CONCISE COMMUNICATIONS

Risk Factors for Human T Cell Lymphotropic Virus Type II Infection among the Guaymi Indians of Panama

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To examine risk factors for human T cell lymphotropic virus type II (HTLV-II) infection, a case-control study was conducted among the Guaymi Indians of Panama. In females, HTLV-II seropositivity was associated with early sexual intercourse (≤13 vs. >15 years; odds ratio [OR], 2.50; 95% confidence interval [CI], 1.11–6.14) and number of lifetime sex partners. One partner increased risk of seropositivity by 30% (OR, 1.30; CI, 1.05–1.64), and risk increased with number of partners. Similar risk was associated with number of long-term sexual relationships. Among males, intercourse with prostitutes was associated with HTLV-II seropositivity (OR, 1.68; CI, 1.04–2.72). These data support a role for sexual transmission in HTLV-II infection. Association of seropositivity with primary residence in a traditional village (OR, 3.75; CI, 1.02–15.38) and lack of formal education (0 vs. >6 years [OR, 3.89; CI, 1.67–9.82]) observed in males may reflect differences in sexual practices associated with acculturation.

Human T cell lymphotropic virus type II (HTLV-II) is endemic among Amerindians in North, Central, and South America, including the Ngöbe-Bugle people (Guaymi Indians) of Panama, among whom other retroviral infections, intravenous drug (IVD) use, scarification, and tatooing are rare. HTLV-II seroprevalence among the Guaymi approaches 10%, is similar in males and females, and increases with age [1]. Concordance of seropositivity among spouses and mother-child pairs is consistent with sexual and maternal-to-child transmission of HTLV-II in this and other populations [1–3]. The objective of the present study was to identify and quantify sexual, socioeconomic, and lifestyle factors associated with HTLV-II infection among the Guaymi.

Methods

Between January 1991 and May 1993, 3686 (82%) of 4451 Guaymi >1 year of age residing on 10 banana plantations (*fincas*) in and around Changuinola, Bocas del Toro Province, Panama, were recruited for a serosurvey of HTLV-II [1]. This represented 74% of the estimated Guaymi population in this area. Of these, 352 (9.5%) were seropositive. Subsequently (between August 1994 and June 1996), we attempted to enroll all seropositive participants and seronegative controls (frequency matched in a 1:2 ratio by random selection within age [5-year intervals]-sex strata) in a nested case-control study to assess risk factors for infection. Participants in the case-control study were interviewed in their home by a trained interviewer of the same sex, blinded to the participant's HTLV-II status. Controls lost to follow-up or who refused participation were replaced, resulting in an excess of seronegative persons.

This analysis is based on Guaymi ≥12 years old and includes 198 (59%) of 334 seropositive persons and 460 (69%) of 668 matched seronegative controls. The initial serostatus was confirmed for all participants. The 17 participants who seroconverted and 4 who seroreverted were excluded from analysis. Data were obtained for demographic variables: education (none, 1–6 years, >6 years), residential history (on the *finca* or in traditional dwellings), and

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markers of sanitation (plumbing, water source, type of flooring) in the current (≥3 of the last 5 years) and early childhood residence (≥3 of the first 5 years). Data were collected on traditional practices initially postulated to be related to transmission: drinking *chicha fuerte* (a mildly alcoholic beverage made from masticated corn) and hunting or skinning monkeys. Sexual and health histories (including transfusions, IVD use, and sexually transmitted diseases [STDs]) were obtained. Numbers of sex partners and numbers of sexual relationships were treated as continuous variables. Age at first sexual intercourse was treated as a categorical variable with categories determined by sex based on median values in these groups.

Blood, obtained by a trained phlebotomist, was separated, stored at −80°C, and tested by an HTLV-I EIA (Cambridge Bioscience, Cambridge, MA). Reactive samples were confirmed by HTLV Western blot 2.3, and recombinant envelope proteins MTA-1 (rgp46-I) and K55 (rqp46-II) (Diagnostic Biotechnology, Singapore) were used to differentiate HTLV-I from HTLV-II reactives. Herpes simplex virus type 2 (HSV-2) was tested for using an immunoblot containing recombinant baculovirus–infected insect cells expressing HSV-2 glycoprotein (gG2) [4].

Bivariate analyses were done with χ^2 or Fisher's exact tests. To compare mean values of continuous variables between study groups, a *t* test was used. To test for trend in proportions, a χ^2 test for trend was used. Unconditional logistic regression was used to perform an unmatched analysis of risk factors, adjusted for age (quartiles), sex, and *finca* distribution. Odds ratios (ORs) were computed as estimates of risk, and 95% confidence intervals (CIs) calculated to assess precision. Final multivariate models were computed separately for males and females.

Results

Demographic and Cultural Factors

HTLV-II–seropositive and –seronegative persons were similar in age (range, 12–58 and 12–59 years, respectively), mean ages (33.9 ± 0.7 vs. 33.2 ± 0.5 years; $P = .36$), sex (60% vs. 57% male; $P = .49$), and *finca* distribution (data not shown). No participants reported IVD use or IVD use by a sex partner. Overall, transfusion history was similar among seropositive and seronegative persons (9.6% vs. 7.8%; $P = .45$). However, a higher proportion of seropositive males had a history of transfusion (5.6% vs. 1.9%; $P = .05$). No difference was found in transfusion history among females (15.2% vs. 15.7%; $P = .91$).

Guaymi who reported no formal education were more likely to be HTLV-II seropositive than those with 1–6 years of education (OR, 1.73; CI, 0.95–3.31) and were three times more likely to be seropositive than those with >6 years of education (OR, 3.06; CI, 1.62–6.05; χ^2 trend, $P = .0002$). This risk was similar for males and females. Overall, current primary residence in a traditional village was significantly associated with seropositivity (OR, 2.43; CI, 1.05–5.57). This association was stronger for males than females, with seropositive males 4× more likely to report their current primary residence as the traditional village (OR, 4.43; CI, 1.28–17.49). However, HTLV-II seropositivity was not associated either with current or childhood primary residence in a traditional village or with the type of flooring, water source, or toilet facility. Seropositive persons were more likely to report drinking *chicha fuerte* (OR, 1.54; CI, 1.04–2.29). This was significant only among females (40.5% vs. 27.9%; OR, 1.78; CI, 1.02–3.13). Neither hunting nor skinning monkeys was associated with HTLV-II seropositivity.

Sexual Risk Factors

Females. The median ages at first sexual intercourse for seropositive and seronegative females were 13 and 14, respectively. The risk of infection was higher in those reporting first sexual intercourse at ≤13 compared with >15 years (OR, 2.81; CI, 1.22–6.60; table 1). The trend of increasing seropositivity with decreasing age of first sexual intercourse was statistically significant ($P = .001$). The median number of sex partners among women was 1; 95% reported ≤4. Females reporting 1 partner were more likely to be seropositive than were females reporting none (OR, 1.32; CI, 1.14–1.74), and risk increased with number of partners. Reporting ≥4 partners was associated with an OR of 3.25 (CI, 1.33–7.93).

Of females, 95% reported ≤3 long-term (>6 months) sexual relationships (median = 1). Females who reported 1 sexual relationship were 1.52 times more likely to be HTLV-II seropositive than females who reported no sex partners (OR, 1.52; CI, 1.11–2.17). Again, this risk increased with the number of re-

Table 1. Factors associated with HTLV-II infection among Guaymi Indian females.

Factor	HTLV-II⁺ no. (%)	HTLV-II⁻ no. (%)	Adjusted OR[a,c] (95% CI)	Adjusted OR[b,c] (95% CI)
Age at first sexual intercourse (years)				
≤13	44 (58.7)	66 (36.5)	2.81 (1.22–6.60)	2.50 (1.11–6.14)
14–15	22 (29.3)	72 (39.8)	1.32 (0.53–3.14)	1.17 (0.48–3.05)
>15	9 (12.0)	43 (23.8)	1.00 (...)	1.00 (...)
Lifetime sex partners				
0	4 (5.1)	14 (7.1)	1.00	1.00
1	31 (39.2)	95 (48.4)	1.32 (1.14–1.74)	1.30 (1.05–1.64)
2	25 (31.6)	53 (27.0)	1.80 (1.15–2.83)	1.72 (1.07–2.75)
3	6 (7.6)	23 (11.7)	2.42 (1.24–4.73)	2.25 (1.11–4.57)
≥4	13 (16.5)	11 (5.6)	3.25 (1.33–7.93)	2.95 (1.15–7.57)
Sexual relationships >6 months duration				
0	4 (5.1)	19 (10.0)	1.00	1.00
1	39 (49.4)	123 (62.8)	1.52 (1.11–2.17)	1.59 (1.13–2.26)
2	22 (27.9)	37 (18.9)	2.55 (1.27–5.10)	2.55 (1.27–5.10)
≥3	17 (21.5)	17 (8.7)	4.50 (1.45–14.30)	4.06 (1.44–11.52)

NOTE. HTLV-II, human T cell lymphotropic virus type II; CI, confidence interval; OR, odds ratio.

[a] Adjusted for age, *finca*, and education.

[b] Adjusted for age, *finca*, education, and other sexual variables shown in table. (No. of partners and no. of relationships are highly correlated and not included simultaneously.)

[c] OR and CI based on inclusion of these variables as continuous variables in logistic regression models.

ported sexual relationships: ≥3 relationships was associated with an OR of 4.56 (CI, 1.45–13.30). After accounting for significant sexual risk factors among females, the risks associated with a history of drinking *chicha fuerte* (OR, 1.47; CI, 0.80–2.65) and lack of formal education (OR, 3.13; CI, 0.89–14.75) were no longer statistically significant.

Reporting a history or symptoms of STDs (vaginal discharge, genital ulcers), sexual intercourse during menses, or cohabitation with a spouse or other sex partner was not associated with HTLV-II risk. Although the presence of HSV-2 antibody was similar among HTLV-II–seropositive and –seronegative females (34% and 29%, respectively; $P = .52$), HSV-2 antibody status was significantly associated with number of lifetime sex partners and number of long-term sexual relationships ($P < .001$ for both). However, HSV-2 was not associated with age at first sexual intercourse ($P = .26$).

Males. Compared with females, males reported being older at first sexual intercourse (median = 17 years) and reported more lifetime sex partners (median = 5). However, the reported number of sex partners was relatively small (75% ≤ 10, 50% ≤ 5). Neither age at first sexual intercourse nor number of partners was associated with HTLV-II seropositivity in males. Almost 90% reported cohabitation with a spouse or other sex partner, 8% reported a previous STD, and 2% reported a history of penile ulcers. Again, seropositivity was not associated these factors. Thirty-eight percent of men reported having sex with a prostitute. A greater proportion of seropositive males reported having sex with a prostitute (44.2% vs. 35.5%). This risk remained significant after mutual adjustment for all factors significant in univariate analyses (OR, 1.68; CI, 1.04–2.72; table 2). After adjustment for the risk associated with ever having had sex with a prostitute, the risk associated with a history of transfusion was no longer significant (OR, 1.89; CI, 0.53–6.94). HSV-2 seroprevalence was similar in HTLV-II–seropositive and –seronegative males (31% vs. 27%; $P = .55$) and was not associated with number of sex partners or age at first sexual intercourse ($P = .29$ and .33, respectively). However, HSV-2 antibody prevalence was significantly higher among those with a history of STD ($P = .01$) or with sex with prostitutes ($P = .05$).

After the effect of history of sex with prostitutes was taken into account, the association of HTLV-II risk with primary current residence in a traditional village remained statistically significant, as did the risk associated with lack of formal education (table 2). Compared with the most highly educated males, males without formal education were older (43.2 vs. 31.3 years; $P < .001$) and more frequently reported traditional lifestyle factors (hunting monkeys, 21.1% vs. 7.1%, $P = .04$; skinning monkeys, 37.9% vs. 21.7%, $P = .06$; drinking *chicha fuerte*, 83.5% vs. 69.7%, $P = .04$). The small proportion of males who claimed current primary residence in a traditional village precluded further analysis of specific lifestyle factors in this group.

Table 2. Factors associated with HTLV-II infection among Guaymi Indian males.

Factor	HTLV-II⁺ no. (%)	HTLV-II⁻ no. (%)	Adjusted OR[a] (95% CI)	Adjusted OR[b] (95% CI)
History of sex with prostitute				
Yes	50 (44.2)	85 (35.5)	1.89 (0.99–2.56)	1.68 (1.04–2.72)
No	63 (56.6)	160 (64.5)	1.00	1.00 (...)
Primary current residence in traditional village				
Yes	6 (5.3)	4 (1.6)	4.43 (1.28–17.49)	3.75 (1.02–15.38)
No	107 (94.7)	243 (98.4)	1.00	1.00 (...)
Years of education				
0	57 (48.3)	91 (34.7)	2.87 (1.34–6.49)	3.89 (1.67–9.82)
1–6	50 (42.4)	130 (49.6)	1.44 (0.71–3.05)	1.82 (0.83–4.38)
≥6	11 (9.3)	41 (15.7)	1.00[c] (...)	1.00 (...)

NOTE. HTLV-II, human T cell lymphotropic virus type II; CI, confidence interval; OR, odds ratio.

[a] First two variables adjusted for age, *finca*, and education; years of education adjusted for age and *finca*.

[b] History of sex with prostitute and current primary residence in traditional village adjusted for their effects on each other as well as for age, *finca*, and education. Education adjusted for age, *finca*, and the other two variables in the table.

Discussion

Previous studies found an association between sexual factors and HTLV-II infection. A history of receiving money for sex [5], total lifetime sex partners [6, 7], and length of sexual relationships [8] have been associated with HTLV-II seropositivity. These studies were conducted in populations in which IVD use and/or sex with an IVD user were dominant sources of infection. Preferential male-to-female transmission was suggested in both populations [5, 8]. Our present study also demonstrated an association between HTLV-II seropositivity and sexual risk factors in both men and women. Among females, risk of HTLV-II infection was associated with early onset of sexual activity, number of sex partners, and long-term sexual relationships. Among males, having sex with prostitutes was the only sexual factor associated with HTLV-II seropositivity.

Lack of formal education and primary current residence in a traditional village were associated with HTLV-II seropositivity among males. Due to the small proportion of Guaymi males claiming the traditional village as their current primary residence, we could not further explore specific lifestyle factors associated with risk in this group. Low level of education is usually thought of as a marker of low socioeconomic status and is a significant risk factor for HTLV-II infection among blood donors in the United States [7]. However, residence in Changuinola provides a homogeneous standard of living, since housing, health care, and education are provided to all *finca* residents. Formal education in this group may be a surrogate for acculturation. Men without formal education may be at risk for infection because of behaviors or exposures affecting risk that were not directly measured in this study.

In summary, we examined risk factors for HTLV-II infection

among the Guaymi Indians of Panama, a non–IVD-using population. Among both female and male Guaymi, we quantified sexual risk factors associated with HTLV-II seropositivity. Lack of formal education was associated with HTLV-II seropositivity among males and may identify a subgroup with additional unmeasured risk factors. Our data offer further evidence that HTLV-II is sexually transmitted.

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