

Lack of Age Dependence in KSHV Seroprevalence Among Children in a Population-Based Study in South Africa: Evidence for at Least Two Epidemiologic Patterns of KSHV Transmission in Africa

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Background

It has been established that Kaposi's sarcoma-associated herpesvirus (KSHV) infection is endemic among most African adult populations. The prevailing view is that a single mode of KSHV spread – horizontal transmission in childhood – is primarily responsible for endemic infection throughout the continent. However, few studies have directly examined children, particularly in population-based samples in areas where the endemic form (non-HIV-related) of Kaposi's sarcoma (KS) is uncommon.

Objective

To determine KSHV seroprevalence in children in a region where endemic KS is uncommon – South Africa – compared to a region where endemic KS is common – Uganda.

Participants

South Africa: door-to-door community sample of children ages 2, 4, or 8 years, and their primary female caregiver, in Cato Manor, an urban settlement in Durban, and KwaXimba, a rural area ~ 70 km outside of Durban.

Uganda – community sample: global positioning system (GPS)-driven door-to-door sample of children ages 2 to 8 years old in the Mulago III Parish, Kampala.

Uganda – clinic sample: consecutive sample of children ages 2 to 8 years old at Mulago Hospital in Kampala with an indication for blood transfusion but no transfusions in the prior 6 months.

Measurements

Antibodies to KSHV. Plasma from all participants was tested for antibodies to KSHV by the same personnel at the CDC using two different enzyme immunoassays (EIAs) and one indirect immunofluorescence assay (IFA):

• The EIAs target antibodies to ORF K8.1 and ORF 65, respectively, using synthetic peptides as antigen substrate. The optical density cutoff for reactivity was the mean corrected optical density of a 1:100 diluted sample at 450 nm from negative control sera plus 5 standard deviations.

• The IFA used an induced KSHV-containing BCBL-1 cell line. Specimens were evaluated at a dilution of 1:80. Equivocal results on the IFA were defined as weak reactivity that was considered neither positive nor negative.

• Positive overall result assigned when: reactive on both EIAs and/or reactive on IFA

South African children also tested at NCI-Frederick using two different EIAs, targeting antibodies to ORF K8.1 and ORF 73.

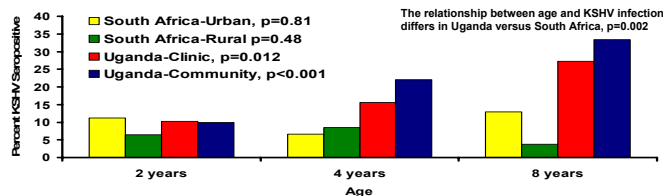
HIV testing. HIV antibody testing performed in South African samples used two EIAs (Vironostika HIV-1 Microelisa, bioMérieux, Durham, N.C.; and Genetic Systems rLAV EIA, Bio-Rad, Redmond, WA) and in Uganda used an EIA (MUREX HIV-1.2.O; Murex Biotech, Kent, United Kingdom).



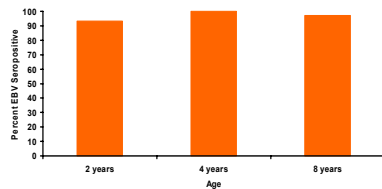
Characteristics of Participants

Characteristic	South Africa Urban community N=201	South Africa Rural community N=226	Uganda Clinic N=388	Uganda Urban community N=409
Age				
2 years	36%	34%	45%	10%
4 years	37%	31%	46%	43%
8 years	27%	35%	8.5%	47%
Female gender	53%	54%	49%	54%
HIV-infected	7.0%	5.8%	9.8%	n/a

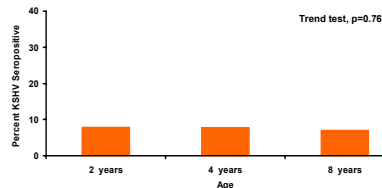
KSHV Seroprevalence in South African and Ugandan Children



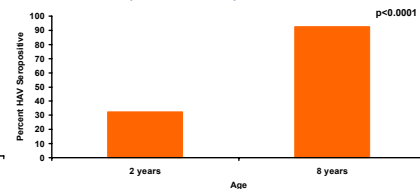
Assessing the Viability of South African Specimens by Evaluation of the Presence of Antibodies to Other Herpesviruses: Epstein-Barr Seroprevalence in South Africa



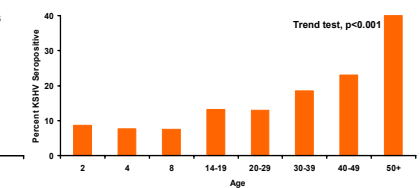
Independent Verification of KSHV Antibody Testing: KSHV Seroprevalence in South Africa – Testing at NCI-Frederick



Assessing the Viability of South African Specimens by Evaluation of the Presence of Antibodies Expected to Increase with Age: Hepatitis A Virus Seroprevalence in South Africa



Evaluation of Age Dependence in KSHV Seroprevalence in South Africa: Comparison of Children to Adult Caregivers



Conclusions

In a contemporary population-based sample in South Africa:

- low overall KSHV seroprevalence (<10%) in children
- lack of age dependence in childhood
- suggests little ongoing horizontal transmission in childhood
- higher KSHV seroprevalence is only seen in adults

In contrast, in Uganda:

- KSHV seroprevalence already 10% by age 2
- further increases throughout childhood
- suggesting ongoing horizontal transmission in childhood

Implications

At least two patterns of KSHV transmission exist in Africa.

Possible explanations:

- host genetic susceptibility
- environmental co-factors
- differences in human behaviors
- viral genotypic differences

These patterns track with underlying incidence of endemic KS. Whether childhood KSHV infection is a critical determinant for KS development as an adult merits further study

Acknowledgements

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