MAJOR ARTICLE

Transmission of Human Herpesvirus Type 8 Infection Within Families in American Indigenous Populations From the Brazilian Amazon

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Background. The intrafamilial dynamics of endemic infection with human herpesvirus type 8 (HHV-8) in Amerindian populations is unknown.

Methods. Serum samples were obtained from 517 Amerindians and tested for HHV-8 anti–latent nuclear antigen (anti-LANA) and antilytic antibodies by immunofluorescence assays. Logistic regression and mixed logistic models were used to estimate the odds of being HHV-8 seropositive among intrafamilial pairs.

Results. HHV-8 seroprevalence by either assay was 75.4% (95% confidence interval [CI]: 71.5%–79.1%), and it was age-dependent ($P_{trend} < .001$). Familial dependence in HHV-8 seroprevalence by either assay was found between mother–offspring (odds ratio [OR], 5.44; 95% CI: 1.62–18.28) and siblings aged ≥10 years (OR 4.42, 95% CI: 1.70–11.45) or siblings in close age range (<5 years difference) (OR 3.37, 95% CI: 1.21–9.40), or in families with large (>4) number of siblings (OR, 3.20, 95% CI: 1.33–7.67). In separate analyses by serological assay, there was strong dependence in mother–offspring (OR 8.94, 95% CI: 2.94–27.23) and sibling pairs aged ≥10 years (OR, 11.91, 95% CI: 2.23–63.64) measured by LANA but not lytic antibodies.

Conclusions. This pattern of familial dependence suggests that, in this endemic population, HHV-8 transmission mainly occurs from mother to offspring and between close siblings during early childhood, probably via saliva. The mother to offspring dependence was derived chiefly from anti-LANA antibodies.

Human herpesvirus type 8 (HHV-8) is the etiologic agent of all forms of Kaposi sarcoma (KS) [1, 2], primary effusion lymphoma [3], and the variant of multicentric Castleman disease associated with human immunodeficiency virus (HIV) [4, 5]. In HIV-seronegative populations, HHV-8 seroprevalence varies geographically and does not always correlate with the incidence of KS [6, 7]. Very high HHV-8 seroprevalence, ranging from 24% to 100%, has been reported in American indigenous populations from Brazil [8–10], Ecuador [11], and French Guiana [12]. Although occurrence of classic KS has been reported in populations originating from the Peruvian Andes [13], the very high prevalence of HHV-8 infection found in Amazonian Amerindians [14] does not mirror the apparent low incidence of KS in these populations. HHV-8 can be transmitted through blood products and vaginal and anal sexual intercourse, but saliva has been predominantly implicated in the spread of HHV-8 among men who have sex with men [15, 16] and within families living in endemic areas, from mother to child and between siblings [17, 18].

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In a previous population-based study [14], we reported a very high prevalence of HHV-8 in American indigenous groups living in a remote area of the Brazilian Amazon, but the intrafamilial associations of HHV-8 infection remain unknown in these populations. We hypothesized both horizontal and vertical transmission of HHV-8 within families via saliva.

The goal of this study was to investigate the actual familial clustering of HHV-8 infection to better understand possible patterns of acquisition and transmission of HHV-8 in this endemic South American population.

METHODS

Study Setting and Populations

The study was conducted in the Mapuera village along the Trombetas River, a tributary of the Amazon River, in Para State, Brazil. American indigenous populations originating from 7 different ethnic groups (ie, Wai Wai, Katwena, Xerew, Mawayana, Tyrió, Hixkariana, and Twnayana, all belonging to the Karib linguistic family), comprising 986 adults and children living in the village. The only inclusion criterion was being a resident in the village. The village is made up of densely clustered huts along the river, each hut measuring approximately 5 meters in diameter, and sheltering from 2 individuals to several families from the same ethnic group or not. In this study, a "'family" was defined as a group consisting of parents and their offspring. Cousins, aunts, and other relatives were excluded from data analysis. In this population, polygamy is not practiced, so spouses were considered to be in monogamous relationships.

The purpose and methods of the study were explained to community leaders and to all through community meetings. Informed consent procedures were carried out individually, with the assistance of local indigenous health agents for translation. Consent was provided mostly verbally and by a parent or guardian for children under the age of 15 years. The study was approved by the American indigenous traditional chiefs, the National Indigenous Health Agency of Brazil (FUNASA), and the ethics research committee of the Ministry of Health of Brazil (CONEP).

Study Procedures

Fieldwork was conducted between May and June 2007. Each day, 10 huts were scheduled for enumeration of inhabitants, interview, and blood sample collection from consenting individuals. Participants' demographic information, including sex, age, ethnic group, marital status, and number of individuals living in the same hut, was recorded by use of a simple interviewer-administered questionnaire. Information on family structure and genealogical data were checked with the local indigenous health agents and against data obtained in a prior census conducted in 2006 by MEVA (Missão Evangélica da Amazônia). Because participation was totally voluntary, this resulted in uneven representation of some families, even those living in the same hut. The Mapuera community chief requested that all village residents be offered participation in the study. Because participation was entirely voluntary and there were no direct benefits for participants, it was not deemed possible nor desirable to obtain information on nonparticipation in the study, including information on absenteeism or refusal.

From each consenting participant, a 5 mL blood sample was collected for serological testing. Samples were stored at −20°C in a generator-operated freezer for up to 3 weeks and shipped to the São Paulo Instituto de Medicina Tropical, where they were stored at −20°C until testing.

HHV-8 Serology

The presence of antibodies against HHV-8 latency-associated nuclear antigen (LANA) and HHV-8 lytic antigens was determined by immunofluorescence assays (IFAs), at a 1:40 starting dilution, using a body cavity–based lymphoma (BCBL)–1 cell line. Punctuate nuclear staining in noninduced BCBL-1 cells was considered to indicate seropositivity for antibodies against LANA. The viral lytic cycle was induced by incubating BCBL-1 cells with 20 ng/mL 12-*O*tetradecanoylphorbol-13–acetate (TPA) (Sigma) for 96 hours. Entire-cell fluorescence in approximately 20% of TPA-treated cells was considered to indicate seropositivity for antibodies against lytic-phase antigen. In a prior validation study, these assays yielded relatively low sensitivities (54% and 55%, for IFA LANA and lytic, respectively) but very high specificity (98% and 99%, respectively) in a latent class model analysis [19].

Statistical Analyses

HHV-8 infection was defined as seropositivity by either LANA or lytic serological assay and then separately by each serological assay. Further, χ^2 tests for categorical variables were used to determine significant differences between prevalence of HHV-8 infection across each variable of interest. The risk associated with HHV-8 infection in a wife given that her husband was HHV-8 seropositive was estimated using ordinary logistic regression. Mixed logistic models were used to estimate the odds ratios (ORs) of being HHV-8 seropositive among relative pairs (ie, parent–offspring and sibling–sibling). Because of the correlation of observations between members of the same family (ie, offspring born to the same mother, or younger siblings with the same older sibling), ordinary logistic regression may lead to standard errors that are either too large or too small and, hence, to confidence intervals (CIs) and *P* values that are invalid. Mixed logistic models allow for the correlation observations by including a random effect along with the standard fixed effect. In this study, results obtained

from mixed models were considered for interpretation of results for clustered observations within families. Results obtained with ordinary logistic regression are reliable for spouse pairs, as there is only one such pair per family.

A family specific random intercept was used for parent–offspring analysis. For the sibling analyses, clusters were defined on the basis of sibling pairs having the same older sibling, and a cluster-specific random intercept nested within families was used. When modeling the risk of infection among sibling pairs, the younger sibling's infection was treated as the response to the older sibling's infection status. The familial dependences of HHV-8 infection in pairs of relatives, given that the first individual of the pair was HHV-8 seropositive, was calculated first by seropositivity with either serological assay, and then separately by each assay.

All statistical analyses were performed using STATA version 9.0 (StataCorp, College Station, Texas) [20].

RESULTS

The 2006 MEVA census indicated that 986 American indigenous people (495 males and 491 females) lived in 193 huts in Mapuera village. The median number of household residents was 5.0 (range, 2–13). A total of 517 (52%) of the enumerated individuals aged 1–87 years-old (233 males and 284 females) consented for inclusion in the study, Reasons for nonparticipation were not elucidated from other residents. Study participants were recruited from 124 huts (64%); in 40 huts, all residents agreed to participate. The median age of participants was 22 years (interquartile range [IQR], 4–72) in males and 20 years (IQR, 4–72) in females.

The overall HHV-8 seroprevalence was 70.2% (363 of 517; 95% CI, 66.1–74.1) by IFA-LANA, 38.9% (201 of 517; 95% CI, 34.6–43.2) by IFA lytic, and 75.4% (390 of 517; 95% CI, 71.5 to 79.1) by either serological assay. HHV-8 seroprevalence increased with age from 45.6% in children aged 1–9 years to 87.5% in individuals aged ≥45 years ($P_{trend} < .001$). When assessed separately by serological assay, the prevalence of HHV-8 infection measured by IFA-LANA increased from 39.2% among those aged 1–9 to 85% among those aged ≥45 years ($P_{trend} < .001$). In contrast, the HHV-8 prevalence measured by IFA-lytic assay was stable from age 10 to 14 years onward (around 40%–46%). HHV-8 seroprevalence was highest (84.3%) among members of the Katwena ethnic group ($P < .001$). There was no significant difference by sex or number of household residents (Table 1).

The probability of HHV-8 seropositivity by either serological assay between spouses given that the other spouse in the pair was also seropositive could be analyzed in 110 couples (Table 2). Both spouses tested HHV-8 seropositive in 81 of 110 couples (73.6%), whereas only 4 couples (3.6%) were concordant seronegative, and 25 couples (22.7%) were serodiscordant. There was no significant evidence of dependence of HHV-8 seropositivity by either assay between spouses (OR from husband to wife, 2.16; 95% CI, 0.60–7.8; $P = .24$). Regarding the offspring, there were significant associations in the mixed models between being HHV-8 seropositive by either assay given that their mother was HHV-8 seropositive (OR, 5.44; 95% CI, 1·62–18.28; $P = .01$) or their sibling was HHV-8 seropositive (OR, 2.49; 95% CI, 1.36–4.54; $P = .003$). In particular, we found a strong dependence of HHV-8 seropositivity among older sibling pairs in which both members of the pair were aged ≥10 years (OR, 4.42; 95% CI, 1.70–11.45; $P = .002$). However, the number of pairs with both siblings aged <10 years was much smaller, limiting our power to detect any dependence among such pairs or its difference from older pairs. There was no significant association between the serostatus of father and their offspring ($P = .08$) (Table 2).

Ordinary logistic regression showed a dependence at the marginal level of significance between spouses when husband tested HHV-8 seropositive by LANA (OR, 3.29; 95% CI, 1.14–9.52; $P = .03$) but not lytic antibodies (Table 3). The lack of significant dependence between father and offspring remained when analyses were performed separately by serological assay (Table 3). The familial dependence in pairs of mother–offspring of any age remained strong when the mother was seropositive to LANA (OR, 8.94; 95% CI, 2.94–27.23; $P < .001$) but not to lytic antibodies (OR, 1.64; 95% CI, 0.80–3.34; $P = .17$). This association with LANA, but not lytic antibodies, was even stronger to offspring aged ≥10 years (OR, 11.91; 95% CI, 2.23–63.64; $P = .004$). In the sibling pairs, there was association with the presence of both LANA (OR, 2.22, 95% CI, 1.28–3.87; $P = .005$) and lytic antibodies (OR, 3.10; 95% CI, 1.53–6.27; $P = .002$) (Table 3).

To further explore the familial dependence between siblings, a separate analysis was performed stratified by age difference between siblings and by the sibship size per family (Table 4). A statistically significant association in HHV-8 seropositivity by either serological assay was observed among siblings close in age (OR, 3.37; 95% CI, 1.21–9.40; $P = .02$) but not when the age difference was >5 years (OR, 1.89; 95% CI, 0.80–4.46; $P = .15$). In this sensitivity analysis, the association was significant amongst families with >4 siblings (OR, 3.20; 95% CI: 1.33–7.67, $P = .01$), and marginally nonsignificant, with a lower odds ratio, in families with <4 siblings (OR, 2.17; 95% CI, 0.97–4.82, $P = .06$). The association in larger families was strongest for lytic antibodies (OR, 9.66; 95% CI: 2.84–32.82; $P < .001$) compared to LANA antibodies (OR, 1.92; 95% CI, 0.89–4.16; $P = .10$) (data not shown).

DISCUSSION

We investigated the familial dependence of HHV-8 infection within American indigenous families living in the Brazilian

Table 1. Seroprevalence of Human Herpesvirus Type 8 (HHV-8) by Anti-LANA and Antilytic Immunofluorescence Assays (IFAs) among 517 Residents of the Mapuera Village, Para State, Brazil

Characteristic	LANA IFA No. Positive/No. Tested (%)	Lytic IFA No. Positive/No. Tested (%)	Either LANA or Lytic IFA No. Positive/No. Tested (%)
Sex			
Male	157/233 (67.4)	99/233 (42.5)	171/233 (73.4)
Female	206/284 (72.5)	102/284 (35.9)	219/284 (77.1)
P value*	.20	.12	.33
Age groups, years			
1–9	31/79 (39.2)	21/79 (26.6)	36/79 (45.6)
10–14	61/89 (68.5)	36/89 (40.4)	65/89 (73.0)
15–19	47/71 (66.2)	27/71 (38.0)	51/71 (71.8)
20–24	42/60 (70.0)	25/60 (41.7)	47/60 (78.3)
25–34	56/71 (78.8)	27/71 (38.0)	60/71 (84.5)
35–44	58/67 (86.6)	31/67 (46.3)	61/67 (91.0)
45–87	68/80 (85.0)	34/80 (42.5)	70/80 (87.5)
P value*	<.001**	.29**	<.001**
Ethnic group			
Wai Wai	126/178 (71.1)	87/178 (48.0)	139/178 (78.1)
Katwena	119/147 (81.0)	63/147 (43.0)	124/147 (84.3)
Other Amerindian[a]	113/171 (66.1)	48/171 (28.1)	122/171 (71.3)
Other groups[b]	5/21 (23.8)	3/21 (14.3)	5/21 (23.8)
P value*	<.001	.001	<.001
No. of inhabitants in the same hut			
2	18/24 (75.0)	7/24 (29.2)	19/24 (79.2)
3	16/23 (69.6)	8/23 (34.8)	17/23 (73.9)
4	63/82 (76.8)	37/82 (45.1)	69/82 (84.1)
5–7	157/239 (65.7)	85/239 (35.6)	171/239 (71.5)
8–13	109/149 (73.2)	64/149 (43.0)	114/149 (76.5)
P value*	.29**	.33**	.23**

Abbreviation: LANA, latent nuclear antigen.

[a] Other Amazonian American indigenous groups included: Xerew (n = 79), Mawayana (n = 45), Hixkariana (n = 29), Tyrió (n = 18), and Twnayana (n = 1).

[b] Others include non-Amerindians (n = 2) and mixed race (n = 18).

* For comparisons within the whole group in the category with results to either IFA assay.

** *P* for trend.

Amazon, using 2 serological assays to detect antibodies against LANA and lytic antigens separately and in combination.

This study confirms the very high seroprevalence of antibodies against both HHV-8 LANA and lytic antigens amongst Amazonian American populations. Seroprevalence of anti-LANA antibodies increased linearly from 39% among 1–9 year-olds to >85% in the oldest age groups, whereas the prevalence of lytic antibodies remained stable at around 40% throughout age groups. This age distribution pattern is consistent with other studies in settings where HHV-8 infection is endemic [17, 18], and it suggests that HHV-8 transmission starts early in life and continues throughout life. Reasons why HHV-8 becomes hyperendemic have remained unclear. Studies in Africa indicate that the acquisition of HHV-8 infection during childhood is associated with the presence of a family member who is also infected [17, 18]. In agreement with previous studies in endemic populations [17, 18, 21, 22], we found a positive association between the serostatus of the mother and her offspring. Our data suggest that HHV-8 transmission is more intense when siblings are close in age (that is, when they were more likely to have played and shared meals together), and when living in larger families, which may also increase the possibility of exchange of oral fluids. The persistently strong dependence of HHV-8 infection observed in sibling pairs aged ≥10 years indicates that exposure may be cumulative and not restricted to early childhood.

Our data provide a unique opportunity to examine the associations between pairs of relatives separately by antibody profile, which may shed light on transmission dynamics. The dependence of HHV-8 seropositivity between mother–offspring pairs was derived chiefly from LANA, whereas it was independent of serological assay among siblings. Like other

Table 2. Distribution of Pairs According to Familial Relationships and HHV-8 Serological Status, and Estimates of Odds Ratios for HHV-8 Seropositivity by Either Assay (Anti-LANA or Antilytic IFA)

Type of Pair	No. of Pairs[a]				Total	OR (95% CI)	*P* Value
	+, +	+, −	−, +	−, −			
Husband–wife[b]	81	10	15	4	110	2.16 (0.60–7.80)	.24
Mother–offspring[c]							
Child <10 years	31	33	3	9	76	5.21 (0.50–54.69)	.17
Child ≥10 years	149	44	5	6	204	5.62 (0.58–54.36)	.14
All children	180	77	8	15	280	5.44 (1.62–18.28)	.01
Father–offspring[c]	142	74	17	18	251	2.20 (0.91–5.35)	.08
Sibling pairs[d]							
Both siblings <10 years	7	6	4	10	27	7.67 (0.11–534.94)	.35
Both siblings ≥10 years	146	33	35	25	239	4.42 (1.70–11.45)	.002
All sibling pairs	214	107	55	58	434	2.49 (1.36–4.54)	.003

Abbreviations: CI, confidence interval; HHV-8, human herpesvirus type 8; IFA, immunofluorescence assay; LANA, latent nuclear antigen; OR, odds ratio.

[a] HHV-8 status of first and second in pair.

[b] OR calculated with ordinary logistic regression.

[c] Mixed logistic regression model with family specific random intercept.

[d] Mixed logistic regression model with random intercepts for family and oldest sibling within family.

herpesviruses, HHV-8 has latent and lytic cycles of replication, and reactivation from latency to lytic replication is a necessary step for HHV-8 transmission [23]. The presence of antibodies against lytic antigens is strongly associated with both viral replication and viral transmission. This was observed in a Kaposi's sarcoma–associated herpesvirus (KSHV) transmission study among mother–child pairs in South Africa, where the detection of KSHV in saliva, a marker of active replication, was associated with increased titters of lytic antibodies, whereas there was no association between anti-LANA antibodies and the presence of HHV-8 DNA in saliva among mothers [24].

We found associations with LANA antibodies in all types of family member pairs, but there was no significant evidence of dependence between spouses measured by lytic antibodies, a marker of ongoing transmission confirming that, as in other endemic populations, sexual intercourse is not likely to be the predominant mode of HHV-8 transmission in Brazilian Amerindians [17]. We did not assess the duration of cohabitation of spouses and thus could not determine whether this could have been a factor of HHV-8 transmission in this population.

The dependence between mother and offspring and between spouses measured by IFA-LANA in our study may reflect older transmission events, whereas the associations with both LANA and lytic antibodies among siblings may indicate old as well as more recent or ongoing transmission. We did not assess antibody titers in this study, although it has been demonstrated that lytic antibody levels did not influence HHV-8 dependence between close relatives in an isolated and hyperendemic community in Cameroon [25].

It has been widely reported that in asymptomatic HHV-8 infected individuals, the prevalence of antilytic HHV-8 antibodies is higher than anti-LANA [26–29]. This antilytic/anti-LANA antibody profile ratio is strikingly different in some populations in Africa [30] and in the Amazon [9, 11, 14], where more subjects have antibodies against LANA than lytic antigens. This is more evident among Brazilian Amerindians, where the prevalence of anti-LANA antibodies is consistently much higher than the prevalence of antilytic antibodies [14]. Further studies are needed to evaluate the significance of this finding and its associations with genetic characteristics of the virus in certain populations, the genetic makeup of these populations, or both.

It has been speculated that 3 types of behavioral practices associated with saliva exchange may enhance the risk of HHV-8 transmission in sub–Saharan Africa through (1) healing and medical practices, (2) initiation or ritual practices, and (3) feeding practices [31]. Yet epidemiological surveys have failed to demonstrate strong associations between specific cultural habits and the risk of HHV-8 infection in endemic populations. In one study conducted in a rural community in Uganda, the report of sharing food and/or sauce plates with other household members was only marginally associated with HHV-8 infection, whereas children exposed to premasticated food from the mother did not have an increased risk of HHV-8 infection [32]. Our study did not explore which cultural habits of Amazonian American populations could be associated with their very high HHV-8 prevalence. We could not assess whether our finding of an association between HHV-8 seropositivity and ethnic group might be related to

Table 3. HHV-8 Seroprevalence Dependency According to Familial Relationships and Type of HHV-8 Serological Assay (Immunofluorescence Assays for Anti-LANA or Anti-Lytic Antibodies)

Type of Pair	OR (95% CI)	*P* Value
Husband–wife[a]		
LANA pos	3.29 (1.14–9.52)	.03
Lytic pos	1.05 (0.49–2.27)	.89
Mother–offspring[b]		
Offspring <10 years		
LANA pos	6.65 (0.82–53.62)	.07
Lytic pos	3.17 (0.32–31.70)	.33
Offspring ≥10 years		
LANA pos	11.91 (2.23–63.64)	.004
Lytic pos	1.40 (0.57–3.46)	.46
All offspring		
LANA pos	8.94 (2.94–27.23)	<.001
Lytic pos	1.64 (0.80–3.34)	.17
Father–offspring[b]		
LANA pos	2.39 (0.94–6.08)	.07
Lytic pos	0.94 (0.48–1.81)	.85
Sibling pairs[c]		
LANA pos	2.22 (1.28–3.87)	.005
Lytic pos	3.10 (1.53–6.27)	.002

Abbreviations: CI, confidence interval; HHV-8, human herpesvirus type 8; LANA, latent nuclear antigen; OR, odds ratio; pos, positive.

[a] OR calculated with ordinary logistic regression.

[b] Mixed logistic regression model with family-specific random intercept.

[c] Mixed logistic regression model with random intercepts for family and oldest sibling within family.

specific cultural habits or genetic characteristics of certain American indigenous subgroups. Further studies are required to evaluate the relationship between specific behavioral and sociocultural practices and the risk of HHV-8 infection within families.

We could not include all of the population in our study, which would have been useful to study transmission routes exhaustively. Information on reasons for nonparticipation through absenteeism, refusal, or other reason could not be collected, but this would only have contributed to reduce the power of our study, as it is unlikely that nonparticipation would be related to the outcome (asymptomatic HHV-8 infection). It is possible that working-age men were not always present at the time of sample collection, but odds ratios presented were adjusted for age and sex on data analysis, reducing any selection bias arising from nonparticipation of working-age males.

HHV-8 DNA was commonly detected in the saliva of this Amazonian American population, particularly among the youth [14]. There have been reports of an association between certain human leukocyte antigen (HLA) alleles and shedding of HHV-8 in saliva in endemic populations in Uganda [33] and South Africa [34]. Further work on HLA typing is being conducted by our group to investigate associations between HLA types and shedding of HHV-8 in saliva in this population.

Brazilian Amerindians are infected with a particular HHV-8 viral subtype (E) [14], also described in native Amerindians from Guyana [12] and Ecuador [11]. Although the incidence of Kaposi's sarcoma (KS) is unknown in these populations, there have been reports of subtype E-associated KS in AIDS patients from Peru [35]. However, the very high HHV-8 seroprevalence is in stark contrast with the rarity of classic KS in Amazonian American indigenous populations, suggesting a host adaptation to HHV-8 infection or a peculiar virus. It has been suggested that a major recessive gene may be associated with host susceptibility or resistance to HHV-8 infection in other endemic populations [36]. Alternatively, it can be hypothesized that a yet unidentified subtype E viral gene, absent in other HHV-8 subtypes, might be responsible for controlling viral latency and lytic replications in this population. Such gene candidates include the recently described HHV-8 microRNAs [23], which are viral regulators recognized as inhibitors of lytic replication and thus of the development of KS [37], which have never been investigated for the HHV-8 E subtype.

Table 4. Distribution of Sibling Pairs According to Age Difference Between Siblings and Number of Siblings Per Family, and Association of HHV-8 Seropositivity Within Pairs

	Number of Pairs[a]						
Type of Pair	+, +	+, −	−, +	−, −	Total	OR (95% CI)[b]	*P* value
Age difference, years [range 0–40]							
<5 years	86	30	25	29	170	3.37 (1.21–9.40)	.02
≥5 years	128	77	30	29	264	1.89 (0.80–4.46)	.15
Number of siblings per family [range 2–8]							
≤4	84	32	33	25	174	2.17 (0.97–4.82)	.06
>4	130	75	22	33	260	3.20 (1.33–7.67)	.01

Abbreviations: CI, confidence interval; HHV-8, human herpesvirus type 8; OR, odds ratio.

[a] In order, HHV-8 status of oldest and youngest sibling of the pair.

[b] Hierarchical mixed logistic regression model with random intercepts for family and oldest sibling within family.

In conclusion, our study confirms that, in this highly endemic population, HHV-8 is mainly transmitted from mother to offspring early in childhood and between siblings of close age range, also probably at toddlers' age, although transmission may continue throughout life, likely through intermittent but ongoing saliva HHV-8 shedding.

Notes

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