Original Research

Risk factors for common cancers among patients at Kamuzu Central Hospital in Lilongwe, Malawi: A retrospective cohort study

Agnes Moses[1,3,4], Albert Mwafongo[1], Maria Chikasema[1], Laureen Kafantenganji[1], Christopher Stanely[1], Emma Chimzukira[1], Coxcilly Kampani[1], Robert Krysiak[1], Satish Gopal[1–4], Nora E. Rosenberg[1,2], Carol G. Shores[1,2], Mina C. Hosseinipour[1,2,3]

1. UNC Project–Malawi, Lilongwe, Malawi
2. University of North Carolina, Chapel Hill, North Carolina, USA
3. College of Medicine, University of Malawi, Blantyre, Malawi
4. Kamuzu Central Hospital, Lilongwe, Malawi

Correspondence: Dr Agnes Moses (amoses@unclilongwe.org)

Abstract

Background

Little is known about risk factors for different cancers in Malawi. This study aimed to assess risk factors for and epidemiologic patterns of common cancers among patients treated at Kamuzu Central Hospital (KCH) in Lilongwe, and to determine the prevalence of Human Immunodeficiency Virus (HIV) infection in the same population.

Methods

We analysed data from the hospital-based KCH cancer registry, from June 2009 to September 2012, including data from a nested substudy on coinfections among cancer patients. Demographics and behavioural variables, including smoking and alcohol use, were collected through personal interviews with patients. We assessed HIV prevalence across cancer types. The distribution of cancer types was reported overall and by gender. Logistic regression was used to assess risk factors associated with common cancer types.

Results

Data from 504 registered cancer patients were included—300 (59.5%) were female and 204 (40.5%) were male. Mean age was 49 years (standard deviation, SD = 16). There were 343 HIV-negative patients (71.2%), and 139 (28.8%) were HIV-positive. The commonest cancers were oesophageal (n = 172; 34.5%), cervical (n = 109; 21.9%), and Kaposi's sarcoma (KS) (n = 52; 10.4%). Only 18% of cancer cases were histologically confirmed. Patients with oesophageal cancer were likely to be older than 50 years (odds ratio, OR = 2.22), male (OR = 1.47), and smokers (OR = 2.02). Kaposi's sarcoma patients had the highest odds (OR = 54.4) of being HIV-positive and were also more likely to be male (OR = 6.02) and smokers. Cervical cancer patients were more likely to be HIV-positive (OR = 2.2) and less than 50 years of age.

Conclusions

Age, smoking, and HIV are important risk factors for the 3 commonest cancer types (oesophageal, KS, and cervical) at this teaching hospital in Malawi. HIV is the single most important risk factor for Kaposi's sarcoma and cervical cancer.

Introduction

Cancer is the leading cause of death in the world and is attributable to 13% of total worldwide mortality, according to the World Health Organization (WHO).[1,2] In Africa, the 5 commonest cancers in males are Kaposi's sarcoma (12.9% of all cancers in males) and cancer of the liver (14.8%), prostate (9.5%), bladder (6.1%), and non-Hodgkin's lymphoma (NHL) (5.7%). In females, cancer of the cervix (23.3% of all cancers in females) and breast (19.2%), Kaposi's sarcoma (5.1%), cancer of the liver (5.0%), and NHL (3.7%) are the 5 most common cancers.[1–2] Environmental factors (such as tobacco use, alcohol, maize flour-based diet, as well as parasite and mold exposure), oncogenic viral infection (such as with hepatitis B, hepatitis C, human papillomavirus [HPV], or human immunodeficiency virus [HIV]) are known risk factors for development of cancers.[11] With the higher prevalence of HIV and other infectious diseases in Africa compared to the developed world, the rate of infection-related cancers (thought to be 36% in Africa) is twice the world average.[22] Mortality rates are drastically higher for cancer patients in the developing world for a multitude of reasons, including unavailable or disorganised screening modalities, delayed diagnosis, and limited treatment options.

In Malawi, cancer data are sparse but recent estimates from population-based cancer registries show that the age-standardised incidence rates per 100,000 people for all types of cancer have increased, especially AIDS-defining cancers.[10] In males, the incidence increased from 31 per 100,000 in 1999–2002 to 56 per 100,000 people in 2007–2010, and in females it increased from 29 to 69 per 100,000 people.[10] Kaposi's sarcoma, oesophageal cancer, and cervical cancer were the main causes for the increased incidence.

Malawi's HIV prevalence is estimated to be 10.6% among adults 15 to 49 years of age, and the country has seen an increase in antiretroviral therapy (ART) coverage from 4% in 2004 to 76% in June 2011.[9] The high HIV incidence may partially explain Malawi's high Kaposi's sarcoma and cervical cancer rates.[17] In contrast, HIV infection does not seem to confer increased risk of breast, oesophageal, prostate, or many other common types of cancer. To our knowledge, these factors have not been fully explored in our local setting.

Table 1: Cancer types diagnosed among patients at Kamuzu Central Hospital, Lilongwe, between June 2009 and September 2012

	Total	Male	Female
Type of cancer	**n (%)**	**n (%)**	**n (%)**
Oesophageal	172 (34.5)	92 (45.8)	80 (26.9)
Cervical	109 (21.9)	0 (0.0)	109 (36.7)
Kaposi Sarcoma	52 (10.4)	40 (19.9)	12 (4.0)
Breast	37 (7.4)	0 (0.0)	37 (12.5)
Head and neck	22 (4.4)	12 (6.0)	10 (3.4)
Bladder	20 (4.0)	10 (5.0)	10 (3.4)
Other genitourinary	16 (3.2)	14 (7.0)	2 (0.7)
Lymphoma	13 (2.6)	7 (3.5)	6 (2.0)
Gastrointestinal	10 (2.0)	4 (2.0)	6 (2.0)
Eye	8 (1.6)	2 (1.0)	6 (2.0)
Other gyanaecologic	6 (1.2)	0 (0.0)	6 (2.0)
Sarcoma	6 (1.2)	3 (1.5)	3 (1.5)
Other skin	5 (1.0)	4 (2.0)	1 (0.3)
Leukaemia	5 (1.0)	4 (2.0)	1 (0.3)
Others	17 (3.4)	9 (4.5)	8 (2.7)
Missing	6	3	3
Total	504	204	300

Methods

Patients and procedures

This was a retrospective descriptive analysis of data collected on patients enrolled into Cancer and Comorbid Infections (CANCO) study at Kamuzu Central Hospital (KCH), in Lilongwe, Malawi, from June 2009 to September 2012. KCH is a 1250-bed referral hospital, which serves about 5 million people annually. It serves as cancer referral hospital for the Northern and Central regions of Malawi, whose total population is roughly 9 million. The CANCO study was nested within the KCH cancer registry, which sought to assess comorbid infections in cancer patients. Inclusion criteria for CANCO were: adult patients 18 years of age or older, presenting to a KCH ward or clinic with a clinically suspected or histologically confirmed diagnosis of cancer at any site, and having not had received treatment (chemotherapy, surgery, or radiotherapy) more than 4 weeks prior to enrolment. Cancer cases were identified by data clerks through daily review of departmental registers, as well as weekly attendance at specialty clinics. Demographic and behavioural variables, such as smoking and alcohol use, were collected through personal interviews with patients by study physicians and nurses, using a structured questionnaire administered to eligible participants. Self-reported tobacco and alcohol use was not quantified. Clinical assessments of participants included tumour measurements in the 3 longest dimensions, using a tape measure. Tumours not obviously identifiable on physical exam were evaluated using an imaging device (ultrasound and x-ray, or occasionally computed tomography [CT] scan, or magnetic resonance imaging [MRI]).

Performance status, using the Karnofsky Performance Scale, was determined. Diagnostic testing for HIV, CD4 count, hepatitis B, schistosomiasis ova in urine and stool, and malaria (thick film) were carried out where resources permitted. This analysis does not include all the variables in the database.

Data management and analysis

Data were entered into the KCH Malawi cancer registry database, as well as the AIDS Malignancy Clinical Trials Consortium surveys for AIDS-related malignancies (lymphoma, cervical cancer, and Kaposi's sarcoma). The data were extracted from the database into Microsoft Excel. Baseline characteristics were summarised using frequencies with percentages or means with standard deviations (SDs). We compared differences in distribution between each risk factor variable, according to cancer site and stage, using Fisher's exact test. We estimated the odds of being HIV-positive with a particular cancer diagnosis using a logistic regression model to assess risk factors for common types of cancer. We considered a P-value of 0.05 or less to be significant. All analyses were performed using Stata SE version 12.1 (StataCorp, College Station, TX, USA)

Ethical approval

The CANCO study was approved by the National Health Science Research Committee (NHSRC) in 2009 (Approval number NHSRC #732).

Results

Overall, 1453 cancer cases were recorded into the KCH cancer registry between June 2009 and September 2012. The participants were referred from 6 hospital departments, namely Medicine, Surgery, Obstetrics and Gynaecology, Ophthalmology, and Dentistry. Data from 504 registered cancer patients, who were enrolled into the CANCO study, were included, 300 (59.5%) of whom were female and 204 of whom (40.5%) were male. The mean age was 49 years (SD = 16). The mean age for males was 50 years (SD = 16), and the mean age for females was 49 years (SD = 15). There were 139 (28.8%) HIV-positive patients included in the analysis, for whom CD4 count and viral load were not routinely tested.

The 4 most common cancers were oesophageal (n = 172; 34.5%), cervical (n = 109; 21.9%), Kaposi's sarcoma (n = 52; 10.4%), and breast cancer (n = 37; 7.4%). Other cancers included in the registry were: head and neck cancers (n = 22; 4.4%), bladder cancer (n = 20; 4.0%), other genitourinary cancers (n = 16; 3.2%), lymphoma (n = 13; 2.6%), gastrointestinal cancers (n = 10, 2.0%), eye cancer (n = 8; 1.6%), other gynaecologic cancers (n = 6; 1.2%), sarcoma (n = 6; 1.2%), other skin cancers (n = 5; 1.0%), and leukaemias (n = 5; 1.0%) (Table 1).

Patients with oesophageal cancer were likely to be older than 50 years (odds ratio, OR = 2.22), male (OR = 1.47), and tobacco smokers (OR = 2.02). Kaposi's sarcoma patients were more likely to be HIV-positive (OR = 54.4) and male (OR = 6.02). Cervical cancer patients were more likely to be HIV-positive (OR = 2.2).

Working diagnoses were documented for 498 of the 504 cases. Owing to the limited scale and availability of pathology services during the patient enrolment period, only 90 (18%) of the cases had histologically confirmed cancer diagnoses. Other diagnoses were made by clinical assessment. Most (96%) of the Kaposi's sarcoma cases were clinically diagnosed, except for the 4% of endemic Kaposi's sarcoma cases that were confirmed histologically. For cervical, breast, head and neck, and oesophageal cancers, clinical diagnoses were made in 91%, 81%, 82%, and 68% of cases, respectively. The highest proportion of histological diagnoses was among oesophageal cancers (32%).

Table 2: Common cancer types by age group among patients at Kamuzu Central Hospital, Lilongwe, between June 2009 and September 2012

Age group (years)	Oesophagus	Kaposi's sarcoma	Cervix	Breast	P-value
	n (%)	n (%)	n (%)	n (%)	(Fisher's exact)
< 25	6 (3.5)	3 (5.8)	4 (3.7)	2 (5.4)	
25 to 34	10 (5.8)	23 (44.2)	13 (11.9)	5 (13.8)	
35 to 44	28 (16.3)	15 (28.9)	34 (31.2)	11 (29.7)	0.004
45 to 54	39 (22.7)	6 (11.5)	28 (25.7)	10 (27.0)	
≥ 55	89 (51.7)	5 (9.6)	30 (27.5)	9 (24.3)	
Total	172	52	109	37	

Table 3: Smoking and alcohol consumption history by cancer type among patients at Kamuzu Central Hospital, Lilongwe, between June 2009 and September 2012

Variable	Oesophagus n (%)	Kaposi's sarcoma n (%)	Cervix n (%)	Breast n (%)
Tobacco use				
Never	101 (60.8)	33 (63.5)	102 (93.6)	35 (94.6)
Past and current	65 (39.2)	19 (36.5)	7 (6.4)	2 (5.4)
Alcohol use				
Never	111 (66.9)	28 (53.8)	103 (94.5)	35 (94.6)
Past and current	55 (33.1)	24 (46.2)	6 (5.5)	2 (5.4)
Total	166	52	109	37

Among patients with the 4 most common cancers (oesophageal, cervical, Kaposi's sarcoma, and breast), 64% were younger than 55 years of age, 26 % were either past or current smokers, and 24% were alcohol drinkers of any amount and any duration. The ages of oesophageal cancer patients ranged from 23 to 83 years, and 52% of them were older than 55 years. The majority of the Kaposi's sarcoma patients (79%) were under the age of 45. Seventy-two percent of cervical cancer patients and 76% of breast cancer patients were less than 55 years old.

Tobacco use was most common among oesophageal cancer and Kaposi's sarcoma patients, of whom 39% and 37% were smokers, respectively. For alcohol use, the highest prevalence (46%) was observed among patients with Kaposi's sarcoma, while 33% of oesophageal cancer patients were alcohol consumers. Most of the breast cancer (94%) and cervical cancer (95%) patients had no history of smoking or alcohol consumption (Table 3).

HIV status was documented in 482 (96%) of the 504 cases included in the analysis; 139 patients (28%) were documented as HIV-positive. Although oesophageal cancer was the most common cancer among those included in the analysis, patients with Kaposi's sarcoma were 54.4 times were more likely to be HIV-positive than those with cancer of oesophagus ($P \leq 0.001$). Of the cancer diagnoses among patients with HIV, 32% were Kaposi's sarcoma and 28% were cervical cancer. Patients with cervical cancer were 2.21 times more likely to be HIV-positive than those with cancer of oesophagus ($P = 0.009$). Patients with breast cancer were 1.73 times more likely to be HIV-positive than those with oesophageal cancer ($P = 0.231$). HIV-associated cancers (Kaposi's sarcoma, cervical cancer, and NHL) constituted 36% of all cancer diagnoses in the analysis. Ninety percent of Kaposi's sarcoma patients were HIV-positive, as were 27% of cervical cancer patients and 46% of lymphoma patients. Among HIV-positive individuals included in the study, 54% reported being on antiretroviral therapy (ART) and 24% were not on ART. ART status was undocumented for 22% of HIV-positive patients. Among HIV-positive patients with cervical cancer, Kaposi's sarcoma, and lymphoma, 60%, 45%, and 67% were on ART, respectively.

Discussion

The 4 commonest cancers among patients at KCH during the study period were cancer of the oesophagus, Kaposi's sarcoma, cervical cancer, and breast cancer—together contributing to more than 70% of all cancer cases in the study population. Cancer of the oesophagus alone comprised over one-third of the cases, followed by cervical cancer contributing to over one-fifth (21%) and then Kaposi's sarcoma and breast cancer. Among the females, cervical cancer was the commonest cancer contributing to more than one third (36.7%) of all cancers in females, followed by cancer of oesophagus, breast cancer, and Kaposi Sarcoma. Among males, oesophageal cancer was most common, accounting for 45% of cancer diagnoses in men.

The findings of this clinic-based study are similar to those of a recent analysis of data from a nationwide population-based Malawian cancer registry,[10] with oesophageal cancer, Kaposi's sarcoma, and cervical cancer being among the most common cancers in both analyses. In contrast to our findings, however, Kaposi's sarcoma (and not oesophageal cancer) was found to be the commonest diagnosis in the nationwide registry. This difference may be partly explained by the differences in study populations. Additionally, an

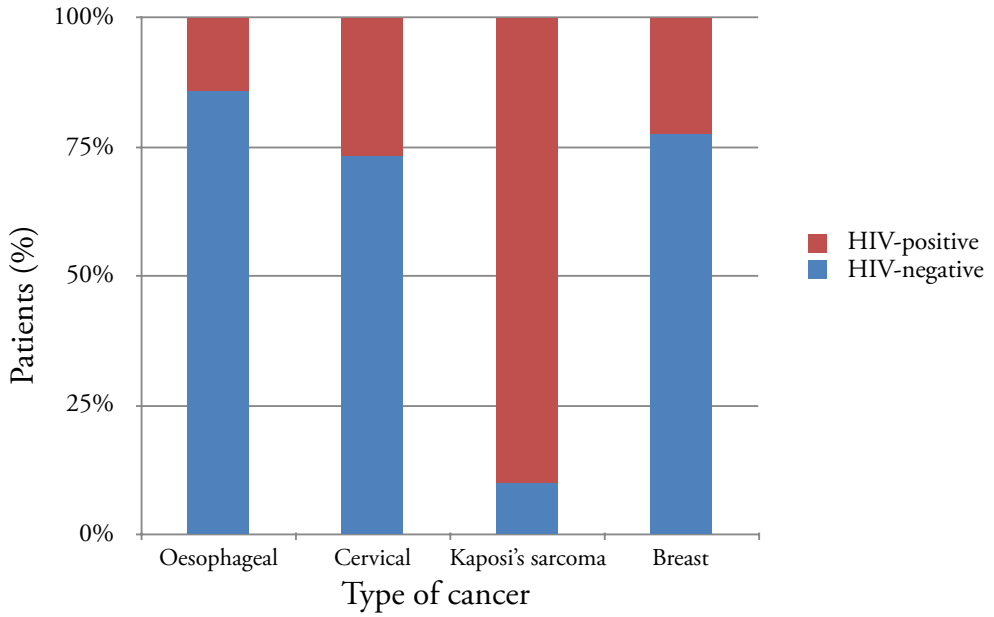

Figure 1: HIV status among patients diagnosed with common cancer types at Kamuzu Central Hospital between June 2009 and September 2012

oesophageal cancer study, which enrolled patients within the time period captured by our study, may have introduced a sampling bias in favour of including more oesophageal cancer patients in the KCH cancer registry during the period under investigation.

The high prevalence of oesophageal cancer in males may be attributable to the higher prevalence of smoking (39%) in our population, compared to 25.9% overall in Malawi.[26] Tobacco and alcohol consumption, known risk factors for the development of oesophageal cancer in many countries, have also been documented as important factors in Africa in studies conducted from the 1980s onward. The effect of increased alcohol and tobacco consumption on oesophageal cancer incidence in Africa has not been delineated. It is unclear why, for example, lung cancer (which has a well established association with smoking) was not commonly observed in our study population. It is also unclear why (with a mean age of 55 years among affected individuals) oesophageal cancer affects younger people in our study population than, for example, the United States, where the mean age at diagnosis of oesophageal cancer is 67 years.

HIV infection did not seem to be associated with cancer of the oesophagus in our study population. This is consistent with previous findings in other cohorts.[3,10,12,13]

Cancer of the cervix was classified as an AIDS-defining cancer by the U.S. Centers for Disease Control and Prevention as early as 1993.[43] HIV has been found to be associated with cervical cancer in case–control and cohort studies in South Africa and Uganda, with odds ratios between 1.6 and 2.4.[40] It is now recognised that most cervical cancer is caused by HPV. In our study, the odds of HIV infection among cervical cancer patients were not much different from the odds of HIV infection among breast cancer patients (OR of 2.2 vs 1.7), and were much lower than the odds among Kaposi's sarcoma patients (OR = 54). These associations differ from those found by other researchers.[4] The lower OR for cervical cancer (as compared to Kaposi's sarcoma) may suggest that increased incidence resulting from HIV infection may be less pronounced for cervical cancer than Kaposi's sarcoma. In this study, it may also be explained by the lack of histological diagnoses, which may have led to overestimation of cervical cancer cases by clinical misdiagnosis (among both HIV-positive and HIV-negative individuals). Our observation that cervical cancer was the commonest cancer among young nonsmoking females is consistent with findings by others in South Africa and Malawi.[10]

We observed that Kaposi's sarcoma was 3 times more common in the males than females and commoner in the younger individuals (less than 45 years of age), with half of the cases occurring in people less than 35 years of age. These findings regarding gender and age patterns are consistent with other studies.[28,29] The high Kaposi's sarcoma prevalence can be explained by the high HIV prevalence in this age group. We also observed that Kaposi's sarcoma was the commonest HIV-associated cancer in our study population. This is in agreement with findings from elsewhere that report that HIV infection increases the risk of Kaposi's sarcoma by 50- to 100-fold.[28] Three case–control studies from Africa showed increased Kaposi's sarcoma risk of 30- to 50-fold in association with HIV, rising to 1600-fold in HIV-positive individuals with high HHV8 antibody titres.[4,13] ART for treating HIV in adults has been reported to cause a decline in the incidence of Kaposi's sarcoma in Western countries.[43] In Malawi, data are needed to establish if this is true in our setting.

In this study, we have not determined whether the incidence of AIDS-defining cancers have decreased since the beginning of the ART scale-up, in 2005. The first reason for this is that we did not have prevalence data until 2012, and the second reason is that determination of incidence rates requires longitudinal studies or the use of population-based cancer registries, both of which require more time and resources than are normally available in our setting. The careful characterisation of incidence trends of HIV-associated malignancies would require the availability of comprehensive population-based cancer registry data, including careful determination and documentation of HIV status.

The main strength of this study lies in its comprehensive dataset, which is more extensive than what can usually be obtained from routine clinical data in our setting. The demographic characterisation of participants was comprehensive. However, diagnostic errors resulting from

the lack of pathological diagnostic capacity, may have led to errors in prevalence estimates, especially for cancers with wide differential diagnoses.

Conclusions

This study systematically described cancer burden, distribution, and risk factors at a central teaching hospital in Malawi. It has demonstrated that age, smoking, and HIV are important risk factors for some of the most common cancer types. Further research is required to confirm associations and to assess trends in cancer burden, as well as to evaluate the impact of ART on the incidences of all AIDS-defining cancers in Malawi.

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Competing interests

All authors declare that they have no competing interests related to this work.

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