TRANSMISSION PATTERNS AND SEROEPIDEMIOLOGY OF KAPOSI'S SARCOMA ASSOCIATED HERPES VIRUS – KSHV (HUMAN HERPES VIRUS 8 – HHV-8) IN SOUTH AFRICA

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Abstract

Factors associated with the transmission of Kaposi's sarcoma-associated herpesvirus (KSHV) are inconclusive. In countries where KS and KSHV are confined to men who have sex with other men (MSM), KSHV is associated with sexual risk factors. In countries where KSHV is endemic, it affects adults and children of all ages and irrespective of sexual orientation, suggesting the existence of non-sexual risk factors for KSHV infection.

In this thesis, three distinct cross sectional studies aiming to define the seroprevalence of KSHV in South African populations and to identify plausible risk factors for KSHV infection were undertaken. The studies measured KSHV seropositivity in relation to sociodemographic factors and HIV status. In children, factors associated with horizontal mother to child transmission were also explored. In adults KSHV seropositivity was also measured in relation to sexually transmitted infections and/or measures of sexual behaviour. Calculated risk factors were expressed as odds ratios (95% confidence interval) for KSHV.

Methods

Mother to Child KSHV seroepidemiology Study: KSHV seroprevalence (reactive to either lytic K8.1 or latent Orf73) was measured in 1287 children and their 1179 biological mothers. Association between KSHV seropositivity in children was measured against KSHV seropositivity and HIV status of their mothers.

KSHV seroepidemiology in women attending antenatal clinics: Antibodies to KSHV lytic K8.1 and latent Orf73 antigens were tested in 1740 pregnant women attending antenatal clinics in South Africa in 2001. Information on HIV and syphilis serology, age, education, residential area, gravidity, and parity was anonymously linked to evaluate risk factors for KSHV seropositivity. Clinics were grouped by municipal regions and their proximity to the two main river catchments defined.

Carletonville Community KSHV seroepidemiology Study: Sera from 2103 South African individuals (862 miners, 95 sex workers, 731 female and 415 male township residents) were tested for antibodies to KSHV lytic K8.1 and latent Orf73, HIV gonococcus, herpes simplex virus type 2 (HSV-2), syphilis and chlamydia. Information on social, demographic and high-risk sexual behaviour was linked to laboratory data.

Results

Mother to Child KSHV seroepidemiology Study: KSHV seroprevalence (reactive to either lytic K8.1 or latent Orf73) was 15.9% (204 of 1287 subjects) in children and 29.7% (350 of 1179 subjects) in mothers. The risk of KSHV seropositivity was significantly higher in children of KSHV seropositive mothers compared with those of KSHV-seronegative mothers. The HIV status of mothers was marginally associated with an increased risk of KSHV seropositivity in their children (AOR = 1.6, 95% CI: 1.0 to 2.6; P = 0.07). KSHV seroprevalence was significantly higher in HIV-infected subjects (P = 0.0005), and HIV-infected subjects had significantly higher lytic and latent KSHV antibody levels than HIV-negative subjects.

KSHV seroepidemiology in women attending antenatal clinics: KSHV seroprevalence was nearly twice that of HIV (44.6% vs. 23.1%). HIV and syphilis seropositivity was 12.7% and 14.9% respectively in women without KSHV, and 36.1% and 19.9% respectively in those with KSHV. Women who were KSHV seropositive were 4 times more likely to be HIV positive than those who were KSHV seronegative (AOR 4.1 95%CI: 3.4 - 5.7). Although, women with HIV infection were more likely to be syphilis seropositive (AOR 1.8 95%CI: 1.3 - 2.4), no association between KSHV and syphilis seropositivity was observed. Those with higher levels of education had lower levels of KSHV seropositivity compared to those with lower education levels. KSHV seropositivity showed a heterogeneous pattern of prevalence in some localities.

Carletonville Community KSHV seroepidemiology Study: Overall KSHV and HIV prevalences were 47.5 and 40%, respectively (P<0.43). The risk of HIV infection was highest in sex workers followed by female residents and miners, compared with male residents (P<0.001). HSV-2 infection was highly prevalent (66%) and lower, but still substantial, prevalence (6–8%) was observed for other sexually transmitted infections (STI). No significant difference in KSHV infection was observed among the residential groups (P>0.05). KSHV was not associated with any of the STI or any measures of sexual behaviour.

Conclusion

The findings of these three studies contribute substantially to global KSHV seroepidemiology and show that in Southern African settings KSHV is associated with non-sexual mode of transmission. Firstly KSHV is common in very young children up to ten years of age and increases with age until adulthood. The high prevalence of KSHV in the South African populations remained evident in all populations. In children, the risk of acquisition of KSHV was higher among children of KSHV-seropositive mothers than if the mother was KSHV negative. The association between KSHV and HIV was also noted in the study of pregnant

women attending antenatal clinics and in the mother to child study. However this association was not evident in the Carletonville population where both KSHV and HIV were highly prevalent.

In both the adult studies the lack of association between KSHV and syphilis was evident. KSHV infection was also not associated with other sexually transmitted infections and measures of sexual behaviour. As expected, the pattern of HIV and STI in sex workers suggests high rates of high-risk sexual behaviour in this population; however KSHV seropositivity was the same amongst sexworkers and all the other community groups. This pattern of the lack of association with high-risk sexual behaviour, particularly in sex workers and with any markers of STI strongly suggests that the sexual mode does not play a significant role in KSHV transmission in this South African population. This may also suggest that KSHV transmission may involve geographical and cultural factors other than sexual transmission.