

Prognostic factors and survival outcomes among oncology patients with known and unknown HIV status in Kisumu County, Kenya

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ABSTRACT

Introduction: Human immunodeficiency virus (HIV) and cancer have a complicated interplay in their pathobiology, resulting in malignancies associated with viral infection. This study sought to establish the prognostic factors and survival outcomes among patients diagnosed with cancer with known and unknown HIV status.

Methods: The study employed a hybrid design, combining retrospective and prospective cohorts from 2019 to 2021. Three hundred and seventy-nine cancer patients with known and unknown HIV status enrolled at the oncology clinic in Kisumu County were recruited via multi-stage and stratified sampling.

Results: The mean age was 57.2 years (SD 15.2). The study population comprised 31.1% (118) males and 68.9% (261) females. Among the study participants, 53.6% (203) were HIV-negative, 39.8% (151) were HIV-positive, and 6.6% (25) had an unknown HIV status. Multivariable Cox regression showed HIV status had no statistical impact on survival. Metastasis at diagnosis increased the risk of death (HR 3.1, $p<0.001$, 95% CI 1.7-5.6) as did late cancer stage (HR 3.1, $p=0.035$, 95% CI 1.1-8.7). Longer duration of care reduced risk of death (HR 0.8, $p<0.001$, 95% CI 0.7-0.9), as did non-tobacco usage (HR 0.3, $p=0.042$, 95% CI 0.1-0.9).

Conclusion: Tumour stage, metastasis, tobacco use, and duration of care had a statistically significant influence on the survival of the oncology patients.

Keywords: HIV status, cancer survival, prognostic factors, tumour stage, cancer patients, Kenya

Citation: Mogire et al. Prognostic factors and survival outcomes among oncology patients with known and unknown HIV status in Kisumu County, Kenya. *South Sudan Medical Journal*, 2026;19(1):5-12 © 2026 The Author(s) **License:** This is an open access article under [CC BY-NC](https://creativecommons.org/licenses/by-nd/4.0/) DOI: <https://doi.org/10.4314/ssmj.v19i1.2>

Introduction

The global cancer burden, based on the Global Cancer Observatory (GLOBOCAN) (2020) estimates of cancer incidence and mortality from the International Agency for Research on Cancer, revealed approximately 19.3 million new cancer cases (18.1 million excluding non-melanoma skin cancer) and nearly 10.0 million cancer-related deaths (9.9 million excluding non-melanoma skin cancer) in 2020.^[1]

In the United States (US), from 1991 to 2021, cancer mortality has been on the decline due to early detection, reduced smoking practices, and advanced treatment, preventing over 4 million deaths.^[2] In the first year of cancer diagnosis, age, cancer type and stage, presence of comorbidities, and treatment type significantly influence the cancer-patient survival rates.^[3] The key indicator that is used to assess the effectiveness of anticancer treatments is the overall survival of cancer patients from initiation of therapies to death from any cause.^[4] Advancements in the treatment of human immunodeficiency virus (HIV) have led to an extended lifespan by reducing acquired immunodeficiency syndrome (AIDS) related deaths and decreasing the incidence of AIDS-defining cancers. However, with the increase in survival time, there has been an increase in non-AIDS-defining cancers among persons with HIV.^[5,6] People living with HIV who have malignancies, even though their viral load is suppressed by effective antiretroviral therapy, require more personalised care.^[7] Multiple factors influence the intricate relationship between cancer and HIV, making them more complex to treat compared to cancer patients without HIV.^[8]

This study aimed to determine the prognostic factors that affect the survival outcomes among cancer patients based on their HIV status. By examining these factors, the study sought to provide evidence to guide treatment decisions, highlight areas for better healthcare integration, and improve survival outcomes for oncology patients in this context.

Method

This was a hybrid retrospective and prospective cohort study conducted from 2019 to 2021 at the Oncology Clinic of Jaramogi Oginga Odinga Teaching and Referral Hospital (JOOTRH) in Kisumu County, Kenya, a referral hospital for patients across the western region of Kenya. In this study, a multi-stage sampling method was employed, where in the first stage, JOOTRH was purposively selected because it serves as the regional referral oncology centre for the western part of Kenya. In the second stage, the study listed all adult cancer patients at Oncology Clinic between 2019 and 2021. In the third stage, all eligible participants with complete medical records were recruited into the study through random sampling.

Participants and materials

Medical records and in-depth interviews were used to collect data from diagnosed cancer patients aged 18 years and above. The retrospective component involved all

oncology patients who were already receiving care from 2019 onwards, who had complete medical records from 2019 to 2021. The prospective component involved follow-up of newly diagnosed patients receiving oncology care during the study period from 2019 to 2021. Patients were randomly selected using a random number table with a view of minimizing selection bias. The selection process did not stratify oncology patients by HIV status; instead, the HIV status was documented alongside other clinical information and considered during the analysis.

Data collection

The cancer patients were stratified in the analysis based on their HIV status as HIV positive, HIV negative and unknown status as recorded at the time of their initial contact with the oncology clinic. Collected data included demographic information, cancer diagnosis, HIV status, treatment history, and follow-up outcomes (survival, relapse, treatment response, lost to follow-up). Data were extracted from the hospital's Health Information Management System. The cancer registry and special reports were used for verification and to supplement patient data. The study used both telephone and face-to-face interviews to get information from the participants, depending on their availability and accessibility. Contact information of the patients was obtained from the hospital files. Through telephone interviews, the study was able to gather information on the patients' current health status, including whether they were alive or deceased, ongoing treatment and other relevant health outcomes. Face-to-face interviews were conducted with patients who continued to visit the hospital for their scheduled treatment follow-ups or when they presented with illness.

Statistical analysis

Descriptive statistics, the chi-square test, a Kaplan-Meier plot, multivariable logistic regression, and Cox proportional hazards regression model were used. Analyses were conducted using Stata version 15.1 (StataCorp LLC, College Station, TX, USA).

Results

A total of 379 participants were included. Of these, 151 (39.8%) were HIV negative, 203 (53.6%) HIV positive and 25 (6.6%) had unknown HIV status. The mean age varied significantly (Kruskal-Wallis test $p < 0.001$) across the HIV status groups, with an overall mean age of 57.2 years (SD 15.2). Marital status, alcohol and tobacco use did not differ significantly ($p > 0.05$) across the groups,

Table 1. Characteristics of the study participants

| | | HIV status | | | Total | p-value |
|--|------------------|-------------------|-------------------|------------------|------------------|---------|
| | | Negative n (%) | Positive n (%) | Unknown n (%) | | |
| Ages (Years) | Mean (SD) | 50.3 (11.5) | 62.5 (15.2) | 56.4 (18.1) | | |
| | Median (IQR) | 49.7 (41.3,56.2) | 64.3 (50.7,74.7) | 52.7 (42.5,70.0) | 55.9 (45.7,70.0) | <0.001 |
| | Min, Max | 26.3, 85.7 | 24.6, 95.7 | 28.0, 89.7 | 24.6, 95.7 | |
| Marital status | Single* | 47 (31.1) | 52 (25.6) | 10 (40.0) | 109 (28.8) | 0.231 |
| | Married | 104 (68.9) | 151 (74.4) | 15 (60.0) | 270 (71.2) | |
| Sex | Female | 120 (79.5) | 122 (60.1) | 19 (76.0) | 261 (68.9) | <0.001 |
| | Male | 31 (20.5) | 81 (39.9) | 6 (24.0) | 118 (31.1) | |
| Cancer stage | 1 | 11 (7.3) | 9 (4.4) | 2 (8.0) | 22 (5.8) | |
| | 2 | 18 (11.9) | 50 (24.6) | 1 (4.0) | 71 (18.7) | |
| | 3 | 69 (45.7) | 74 (36.5) | 6 (24.0) | 149 (39.3) | <0.001 |
| | 4 | 31 (20.5) | 62 (30.5) | 6 (24.0) | 99 (26.1) | |
| | Not recorded | 22 (14.6) | 8 (3.9) | 10 (40.0) | 40 (10.6) | |
| Tobacco use | Current/Previous | 9 (6.0) | 14 (6.9) | 3 (12.0) | 26 (6.9) | |
| | Never | 141 (93.4) | 185 (91.1) | 22 (88.0) | 348 (91.8) | |
| | Not recorded | 1 (0.7) | 4 (2.0) | 0 | 5 (1.3) | 0.608 |
| Alcohol use | No | 138 (91.4) | 175 (86.2) | 22 (88.0) | 335 (88.4) | |
| | Yes | 13 (8.6) | 25 (12.3) | 3 (12.0) | 41 (10.8) | |
| | Not recorded | 0 | 3 (1.5) | 0 (0) | 3 (0.8) | 0.406 |
| Family history of cancer | No | 141 (93.4) | 180 (88.7) | 18 (72.0) | 339 (89.4) | |
| | Yes | 4 (2.6) | 11 (5.4) | 0 | 15 (4.0) | |
| | Unknown | 5 (3.3) | 9 (4.4) | 7 (28.0) | 21 (5.5) | |
| | Not recorded | 1 (0.7) | 3 (1.5) | 0 | 4 (1.1) | <0.001 |
| Duration since Cancer Diagnosis | N | 149 | 202 | 20 | 375 | |
| | Mean (SD) | 3.2 (1.5) | 3.4 (1.6) | 3.5 (1.7) | 3.3 (1.6) | |
| | Median (IQR) | 3.0 (1.9, 4.1) | 3.1 (2.2, 4.9) | 3.5 (1.7, 4.7) | 3.1 (2.0, 4.6) | 0.566 |
| | Min, Max | 0.2, 6.7 | 0.2, 6.7 | 1.2, 6.4 | 0.2, 6.7 | |
| Total | Missing data | 2 | 1 | 5 | 8 | |
| | | 151 (39.8) | 203 (53.6) | 25 (6.6) | 379 (100) | |

* Single / Divorced /Widowed

Research Article

Table 2. Regression Analysis of clinical characteristics as predictors of death/LTFU

| Variable | Univariable OR (95% CI) | p-value | Multivariable OR (95% CI) | p-value |
|---|----------------------------|---------|------------------------------|---------|
| HIV status | | | | |
| Negative | Ref | | | |
| Positive | 1.2 (0.8-1.8) | 0.278 | | |
| Unknown | 2.1 (0.8-5.3) | 0.121 | | |
| Duration (months) since Cancer Diagnosis | 0.8 (0.7 - 0.9) | 0.024 | 0.8 (0.7 - 1.0) | 0.127 |
| Tumour Stage | | | | |
| Stage 0-2 | Ref | | Ref | |
| Stage 3-4 | 3.2 (1.8 - 5.5) | <0.001 | 2.0 (0.8 - 5.5) | 0.157 |
| Metastasis at Diagnosis | | | | |
| No | Ref | | Ref | |
| Yes | 3.1 (1.9 - 5.1) | <0.001 | 2.6 (1.3 - 5.2) | 0.006 |
| Age (years) at Cancer Diagnosis | 1.0 (0.9 - 1.0) | 0.691 | | |
| Duration of Symptoms | | | | |
| 0 to 3 months | Ref | | | |
| >3 to 6 months | 0.6 (0.3 - 1.1) | 0.378 | | |
| >6 to 12 months | 0.8 (0.4 - 1.4) | 0.389 | | |
| >12 months | 0.8 (0.5 - 1.5) | 0.412 | | |
| Treatment Goal | | | | |
| Curative | Ref | | Ref | |
| Palliative | 2.5 (1.4 - 4.2) | 0.001 | 1.6 (0.6 - 4.0) | 0.317 |
| Consistent with Treatment/Adherent | | | | |
| No | Ref | | Ref | |
| Yes | 0.2 (0.1 - 0.4) | <0.001 | 0.2 (0.1 - 0.5) | <0.001 |
| Reported Treatment Complications | | | | |
| No | Ref | | | |
| Yes | 1.3 (0.6 - 2.5) | 0.497 | | |
| Duration on Care (months) | 0.9 (0.9 - 1.0) | <0.001 | | |
| Tobacco Use | | | | |
| Current/Previous use | Ref | | Ref | |
| Never | 0.4 (0.2 - 1.0) | 0.055 | 0.9 (0.1 - 5.8) | 0.944 |
| Alcohol Use | | | | |
| No | Ref | | Ref | |
| Yes | 1.9 (0.9 - 3.6) | 0.055 | 3.2 (0.7 - 13.5) | 0.117 |

Table 3. Cox proportional hazard regression of clinical characteristics as predictors of death/LTFU

| Variable | Univariable HR (95% CI) | p-value | Multivariable HR (95% CI) | p-value |
|---|----------------------------|---------|------------------------------|---------|
| HIV status | | | | |
| Negative | Ref | | Ref | |
| Positive | 1.4 (1.0-2.0) | 0.054 | 1.0 (0.6-1.8) | 0.978 |
| Unknown | 1.8 (1.0-3.3) | 0.598 | 1.1 (0.3-3.6) | 0.914 |
| Duration (months) since Cancer Diagnosis | 0.8 (0.7-0.9) | <0.001 | 1.0 (0.8-1.2) | 0.797 |
| Tumour Stage | | | | |
| Stage 0-2 | Ref | | Ref | |
| Stage 3-4 | 2.4 (1.5-3.9) | <0.001 | 3.1 (1.1-8.7) | 0.035 |
| Metastasis at Diagnosis | | | | |
| No | Ref | | Ref | |
| Yes | 1.8 (1.3-2.6) | 0.001 | 3.1 (1.7-5.6) | <0.001 |
| Age (years) at Cancer Diagnosis | 1.0 (0.9-1.0) | 0.299 | | |
| Duration of Symptoms | | | | |
| 0 to 3 months | Ref | | Ref | |
| >3 to 6 months | 0.6 (0.4-1.0) | 0.133 | 0.9 (0.4-1.9) | 0.789 |
| >6 to 12 months | 0.6 (0.4-0.9) | 0.029 | 1.1 (0.6-2.1) | 0.821 |
| >12 months | 0.8 (0.5-1.2) | 0.430 | 0.6 (0.3-1.3) | 0.421 |
| Treatment Goal | | | | |
| Curative | Ref | | Ref | |
| Palliative | 1.9 (1.2-3.0) | 0.006 | 0.5 (0.2-1.3) | 0.178 |
| Consistent with Treatment/Adherent | | | | |
| No | Ref | | Ref | |
| Yes | 0.4 (0.3-0.6) | <0.001 | 0.6 (0.4-1.1) | 0.078 |
| Reported Treatment Complications | | | | |
| No | Ref | | | |
| Yes | 1.2 (0.7-2.0) | 0.557 | | |
| Duration on Care (months) | 0.9 (0.8-0.9) | <0.001 | 0.8 (0.7-0.9) | <0.001 |
| Tobacco Use | | | | |
| Current/Previous use | Ref | | Ref | |
| Never | 0.5 (0.3-0.8) | 0.007 | 0.3 (0.1-0.9) | 0.042 |
| Alcohol Use | | | | |
| No | Ref | | Ref | |
| Yes | 2.0 (1.2-3.1) | 0.004 | 0.6 (0.2-1.6) | 0.289 |

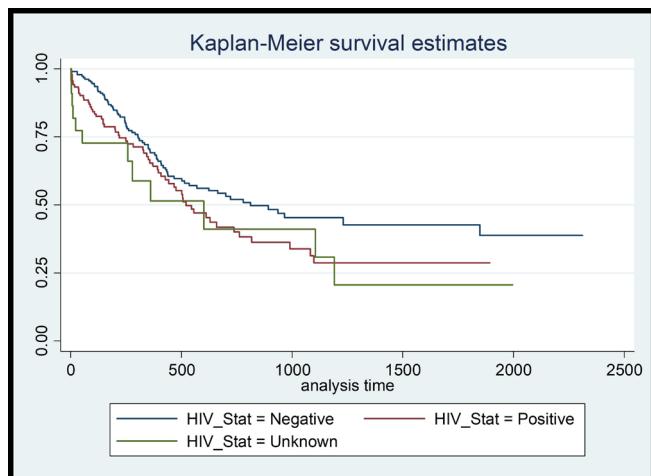


Figure 1. Kaplan-Meier survival estimates by HIV status

whereas sex, family history of cancer and cancer stage at diagnosis showed statistically significant differences ($p<0.001$), as shown in Table 1.

HIV status was considered a primary variable of interest due to its known influence on cancer outcome. The survival status of the oncology patients was classified as alive, dead or lost to follow-up (LTFU). HIV status was explicitly included as a covariate in the logistic regression to assess its association with the disease status outcomes.

Table 2 presents the results of a logistic regression analysis using death or loss to follow-up (LTFU) as the outcome measure. In the univariable analysis, significant predictors of death or LTFU were short duration since diagnosis, late tumour stage, metastasis at diagnosis, palliative treatment goal, non-adherence to treatment, and shorter duration of care. Although HIV was a key variable of interest, it was not a statistically significant predictor of death or LTFU. Multivariable analysis was performed using the variables that were significant in the univariable analysis, excluding time-related variables that were considered co-linear. In this analysis, only metastasis at diagnosis (OR 2.6, 95% CI 1.3-5.2, $p=0.006$) and non-adherence to treatment (OR 0.2, 95% CI 0.1-0.5, $p<0.001$) were significant predictors of death or LTFU.

Using data from patients with reliable time-to-event information, Kaplan-Meier survival estimates were plotted (Figure 1) and a Cox proportional hazard regression was performed (Table 3). The Cox regression allowed the study to estimate the hazard ratio for mortality over time, complementing the logistic regression findings.

A Kaplan-Meier curve (Figure 1) was used to assess the survival probability according to HIV status (negative, positive, and unknown). An unadjusted log-rank test, comparing the survival distributions of the three HIV groups, revealed a significant difference ($p= 0.047$). The HIV negative group had fewer observed deaths than expected (75 observed vs 88.8 expected), suggesting a better-than-expected survival, whereas the HIV positive group had more observed deaths than expected (61 observed vs 51.4 expected), suggesting that HIV status might have played a meaningful role in predicting survival outcomes among oncology patients.

While the unadjusted Kaplan-Meier analysis showed a statistically significant difference in the survival outcome by HIV status, this finding was not supported in the Cox regression analysis (below), suggesting that HIV status alone was not an independent predictor of survival.

Table 3 shows the results of Cox proportional hazards regressions. In the univariable analysis, significant predictors of death or loss to follow-up were: a shorter duration since cancer diagnosis, later tumour stage, metastasis at diagnosis, palliative treatment goal, non-adherence to treatment, shorter duration on care, tobacco use and alcohol use. However, in the multivariable analysis, only tumour stage (HR 3.1, 95% CI 1.1-8.7, $p=0.035$) metastasis at diagnosis (HR 3.1, 95% CI 1.7-5.6, $p<0.001$), short duration of care (HR 0.8, 95% CI 0.7-0.9, $p<0.001$) and past or current tobacco use (HR 0.3, 95% CI 0.1-0.9, $p=0.042$) remained significant predictors of death/LTFU.

Discussion

The Cox regression showed that HIV status did not statistically influence survival. This suggests that HIV status alone might not be a strong determinant of survival in this cohort. Findings of this current study were consistent with Atwine et al^[6] who observed that, although people with human immunodeficiency virus (PWH) had higher mortality rates than those without HIV, the differences in overall survival and cancer-specific survival were not statistically significant, indicating no notable survival disparities between the two groups in the era of modern treatment. The results of this study agree with a study done among PWH in Japan,^[9] which also concluded that HIV status did not significantly influence survival among patients with non-AIDS-defining malignancies. Additionally, a prognostic study done among women with cervical cancer in Thailand also found that HIV status did not significantly influence long-term survival.^[10] The

results of the current study, however, differ from those of the 2023 US Cancer database, which reported poorer survival outcomes in HIV-positive individuals, especially when cancer was diagnosed at later stages.^[11]

These results emphasise the importance of early-stage detection and metastasis management in improving cancer patients' survival outcomes. However, when tumour stage was included in the multivariable model, an interesting shift emerged: although tumour stage was significant in the univariable analysis, it lost significance after accounting for other factors in the multivariable analysis. The loss of statistical significance may be due to a complex interplay between the cancer stage and other prognostic factors.

The current study observed that cancer patients who used tobacco had a poorer survival rate compared to non-smokers. This result is consistent with the existing literature that pointed out that tobacco use is a significant risk factor that enables cancer development and results in adverse outcomes among such patients. As noted in the previous studies, lung cancer has been linked to tobacco smoking and increased cancer-related deaths globally.^[12, 13] While in this study, we did not specifically analyse the cancer types in relation to the tobacco usage, the analysis showed that poor survival among tobacco users supports the continued need for cessation of tobacco use as an intervention among oncology patients. Among patients with lung cancer, tobacco smoking remains the leading causative agent and was estimated to be 67% of lung cancer deaths globally in 2019.^[14]

Conclusion

The study observed that tumour stage, metastasis, tobacco use and duration of care had a statistically significant influence on the survival of the oncology patients.

Acknowledgements

The authors express their gratitude to the ISERC (Institutional Ethical Review Committee) and JOOTRH (Jaramogi Oginga Odinga Teaching and Referral Hospital). They also appreciate the contributions of everyone who took part in this study. Additionally, the authors thank Dr. Benard Samba for his assistance with the statistical analysis.

Author contributions

RND and GKM conceptualized and designed the study. RND, GKM, and GA oversaw data collection. RND and Dr. Benard Samba conducted the statistical analysis and interpretation. RND, GKM, and GA contributed to

writing the manuscript. RND and GKM were primarily responsible for the final content. All authors have reviewed and approved the final manuscript.

Funding

This study did not receive any external funding. All costs were funded by the principal investigator, as this research was conducted as part of her post-graduate studies.

Data availability

The data presented in this manuscript will be made accessible upon request to the corresponding author.

Ethics approval and consent to participate

All procedures involving human participants were conducted in accordance with the ethical guidelines set by the institutional and/or national research committees, as well as the 1964 Helsinki Declaration and its subsequent ethical standards. Ethical approval for the study was granted by the JOOTRH Institutional Ethical Review Committee (ISERC/JOOTRH/708/23), and permission to access patient medical records was provided by the hospital administration. Additionally, the research received authorization from the National Commission for Science, Technology, and Innovation, which issued the research license (License No: NACOSTI/P/23/29542).

Competing interests: None.

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