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Human T-cell leukaemia virus type 1 and Adult T-cell leukaemia/lymphoma in Queensland, Australia: a retrospective cross-sectional study

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ABSTRACT

Objectives Human T-cell leukaemia virus type 1 (HTLV-1), an STI, is reported to be highly prevalent in Indigenous communities in Central Australia. HTLV-1 is an incurable, chronic infection which can cause Adult T-cell leukaemia/lymphoma (ATL). ATL is associated with high morbidity and mortality, with limited treatment options. We studied the prevalence of HTLV-1 and ATL in the state of Queensland, Australia.

Methods Serum samples stored at healthcare services in Brisbane, Townsville and Cairns and at haemodialysis units in Brisbane (2018–2019) were screened for HTLV-1/2 antibodies using the Abbott ARCHITECT chemiluminescent microparticle immunoassay (CMIA) for antibodies against gp46-I, gp46-II and GD21 (Abbott CMIA, ARCHITECT). Reactive samples were confirmed through Western blot. Pooled Australian National Cancer Registry surveillance data reporting on cases coded for ATL (2004–2015) were analysed.

Results Two out of 2000 hospital and health services samples were confirmed HTLV-1-positive (0.1%, 95% CI 0.02% to 0.4%), both in older women, one Indigenous and one non-Indigenous. All 540 haemodialysis samples tested negative for HTLV. All samples were HTLV-2-negative. Ten out of 42 (24.8%) reported cases of ATL in Australia were from Queensland (crude incidence rate 0.025/100 000; 95% CI 0.011 to 0.045); most cases were seen in adult men of non-Indigenous origin. Nineteen deaths due to ATL were recorded in Australia.

Conclusion We confirm that HTLV-1 and ATL were detected in Queensland in Indigenous and non-Indigenous people. These results highlight the need for HTLV-1 prevalence studies in populations at risk of STIs to allow the implementation of focused public health sexual and mother-to-child transmission prevention strategies.

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INTRODUCTION

Human T-cell leukaemia virus type 1 (HTLV-1) is an STI similar to HIV-1[1–3] and can also be acquired through infected blood and mother-to-child transmission.[4 5] Because it is an STI, worldwide, women mostly carry the burden of HTLV infection, acquiring HTLV-1 through condomless sex and transmitting HTLV-1 unknowingly to their babies.[5]

Unlike HIV-1, there is no antiretroviral treatment for HTLV-1, but most people who live with HTLV-1 (PLHTLV) do not become seriously ill. About 5% of PLHTLV develop Adult T-cell leukaemia/lymphoma (ATL), which is caused by HTLV-1, and the incidence of ATL is a clinical surrogate marker of HTLV-1 prevalence. Survival of aggressive ATL is usually less than 1 year even with treatment.[6]

HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) is also caused by HTLV-1. It is a chronic, progressive and painful walking disability most prevalent in middle-aged women and is associated with increased mortality.[7]

There are four types of HTLV and a systematic review of HTLV-1 and HTLV-2 prevalence data showed that it is a virus of complex global distribution and that it is highly endemic in regions of Australia, Iran, Japan, Romania, Gabon, Nigeria, Central African Republic, Jamaica, Martinique, Peru, Argentina and Brazil.[8]

In Australia, HTLV-1 was first described in certain Aboriginal communities in 1988 (prevalence 15%–18%). Recently 30%–50% of Indigenous people living in Central Australia have tested positive.[9–11] Unlike international reports, HTLV-1 was most prevalent in men >50 years of age instead of middle-aged women.

We tested the hypothesis that HTLV-1 and ATL are prevalent in Queensland similar to levels observed in other low-endemic industrialised countries and that this STI can be detected in both Indigenous and non-Indigenous persons. To this aim we conducted HTLV testing of stored serum of adults who accessed hospital and health services (HHS) or haemodialysis services and analysed national ATL cancer registry data retrieved from the Australian Institute of Health and Welfare (AIHW).

METHODS

Laboratory study

The population prevalence of HTLV in Queensland is unknown and a purposeful large sample size was chosen. In 2018/2019, at the Pathology Central, 2000 de-identified serum HHS samples were stratified: 25% in each age category of 18–24, 25–39, 40–54 and >55 years, 50% from women, and 50% from First Nations Peoples. Samples had been collected in Brisbane, Townsville and Cairns catchment areas. Additionally, 540 unstratified, de-identified, stored haemodialysis samples, collected in Brisbane, were also included.

All samples were screened for HTLV-1/2 antibodies using the Abbott ARCHITECT

Table 1 Demographic structure of the samples selected for testing and the results

HHS data	n	Age median (range)	Female:male	Non-Indigenous:Indigenous	HTLV-1-positive WB	Prevalence, % (95% CI)
Total	2000	45 (18–78)	50:50	50:50	2	0.1 (0.01 to 0.36)
Reported by age category		**Age category**				
Group A	500	18–25	50:50	50:50	0	–
Group B	500	26–40	50:50	50:50	0	–
Group C	500	41–55	50:50	50:50	1	0.2 (0.01 to 1.11)
Group D	500	>56	50:50	50:50	1	0.2 (0.01 to 1.11)

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2 out of 2000 HHS samples were confirmed to be HTLV-1-positive.
CI, Confidence interval; HHS, Hospital and Health Services; HTLV-1, Human T-cell leukaemia virus type 1; WB, Western blot confirmatory laboratory test.

chemiluminescent microparticle immunoassay (CMIA) for antibodies against gp46-I, gp46-II and GD21 (Abbott CMIA, ARCHITECT). Reactive sera were confirmed and typed by Western blot (WB); MP Diagnostics HTLV Blot V.2.4 was performed at the National Serology Reference Laboratory and interpreted using the HTLV European Research Network guidelines.

ATL study

The National Cancer Registry at the AIHW uses the International Classification of Diseases Version 10 Australian Modification (ICD-10-AM) codes to report the incidence of diseases in Australia. The National Cancer Registry surveillance records on ATL coded through the ICD-10-AM codes (2005–2014) were retrieved from the Cancer Data and Monitoring Unit at the AIHW. Data were analysed by incidence, mortality, age, sex, Indigenous or non-Indigenous heritage, and State/Territory of residence. Crude incidence rates (CIR) and crude mortality rates (CMR) were calculated using the December 2009 Australian population data from the Australian Bureau of Statistics.

RESULTS

HTLV-1 prevalence study

The median age of the patients of the 2000 HHS samples was 45 years (mean 31 years, range 18–78).

Out of six reactive samples two were confirmed to be HTLV-1-positive on WB: 2 in 2000 (0.1%, 95% CI 0.02 to 0.4%) samples, that is, 1 in 250 (0.4%, 95% CI 0.02% to 2.6%) Indigenous women (45–54 years) and 1 in 250 (0.4%, 95% CI 0.02% to 2.6%) non-Indigenous women (>55 years) (table 1).

The median, mean and age range of the 540 de-identified haemodialysis patient samples were 63 years, 62 years and 19–94 years, with a distribution of 63% from men and 91% from non-Indigenous patients. One sample was reactive but was confirmed HTLV negative on WB. Therefore, HTLV was not detected in the haemodialysis samples.

ATL prevalence study

From 2005 to 2014, 42 ATL cases were recorded (CIR: 0.021/100 000 person years, 95% CI 0.015 to 0.029), and 10 (24%) cases lived in Queensland (CIR: 0.025/100 000 person years, 95% CI 0.011 to 0.045). The median age of the patients was 67 years (mean: 65 years (3–92)), and 92% of the cases were of non-Indigenous origin and 67% (n=28) were men.

Nineteen people (CMR: 0.010/100 000 person years, 95% CI 0.006 to 0.015) had died of ATL (median age: 78 years, mean: 75 years (39–92)). More men (12, 63%) than women were reported to have died of ATL. Fourteen (88%) people were non-Indigenous and 63% (n=12) were men.

DISCUSSION

We hypothesised that the prevalence of HTLV-1 in Queensland should be at levels similar to other industrialised countries. In common with other STIs, it should be detected in the sexually active population.[8]

HTLV-1 was prevalent at 0.1% in 2000 samples of patients accessing HHS. In particular, HTLV-1 was detected in both Indigenous and non-Indigenous peoples in Queensland. These cases we observed were in older women (>45 years), similar to other studies.[4 12]

Patients who attend haemodialysis units are routinely tested for HIV, syphilis and hepatitis, but not for HTLV-1, although it is a bloodborne virus. HTLV-1 was not confirmed in the haemodialysis samples of 540 patients in Brisbane.

We also confirm that the HTLV-1-associated haematological cancer, ATL, is present in Queensland.[13] From 2004 to 2015, 42 people were diagnosed with ATL in Australia, 10 were in Queensland. In the same time frame, 19 people were reported to have died of ATL in Australia. The reason for the discrepancy between disease and death is unknown. As these data were derived from coding, it may be inaccurate and some of those who have died may not have ATL as the direct cause of death.

The majority of ATL cases were found in male and non-Indigenous people, which was surprising since internationally HTLV-1 is more commonly detected in older women[4 8 12] and in Central Australia HTLV-1 is reported to be more common in Indigenous older men.[9–11] We do not know the reason for this discrepancy, but perhaps men are more at risk of HTLV-1 transmission in Central Australia.

We acknowledge that our data were derived from a convenience sample, rather than a random sample of people from Queensland. As a result, we oversampled the age group 18–24 years and undersampled the 55+ years group, and deliberately oversampled the Indigenous population, therefore, the prevalence of HTLV-1 in Indigenous people may be even lower. Due to the low number of positive tests, we did not weight the data. The true prevalence of HTLV-1 may be higher than our estimates, since HTLV-1 is not notifiable and asymptomatic HTLV-1 carriers may not present to HHS. In addition, despite HTLV-1 being sexually transmitted, HTLV-1 is not routinely tested for in at-risk population in antenatal or sexual health clinics.

In 2010, about 4.51 million people lived in Queensland. Extrapolating from our HTLV-1 prevalence estimate of only 0.1%, potentially 4500 people could be living with HTLV-1 in Queensland. With a 4%–5% lifetime risk of developing ATL if HTLV-1-positive, an estimated 180 cases of ATL would be expected to occur. However, the National Cancer Registry recorded only 10 ATL cases over a decade; maybe it is difficult to diagnose ATL and cases are missed as reported in Brazil[14]

and the Netherlands.[15] The other specific HTLV-1 disease is HAM/TSP, with a similar 4%–5% lifetime risk. HAM/TSP has been observed but not systematically recorded in Australia, since there is no Australian modification of the ICD-10 code for HAM/TSP. In summary, it is possible that people suffering from ATL and HAM/TSP are not diagnosed without specific training and experience.

HTLV-1 causes disease in Queensland and other states of Australia, but due to a lack of obligatory notification HTLV-1 remains underdiagnosed. This may have led to the conclusion that a public health response to HTLV-1 is not necessary in Australia. However, the World Health Organization is considering to formally adopt HTLV-1 as a health topic and recommends testing and counselling of at-risk population to prevent further transmission of this STI.[16]

While HTLV-1 is highly endemic in Central Australia, we demonstrate that it is an ubiquitous virus and not confined to the Indigenous population. It is present in Queensland's general population at low prevalence levels, similar to other industrialised countries such as the UK. It is therefore important to ensure that all people at risk of an STI and/or presenting with HTLV-1 disease-like symptoms are considered for an HTLV-1 screen.

HTLV-1 infection and its diseases are not overt. If not tested for, cases will not be identified. As a first step, making HTLV-1 a notifiable infection, similar to UK and Japan, would improve the mapping of HTLV-1 Australia-wide. In Queensland further research is required to identify at-risk groups, to be able to implement tailored public health prevention strategies to stop the HTLV-1 transmission between sexual partners and from the mothers to children.

Key messages

- ⇒ Human T-cell leukaemia virus type 1 (HTLV-1) is a sexually transmitted virus, which is also transmitted from the mother-to-child through body fluid, similar to HIV-1.
- ⇒ HTLV-1 causes Adult T-cell leukaemia/lymphoma (ATL), which is a blood cancer with high disease burden and mortality.
- ⇒ HTLV-1 and ATL were detected in Indigenous and non-Indigenous persons living in Queensland.
- ⇒ Australia urgently needs a public health strategy to identify people at risk and prevent the transmission of HTLV-1, similar to HIV-1 public health strategies.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study involves human participants. Ethics approval for serological studies was received from the Royal Brisbane Women's Hospital Research Ethics Committee (HREC/2018/QRBW/44416) and from each of the eight Australian member states of the AIHWF to use ATL cancer registry data. This was an anonymous retrospective study of stored samples which were de-identified before testing.

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