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HIV among cancer patients: prevalence and cancer description by HIV status

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HIV AMONG CANCER PATIENTS:

PREVALENCE AND CANCER DESCRIPTION BY

HIV STATUS

By

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ABSTRACT

Background: Antiretroviral therapy (ART) has resulted in a higher life expectancy of persons living with Human Immunodeficiency Virus (PLHIV) leading to an aging population at risk for non-AIDS defining cancers (NADCs) rather than AIDS-defining cancers (ADCs). Identification of HIV-cancer comorbidity through diagnostic HIV testing of patients presenting for cancer care is not offered routinely. The HIV prevalence among cancer patients in Kenya is undefined. In addition, the spectrum of malignancies in PLHIV has not been well characterized outside of ADCs.

Objective: Our primary objective was to determine the prevalence of HIV among patients with cancer**.** Secondary objectives were to determine the proportion of ADCs and NADCs in HIV positive patients and to describe the spectrum of malignancies seen among HIV-positive and negative patients with cancer.

Methods: This was a cross sectional study done at the Aga Khan University Hospital, Nairobi between February and September 2021 where patients with a histological cancer diagnosis were enrolled and demographic data collected. HIV pre-test counselling and consent were done prior to testing. Diagnostic HIV testing was done using a rapid fourth generation HIV assay. Positive HIV results were confirmed with a rapid third generation assay. HIV and cancer related clinical variables were obtained from medical records including cancer stage, Eastern Cooperative Oncology Group status, CD4 count, HIV viral load, ART regime and history of defaulting on ART.

Results: During our study period**,** 301 cancer patients were enrolled; 67.8% (204/301) were female; mean age was 50.7 ± 12.5 years. From our cohort 10.6% (32/301) patients were HIV-positive. Of the HIV-positive patients, 59.4% (19/32) had a NADC. The commonest NADC among HIV positive patients was breast cancer (18.8%; 6/32). The most prevalent ADCs among HIV positive patients were non-Hodgkin's lymphoma (18.8%; 6/32) and cervical cancer (18.8%; 6/32).

Conclusion: The prevalence of HIV infection among patients with cancer was twice the Kenya national HIV prevalence. NADCs comprised a larger percentage of the cancer burden. Universal opt-out HIV testing of patients attending for cancer care regardless of cancer type may facilitate

early recognition of HIV infected patients, aid in appropriate selection of ART and cancer therapies and preventive strategies.

LIST OF ABBREVIATIONS

ABC:	Abacavir
ADC:	AIDS Defining Cancers
AIDS:	Acquired Immunodeficiency Syndrome
AKUHN:	Aga Khan University Hospital, Nairobi
ART:	Antiretroviral Therapy
ATV/r:	Atazanavir/ritonavir
AZT:	Zidovudine
CLL:	Chronic Lymphocytic Leukaemia
DNA:	Deoxy Ribonucleic acid
DTG:	Dolutegravir
ECOG:	Eastern Cooperative Oncology Group
EBV:	Epstein Barr Virus
EFS:	Event Free Survival
EFV:	Efavirenz
FTC:	Emtricitabine
GI:	Gastrointestinal
GLOBOCAN:	Global Cancer Incidence, Mortality and Prevalence
HBV:	Hepatitis B Virus
HCV:	Hepatitis C Virus
HIV:	Human Immunodeficiency Virus

HL:	Hodgkin's Lymphoma
HPV:	Human papilloma virus
IERC:	Institutional Ethics Review Committee
IQR:	Interquartile range
KS:	Kaposi Sarcoma
NACC:	National AIDS Control Council
NACOSTI:	National Commission for Science, Technology and Innovation
NADC:	Non AIDS Defining Cancers
NCCN:	National Comprehensive Cancer Guidelines
NHL:	Non-Hodgkin's Lymphoma
OS:	Overall Survival
PLHIV:	Persons Living with HIV
REDCap:	Research Electronic Data Capture
RNA:	Ribonucleic acid
SIR:	Standardized Incidence Ratio
SPSS:	Statistical Product and Service Solution
SSA:	Sub Saharan Africa
START:	Strategic Timing of Antiretroviral Treatment
Tat:	Transactivator of transcription
TAF:	Tenofovir alafenamide
TDF:	Tenofovir disoproxil fumarate
TNM:	tumour (T), nodes (N), and metastases (M)
UCI:	Uganda Cancer Institute

UNAIDS:	Joint United Nations Programme on HIV/AIDS
US:	United States
3TC:	Lamivudine

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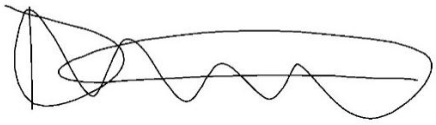
Lastly, I would like to thank God for seeing me through the academic journey thus far and giving me victory over every hurdle.

DECLARATION

"I declare this dissertation does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any university and that to the best of my knowledge it does not contain any material previously published or written by another person except where due reference has been made in the text".



Signature of candidate

30th May, 2022

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CHAPTER 1: INTRODUCTION

1.1 Background

The relationship between Human Immunodeficiency Virus (HIV) and malignancies became evident early in the epidemic with Kaposi sarcoma (KS) being among the first described AIDS defining conditions after a report of 26 cases of KS among homosexuals (1). There are three cancers classified as AIDS-defining cancers (ADCs) and they include KS, cervical cancer and non-Hodgkin lymphoma (NHL) (2). These cancers are due to decreased immune surveillance by virtue of T cell reduction by the HIV virus and subsequent immunosuppression. Nearly a third of persons living with HIV (PLHIV) received a cancer diagnosis prior to HIV treatment with antiretroviral therapy (ART) (3).

Non-AIDS defining cancers (NADCs) comprise malignancies that occur among PLHIV and are not due to host's immune deficiency. These include Hodgkin's Lymphoma (HL), conjunctival squamous cell cancer, hepatocellular carcinoma, anal, lung and head and neck cancers. The increased frequency of NADCs in PLHIV may be due to a number of factors. The HIV virus encodes for a protein known as transactivator of transcription (Tat) which impairs the tumour suppressor function of the p53 gene (4). HIV Tat protein may activate cellular proto-oncogenes such as c-myc genes with potential to induce oncogenicity such as in Burkitt's lymphoma (5). Microsatellite alterations causing genomic instability are also found in HIV- associated cancers. Wistuba et al showed a six times higher occurrence of microsatellite alterations in HIV-associated lung cancers compared to sporadic lung tumours ($p<0.001$) (6). PLHIV are at increased risk of infection with oncogenic viruses such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human papilloma virus (HPV) as a result of shared route of transmission and other viruses like Epstein Barr Virus (EBV) (7-10). For example, EBV-associated HL is found more frequently among PLHIV than in patients with HL and who were HIV-negative. HIV increases susceptibility to effects of carcinogens such as tobacco. Smoking among PLHIV is associated with NADCs such as primary lung and head and neck malignancies. Kirk et al found an elevated lung cancer occurrence in PLHIV (hazard ratio, 3.6; 95% confidence interval, 1.6–7.9) even after adjusting for smoking status (11). PLHIV are also at risk of sporadic cancers present in the general population including those of the breast, colon and prostate (9, 12).

Cancer epidemiology among PLHIV has been influenced by the introduction of ART (13, 14). Its impact was illustrated by the cohort study among HIV positive patients in Switzerland that assessed the incidence of ADCs and NADCs during three periods: pre-ART, early ART and late ART. This study showed that the ADCs comprised a progressively smaller percentage of cancers in PLHIV with increasing utilization of ART, (88%, 47% and 33%), for each of the three periods respectively (15). Another study in the United States (US) by Shiels on proportion of cancers in PLHIV also showed a greater than threefold reduction in ADCs $p<0.001$ with a concurrent triple increase in NADCs $p<0.001$ in the post ART period (16). The Strategic Timing of Antiretroviral Treatment (START) study was a randomized trial on HIV infected adults who were asymptomatic and it compared early ART initiation irrespective of CD4 cell count versus deferred ART initiation once patients had a CD4 cell count of below 350 cells/ mm^3. The study was aimed to establish whether there were any benefits of early ART commencement in PLHIV. In the study, the hazard ratio was found to be 0.36 (95% CI, 0.19 to 0.66; P=0.001) for ADCs and NADCs (17).

Despite marked improvements in HIV treatment and outcomes since the onset of the HIV pandemic there is still an increased cancer incidence and mortality among PLHIV (13-15, 18). A registry linked population study in the US by Hernández-Ramírez RU found a 4.8% (n= 21,294/448,258) incident cancers among PLHIV. There was a two-thirds increase of malignancy among PLHIV in comparison to the general populace (standardized incidence ratio (SIR) 1.69,95% CI 1.67-1.72) for all cancers (18). Thirty four percent (n=250/728) deaths among PLHIV were as a result of cancers in a study by Morlat in France (19). Longevity for PLHIV has also increased, leading to a large cohort of older adults with a lifespan similar to the general population (20). Cancer risk increases with age (21) and this is projected to contribute to higher cancer cases in PLHIV following widespread use of ART. As an example, Shiels et al projected a threefold increase in the number of HIV infected adults above 65 years of age in 2030 (22).

A significant proportion, approximately 69%, of PLHIV reside in Sub-Saharan Africa (SSA) (23). Several factors make it difficult to assess cancer epidemiology and trends in this population and whether there is as a similar shift from ADC to NADC (24). One such factor is that most African countries lack real time population-based cancer registries. A study by Crocker et al critically appraised the standard and constitution of cancer registries in SSA used to generate

global cancer incidence, mortality and prevalence (GLOBOCAN) estimates. Twenty countries (300 million people) had no cancer registries. The registries' population coverage differed from two percent to one hundred percent and nearly all had a bias towards their urban population (25). A cross sectional medical review study at the Uganda Cancer Institute (UCI) demonstrated a HIV prevalence of 23% among cancer patients, which was three times higher than the HIV prevalence in Uganda (26). In this study, 42% of persons who had a documented HIV- positive status had a NADC. Another retrospective, descriptive study on HIV prevalence among cancer patients in Guinea demonstrated a 79% proportion of NADCs (27). In Tanzania, a retrospective study in a zonal referral hospital showed a proportion of 72% NADCs among PLHIV(28).

Cancer incidence has been on the rise in Kenya. Recent GLOBOCAN data of 2018 estimated that there would be an incidence of 47,000 new cancer cases per year with a mortality of 32,000 annual cancer cases in Kenya (29). In 2013, the incidence of cancer was about 28,000 new cases per year with a mortality of 22,000 cases per year (30).

In Kenya, the HIV prevalence among cancer patients as well as cancer epidemiology in PLHIV is undefined. Most studies have determined prevalence of individual cancers. The only study found describing various HIV- associated cancers was a laboratory-based study carried out in Kenyatta National Hospital by Rogena et al who reviewed 173 histological blocks and reports from 2000 to 2011. They demonstrated KS and conjunctival squamous cell cancer as the leading ADC and NADC in Kenya respectively. In addition, NADCs constituted 29.3% of all malignancies (31).

Knowledge of the HIV status of patients presenting for cancer care is important given this background. HIV positive patients who are either unaware of their status or not on ART remain at risk of severe immunosuppression once treated with various cancer treatment modalities like chemotherapy (32-34). Starting ART and preventing further immunosuppression in addition to appropriate opportunistic infection prophylaxis has demonstrated good outcomes and increased survival among HIV positive cancer patients. Some malignancies have comparable outcomes to those patients without HIV diagnosed with the same cancer (8, 34-39). A retrospective study by Montoto compared outcomes of patients with newly diagnosed HL among HIV positive patients on ART and those without HIV following treatment with the standard HL chemotherapy protocol. The HIV positive group had unfavourable prognostic factors and yet the five year

overall survival (OS) and five year event free survival (EFS) was not significantly different from the HIV negative group (81% vs 88% (p=0.15)) and (59% vs 66% (p=0.5)) respectively (39).

The use of combination ART with systemic chemotherapy introduces the probability of drug-to-drug interactions. In addition, the cytochrome P450 liver enzymes metabolize many chemotherapy drugs with potential to cause adverse events, reduced efficacy of either group of drugs if personalized care is not offered in view of the two comorbidities (32, 38, 40, 41).

The main aim of this study was to explore the HIV prevalence among cancer patients in a tertiary cancer centre in Kenya and characterize the spectrum of malignancies in this population as well as seek to answer the question of whether there was a similar observation of a shift from ADCs to NADCs.

1.2 Justification

The prevalence of HIV among cancer patients in Kenya is undefined and diagnostic HIV testing is not routine in our cancer care sites. Moreover, the spectrum of malignancies in PLHIV in Kenya has not been well characterized outside of ADCs.

Knowledge of the proportion and range of HIV-associated cancers informs the extent of HIV-cancer comorbidity on the health system and therefore facilitate planning of preventive strategies among PLHIV including smoking cessation, annual cervical cancer screening, HBV testing and vaccination, HPV testing and vaccination and age appropriate screening such as colonoscopy for those over 50 years of age.

Early identification of HIV and treatment with ART is a contributing factor of treatment outcomes for cancer patients who are also HIV positive. Furthermore, HIV testing among patients presenting for cancer care could enable selection of individualized ART and cancer therapies thus minimizing toxicity, improving efficacy and improve outcomes of these patients.

1.3 Research Questions

What is the HIV prevalence in patients with a cancer diagnosis, and what is the spectrum of malignancies seen in those with HIV?

1.4 Study Objectives

Primary Objective

To determine the prevalence of HIV in patients with a histological cancer diagnosis at the Aga Khan University Hospital, Nairobi (AKUHN).

Secondary Objective:

1. To describe the spectrum of malignancies seen in HIV-positive and negative patients at AKUHN.
2. To determine the proportion of ADCs and NADCs in HIV positive patients at AKUHN.

CHAPTER 2: METHODOLOGY

2.1 Study Setting

The study was done at the Aga Khan University Hospital Nairobi (AKUHN), a private teaching hospital offering tertiary care and with a robust haemato-oncology service. All patients with a suspected or confirmed hematologic or solid cancer are enrolled into the AKUHN hemato oncology outpatient unit and are attended to by oncologists and haematologists situated there . Similarly there is one hemato-oncology ward dedicated for patient requiring inpatient services.

2.2 Study Design

This was a cross-sectional study.

2.3 Study Population

Patients with a histological confirmed cancer diagnosis at the AKUHN.

Inclusion Criteria

1. Patients aged 18 years and above.
2. No documented HIV test result
3. Known infection with HIV

Exclusion Criteria

1. Patients who declined HIV testing.
2. Patients who did not give consent for study enrolment.

2.4 Sample Size

A study at the UCI in 2015 demonstrated a HIV prevalence of 23% among cancer patients (15). Based on this and the prevalence sample size formula below, using a precision level of 5% and 95% confidence, the minimum sample size required for the study was 273 patients and adding an attrition rate of 10%, the sample size required was 300.

$$n = deff \times \frac{N \times \hat{p} \times \hat{q}}{\frac{d}{Z_{\alpha/2}} \times (N-1) + (\hat{p} \times \hat{q})}$$

Where

$n =$ sample size

$deff =$ design effect

$N =$ population size

$\hat{p} =$ the estimated proportion

$\hat{q} = 1 - \hat{p}$

$d =$ desired absolute precision

Z=confidence level

2.5 Sampling procedure, recruitment and sample collection

Consecutive sampling was done from the hemato-oncology inpatient ward and outpatient clinic simultaneously until desired sample size was reached. The study was conducted between February 2021 and September 2021. The study staff underwent training on purpose of study, patient recruitment, data collection and management procedures to ensure privacy and confidentiality. The study staffs were alerted by clinicians whenever patients meeting the inclusion criteria were encountered. Patients were reviewed by the resident and informed on the aim of the study, and thereafter assessed for eligibility and willingness of study participation. Following written informed consent, each patient was allocated a unique identification number. Study staff drew four millilitres of blood into a serum separator clot activator tube and sample labelling done. The sample was then immediately transported to the laboratory for analysis. Diagnostic HIV testing was done using a fourth generation HIV assay (Cobase 411/601 HIV Combi gen.2 assay). Positive HIV results were confirmed with uni-gold rapid third generation assay as per the HIV testing algorithm. Patients who were confirmed HIV positive received post-test counselling and their attending clinician was informed. They were then linked to an Infectious disease specialist for further management.

2.6 Data Collection

Data were collected based on a data abstraction tool (Appendix 1) using the Research Electronic Data Capture (REDCap) platform (Vanderbilt and National Institute of Health) (42) from electronic clinician and laboratory records. The tool captured patient demographic details, cancer characteristics and HIV disease characteristics. Demographic details included age, gender, race, patient comorbidities, smoking and alcohol history. The latter variable was categorised as past or present smoking and alcohol use and never for those who had no exposure. HIV disease characteristics included date of HIV diagnosis, date of ART initiation, current ART regime, CD4 count at diagnosis, current HIV viral load, and known HBV status from the laboratory records. Patients were categorised as having a history of defaulting ART if they had stopped taking their ART at any point since ART commencement. Duration of ART was calculated from entry date of the study and date of ART initiation.. The study used designated tumour (T), nodes (N), and metastases (M) "TNM" one through four staging as per National Comprehensive Cancer Guidelines (NCCN) to stage each type of tumour. KS was staged as per AIDS Clinical Trials Group staging with designation of (T) for extent of tumour, (I) for immune status and (S) for severity of systemic illness. Binet staging was used for chronic lymphocytic leukaemia (CLL.) Early cancer was defined as TNM stages one and two and TNM stages three and four set as late stage. KS was designated T0S0 or T1S0 when early with any other designation classified as late stage (43). Binet C for CLL was set as late stage. Functional status was evaluated with the Eastern Cooperative Oncology Group (ECOG) score zero through five. Poor functional status was assigned for an ECOG score greater than two (44). HIV viral load obtained while on ART was grouped into three categories, < 50 cells/ul, 51-200 cells/ul and >200 cells/ul. Patients with a viral load of >200 cells/ul were classified as having inadequate HIV viral suppression and ART treatment failure.

2.7 Data Management

The REDCap data was checked for completion and assessed for any errors. All the data were de-identified for analysis. The REDCap data was stored under the institution server. On study

completion, the data sets were handed over to the Aga Khan University Faculty of Health Sciences for archiving and disposal as regulated by institutional guidelines.

2.8 Data Analysis

Continuous variables were summarized using median and interquartile range (IQR), and categorical variables using frequency and percentages. Cross-tabulations with Chi-square test or Fisher's exact test were performed to relate variables of interest. All the analyses were performed using SPSS version 23 and a p value < 0.05 was considered statistically significant wherever applicable.

2.9 Ethical Considerations

Ethical approval was sought from the Aga Khan University, Nairobi Institutional Ethics Review Committee (Approval Number 2020/IERC-106). Approval was also obtained from National Commission for Science, Technology and Innovation (NACOSTI). Written informed consent was obtained prior to entry into the study (Appendix 2). Information collected was only available to the study team to ensure privacy and was password protected. All staffs working on this study were trained on how to respect participant confidentiality. The enrolled participants were only identified using the unique identification number assigned to them that was linked to their hospital numbers and they were consequently de-identified for analysis to maintain confidentiality. Potential risks were communicated to the participants and included pain during blood draw for diagnostic HIV testing, skin infection at the site of blood collection and bruise or swelling on the skin. Aseptic procedure was used to draw blood and was done professionally and gently to minimize discomfort.

CHAPTER 3: RESULTS

3.1 Sample characteristics

Three hundred and one cancer patients were enrolled. The median age of the participants was 52.0 (IQR: 44.0-61.0) years, 67.8% of the study population were female, and majority (92.0%; n=277) were of African origin. The most prevalent comorbidity among the participants was hypertension 26.6% (n=80) followed by diabetes at 13.3% (n=40). Majority of the respondents (86.4%, n=260) had never smoked in their lifetime while 12.6% (n=38) were former smokers and only 1.0% (n=3) were current smokers. In terms of history of alcohol consumption, 64.8% (n=195) of the respondents had never consumed alcohol, 25.6% (n=77) and 9.6% (n=29) were former and current users respectively (Table 1).

Characteristics		n	%
Age (Years), median (IQR)		52.0 [44.0-61.0]	
Gender	Male	97	32.2
	Female	204	67.8
Ethnicity	African	277	92.0
	Asian	13	4.3
	Caucasian	11	3.7
Comorbidities	Diabetes	40	13.3
	Hypertension	80	26.6
	Chronic Kidney Disease	9	3.0
	Others*	19	6.3
	None	180	59.8
Smoking History	Current	3	1.0
	Former	38	12.6
	Never	260	86.4
Alcohol History	Current	29	9.6
	Former	77	25.6
	Never	195	64.8

Table 1: Characteristics of the enrolled participants (n=301).

*Other included: asthma), coronary artery disease, dystonia), epilepsy, hepatitis B, hypothyroidism, idiopathic pulmonary fibrosis, neurofibromatosis, osteoarthritis, rheumatoid arthritis

3.2 HIV characteristics

The results indicate that the prevalence of HIV was 10.6% (95%CI: 7.4% - 14.7%) from 32 participants, out of who 30 participants were known to be HIV infected prior and 2 were picked during the study. The median age of HIV positive patients was 49 (IQR: 44-57) years of whom, females were 65.6% (n=21/32). Among HIV positive patients, 93.9% (n=30/32) had a HIV-1 viral load test done, 76.7% (n=23/30) of whom viral load was recorded as less than 50 copies/ml, 6.6% (n=2/30) had viral load in the range of 51-200 copies/ml and the remaining 16.7% (5/30) had theirs above 200 copies/ml. Only 50.0% (n=16/32) had CD4 counts recorded at diagnosis. For these patients, the median CD4 count was 73.0 cells/ mm^3 (IQR: 40.0 – 157.0). The different ART regimens the patients were on are shown in Figure 1. The most common ART regimen was TDF/3TC/DTG while the least common were TDF/3TC/EFV and TDF/FTC/EFV, each used by 3.2% of the patients. One patient had a new HIV diagnosis and was yet to start ART. Only 12.5% (n=4) patients had a history of defaulting on ART. Only 5.3% (n=1/19) was positive for HBV (Table 2).

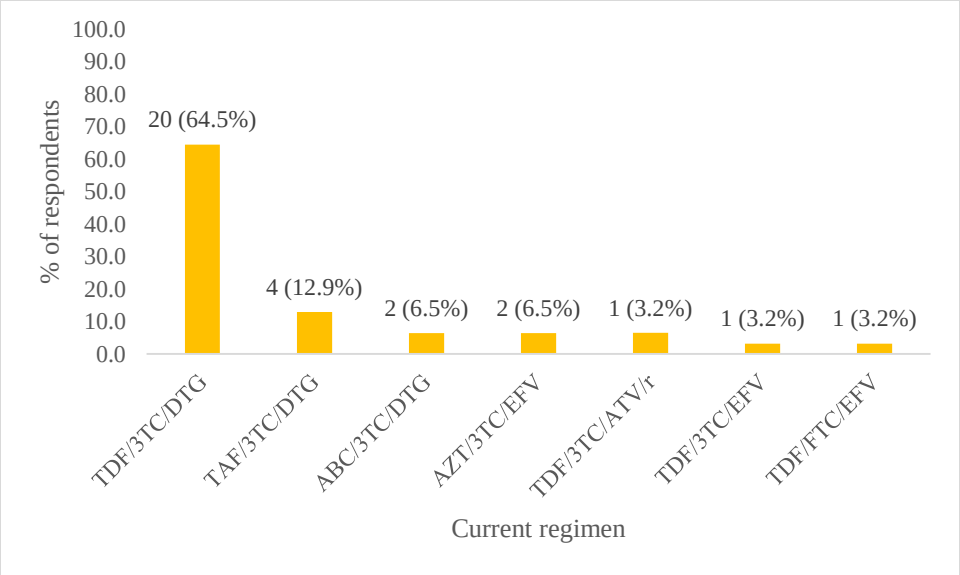

Figure 1: ART regimen used

Characteristics		n	%
HIV Test	Positive	32	10.6%
Gender	Males	11	34.4%
	Females	21	65.6%
Age, median (IQR) years		49 [44-57]	
Viral Load Done Before	Yes	30	93.8%
	No	2	6.3%
Duration of ART, median (IQR) months		45 [10-58]	
History of ART Defaulter	Yes	4	12.9%
	No	27	87.1%
Specify Defaulter Months	4 Months	1	25.0%
	12 Months	2	50.0%
	36 Months	1	25.0%
Last Viral Load Count	< 50	23	76.7%
	51 - 200	2	6.6%
	> 200	5	16.7%
CD4 Count at diagnosis, median (IQR) (n = 16)		73.0 [40.0-157.0]	
Hepatitis B Status	Positive	1	3.1%
	Negative	18	56.3%
	Not Available	13	40.6%

Table 2: HIV characteristics

Table 3 shows gender and cancer stage stratified by HIV status. The HIV prevalence among males and females were 11.3% and 10.3% respectively. Majority of the study participants had stage four cancers irrespective of the HIV status.

	HIV status		
	Positive n (%)	Negative n (%)	Total N
Gender			
Male	11 (11.3)	86 (88.7)	97
Female	21 (10.3)	183 (89.7)	204
Age at cancer diagnosis ,median (IQR) years	49 (45-55.2)	52 (42-50.7)	301
Cancer stage			
1	1 (12.5)	7 (87.5)	8
2	6 (14.6)	35 (85.4)	41
3	8 (8.8)	83 (91.2)	91
4	16 (12.8)	109 (87.2)	126
Others	1 (2.9)	34 (97.1)	35
Total	32 (10.6)	269 (89.4)	301

Table 3: HIV status by gender and cancer stage

3.3 Cancer characteristics

Table 4 summarizes cancer characteristics and cancer sites of the study population. Breast cancer was the most frequent cancer diagnosis 33.6% (n=101). Majority of the patients, 41.9% (n=126) had stage IV cancer, 30.2%, 13.6% and 2.7% had stages III, II and I respectively. Five of the participants had cancers with different staging systems including BINET C (n=4) in CLL and T1I1S1 in the only patient with Kaposi Sarcoma. The remaining 30 patients had cancers with no standardized staging system including multiple myeloma and acute leukaemia. The prevalence of late stage (stage III and IV) cancer was 81.6 %(95%CI: 76.4% - 86.1%). Majority of the participants 66.4% (n=200) had an ECOG score of 1, 21.3% had a score of 0 while 9.6%, 2.0% and 0.7% had scores of 2, 3 and 4 respectively. HIV status across the different cancer types is shown in figure 3.

Characteristics	(N = 301)	n	%
Cancer Stage	I	8	2.7
	II	41	13.6
	III	91	30.2
	IV	126	41.9
	Other*	35	11.6
Cancer Stage	Early (I& II)	49	18.4
	Late (III& IV)	217	81.6
Other Cancer Stage* (n = 35)	None	30	85.7
	BINET C	4	11.4
	T1I1S1	1	2.9
ECOG Status	< = 2	293	97.3
	> 2	8	2.7
Site	Breast	101	33.6
	Cervical	21	7.0
	Gastrointestinal	52	17.3
	Hematologic	42	14.0
	Head and Neck	19	6.3
	Prostate	16	5.3
	Others	50	16.6

Table 4: Cancer characteristics of the patients (n=301)

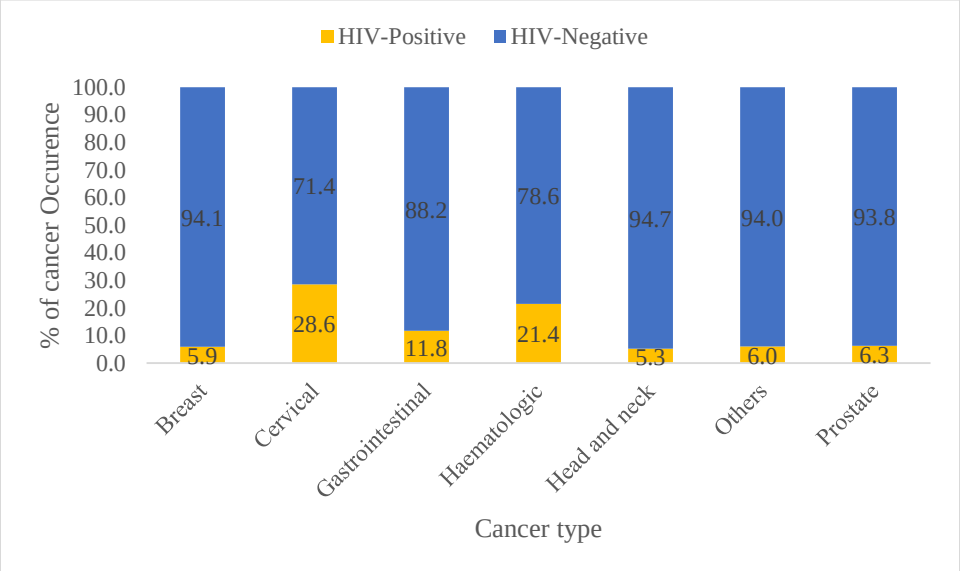

Figure 2: Different types of cancers and HIV status

3.4 Types of cancers among HIV-positive patients

Different types of cancers diagnosed among the 32 HIV positive patients are shown in Figure 4. The most common NADC among HIV positive patients was breast cancer 18.8% (n=6) with 9.4% diagnosed with Hodgkin's lymphoma and 6.3% had lung adenocarcinoma. The gastrointestinal (GI) cancers included anal signet ring carcinoma, anal squamous carcinoma, cholangiocarcinoma, oesophageal squamous cell carcinoma, gall bladder adenocarcinoma and gastric adenocarcinoma, each diagnosed in one patient. The most common ADCs were cervical cancer and NHL in equal proportions 18.8% (n=6). Of interest was the low frequency of Kaposi Sarcoma 3.1% (n=1) in the study.

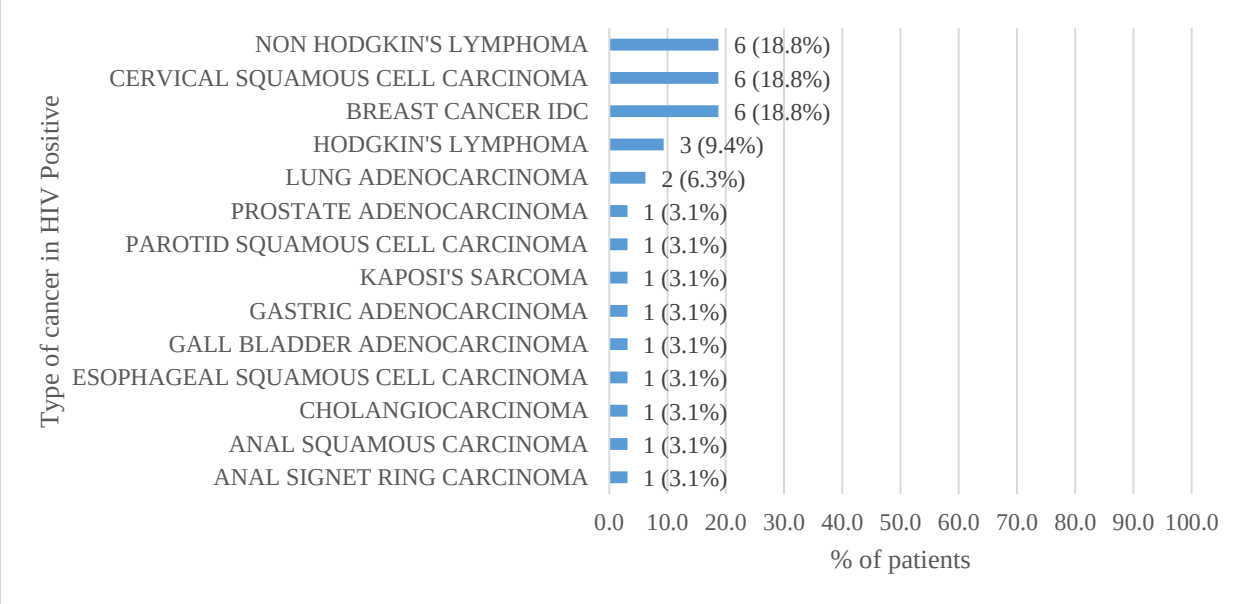

Figure 3: Spectrum of malignancies among HIV positive patients (n=32)

HIV positive patients with a detectable HIV viral load above 50 copies/ml were 23.3% (n=7/30). Majority of these patients had ADCs with 13.3% (n=4/30) for NHL, 3.3% (n=1/30) each for KS and cervical cancer. One patient with anal cancer also had a detectable HIV viral load (figure 5).

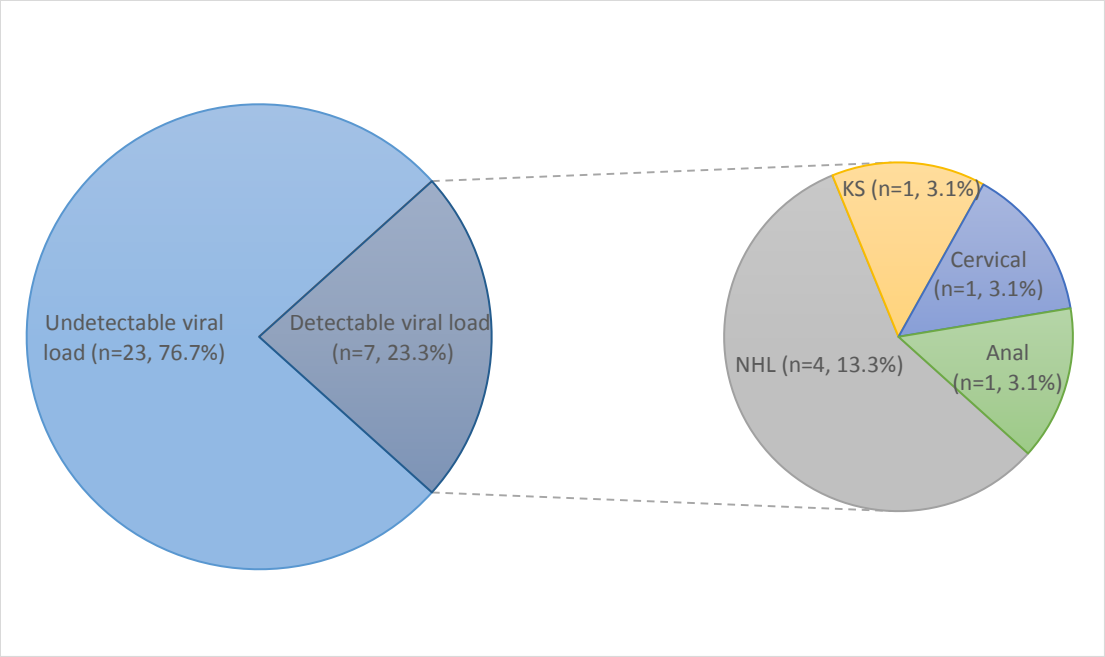

Figure 4: HIV viral load by cancer type

3.5 Proportion of ADCs and NADCs and HIV status

Of the 32 HIV-positive participants, 59.4% (n=19) had a NADC while 13 40.65% (n=13) had an ADC. The prevalence of NADC and ADC among HIV negative patients were 248 (82.2%) and 21 (17.8%) respectively **(**Figure 5).

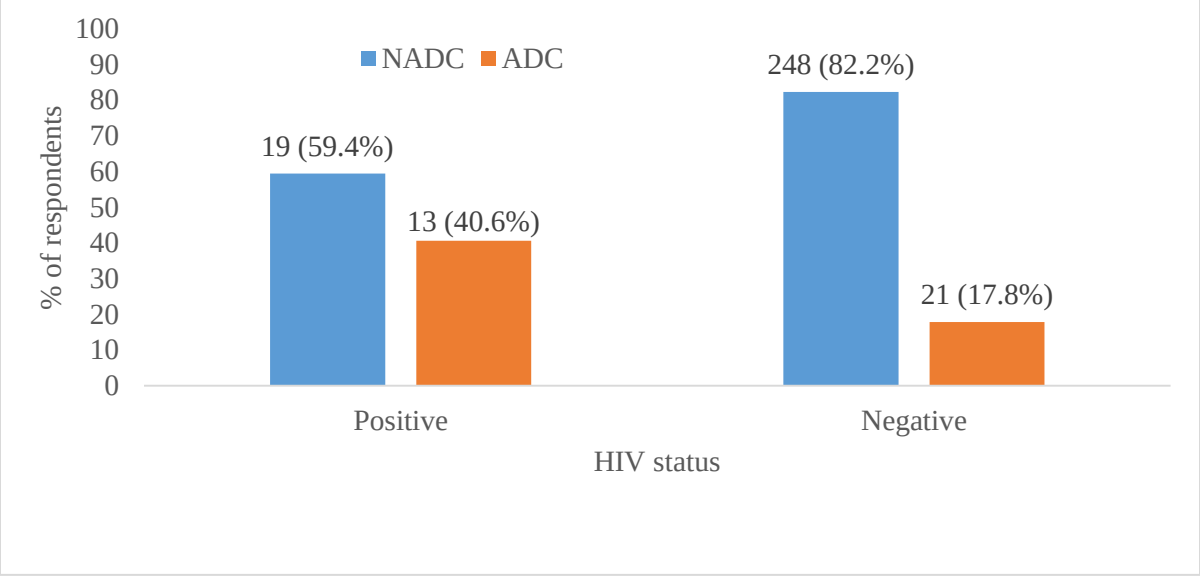

Figure 5: Proportion of NADCs and ADCs by HIV status

CHAPTER 4: DISCUSSION

The present study documented the prevalence of HIV and the spectrum of malignancies among cancer patients attending AKUHN haemato-oncology outpatient and inpatient units. In this cohort of 301 cancer patients, we found a HIV prevalence of 10.6% which was twice that recorded as the national HIV prevalence among an adult general population aged 15-64 years in the 2018 Kenya population- based HIV impact assessment (KENPHIA) survey (45).

This was similar to the nine percent prevalence of HIV-cancer comorbidity in a study by Mremi et al in a Tanzanian zonal hospital (28) but lower than what was described in a Ugandan study which demonstrated a 23% prevalence (26). The lower prevalence in our study may be influenced by patient catchment and may not reflect that in a middle or lower socio economic population.

Identification of HIV-cancer comorbidity through diagnostic HIV testing of patients attending haemato oncology units is not offered routinely. The higher HIV prevalence demonstrated in this population compared with the national HIV prevalence implies a missed opportunity for HIV diagnosis, initiation of ART and chemoprophylaxis for prevention of opportunistic infection, all of which may ultimately improve outcomes.

Sixty percent of the cancers among HIV positive patients in the study were NADCs demonstrating a shift in cancer epidemiology from ADCs to NADCs in PLHIV similar to that observed in developed countries with ART availability (15, 16). A study done a decade ago by Rogena et al at the largest referral hospital in Kenya, Kenyatta National Hospital, showed that ADCs dominated the cancer burden among PLHIV in Kenya (31). Since then, Kenyan HIV treatment guidelines have changed to recommend universal testing, and treatment of all found to have HIV with ART as recommended by World Health Organisation (WHO) (46). This is projected to result in higher survival rates among PLHIV and a large cohort of older HIV positive adults with cancer risks similar to the general population and not necessarily cancers associated with profound immunosuppression attributable to HIV infection.

The changing trend and shift towards NADCs among PLHIV in Sub Saharan Africa (SSA) was demonstrated in Guinea and Tanzania with 79% and 72% prevalence of NADCs respectively

underscoring the need to perform diagnostic HIV testing in cancer patients irrespective of cancer type (27, 28).

Among the NADCs, the commonest malignancy among HIV positive patients in the study group was breast cancer (18.8 %). The predominance of breast cancer among NADCs has been shown in SSA. A study done in Soweto, South Africa among patients with breast cancer demonstrated a HIV prevalence of 19.7% (47). The high breast cancer prevalence in our study could be because it is also the most frequent cancer among Kenyan women. As per the 2020 GLOBOCAN estimates, breast cancer had the highest incidence 16.1% (n= 6,799/42,116) (48). Contrary to the present study Mpunga et al showed conjunctival, HL and anal malignancies were the most frequent NADCs in Rwanda (49). HL, lung and anal malignancies and hepatocellular carcinoma were the most common NADCs in developed countries (16).

Cervical cancer and NHL were the most prevalent ADCs in our study, occurring in equal proportions. These findings were comparable to those described in other SSA countries (24, 28, 49-52). ADCs, which accounted for 40% of all cancers among HIV positive patients, are a result of advanced immunosuppression suggested by the median CD4 count well below 200 cells/ul at HIV diagnosis among the study population. Advocacy is needed for routine HIV testing to ensure early ART initiation to reduce the ADC burden among PLHIV.

There was a low rate of KS in our study with only one case identified. This is in contrast to various SSA studies, which showed KS as the most common ADC among PLHIV (28, 31, 49, 53). In the present study, majority of the patients who were HIV positive were virally suppressed and the frequency of ADCs such as KS would be expected to be lower although there was no record of current CD4 counts. A higher socioeconomic status in our patient catchment was also a possible explanation for this finding of low KS frequency.

ART coverage was nearly 100% among PLHIV in our study in keeping with the 90% WHO recommendation (46). Among the HIV positive patients, 18% had not achieved HIV viral suppression placing them at potential risk of further immune suppression when various cancer treatment modalities such as chemotherapy are used. Cross referral among oncologists and infectious disease specialists would assist in optimal control of both illnesses thereby improved survival and outcomes for these patients.

3.1 Limitations of the study

The cross-sectional nature of the study determined the proportion of patients with both cancer and HIV but was not able to determine any cause-effect relationship or HIV associations with individual cancer types.

Our study gave a HIV prevalence and spectrum of malignancies at AKUHN. It may not be generalizable to the remaining Kenyan regions as it was biased by patient catchment and may not have reflected the prevalence in a middle or lower socioeconomic population. AKUHN, being a private tertiary care facility, may have had clients with different health seeking behaviour patterns.

Potential for selection bias may have misstated the estimated prevalence of HIV among cancer patients and some patients may have felt that clinician knowledge of their status may affect their overall cancer care and as a result held back giving consent.

The design of prospective cross section study over the seven months did not allow comparison of post-ART with pre-ART period.

CHAPTER 5: CONCLUSION

To our knowledge, this is the first study on HIV prevalence among patients with malignancies in Kenya and the study demonstrated one that was double that of the Kenya national HIV prevalence.

NADCs comprised a larger percentage of the cancer burden among PLHIV suggesting that universal opt-out HIV testing of patients presenting to haemato-oncology units regardless of cancer type may facilitate early identification of HIV infected patients and aid in appropriate selection of ART and cancer therapies.

The burden of ADCs among PLHIV is still significant despite widespread availability of ART suggesting that efforts need to be continually placed for early identification of HIV infection and early ART commencement before severe immunosuppression sets in.

The most prevalent cancers among HIV positive patients were breast cancer, cervical cancer and NHL. Most of these cancers offer an opportunity for deployment of preventive strategies such as HPV vaccination to prevent cervical cancer and mammogram for detection of early breast cancer among PLHIV.

CHAPTER 6: RECOMMENDATIONS

We recommend a Kenyan population HIV/AIDS-cancer match study to obtain an accurate HIV prevalence among cancer patients to assess the magnitude and put measures towards optimal management for patients with the two comorbidities.

Being an HIV endemic country, we also recommend universal opt-out HIV testing to patients on enrolment to cancer care units in order to offer optimal ART treatment regimen, opportunistic infection prophylaxis and plan for chemotherapy so as to avoid further immunosuppression that may occur on initiation of chemotherapy.

Through the study, a cohort of HIV positive and negative cancer patients was established and can act as a foundation to further studies that can be carried out in the subject area of HIV-associated cancers including long term follow up and whether overall survival and outcomes are comparable between the two groups.

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APPENDICES

Appendix 1: Data Collection Tool

Section A – Demographics and Contacts

1. Study ID
2. Name: 2.1 First Name
   2.2 Middle Name
   2.3 Last Name
3. Hospital Number:
4. Date of Birth (DD/MMM/YY)
5. Gender (Tick as appropriate) □ Male □ Female
6. Tel. No.: 6.1 Tel. No. (1)
   6.2 Tel. No. (2)
7. Email Address
8. Postal Address
9. Race (Check as appropriate) □ African □ Asian □ Caucasian
10. Comorbidities
11. Smoking history
12. Alcohol history
13. Hepatitis B status

Section B: HIV Testing

14. HIV test result

Section C: Cancer Details

15. Date of cancer diagnosis _____
16. Histological type of cancer
17. Cancer stage
18. Eastern Cooperative Oncology Group (ECOG) performance status

_____

Section C: HIV Treatment Details

19. Date of diagnosis of HIV
20. CD4 count at diagnosis
21. Time (months) since ART initiation
22. Current ART regime
23. Last tested HIV-1 RNA count
24. Date of last tested HIV-1 RNA count
25. Previous history of defaulter status and duration in (months) Yes…… No …

Appendix 2: Consent form

Approval Number: 2020/IERC-106

STUDY TITLE: PREVALENCE AND CANCER DESCRIPTION BY HIV STATUS

Introduction

My name is ……from the Aga Khan University Hospital, Nairobi. We are conducting a research to investigate the burden of HIV disease among patients with cancer and the different type of cancers among patients with and without HIV.

Purpose of this study

The aim of this study is to determine HIV prevalence among patients with cancer in order to plan effective preventive strategies. Treatment of cancer can negatively affect a person who has HIV and is not on treatment. One can be affected by further decrease in their immunity leading to deterioration of one's health. If HIV disease is detected early, a patient is started on HIV treatment that is carefully selected bearing in mind one's cancer treatment. In this way, healthcare providers ensure that the two treatments will be beneficial to you.

Benefits of the study

The study will help us to implement routine HIV testing among patients with cancer, help us modify our current practice for the better and improve outcomes and survival of our patients.

Risks/side effects

Blood sample collection: The risks of harm because of having blood drawn are very small. They include pain during blood draw, skin bruising and infection at the site of blood collection. We will ensure all necessary sterilization has taken place to prevent this and assure you that the pain disappears after a short while.

Voluntary participation

Participation in this study is voluntary and you can withdraw your participation freely without jeopardy to care.

Confidentiality

We have taken a number of steps to ensure utmost confidentiality. The information given is only accessible to the researchers. Data sets will not contain names or unique hospital numbers and will be de-identified for analysis.

Conduct of Study and Follow up

We will first gather some information about you together with details about cancer illness. We will then talk about HIV disease and benefits of testing you for HIV and get consent to perform the test. All patients with cancer who have not had a documented HIV test within the last 1 year or are unaware of their HIV status are eligible to participate. After HIV pre-test counselling, a blood sample will then be drawn and taken to the laboratory for testing. We will discuss the results, impact of results with you, and provide appropriate referral based on the results. If test result is positive, we will discuss positive living with HIV and link you to the Infectious Disease Specialist Clinic for commencement of care. If HIV negative, we will discuss recommendations for HIV re-testing.

Costs

There are no additional costs of participating in the study. The HIV test will be free for all patients diagnosed with cancer.

Who to contact

The study has been approved by the Aga Khan University, Nairobi Institutional Ethics Review Committee (IERC) that makes sure study participants do not suffer harm. If you have some questions or wish to contact the investigators of this study, please call Dr. Diana Muturi +254711649040 for any further questions or clarifications that you have.

Consent Agreement

I have read the foregoing information and I give my consent to enrol as a participant in the study.

Print Name of Participant

_____

Signature of Participant

_____

Signature of Person Obtaining Consent

_____

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