentation (12). KS is an endothelial cell multicentric malignant neoplasm with the oral cavity being the first site of the lesion. It frequently involves the palate, gingivae and tongue, but may involve any mucosal surface. It is interesting to note that OKS has been reported to be the first sign of KS in up to 70% of cases of disseminated disease as well as the most common sign of HIV infection (13). KS in an HIV-infected patient classifies into an AIDS stage IV (CDC classification of HIV-Related Diseases) (14). The prevalence of OKS is generally lower than the prevalence of KS affecting the skin and other organ sites. In 1997 it was found that oral lesions were the initial tumours in 20-25% of patients with AIDS-associated KS and may be found along with skin lesions in 45-50% of patients (15,16,17,18). By world statistics, reports of AIDS-associated OKS prevalence range from 0% to 12% in Africa, and from 0 to 38% in the US and in Europe (19,20,21). AIDS patients with OKS have a higher death rate than those with skin involvement; and OKS is identified as a prognostic factor for patients not on highly active anti- retroviral treatment (HAART) (22).

Non-Hodgkin's Lymphoma (NHL)

Lymphomas have long been some of the most devastating and complex opportunistic diseases of HIV infection. NHL is a malignancy of the lymphoid tissue which has been frequently observed with the emergence of the HIV pandemic. It is now a well-established complication of HIV disease but it was not until 1985 that the CDC included NHL as an AIDS-defining diagnosis (23). At present, NHL is after KS, the second most common malignancy affecting people with HIV infection in western countries (24). However, in Thailand NHL is the

most common oral tumour among HIV-infected individuals (25). The anatomic distribution of NHL is not altered in the presence of HIV infection with the head and neck region (63%) most often involved overall. However, within the head and neck region, extra-lymphatic disease is significantly more common in HIV-infected (59%) than non-infected patients (31%) (26). Primary oral NHLs were rare before the AIDS era, constituting only 4% to 5% of the extranodal NHLs. Of these tumours, approximately 20% to 35% originated in the palate and only 35% showed osseous involvement (27,28). NHL of the oral cavity accounts for 3% of all malignant lymphomas in patients with HIV infection (29). The oral cavity may be the first or only site of involvement presenting as a firm elastic often reddish or purplish swelling, with or without ulceration. NHL can occur anywhere on the oral mucosa, but the gingivae, palatal mucosa and fauces are sites of predilection (30). Oral ulceration is a common manifestation of NHL. It is suggested that if oral ulcers appear in a patient with HIV infection, NHL should be included in the differential diagnosis of the lesion (31).

Remarkably, HIV-infected individuals develop Hodgkin's disease (HD) in addition to NHL; and this AIDS-related HD is biologically and clinically distinct from the HD of the immunocompetent host (32,33,34). Burkitt's lymphoma (BL) comprises 30-40% of HIV-associated NHL. Their morphologic, clinical, cytogenetic and molecular genetic characteristics are similar to those of the sporadic BL unassociated with HIV infection (35). Two thirds of all AIDS-related NHL are diffuse large cell lymphomas (which include all immunoblastic lymphomas) while one third are small non-cleaved cell lymphomas (which include BL) (36,37,38). In general, patients with AIDS-associated BL are younger and have higher CD4 cell counts than those who develop diffuse large cell/immunoblastic NHL (39,40). Moreover BL, more often involves the bone marrow and lymph nodes while the diffuse large cell/immunoblastic tumours more frequently present with extranodal disease involving the gastrointestinal tract and include all the primary cerebral lymphomas (40,41).

Squamous Cell Carcinoma (SCC)

SCC has been reported in HIV-infected patients although epidemiological evidence documenting increased risk of this has not been convincing. Case reports appear in the literature, some involving younger people without other risk factors commonly associated with SCC. In addition to tobacco and alcohol use, the Human papilloma virus (HPV) infection, immunodeficiency; and possibly genetic changes represent risk factors for SCC in HIV infection (42). In general, this malignancy has been described in a younger age group and in individuals lacking the common risk factors associated with oral cancer and may be associated with a poorer overall survival. Flaitz et al. (1995) reported four patients in whom the tumour appeared as an ulcer or fungating mass or erythroplakia (43). Two cases were positive to human papilloma virus types 16, 18, 31, 33 and 35 (44). SCC of the upper aerodigestive tract (UAT) in HIV-infected individuals may be more aggressive than in those who are not HIV-infected. The majority of patients present with advanced disease. In one study the overall experience with 30 cases of SCC of the UAT in HIV-infected patients, stage III or IV cancer occurred in all but one patient at presentation. In contrast, the advanced stage occurred in only 49% of the non-infected population (45).

The purpose of this project was to study the pattern of malignant neoplasms associated with HIV-infected/AIDS patients presenting at the Kenyatta National Hospital (KNH), a major referral centre. The information obtained from this audit would be used to closely monitor such patients with a high index of suspicion and; therefore, reduce the increased morbidity and mortality associated with these malignancies in addition to the HIV disease. Furthermore, the data obtained could be used to compare with those from different regions to aid in the understanding of HIV infection.

2. RESEARCH PROBLEM

The pattern of head and neck malignancy is not clear in HIV-infected patients presenting at the Kenyatta National hospital posing a challenge in the management of the lesions and subsequently the disease.

3. JUSTIFICATION

This study provides a pattern of head and neck malignancies in HIV positive patients presenting at the KNH. A literature search has shown that few studies have been documented worldwide and hardly any in Kenya, correlating HIV with head and neck malignancy. Clinically, HIV-infected patients present with malignancy not only at an early age but also as an aggressive form of the disease which is inconsistent with the pattern of these lesions known to present in the non-HIV infected patients. This study illustrates the various types of malignancy, their behaviour including, the site, age of presentation and clinical aggressiveness. This information can be used to carry out a clinical staging of the HIV disease, which may act as a guide for the purposes of instituting both treatment for the HIV infection and the neoplasm in addition to the overall prognosis. The presence of these neoplasms may also serve as a guide to judging the immune status of the patient. The results of the study will increase the awareness of the relationship between HIV and head and neck malignancy. This will lead to an increased awareness among clinicians regarding head and neck malignancies in HIV-infected subjects, hence facilitating their screening when these lesions are detected.

4. OBJECTIVES

4.1 BROAD OBJECTIVE

To describe the pattern of occurrence of head and neck malignancy in HIV-infected patients at the KNH.

4.2 SPECIFIC OBJECTIVES

1. To describe the socio-demographic characteristics of HIV-infected patients
2. To determine the spectrum of malignancies in the head and neck area among HIV-infected patients
3. To clinically correlate the malignancy according to the WHO clinical staging of HIV presentation.

CHAPTER 2

5. MATERIAL AND METHODS

5.1 Study Area: Patients were recruited from all medical wards and general surgical wards, Dental outpatient clinics and Ear, Nose and Throat Clinics of the hospital within the study period.

5.2 Study population: This was defined as all HIV positive patients admitted at the hospital and those attending out-patient clinics.

5.3 Study Period: February 2006 to June 2006

5.4 Study design: This was a descriptive cross-sectional study conducted at the KNH using hospital based study subjects. KNH is the leading national teaching and referral hospital in the country.

5.5 Study Variables:

I Dependent variable

- Presence or absence of malignancy

II Independent variable:

- Alcohol and tobacco consumption
- History of viral infection including the viruses.

III Sociodemographic characteristics:

- Age
- Gender
- Occupation

5.6 Sample size: This was a descriptive cross-sectional study to determine the pattern of occurrence of head and neck malignancy among HIV-infected

patients. The sample size was calculated using the Fisher et al. (1998) formula for population studies:

$$n = z^2pq / d^2$$

Where n is the desired sample size, z is the standard normal deviation, p is the proportion of the target population estimated to have a particular malignancy. In this case p was estimated at 0.5 (since there is no available data on malignancy in HIV-infected patients), z = 1.64(one-tailed test), d = 0.05 and q = 0.6 (1-p), with a 95% confidence interval (CI) = 1.64.

$$n = 1.64^2 \times 0.5 \times 0.5 / 0.05^2 = 269 \text{ patients}$$

The desired sample size was therefore, 269. Two hundred and fifty patients were examined among whom 200 (74.4% of n) were recruited.

6. Patient Selection Criteria

6.1 Inclusion Criteria:

1. All HIV positive patients.
2. Patients aged 18 years and above.
3. Patients who gave consent voluntarily (Appendix I).

6.2 Exclusion Criteria:

1. Those patients who were HIV negative.
2. Those who declined to participate in the study.

7. Data Collection Procedure/Tools

7.1 Demographic details:

Demographic parameters such as gender, age, ethnicity, level of education and occupation were recorded in a specially structured questionnaire (Appendix II).

7.2 Clinical procedure:

HIV positive patients whose HIV status had been confirmed through laboratory examination (using the fourth generation Enzyme linked immunosorbent assay)

were recruited into the study. A general head and neck examination was performed and the presence of non-neoplastic lesions (candidiasis, aphthous ulceration) and /or neoplastic (KS, NHL, SCC) lesions were recorded. An incisional biopsy under local anaesthesia utilizing a strict aseptic technique was performed of all lesions suspected of having been malignant. There is a wide spectrum of malignancies in the head and neck region necessitating biopsy procedures for histopathological diagnosis. Clinical photographs were taken before biopsy. The biopsy was reviewed by the investigator with a senior histopathologist and 10% of the biopsies were submitted to a second independent pathologist as quality assurance. There were no discrepancies with the histopathological diagnosis. The clinical stage of each patient according to the WHO clinical stage of the HIV disease was recorded in the chart to correlate the malignancy with the stage of the disease (Appendix III). The histopathological diagnosis was communicated to the ward doctor with a copy for the file for further management of the affected patients.

8. Data Management:

Data analysis for this study has been executed according to the statistical package for social sciences (SPSS) soft ware version 12. Descriptive statistics were employed for categorical and continuous variables. Descriptive ones were for continuous variables and were measures of central tendency and dispersion. Those for categorical variables were those of frequency and proportional inferential statistics used to determine the associations. Chi-square tests were used to determine association between categorical variables. Statistical significance was accepted at 5% interval.

9. Ethical consideration:

Consent to conduct this study was sought from the Ethics, Research and Standards Committee of KNH and the University of Nairobi (Reference number KNH-ERC/01/3317). Strict ethical values of patient confidentiality were maintained by the use of codes for each patient instead of their names. An informed consent form was signed by each patient before their recruitment to declare their voluntary participation in the study.

10. Benefits of the study

One of the benefits of the study is partial fulfillment of the requirements for the degree of Master of Dental Surgery in Oral and Maxillofacial surgery. The histopathological diagnosis was communicated to the ward doctor with a copy for the file to enhance further management of the HIV-patients. The data collected will be used to aid in the appreciation of the effects of HIV infection and provide a better understanding of the relation between HIV and malignancy.

11. Limitations of the study

Accessibility to surgical armentarium in the wards was tedious, since at any one time only one sterile tray was available. The lighting was poor and performing a biopsy with using a torchlight was challenging.

CHAPTER 3

11. RESULTS

Out of the 250 patients examined, 200 were recruited for the study while the remaining 50 could not be included due to discordant seropositive results. Others were discharged and some changed their minds towards participating, while others succumbed to the HIV-disease. There were 132 patients from the wards and 68 from outpatient clinics among whom 116 were males and 84 females. The overall age range among the study participants was 18-61 years (mean=37yrs) while among females; it was 18-57yrs (mean=33.5yrs); and 18-61yrs (mean=37.3yrs) among males. The majority of the patients (88%) were in the age group of 18-34 and 35-45 years according to gender respectively, with the minority having been above the age of 55 years (Fig.1).

Age group (yrs)	Frequency	Percentage%
18-34	103	51.5
35- 45	73	36.5
46- 55	18	9.0
55+	6	3.0

Fig. 1. Distribution of the study population according to age groups.

The level of literacy among the participants was relatively high since only 9.5% had not attended any form of education, with the majority of 97% having at least achieved primary and 15% tertiary education (Fig. 2).

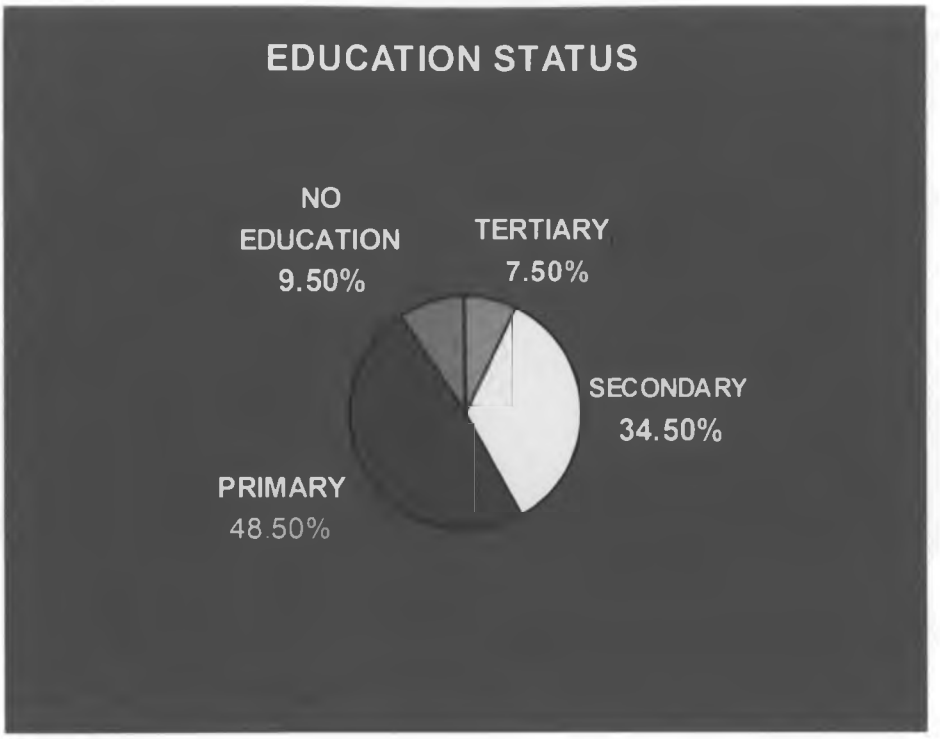

Fig. 2. Distribution of the study participants according to the level of education.

Regarding alcohol and tobacco use, 28.5% (57) and 18.5% (37) of the participants had a history of their consumption respectively. The prevalence of malignancy among the group that used alcohol and tobacco was 22.8% and 27.0% respectively. The various types of medication the study participants were taking included, anti-retrovirals (28%), anti-tuberculosis (34%), anti-meningitics (4.3%) while some were on more than one type in addition to anti-retrovirals (28.6%).

According to the WHO clinical staging classification, 7 (3.5%) were in stage II, 86 (43%) in stage III and 107 (53.5%) in stage IV of the disease, the majority (96.5%) having been in the advanced stage of the disease (Fig. 3).

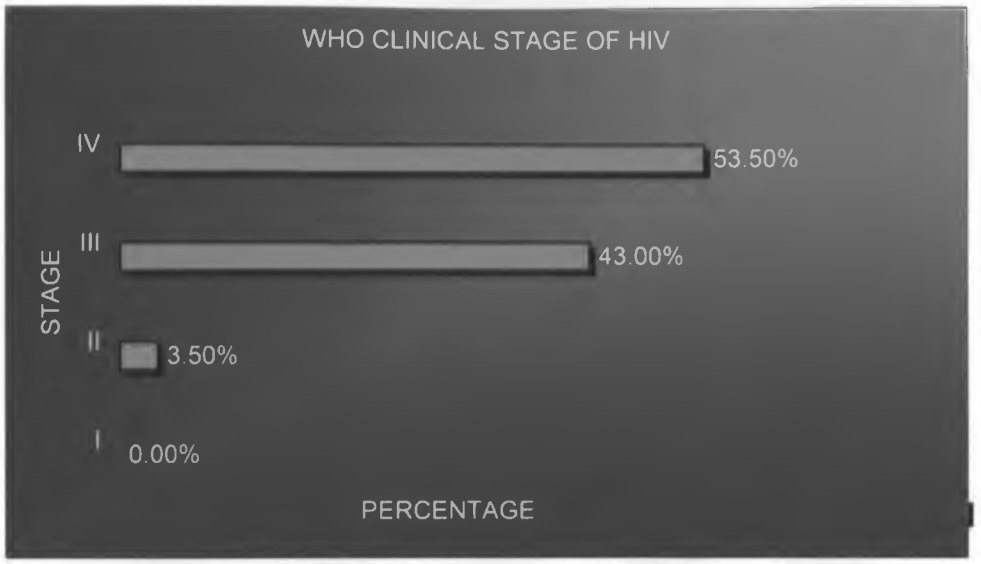

Fig. 3. Distribution of study participants according to the WHO clinical stage of the HIV disease.

Clinical examination revealed the presence of oral manifestations (both neoplastic and non-neoplastic) with the progressive stage of the disease. The most prevalent non-neoplastic lesion in decreasing order was hyperplastic candidiasis 45.5% (91), erythematous candidiasis 22.5% (45), angular cheilitis 21.5% (43) aphthous ulceration 5.5% (11) and herpetic ulcers 4.5%(9) (Fig. 4). Some of the uncommon manifestations found among the study participants were orofacial necrotizing fascitis, osteomyelitis, ranulae, cervical tuberculosis (TB), adenitis, TB ulceration of the lower lip, molluscum contagiosum, facial and hypoglossal nerve palsy.

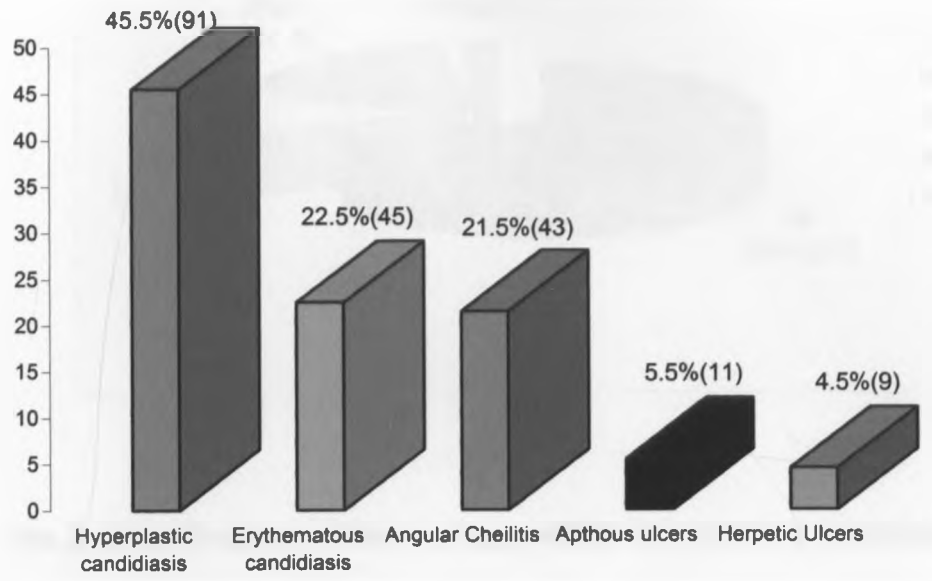

Fig. 4. Distribution of the clinical presentation of the HIV infection associated oral conditions among the participants

Among the neoplastic lesions, 37(68%) patients presented with KS/OKS followed by 9(17%) of SCC, 7(13%) of NHL and 1(2%) with BL (Fig. 5). The clinical and histological illustration of the various neoplastic lesions is depicted in plates I to III.

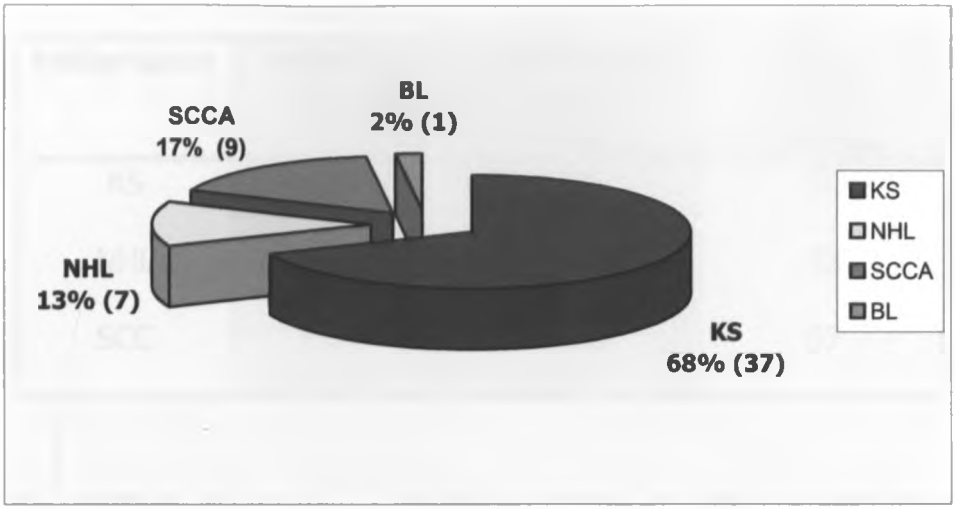

Fig.5. Distribution of the various AIDS-associated neoplasms.

Majority of the KS lesions were seen on the palate followed by the maxillary alveolus and gingivae, unlike NHL and SCCA which presented mostly in the maxillary/mandibular alveolus (Fig 6).

NEOPLASM/SITE	PALATE	MAXILLARY ALVEOLUS	MANDIBULAR ALVEOLUS	GINGIVAE
KS	30	4	1	2
SCCA	2	3	4	0
NHL	2	3	2	0
BL	1	0	0	0

Fig.6. Site distribution of the neoplastic lesions in the study population.

The age distribution of patients with malignant lesions varied, the youngest patient with SCC was 18 years followed by a 23-year-old with KS/OKS and a 33-year-old with NHL. NHL had an older group of patients presenting with the lesion and SCC the youngest among our study participants (Fig.7).

Malignancy	Mean Age (n-years)	Youngest patient (years)	Oldest patient (years)
KS	36.3	23	55
NHL	43.9	33	53
SCC	35.7	18	57

Fig.7. Age distribution among study participants who manifested neoplasms.

In this study population the number of females presenting with KS and SCC was higher than in males, the converse was true for NHL with more of a male predilection. A remarkably higher number of female participants 20 (54.1%) than males 17 (45.9%) presented with KS. Similarly, more females 6 (66.7%) than males 3 (33.6%) presented with SCC, the converse was true for NHL with 6 (85.7%) of males compared to 1 (14.3%) of females (Fig.8).

Sex	KS	NHL	SCC	BL
Males	17 (45.9%)	6 (85.7%)	3 (33.6%)	1 (100%)
Females	20 (54.1%)	1 (14.3%)	6 (66.7%)	0
Total	37	7	9	1

Fig.8. Gender distribution among patients with neoplasms.

All the patients with neoplastic lesions were in stage III and IV of the HIV disease while none was in stage II of the HIV disease. The only malignancy that appeared in stage III was KS (1.2%), the rest were in stage IV. The most prevalent malignancy in the latter was KS and SCC followed by NHL (Fig.9).

Malignancy	Stage of HIV Infection		
	II	III	IV
KS	0%	1.2%	33.6%
NHL	0%	0%	6.5%
SCC	0%	0%	8.4%

Fig. 9. Distribution of malignancies according to the clinical stage of the HIV infection.

CHAPTER 4

12 DISCUSSION

The results in the present study show a similar pattern of head and neck malignancy in HIV-infected patients as reported in other studies (3). The prevalence of any neoplastic lesion from this group of HIV-infected patients is 27% (95%CI) and; therefore, the true prevalence in any population is between the range of 20.85% - 33.15%. HIV-infected patients have an overall two-fold increase in the risk of malignant disease with the following sequence of development of these lesions in the immunosuppresssed individuals appearing as KS/OKS, NHL and SCC (2). The head and neck region was the initial and only site of presentation for most of the neoplastic lesions and the frequency in our population in decreasing order of occurrence was KS/OKS (68%), SCC (17%), NHL (13%), and BL (2%). SCC, was the second most common neoplastic lesion and not NHL as indicated from the literature review. Although the patients' age group had a wide range, it was apparent that the malignancies presented at an earlier age than is generally observed in the non-HIV infected patients occurring in the 5^{th} to 6^{th} decades.

Kaposi's Sarcoma

KS/OKS was most prevalent among the female participants in the study in the ratio of female: male = 1:0.85. Yet it has been reported that the risk of KS/OKS is 5 to 10 times greater in male homosexuals than in other HIV-infection risk groups (46,47). In the developed world the incidence of HIV-related KS began to decline before HAART became available but became more pronounced thereafter. In contrast, the prevalence of KS has risen alarmingly in Africa (48). Since the advent of AIDS, KS/OKS has become more frequent in both genders, the male to female ratio changing from 19:1 to 1.7:1 particularly in East Africa (49). There was no apparent reason as to why females were predominant, hence

the need for further investigation of the difference. The site predilection was in accordance with the findings by Lager et al. (2003) with the palate having been the most common site (12). AIDS patients with OKS have a higher death rate than those with skin involvement; and OKS has been identified as a prognostic factor for patients not on HAART (21). It was apparent that as the disease stage advanced, most patients presented with KS in stage IV of the disease which showed a deteriorating state of immunosuppression. Hence, AIDS patients with OKS have a higher death rate and; this has also been identified as a prognostic factor for patients not on HAART (21).

Squamous cell carcinoma

The second most prevalent neoplasm after KS/OKS was SCC in the present study with a mean age of 35.6years, the youngest victim having been 18 years old and the female to male ratio was 2:1. This was unusual since in the non-HIV-infected patients males have had a predominance of developing SCC due to the association of the consumption of alcohol and cigarette smoking among males more than females. Most of the afflicted had an advanced and aggressive form of the disease at the time of presentation. SCC, the most common cancer in the head and neck region, is overshadowed by KS/OKS and NHL in patients with HIV infection (49, 29, 17, 50, 51,52). An overall younger (less than 45 years) population is affected by HIV-associated SCC (44). The results of a study in non-HIV infected patients at the KNH, showed a relative frequency of oral cancer of 2-3% with a peak incidence in the 50-60-year age bracket (53). In this study 28.5% and 18.5% of the patients who used alcohol and tobacco respectively, developed the neoplasm. Patients with malignancy had in common, a history of significant exposure to tobacco and/or alcohol, suggesting that carcinoma may develop in these patients as a result of a multifactorial aetiology of carcinogenic exposure, viral stimulation and immune dysfunction. It is important to take into consideration that the patients who were 18 years of age did not have a history of alcohol/tobacco use, making it difficult to rule out a genetic predisposition in

such cases. Therefore, in accordance with other studies, patients in the present study were of a younger age, had an advanced form of malignancy and were in stage IV of the HIV disease. This clearly explains that HIV infection may accelerate the development of SCC by probably impairing normal immune surveillance mechanisms in the background of HIV-infection. The alteration in the age distribution of SCC indeed mandates aggressive screening of all HIV-infected patients (45).

Non-Hodgkin's lymphoma

Head and neck involvement with NHL occurs in a significant number of HIV-infected patients. NHL accounts for over 95% of the cases and is the only immune malignancy to be considered AIDS-defining by the CDC (25). It is the second most common malignancy in HIV-infected patients, featured as the third common (24). This is a significant finding in this group of study participants from a major referral centre and it may be depicting a different pattern in comparision to the available literature. In comparison to KS/OKS and SCC, NHL presented in older individuals with the highest mean age of 43.9years; and the youngest patient having been 33 years, both of who were in stage IV of the HIV disease. NHL is described as a disease of adults in their 5^{th} to 6^{th} decades of life having an equal female to male ratio (54). However, in the face of HIV infection, a lower age group is emerging at 30 to 40 years (55). In the present group of participants the male to female ratio was a 6:1; the males as the majority all appeared in stage IV of the disease with the alveolar ridge and palate as the most common extra-lymphatic sites. Oral NHL gives rise to intra-oral soft tissue masses with or without ulceration and tissue necrosis usually involving the gingival, palatal and alveolar mucosa (56). The distribution and course of NHL is unique and; therefore, a high level of suspicion for NHL is required in all cases of head and neck lesions with HIV infection to facilitate appropriate management (25).

13 CONCLUSIONS

The most prevalent malignant neoplasms were OKS/KS, SCC and NHL. A rather younger age group developed malignancy at a mean age of 37 years. Younger females than males presented with KS and SCC. Majority of these neoplasms occurred in stages III and IV of the HIV disease.

14 RECOMMENDATIONS

- Clinicians need to be sensitized on comprehensive oral examination of all HIV-infected patients for early detection and management.
- All patients presenting with malignancy should be advised about screening for HIV infection. This will enhance HIV infection screening and help in reducing the associated morbidity and mortality.
- Similar studies should be carried out in major hospitals across the country to determine the actual occurrence of malignancies in the Kenyan population.

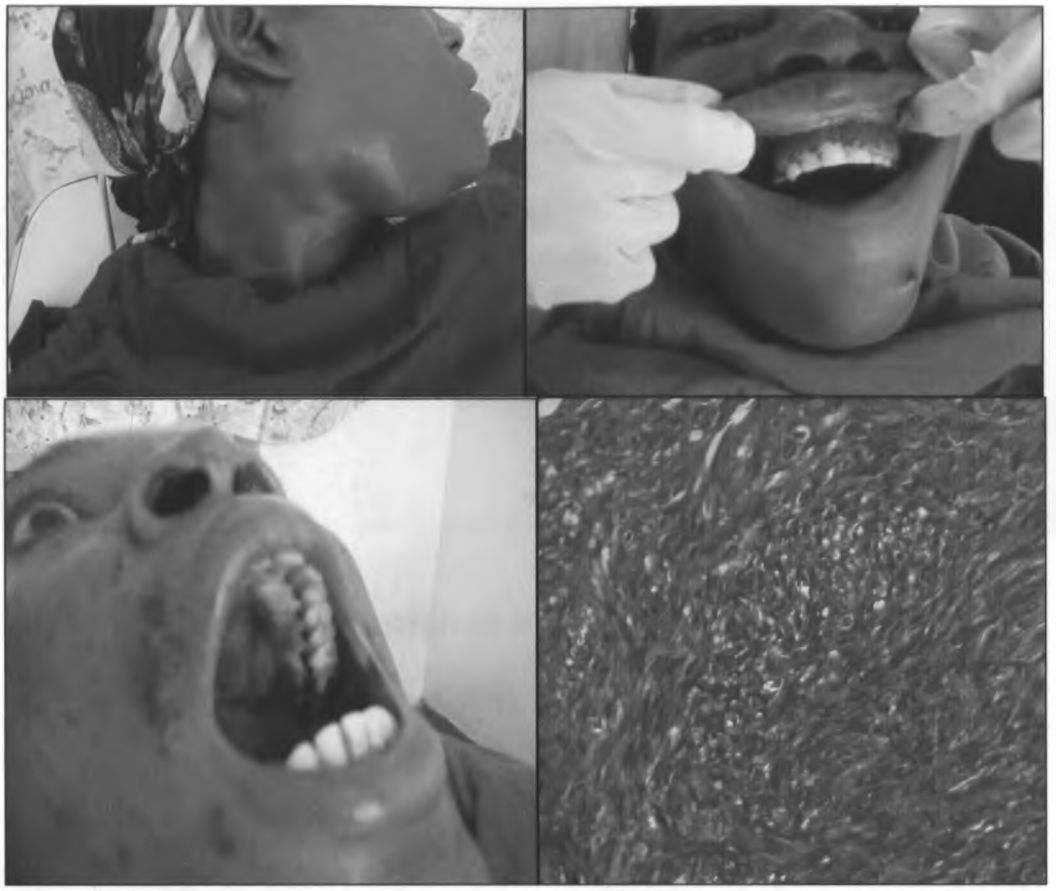

Plate I : Extra- and intra-oral clinical presentation of KS/OKS : A-in neck lymph nodes,

Plate I B - in the gingivae,

Plate I C - in the palate,

Plate I D - a photomicrograph of KS/OKS (Haematoxylin and Eosin staining/ magnification x 40).

Histopathology: *Tumour is composed of pleomorphic spindle shaped cells with slit-like spaces not lined by endothelium and containing extravasated red blood cells.*

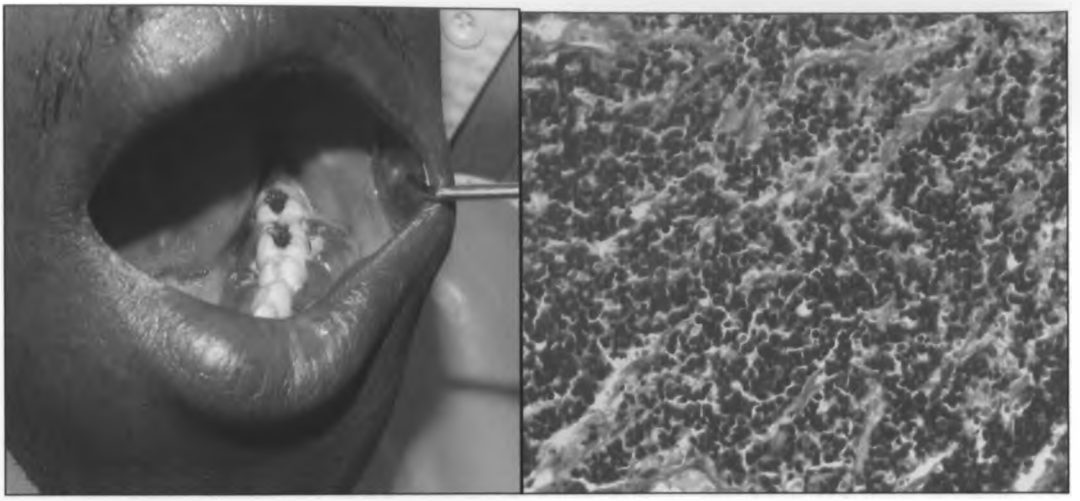

Plate II A: Clinical presentation of NHL in the mandibular gingivae.

Plate II B: Photomicrograph of NHL (Haematoxylin and Eosin staining/magnification x 40).

***Histopathology**: Tumour composed of monomorphic population of round, non-cleaved malignant lymphoid cells; these are features of a diffuse large cell type of non-Hodgkin's lymphoma*

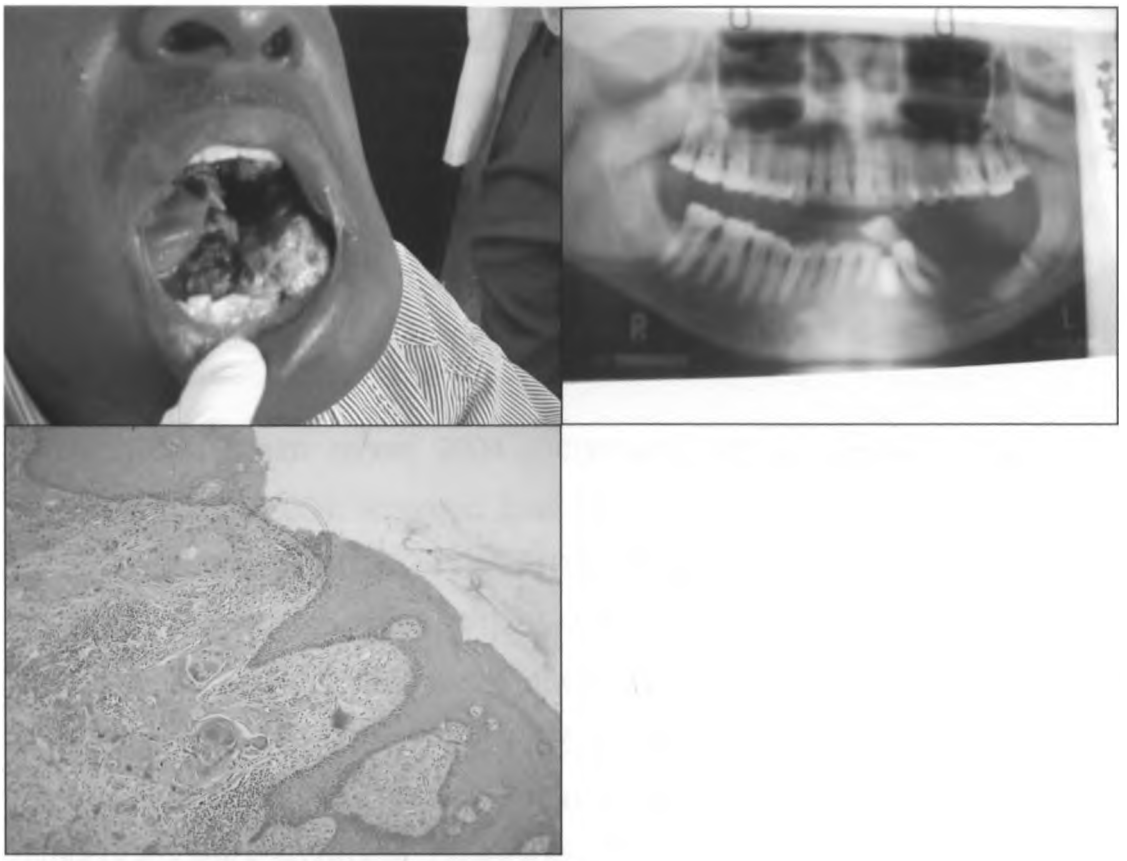

Plate III A Clinical presentation of oral SCCA in the mandibular gingivae.

Plate III B: An orthopantomogram depicting extensive erosion of the left body of the mandible by SCCA.

Plate III C: A photomicrograph of an HIV-infection associated SCCA. (Haematoxylin and Eosin staining/magnification x 40).

Histopathology: *Tumour composed of nests and anastomosing islands of moderately differentiated malignant squamous cells exhibiting intracellular and extracellular keratinization. Mitoses are noted.*

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16 APPENDICES

I PATIENT INFORMATION AND CONSENT FORM

In partial fulfillment of the master of dental surgery in oral and maxillofacial surgery I am required to conduct a research project as a post graduate student of the University of Nairobi. My research involves a **descriptive study of the pattern of head and neck neoplasms in HIV-infected patients seen Kenyatta National Hospital**.

I would like you to participate in this study, which will look at different problems in the head and neck region. This participation is entirely voluntary and you have the choice of withdrawing at any stage during the study. As part of the audit your present results will be used and you will be requested to fill a specially designed chart with questions routinely raised by health care providers. It is entirely dependent on your will to consent to these questions should you refrain from the exercise not in under any circumstances will this adversely affect your care. A thorough head and neck examination will be done using adequate light, clean instruments, disposal gloves and face masks. Where necessary a piece of your tissue from the area of the swelling depending on its location in the head and neck area, will be taken for accurate diagnosis using sterile instruments under the influence of local anesthesia (painkiller) to minimize discomfort during the procedure. Antibiotics and painkillers will be prescribed after the procedure to protect from infections and to control pain. To ensure confidentiality your personal identity will not be included in the records. Relevant findings from this exercise will be provided to your current health care provider to facilitate your health management. The results from this study may be used in the future treatment of those infected with the HIV infection.

I _ _ _ _ _ _ _ _confirm that I have explained the relevant parts of the audit and do hereby give consent to participate.

Signed _ _ _ _ _ _ _ _

I, the participant, confirm that I have understood the relevant parts of this exercise and do herby give consent to participate.

Signed _ _ _ _ _ _ _ _

Should you wish to contact me over any issues related to the study and your participation please use the following address.

Dr Fawzia Butt

P.O.Box 00603-25361, Nbi Mobile 0722 703347.

II SPECIALLY STRUCTURED QUESTIONNAIRE

NAME	
I/P NUMBER	
AGE	
SEX	
LOCATION	
RELIGION	
WARD/CLINIC	

MARITAL STATUS ☐

0-Single, 1-Married, 2-Divorced 3-Widow 4- Separated

OCCUPATION 0-Unemployed, 1-Employed ☐

Type _____

EDUCATION 0-Uneducated, 1-Educated ☐

Level of Education _____

RESIDENCE 0-Nairobi, 1-Outside Nairobi ☐

If 1 state location _____

DURATION OF ILLNESS (since diagnosis)

0-first time, 1-long duration ☐

State Duration _____

MEDICAL HISTORY

	0-NO	1-YES
Respiratory problems		
Liver disease		
Renal disease		
Blood disease		
Bleeding disorder		
Anaemia		
Leukemia		
Endocrine disorders		
Diabetes Mellitus		
Steroid use(Period)		
Previous cancer treatment		
Radiotherapy		
Chemotherapy		
Allergies		
Are you pregnant		
Current Medication		
Type of Medication		

SMOKING

0-Non-smokers, 1-Current smokers, 2-ex-smokers ☐

Type and Duration _____

ALCOHOL 0-No, 1-Yes ☐

Local/Modern Brew _____ Duration _____

EXAMINATION

Extra oral examination

	O-NO	1YES(Site)
Squamous cell carcinoma		
Kaposis Sarcoma		
Hodgkin's Lymphoma		
Non-Hodgkin's lymphoma		

Lymphadenopathy

	0-NO	1-YES
Submental/Submandibular		
Parotid		
Auricular(Pre/Post)		
Level II		
Level III		
Level IV		
Level V		
Level VI		

Salivary glands Enlargement

		0-NO	1-YES
Parotid	Right		
	Left		
Submandibular	Right		
	Left		
Sublingual			
Minor			

Intra oral examination

Code	Condition	Location (Fairly Accurate)
1	Pseudomembranous candidiasis	
2	Erythematous candidiasis	
3	Hyperplastic candidiasis	
4	Angular cheilitis	
5	Herpetic ulceration	
6	Apthous ulceration	
7	Oral hairy leucoplakia	
8	Kaposi's sarcoma	
9	Non-hodgkins lymphoma	
10	Molluscum Contagiosum	
11	Melanotic hyperpigmentation	
12	Squamous cell carcinoma	
13	Verrucous cell carcinoma	
14	Burkitt's lymphoma	

Other.....

CONDITION	LOCATION

HISTOPATHOLOGY _____

III WHO STAGING SYSTEM FOR HIV-INFECTION AND DISEASE.

This was first published in 1990 by the WHO and updated in September 2005. It is an approach for use in resource limited setting and is widely used in Africa and Asia and has been a useful research tool in studies of progrssion to symptomatic disease.

Stage I: HIV disease is asymptomatic and not categorized as AIDS.

Stage II: Includes minor mucocutaneous manifestations and recurrent upper respiratory tract infections.

Stage III: includes unexplained chronic diarrhea for longer than a month, severe bacterial infections and pulmonary tuberculosis.

Stage IV: includes toxoplasmosis of the brain, candidiasis of the esophagus, trachea, bronchi or lungs and Kaposi's sarcoma; these are used as indicators of AIDS.

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Ref: KNH-ERC/ 01/ 3317

Date: 23rd February 2006

Dr. F. Butt
Dept. of Oral & Maxillofacial Surgery
Faculty of Dental Sciences
University of Nairobi

Dear Dr. Butt

RESEARCH PROPOSAL: "INCIDENCE OF HEAD AND NECK NEOPLASMS IN HIV-INFECTED PATIENTS SEEN AT K.N.H" (P151/8/2005)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** revised version of your above cited research proposal for the period 23rd February 2006 – 22nd February 2007.
You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M.Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
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