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Causes of Death Among Adults with HIV-Associated Kaposi Sarcoma in East Africa in the "Treat All" Era

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Background

- Kaposi sarcoma (KS) is among the most common cancers in sub-Saharan Africa in the general population.
- One-year mortality of HIV-associated KS in the "Treat All" era in East Africa was recently estimated to be 41%.
- Understanding causes of death among patients with KS might improve management and, hence, survival or suggest other strategies.

Objectives

To describe the causes of death among adults with HIV-associated KS in East Africa in the "Treat All" era.

Study Design

- Cross sectional study of adults (age ≥ 18 years) who died after a new diagnosis of HIV-associated KS.

Participants

- KS confirmed by histopathology except where lesions deemed unsafe for biopsy.
- Deaths arising in a cohort of adults with HIV-associated KS diagnosis made from 2021 and 2024.
- At 5 primary care networks in East Africa.
  - AMPATH Network, Western Kenya
  - Masaka Regional Referral Hospital, Uganda
  - Mbarara Regional Referral Hospital, Uganda
  - Infectious Diseases Institute (IDI), Uganda
  - Muhimbili University of Health and Allied Sciences (MUHAS), Tanzania



Study Sites in East Africa

Participant Characteristics

Characteristics at KS Diagnosis (N=163)	
Age, years	36 (29-42)*
Male, sex	63%
CD4 count, count/mm³	
≤50	34%
51-200	34%
201-500	26%
≥500	6%
Viral load, copies/ml	
≤40	29%
40-1000	30%
1001-10,000	11%
≥10,000	30%

*Median (interquartile range)

Information at Death (N=163)	
Source of Information Death	
Family member	84%
Non-family member	4%
Medical record	25%
Location of Death	
Health facility	58%
Community	40%
Unknown	2%
Autopsy performed	
Yes	4%
No	85%
Unknown	11%
Ever Initiated chemotherapy	
Yes	38%
No	62%

Suspected Causes of Death Among Adults with HIV-Associated KS in East Africa (N=163)

Condition	% of Deaths in which Condition Contributed % (95% CI)‡	Certainty of Condition's Presence*			Certainty of Contribution to Death†		
		Definite	Likely	Possibly	Highly	Likely	Possibly
Kaposi sarcoma	100% (98%-100%)	99%	--	1%	73%	14%	13%
Tuberculosis	31% (24%-38%)	54%	32%	14%	56%	24%	10%
Anemia	7% (4%-13%)	33%	50%	17%	8%	50%	42%
Cryptococcosis	5% (3%-10%)	50%	50%	--	50%	25%	25%
Renal insufficiency	3% (1%-6%)	75%	--	25%	50%	50%	--
Septicemia	3% (1%-6%)	25%	--	75%	--	--	100%
Medication toxicity	4% (2%-8%)	--	--	100%	33%	--	67%

‡ Only conditions that contributed to ≥ 3% of deaths are shown.

*Certainty of condition's presence defined as "Definite" if histopathology, direct visualization, microscopy, culture or polymerase chain reaction were available, "Possibly" if based on clinical history, signs and symptoms, "Likely" if based on clinical history, imaging or laboratory markers.

†Certainty of contribution was defined as highly (95%-100%), likely (80%-95%) or possibly (50%-80%)

- In 6% of cases, an unexplained sudden onset of malaise occurred following improvement on chemotherapy, often with fever and respiratory symptoms, was followed shortly by death.

Measurements

- Adjudication of each death performed using information obtained from, when possible, next of kin, review of medical records and interview of attending clinicians.
- Information on circumstances surrounding death was collected using a standardized interviewer-administered questionnaire.
- Contributing cause defined as suspicion that the condition mechanistically/causally contributed to death as guided by Rothman's sufficient component cause ("causal pie") model..

Conclusions

Among adults who died after a new diagnosis of HIV-associated KS in East Africa in the "Treat All" era:

- KS was deemed to be possibly contributing in all cases.
- There was often other suspected causes, especially TB.

Implications

- Without autopsy, it is impossible to know all causes or sequence of events.
- Improving survival in this population will need better access to more potent anti-KS therapy AND better diagnostic capacity (and treatment) for other complications of HIV infection.
  - Short-term likelihood of accomplishing this is low.
  - Instead, earlier detection and treatment of KS seems more feasible.
- Some scenarios beg the question regarding the causal role in death of non-KS KSHV-related disease that is difficult to diagnose (e.g., KSHV-related inflammatory conditions).

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