

Table 2.4. Nested case–control studies HTLV-I and ATLL – viral and serum immune markers

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk (95% CI)	Adjusted potential confounders	Comments
Hisada et al. (1998b) Japan, Miyazaki Cohort Study (MCS) –cross-sectional case-control analysis, 1988–91	Within the MCS, 215 HTLV-1 carriers (67 men, 148 women) had multiple measures of abnormal lymphocytes (Ably) on peripheral blood smear; 36% Ably+. Mean age: 62.5 yrs.	Within the MCS, 215 HTLV-1 carriers had multiple measures of Ably on peripheral blood smear. 137 defined as Ably–.	Anti-HTLV-1 by passive particle agglutination assay (PAA) with Western blot confirmation, anti-tax by reactivity to recombinant tax; proviral load by semiquantitative PCR; each slide read blindly by 2 technicians, with confirmation of positives by clinician.	Those with Ably $\leq 0.6\%$ = Ably–.	<u>Ably+</u> <i>n</i> = 64	<i>High proviral load</i> : OR = 8.9 (4.1, 19.5) <i>Male gender</i> OR = 1.5 (0.73, 3.1) <i>High proviral load</i> : OR = 19.7 (6.9, 56.1) <i>Male gender</i> OR = 2.8 (1.0, 7.8)	Age, gender, leukocyte categories Age, proviral load, leukocyte categories Age, gender, leukocyte categories Age, proviral load, leukocyte categories	This study is among HTLV1+ persons and can examine co-factors only
				Those with $> 0.6\%$ Ably at least once = Ably+; of these, 30 with $> 0.6\%$ Ably at all screens and $> 1.6\%$ at least once = Ably++.	<u>Ably++</u> <i>n</i> = 18			
				Proviral load $\geq 10\text{ng}$ DNA = high; anti-tax $\geq 1:500$ = high titre.	<i>n</i> = 30			

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Hisada et al. (1998b) (contd)					Males: <u>Ably+</u> n=25 Males: <u>Ably++</u> n=9 Females <u>Ably+</u> n=27 Females <u>Ably++</u> n=9	<i>High proviral load</i> : OR=15.5 (0.33,6.6) <i>High proviral load</i> : OR=30.2 (4.4,209.5) <i>High proviral load</i> : OR=5.5 (2.0,15.2) <i>High proviral load</i> : OR=18.1 (4.1,80.6)	Age, leukocyte categories Age, leukocyte categories Age, leukocyte categories Age, leukocyte categories	
Hisada et al. (1998a) Japan, Miyazaki MCS, nested case-control study (1984–1995)	Five HTLV-1+ incident ATLL cases: 3 men, 2 women Range of ages at death: 64–83 yrs	38 HTLV-1+ subjects matched for age, gender, study screens	Anti-HTLV-1, anti-tax, Ably, as in Hisada (1998b) above			<i>Anti-HTLV-I per level</i> ↑: OR=1.6 (0.94–3.8) <i>Anti-tax per unit</i> ↑: OR=0.78 <i>Leukocyte count</i> (continuous)	Other viral markers, smoking, leukocyte count Other viral markers, smoking leukocyte count Viral markers, smoking	

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Arisawa et al. (2002) Japan Nagasaki, K Islands; nested case-control study (1985–96) within population of 23922 screened at K hospital or at public health exams	29 incident ATLL cases identified by Prefecture Cancer Registry. 18 men, 11 women. Age at baseline: 33–76 yrs	All cohort members matched for sex, birth year, date of first blood draw, HTLV-1+: 83 men, 75 women. Age at baseline: 33–76 yrs	Anti-HTLV-1 by PAA and indirect immunofluorescence with Western blot confirmation; sIL-2R measured by sandwich enzyme immunoassay. Anti-tax by enzyme-linked immunosorbent assay.	sIL-2R	↑ <u>sIL-2R</u> <i>n</i> = 18	OR = 20.5 (4.5–194)	matching factors	
				anti-HTLV-I titre ≥ 1024 v. < 1024	↑ <u>HTLV-1 titres</u> <i>n</i> = 17	OR = 2.9 (0.98–9.5)	matching factors	
					<u>anti-tax</u> <i>n</i> = 18	OR = 0.59 (0.15–2.0)	matching factors	
Okayama et al. (2004) Japan Miyazaki, MCS, nested case-control study 1984–2000	4 incident ATLL cases with prediagnosis PBC samples – 2 men, 2 women, ages 64–83 yrs	37 randomly selected controls matched for age, sex	Proviral load measured by AmpliSensor assay; Clonality by inverse long PCR			Proviral load ↑ <i>per 1000 copies</i> OR = 1.42 (1.04–2.10)	matching factors	Preleukaemic clone detected 8 years before diagnosis in one case