INFECTION WITH HUMAN HERPESVIRUS-8 AND ITS CORRELATION WITH HEPATITIS B VIRUS AND HEPATITIS C VIRUS MARKERS AMONG RURAL POPULATIONS IN CAMBODIA

LOREDANA SARMATI, MASSIMO ANDREONI, BARBARA SULIGOI, ROBERTO BUGARINI, ILARIA UCCELLA, EDOARDO POZIO, AND GIOVANNI REZZA

Department of Public Health, Tor Vergata University, Rome, Italy; AIDS & STD Unit, Laboratory of Epidemiology and Biostatistics, and Laboratory of Parasitology, Istituto Superiore di Sanità, Rome, Italy

Abstract. Among 164 individuals in a rural population of Cambodia, antibodies to human herpesvirus-8 (HHV-8) were found among 56.6% of the women and 50.6% of the men. Seropositivity for HHV-8 tended to decrease with age ($P < 0.001$) and was not associated with exposure to hepatitis B virus (HBV) or HCV. Human herpesvirus-8, which shows a high rate of infection during childhood, does not seem to have the same pattern of transmission as HBV. This suggests very early acquisition of infection with HHV-8 in Cambodia.

INTRODUCTION

Human herpesvirus 8 (HHV-8), the major determinant of Kaposi’s sarcoma, is highly prevalent in tropical areas, and is transmitted primarily in childhood.\(^1\) To assess the prevalence of HHV-8 in rural areas of southeastern Asia, we conducted a study on a relatively isolated population in Cambodia. The association of HHV-8 infection with markers of exposure to hepatitis B virus (HBV) or HCV was also studied to evaluate similarities in the epidemiologic pattern and to suggest possible routes of transmission.

MATERIALS AND METHODS

**Study population.** The study was conducted in January 1997 in the village of Sdau, Cambodia, and was originally designed as a cross-sectional survey to assess the prevalence of infection with *Schistosoma mekongi*. One-third of the population is usually absent from the village after the rice harvest for due to travel and cutting of wood (males). Adolescents and young adults often move to neighboring areas, in particular to Stung Treng, the provincial capital. Individuals in the village between 4 and 17 years of age (131 subjects) were enrolled in the study. Thirty-three adults were also studied.

Serum samples were collected and kept at −20°C until use. This study was reviewed and approved by the Cambodian Health Ministry in accordance with World Health Organization guidelines. Informed consent was obtained prior to enrollment.

**Serologic assays.** Serum samples were tested for antibody to HCV (Serodia HCV; Fujirebio, Inc., Tokyo, Japan), hepatitis B virus surface antigen (HBsAg) (Serodia Hbs; Fujirebio, Inc.), and antibody to hepatitis B virus core antigen (HBc) (Monolisa anti-HBc; Sanofi-Diagnostic Pasteur, Marnes-la-Coquette, France). To detect antibodies against lytic antigens of HHV-8, an immunofluorescent assay based on the BCBL-1 cell line (AIDS Research and Reference Reagent Program, Rockville, MD) was used. Positive samples were defined as having reactivity at a dilution of 1:20 in the anti-lytic test.\(^2\)

**Statistical analysis.** The prevalence of antibodies to HHV-8, HBc, and HCV and positivity for HBsAg were defined as the number of positive individuals per total number of those tested. Odds ratios (ORs) were used to evaluate the association between HHV-8 positivity and demographic variables (i.e., age and gender) or serology for HBV and HCV. Ninety-five percent confidence intervals (CIs), a chi-square, test, and a chi-square test for trend were used to evaluate the statistical significance of the associations at a level of $P < 0.05$.

RESULTS

A total of 164 individuals were studied, of whom 83 were females (50.6%). The median age of the population was 13 years (range = 4–69 years), and 79.9% (131 of 164) of the participants were ≤17 years old. Eighty-eight (53.7%) had antibodies to HHV-8, 33 (20.1%) had antibodies to HBc, 17 (10.4%) had antibodies to HCV, and 15 (9.1%) were positive for HBsAg.

The seroprevalence of HHV-8 tended to decrease with age (OR = 0.93 per year of increase, 95% CI = 0.90–0.97). Positivity for HBc showed a large increase in the adult age groups (OR = 1.06 per year of increase, 95% CI = 1.03–1.10). Those individuals who were more than 17 years old had a 4.34 (95% CI = 1.87–10.1) increased risk of exposure compared with the younger participants. Individuals positive for HCV (OR = 1.02 per each year increase, 95% CI = 0.98–1.06) were more likely to be detected after childhood. The OR was 4.73 (95% CI = 1.30–17.2) for those who were at least 13 years old compared with the youngest group (Table 1).

The distribution of antibody titers to HHV-8 did not show a wide variation across the different age groups. Antibodies to HHV-8 were found in 47 (56.6%) of 83 women and 41 (50.6%) of 81 men. Seropositivity for HHV-8 tended to be inversely associated with HBV markers and was not associated with HCV markers (neither association was statistically significant). Antibodies to HHV-8 were detected in 14 (42.4%) of 33 HBc-positive individuals compared with 74 (56.5%) of 131 HBc-negative individuals (OR = 0.57, 95% CI = 0.26–1.23, $P = 0.15$), and in 8 (47.1%) of 17 HCV-positive individuals compared with 80 (54.4%) of 147 HCV-negative individuals (OR = 0.74, 95% CI = 0.27–2.03, $P = 0.57$).

When we adjusted for age in a multivariate logistic model, the association between HHV-8 and exposure to the other viral agents did not change significantly. The adjusted OR (0.91) for the association between antibodies to HHV-8 and HBc tended to increase towards 1.0 (95% CI = 0.38–2.14, $P = 0.82$). The adjusted OR for the association with HCV was 0.89 (95% CI = 0.310–2.580, $P = 0.84$) and remained similar.
to the crude OR. Exposure to HBV, as defined by positivity for HBsAg, and HCV were associated (OR = 0.22, 95% CI = 0.03–1.76).

**DISCUSSION**

The prevalence of antibodies to HHV-8 was high in the studied rural population. Other studies conducted in other areas of southeastern Asia showed inconsistent results. A low prevalence of infection with HHV-8 was observed in Malaysia, India, Sri Lanka, and Thailand in both healthy individuals and those infected with human immunodeficiency virus HIV; the seroprevalence was 3.7% among persons with nasopharyngeal and oral carcinoma from Malaysia, Hong Kong, and Sri Lanka. Another study conducted in Taiwan showed that the seroprevalence was 3.7% among persons with nasopharyngeal and oral carcinoma.

The high prevalence detected in the Cambodian village might be attributable to the special local situation, which is characterized by a very low socioeconomic level and poor hygiene. It is not known whether the rural setting and underdevelopment contribute to the observed difference in comparison with other neighboring countries. However, these results do not explain the rarity of Kaposi’s sarcoma in this region.

The seroprevalence of HHV-8 tended to decrease with age. Similar age patterns have been observed in Uganda and Ghana, which have high seroprevalences for HHV-8. The significance of this finding is unclear. It is likely that levels of antibodies to HHV-8 decrease with age. A similar pattern, which shows a decreasing seroprevalence with age, has also been observed for HHV-6, which is acquired early in childhood. However, these results need to be interpreted cautiously because the sample size of the adult population was limited.

In conclusion, we have found a high prevalence of HHV-8 infection in a rural village in Cambodia. The seroprevalence of HHV-8 tended to be high in children, suggesting a very early acquisition of the infection in the studied area. Further studies are needed to determine the mechanisms of transmission and reasons for the rarity of HHV-8-associated conditions in this region.

**REFERENCES**


