Adherence to Antiretroviral and Cancer Chemotherapy, and Associated Factors Among Patients with HIV–Cancer Co-Morbidity at the Uganda Cancer Institute: A Cross Sectional Study

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Abstract

Background: Human Immunodeficiency Virus is a major global public health issue affecting millions of people, and sub-Saharan Africa where Uganda lies is is disproportionately affected. There has been an increase in cancer among HIV patients which has resulted into use of co-medications that sometimes affect ART and cancer chemotherapy adherence. We aimed to determine adherence to antiretroviral and cancer chemotherapy and the associated factors among patients with HIV-cancer co-morbidity at the Uganda Cancer Institute.

Methods: We conducted a cross-sectional study among 200 randomly selected adult cancer patients infected with HIV, attending Uganda cancer institute. Antiretroviral and anti-cancer chemotherapy adherences with associated factors were assessed quantitatively. We collected the data using interviewer administered semi-structured questionnaires**.** Modified Poisson regression with robust standard errors was used to estimate prevalence ratios at 95% confidence intervals for factors associated with adherence to ART and cancer chemotherapy.

Results: Overall, 54% (107/200) of the study participants adhered to both ART and chemotherapy, and 55% (110/200) adhered to ART while 65% (129/200) adhered to cancer chemotherapy. A majority, 61% (122/200) of the respondents were males. The mean age of the respondents was 42(SD±11years), and at least 43% (86/200) belonged to protestant religion. More than half, 56.5% (113/200) were married and at least 45% (90/200) had attained a primary level of education. Patients with good adherence to antiretroviral therapy and chemotherapy were 107(54%, 95% CI=46.5-60.4). No knowledge of cancer stage (PR=0.4, 95% CI=0.25-0.56, P<0.0001), having an AIDS defining cancer (PR=0.7, 95% CI=0.50-0.88, P=0.005), ART clinic in district not near Uganda Cancer Institute (PR=0.7,95% CI=0.84-0.96, P=0.027) and affordability of cancer chemotherapy (PR=1.4, 95% CI=1.02-1.87, P=0.037) were associated with adherence to both ART and cancer chemotherapy.

Conclusion: Adherence to both ART and cancer chemotherapy was low. Factors significantly associated with adherence were: knowledge of the cancer stage by the patient, the type of cancer diagnosis, source of ART and affordability/ availability of medications. There is need to provide information on stage of cancer and adherence counseling to patients. Furthermore, Integration of HIV- cancer care will be necessary for efficient and effective care for the patients.

Background

Globally, an estimated 37.7 million people were living with HIV in 2020, and about 680,000 died due to AIDS-related illnesses in the same year [1]. Recently, there has been a rise in cancer among the people living with HIV (PLWHIV) with nearly 25–35% of the global HIV-associated deaths occurring among cancer patients and Sub-Saharan Africa (SSA) bears the greatest burden [2, 3]. People Living with HIV (PLWH) are at an elevated risk of developing cancer [4], and have a higher incidence of both AIDS-defining cancers (ADCs) and non-AIDS-defining cancers (NADCs) due to HIV-induced immunodeficiency

compared with the general population [5]. Some of the cancers that have been associated with HIV infection include; Kaposi sarcoma is the most common HIV-associated malignancy, followed by cervical cancer, lymphoma and anal cancer, lung cancer and hepatocellular carcinoma [6].

Uganda had an estimated 1.4 million people living with HIV in 2019, and in the same year approximately 23,000 people died of AIDS-related illnesses [7]. The number of documented new cancer cases has increased over the past years in Uganda with approximately 4,000 cancer patients in registered in 2016 and 1,500 cancer-related deaths[8]. Previous studies in Uganda have established an association between HIV infection and cancers with the prevalence ranging from 23–57% [9, 10].

Previous studies have demonstrated that adherence to ART and chemotherapy among HIV-infected cancer patients reduce morbidity associated with opportunistic infections which improves prognosis among these patients [11]. While evidence has found an association between HIV and cancer [10], adherence to medication among cancer patients is sub-optimal. Documented literature elsewhere indicate that adherence to ART and chemotherapy improves patients prognosis [11]. This adherence to care has been associated with; having comorbid conditions, socio-demographic factors, health system factors such as cost of medication, and therapy-related factors such as; the dosing frequency and side effects [12–15].

There is limited data on the ART and chemo adherence in Uganda. Even the available data on ART and cancer chemotherapy has estimated adherence separately. For instance, the average adherence to ART ranges from 50–95% [15, 16] which is lower than the UNAIDS cut off, while adherence to chemotherapy is much lower at 14%[17]. Further still, being on ART and taking cancer chemotherapy increases the pill burden, side effects, toxicity which affect adherence [18]. Data on adherence to ART and cancer chemotherapy as well as the associated factors among HIV-infected cancer patients is limited in Uganda. Yet, high levels of adherence to medications have been found to be predictors of better health-related quality of life among HIV-cancer patients [10, 19]. We aimed to determine adherence to antiretroviral and cancer chemotherapy and the associated factors among patients with HIV-cancer co-morbidity at the Uganda Cancer Institute. These findings will inform the interventions aimed at improving adherence to care among HIV-cancer patients in Uganda.

Methods

Study design and setting

This study utilized a cross sectional study design in which we quantitatively collected data from the patients with HIV-cancer co-morbidity at the Uganda cancer institute (UCI). UCI is a public, specialized, tertiary cancer research and treatment center in Uganda. It is located along upper Mulago Hill road on Mulago Hill, central division, Kampala. It is located about 5km North East of the central business district. The UCI provides services on research, training, consultation, prevention and cancer treatment in areas of Pediatrics, Oncology, Gynecology, and Radiotherapy, surgery, pharmacy and recently venturing into bone marrow transplants. The facility has an in-patient's facility with a capacity of 80 beds and receives an

average of about 200 patients daily. The facility serves approximately 10 million people from Uganda and the neighboring countries of; The democratic Republic of Congo (DRC), Rwanda, Burundi, Tanzania, south Sudan and Kenya.

Study population

We included a sample of 200 patients who were on both ART and cancer chemotherapy, and attending UCI in the months of July, August and September 2018. These patients were obtained using simple random sampling, whihch was done through obtaining a list of patients with HIV-cancer co-morbidity from the UCI patient database with the guidance of the UCI data manager. This list was used as a sampling frame from which the study participants were then randomly selected and interviewed for the study using a pre-coded interviewer administered questionnaire. This questionnaire was formulated with guidelines from a tool used to measure adherence to ART with an African resource-constrained setting in South Africa and the WHO five dimensions of adherence [20].

Measures

The outcome variable was adherence to both ART and chemotherapy. This was measured using a self-report recall of missed doses method using the four-item Morisky Medication Adherence Scale that has been used in similar studies in South Africa [21]. The Morisky Medication Adherence Scale measures medication adherence by asking the following four questions: (1) Do you sometimes find it difficult to remember to take your medication? (2) Many patients have troubles in taking their medication doses as prescribed; did you miss any doses in the last 7 days? (3) When you feel better, do you sometimes take a break from your medicine? (4) When you feel worse, do you sometimes stop taking your medicine? Adherence was categorized into adherent or not adherent. A patient was considered to be non-adherent if they responded with a 'Yes' to any of the questions. A patient was considered adherent if they said 'No' to all the four questions. Independent variables included; age, sex, education level, marital status, occupation, residence, regimen complexity (ARV complexity and chemotherapy complexity), side effects of the regimen, stage of the cancer, stage of HIV infection and type of cancer.

Data collection and analysis

Data were collected using a tested questionare [20]. Each questionnaire was given a unique numerical identifier, and all completed questionnaires were locked in the principal investigator's cabinet. The principal investigator (PI) kept the key to the cabinet throughout the study to ensure confidentiality. Data was double entered by trained data entrants. Controls were put in place to rule out any wrong entries or skipped fields. Each questionnaire was thoroughly checked for missing data and errors while still at the data collection area. Data was field edited, coded, cleaned and checked for consistency. Coding was done to clearly identify the required variables for analysis. Data was entered in the EPI-Data version 3.1, transferred to Microsoft excel for cleaning, and then exported to STATA version 15 software for statistical analysis.

Data analysis

Data were analyzed using STATA version 15. All continuous variables were summarized using means with their standard deviations (SD) while categorical variables were recoded as proportions. Modified Poisson regression with robust variances was used at bivariable and multivariable analysis to identify factors associated with adherence to ART and cancer chemotherapy. Prevalence ratios (PRs) were used to estimate the strength of association between the outcome and indicator variables and associations were tested at a 95% confidence interval (CI). Factors with p-value less than 0.05 at multivariate stage were considered significant.

Results

Socio-demographic characteristics of the HIV- Cancer comorbidity patients at the Uganda Cancer Institute.

As depicted in Table 1; of the 200 recruited respondents, 61% (122/200) were males. The mean age of respondents was 42±11years. More so, 43% (86/200) of the respondents were Protestants and 56.5% (113/200) were married. Table 1 further shows that near half, 45% (90/200) had at least attained a primary education and 40% (80/200) were in informal-employment. Additionally, more than half, 55.5% (111/200) were from a rural residence.

Table 1: Socio-demographic characteristics of HIV-Cancer comorbidity patients at the Uganda Cancer Institute

Variable	n(%)
Age	
18-35	66 (33)
36-45	74(37)
46-55	39(19.5)
Over 55 years	21(10.5)
Sex	
Female	78(39)
Male	122(61)
Religion	
Catholic	74(37)
Protestant	86(43)
Muslim	32(16)
Others*	8(4)
Marital status	
Single	46(23)
Married	113(56.5)
Divorced	25(12.5)
Others**	16(8)
Level of education	
None	28(14)
Primary	90(45)
Secondary	60(30)
Tertiary	22(11)
Occupation	
None	48(24)
Peasant	47(23.5)
Self Employed	80(40)
Employed	25(12.5)

Residence	
Rural	111(55.5)
Urban	89(44.5)

Others religions included; born again, orthodox, Seventh day Adventists and Jehovah's Witness.

Other marital status included; separated, widowed and not living together.

Adherence to ART and cancer chemotherapy

More than half, 54% (107/200) of the respondents adhered to both ART and chemotherapy. Additionally, 55% (110/200) adhered to ART and 65% (129/200) adhered to chemotherapy. See Table 2.

Table 2: Adherence to ART and Cancer Chemotherapy among patients with HIV-Cancer comorbidity at the Uganda Cancer Institute

Outcome	Frequency (n=200)	Percentage (%)	95% CI	
ART Adherence	110	55	48.0	61.8
CHEMO Adherence	129	65	57.6	70.9
Overall Adherence	107	54	46.5	60.4

Multivariable analysis of the factors associated with adherence to ART and chemotherapy among HIV cancer patients attending Uganda cancer institute

Knowledge of cancer stage, type of cancer diagnosis, source of ARVs and affordability of cancer chemotherapy were significantly associated with adherence to ART and cancer chemotherapy. Respondents who did not know their cancer stage (APR=0.4, 95%CI=0.25-0.56, P<0.0001) were 0.4 times less likely to adhere to their treatments than those in the early stage; Patients with AIDS defining cancers (APR 0.7, 95%CI=0.50-0.88, P=0.005) were 0.7 times less likely to adhere to both ART and cancer chemotherapy than those with NADCs. ART clinic near UCI was associated with better adherence to the medications (APR=0.7, 95%CI=0.84-0.96, P-value=0.027). Cancer chemotherapy affordability was positively significant to adherence (APR 1.4, 95%CI=0.02-0.87, P-value=0.037). See Table 3.

Table 3: Factors associated with adherence to ART and chemotherapy among HIV cancer patients attending Uganda cancer institute

Variable	Adherence (n=107)		Non-Adherence (n=93)		UPR (95% CI)	P-value	APR (95% CI)	P-Value
	n	%	n	%				
Sex								
Male	63	58.9	59	63.4	1		1	
Female	44	41.1	34	36.6	1.1 (0.84-1.42)	0.506	0.8 (0.60-1.01)	0.056
Side effects								
Yes	78	72.9	75	80.6	1		1	
No	29	27.1	18	19.4	1.2 (0.92-1.59)	0.173	1.1 (0.80-1.40)	0.705
Knowledge of cancer stage								
Early	49	45.8	21	22.6	1		1	
Late	36	33.6	12	12.9	1.1 (0.86-1.34)	0.547	0.9 (0.67-1.10)	0.239
Unknown	22	20.6	60	64.5	0.4 (0.26-0.57)	0.000*	0.4 (0.25-0.56)	0.000*
Cancer diagnosis								
Non-AIDs defining	40	37.4	18	19.4	1		1	
AIDs defining	67	62.6	75	80.6	0.5 (0.40-0.51)	0.000*	0.7 (0.50-0.88)	0.005*
Last time that missed taking pills								
Ever missed	22	20.6	40	43	1		1	
Never missed	85	79.4	53	57	1.7 (1.21-2.49)	0.003*	0.93-1.47	0.125
Ever missed appointment dates								
Yes	29	27.1	42	45.2	1		1	
No	78	72.9	51	54.8	1.5 (1.08-2.03)	0.014*	1.1 (0.84-	0.473

							1.47)	
Source of ARVs								
ART clinic nearby UCI	13	12.1	20	21.5	1		1	
ART clinic near home	59	55.1	70	75.3	1.2 (0.73-1.85)	0.529	0.7 (0.84-0.96)	0.027*
Other	35	32.7	3	3.2	2.3 (1.51-3.61)	0.000*	0.9 (0.61-1.44)	0.759
Chemotherapy affordable?								
No	35	32.7	65	69.9	1			
Yes	72	67.3	28	30.1	2.1 (1.53-2.76)	0.000*	1.4 (0.02-0.87)	0.037*

***= Statistically significant (P-value< 0.05), UPR= unadjusted prevalence ratio, APR=adjusted prevalence ratio, CI= confidence interval.**

Discussion

We found adherence to both ART and cancer chemotherapy at 54%. Adherence to ART alone in HIV-cancer patients was 55% while that of cancer chemotherapy alone was (65%). These findings are lower than those in a related previous study conducted in Uganda [15]. These findings could be different because of the presence of the co-morbidity of HIV and cancer where one ailment could affect the adherence to the other. Comparable findings were reported by Greer, Amayol et al in their study where they found rates of adherence to cancer chemotherapy varying from as low as 46% [22]. These findings are also in-line with a review study for adherence in chronic illness that stated that achieving adherence rates above 80% is difficult even in resource –rich countries [23].

Our study found that individuals who did not know their stage of cancer were less likely to adhere well to both their ART and cancer chemotherapy. This could be because knowledge of one's cancer stage contributes to the way they adhere to medications. It is important for the patients to know whether the cancer is in an early or late stage so as to plan on medication in time. These findings are different from those in studies that found late cancer stage [24, 25], associated with poor adherence [26-28], and another study that found patients with metastatic cancer more likely to become over-adherent to oral chemotherapy [27].

Our study further found the type of cancer diagnosis significantly associated with ART and cancer chemotherapy adherence. Individuals with the AIDS defining cancers such as Kaposi's sarcoma, Non Hodgkins lymphoma were less likely to adhere well to their co- medications. These findings suggest that

patients with advanced HIV disease or AIDS may not adhere well to their medications; this could be explained by the high pill burden, and possibly because of the presence of other comorbidities which may hinder proper adherence to medications.

Accessing ART from a clinic near UCI was found to be positively associated with both ART and cancer chemotherapy than picking ART from in district away from UCI. This could be because the patients find it easy to access the both treatments since the ART treatment Centre and cancer treatment Centre are near each other. Our study found that affordability of chemotherapy to be positively associated with ART and chemotherapy adherence. This is explained by the fact that, at Uganda Cancer Institute most of the chemotherapy is given at a free cost and patients only buy the drugs if they are out of stock. These findings are comparable to those in studies that found supplying medication to patients from the health facility improved medication adherence ,and reducing patient out-of-pocket expenses was associated with improved drug adherence [29]. Therapies that are high-value on high-risk patients like those with the HIV-cancer comorbidity may affect adherence and lead to undesired adherence and health outcomes [29].

The study found that the patients with both HIV and cancer on both ART and cancer chemotherapy generally felt weak most of the times, experienced a number of treatment challenges including drug side effects, missing their doses, stigma and financial challenges. They experienced a number of hospital visits and hospital admissions. These findings are similar to those in other studies that found disease correlates, such as the number of co morbidities, cancer stage, and nodal involvement, associated with negative medication adherence [24, 25], also treatment factors, such as higher doses of medication, worse side effects, switching therapy types, and higher utilization of medical care were associated with poor adherence [26, 27].

Strength and limitations

This study collected primary data from the patients with HIV and cancer, which was considered reliable information from which adherence was measured. The method (Moriscky scale) used to estimate adherence was a reliable and it validated tool.

Due to limited time and resources, our study did not assess the level of adherence per specific type of cancer which could have overestimated the outcome. Future studies will be necessary to determine the level of adherence to ART and Cancer chemotherapy per specific type of cancer.

Conclusion And Implications

Overall, adherence to both ART and cancer chemotherapy was low. Factors that were found to be associated with adherence were; Knowledge of the cancer stage by the patient, the type of cancer diagnosis, source of ART and affordability of the medications. Our findings suggest a need health promotion awareness campaigns and adherence counseling to increase knowledge of cancer stages and adherence among patients with cancer and HIV-comorbidity. Furthermore, there is need to integrate free and/ or subsidized HIV treatment services with cancer care services to ease access by the patients.

Abbreviations

UCI	Uganda Cancer Institute
IRB	Institutional Review Board
HDREC	Higher Degrees Research and Ethics Committee
UBOS	Uganda Bureau of Statistics
MOH	Ministry of Health

Declarations

Ethics approval and consent to participate

We obtained ethical approval to conduct the study from Makerere University School of Public Health Higher Degrees Research and Ethics Committee (HDREC) and Uganda Cancer institute Institutional Review Board (IRB). The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki. Informed voluntary consent was sought from the participants . They were assured of privacy and confidentiality of the information collected by leaving the questionnaires anonymous and no personal identifiers were used. The aims of the study were well explained to study participants and those that accepted to take part in the study were requested to sign a written consent form.

Consent for publication

Not applicable.

Availability of data and material

The data used and/or analyzed during the study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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The authors did not receive any particular funding for this study.

Authors' contributions

C.A led the conceptualization of the first draft of the study. C. A and N.B contributed towards literature search, data analysis, and drafting of the first version of the manuscript. J.K and F.N offered guidance

and contributed towards reviewing the initial drafts of the manuscript. All authors contributed to data interpretation and critical comments on the first and subsequent drafts of the manuscript. All authors read and approved the final manuscript for submission.

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