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# Epidemiology of oral Kaposi's sarcoma in Zimbabwe 1988-1997: a population-based study

C MARIMO

## Abstract

**Objective:** Sub-Saharan Africa has the highest number of HIV/AIDS cases globally which contrasts with the lack of population-based studies of oral Kaposi's sarcoma (OKS); one of the clinical cardinal signs of HIV/AIDS. To date, no study has investigated the incidence of OKS in African populations affected by the HIV/AIDS epidemic. It is, therefore, the purpose of this study to assess the burden of OKS in the Zimbabwean population over a 10 year period.

**Design:** A descriptive epidemiological study was undertaken to assess the burden of OKS by determining the frequencies, incidence and cumulative rates, the lifetime risk and chances of developing OKS according to site (topography), gender, age, race/ethnic origin of the Zimbabwean population. A total of 445 incident cases of OKS from the upper and lower lips, oral vestibule, retromolar area, floor of mouth, tongue, cheek, mucosa, gums, hard and soft palate were accessed from the Zimbabwe National Cancer Registry (ZNCR). Cases from the skin, pharynx, larynx and the major salivary glands were excluded from the study.

**Setting:** This comprised the population of Zimbabwe during the 10 year period 1988-1997. The population figures used for this study were from the 1992 Census Zimbabwe National Report. The study population was standardized by the direct method against the world standard population to calculate the age standardized incidence rate (ASIR). The SPSS statistical software programme (SPSS Inc. 2001, USA) was used for the statistical analysis.

**Results:** OKS comprised 0.92% of total body malignancies and 51% of oral malignancies with a mean age of study cases of 37.6 years and median age of 32 years. Histology of the primary (64.5%) and clinical diagnosis (34.6%) were the predominant methods of diagnosis. OKS affected nearly only blacks and males more than females, with a male to female ratio of 1.9:1. The most affected age groups by OKS were the 30 to 34 years for male and 25 to 29 years for both females and the whole population. Other notable peaks in OKS rates were in the 0 to 4 year and the 75+ age groups. OKS mostly affected the palate (70.2%) followed by, in descending order, the tongue (13.3%) and mouth (8.3%). The age adjusted age standardized incidence rate (ASIR) of OKS exponentially increased the entire study period bypassing oral squamous cell carcinoma (OSCC) as the predominant oral malignancy in 1994. Among AIDS-associated malignancies, OKS accounted for 98% while the balance comprised Burkitt's lymphoma, Hodgkin's and Non-Hodgkin's lymphomas,

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haemangiosarcoma and lymphoma not specified.

**Conclusion:** OKS was the commonest malignancy of young adults affecting males more than females. OKS steady increased for the entire study period overtaking SCC in 1994 to become the commonest oral malignancy for the remainder of the study period. The palate was the most affected intra-oral site by OKS. These findings are attributable to the high human immunodeficiency virus infection (HIV) rates recorded for

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## Introduction

Studies from Uganda, Rwanda and Zimbabwe have reported sharp increases in the incidence of Kaposi's sarcoma (KS)<sup>1-5</sup> which has become the most common malignancy associated with human immunodeficiency virus (HIV) infection and auto-immune deficiency syndrome (AIDS) epidemic<sup>1,2,6,7</sup>. Oral Kaposi's sarcoma (OKS) is one of the seven cardinal lesions strongly associated with HIV infection and indicates HIV infection. OKS presents as one of the early clinical features and is a marker of HIV disease progression into full-blown AIDS<sup>11</sup> as well as being a prognostic marker during antiretroviral treatment (ART). Sub-Saharan Africa has the highest number of HIV/AIDS cases globally which contrasts with the lack of population-based studies on OKS; one of the clinical cardinal signs of HIV/AIDS. To date, no study has investigated the incidence of oral KS (OKS) in African populations affected by the HIV/AIDS epidemic. It is, therefore, the purpose of this study to assess the burden of OKS in the Zimbabwean population over a 10 year period.

## Materials and Methods

The burden of oral Kaposi's sarcoma in Zimbabwe was assessed by determining the frequencies, incidence and cumulative rates, the lifetime risk and chances of developing OKS according to site (topography), gender, age and race/ethnic origin. During the study period, 1 January 1988 to 31 December 1997, 445 case of incident OKS out of a total of 873 oral malignancies and 47 906 cases of whole body malignancies were recorded by the Zimbabwe National Cancer Registry (ZNCR). The intra-oral sites investigated included, upper and lower lips; oral vestibule; retromolar area; floor of mouth; tongue; cheek, mucosa' gums; hard and soft palate. Cases from the skin, pharynx, larynx and the major salivary glands were excluded from the study. Distinction between lip vermilion and lip mucosal malignancies was not clarified in the original ZNCR data; hence the inclusion of some lip vermilion KS among intra-oral KS was a distinct possibility. Oral squamous cell carcinoma (OSCC) is a common oral malignancy that was used to assess the relative rate of increase of OKS. The accessed data for each case comprised information on age; gender; race; date of diagnosis; basis of diagnosis and site/topography. Absolute anonymity of identities of patients whose case details comprised the raw data for this study was maintained throughout the study.

## Population.

The population figures used for this study were from the 1992 Census Zimbabwe National Report. Zimbabwe had a total of 10 412 548 persons comprising 5 083 537 males and 5 329 011 females.<sup>12</sup>

## Statistical Methods.

The data was sorted into tables for males, females and the whole population in five year age groups against the site. The five year age groups and the upper limit of 75+ were set for concordance with the 1992 Census population figures. Statistical analysis was done using the SPSS statistical software program (SPSS Inc. 2001, USA). The age specific incidence rate; crude rate; age standardized incidence rate (ASIR); cumulative rate; the cumulative (lifetime) risk and chances of developing OKS were calculated using Microsoft Excel on Windows 98. The ASIR was age adjusted and standardized by the direct method against the world standard population. The cumulative rate was calculated using a defined life span of 0 to 74 years. It follows, therefore, that the chances of developing OKS that were calculated apply to the same life span of 0 to 74 years.

## Results

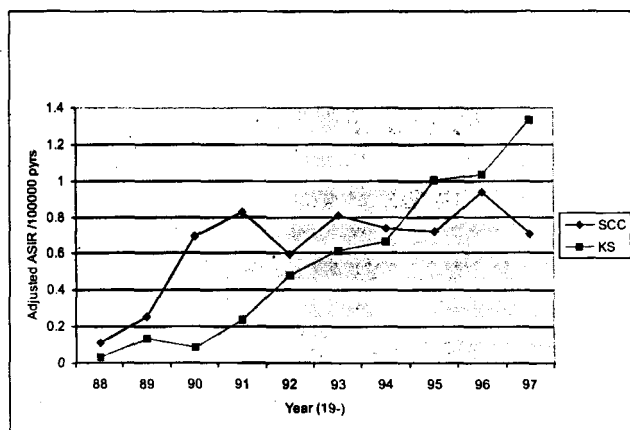
OKS comprised 51% of oral malignancies and 0.92% of total body malignancies recorded during the study period. The mean age of recorded patients was 37.6 years while the median age was 32 years. The racial distribution was almost exclusively blacks as only one case was recorded in a 25 year old European female. Males bore the greater burden of OKS with 65.6% of recorded cases and a male:female ratio of 1.9:1. The majority of cases were diagnosed from the histology of the primary (64.5%) followed by clinically only (34.6%) while clinical, X-ray and ultra sound accounted for only 0.6%. Only one case of metastatic KS (0.2%) was recorded in the oral cavity. OKS mostly affected the palate (70.2%) followed by, in descending order, the tongue (13.3%) and mouth (8.3%). Frequencies for the other oral sites are as shown in Table I.

Table I: Site/topographical distribution of oral Kaposi's sarcoma.

Site	Count	Frequency (%)
External upper lip	2	0.4
Mucosa of upper lip	1	0.2
Lip NOS	2	0.4
Tongue NOS	59	13.3
Gum NOS	16	3.7
Floor of mouth NOS	1	0.2
Hard palate	6	1.3
Soft palate	6	1.3
Palate NOS	312	70.2
Cheek mucosa	3	0.7
Mouth NOS	37	8.3
<b>Total</b>	<b>445</b>	<b>100.0</b>

The most affected five year age groups by OKS were the 30 to 34 for males and 25 to 29 for both females and the whole population. Other notable peaks in OKS rates were in the 0 to 4 and the 75+ age groups. The ASIR of OKS increased steadily in all three population categories.

Figure I: Trends of OKS and OSCC for the whole population by year of study.



A graphical plot of the ASIRs of OKS and OSCSS by year of study in Figure I shows OKS steadily increasing for the entire study period overtaking SCC in 1994. Interestingly, the ASIR of OSCC did not increase but stayed within a narrow range of 0.6 to 1.0 per 100 000 person years for eight of the 10 years of study. The crude rate, age adjusted ASIR, cumulative rate, the lifetime risk and the chances to develop OKS of the study population are as given in Table II.

Table II: Rates, risks and chances of developing oral Kaposi's sarcoma among males, females and the whole population.

Variable	Oral Kaposi's sarcoma (OKS)		
	Male	Female	Population
Age specific incidence rate (crude rate)/100 000 p/yr	0.57	0.29	0.43
Age standardised incidence rate/100 000 p/yr	7.87	3.56	5.62
Cumulative rate (%)	0.76	0.33	0.53
Cumulative (lifetime) risk (%)	0.8	0.3	0.5
Chances of developing OKS	1:132	1:299	1:188

The corresponding figures for OSCC were 0.32/100 000 person years, 0.64/100 000 person years, 0.08% and 0.01% with one chance in 1 331 of developing OSCC for the study population. Males had higher ASIR for OKS (7.87 per 100 000 person years) and OSCC (9.18 per 100 000 person years) than females with 3.56 and 3.69 person years respectively. Males had the highest ASIR for OSCC a decade earlier (50 to 54 five year age group) than females (60 to 64 five year age group) as depicted in Figures II and III. Among AIDS-associated malignancies, OKS accounted for 98% while the balance comprised Burkitt's lymphoma, Hodgkin's and Non-Hodgkin's lymphomas, haemangiosarcoma and lymphoma not otherwise specified.

Figure II: Trends of OKS and OSCC among females by five year age groups.

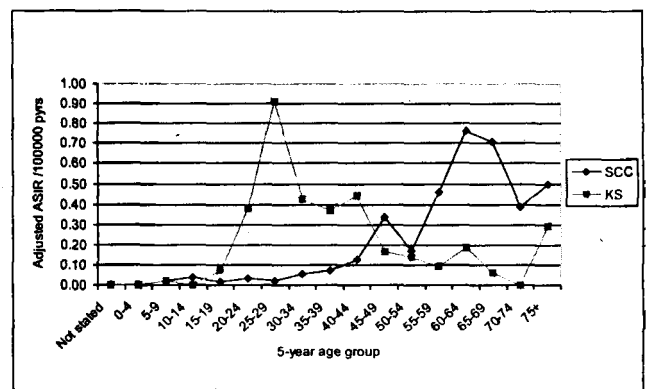
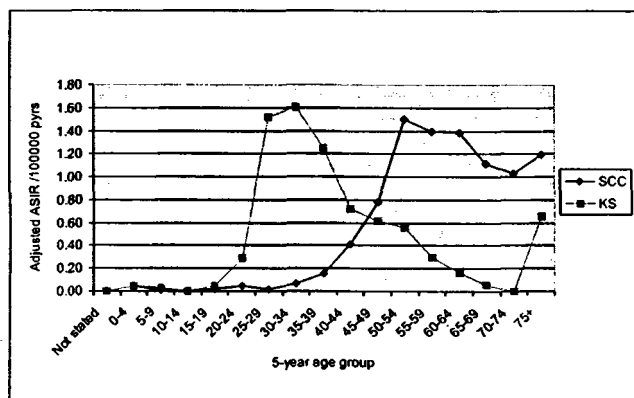


Figure II: Trends of OKS and OSCC among males by five year age groups.



## Discussion

This study was promoted by a previous population-based study of the burden of oral malignancies in Zimbabwe where OKS was the commonest oral malignancy and mostly affected the palate.<sup>13</sup> Previous studies from Zimbabwe<sup>6,13</sup> on general cancer trends have reported dramatic increases in the incidence of Kaposi's sarcoma (KS) making KS the most common cancer in males and the second most common in females after cervical cancer. In this study, the study population is seven times more likely to develop OKS than OSCC while males have double the chances of developing OKS compared to females. Consequently Kaposi's sarcoma has overtaken squamous cell carcinoma to become the most common form of oral malignancy in the three population categories of males, females and the whole population during the study period. These changes were due to the HIV/AIDS epidemic in Zimbabwe where some of the highest HIV infection rates have been reported<sup>14</sup> and non-provision of highly active antiretroviral therapy (HAART) in the public health sector during the study.

The frequency of other AIDS associated malignancies in this study is very low. This may either be due to occurrence of the bulk of such malignancies at extra-oral sites or death of the patients before intra-oral involvement. It has been reported that survival of cases with AIDS related KS is worse in younger than in older age groups and the median survival for AIDS patients presenting with KS is between 19 and 22 months.<sup>15</sup> This could explain the low frequency of other AIDS associated malignancies in this study as patients died before developing these malignancies. The non-provision of HAART during the study period at state hospitals in Zimbabwe worsened the prognosis of patients with KS.

The role of  $\gamma$  herpes virus, human herpes virus 8 (HHV-8), in the pathogenesis of KS presents conflicting views. There is a widely held view that HHV-8 plays a synergistic role in the pathogenesis of KS<sup>15-19</sup>. HIV-1 is the most prevalent HIV strain in Zimbabwe.<sup>13</sup> However, evidence from Ivory Coast in

West Africa prompts a revision of this view. A study from Ivory Coast reported high ant-HHV-8 antibodies comparable to complication of HIV-2 infection than it was of HIV-1 infection.<sup>21</sup> The same authors also reported that increases in infection rates since 1987 had been largely due to the transmission of HIV-1, whereas the infection rates of HIV-2 had remained stable or had declined. Furthermore, the same group of authors found that prior to the AIDS epidemic, KS was a relatively rare cancer in West Africa compared with the endemic areas in east and southern Africa. In their opinion, this did not appear to reflect a marked difference in the prevalence of infection with the causative agent, HHV-8 because seroprevalence of ant-HHV-8 antibodies in West Africa was high and quite comparable to that seen in the high incidence areas for KS. In view of these findings, it can be hypothesized that in sub-Saharan Africa, HHV-8 plays a HIV strain selective synergistic role in the pathogenesis of KS. Such a role is illustrated with the HIV-1 strain and not HIV-2 strain. The high HHV-8 infection levels already prevalent in West Africa are fertile ground for the HIV-1 strain and dramatic increases in the incidence of KS more specifically OKS can be anticipated. This point calls for further studies from West Africa where HIV-1 infection has been on the increase and strengthening of oral health screening programmes.

### Oral KS by Age.

The high rates of OKS in the 0 to 4 age group suggest that a high proportion of babies were born HIV positive then developed OKS in infancy as observed in a Zimbabwean study of total body KS.<sup>13</sup> At the other end of the age spectrum, the 75+ age group also had high OKS rates. The latter increase most likely reflects rates of the endemic form, which usually affects the lower extremities of the elderly than the epidemic form of KS or a mixture of the two. However, at which age group the epidemic form ends and the endemic form starts remains imprecise. This is further complicated by the reported increase of classic KS in Greece and a speculative role of HHV-8 in this increase.<sup>22</sup> This study illustrates that OKS is predominantly a disease of young adults, which is attributable to the HIV/AIDS epidemic.

### Oral KS by Site.

The oral KS frequency of 51% in this study represents a tenfold increase of KS frequencies reported in an earlier study in Zimbabwe.<sup>5</sup> Though the palate is the most commonly affected intra-oral site in this study and Uganda<sup>23</sup> there are differences in subsequent intra-oral sites affected by OKS as the Ugandan study had the palate followed by the gingiva, tongue and tonsil. Ziegler and Katongole-Mbidde (1996) reported a similar intra-oral site distribution of OKS in another study from the same geographical region of east Africa. Canto and Devesa (2002) reported that OKS accounted for 1.2% mainly occurring on the hard palate and only 10% of total KS cases were found in the pharynx. It can

be concluded that even though the palate is the most commonly affected intra-oral site, differences do occur at other intra-oral sites affected by OKS possibly due to geographical and or intrinsic factors.

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