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Changes in the pattern of Kaposi's sarcoma at Ocean Road Cancer Institute in Tanzania (2006-2011)

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Abstract

Tanzania has high HIV and human herpes virus-8 rates linked to Kaposi's sarcoma (KS). We conducted a study at the Ocean Road Cancer Institute (ORCI) in Dar es Salaam, Tanzania, to examine changes in proportions of KS to all cancers over the period (2006-2011) of increased AIDS management by ART. We included 1504 KS from ORCI and abstracted information regarding age, sex, HIV and TB, ART duration and KS lesions. Male KS patients (59.6%) were older (42.1±11.5 years) than females (40.4%) (36.2± 9.6 years). KS proportions declined from 10.1% in 2003 to 7.4% in 2011. Being female was associated with increased oral and generalized lesions and higher numbers of lesion locations (OR=2.17, CI: 1.35, 3.51; OR=1.49, CI: 1.08, 2.06; OR=1.06, CI: 0.79, 1.41, respectively). TB was associated with oral, generalized and number of lesion locations (OR=2.08, CI: 1.10, 3.93; OR=2.06, CI: 1.28, 3.33; OR=1.88, CI: 1.19, 2.97, respectively). ART duration showed a protective effect with oral, generalized and number of lesion locations (OR=0.55, CI: 0.33, 0.91; OR=0.73, CI: 0.52, 1.01; OR=0.89, CI: 0.67, 1.18, respectively). With increasing number of patients receiving prolonged ART, future studies should investigate long-term effect of ART and tuberculosis in Tanzania and countries with HIV infection.

Keywords

HIV; Kaposi's sarcoma; Tanzania; Trend

Introduction

Tanzania is located in East Africa, a region of the world that experiences a high burden of human immunodeficiency virus (HIV)[1,2]. The estimated adult prevalence of HIV in Tanzania is approximately 5.8%, with over 1.6 million people living with HIV in 2009[3]. Additionally, there is also a high burden of human herpes virus-8 (HHV-8) in the region[4]. A study by Pfeiffer et al. estimated that approximately 50% of males and 42% of females were seropositive for HHV8 in a district of Tanzania[5]. Furthermore, Mbulaiteye et al. found that

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the prevalence of HHV8 infection was high among rural adults of Tanzania. HHV8 seropositivity was associated with having at least 1 seropositive first degree relative or having a seropositive spouse, suggesting both non-sexual, such as saliva, and sexual routes of transmission[6]. HHV-8 is required for the development of Kaposi's sarcoma (KS) and progression to KS malignancies increases rapidly among HIV-positive patients[7-10]. Thus, due to the burden of HIV and HHV-8 in sub-Saharan Africa, KS is one of the most prevalent acquired immune deficiency syndrome (AIDS)-defining cancers in Tanzania[4,9,11,12]. According to the International Agency for Research on Cancer, KS accounts for approximately 12.3% of all cancer deaths in the East African region[2].

There are several types of Kaposi's sarcoma, although the most common type is AIDS-associated. Classic KS, which is not associated with AIDS, is identified most commonly in elderly men, especially from the Mediterranean and Eastern European regions. Another form of KS, called endemic KS, usually affects both children and older men of Africa and has been documented since the early 1900's[13]. Endemic KS was estimated to account for 3% to 10% of cancers diagnosed before the AIDS epidemic. However, in 1981, young men presented with KS lesions and provided evidence of AIDS-associated KS. The incidence of KS among white males before the AIDS epidemic was 0.3 per 100,000 and increased to nearly 9 per 100,000 between 1989 and 1991. Additionally, AID-associated KS occurs at a younger age compared to endemic KS, and is significantly influenced by HIV exposure[13].

It has been established that since the widespread introduction and access of anti-retroviral treatments (ART) in 1995, there has been a substantial decrease in the incidence of HIV-related cancers, particularly KS, in the developed world[7,8]. ART reduces the severity of most cutaneous and oral KS lesions in HIV-infected individuals[14,15]. In Tanzania, the National AIDS Control Program has implemented many campaigns to increase access and uptake of ART, including establishing care treatment clinics (CTCs)[16]. These clinics provide testing, treatment and counseling services to HIV-infected individuals[17]. By the end of 2005, there were almost 1000 CTCs, and the proportion of individuals receiving ART in Tanzania increased from 1% to approximately 31%[16,18]. Due to strategic ART administration, the prevalence and incidence of HIV has been decreasing in individuals aged 15-49 in Tanzania in recent years[4]. However, there still are needs for improving treatment services, reducing the overall burden of HIV and understanding the impact of ART administration to HIV patients on the rate of KS in the population[4].

This study was conducted at the Ocean Road Cancer Institute (ORCI) in Dar es Salaam, Tanzania, the only cancer hospital in the country, to examine the trend and possible changes in annual proportions of KS in relation to all cancers over a 10-year period (2002-2011) that correlated with increased access to ARTs. The study also aimed at examining the socio-demographic, clinical, and treatment characteristics of patients with KS during the study period.

Methods

Study population

This study was conducted at ORCI in Dar es Salaam, Tanzania from January to August 2012. ORCI is the only government hospital that offers chemotherapy and radiotherapy to patients, and nearly all Tanzanian KS patients are referred to this hospital for treatment. All hospital logbooks containing KS from 2002 through 2011 were reviewed and information about patient name, date of diagnosis and place of residence were abstracted.

The final study population for this analysis included all adults who presented at ORCI with clinically and/or histolopathologically-confirmed KS between January 2006 and December 2011 (n =1504). Patient medical records before 2006 were not available for abstraction of the detailed variables. Only patients with clear KS diagnosis were included in this study.

Data management

The number of KS cases and cases of other cancers were gathered from hospital logbooks which used unique patient identification codes to prevent duplicate cases. Medical records of KS patients were retrieved and the following variables were abstracted: date of admission, pathology report information, previous clinic of referral information, HIV status and other infectious or chronic co-morbidities, history of ART, cancer treatment regimens (chemotherapy or radiotherapy), HIV testing dates and date of death, if appropriate. Additional abstracted information included location and number of skin lesions at the time of their first visit to ORCI. Microsoft Excel was used for data entry and data management.

Data analysis

We calculated annual proportions of KS by including all identified KS cases in the numerator and using the total number of cancer cases for any given year as the denominator. Univariate and bivariate analyses were performed to assess demographic and treatment characteristics of the study population. The data was also stratified by year of treatment at ORCI to determine changes over the six-year period (2006-2011). All categorical variables were examined using chi-squared tests and continuous variables using t-tests or Wilcoxin signed-rank test.

Oral lesion presentation (yes/no), generalized lesion presentation (yes/no) and number of lesion locations (one or more than one) were dependent variables used for logistic regression. Independent variables included sex, age, tuberculosis (TB) status, HIV status, and ART administration. Multivariable analysis was performed to further evaluate prediction of dependent outcome variables by the independent variables.

To assess these outcomes separately, we constructed three logistic regression models using ART duration as the main covariate of interest. ART duration was dichotomized for those who received ART for five months or less prior to the first visit to ORCI, and those who received ART longer than five months prior to first visit to ORCI. The five-month cutoff was determined by assessing the median of the original ART duration. The final logistic regression models included only HIV-positive patients with confirmed ART at the time of

diagnosis. The predictors included ART duration and number and location of lesions, while adjusting for age, sex and TB status. Odds ratios (ORs) were reported with statistical significance determined at the 95% confidence interval. Statistical Analysis Software (SAS 9.0) was utilized for all data analysis. The study was approved by the Institutional Review Boards of the University of Michigan and of Ocean Road Cancer Institute.

Results

The decline in annual percentage of KS cases at ORCI, which ranged from 7.4% to 13.5%, with the highest proportion in 2003 and the lowest in 2011. The number of KS, total cancer cases, and proportion of KS patients over the study period of 2002-2011 were 227/1897 (12%), 272/2013 (13.5%), 315/2367 (13.3%), 303/2460 (12.3%), 257/2550 (10.1%), 304/2738 (11.1%), 311/3114 (9.9%), 297/3204 (9.3%), 278/3414 (8.1%) and 228/3102 (7.4%), respectively.

Table 1 shows the characteristics of KS cases from 2006 to 2012. More men presented with KS (59.6%) than women (40.4%) during the six-year period ($p = 0.0418$). The mean age at diagnosis for men was generally older (42.1±11.5 years) than women (36.2±9.6 years), with the p-value showing a marginal significance over the six-year period ($p=0.0618$). More women presented with oral KS lesions (59.2%) and more men presented with lesions in the lower half of the body (65.3%). Overall, almost three-quarters of the patients presented with lesions in the lower half of the body (74.3%,) with significant changes throughout the study period ($p<0.0001$, Table 1). Lesions in the upper half of the body were present in 19.9% of the study population on average, with significant changes over the study period ($p < 0.0001$, Table 1). Additionally, 18.3% of patients presented with lesions on the face and neck. However, the changes over the study period were insignificant ($p = 0.0906$, Table 1). Similarly, 8.4% of patients presented with oral lesions, but the changes over the study period were insignificant ($p = 0.4252$, Table 1). These findings were relatively consistent when stratified by year (Table 1).

Table 1 also shows HIV characteristics for the study population, stratified by year. There was a significant difference over the years with respect to sex ($p=0.0418$), lower and upper body lesions ($p < 0.0001$ for both), HIV status ($p < 0.0001$), TB status ($p= 0.0409$) and ART treatment ($p < 0.0001$). Age was marginally significant ($p = 0.0618$), and face/neck lesions ($p = 0.091$), oral lesions ($p = 0.4252$) and ART duration ($p = 0.6870$) did not show statistically significant differences over the study period (Table 1).

Most of the patients presenting with KS were confirmed HIV-positive (72.5%). Patients who were HIV-negative were grouped with patients with unknown status, as it was sometimes difficult to ascertain if the patient was confirmed negative, or their sero-status was unknown (Table 1). In 2006, patients who reported being on ART were treated on average for 8.0±7.2 months, with a median of 5 months, prior to diagnosis. In 2011, the average duration of treatment prior to diagnosis increased to 12.5±19.1 months, with a median of 6 months. In 2006, a test was conducted for 44.6% of the new patients, and in 2011 only 22.3 % were administered an HIV test.

Table 2a shows characteristics of KS patients stratified by sex. Overall, about half of the KS patients in the study population were between 36 and 50 years old (49.8%), which was for both men (48.7%) and women (51.4%). Age ($p < 0.0001$), HIV-positive status ($p < 0.0001$) and ART treatment ($p < 0.0001$) all showed significant differences between sexes. TB positive status ($p = 0.1554$) and ART duration ($p = 0.1203$) showed insignificant differences between sexes. A higher proportion of women reported being on ART at first visit (71.6%) than men (53.0%), which suggests that women may be more likely to seek treatment than men. Furthermore, among patients on ART, only about one-fourth of men (23.5%) and women (25.5%) reported being on treatment for five months or longer, and the difference between men and women was not significant ($p = 0.1203$).

Table 2b shows the characteristics of KS cases stratified by HIV status. The vast majority of the study population was HIV-positive (N= 1250), while only 142 of the 1504 total patients were HIV-negative. The mean age of those who were HIV-negative was 47.9 + 16.5 years, whereas the mean age for HIV-positive patients was 38.4 + 9.3 years. There were more HIV-positive patients than HIV-negative, and more men (N=692) than women (N= 558) were HIV-positive. The majority (52.5%) of HIV-positive patients were between 36 and 50 years of age and the majority of HIV-negative patients were 50 years old or older. Furthermore, 72% of HIV-positive patients received ART treatment.

Table 3 shows characteristics by lesions presentation outcomes. Age, TB-positive status, HIV-positive status and ART showed statistically significant associations with all lesion outcomes. Although not statistically significant, it is interesting to note that for all lesion outcomes, a much larger proportion of patients reported having been on ART for five or fewer months (Table 3). Table 4(a) shows the crude and adjusted ORs for the important covariates of interest related to the different outcomes of lesion severity. Being female ($p = 0.0006$), TB status ($p = 0.0173$) and ART duration ($p = 0.0131$) were all significant predictors of oral lesions. Being female ($p = 0.0006$), HIV status ($p < 0.0001$), TB status ($p < 0.0001$) and ART duration ($p = 0.0279$) were significant predictors of generalized lesions. HIV status and TB status were significant predictors of the number of lesion locations ($p = 0.0032$ and $p = 0.0005$, respectively). The other variables shown in Table 4(a) yielded insignificant p-values.

Women had 2.30 times odds (95% CI: 1.58, 3.33) of having an oral lesion presentation than men, which remained significant after adjusting for age (adjusted OR=1.96, CI:1.33, 2.89). TB-positive patients were 1.84 (95% CI: 1.08, 3.14) times more likely to present with an oral lesion. Generalized lesions and the number of lesion locations exhibited the same trend. Those who were on ART for five months or longer had 0.53 (95% CI: 0.32, 0.88) times the odds of having an oral lesion and 0.66 (95% CI: 0.48, 0.70) times the odds of having generalized lesions than those who reported having been on ART for less than five months. There was also a protective effect when assessing having more than one lesion location (OR = 0.85; 95% CI: 0.64, 1.14), however, this relationship was not significant.

Table 4(b) shows that these relationships remained relatively the same when constructing the full logistic models. Sex and TB status remained significant predictors for oral and general lesions, however only TB status was a significant predictor of number of lesion

locations. ART duration shows a protective effect for all three lesion outcomes among those who were HIV-positive and on ART, even when controlling for all other covariates.

Discussion

This study was the first evaluation of the burden of Kaposi's sarcoma at Ocean Road Cancer Institute, the only cancer center in Tanzania. The study revealed several interesting observations. First, there has been a declining trend of KS over the 10-year period. Second, we observed that more men presented with KS than women, and men on average were older than women. Third, we found significant relationships between sex, TB status, HIV status, and ART duration for oral and generalized lesions and number of lesion locations. We were also able to use logistic regression to predict the likelihood of the same lesion outcomes based on covariates such as sex, TB status, and ART duration. We found that being female, having TB and being HIV-positive increased the odds of the lesion outcomes. Prolonged ART duration showed to be protective and decreased the odds of the lesions outcomes studied. Previous researchers have identified biomarkers that can predict KS outcomes [19]. Similarly, our study was able to use significantly associated risk factors to predict lesion severity.

It is difficult to identify the reason for the trend decline in proportions of KS. Although the trend is informative, it would also be important to consider the increase in total number of cancer cases at the hospital in any given year. For example, the denominator of the KS proportion may change if there was an increase in cervical cancer due to higher screening rates. The establishment of CTCs in Tanzania may not be the only factor reducing the proportion of KS cases at ORCI, but these data support the prediction of the decrease in KS relative to all other cases seen at the hospital. The proportion of suspected KS cases that needed HIV confirmation declined in 2006 and 2011. This could likely be due to the increased access to CTC clinic resources and that patients were more likely to be tested prior to being referral to ORCI [16]. This could also explain the increase in mean duration of ART administration prior to diagnosis during the same time period. Some of the findings of this study have been discussed in previous studies, particularly when assessing the sex disparities of severe lesion presentation. Our findings related to Tanzania could be due to the observation that more women than men have HIV[20].

Although endemic KS has been affecting African populations for several decades, this study focused on HIV-associated KS. Recent studies have examined how the distribution and sex differences for HIV-related KS are changing in clinical settings [11,14,21-23]. It was observed that there was a dramatic increase in women diagnosed with KS and that women have larger oral lesions than men[11,21,23]. In South Africa, it was estimated that the incidence of KS has doubled in men, while increasing by seven folds in women since the early 1990's. Furthermore, women are also more likely than men to present with oral lesions when diagnosed with KS[22]. Nigerian women presented with KS at a younger age (~35 years) than men (~38 years) at the time of the first visit[14]. Women were more likely to have oral and generalized lesions and increased numbers of lesion locations, as well as a significantly lower mean age of diagnosis than men. These and other differences among men and women are important to consider when initiating treatment and implementing strategies to prevent

KS and HIV progression in populations with high HIV infection rates. There should be more intense screening for women for skin lesions because they are at higher risk, and women should be given more attention during ART treatment.

An objective of this study was to determine if duration of ART administration prior to diagnosis had association with lesion presentation severity. It is possible that with a reduced viral load, HIV-positive individuals will have improved clinical presentation of KS lesions due to better immune function after ART administration[21]. In this study, severe lesion presentation was defined by 3 separate outcomes: oral and generalized lesion presentation, and the number of lesion locations. It is important to note that for the outcomes, it was not easy to determine the effect of ART based on whether or not the patient reported being on ART. After the inclusion of duration, ART had a protective effect on the association. This supports an observation by Taiwo and Hassan that KS lesions had delayed responses to ART[12]. While it is possible that ART could have a protective effect even if the response to treatment was immediate, our data suggests greater protection with a longer duration of treatment. In our study, patients who reported being on ART for five months or longer were less likely to have oral or generalized lesion presentation. Although the association was not significant, patients also had lower odds of having more than one lesion at the time of diagnosis. These findings are informative but successful ART uptake in the population cannot be derived from analysis of a hospital population. It is possible that with establishment of more CTC clinics, more patients are diagnosed and treated before arriving to ORCI.

Strengths of this study include that it was the first study at ORCI examining the burden of KS and the changing trends in distribution over recent years. Furthermore, the study population was large and the data addressed both HIV and KS in patients. Although all of the cases came from ORCI, it is the only referral cancer hospital in Tanzania, which makes the study population more generalizable to the overall Tanzanian population as patients seek care from all over the country.

A possible limitation of this study is relying on ART duration from medical records with little validation if no documentation was included. Other limitations include the number of patients with unknown HIV status and the use of medical records from a specialized center without a well-defined catchment area. The findings from this study suggest that ART administration duration prior to KS diagnosis can reduce severity of KS lesion presentation at the time of diagnosis. Future interventions need to increase provisions of ART and manage co-infections related to KS. Interventions should also closely monitor HIV and KS patients to better characterize the impact of ART on the changing epidemiologic profile of KS in this population and other populations with HIV infection.

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Table 1

Characteristics of 1504 KS cases at ORCI from 2006 through 2011, stratified by year

	Overall		2006		2007		2008		2009		2010		2011		
Total N	**1504**		**241**		**269**		**257**		**269**		**253**		**215**		**p-value***
	Mean (SD)		Mean (SD)		Mean (SD)		Mean (SD)		Mean (SD)		Mean (SD)		Mean (SD)		
Age															
Overall	39.7	(11.2)	39.4	(11.6)	39.3	(11.4)	39.1	(10.4)	39.0	(10.6)	40.6	(11.6)	41.5	(11.4)	0.0618
Men	42.1	(11.5)	42.5	(12.2)	42.1	(11.5)	40.8	(10.9)	42.0	(11.2)	43.0	(12.5)	42.7	(10.8)	
Women	36.2	(9.6)	35.5	(9.5)	35.8	(10.4)	36.0	(8.7)	34.8	(7.8)	37.0	(8.9)	39.3	(12.2)	
	N(%)		N(%)		N(%)		N(%)		N(%)		N(%)		N(%)		
Sex															
Men	897	(59.6)	133	(55.2)	148	(55.0)	168	(65.4)	158	(58.7)	150	(59.3)	140	(65.1)	0.0418
Women	607	(40.4)	108	(44.8)	129	(45.0)	89	(34.6)	111	(41.3)	103	(40.7)	75	(34.9)	
Location of Lesion															
Lower Body *	1111	(73.9)	165	(68.5)	191	(71.0)	168	(65.4)	203	(75.5)	204	(80.6)	180	(83.7)	<0.0001
Men	725	(65.3)	107	(64.9)	121	(63.4)	113	(67.3)	131	(64.5)	130	(68.7)	123	(68.3)	
Women	386	(34.7)	58	(35.2)	70	(36.6)	55	(32.7)	72	(35.5)	74	(36.3)	57	(31.4)	
Upper Body *	298	(19.8)	33	(13.7)	40	(14.9)	43	(16.7)	67	(25.0)	63	(24.9)	52	(24.2)	<0.0001
Face/Neck	273	(18.2)	51	(21.2)	52	(19.3)	38	(14.8)	59	(22.0)	43	(17.0)	30	(14.0)	0.0906
Oral	125	(8.4)	18	(7.5)	20	(7.4)	24	(9.3)	20	(7.4)	21	(8.3)	22	(10.3)	0.4252
Men	51	(40.8)	6	(33.3)	8	(40.0)	12	(50.0)	5	(25.0)	9	(42.8)	11	(50.0)	
Women	74	(59.2)	12	(66.7)	12	(60.0)	12	(50.0)	15	(75.0)	12	(57.1)	11	(50.0)	
Co-infections															
TB	133	(8.8)	29	(12.0)	27	(10.0)	26	(10.1)	11	(4.1)	26	(10.3)	14	(6.5)	
HIV status **															
Pos	1250	(83.1)	193	(80.0)	218	(81.0)	217	(84.4)	229	(85.1)	210	(83.0)	183	(85.1)	<0.0001
Neg	142	(9.4)	18	(7.4)	25	(9.3)	20	(7.8)	22	(8.1)	32	(12.6)	27	(12.6)	

	Overall		2006		2007		2008		2009		2010		2011		
Total N	**1504**		**241**		**269**		**257**		**269**		**253**		**215**		**p-value***
Unknown	8	(0.5)	2	(0.8)	2	(0.7)	0		1	(0.4)	0		3	(1.4)	
ART treatment	905	(60.1)	110	(45.6)	147	(54.6)	155	(60.3)	180	(66.9)	168	(66.4)	145	(67.4)	<0.0001
Duration Months (SD)	8.7	(12.3)	8.0	(17.2)	7.6	(9.5)	7.4	(8.3)	7.6	(8.5)	9.2	(11.1)	12.5	(19.1)	0.6870
Q1	2.0		2.0		2.0		2.0		3.0		2.0		3.0		
Med	5.0		5.0		4.0		5.0		5.0		5.0		6.0		
Q3	10.0		7.0		10.0		10.0		10.0		12.0		12.0		

Percentages are column percent and comparisons are between columns.

* Patients who had both upper and lower body lesions represented the remaining percentage of cases, totaling to 100%.

** Patients with missing HIV status represented the remaining percentage of cases totaling to 100%

Table 2a
Characteristics of KS cases ORCI from 2006 through 2011, stratified by sex

	Overall		Male		Female		P-value
Total N	**1504**		**894**		**607**		
	Mean	(SD)	Mean	(SD)	Mean	(SD)	
Age	39.7	(11.2)	42.1	(11.5)	36.2	(9.6)	<0.0001
	N	(%)	N	(%)	N	(%)	
Age							
18-35 years	331	(22.1)	137	(15.3)	194	(32.0)	<0.0001
36-50 years	747	(49.8)	435	(48.7)	312	(51.4)	
>50 years	423	(28.2)	322	(36.0)	101	(16.6)	
TB Positive Status							
Yes	133	(8.8)	87	(9.7)	46	(7.6)	0.1554
HIV Positive Status							
Yes	1250	(72.5)	581	(65.0)	508	(83.7)	<0.0001
No	149	(9.9)	129	(14.4)	20	(6.5)	
ART							
Yes	905	(60.5)	472	(53.0)	433	(71.6)	<0.0001
No	590	(39.2)	418	(47.0)	172	(28.4)	
ART Duration							
≥5 months	353	(23.5)	198	(22.1)	155	(25.5)	0.1203
<5 months	1151	(76.5)	699	(77.9)	452	(74.5)	

Categorical variables were analyzed using chi-square test, continuous variables were analyzed using t-test or Wilcoxin Exact Test. Significance determined at the 95% confidence level.

Table 2b
Characteristics of KS cases ORCI from 2006 through 2011, stratified by HIV status

	Overall		HIV+		HIV−		P-value
Total N	**1504**		**1250**		**142**		
	Mean	(SD)	Mean	(SD)	Mean	(SD)	
Age	39.7	(11.2)	38.4	(9.3)	47.9	(16.5)	<0.0001
	N	(%)	N	(%)	N	(%)	
Sex							
Male	894	(59.6)	692	(55.4)	124	(87.3)	<0.0001
Female	607	(40.4)	558	(44.6)	18	(12.7)	
Age							
18-35 years	331	(22.1)	287	(23.0)	22	(15.6)	<0.0001
36-50 years	747	(49.8)	656	(52.5)	47	(33.3)	
>50 years	423	(28.2)	306	(24.5)	72	(51.6)	
TB Positive Status							
Yes	133	(8.8)	124	(9.3)	2	(1.5)	0.0024
ART							
Yes	905	(60.5)	900	(72.0)	1	(0.7)	<0.0001
No	590	(39.2)	348	(27.8)	141	(99.3)	

*Categorical variables were analysed using chi-square test, continuous variables were analysed using t-test or Wilcoxin Exact Test. Significance determined at the 95% confidence level.

Table 3

Characteristics of KS cases at ORCI from 2006 through 2011, by lesion presentation outcomes

	Oral		Generalized		Number of Lesions (>1)	
Total N	**125**		**305**		**494**	
	N	(%)	N	(%)	N	(%)
Age *A,B,C*						
18-35 years	33	(26.4)	88	(29.0)	65	(30.0)
36-50 years	74	(59.2)	167	(54.9)	122	(56.2)
>50 years	18	(14.4)	49	(16.1)	30	(13.8)
TB Positive Status *A,B,C*						
Yes	18	(14.4)	46	(15.1)	62	(12.6)
HIV Positive Status *A,B,C*						
Yes	117	(97.5)	280	(95.9)	203	(97.1)
No	3	(2.5)	12	(4.1)	6	(2.9)
ART *A,B,C*						
Yes	91	(72.8)	224	(73.4)	156	(71.9)
No	34	(27.2)	81	(26.6)	61	(28.1)
ART Duration *A,B,C*						
≥ 5 months	24	(26.1)	71	(31.6)	41	(26.0)
<5 months	68	(73.9)	154	(68.4)	117	(74.0)

A Significant at the 95% confidence level for oral lesion presentation.

B Significant at the 95% confidence level for generalized lesion presentation.

C Significant at the 95% confidence level for number of lesion locations

Table 4(a)

Crude and adjusted ORs (95% CI) for oral lesion presentation, general lesion presentation, and number of lesion locations

		Unadjusted OR (95% CI)	Adjusted OR (95% CI)[A]	P-value[B]
Oral lesions	Sex	2.30 (1.58, 3.33)	1.96 (1.33, 2.89)	0.0006
	HIV status	2.05 (1.26, 3.36)	1.61 (0.97, 2.66)	0.0650
	TB status	1.84 (1.08, 3.14)	1.94 (1.12, 3.33)	0.0173
	ART[C]	1.37 (0.77, 2.41)	1.32 (0.74, 2.34)	0.3430
	ART Duration[D]	0.50 (0.31, 0.83)	0.53 (0.32, 0.88)	0.0131
General lesions	Sex	1.85 (1.44, 2.38)	1.58 (1.22, 2.06)	0.0006
	HIV status	2.67 (1.89, 3.77)	2.20 (1.55, 3.13)	<0.0001
	TB status	2.25 (1.54, 3.30)	2.36 (1.60, 3.49)	<0.0001
	ART	1.41 (0.96, 2.07)	1.39 (0.94, 2.05)	0.0979
	ART Duration	0.66 (0.48, 0.90)	0.70 (0.50, 0.96)	0.0279
Number of lesion locations	Sex	1.28 (1.03, 1.59)	1.13 (0.90, 1.42)	0.2777
	HIV status	1.66 (1.29, 2.14)	1.48 (1.14, 1.93)	0.0032
	TB status	1.90 (1.33, 2.72)	1.89 (1.32, 2.72)	0.0005
	ART	1.05 (0.76, 1.46)	1.07 (0.77, 1.48)	0.6977
	ART Duration	0.83 (0.62, 1.01)	0.85 (0.64, 1.14)	0.2750

[A] Estimates are adjusted for sex and age.

[B] Significance determined at the 95% confidence interval.

[C] Includes only those who are HIV positive.

[D] Includes only those who are HIV positive and on ART.

Table 4(b)

Adjusted full models, reported ORs and 95% CIs for associations between individual covariates and oral lesion presentation

	Sex[A]	HIV status (y/n)	TB status(y/n)	ART (y/n)	ART duration (<5, >5mo)
OLP (y/n)	2.17 (1.35, 3.51)	*	2.08 (1.10, 3.93)	*	0.55 (0.33, 0.91)
GLP (y/n)	1.49 (1.08, 2.06)	*	2.06 (1.28, 3.33)	*	0.73 (0.52, 1.01)
NLL (1, >1)	1.06 (0.79, 1.41)	*	1.88 (1.19, 2.97)	*	0.89 (0.67, 1.18)

OLP: Oral lesion presentation

GLP: Generalized lesion presentation

NLL: Number of lesion locations

[A] Male is identified as the reference group. Adjusted for age.

[B] All models are stratified by those patients who were HIV positive and indicated to be on ART at the time of their first visit to ORCI.