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RESEARCH ARTICLE

REVISED Burden of cancer in Kenya: types, infection-attributable and trends. A national referral hospital retrospective survey [version 2; referees: 2 not approved]

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Abstract

Background: Cancer in Africa is an emerging health problem. In Kenya it ranks third as a cause of death after infectious and cardiovascular diseases. Nearly 31% of the total cancer burden in sub-Saharan Africa is attributable to infectious agents. Information on cancer burden is scanty in Kenya and this study aimed to provide comprehensive hospital based data to inform policies.
Method: A cross-sectional retrospective survey was conducted at Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH) from 2008 to 2012. Data was obtained from the patients files and the study was approved by the KNH/University of Nairobi and MTRH Ethics and Research Committees.
Results: In KNH, the top five cancers were: cervical (62, 12.4%), breast (59, 11.8%), colorectal (31, 6.2%), chronic leukemia (27, 5.4%) and stomach cancer 26 (5.2%). Some 154 (30.8%) of these cancers were associated with infectious agents, while an estimated 138 (27.6%) were attributable to infections. Cancers of the cervix (62, 12.4%), stomach (26, 5.2%) and nasopharynx (17, 3.4%) were the commonest infection-associated cancers. In MTRH, the five common types of cancers were Kaposi's sarcoma (93, 18.6%), breast (77, 15.4%), cervical (41, 8.2%), non-Hodgkin's lymphoma (37, 7.4%) and colorectal, chronic leukemia and esophageal cancer all with 27 (5.4%). Some 241 (48.2%) of these cancers were associated with infectious agents, while an estimated 222 (44.4%) were attributable to infections. Kaposi's sarcoma (93, 18.6%), cancer of the cervix (41, 8.2%) and non-Hodgkin's lymphoma (37, 7.4%) were the commonest infection-associated cancers.
Conclusion: Our results suggest that 30.8% and 48.2% of the total cancer cases sampled in KNH and MTRH respectively were associated with infectious agents, while 27.6% and 44.4% were attributable to infections in the two hospitals respectively. Reducing the burden of infection-attributable cancers can translate to a reduction of the overall cancer burden.

Keywords
Cancer burden, infectious agents, sub-Saharan Africa, Kenya

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> **REVISED** **Amendments from Version 1**
>
> We have performed major revision in the new manuscript taking all suggestions from the reviewers into account. We have applied the PAF/AF standard formula of calculating the cancers attributable to infections. We have updated the methodology section and ensured that the results or tables are listed according to the third edition of the International Classification of Diseases for Oncology (ICD-O). We have only reported the results as generated from the data from the two hospitals and highlighted where necessary that we were comparing our hospital-based data with other population-based studies. We have inserted a new paragraph in the new manuscript highlighting the limitations of this study.
>
> We are thankful to the reviewers for their suggestions.
>
> **See referee reports**

Background

Cancer in Africa is an emerging health problem where about 847,000 new cancer cases and 591,000 deaths occurred in 2012, with about three quarters of these occurring in the sub-Saharan region[1]. In Kenya, cancer ranks third as a cause of death, after infectious and cardiovascular diseases, and in 2012 there was an estimated 37,000 new cancer cases, and 28,500 cancer deaths reported[2]. Infectious agents are an important cause of cancer, particularly in less developed countries. According to the International Agency for Research on Cancer (IARC), 11 infectious agents have been classified and established as carcinogenic agents in humans namely: *Helicobacter pylori*, hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus type 1 (HIV-1), human papillomavirus (HPV), Epstein-Barr virus (EBV), human herpes virus type 8 (HHV-8; also known as Kaposi's sarcoma herpes virus), human T-cell lymphotropic virus type 1 (HTLV-1), *Opisthorchis viverrini*, *Clonorchis sinensis*, and *Schistosoma haematobium*[3].

Nearly 31% of the total cancer burden in sub-Saharan Africa is attributable to infections[4]. Specifically, *H. pylori*, HPV, HBV, and HCV are the leading infectious agents contributing to the global cancer burden. When summed together they account for 92% of all infection-attributable cancers worldwide with 35.4%, 29.5%, 19.2%, and 7.8% respectively[4]. The rise of the HIV epidemic concentrated in low and middle-income countries has resulted to an increase in HIV-associated malignancies[5]. In Kenya, a HIV prevalence of 5.6% (95% CI: 4.9 to 6.3), and HIV incidence of 0.5% (95% CI: 0.2 to 0.9), corresponding to an annual HIV transmission rate of 8.9 per 100 HIV-infected persons has been reported[6]. This population is at greater risk of acquiring HIV associated cancers such as Kaposi's sarcoma (KS), non-Hodgkin lymphoma (NHL) and invasive cancer of the cervix (ICC)[7]. According to a recent study, KS was the second largest contributor to the cancer burden in sub-Saharan Africa[4], while NHL is the second most common malignant disorder associated with HIV infection worldwide[7]. Previous studies done in Africa have been discussed in details in the methodology section.

Information on the burden of cancer and especially the burden attributable to infections is sparse in Kenya. In this study, we highlight the results from two national referral hospitals in Kenya for five-year period between 2008–2012.

Methods

This was a retrospective cross-sectional study conducted at Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH) in Kenya. Initially the study targeted four teaching and referral hospitals located in the former Nairobi, Rift Valley, Coast and Nyanza Provinces, but the authorization to access medical records was only granted by the above mentioned hospitals. Kenya was divided into eight provinces (see map from the Kenya bureau of statistics[8]) before the new constitution of Kenya that came into force in 2013. KNH is located in the former Nairobi Province which is the capital and the largest city of Kenya and according to the last official census taken in 2009 it had a population of 3,138,369 whose number has since grown to approximately 3.5 million people. MTRH is located in the former Rift Valley Province (Kenya's largest Province) with a population of 10,006,805[8]. According to the Kenyan network of cancer organizations KNH and MTRH are amongst the oldest and largest public referral hospitals with cancer treatment services. The two national hospitals are also the largest source of data for the two main cancer registries in Kenya. KNH provides data to the Nairobi cancer registry located in Nairobi while MTRH provides data to the Eldoret cancer registry located in Rift Valley. Recently, with an aim to decongest the national hospitals more (private, mission and public) health facilities have been equipped with the cancer services. However, because of the affordability of the services many patients opt for the public health facilities.

Data source

Data for this study was obtained from hospital records of patients as this was the most convenient data source for all the information targeted.

Inclusion criteria

- Hospital records of patients diagnosed with cancer during the period 2008 to 2012.

- Records of patients above the age of 18 at the time of diagnosis and with a confirmed diagnosis either by histology, radiology or haematology.

Exclusion criteria

- Hospital records with incomplete data or not meeting the above criteria.

Sample size calculation

The sample size (n) was calculated according to the guidelines outlined for calculating sample sizes for cross-sectional studies (qualitative variable) as explained by 9–11 and as shown below;

$$n = \frac{z^2 \hat{p}(1-\hat{p})}{d^2}$$

Where:

p = Prevalence of condition or health state or the expected prevalence or proportion or estimated proportion of a disease

d = degree of precision of the estimate or the absolute error

z = Z statistic for a level of confidence or is the normal distribution critical value for a probability of $\alpha/2$ in each tail. For a 95% CI, z=1.96. A 95% level of confidence and a ±5% (0.05) degree of precision were considered.

The prevalence of cancer in Kenya was not known at the time of the study and therefore a prevalence of 50% (0.5) was used in calculating the sample size. Elsewhere, it has been highlighted that when d =0.05 and a z=1.96, using a p of 0.5 (50%) yields the highest estimates for n (sample size)[12].

Therefore,

$$n = \frac{1.96^2 * 0.5(1 - 0.5)}{0.05^2}$$

$$n = 384$$

A sample size of 384 was estimated as the minimal necessary to achieve the required power of the study. However, a 30% (116) non-response allowance was factored in resulting to a final sample size of 500. In KNH an estimated 17,584 (inpatient and outpatient) cancer files were reported while in MTRH 4304 (inpatient) cancer cases were reported during the five year period. Due to cost and time constraints, it was only feasible to study 500 files as calculated from the sample size. To obtain the final number of 500 files from the totals in each hospital, a proportional stratified sampling method was used as described by 10. (see Table 1)

$N_1 = 3168; N_2 = 2834; N_3 = 3048; N_4 = 4161; N_5 = 4373$

so $N = \sum_{i=1}^{5} N_i = 17.584$

and $n_1 = 90; n_2 = 80; n_3 = 85; n_4 = 120; n_5 = 125$

so $n = \sum_{i=1}^{5} n_i = 500.$

To randomly select the calculated proportions of files for each year obtained in the previous step, a systematic random sampling method was used as described by 10. At KNH, the files were all available at the health information department, and in the databases where systematic random sampling was an automated

process. At the time of data collection, MTRH was in the process of updating the database and only 2012 files were available at the health information department. The files for 2008 to 2011 were obtained from the oncology centre at the Academic Model for the Prevention and Treatment of HIV/AIDS (AMPATH), and convenient sampling was used to achieve the required number of files.

Data collection
A pre-designed questionnaire was used to abstract the information (Supplementary File 1). The information abstracted from the files included patients age, sex, origin, type of cancer, method of cancer diagnosis, year of diagnosis and whether the patient was referred from another hospital.

Ethical consideration
The study was approved by the Kenyatta National Hospital/ University of Nairobi (KNH/UoN-ERC) and the Moi Teaching and Referral Hospital (IREC/MTRH) Ethics and Research Committees with approval numbers P24/01/2013 and FAN:IREC 1027 respectively. Endorsement for the study was obtained from the Director of Medical Services while the permission to access data from the hospital databases and patients files was obtained from the director of the Health Information Department. Although, the study aimed at conducting the research at four referral hospitals in Kenya, only two hospitals granted permission to access the patient files while the other two refused and the reasons for refusal were unknown. The study was a minimal risk study and patient consent was not sought since there was no direct patient involvement but a retrospective review of patients' files. However, the patient identifying information was not included in the data collection forms.

Data handling and analysis
Data was entered into statistical package for social sciences programme (IBM-SPSS) version 23 that was labeled using the exact fields as the questionnaires and the excel files. Quality control checks were performed to prevent double entry and to ensure accurate entry of the data. The proportions of cancer cases were analyzed with reference to the study site, sex and the age group. GraphPad Prism 6 (GraphPad Software Inc., San Diego, CA, USA) was used to draw the figure images. The cancers were listed according to the third edition of the International Classification of Diseases for Oncology (ICD-O).

Table 1. Sample calculations for Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH).

	KNH			MTRH		
Year	Estimated Files (N)	Sampling fraction	Final sample size (Proportion)	Estimated Files (N)	Sampling fraction	Final sample size (Proportion)
2008	3168	18%	90	947	22%	110
2009	2834	16%	80	1325	31%	154
2010	3048	17%	85	489	11%	57
2011	4161	24%	120	732	17%	85
2012	4373	25%	125	811	19%	94
Total	**17,584**	**100%**	**500**	**4,304**	**100%**	**500**

For cancers like BL (9687/3), HL (9650/3), NHL (9596/3), adult T-cell leukemia (9827/3), KS (9140/3), acute leukemia (9835/3 & 9861/3), chronic leukemia (9863/3 & 9823/3) and multiple myeloma (9732/3) where ICD-0-3 topographical code was not clear, we converted the IDC-0-3 morphological code to ICD10 topographical code for clarity.

Although many studies have shown a variety of cancers associated with infectious agents, the attributable fraction (AF) standard formula was applied to a group of cancers classified as carcinogenic in the IARC monograph 100b[3] namely; cervix (C53), liver (C22.0), stomach (C16), Kaposi's sarcoma (C46), non-Hodgkin's lymphoma (C82-85, C96), Hodgkin's lymphoma (C81), nasopharynx (C11), oropharynx (C10), bladder (C67), vulva (C51), vagina (C52), penis (C60), anus (C21) and bile duct (C22.1). Calculation of the attributable fraction (AF) relies upon the standard formula for population attributable risk as shown by 13,14:

$$AF = p(r-1) / [p(r-1)+1]$$

Where:

p=prevalence of exposure to the infectious agents to the population

r=relative risk of exposure

However, the use of this formula requires prior knowledge on p and r as defined above and since this information is limited in Kenya, we used AF derived from other studies done elsewhere either in developing countries, sub-Saharan Africa, or world estimates that used data from developing countries. The formula results in a proportion that is applied to the total number of cases in the target population to obtain the number of cases that can theoretically be attributed to the factor in that population[13].

In determining AF estimates for cervical cancer, we identified other African studies that reported the prevalence of HPV in cervical cancer to be between 76% to 91%[15–17]. However, an AF of 100% was used for this study since the causality of HPV in cervical cancer is generally known[4,18,19]. For vulvar cancer, studies from Botswana reported a HPV prevalence of 56.8 to 100%[20,21], but an AF of 40% derived from developing countries estimates was used[13]. We did not find any clear study showing the prevalence of HPV in vaginal cancers in sub-Saharan Africa, but an AF of 78% derived from world estimates was used[4,19]. Studies from Central African Republic and Botswana identified a prevalence of HPV in anal cancer to be 69.1%[20,22], but a world estimate AF of 88% was used[4,19]. The prevalence of HPV in penile cancer has been shown to be 41.9% to 68% from Kenya and Botswana studies[20,23] but a world estimate AF of 50% was used[4,19]. A study from South Africa showed the prevalence of HPV in oropharyngeal cancer to be 5.6% among men (N=125)[24], while another from Ghana found a HPV prevalence of 13.8% (4 of 29) from the oral cavity, and 18.2% (2 of 11) from the pharynx[25], but an AF of 30.8% derived from world estimate was used[4,19] (Table 2).

Table 2. Previous prevalence studies on infectious agents and cancers.

Infectious agent	Cancer Site	ICD-0 code	Studies done in sub Saharan Africa	Prevalence of the infectious agent (%)	AF estimates used for this study (%)
HPV	Cervix uteri	C53	South Africa, Gabon[15–17]	76–91	100[4,18,19]
	Vulva	C51	Botswana[20,21]	57–100	40[13]
	Vagina	C52	-	-	78[4,19]
	Anus	C21	Central African Republic, Botswana[20,22]	69	88[4,19]
	Oropharynx	C10	South Africa, Ghana[24,25]	6–18	31[4,19]
	Penis	C60	Kenya, Botswana[20,23]	42–68	50[4,19]
HHV8/HIV	KS	**C46**	Kenya[26]	50–64	100[4,7,19]
EBV	HL	**C81**	Kenya,Zambia, Malawi[27–29]	41–100	74[4]
	Nasopharynx	C11	-	-	96[4]
EBV/HIV	NHL	**C82-C85, C96**	Zambia[27]	55	100[13,14]
HBV/HCV	Liver	C22.0	Gambia[30]	70	71[31]
H. pylori	Stomach	C16	Nigeria, Uganda[32,33]	82–86	89[4]
Schistosoma	Bladder	C67	South Africa[34]	10–85	41[4]
O. viverrini C. sinensis	Bile duct	C22.1	-		-

Helicobacter pylori (H. pylori), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus type 1 (HIV-1), human papillomavirus (HPV), Epstein-Barr virus (EBV), human herpes virus type 8 (HHV-8), human T-cell lymphotropic virus type 1 (HTLV-1), Opisthorchis viverrini, Clonorchis sinensis, Schistosoma haematobium, non-Hodgkin's lymphoma (NHL), Kaposi's sarcoma (KS), Hodgkin's lymphoma (HL)

AF=attributable fraction, - = not available or not obtainable

In determining AF estimates for KS, a study from Western Kenya found a Kaposi´s sarcoma-associated herpes virus (KSHV) positivity of 50.1 to 63.5% using 228 surgical cases[26] but a world estimate AF of 100% was used since HHV8 is recognized as a necessary cause of KS in HIV infections[4,7]. For EBV in NHL, A study from Lusaka, Zambia, detected EBV in 54.5% of the cases[27]. We used an estimated AF of 100% based on meta-analysis studies from developing countries[13,14]. Elsewhere in Malawi, EBV in HL was present in 18 of 24 (75%) tumor specimens, including 14 of 20 (70%) HIV- and 4 of 4 (100%) HIV+[28]. Similarly a study from Kenya found an EBV in HL positivity of 100% present in pediatric cases[27] while Zambia, detected EBV in HL of 40.9%[26]. However, an AF of 74% derived from African estimates was used[4]. No studies were encountered showing the prevalence of EBV in nasopharyngeal cancer in sub-Saharan Africa, therefore an AF of 95.5% derived from world estimates was used[4].

A study aiming to study the prevalence of HBV/HCV in hepatocellular carcinoma (HCC) patients in Gambia found that HBV carriage was present in 61% (129/211) of HCC while HCV present in 19% (36/191) of HCC patients[30]. An AF of 50% for HBV and 21% for HCV obtained from sub-Saharan estimates was used[31]. A study aiming to study the prevalence of *H. pylori* in Kano, Nigeria found a prevalence of 81.7%[32] while in Uganda 18 of the 21 cases of stomach cancer had *H.pylori*[33]. However, an AF of 89% derived from world estimates was used[4] (Table 2).

In South Africa, ova of *Schistosoma haematobium* were seen in microscopic sections of bladder tumours in 85% of the patients with squamous cell carcinoma, in 50% of those with undifferentiated tumours and adenocarcinoma, in 17% of those with mixed tumours or sarcoma, and in only 10% of the patients with transitional cell carcinoma (all classifications of the bladder tumours)[34]. However, an AF of 41% was used derived from endemic areas in Africa[4].

We did not come across any studies in Africa showing the prevalence of *Opisthorchis viverrini* and *Clonorchis sinensis* in cancer of the bile duct. Similarly the AF could not be obtained. Burkitt's lymphoma (BL) was first described in Eastern Africa where the highest incidence and mortality rates are seen. It has been associated with EBV and affects mainly children, where boys are more susceptible than girls[35]. However, we did not come across any cases of BL or Adult T-cell leukaemia/lymphoma (ATLL) from our study.

Results
Demographics
An estimated total of 17,584 and 4304 cancer files were recorded in the KNH and MTRH respectively from 2008 to 2012. For the purpose of this study data was only obtained from 500 randomly selected files per hospital. In KNH, 60% of these were females while 40% were males with a mean age of 50.57 (18 to 95 years), giving a male to female (M:F) ratio of 1:1.5. In MTRH, 56% were females while 44% were males with a mean age of 48 years (18 to 90 years) giving a M:F ratio of 1:1.2. More than 70% of patients were within the age group of 25 to 64 years in both hospitals,

largest age group being 45 to 64 years (43.4%) in KNH, and 25 to 44 years (39.4%) in MTRH. By Province, most KNH patients were from Central, Eastern and Western, (44%, 24.8% and 10.2% respectively), with specific regions being Muranga, Kiambu, Machakos, Nyeri and Kisii (11.2%, 10.2%, 8%, 8% and 5.4% respectively) with 66% of these patients being referred from other hospitals. On the other hand, most MTRH cancer patients were from the Rift valley, Western and Nyanza Provinces with 66.8%, 24.8% and 6.4% respectively with specific highest regions being Uasin Gishu, Nandi, Lugari, Trans Nzoia and Bungoma (22.8%, 8.4%, 8.4%, 7.4% and 6% respectively). 41% of these cancer cases were referrals from other hospitals (Table 3).

Types of cancers
In KNH (n=500), the top five types of cancers were: cervical (62, 12.4%), breast (59, 11.8%), colorectal (31, 6.2%), chronic leukemia (27, 5.4%) and stomach cancers with 26 (5.2%). In females (n=300) the five most common cancers were cervical (62, 20.7%), breast (59, 19.7%), ovarian (22, 7.3%), chronic leukemia (16, 5.3%), and endometrial and stomach cancers both with 15 (5%). In males (n=200) the five most common types of cancers were prostate (23, 11.5%), laryngeal (19, 9.5%), colorectal (17, 8.5%), esophageal (14, 7.0%) and nasopharyngeal cancers with 12 (6.0%). In MTRH (n=500), the five most common types of cancer were Kaposi's sarcoma (93, 18.6%), breast (77, 15.4%), cervical (41, 8.2%), non-Hodgkin's lymphoma (37, 7.4%) and colorectal, chronic leukemia and esophagus cancer all with 27 (5.4%). In females (n=282) the five most common types of cancers were breast cancer (74, 26.2%), cervical (41, 14.5%), Kaposi's sarcoma (38, 13.5%), non-Hodgkin's lymphoma (15, 5.3%) and ovarian cancer with 14 (5%). In males (n=218) the five most common types of cancers were Kaposi's sarcoma 55(25.2%), non-Hodgkin's lymphoma 22(10.1%), chronic leukemia 17(7.8%), colorectal and esophageal cancer both with 16 (17.3%) (Table 4 and Figure 1).

Cancer cases by age groups
From the results generated from both hospitals, it was suggestive that some cancers were predominant in specific age groups. Acute leukemia, NHL, cancer of the bone, genitalia, HL and nasopharyngeal were predominant in the age group of 24 years and below. Cancer of the cervix was predominant in the age group of 22 to 44 years while breast and bile duct cancers were predominant between 45 to 64 years. The age-group of 65 to 84 years was predominated by esophagus, prostrate, larynx, endometrium and lip and oral cavity cancers. A larger age group ranging from 45 to 65 years was predominated by colorectal, stomach, ovary, lung and bronchus, liver, bladder and multiple myeloma cancers (Table 5 and Table 6). This information is particularly important for estimating the age to go for the cancer checkups.

Infection-attributable cancers
The cancers listed here are cancers associated with the 11 infectious agents as classified and established by the International Agency for Research on Cancer (IARC). In KNH, 154 (30.8%) of the total cancers sampled were associated with infectious agents, while an estimated 138 (27.6%) were attributable

Table 3. Cancer cases by age groups, gender, method of cancer diagnosis, region and referral information in KNH/MTRH: 2008–2012.

Site	KNH						MTRH					
Year	08	09	10	11	12	All	08	09	10	11	12	All
Age groups												
≤24	5	4	6	9	7	31	8	11	4	2	3	28
%	5.6	5	7.1	7.5	5.6	6.2	7.3	7.1	7	2.4	3.2	5.6
25-44	30	22	24	34	39	149	42	70	20	35	30	197
%	33.3	27.5	28.2	>28.3	31.2	29.8	38.2	45.5	35.1	41.2	31.9	39.4
45-64	35	35	36	52	59	217	45	50	21	34	39	189
%	33.9	43.8	42.4	43.3	47.2	43.4	40.9	32.5	36.8	40	41.5	37.8
65-85	19	18	18	25	18	98	15	21	10	14	17	77
%	21.1	22.5	21.2	20.8	14.4	19.6	13.6	13.6	17.5	16.5	18.1	15.4
≥85	1	1	1	0	2	5	0	2	2	0	5	9
%	1.1	1.3	1.2	0	1.6	1	0	1.3	3.5	0	5.3	1.8
Total	90	80	85	120	125	500	110	154	57	85	94	500
%	100	100	100	100	100	100	100	100	100	100	100	100
Gender												
Male	39	37	33	51	40	200	50	74	17	25	52	218
%	43	46.3	38.8	42.5	32	40	45.5	48.1	29.8	29.4	55.3	43.6
Female	51	43	52	69	85	300	60	80	40	60	42	282
%	56.7	53.7	61.2	57.5	68	60	54.5	51.9	70.2	70.6	44.7	56.4
Total	90	80	85	120	125	500	110	154	57	85	94	500
%	100	100	100	100	100	100	100	100	100	100	100	100
Method of Cancer Diagnosis												
Radiology	61	68	63	95	107	394	7	12	20	28	84	151
%	67.8	85	74.1	79.2	85.6	78.8	6.4	7.8	35.1	32.9	89.4	30.2
Biopsy	90	80	85	120	125	500	110	154	57	85	94	500
%	100	100	100	100	100	100	100	100	100	100	100	100
Cancer Cases by Province												
Central	40	30	37	57	56	220	1	1	1	3	1	7
%	44.4	37.5	43.5	47.5	44.8	44	0.9	0.6	1.8	3.5	1.1	1.4
Coast	2	1	1	0	2	6	0	0	0	0	0	0
%	2.2	1.3	1.2	0	1.6	1.2	0	0	0	0	0	0
Eastern	24	22	22	30	26	124	0	0	0	0	1	1
%	26.7	27.5	25.9	25	20.8	24.8	0	0	0	0	1.1	0.2
Nairobi	2	1	3	6	8	20	0	0	0	0	0	0
%	2.2	1.3	3.5	5	6.4	4	0	0	0	0	0	0
Nyanza	4	8	12	7	9	40	4	15	4	5	4	32
%	4.4	10	14.1	5.8	7.2	8	3.6	9.7	7.0	5.9	4.3	6.4
Rift Valley	7	7	4	6	13	37	77	95	33	60	69	334
%	7.8	8.8	4.7	5	10.4	7.4	70	61.7	57.9	70.6	73.4	66.8
Western	11	11	5	13	11	51	28	41	19	17	19	124
%	12.2	13.8	5.9	10.8	8.8	10.2	25.5	26.6	33.3	20	20.2	24.8
Others	0	0	1	1	0	2	0	2	0	0	0	2
%	0	0	1.2	0.8	0	0.4	0	1.3	0	0	0	0.4
Total	90	80	85	120	125	500	110	154	57	85	94	500
%	100	100	100	100	100	100	100	100	100	100	100	100
Referral												
Yes	57	48	57	85	83	330	44	64	19	39	41	207
%	63.3	60	67.1	70.8	66.4	66	40	41.6	33.3	45.9	43.6	41.4
No	33	32	28	35	42	170	66	90	38	46	53	293
%	36.7	40	32.9	29.2	33.6	34	60	58.4	66.7	54.1	56.4	58.6
Total	90	80	85	120	125	500	110	154	57	85	94	500
%	100	100	100	100	100	100	100	100	100	100	100	100

% = percentage

Table 4. Cancer cases by gender in Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH) from 2008–2012.

Cancer site	ICD-0 code	KNH						MTRH					
		No. of cases	P	Males		Females		No. of cases	P	Males		Females	
		N	%	n	%	n	%	N	%	n	%	N	%
Cervix uteri	C53	62	12.4	0	0	62	20.7	41	8.2	0	0	41	14.5
Breast	C50	59	11.8	0	0	59	19.7	77	15.4	3	1.4	74	26.2
Colon & Rectum	C18,C20	31	6.2	17	8.5	14	4.7	27	5.4	16	7.3	11	3.9
Chronic leukemia	C91.1,C92.1	27	5.4	11	5.5	16	5.3	27	5.4	17	7.8	10	3.5
Stomach	C16	26	5.2	11	5.5	15	5	15	3	5	2.3	10	3.5
Esophageal	C15	25	5	14	7	11	3.7	27	5.4	16	7.3	11	3.9
Prostate	C61	23	4.6	23	11.5	0	0	7	1.4	7	3.2	0	0
Ovary	C56	22	4.4	0	0	22	7.3	14	2.8	0	0	14	5
Larynx	C32	21	4.2	19	9.5	2	0.7	3	0.6	3	1.4	0	0
Skin	C44	19	3.8	11	5.5	8	2.7	11	2.2	7	3.2	4	1.4
Nasopharynx	C11	17	3.4	12	6	5	1.7	11	2.2	8	3.7	3	1.1
Endometrium	C54.1	15	3	0	0	15	5	5	1	0	0	5	1.8
Pancrease	C25	14	2.8	6	3	8	2.7	11	2.2	3	1.4	8	2.8
Acute leukemia	C91.0,C92.0	13	2.6	5	2.5	8	2.7	8	1.6	4	1.8	4	1.4
Non Hodgkin´s lymphoma	C82-C85, C96	13	2.6	7	3.5	6	2	37	7.4	22	10.1	15	5.3
Lung and bronchus	C34	11	2.2	8	4	3	1	3	0.6	1	0.5	2	0.7
Lip and oral cavity	C00-C14	11	2.2	6	3	5	1.7	9	1.8	4	1.8	5	1.8
Hypopharynx	C13	11	2.2	4	2	7	2.3	0	0	0	0	0	0
Liver	C22	10	2	5	2.5	5	1.7	16	3.2	13	5.9	3	1.1
Bone	C40-C41	8	1.6	6	3	2	0.7	10	2	7	3.2	3	1.1
Bladder	C67	7	1.4	5	2.5	2	0.7	2	0.4	1	0.5	1	0.4
Thyroid	C73	7	1.4	0	0	7	2.3	0	0	0	0	0	0
Genitalia	*	6	1.2	3	1.5	3	1	8	1.6	3	1.4	5	1.8
Eye	C69	6	1.2	3	1.5	3	1	0	0	0	0	0	0
Multiple myeloma	C90.0	6	1.2	4	2	2	0.7	7	1.4	5	2.3	2	0.7
Hodgkin´s lymphoma	C81	5	1	2	1	3	1	14	2.8	7	3.2	7	2.5
Parotid gland	C07	4	0.8	3	1.5	1	0.3	0	0	0	0	0	0
Bile duct	C22.1	4	0.8	3	1.5	1	0.3	3	0.6	1	0.5	2	0.7
Kaposi's sarcoma	C46	2	0.4	1	0.5	1	0.3	93	18.6	55	25.2	38	13.5
Others	**	15	3	11	5.5	4	1.3	14	2.8	10	4.6	4	1.4
Adult T cell Leukemia	C91.5	0	0	0	0	0	0	0	0	0	0	0	0
Burkitt´s Lymphoma	C83.7	0	0	0	0	0	0	0	0	0	0	0	0
Total		**500**	**100**	**200**	**100**	**300**	**100**	**500**	**100**	**218**	**100**	**282**	**100**

*Genitalia included cancer of the penis (C60), vagina (C52), vulva (C51), testis (C62) and pelvis (C63) while **others included cancers of renal (C65), head (C76), brain (C71), anus (C21), ear (C30), rhabdomyosarcoma (C49) and meninges (C70). N = number of cases P = percentage.
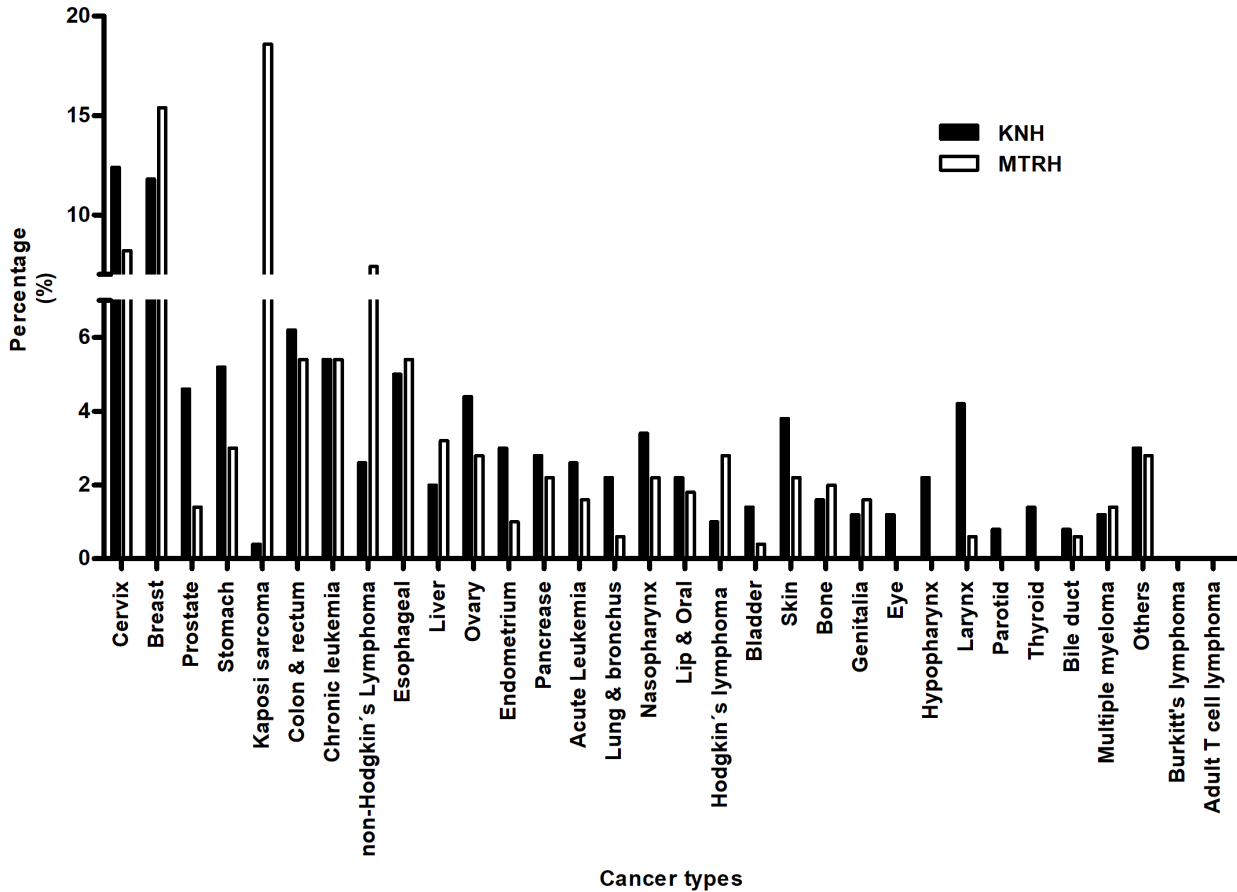
Figure 1. Types of cancers at Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH).

to infections. Cancers of the cervix (62, 12.4%), stomach (26, 5.2%), nasopharynx (17, 3.4%), non-Hodgkin's lymphoma (13, 2.6%) and liver (10, 2%) were the commonest infection-associated cancers. In MTRH, 241 (48.2%) of the 500 cancers cases sampled were associated with infectious agents, while an estimated 222 (44.4%) were attributable to infections. Kaposi's sarcoma (93, 18.6%), cancer of the cervix (41, 8.2%) and non-Hodgkin's lymphoma (37, 7.4%), liver (16, 3.2%) and stomach (15, 3%) were the commonest infection-associated cancers (Table 7).

Trends of the top most cancer cases

To show the trends of the top two cancers by gender, a trend graph was drawn. The percentage was obtained by dividing the total number of each cancer case over the total number of cancers per year with reference to gender. In KNH, the number of cervical cancers among the women has steadily been going up since 2008 to 2011 with a slight decrease in the year 2012. Prostate cancer maintained its high percentage throughout the years apart from 2011 where there was a sharp increase (Figure 2). On the other hand, in MTRH, both cervical and breast cancers have been seemingly increasing since 2008 to 2011 where in 2012 there was a reduction. It was also clear that that from 2011, four of the cancers namely: Kaposi´s sarcoma, non-Hodgkin´s lymphoma, breast and cervical cancers were steadily reducing (Figure 3).

Discussion

Results from the current study conducted at two referral hospitals between the period of, 2008 to 2012, suggest that the top five types of cancers in KNH (n=500) were cervical, breast, colorectal and , chronic leukemia and stomach while in MTRH (n=500) they were Kaposi's sarcoma, breast, cervical, non-Hodgkin's lymphoma, colorectal, chronic leukemia and esophageal cancers.

In females (n=300) the five most common cancers in KNH were cervical, breast, ovarian, chronic leukemia, endometrial and stomach while in MTRH (n=282), they were breast, cervical, Kaposi's sarcoma, non-Hodgkin's lymphoma and cancer of the ovary (Table 4 and Figure 1). These results are comparable with the data obtained from a previous study conducted retrospectively in Tenwek Hospital, in Bomet District, western Kenya in the period of 1999 to 2007, that showed that the common types of cancer in women were cervical, breast, stomach, uterus and esophageal[36]. Another study aiming to study the burden of cancer in Malawi using population based data in the period of 2007–2010, found that amongst females, cancer of the cervix was the commonest accounting for 45.4% of all cases followed by Kaposi's sarcoma (21.1%), cancer of the esophagus (8.2%), breast (4.6%) and non-Hodgkin lymphoma (4.1%)[37]. It was suggestive from the trend curves (Figure 2 and Figure 3) that cervical cancer has

Table 5. Cancer cases by age groups in Kenyatta National Hospital (KNH) from 2008–2012.

KNH											
Cancer site	**ICD-0 code**	**Age groups**									
		≤24		24–44		45–64		65–84		≥85	
		cases	%	cases	%	cases	%	cases	%	cases	%
Cervix uteri	C53	3	9.7	26	**17.4**	29	13.4	4	4.1	0	0
Breast	C50	2	6.5	19	12.8	30	**13.8**	8	8.2	0	0
Colon & Rectum	C18,C20	1	3.2	4	2.7	19	**8.8**	7	7.1	0	0
Chronic leukemia	C91.1,C92.1	1	3.2	12	**8.1**	10	4.6	4	4.1	0	0
Stomach	C16	1	3.2	3	2	14	**16.5**	6	6.1	2	40
Esophageal	C15	0	0	2	1.3	14	6.5	9	**9.2**	0	0
Prostate	C61	0	0	0	0	10	4.6	12	**12.2**	1	20
Ovary	C56	1	3.2	7	4.7	11	**5.1**	3	3.1	0	0
Larynx	C32	0	0	1	0.7	13	6	6	**6.1**	1	20
Skin	C44	2	**6.5**	9	6	4	1.8	4	4.1	0	0
Nasopharynx	C11	2	**6.5**	5	3.4	7	3.2	3	3.1	0	0
Endometrium	C54.1	0	0	4	2.7	6	2.8	5	**5.1**	0	0
Pancrease	C25	4	12.9	4	2.7	6	2.8	1	1.0	0	0
Acute leukemia	C91.0,C92.0	0	0	4	2.7	5	2.3	5	**5.1**	0	0
Non Hodgkin´s lymphoma	C82-C85, C96	2	**6.5**	9	6	1	0.5	1	1	0	0
Lung and bronchus	C34	3	**9.7**	5	3.4	4	1.8	1	1	0	0
Lip and oral cavity	C00-C14	0	0	4	2.7	6	**2.8**	1	1	0	0
Hypopharynx	C13	1	3.2	4	2.7	1	0.5	5	**5.1**	0	0
Liver	C22	0	0	2	1.3	6	2.8	3	3.1	0	0
Bone	C40-C41	0	0	3	2	6	**2.8**	1	1	0	0
Bladder	C67	4	**12.9**	3	2	1	0.5	0	0	0	0
Thyroid	C73	0	0	3	2	1	0.5	3	**3.1**	0	0
Genitalia	*	0	0	3	2	4	1.8	0	0	0	0
Eye	C69	1	**3.2**	4	2.7	1	0.5	0	0	0	0
Multiple myeloma	C90.0	1	3.2	3	2	1	0.5	1	1	0	0
Hodgkin´s lymphoma	C81	0	0	1	0.7	4	**1.8**	0	0	1	20
Parotid gland	C07	2	**6.5**	3	2	0	0	0	0	0	0
Bile duct	C22.1	0	0	2	1.3	1	0.5	1	1	0	0
Kaposi's sarcoma	C46	0	0	0	0	2	**0.9**	2	2	0	0
Others	**	0	0	0	0	0	0	2	1	0	0
Adult T cell Leukemia	C91.5	0	0	0	0	0	0	0	0	0	0
Burkitt´s Lymphoma	C83.7	0	0	0	0	0	0	0	0	0	0
Total		**31**	**100**	**149**	**100**	**217**	**100**	**98**	**100**	**5**	**100**

*Genitalia included cancer of the penis (C60), vagina (C52), vulva (C51), testis (C62) and pelvis (C63) while **others included cancers of renal (C65), head (C76), brain (C71), anus (C21), ear (C30), rhabdomyosarcoma (C49) and meninges (C70). N = number of cases P = percentage

Table 6. Cancer cases by age groups in Moi Teaching and Referral Hospital (MTRH) from 2008–2012.

MTRH											
Cancer site	**ICD-0 code**	**Age groups**									
		≤24		24–44		45–64		65–84		≥85	
		Cases	**%**	**Cases**	**%**	**Cases**	**%**	**Cases**	**%**	**Cases**	**%**
Cervix uteri	C53	0	0	20	**10.2**	16	8.5	4	5.2	1	11.1
Breast	C50	3	10.7	28	14.2	37	**19.6**	8	10.4	1	11.1
Colon & Rectum	C18,C20	0	0	9	4.6	10	5.3	7	**9.1**	1	11.1
Chronic leukemia	C91.1,C92.1	1	3.6	10	5.1	10	5.3	6	**7.8**	0	0
Stomach	C16	0	0	4	2	6	3.2	4	**5.2**	1	11.1
Esophageal	C15	0	0	3	1.5	15	7.9	8	**10.4**	1	11.1
Prostate	C61	0	0	0	0	2	1.1	4	**5.2**	1	11.1
Ovary	C56	0	0	6	3	4	2.1	4	**5.2**	0	0
Larynx	C32	0	0	1	0.5	1	0.5	1	**1.3**	0	0
Skin	C44	1	3.6	2	1	3	1.6	4	**5.2**	1	11.1
Nasopharynx	C11	2	**7.1**	5	2.5	3	1.6	1	1.3	0	0
Endometrium	C54.1	0	0	0	0	2	1.1	3	**3.9**	0	0
Pancrease	C25	0	0	5	2.5	7	3.7	2	0.6	0	0
Acute leukemia	C91.0,C92.0	1	**3.6**	2	1.0	6	3.2	0	0	2	**22.2**
Non Hodgkin´s lymphoma	C82-C85, C96	2	**7.1**	4	2.0	1	0.5	1	1.3	0	0
Lung and bronchus	C34	6	**21.4**	9	4.6	17	9	5	6.5	0	0
Lip and oral cavity	C00-C14	0	0	0	0	1	0.5	2	**2.6**	0	0
Hypopharynx	C13	1	3.6	3	1.5	1	0.5	4	**5.2**	0	0
Liver	C22	0	0	0	0	0	0	0	0	0	0
Bone	C40-C41	1	3.6	6	3	5	2.6	4	**5.2**	0	0
Bladder	C67	2	**7.1**	5	2.5	2	1.1	1	1.3	0	0
Thyroid	C73	0	0	0	0	2	**1.1**	0	0	0	0
Genitalia	*	0	0	0	0	0	0	0	0	0	0
Eye	C69	1	**3.6**	6	3	1	0.5	0	0	0	0
Multiple myeloma	C90.0	0	0	0	0	0	0	0	0	0	0
Hodgkin´s lymphoma	C81	0	0	0	0	5	**2.6**	2	**2.6**	0	0
Parotid gland	C07	3	**10.7**	7	3.6	3	1.6	1	1.3	0	0
Bile duct	C22.1	0	0	0	0	0	0	0	0	0	0
Kaposi's sarcoma	C46	0	0	1	0.5	2	**1.1**	0	0	0	0
Others	**	4	14.3	61	31	27	14.3	1	1.3	0	0
Adult T cell Leukemia	C91.5	0	0	0	0	0	0	0	0	0	0
Burkitt´s Lymphoma	C83.7	0	0	0	0	0	0	0	0	0	0
Total		**28**	**100**	**197**	**100**	**189**	**100**	**77**	**100**	**9**	**100**

*Genitalia included cancer of the penis (C60), vagina (C52), vulva (C51), testis (C62) and pelvis (C63) while **others included cancers of renal (C65), head (C76), brain (C71), anus (C21), ear (C30), rhabdomyosarcoma (C49) and meninges (C70). N = number of cases P = percentage

Table 7. Attributable fraction (AF) and estimated number of cancers attributable to infectious agents in KNH/MTRH from 2008–2012.

Infectious agent	Cancer site	ICD-0 code	AF%	No. of cancer cases KNH	No. of cancer cases attributable to infections KNH	No. of cancer cases MTRH	No. of cancer cases attributable to infections MTRH
Female							
HPV	Cervix	C53	100	62	62	41	41
	Vulva	C51	40	2	1	3	1
	Vagina	C52	78	1	1	0	0
	Anus	C21	88	2	2	0	0
	Oropharynx	C10	31	0	0	0	0
Schistosoma	Bladder	C67	41	2	1	1	0
HBV/HCV	Liver	C22.0	71	5	4	3	2
EBV	Nasopharynx	C11	96	5	5	3	3
	HL	**C81**	74	3	2	7	5
H. pylori	Stomach	C16	89	15	13	10	9
EBV/HIV	NHL	**C82-85,C96**	100	6	6	15	15
HIV/HHV8	KS	**C46**	100	1	1	38	38
O. viverrini C. sinensis	Bile duct	C22.1	*	1	**	2	**
Total (% female cancers)				105(35.0%)	98 (32.7%)	123(43.6%)	114 (40.4%)
Male							
HPV	Penis	C60	50	0	0	2	1
	Anus	C21	88	3	3	4	4
EBV	Oropharynx	C10	31	0	0	0	0
Schistosoma	Bladder	C67	41	5	2	1	0
HBV/HCV	Liver	C22.0	71	5	4	13	9
EBV	Nasopharynx	C11	96	12	12	8	8
	HL	**C81**	74	2	1	7	5
H. pylori	Stomach	C16	89	11	10	5	4
EBV/HIV	NHL	**C82-85,C96**	100	7	7	22	22
HIV/HHV8	KS	**C46**	100	1	1	55	55
O. viverrini C. sinensis	Bile duct	C22.1	*	3	**	1	**
Total (% of male cancers)				49 24.5%	40 20%	118 54.1%	108 49.5%
Total (% of cancers in both sexes)				154 30.8%	138 27.6%	241 48.2%	222 44.4%

Over the 5-year period the total number of cases sampled in each hospital were 500. KNH had 300 female and 200 male cases while MTRH had 282 female and 218 male cases. *AF not available, ** Not possible to estimate without AF,

been steadily increasing over the years in the two hospitals. The high number of cervical cancer could reflect a potential higher prevalence of HPV infection, low screening rates or late detection of the disease. This is particularly alarming especially because there are free cervical cancer checkup programs available in both hospitals. Most patients with cervical cancer were between in the age groups of 35 to 44 and 45 to 54 years while for breast cancer, they were in the age group of 45 to 54 years followed by 24 to 44 years with 35.5% and 29% respectively (Table 5 and Table 6). With increased awareness and strict policies that
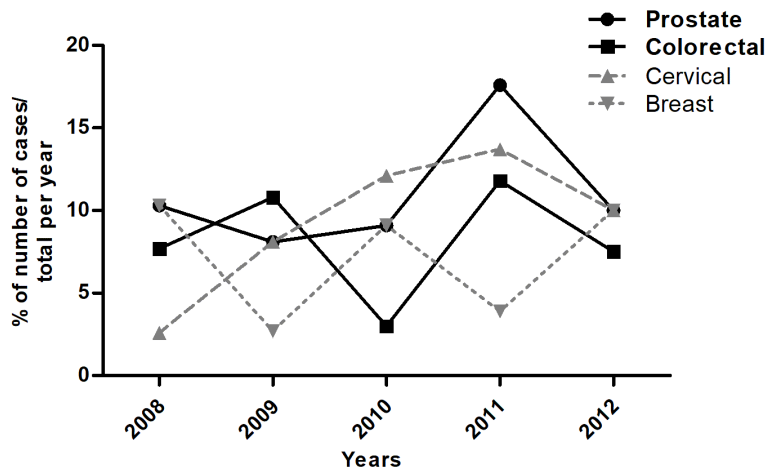
Figure 2. Trends of top 2 common cancers per gender in Kenyatta National Hospital (KNH).
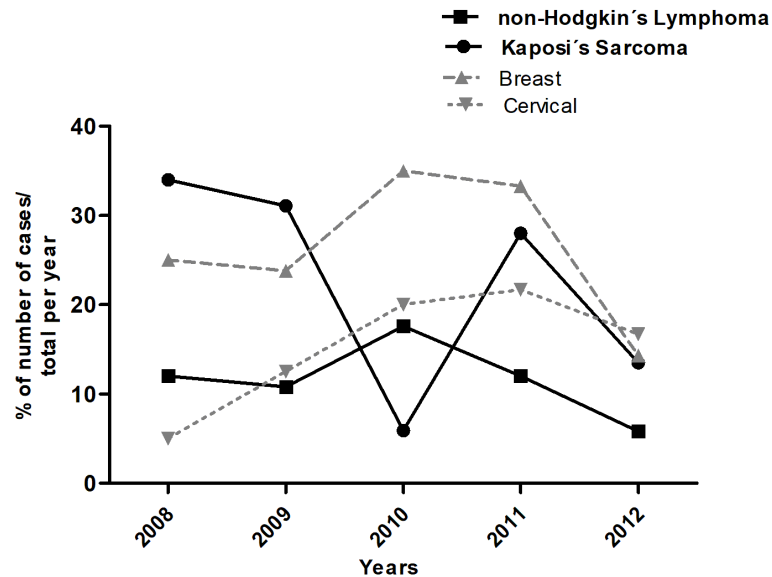

Figure 3. Trends of top 2 common cancers per gender in Moi Teaching and Referral Hospital (MTRH).

oblige the women to go for routine checkups and vaccination, the burden of some of these cancers could be reduced. The risk factors associated with breast cancer include early menarche, late childbearing, having fewer children, obesity, lack of awareness and early detection[38].

In males, (n=200) the five most common types of cancers in KNH were prostate, laryngeal, colorectal, esophageal and nasopharyngeal carcinoma while in MTRH, (n=218) they were: Kaposi's sarcoma, non-Hodgkin's lymphoma, chronic leukemia, colorectal and esophageal cancers (Table 4 and Figure 1). The high number of prostate and esophageal cancer is comparable with the data from the Kenya national cancer control strategy that showed that Kaposi's sarcoma, prostate and esophageal cancer are the most common cancers in men[39]. Similarly the retrospective study done in Tenwek Hospital in Western Kenya

from 1999 to 2007 showed that the most common cancers in men were esophagus, stomach, prostate and colorectal and non-Hodgkin's lymphoma (NHL). Specifically, esophageal was the top cancer accounting for 35% of all cancer cases with esophageal squamous cell carcinoma being the most common subtype[36]. Although various other studies show that esophageal is the leading cause of death among both men and women in East Africa[36,38,40] this did not reflect in our hospital based study as esophageal cancer was among the most common but not the leading cancer. The majority of the esophageal cancers were in patients aged 65 to 84 years, followed by 45 to 64 years (Table 5 and Table 6), and was more common in males than women. Some of the risk factors independently associated with esophageal cancer ($P < 0.05$) identified from a study conducted at MTRH were low socio-economic status, smoking, alcohol consumption, tooth loss, cooking with charcoal and firewood,

consumption of hot beverage and use of a traditional fermented milk referred to as *mursik*[40].

Elsewhere, a study aiming to determine the burden and pattern of cancer in Western Kenya by use of data from the Eldoret cancer registry, from 1999 to 2006, found out that about 21% of the patients had haematological malignancies while 79% of the patients had solid tumors. Among the haematological malignancies reported, lymphomas were the most common (11.9%) followed by acute and chronic leukemia with 4.0% and 3.2% respectively. Esophageal (10.5%), breast (6.2%) and Kaposi's sarcoma (5.9%) were the top most non-haematological cancers. This is comparable to what was observed from our hospital based study where Kaposi's sarcoma, non Hodgkin's lymphoma and chronic leukemia were high especially in MTRH[41]. Chronic leukemia was specifically the 4th most common type of cancer in KNH and 5th most common in MTRH (Table 4) while acute leukemia was also high and highest in the age-group of 24 years and below (Table 5 and Table 6). There were high numbers of prostate cancer cases at KNH compared to MTRH as this type of cancer can be prevented if detected early. From the trend curve (Figure 2) the numbers were steadily increasing over the years and it was clear from this study that prostate cancer commonly affected males in the age-group of 65 to 84 years in both hospitals and with notable higher occurrence also in the age-group of 45 to 64 years (Table 5 and Table 6). As Both hospitals offer free prostate cancer checkup programs for men this differences could possibly be attributed to lifestyle choices and family history of the disease which are among the risk factors associated elsewhere with the cancer[42].

Infection-attributable cancers contributed up to 27.6% and 44.4% of the total cancer burden in KNH and MTRH respectively (Table 7). This is closer to estimates of 31.1% for sub-Saharan Africa; higher than 9.2% estimated for developed countries and expectedly higher than global average of 15.4% reported by Plummer *et al* in 2016[4]. Fortunately, the majority of cancers associated with infectious agents can be controlled by controlling the infectious agent[13,43]. Cancers of the cervix, stomach, nasopharynx, liver and non-Hodgkin's lymphoma were the commonest infection-associated cancers in KNH; while in MTRH, Kaposi's sarcoma, cancer of the cervix, non-Hodgkin's lymphoma, liver and stomach cancer were the commonest infection-associated cancers. The high burden of cancers of the cervix, stomach and liver are comparable with other population based studies that show that among infection-related cancers, stomach, liver and cervical cancer, not only account for the vast majority of the total cancer burden associated with infections, but they have the highest incidences[4,13,44]. A study by Msyamboza and collegues also found out that Kaposi`s sarcoma was among the cancers causing the increased burden of cancers in Malawi with 21.1% in women and 50.7% in men[37]. Moreover, a recent study by Plummer and colleagues highlighted that Kaposi's sarcoma was the second largest contributor to the cancer burden in sub-Saharan Africa[4]. It is already known also that infection with HIV entails an increased risk of developing AIDS defining diseases (Kaposi's sarcoma, non-Hodgkin's lymphoma, cervical cancer)[7]. The high number of Kaposi's sarcoma, non-Hodgkin's lymphoma and cervical cancer could have been influenced by the association of the cancers with HIV. From the trend curve, it was suggestive that non-Hodgkin's lymphoma has been decreasing steadily in MTRH since 2010 to 2012 while Kaposi's sarcoma was lower in 2010 and 2012 (Figure 3). The reduction could have been influenced by scaling up of the highly active antiretroviral therapy (HAART) treatment programme. A population based study from Nigeria has also reported high numbers of NHL making it the third most common infection-associated cancer[14].

A high number of liver cancer cases was observed in males rather than females. This can be explained by higher prevalence of risk factors for liver cancer in men as compared to women such as higher alcohol consumption and infection with HBV or HCV[13]. Although the data on HBV/HCV was unavailable to accurately reflect the true proportion of people infected, this kind of cancer could be prevented by vaccination and increased awareness. Our study showed the most affected age group to be 45 to 84 years (Table 5 and Table 6). The high number of gastric cancer in KNH suggested a higher prevalence of the risk factors associated with the cancer including infection with *H. pylori,* poor diet, poor hygiene, lack of awareness or the late stage of diagnosis[13]. Although studies suggest that the age at onset of *H.pylori* infection is generally lower and peaks at 90% among young adults[4,45], this was not the case at MTRH where the highest age-group was 65 to 84 years which also could suggest a late stage of diagnosis.

More than 70% of patients were 25 to 64 years of age in both hospitals with the highest age group being 45 to 64 years in KNH (43.4%) and 25 to 44 years in MTRH (39.4%). According to the latest data published in WHO 2018, life expectancy in Kenya is 64.4 years for males and 64.8 for females and this is the age frequently associated with cancer occurrence[46]. The mean age of the population under study was 50.57 years for KNH and 48 years for MTRH suggesting that with increased awareness and early detection some cancer cases could be prevented. There were more female cases than males with 60% and 56.4% in KNH and MTRH respectively, this could be explained by the fact that probably males fear going to the hospitals, or women tend to have frequent contact with the health professionals and show up in even greater numbers than men during health campaigns. The findings of the study show a high number of referrals at KNH (66%) as compared to the 41.4% at MTRH (Table 3). The possible reasons for the high referral rates at KNH could be explained by the establishment of a functional oncology centre which encourages the referral of patients for care while the decline at MTRH could be due to the establishment of an outreach satellite oncology service sites based at Eldoret where a significant number of patients are attended without the need of going to MTRH. The oncology services at these sites are integrated with the comprehensive care programme run by the Academic Model for the Prevention and Treatment of HIV/AIDS (AMPATH)[41]. The majority of patients were referrals from other regions, indicating that majority of the patients have difficulty accessing cancer

services resulting in distant referrals, and long waiting times that could cause some previously curable cancers to progress to incurable stages.

Our study had several limitations. First, causality could not be proven and we could not ascertain that a given cancer was actually caused by an infectious agent. Therefore, we used AF generated from other studies. Information on associations is sparse in Kenya which opens up new avenues for future research studies. Our study used a sampling faction of the total number of files available at the two hospitals which may have influenced our results. Future studies should focus on population based data as this would be more reflective of the population. Our choice of study population was influenced by the fact that cancer registration in Kenya was in its fairly early stages of development at the time the study was done, and the use of hospital based data seemed suitable. We were not able generate age standardized rates (ASR) for our data that would allow for accurate comparisons between countries and adjusting for population differences. The percentage attributable to infections for certain cancers, such as BL, adult T-cell leukemia or bile duct cancers could not be calculated because we did not come across any cases of the first two cancers while the AF of bile duct was unobtainable.

Conclusion

Our study presented a picture of the burden of cancer and infection-attributable cancer from a hospital point of view. Despite the limitations, the role played by infectious agents in contributing to the overall cancer burden was highlighted. Controlling for the infectious agents could translate to a significant reduction in the cancer burden. Further research is warranted to prove causality between infection-attributable cancers and the infectious agents in Kenya as this may provide new avenues for effective cancer prevention.

Data availability

The data underlying this study is available from the Open Science Framework (OSF) Dataset 1: Burden of Cancer in Kenya; Types, Infection-Attributable and Trends: A National Referral Hospital Retrospective Survey https://doi.org/10.17605/OSF.IO/MD2PY[47]

Data is available under a CC0 1.0 universal license.

Supplementary material

Supplementary File 1: Data collection form

Click here to access the data

References

1. Parkin DM, Bray F, Ferlay J, *et al.*: **Cancer in Africa 2012.** *Cancer Epidemiol Biomarkers Prev.* 2014; **23**(6): 953–966.
   PubMed Abstract | Publisher Full Text

2. Ministry of Health: **National Cancer Control Strategy 2017 – 2022**. 2017.
   Reference Source

3. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans: **Biological agents. Volume 100 B. A review of human carcinogens.** *IARC Monogr Eval Carcinog Risks Hum.* 2012; **100**(Pt B): 1–441.
   PubMed Abstract | Free Full Text

4. Plummer M, de Martel C, Vignat J, *et al.*: **Global burden of cancers attributable to infections in 2012: a synthetic analysis.** *Lancet Glob Heal.* The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY-NC-ND license; 2016; **4**(9): e609–e616.
   PubMed Abstract | Publisher Full Text

5. Chinula L, Moses A, Gopal S: **HIV-associated malignancies in sub-Saharan Africa: progress, challenges, and opportunities.** *Curr Opin HIV AIDS.* 2017; **12**(1): 89–95.
   PubMed Abstract | Publisher Full Text | Free Full Text

6. Kimanga DO, Ogola S, Umuro M, *et al.*: **Prevalence and incidence of HIV infection, trends, and risk factors among persons aged 15-64 years in Kenya:**

results from a nationally representative study. *J Acquir Immune Defic Syndr.* 2014; **66 Suppl 1**: S13–26.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

7. Sasco AJ, Jaquet A, Boidin E, *et al.*: **The challenge of AIDS-related malignancies in sub-Saharan Africa**. Maartens G, editor. *PLoS One.* 2010; **5**(1): e8621.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

8. Kenya National Bureau of Statistics: **The 2009 Kenya Population & Housing. Counting our people for the Vision 2030.** *Population Distribution by Age Sex and Administrative Unit.* 2010; **IC**.
Reference Source

9. Charan J, Biswas T: **How to calculate sample size for different study designs in medical research?** *Indian J Psychol Med.* 2013; **35**(2): 121–6.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

10. Daniel WW: **Biostatistics: A Foundation for Analysis in the Health Sciences**. 7th ed. New York; 1999.
Reference Source

11. Pourhoseingholi MA, Vahedi M, Rahimzadeh M: **Sample size calculation in medical studies.** *Gastroenterol Hepatol Bed Bench.* 2013; **6**(1): 14–17.
PubMed Abstract | **Free Full Text**

12. Arya R, Antonisamy B, Kumar S: **Sample size estimation in prevalence studies.** *Indian J Pediatr.* 2012; **79**(11): 1482–8.
PubMed Abstract | **Publisher Full Text**

13. Parkin DM: **The global health burden of infection-associated cancers in the year 2002.** *Int J Cancer.* 2006; **118**(12): 3030–3044.
PubMed Abstract | **Publisher Full Text**

14. Odutola M, Jedy-Agba EE, Dareng EO, *et al.*: **Burden of Cancers Attributable to Infectious Agents in Nigeria: 2012-2014.** *Front Oncol.* 2016; **6**: 216.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

15. Moussavou PB, Koumakpayi IH, Nkili-Meyong AA, *et al.*: **Molecular analysis of human Papillomavirus detected among women positive for cervical lesions by visual inspection with acetic acid/Lugol's iodine (VIA/VILI) in Libreville, Gabon.** *Infect Agent Cancer.* 2016; **11**(1): 50.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

16. Ebrahim S, Mndende XK, Kharsany AB, *et al.*: **High Burden of Human Papillomavirus (HPV) Infection among Young Women in KwaZulu-Natal, South Africa.** Meyers C, editor. *PLoS One.* 2016; **11**(1): e0146603.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

17. Denny L, Adewole I, Anorlu R, *et al.*: **Human papillomavirus prevalence and type distribution in invasive cervical cancer in sub-Saharan Africa.** *Int J Cancer.* 2014; **134**(6): 1389–98.
PubMed Abstract | **Publisher Full Text**

18. Walboomers JM, Jacobs MV, Manos MM, *et al.*: **Human papillomavirus is a necessary cause of invasive cervical cancer worldwide.** *J Pathol.* 1999; **189**(1): 12–9.
PubMed Abstract | **Publisher Full Text**

19. de Martel C, Plummer M, Vignat J, *et al.*: **Worldwide burden of cancer attributable to HPV by site, country and HPV type.** *Int J Cancer.* 2017; **141**(4): 664–70.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

20. Rantshabeng PS, Moyo S, Moraka NO, *et al.*: **Prevalence of oncogenic human papillomavirus genotypes in patients diagnosed with anogenital malignancies in Botswana.** *BMC Infect Dis.* 2017; **17**(1): 731.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

21. Tesfalul M, Simbiri K, Wheat CM, *et al.*: **Oncogenic viral prevalence in invasive vulvar cancer specimens from human immunodeficiency virus-positive and -negative women in Botswana.** *Int J Gynecol Cancer.* 2014; **24**(4): 758–65.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

22. Mboumba Bouassa RS, Mbeko Simaleko M, Camengo SP, *et al.*: **Unusual and unique distribution of anal high-risk human papillomavirus (HR-HPV) among men who have sex with men living in the Central African Republic.** Mossong J, editor. *PLoS One.* 2018; **13**(5): e0197845.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

23. Davidson CL, Richter KL, Van der Linde M, *et al.*: **Prevalence of oral and oropharyngeal human papillomavirus in a sample of South African men: a pilot study.** *S Afr Med J.* 2014; **104**(5): 358–61.
PubMed Abstract | **Publisher Full Text**

24. Kaba G, Dzudzor B, Gyasi RK, *et al.*: **Human papillomavirus genotypes in a subset of head and neck squamous cell carcinoma.** *West Afr J Med.* 2014; **33**(2): 121–4.
PubMed Abstract

25. Senba M, Buziba N, Mori N, *et al.*: **Human papillomavirus infection induces NF-κB activation in cervical cancer: A comparison with penile cancer.** *Oncol Lett.* 2011; **2**(1): 65–8.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

26. Senba M, Buziba N, Mori N, *et al.*: **Increased prevalence of Kaposi´s**

27. sarcoma-associated herpesvirus in the Kaposi´s sarcoma-endemic area of western Kenya in 1981-2000. *Acta Virol.* 2011; **55**(2): 161–4.
PubMed Abstract | **Publisher Full Text**

27. Kafita D, Kaile T, Malyangu E, *et al.*: **Evidence of EBV infection in lymphomas diagnosed in Lusaka, Zambia.** *Pan Afr Med J.* 2018; **29**: 181.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

28. Westmoreland KD, Stanley CC, Montgomery ND, *et al.*: **Hodgkin lymphoma, HIV, and Epstein-Barr virus in Malawi: Longitudinal results from the Kamuzu Central Hospital Lymphoma study.** *Pediatr Blood Cancer.* 2017; **64**(5): e26302.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

29. Weinreb M, Day PJ, Niggli F, *et al.*: **The consistent association between Epstein-Barr virus and Hodgkin's disease in children in Kenya.** *Blood.* 1996; **87**(9): 3828–36.
PubMed Abstract

30. Kirk GD, Lesi OA, Mendy M, *et al.*: **The Gambia Liver Cancer Study: Infection with hepatitis B and C and the risk of hepatocellular carcinoma in West Africa.** *Hepatology.* 2004; **39**(1): 211–9.
PubMed Abstract | **Publisher Full Text**

31. Maucort-Boulch D, de Martel C, Franceschi S, *et al.*: **Fraction and incidence of liver cancer attributable to hepatitis B and C viruses worldwide.** *Int J Cancer.* 2018; **142**(12): 2471–7.
PubMed Abstract | **Publisher Full Text**

32. Bello A, Umar A, Borodo M: **Prevalence and risk factors for helicobacter pylori infection in gastroduodenal diseases in Kano, Nigeria.** *Afr J Med Health Sci.* 2018; **17**(1): 41–46.
Publisher Full Text

33. Newton R, Ziegler JL, Casabonne D, *et al.*: **Helicobacter pylori and cancer among adults in Uganda.** *Infect Agent Cancer.* 2006; **1**: 5.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

34. Groeneveld AE, Marszalek WW, Heyns CF: **Bladder cancer in various population groups in the greater Durban area of KwaZulu-Natal, South Africa.** *Br J Urol.* 1996; **78**(2): 205–8.
PubMed Abstract | **Publisher Full Text**

35. Orem J, Mbidde EK, Lambert B, *et al.*: **Burkitt's lymphoma in Africa, a review of the epidemiology and etiology.** *Afr Health Sci.* 2007; **7**(3): 166–75.
PubMed Abstract | **Free Full Text**

36. Parker RK, Dawsey SM, Abnet CC, *et al.*: **Frequent occurence of esophageal cancer in young people in Western Kenya.** *NIH.* 2012; **34**: 13–23.

37. Msyamboza KP, Dzamalala C, Mdokwe C, *et al.*: **Burden of cancer in Malawi; Common types, incidence and trends: National population-based cancer registry.** *BMC Res Notes.* BioMed Central Ltd; 2012; **5**: 149.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

38. Jemal A, Bray F, Ferlay J: **Global Cancer Statistics: 2011.** *CA Cancer J Clin.* 2011; **61**(2): 69–90.
PubMed Abstract | **Publisher Full Text**

39. MOPHS & MOMS: **Strategic Plan.** 2011-2016 National Cancer Control Strategies. 2010.
Reference Source

40. Patel K, Wakhisi J, Mining S, *et al.*: **Esophageal Cancer, the Topmost Cancer at MTRH in the Rift Valley, Kenya, and Its Potential Risk Factors.** *ISRN Oncol.* 2013; **2013**: 503249.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

41. Tenge CN, Kuremu RT, Buziba NG, *et al.*: **Burden and pattern of cancer in western Kenya.** *East Afr Med J.* 2009; **86**(1): 7–10.
PubMed Abstract | **Publisher Full Text**

42. Ferlay J, Shin HR, Bray F, *et al.*: **Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008.** *Int J Cancer.* 2010; **127**(12): 2893–2917.
PubMed Abstract | **Publisher Full Text**

43. Pagano JS, Blaser M, Buendia MA, *et al.*: **Infectious agents and cancer: criteria for a causal relation.** *Semin Cancer Biol.* 2004; **14**(6): 453–471.
PubMed Abstract | **Publisher Full Text**

44. Thun MJ, DeLancey JO, Center MM, *et al.*: **The global burden of cancer: priorities for prevention.** *Carcinogenesis.* 2009; **31**(1): 100–110.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

45. Plummer M, Franceschi S, Muñoz N: **Epidemiology of gastric cancer.** *IARC Sci Publ.* 2004; (157): 311–26.
PubMed Abstract

46. Torre LA, Bray F, Siegel RL, *et al.*: **Global cancer statistics, 2012.** *CA Cancer J Clin.* 2015; **65**(2): 87–108.
PubMed Abstract | **Publisher Full Text**

47. Macharia LW: **Burden of Cancer in Kenya; Types, Infection-Attributable and Trends: A National Referral Hospital Retrospective Survey.** 2018.
http://www.doi.org/10.17605/OSF.IO/MD2PY

Open Peer Review

Current Referee Status: ✖ ✖

Version 2

Referee Report 31 December 2018

✖ **Maria Paula Curado**

Postgraduate Program in Health Sciences, Federal University of Goia´s, Goiânia, Brazil

Title

The title is not clear with the aims " Cancer in Kenya data from two National referral hospitals "

It is not possible to have trends as it is a cross sectional study in two hospitals in Kenya.

Abstract

No comments.

Introduction

No comments.

Methods

Why were patients aged less 18 was excluded from the study?
Why was clinical diagnosis not included?
This type of study has limitations it can give more information about the hospital activities. More description about the hospital facilities (number of beds, medical, nurses, etc, radiotherapy etc ..)

Results

Figure 1 please add the period 2008-2012 sample (500/500).
Figure 2 this is not trends it is a proportion of cases treated in the period, it means that more patients has access to treatment in 2008 to 2011 and less in 2012. I suggest to use a histogram instead of lines for this figure and change the title.
Why were only two cancer sites used?
Same observations for figure 3.

Discussion

I was expecting a comparison of your data with Eldoret and Nairobi cancer registry.
The discussion is long for the data, please make it shorter.

ASR are only possible to generate if you have a population based cancer registry database.

References
1. Jedy-Agba EE, Curado MP, Oga E, Samaila MO, Ezeome ER, Obiorah C, Erinomo OO, Ekanem IO, Uka C, Mayun A, Afolayan EA, Abiodun P, Olasode BJ, Omonisi A, Otu T, Osinubi P, Dakum P, Blattner W, Adebamowo CA: The role of hospital-based cancer registries in low and middle income countries-The Nigerian Case Study.*Cancer Epidemiol*. 2012; **36** (5): 430-5 PubMed Abstract | Publisher Full Text

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
No

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Referee Expertise: epidemiology

I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Version 1

Referee Report 01 October 2018

https://doi.org/10.21956/aasopenres.13980.r26613

❌ **Clement A Adebamowo** (ID) [1,2,3], **Michael Odutola** [2]
[1] Greenebaum Comprehensive Cancer Center, Institute of Human Virology, University of Maryland School of Medicine, Baltimore, MD, USA
[2] Institute of Human Virology Nigeria, Garki, Abuja, Nigeria
[3] Center for Bioethics and Research, Ibadan, Nigeria

Overview
This paper provided information on the prevalence of cancers and the proportion of cancers that were

attributable to infections in Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH), Kenya over a 5 year period from 2008 to 2012. These 2 centers are the oldest and largest national referral hospitals in Kenya. The authors randomly selected some cancer cases reported at these centers within the study period and reviewed the charts for cancer types and numbers of cancers attributable to infections. The study reported that 40.0% to 53.2% of cancers that were seen in these referral hospitals were attributable to infections.

Title
In this paper, the numbers and proportions of cancers associated with infections were presented and not the proportion of cancers attributable to infections. In order to obtain the proportion of cancers that were attributable to infections, the author would need to apply the formula for Population Attributable Fraction (PAF) which was not done in this paper.

Introduction

The introduction is repetitive and should be edited. Separate paragraphs should be devoted to those infections that are established as causes of cancer while those will weaker associations should be in a separate paragraph.
The role of HIV infection in cancer etiology, prevalence and incidence in Kenya deserves more discussion than just mentioning HIV in a list of pathogens.
Previous studies of infection-associated cancers in Kenya, East Africa or Sub-Saharan Africa should be discussed briefly to provide more introduction to the field and establish why this study was necessary and what it hopes to accomplish.

Methods
It would be more informative to describe the demographic characteristics of the catchment areas, the pattern of healthcare services including other hospitals, and referral systems for the two hospitals included in this study. While these are the biggest hospitals, they may not see the most cancer patients if specialized cancer hospitals are located in the same region or city.

The rationale, application, and choice of sample size calculation are unclear. This is a retrospective case series. The researchers should analyze all the case records that they can find irrespective of sample size calculation. Further, it is highly unlikely that the prevalence of cancer in adult Kenyan population is 50%.

The justification for randomly selecting case notes to review is not clear. Rather than statistically estimate the number of files, why not obtain the number of patients seen and the number who have a cancer diagnosis directly from the institutions? If this is not possible, the authors should say so.

The randomization procedure is not clear. The authors state that "the first record was selected randomly every year". What is the "first record"? Record of the first patient seen in the institution within a specific year? The first record selected from among all the patients' records for a specific year? If the latter how was the selection done? Were all the records assigned numbers and random number generators used to select records?

Do the authors have an objective assessment of the completeness of the records of these two institutions?

What is the relationship of the two institutions that refused to grant permission for this study and their locations with the institutions that gave permission for the study? A map showing this information would

be informative for international readers

The analytic methods used in the paper and described in the data analysis section should be described better.

Results
The authors should be precise in reporting results. "Around 4304 inpatient cancer cases were available in MTRH" is imprecise and unacceptable.

There is a clear difference in the cases of cancer at the KNH compared to MTRH, most probably because one site hosts AMPATH HIV treatment and prevention programs. It is therefore not justifiable to make too much of the differences in the proportion of cancers seen in these two institutions and attempt to extrapolate that to the general population.

Discussion
The interpretation of the result is not justifiable based on the data, methods, and analyses.

Proportions of cancers presenting in specific institutions may not reflect population level epidemiology of the cancers. See Chapter 1 of the Cancer in Africa (Ed) Max Parkin et al.

The authors suggest that their data shows the incidence of the cancers that they described but this is not correct.
The authors can describe the pattern of cancers presenting to each of these hospitals over a period of time, but this is not "incidence" of those cancers in the population. The pattern of presentation of cancers to specific hospitals is influenced by many factors. An example is illustrated in their paper where the pattern of cancers presenting at the AMPATH related hospital reflects the focus on HIV treatment and prevention at the institution.

General comments
1. There are several grammatical and typographical errors in the paper. For example in the Discussion section, Paragraph 3 "Elsewhere, a study aiming determine the burden and pattern of cancer in ……."
2. There is inconsistency in the format of data presentation. For example, age groups were written as 22 to 44 years, and in another 45-65 years and elsewhere 45-64 years.
3. Some sentences are too long. E.g. "Nearly 15% of the global cancer burden is attributable to infectious agents, with two-thirds of infection attributable cancers occurring in the less developed countries and in which infections accounts for nearly one in four cancers."

Summary
In this paper, the authors described the prevalence of cancers and the proportion of cancers that were associated with infections in two referral hospitals in Kenya.
The data was over-interpreted. The methods are inadequately described and the results are poorly presented. The conclusions drawn from the data are not justifiable.

Is the work clearly and accurately presented and does it cite the current literature?
No

Is the study design appropriate and is the work technically sound?
No

Are sufficient details of methods and analysis provided to allow replication by others?
No

If applicable, is the statistical analysis and its interpretation appropriate?
No

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
No

Competing Interests: No competing interests were disclosed.

Referee Expertise: Cancer epidemiology

We have read this submission. We believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 28 Oct 2018

Lucy Wanjiku Macharia, University of Nairobi (Alumni), Kenya

Authors' Response to Reviewers' Comments:

Journal: AAS Open Research
Manuscript #: 12910

Manuscript Title: Burden of cancer in Kenya: types, infection-attributable and trends. A national referral hospital retrospective survey

We thank the reviewers for having reviewed our manuscript, for the suggestions and for the positive criticism. We have performed a major revision in the manuscript in agreement with the suggestions. We have applied the PAF/AF standard formula in estimating the number of cancer cases attributable to infections. Secondly, we have conformed to the third edition of the International Classification of Diseases for Oncology (ICD-O) way of listing the cancers. For cancers like leukemias and lymphomas where the ICD-0-3 topographical code was not clear, we converted the IDC-0-3 morphological code to ICD10 topographical code for clarity.
We hope that this new version of the manuscript can be reconsidered to be of an acceptable scientific standard.
Kindly find below a point-by-point response to the comments and queries.

 Sincerely,
 L.W.M

Overall Comment:
 "This paper provided information on the prevalence of cancers and the proportion of cancers that were attributable to infections in Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH), Kenya over a 5 year period from 2008 to 2012.

These 2 centers are the oldest and largest national referral hospitals in Kenya. The authors randomly selected some cancer cases reported at these centers within the study period and reviewed the charts for cancer types and numbers of cancers attributable to infections. The study reported that 40.0% to 53.2% of cancers that were seen in these referral hospitals were attributable to infections."

Response:
We are thankful to the reviewers for revising our manuscript, for the positive criticism and for the suggestions. We have revised the manuscript text, tables, figures and reference list as described below and in the revised manuscript. We have also updated our results and discussions section together with additional analysis as suggested.

Main comments
1: Title
"In this paper, the numbers and proportions of cancers associated with infections were presented and not the proportion of cancers attributable to infections. In order to obtain the proportion of cancers that were attributable to infections, the author would need to apply the formula for the Population Attributable Fraction (PAF) which was not done in this paper."

Response:
We agree with the reviewers' concern. We have applied the PAF/AF standard formula in estimating the number of cancer cases attributable to infections. We are thankful for the suggestion.

2: Introduction
"The introduction is repetitive and should be edited. Separate paragraphs should be devoted to those infections that are established as causes of cancer while those will weaker associations should be in a separate paragraph.

The role of HIV infection in cancer etiology, prevalence and incidence in Kenya deserves more discussion than just mentioning HIV in a list of pathogens.

Previous studies of infection-associated cancers in Kenya, East Africa or Sub-Saharan Africa should be discussed briefly to provide more introductions to the field and establish why this study was necessary and what it hopes to accomplish."

Response:
We are grateful for the insightful suggestions. We have edited the introduction as recommended in the new manuscript.

We have included a new paragraph on HIV prevalence and incidence in Kenya together with its associated cancers.

Previous studies on infection-associated cancers in sub-Saharan Africa have been expounded in details in the data analysis section.

Comment 3: Methods
3.1 "It would be more informative to describe the demographic characteristics of the

catchment areas, the pattern of healthcare services including other hospitals, and referral systems for the two hospitals included in this study. While these are the biggest hospitals, they may not see the most cancer patients if specialized cancer hospitals are located in the same region or city."

3.2 "The rationale, application, and choice of sample size calculation are unclear. This is a retrospective case series. The researchers should analyze all the case records that they can find irrespective of sample size calculation. Further, it is highly unlikely that the prevalence of cancer in adult Kenyan population is 50%."

3.3 "The justification for randomly selecting case notes to review is not clear. Rather than statistically estimate the number of files, why not obtain the number of patients seen and the number who have a cancer diagnosis directly from the institutions? If this is not possible, the authors should say so."

3.4 "The randomization procedure is not clear. The authors state that "the first record was selected randomly every year". What is the "first record"? Record of the first patient seen in the institution within a specific year? The first record selected from among all the patients' records for a specific year? If the latter how was the selection done? Were all the records assigned numbers and random number generators used to select records?"

3.5 "Do the authors have an objective assessment of the completeness of the records of these two institutions?"

3.6 "What is the relationship of the two institutions that refused to grant permission for this study and their locations with the institutions that gave permission for the study? A map showing this information would be informative for international readers"

3.7 "The analytic methods used in the paper and described in the data analysis section should be described better. ."

Response:
3.1. We are thankful to the reviewers for the suggestions. We have included the demographic characteristics of the catchment areas together with the pattern of healthcare services in the study site section of the new manuscript. To clarify the reviewers' concern, there are 12 health facilities in Kenya that offer cancer services; seven private hospitals, two mission hospitals and three public facilities (KNH, MTRH and Coast Province General Hospital). Because of the affordability of the cancer services, most patients opt for the public facilities resulting in congestion of the facilities and long waiting times of the patients. Patients with private insurance and the government-sponsored scheme, National Health Insurance Fund, are more likely to undergo treatment than those without insurance.

3.2. We have edited the sample size calculation section and included detailed explanations with references in the new manuscript. We do agree with the reviewers' concern of analyzing all the chart reviews. However, due to cost and time constraints, we were only able to analyze 500 files in each hospital, as this was the minimum necessary sample size needed to achieve the required power of the study. We have also come across an article showing that sampling is also applicable

in retrospective chart review studies **[1]** but to avoid any misunderstanding, we have included this as one of the limitations of the study. Regarding the prevalence, we stated in the sample size calculation section that the prevalence of cancer in Kenya was unknown at the time of conducting the study. For a better clarification, a 50% prevalence (p) was used in calculating the sample size since it is known that when d =0.05 and a z=1.96, using a p of 0.5 (50%) yields the highest sample size required for cross-sectional studies **[2].** A detailed explanation has been included in the new manuscript.

3.3. We thank the reviewers for the positive criticism. For clarification, knowing the number of patients with cancer was not our only objective. We also aimed at knowing the of cancer types, the sex and age of the patients under study, their origin by birth, the method of cancer diagnosis used, year of diagnosis and whether the patient was referred from another health facility. At the time of the study, the hospital databases could not provide all the information needed and therefore we had to use the files. Randomization was done because of the cost and time constraints. In a facility like KNH that had 17,584 cancer files, abstracting all the information needed from the patient files to the data collection form would cost more and need longer time that the time allocated to us by the ethics committee.

3.4. We agree with the reviewer's concern. We have modified the randomization section. For clarification, the files in KNH were captured in a database and randomization was purely an automated process since all files have a hospital number (that cannot be disclosed to protect the privacy of the patients). However, in MTRH, the records department was in the middle of updating their databases when this study was being done and because of this we were only given an estimate of the number of files and to achieve the required sample size we used convenient sampling method.

3.5. Yes, the authors had an objective assessment of the completeness of the records at the two institutions. First, randomization depended on the total number given to us of the number of cancer files available for the five year period. Secondly, to obtain all the data for the questions we had, we needed to use a patient file with complete information.

3.6. We thank the reviewers for the question. The four hospitals initially selected for the study included; Kenyatta National Hospital (KNH), Moi Teaching and Referral Hospital (MTRH), Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH) and Coast General Hospital previously known as Coast Province General Hospital (CPGH). At the time, they were all teaching and referral hospitals. KNH and MTRH are national hospitals (level 6) while JOOTRH and CPGH are level 5 hospitals. KNH is located in the former Nairobi province, MTRH is located in the former Rift Valley province, JOOTRH is located in the former Nyanza province and CPGH is located in the former Coast Province. Although we had ethical approval together with a letter of authority from the Ministry of Health giving us the authorization to conduct research in the four facilities, permission to access the files was only granted by the National hospitals. We have included a map in the new manuscript to guide international readers. We are very grateful for the suggestion.

3.7. We are thankful for the suggestion. We have edited the "data analysis" section in the new manuscript.

Comment 4: Results
"The authors should be precise in reporting results. "Around 4304 inpatient cancer cases were available in MTRH" is imprecise and unacceptable."

"There is a clear difference in the cases of cancer at the KNH compared to MTRH, most probably because one site hosts AMPATH HIV treatment and prevention programs. It is therefore not justifiable to make too much of the differences in the proportion of cancers seen in these two institutions and attempt to extrapolate that to the general population."

Response:
We appreciate the suggestion. We have improved the precision of reporting the results.

We thank the reviewers for the suggestion. We have edited the results section and minimized extrapolating the differences from the two facilities to the general population.

Comment 5: Discussion
5.1. "The interpretation of the result is not justifiable based on the data, methods, and analyses.

5.2. Proportions of cancers presenting in specific institutions may not reflect population level epidemiology of the cancers. See Chapter 1 of the Cancer in Africa (Ed) Max Parkin et al.

5.3. The authors suggest that their data shows the incidence of the cancers that they described but this is not correct.

5.4. The authors can describe the pattern of cancers presenting to each of these hospitals over a period of time, but this is not "incidence" of those cancers in the population. The pattern of presentation of cancers to specific hospitals is influenced by many factors. An example is illustrated in their paper where the pattern of cancers presenting at the AMPATH related hospital reflects the focus on HIV treatment and prevention at the institution."

Response:
5.1. We thank the reviewers for the positive criticism. We have modified the analysis and improved on the interpretation of the data. We have emphasized where necessary that we were comparing our hospital-based results to other results obtained from population-based studies.

5.2. We agree with the reviewer's concern that the proportions of cancers presenting in specific institutions may not be reflective at a population level. We have highlighted this as a limitation of this study.

5.3. The use of the term "Incidence" was an unintended mistake. We have edited the discussion section and thank the reviewers for the observation.

5.4. We agree with the reviewer's observation. We have edited our new manuscript accordingly and avoided the use of the term incidence.

Comment 6: General comments

1. *There are several grammatical and typographical errors in the paper. For example in the Discussion section, Paragraph 3 "Elsewhere, a study aiming determine the burden and pattern of cancer in ……."*
2. *There is inconsistency in the format of data presentation. For example, age groups were written as 22 to 44 years and in another 45-65 years and elsewhere 45-64 years.*
3. *Some sentences are too long. E.g. "Nearly 15% of the global cancer burden is attributable to infectious agents, with two-thirds of infection attributable cancers occurring in the less developed countries and in which infections accounts for nearly one in four cancers."*

Response:

6.1. We thank the reviewer for the observation. We have improved on the wording of the manuscript and corrected the typographical errors.

6.2. We thank the reviewer for the comment. We have ensured consistency in the data presented in the new manuscript.

6.3. We thank the reviewer for the suggestion. We have minimized the use of long sentences in the new manuscript.

Comment 7: Summary

"In this paper, the authors described the prevalence of cancers and the proportion of cancers that were associated with infections in two referral hospitals in Kenya.
The data was over-interpreted. The methods are inadequately described and the results are poorly presented. The conclusions drawn from the data are not justifiable."

Response:

We thank the reviewer for the positive criticism. We have performed major revision in the new manuscript taking all suggestions into account. We have applied the standard formula of calculating the cancers attributable to infections. We have updated the methodology section and we have ensured that the results or tables are listed according to the third edition of the International Classification of Diseases for Oncology (ICD-O). We have only reported the results as generated from the data from the two hospitals and highlighted where necessary that we were comparing our hospital-based data with other population-based studies. We have inserted a new paragraph on the limitations of this study and modified the conclusion. We are thankful for the suggestions.

References

1.   Gearing RE, Mian IA, Barber J, Ickowicz A. A methodology for conducting retrospective chart review research in child and adolescent psychiatry. J Can Acad Child Adolesc Psychiatry. 2006;15: 126–134. doi:10.1186/1478-4505-4-26
2.   Arya R, Antonisamy B, Kumar S. Sample size estimation in prevalence studies. Indian J Pediatr. 2012;79: 1482–1488. doi:10.1007/s12098-012-0763-3

Competing Interests: We have no conflict of interest to declare