Prevalence and transmission of HTLV-I infection in Natal/KwaZulu

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Abstract **A community-based seroprevalence survey for human T-cell lymphotropic virus type I (HTLV-I) was undertaken in the Ngwelezane district of Natal/KwaZulu. A total of 1 018 individuals was interviewed for risk factors and had blood drawn for serological examination. To exclude antibody cross-reactivity between anti-HTLV-I and anti-HTLV-II all Western blot HTLV-I-positive samples were further subjected to a Select HTLV test. For comparison, anonymous HIV testing was done. The areas of residence of patients with myelopathy associated with HTLV-I were also ascertained.**

The seroprevalence of HTLV-I was 2,6% (95% confidence interval (CI) 1,62 - 3,58). An age-related rise in HTLV-I seropositivity from 1,3% in the 15 - 24-year age group to 6,1% in the over 55-year-old group was noted. There was no significant association between HTLV-I antibody positivity and marital status, occupation, history of blood transfusion, scarification, age at first sexual experience and number of sexual partners.

Anti-HIV-1 antibody testing revealed a positivity of 3,5% (95% CI 2,4 - 4,68) and the relative risk for co-infection with both HTLV-I and HIV-1 in the 15 - 24-year group was 1,16 (95% CI 1,08 - 1,24). The study also identified the first HTLV-II-seropositive case in the Natal/KwaZulu region.

Up to December 1991, 90 cases of HTLV-I-associated myelopathy/tropical spastic paraparesis were seen at the Neurology Unit, Wentworth Hospital. The patients came from all parts of Natal, from Pongola in the north to Transkei in the south. The Natal/KwaZulu region is, therefore, an endemic HTLV-I area.

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The human T-cell lymphotropic virus type I (HTLV-I) was first isolated in 1978 and reported on in 1980.[1] It has been aetiologically linked to adult T-cell leukaemia/lymphoma (ATLL)[2] and HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP).[3] The prevalence of HTLV-I infection demonstrates marked geographical variation, ranging from 0% in China[4] to 12% in Japan[5] and 26% in the Melanesian Islands.[6,7] HTLV-I infection is also common in Africa.[8-11] However, the reliability of some of these estimates is questionable. Gross national estimates may obscure foci of high prevalence. For example, the 0,025% seroprevalence in the USA conceals the endemic focus in the south-east region of that country. Furthermore, the serological tests have in some hands lacked specificity. The previously reported high seropositivity (37,7%) among Ethiopian Jews who emigrated to Israel have been shown to be incorrect.[12] The initial controversy that surrounded the Melanesian studies has been resolved by the occurrence of HAM/TSP[13] and isolation of the virus from that region.[14] Similarly in Africa, Ramiandrisoa *et al.*[15] demonstrated lower seroprevalence rates in the Ivory Coast (1,8%), Senegal (0,3%), Burkina Faso (0,8%) and Togo (0,5%) than previously reported.[8]

Seroprevalence of HTLV-I infection in South Africa varies from 0% among blood donors to 5,2% among black female staff at the Kruger National Park (Table I).[9,10,16-18]

HAM/TSP has been described in nearly all the areas reporting seropositivity. Cases have also been reported from countries such as the UK, France, Canada, Italy and Sweden but most of the sufferers have been immigrants from Africa and the Caribbean. There are surprisingly few reports of HAM/TSP in patients still resident in Africa. The first African case was reported in 1986.[19] The first cluster of cases was reported in 1990 from Zaire.[20]

By December 1991, we had seen 90 black patients with HAM/TSP at Wentworth Hospital, Durban. Their areas of residence extend from Pongola in the north to Transkei in the south (Fig. 1). To obtain more information about the extent of HTLV-I infection in the region, and to evaluate the risk factors for the virus, we undertook a seroprevalence study in the Ngwelezane district of Natal/KwaZulu. For comparison, coded samples were tested for HIV-1 and 2 as well.

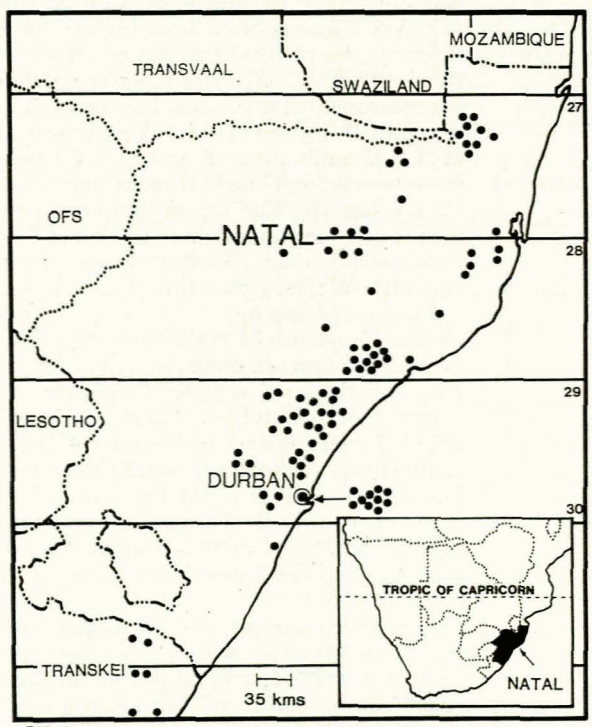

FIG. 1.
Distribution of HAM/TSP cases in the Natal/KwaZulu region and Transkei.

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TABLE I.
Reported HTLV-I seroprevalence rates in South Africa

Area	Seroprevalence (%)	No. tested	Reference	Comment
Durban	5	20	21	Black adults
Johannesburg	0	104	22	Black blood donors
Cape Town	5,3	283	22	Black and white blood donors
Natal and Cape	3,5	543	28	Black blood donors
Kruger Park	3,2	668	29	Black staff
Male	1,2			
Female	5,2			
Natal	0	5 603	30	Blood donors — all races

Methods

The survey was carried out in the Ngwelezane district of KwaZulu. Ngwelezane is situated on the north coast approximately 200 km from Durban. The residents of this district are predominantly semi-skilled and unskilled workers, and live in sub-economic homes. The Ngwelezane district was chosen for the study because: (*i*) it was representative of areas from which patients with HAM/TSP were referred; (*ii*) the local hospital was conveniently located to act as base; and (*iii*) the area was within easy reach of Durban. Apparently healthy individuals over the age of 15 years were recruited from the Ngwelezane township and nearby shopping complexes. The purpose of the study was explained to groups of individuals. Those who volunteered answered a brief questionnaire and donated a sample of blood. The study was approved by the University of Natal Ethics Committee.

Blood was collected in pre-chilled tubes and transported to the laboratory in an ice-box within 5 hours. After separation the serum samples were stored at –20°C. Testing was done within 2 months of sample collection. An enzyme-linked immunosorbent assay (ELISA) kit was used to detect anti-HTLV-I antibodies (Dupont HTLV-I ELISA). A repeatedly positive ELISA was confirmed by means of Western blot (Dupont HTLV-I Western blot, Biotech Research Laboratory, Rockville, Md, USA). The Western blot was considered positive if either the p19 or p24 plus envelope glycoprotein 46 bands were present. In view of the difficulty in distinguishing anti-HTLV-I antibodies from anti-HTLV-II antibodies, all anti-HTLV-I positive results were tested for HTLV-II using the Coulter Select-HTLV test kit. The serum samples were coded and then tested anonymously for HIV-1 and 2 (EIA, Abbott Diagnostic Products, Wiesbaden-Delkenheim, Germany and HIV Western blot IgG Assay, Diagnostic Biotechnology, Singapore).

The prevalence of HTLV-I infection was calculated for each age and sex group, as well as for each age category and the total sample. Crude prevalences were adjusted for age and sex. For the association between HTLV-I infection and the various risk factors, stratified analysis was carried out; stratification for age was as follows: 15 - 24, 25 - 34, 35 - 44, 45 - 54, and 55+ years. In all instances the strata were found to be homogeneous and the Cochran-Mantel-Haenszel test was used for the overall association. The significance level was defined as 0,05.

A stratified analysis was also used to assess the association between HIV and HTLV-I infection. Since differences were found between the different age categories, the chi-square test (or Fisher's exact) was used within each stratum.

Relative risks and 95% confidence intervals (CIs) were calculated where appropriate.

Results

A total of 1 018 individuals, 490 men (48,12%) and 528 women (51,9%), participated in this study. The age range was 15 - 82 years with a mean of 31,5 ± 12,7 years (Table II). Most subjects were unemployed (56,6%), 62,8% were single, 68,7% had evidence of scarification and 13,1% had received a blood transfusion in the past. Sixty-eight persons declined to provide information about their sexual behaviour and a further 10 indicated that they had never been sexually active. Of the remainder the mean age at first sexual experience was 17,9 ± 2,7 years and the mean number of sexual partners was 1,5 ± 1,07.

TABLE II.
HTLV-I seroprevalence rates by age and sex. Differences between men and women are not statistically significant ($P > 0,05$).

Gender and age groups	No. tested	Prevalence	95% CI
Men			
15 - 24	169	0,59	0,00 - 1,74
25 - 34	132	2,27	0,00 - 4,81
35 - 44	66	7,58	1,19 - 13,96
45 - 54	63	4,76	0,00 - 10,02
55+	60	6,67	0,36 - 12,98
Women			
15 - 24	212	1,42	0,00 - 3,01
25 - 34	190	2,11	0,07 - 4,15
35 - 44	76	1,32	0,00 - 3,88
45 - 54	27	3,70	0,00 - 10,82
55+	22	4,55	0,00 - 13,25
Both			
15 - 24	381	1,05	0,03 - 2,07
25 - 34	322	2,17	0,58 - 3,76
35 - 44	142	4,23	0,92 - 7,54
45 - 54	90	4,44	0,18 - 8,69
55+	82	6,10	0,92 - 11,28
Total	1 018	2,60	1,62 - 3,58

A total of 26 (2,6%) sera (95% CI 1,62 - 3,58), of which 16 were from men, tested positive for anti-HTLV-I antibodies (Table II). The age-adjusted rates were 2,65 for men and 1,70 for women. A further 2 gave indeterminate results on Western blot and for the purpose of analysis they were regarded as negative. Another serum demonstrated antibodies to HTLV-II. Apart from the significant age-related rise in HTLV-I infection ($P = 0,01$) (Fig. 2), none of the risk factors showed statistical significance at the 0,05 level.

Thirty-six (3,5%) sera tested positive for anti-HIV-1 antibodies. No sample tested positive for antibodies to HIV-2. The relative risk of co-infection with HIV-1 in individuals who were HTLV-I-positive was significant only in the 15 - 24-year age group (relative risk 1,157; 95% CI 1,08 - 1,24).

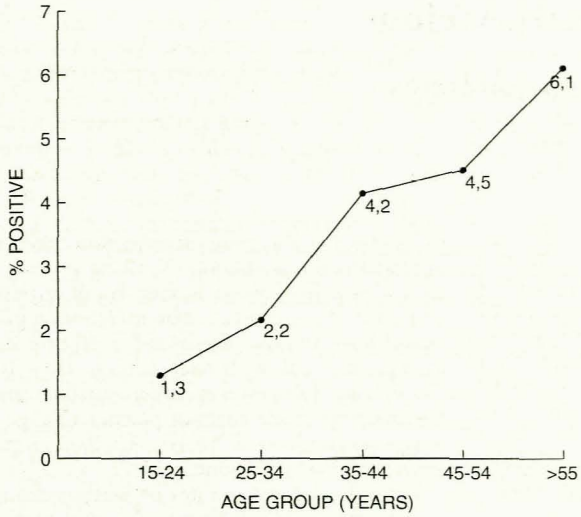

FIG. 2.
Age-related rise in HTLV-I seropositivity.

Discussion

This study showed the seroprevalence of HTLV-I infection in the Ngwelezane district of Natal/KwaZulu to be 2,6% (95% CI 1,62 - 3,58). Of interest, this figure contrasts strikingly with the 0% seropositivity found among black blood donors in Natal.[18] The donor pool may represent a select sample. The problem of HTLV-II cross-reacting antibodies detected by the standard HTLV-I serological tests is in part addressed by using the Coulter Select kit. Further, we have on record 90 cases of HAM/TSP and have isolated the virus from 6 of these patients.[21] Some of these data are unpublished.

In our study more men than women were seropositive for HTLV-I. This finding is contrary to that reported from other parts of the world. The most likely explanation for this is that the sample contained more older men than older women and there is an age-related rise in HTLV-I seropositivity.

The seropositivity rose with age to 6,1% in those over 55 years of age. This finding is consistent with worldwide experience. The rise with age may relate to the age at exposure to the virus and the time to seroconversion.

The modes of transmission of HTLV-I are from mother to child (predominantly through breast-milk), through sexual intercourse, blood transfusion and intravenous drug abuse.[22] Obvious parenteral spread can be excluded in our sample. Intravenous drug abuse is not practised and neither blood transfusion nor tribal scarification showed a significant association with HTLV-I infection. However, the multiply-transfused individual will always be at risk.

This study did not address the problem of mother-to-child transmission. However, in a separate unpublished study of 561 healthy Zulu children under the age of 15 years, we found no cases of seropositivity. The problem of mother-to-child transmission is difficult to evaluate because of the question of latent seronegative infection, variable time of acquisition of infection by the mother in any one family, and premature weaning.

The main mode of transmission in our patients still needs to be defined. However, the increased relative risk for co-infection with HIV-1 would suggest that sexual transmission is important. The finding of one case of HTLV-II seropositivity confirms the presence of HTLV-II in the community. This requires further evaluation as neurological disease has now been associated with this virus as well.[23]

Conclusion

We have established that HTLV-I infection is widespread in the Natal/KwaZulu region. Parts of the Transvaal, Transkei and probably the Cape are endemic areas as well. Awareness of the virus has now led to cases of HAM/TSP being diagnosed in the Transvaal.

We have also established for the first time that there is serological evidence of HTLV-II in our study area.

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