Human T-Cell Lymphotropic Virus Types I and II Infections in Mother–Child Pairs in Nigeria

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Summary

A community-based survey to determine the prevalence of human T-cell lymphotropic type I (HTLV-I) and type II (HTLV-II) virus infections in mothers and children in south-western Nigeria was carried out using blood samples collected in 1993. A multistage cluster, random sampling procedure was used to select 460 mother–child pairs (476 children because there were 16 sets of twins) from 14 enumeration areas. A commercially available, whole HTLV-I lysate antigen-based ELISA method was used to screen for HTLV-I and HTLV-II antibodies in the samples. A synthetic peptide antigen-based ELISA was then used to differentiate between antibody reactivity to either HTLV-I or HTLV-II. Reactivity to HTLV-I or HTLV-II antibodies was found in 4.3 per cent (20/460) of mothers and in 1.1 per cent (5/476) of children in both rural and urban communities and all the positive children were males. None of the 16 sets of twins in this study was positive for either HTLV-I or HTLV-II. Also none of the mother–child paired sera tested showed concordance for either HTLV-I or HTLV-II antibody positivity. The lack of concordance between mother and child sera suggests that vertical transmission may not be the major route of transmission of HTLV infection to children in south-western Nigeria. Other modes of transmission, such as the re-use of unsterilized needles for injections and surgical knives in local scarification, which are common practices in the region, need to be investigated as they may prove to be more important than vertical transmission. These findings have important implications for any control programme for diseases that can be spread by the same routes as HTLV infection (the human immunodeficiency viruses, hepatitis B, and hepatitis C infections).

Introduction

The human T-cell lymphotropic type I (HTLV-I) and type II (HTLV-II) viruses belong to a group of mammalian retroviruses which share a number of similar biological properties, one of which is tropism for T cell lymphocytes.[1] However, each of the two viruses has been associated with different clinical conditions. HTLV-I has been aetiologically linked with adult T-cell leukaemia,[2–4] a myelopathy with tropical spastic paraparesis syndrome,[5–7] and more recently, with paediatric infective dermatitis.[3] HTLV-II, on the other hand, has been linked to hairy cell leukaemia,[8] dermatopathic lymphadenopathy, and lymphoproliferative disorder.[9]

Studies have shown that HTLV-I is endemic to south-western Japan, the Caribbean basin, Central Africa, Islands of West Indies, and the south-eastern United States.[15] In West Africa, two studies from Nigeria[10,11] have shown that both viruses are endemic in the region. However, the epidemiology of both viruses is still being unravelled as better diagnostic tests that can differentiate between antibodies to HTLV-I or HTLV-II are becoming available.[1,12] Transmission of both viruses is known to occur by blood transfusion, needle sharing,

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sexual contact, and from mother to child through breast milk and transplacental and intrapartum infection.[5,13] In a previous study, we found an overall seroprevalence of 5.6 per cent which included 2.5 per cent for HTLV-I, 1.9 per cent for HTLV-II infection, and 1.2 per cent dual reactivity to both viruses in Nigeria.[11] The age and sex distribution of HTLV-I/II infected individuals in that study in which the reproductive age group had the highest prevalence suggested that a major mode of transmission of the virus may be by heterosexual contact.[11] There are few data from Nigeria on other modes of transmission, particularly in children.

In this report, we present the results of our investigation of the prevalence of the viruses in childhood and evidence for the possible modes of transmission to children of these increasingly important human retroviruses using mother–child pair sera collected from rural and urban communities in south-western Nigeria.

Materials and Methods

Selection criteria and sample collection

The opportunity for this study was provided by a nationwide micronutrient survey in 1993 which covered all the four health zones (south east, south west, north east, and north west) in Nigeria. This report is based on the study carried out in the south-west (B) health zone (see Fig. 1).

Sampled localities were drawn from the national master plan for the 1987/92 National Integrated Survey of Households (NISH) implemented by the Federal Office of Statistics as part of the United Nations Household Survey Capability Programme. The enumeration area (EA), which is a geographically defined area, was the unit of sampling. A multistage cluster sampling procedure was used. All the EAs in the south-west zone (B) were stratified into rural and urban communities. Twelve EAs were selected by a systematic random sampling procedure to represent urban and rural EAs in a ratio proportional to their occurrence in the Health Zone. Thirty-five households were randomly selected from a list of households in each EA. Finally, one preschool child (and its mother) was selected from a list of all children aged 6 to 72 months in each household. In a situation where there was more than one preschool child in the household, the child with the earliest birthday and month was selected. Where the chosen child was one of twins, both twins were included in the study. The children selected by a random procedure from two other EAs which were used for the pilot and operations research studies of the micronutrient survey were also included in this report, making a total of 14 EAs. The location of these 14 EAs is shown in Fig. 1.

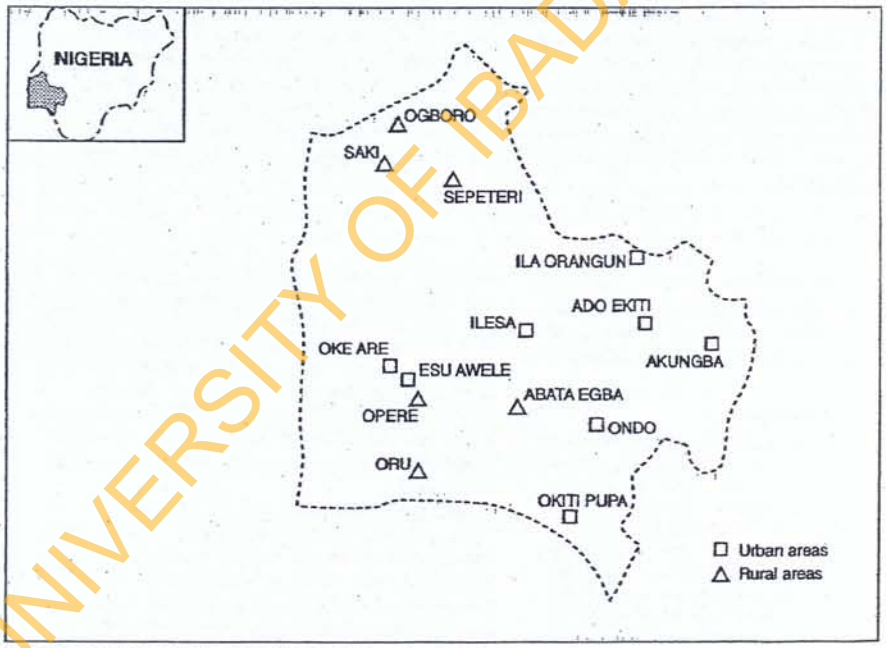

FIG 1. Selected enumeration areas for the study.

Demographic information was collected on the age, education, and occupation of the mother, household head, number of children, and those that were under 6 years old in the household. Venepuncture was carried out on each subject under strict asepsis. The blood was then transferred into vacutainer tubes and allowed to clot at room temperature. The tubes were transferred to the laboratory in a cold box and subsequently kept at 4°C until serum had separated from each blood sample. Each tube was centrifuged at 2000 r.p.m. for 10 min and the serum was collected using an automatic micropipette with sterile tips. One tip was used per sample to prevent cross-contamination during the process of serum transfer to pre-labelled pilot containers according to the mother–child pair number codes. After separation, the sera were stored at −20°C in aliquots, pending analysis.

Laboratory methods

All the sera from mothers and their children were tested for presence of HTLV-I or HTLV-II antibodies as described previously.[11] Briefly, sera were initially screened for antibodies against HTLV-I/II using commercial enzyme-linked immunosorbent assay (ELISA) (Abbott Laboratories, North Chicago, IL, USA). Samples that fulfilled the manufacturer's recommended cut-off value for positivity were retested in duplicate using the same ELISA kit and specimens that were repeatedly reactive were considered HTLV-I/II positive. Then, the SELECT HTLV/I/II (Coulter, Hialeah, FL, USA) was used to differentiate between antibody reactivity of each serum sample to either HTLV-I or HTLV-II. The test uses synthetic peptides to differentiate between HTLV-I and HTLV-II antibodies. After initial separation of HTLV-positive samples to either HTLV-I or HTLV-II reactive, all Coulter SELECT HTLV-I positive sera were confirmed for the presence of HTLV-I antibodies by HTLV-I protein immunoblots as described previously.[11] In addition, all Coulter SELECT HTLV-II positive sera were retested in duplicate using the same ELISA kit. Both HTLV-I and HTLV-II positive and negative control sera were included in each assay.

Statistical methods

Data analysis was done with the Epi Infor software package. Prevalences are presented as proportions and their 95 per cent confidence intervals (CI). Association between HTLV seropositivity in children and their mothers was investigated by means of the McNemar χ^2 test for paired samples.

Results

Serum samples tested for this study were collected from 460 mother–child pairs. Sixteen sets of twins were included, thus giving a total number of 460 mothers and 476 children. Overall, 25 out of 936 sera were confirmed reactive for both viruses (prevalence 27 per cent; 95 per cent CI 1.8–4.0). Twenty of the sera were reactive for HTLV-I and five for HTLV-II antibodies. No sample was dually reactive to both viruses. Twenty of the 25 reactive sera were from mothers, while the other five were from children. There was a higher prevalence of HTLV-I or HTLV-II infection among mothers from urban areas (5.5 per cent) than in mothers from rural areas (2.9 per cent) in our study area, although this was not statistically significant ($\chi^2 = 1.85$, $p = 0.17$).

Comparison of HTLV prevalence in mothers and their children showed a significantly higher rate of HTLV-I or HTLV-II infection among mothers (20/460, prevalence 4.35 per cent; 95 per cent CI 2.8–6.8) than among their children (5/476, prevalence 1.05 per cent; 95 per cent CI 0.4–2.6) ($\chi^2 = 9.78$; $p < 0.002$) (Table 1). There was a higher prevalence of HTLV-I (3.3 per cent) than HTLV-II (1.1 per cent) infection among mothers while all five reactive sera from children were for HTLV-I.

Most of the reactive serum samples from mothers were from those 20–39 years old. All 18 samples from women younger than 20 years were negative and two of 84 sera tested from women 40 years and older (one 40 years, one 42 years) were reactive for HTLV-I antibodies. Prevalence of HTLV infection in the children did not seem to be related to age (Table 2) and all five HTLV-I positive children were males.

TABLE 1

Rural–urban differences in HTLV seropositivity among mothers and their children in south-west Nigeria

	Rural	Urban	p value[a]
Mothers ($n = 460$)	$n = 206$	$n = 254$	
HTLV-I	5 (2.4%)	10 (3.9%)	0.365
HTLV-II	1 (0.5%)	4 (1.6%)	0.499
HTLV-I or HTLV-II	6 (2.9%)	14 (5.5%)	0.174
Children ($n = 476$)	$n = 211$	$n = 265$	
HTLV-I	3 (1.4%)	2 (0.8%)	0.791
HTLV-II	0	0	
HTLV-I or HTLV-II	3 (1.4%)	2 (0.8%)	0.791

[a] p value for Fisher's exact test.

TABLE 2
Age distribution of HTLV infection among mothers and their children in south-west Nigeria

Age	*N*	HTLV-I	HTLV-II	Total HTLV
Mothers				
<20 years	18	0	0	0
20–29 years	197	5 (2.5%)	3 (1.5%)	8 (4.1%)
30–39 years	161	8 (5.0%)	2 (1.2%)	10 (6.2%)
>40 years	84	2 (2.4%)	0	2 (2.4%)
All mothers	460	15 (3.3%)	5 (1.1%)	20 (4.3%)
Children				
<6 months	10	0	0	0
7–24 months	82	1 (1.2%)	0	1 (1.2%)
25–48 months	203	2 (1.0%)	0	2 (1.0%)
49–72 months	181	2 (1.1%)	0	2 (1.1%)
All children	476	5 (1.1%)	0	5 (1.1%)

None of the 16 sets of twins included in this study was positive for either HTLV-I or HTLV-II. In addition, none of the mother–child paired sera tested showed concordance for either HTLV-I or HTLV-II antibody positivity (Table 3).

Discussion

Since the epidemiology of HTLV infection is far from complete, this study has sought to contribute to knowledge about the prevalence of the infection among two important groups, mother and children in south-west Nigeria. To our knowledge, this is the first community-based study of HTLV infection in Nigeria. The results of this study confirm previous findings[10,11] that HTLV infection is endemic in Nigeria.

Results of a previous study on HTLV infection in some urban areas of Nigeria showed an overall higher prevalence of HTLV-I and HTLV-II (5.6 per cent) than the present rate of 2.7 per cent for both viruses in south-western Nigeria. This may be due to differences in sampled population and sampling strategy. However, age- and gender-specific comparison of the results of both studies showed a similar level of infections with both viruses, as previously reported in Nigeria. For example, only three of 337 (0.8 per cent) sera from children 1–9 years old in the previous study were positive for HTLV-I antibodies[11] compared to five of 476 (1.1 per cent) sera tested from children in the present study. Similarly, 105 out of 1929 (5.5 per cent) sera collected from women in the previous study[11] were positive for HTLV-I or HTLV-II antibodies compared to 20 of 460 (4.4 per cent) sera collected from women in this study.

TABLE 3
Concordance in HTLV seropositivity between mother–child pairs in south-west Nigeria

		Child	
		+	−
Mothers	+	+20	0
	−	−5	435

Seroprevalence among mothers = 20/460 (4.3%); seroprevalence among children = 5/476 (1.1%). Each set of twins counted as one child for this paired analysis.

The age pattern of HTLV infection found in this study is also similar to that reported earlier.[10,11] The seroprevalence for both viruses increased from zero among women younger than 20 years of age to 4.1 and 6.2 per cent among those 20–29 years and 30–39 years old, respectively, then declined to 2.4 per cent thereafter. This pattern may suggest heterosexual transmission of both viruses among the sexually active age groups of the population in Nigeria, as earlier suggested.[11] As in the previous study, we found an overall higher prevalence of HTLV-I than HTLV-II. In addition, all the seropositive children were infected with HTLV-I. The reason for this selective HTLV-I infection among the child population is not known at this time.

The results of this study strongly suggest a predominant horizontal route of infection of children with these viruses in Nigeria. Blood transfusion has been reported as the most efficient route of transmission of both viruses.[1,5] In addition, a history of blood transfusion has been identified as a significant risk factor for HTLV-I-related disorders such as adult T-cell leukaemia, myelopathy, and tropical spastic paraparesis.[14–17] It is unlikely that this mode of transmission is the explanation for the findings in the present study because none of the mothers or children in the study had a history of blood transfusion.

The mothers of all five HTLV-positive children found in this study were negative for antibodies to both viruses and none of the mothers who were HLTV-positive had an HTLV-positive child. These observations indicate that the five positive children acquired the infection by means other than vertically or perinatally from their mothers, acquiring it horizontally within the same community.

Possible ways of this horizontal transmission include the re-use of contaminated hypodermic needles and body scarifications with unsterilized instruments. These two practices are very common in both urban and rural areas of south-west Nigeria. In particular, it is known that many people receive intramuscular injections of anti-malarial drugs and/or antibiotics from unqualified personnel in chemist shops, markets, and even car parks. Thus these practices have to be considered as the probable modes of transmission in this study. However, we currently do not have direct evidence for this mode of transmission. It should be noted that such injections have been reported to be a principal mode through which HIV-I was spread among hospitalized children in Romania.[18] The implications of these findings go beyond HTLV infection alone. Programmes to control other diseases that are spread by the same routes as HTLV infection in this region (such as HIV, hepatitis B, and hepatitis C infections) need to note these findings so that intervention is not misdirected, leading to a waste of time and resources.

In conclusion, we have shown that HTLV-I and HTLV-II are endemic in both rural and urban communities in Nigeria. In addition, we have demonstrated that it is unlikely that vertical transmission is the major mode of transmission of these viruses to children and that horizontal modes of transmission, such as by injections and scarification with unsterile instruments, need to be investigated.

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