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

Agnes Moses1,3,4, Albert Mwafongo1, Maria Chikasema1, Laureen Kafantenganji1, Christopher Stanely1, Emma Chimzukira1, Coxilly Kampani1, Robert Krysiak1, Satish Gopal1,2,3,4, Nora E. Rosenberg1,2, Carol G. Shores1,2, Mina C. Hosseinipour1,2,3

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. The aim of this study was to assess risk factors and distribution for common cancers at Kamuzu Central Hospital (KCH), in Lilongwe and to determine prevalence of the Human Immunodeficiency virus (HIV) infection, in the same population.

Methods
We analyzed data from the hospital-based KCH Cancer Registry from June 2009 to September 2012, including data from a nested sub-study on co-infections among cancer patients. Demographics and behavioral variables including smoking, 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 (SD=16) years. 343 (71.2%) were HIV-negative and 139 (28.8%) were HIV-positive. The common cancers were esophageal (172, 34.5%), cervical (109, 21.9%), Kaposi sarcoma (KS) (52, 10.4%). Only 18% of cancer cases were pathologically confirmed. Patients with esophageal cancer were likely to be >50 years (OR=2.22), male (OR=1.47) and smokers (OR=2.02). Kaposi Sarcoma patients had the highest (OR=54.4) odds of being HIV-positive, and were also more likely to be male (OR=6.02) and smokers (OR=2.7). Cervical cancer patients were more likely to be HIV-positive (OR 2.2) and less than 50 years of age.

Conclusions
The study describes cancer burden at a teaching hospital in Malawi, and demonstrates that age, smoking, and HIV are important risk factors for the three commonest cancer types. HIV is a single most important risk factor for Kaposi Sarcoma and cervical cancer.

Introduction
Cancer is the cause of 13% of total worldwide mortality, and the leading cause of death in the world according to the World Health Organization (WHO).1,2 In Africa, the top five cancers in males are Kaposi Sarcoma (KS) (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 Sarcoma (5-1%), cancer of the liver (5-0%), and NHL (3-7%) are the top five cancers.1-3 Environmental factors (such as tobacco use, alcohol, maize flour based diet, parasite and mold exposure), oncogenic viral infection (such as with hepatitis B, hepatitis C, Human Papilloma virus (HPV), or HIV) are known risk factors for development of cancers.11 With the increased prevalence of HIV and other infectious diseases in Africa compared to the developed world, 36% of cancers are thought to be infection-related, which 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 disorganized screening modalities, delayed diagnosis until advanced stage of disease, and limited treatment options.

In Malawi, cancer data are sparse but recent estimates from population based cancer registry show that the age-standardized incidence rate per 100,000 people for all types of cancer have increased, especially AIDS Defining Cancers.19 In males, the incidence increased from 31 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 Sarcoma, esophageal cancer, and cervical cancer were the main causes for the increased incidence. Malawi also has a high HIV prevalence rate, estimated to be 10.6% among adults aged between 15 and 49. Malawi has also seen an increase in antiretroviral therapy (ART) coverage from 4% in 2004 to 76% in June 2011. The high incidence of HIV may partially explain high incidence of Kaposi Sarcoma and Cervical Cancer.17 In contrast, HIV infection does not seem to confer increased risks of breast, esophageal, prostate, or many other common types of cancer. To our knowledge, these factors have not been fully explored in our local setting.

Methods

Patients and procedures
This is a retrospective descriptive analysis of data collected on patients enrolled into Cancer and Comorbid infections (CANCO) study at Kamuzu Central Hospital (KCH) from June 2009 to September 2012. KCH is a 1250-bed referral hospital which serves about 5 million people annually. It
also 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 KCH cancer registry which sought to assess comorbid infections in cancer patients. Inclusion criteria for CANCO were; adult patients 18 years or older, presenting to a KCH wards or clinics with clinically suspected or histologically confirmed diagnosis of cancer at any site, had not received any treatment (chemotherapy, surgery, or radiotherapy) more than 4 weeks prior to enrollment. Cancer cases were identified by data clerks through daily review of departmental registers as well as weekly attendance at specialty clinics. Demographic and behavioral variables like smoking and alcohol use were collected through personal interviews with patients by study physicians and nurses, using a structured questionnaire administered to eligible participants. Clinical assessments of participants included tumor measurements in the three longest dimensions, using a tape measure. Tumors not apparent on physical exam were evaluated by radiological device (ultrasound and x-ray, or occasionally CT scan, or Magnetic Resonance Imaging).

Performance status using Karnofsky Performance Scale was determined. Diagnostic testing of HIV, CD4 count, Hepatitis B, schistosomiasis Ova in urine and stool, malaria thick film, were done 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 excel. Baseline characteristics were summarized using numbers with percentages or means with standard deviations (SD). We compared differences in distribution between each risk factor variable with cancer site and stage using Fischer’s exact test. We estimated the odds of being HIV positive with a particular cancer diagnosis using logistic regression model to assess risk factors for common types of cancer. We considered a p value of < 0.05 as significant. All analyses were performed using STATA SE version 12.1 (Stata Corp., College Station, TX)

**Ethical approval**

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

**Results**

Overall, 1453 cancer cases were recorded into KCH cancer Registry data base from June 2009 to September 2012. The participants were referred from 6 hospital departments; medicine, surgery, obstetrics and gynecology, eye and dentistry. Data from 504 registered cancer patients, who were enrolled into the CANCO study, were included. Three hundred (59.5%) were female and two hundred and four (40.5%) were male. The mean age was 49 years (SD =16). The mean age for males was 50 years (SD = 16). The mean age for females was 49 years (SD = 15). 139 (28.8%) were HIV-positive. CD4 count and viral load were not routinely tested.

The four most common cancers were esophageal (172, 34.5%), cervical (109, 21.9%), Kaposi Sarcoma (KS) (52, 10.4%) and breast cancer (37, 7.4%). The rest of the distribution was: head and neck cancers (22, 4.4%), bladder cancer (20,4.0%), other genitourinary cancers (16,3.2%), lymphoma (13, 2.6%), gastrointestinal cancers (10, 2.0%), eye cancer (8, 1.6%), other gynecology cancers (6, 1.2%), Sarcoma (6, 1.2%) and other skin cancers comprised (5, 1.0%), and leukemia’s comprised (5, 1.0%) (Table 1).

At 95% Confidence Interval, Patients with esophageal cancer were likely to be > 50 years (OR = 2.22), male (OR = 1.47) and smoker (OR = 2.02). Kaposi 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).

Of the 504 cases, 498 had a working diagnosis either clinical or histological. Only 90 (18%) of the cases with working diagnosis of either clinical or histological had histologically confirmed cancer diagnosis due to limited pathology services at the time of the study. Clinical diagnosis was by clinical assessment or anatomical site. Most (96%) of Kaposi’s sarcoma cases were clinically diagnosed, except for the 4% of endemic Kaposi’s sarcoma cases that had a confirmed histology. For cervical, breast, head and neck and esophageal cancer clinical diagnoses were 91%, 81%, 82% and 68% respectively. Esophageal cancer had the most cases with histological diagnosis (32%).

Among patients with the four (esophageal, cervical, Kaposi’s sarcoma and breast) common cancers, 64% were under the age of 55 years, 26% were either past or current smokers, and 24% were alcohol drinkers of any amount and any duration. 52% of the patients with cancer of esophagus were over 55 year of age with age range of 23 to 83. Majority of the Kaposi Sarcomas patients, (7%) were under the age of 45. Seventy-two percent of cervical cancer patients and 76% of breast cancer patients were under 55 years. The tobacco and alcohol history were self-reported by participants and were not quantified.

The esophageal cancer, patients had the highest proportion

---

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

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophageal</td>
<td>172</td>
<td>92</td>
<td>80</td>
</tr>
<tr>
<td>Cervical</td>
<td>109</td>
<td>0</td>
<td>109</td>
</tr>
<tr>
<td>Kaposi Sarcoma</td>
<td>52</td>
<td>40</td>
<td>12</td>
</tr>
<tr>
<td>Breast</td>
<td>37</td>
<td>0</td>
<td>37</td>
</tr>
<tr>
<td>Head and neck</td>
<td>22</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Bladder</td>
<td>20</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Other genitourinary</td>
<td>16</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>13</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>10</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Eye</td>
<td>8</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Other gynaecologic</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Other skin</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>17</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Missing</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>504</td>
<td>204</td>
<td>300</td>
</tr>
</tbody>
</table>
Table 2: Common cancer types by age group among female patients at Kamuzu Central Hospital, Lilongwe, between June 2009 and September 2012

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

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Oesophagus n (%)</th>
<th>Kaposi’s sarcoma n (%)</th>
<th>Cervix n (%)</th>
<th>Breast n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>101 (60.8)</td>
<td>33 (63.5)</td>
<td>102 (93.6)</td>
<td>35 (94.6)</td>
</tr>
<tr>
<td>Past and current</td>
<td>65 (39.2)</td>
<td>19 (36.5)</td>
<td>7 (6.4)</td>
<td>2 (5.4)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>111 (66.9)</td>
<td>28 (53.8)</td>
<td>102 (94.4)</td>
<td>35 (94.6)</td>
</tr>
<tr>
<td>Past and current</td>
<td>55 (33.1)</td>
<td>24 (46.2)</td>
<td>7 (5.6)</td>
<td>2 (5.4)</td>
</tr>
<tr>
<td>Total</td>
<td>166</td>
<td>52</td>
<td>109</td>
<td>37</td>
</tr>
</tbody>
</table>

Discussion

We observed that the four commonest cancers amongst the patients were cancer of the esophagus, Kaposi Sarcoma, cervical cancer and breast cancer together contributing to more than seventy percent of all cancer cases in the study population. Cancer of the esophagus 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 esophagus, breast cancer, and Kaposi Sarcoma. Among the males, the commonest cancer was cancer of Esophagus, contributing to 45% of all cancers in males.

This observation in this clinic-based study is in agreement with recent analysis of population based cancer registry done here in Malawi10 regarding cancer of esophagus, Kaposi Sarcoma and cervical cancer being among the three commonest cancers in Malawi. There is a notable difference in the order of frequency ranking, Kaposi Sarcoma was ranked as the commonest in the aforementioned analysis while in our study esophageal cancer was the commonest. This difference may be partially explained by the differences in study population; population based cancer registry versus hospital based registry. It could also be explained by recruitment bias. There was increased awareness by the esophageal cancer patients of the Esophageal Cancer study that was recruiting patients at the same time this study was going on.

The high prevalence of esophageal cancer in males may be attributed to the elevated 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 esophageal cancer in many countries, have also been documented as important factors in Africa in studies conducted from the 1980s onward. The net effect of increasing commercial alcohol consumption, combined
with increases in some places of tobacco consumption, on esophageal cancer trends is to date unclear. It is surprising and unknown why other cancers reported to be associated with smoking, like lung cancer, was not commonly observed in our study population. It is also unclear why esophageal cancer is occurring at a relatively younger age with mean age of 55 years, much younger than that observed in the Western world, where a mean age at diagnosis of 67 years in the United States.

HIV infection did not seem to be associated with cancer of esophagus in our study population as shown in Table 4 and 5. This is consistent with previous findings in other cohorts. 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. HIV was 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. It is now recognized that HPV constitutes the necessary cause of cervical cancer. In our study the odds of having HIV infection for cervical cancer patient was not very different from breast cancer patient (2.21 vs. 1.7), and was much lower than the odds for Kaposi Sarcoma patients (54). This association is different from what other researchers found. The lower OR as compared to Kaposi Sarcoma (OR 54 vs. 2.2) may suggest that incremental cases due to HIV infection may be less in cervical cancer than Kaposi Sarcoma. In this study, it can also be explained by the lack of histological diagnosis, which may have led to overestimation of cervical cancer cases by clinical misdiagnosis. Our observation that cervical cancer was the commonest cancer among young non-smoking females is consistent with findings by others in South Africa and Malawi.

Regarding Kaposi Sarcoma, we observed that Kaposi Sarcoma was three times more common in the males than females and commoner in the younger age group (less than 45 years), with half of the cases occurring in people less than 35 years of age. These findings regarding gender and age pattern are consistent with other studies. This finding can be explained by the high HIV prevalence in this age group. We also observed that Kaposi Sarcoma was the commonest HIV associated cancer in our study population occurring with odds ratio as high as 54. It is in agreement with findings that HIV infection increases risk of Kaposi Sarcoma by 50 to 100 fold. Three case–control studies from Africa showed increased risks of 30 to 50 fold in association with HIV, rising to 1600 fold in HIV-positive individuals with high HHV8 antibody titers. Antiretroviral therapy for treating HIV in adults has been reported to cause a decline in the incidence of Kaposi's sarcoma in Western countries. In Malawi, data are needed to establish if this is true in our local setting.

In this study, we have not determined whether the incidence of AIDS-defining Cancers have decreased since the ART scale up, in 2005, firstly because we did not have prevalence data until recently in 2012. The second reason is that determination of incidence rates requires longitudinal studies or use of population based cancer registry, both of which require a lot more time and resources to do. The careful characterization of trends in the incidence of HIV-associated malignancies would require availability of comprehensive population based cancer registry data and careful determination and documentation of HIV status. This study’s strength is in its more comprehensive diagnostic data than is available in routine settings. The demographic characterisation of participants was comprehensive. The lack of histological diagnosis provided room for potential errors in diagnosis and eventually errors in estimates especially for cancers with wide differential diagnoses.

Conclusions
The study has systematically described cancer burden, distribution and risk factors at a central teaching hospital in Malawi. It has confirmed 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 over time and evaluate the impact of antiretroviral therapy on incidence of all AIDS defining Cancers in Malawi.

Acknowledgements
This work is supported by UNC PROJECT, Malawi a collaborative health partner of Kamuzu Central Hospital, through support from the Lineberger Comprehensive Cancer Center.
Cancer Center. We acknowledge the contribution of KCH staff, Elizabeth Bigger, Mike Owino, and Wiza Kumwenda for developing Kamuzu Central Hospital Cancer registry. Special acknowledgement to the Principal Investigator for Cancer registry development grant, Prof. Carol Shores for her mentorship.

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

References


