Journal of Infection 86 (2023) 245–247

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

HTLV seroprevalence in people using HIV pre-exposure prophylaxis in England

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ARTICLE INFO

Article history:
Accepted 20 January 2023
Available online 10 February 2023

Keywords:
Human T cell lymphotropic virus type 1 (HTLV-1)
HIV pre-exposure prophylaxis
Gay
Bisexual and other men who have sex with men (GBMSM)

SUMMARY

Objectives: HTLV-1 is predominantly a sexually-transmitted infection but testing is not mentioned in HIV-PrEP guidelines. We ascertained HTLV-1/HTLV-2 seroprevalence amongst HIV-PrEP users in England.
Methods: An unlinked anonymous seroprevalence study.
Results: Amongst 2015 HIV-PrEP users, 95% were men, 76% of white ethnicity and 83% had been born in Europe. There were no HTLV-1/HTLV-2 seropositive cases (95% confidence interval 0% – 0.18%).
Conclusions: There were no HTLV positive cases, likely reflecting the demographic of mostly white and European-born individuals. Similar studies are needed worldwide to inform public health recommendations for HIV-PrEP using populations, particularly in HTLV-endemic settings.

Introduction

HIV pre-exposure prophylaxis (HIV-PrEP) is highly effective in reducing the likelihood of HIV acquisition in HIV-negative people at risk of exposure.[1] Guidelines recommend testing for sexually transmitted infections (STIs) both before starting, and periodically while on HIV-PrEP, including bacterial infections, HIV, hepatitis C virus, and, for those who are non-immune, hepatitis B virus.[2] Diagnosed infections can be treated promptly to reduce onward transmission. HTLV-1 is not mentioned in HIV-PrEP guidelines; however, it is predominantly sexually transmitted, causes adult T-cell leukaemia/lymphoma or myelopathy in 10% of those infected, and is associated with an increased risk of death (Relative Risk 1.57, 95% CI 1.37-1.80) in those without a classically HTLV-associated condition.[3] The 2021 WHO Technical Report on HTLV-1 called for strengthening of global public health measures against its spread. We therefore evaluated the potential risk of HTLV to HIV-PrEP users in England, 96% of whom are gay and bisexual men who have sex with men (GBMSM),[4] through a seroprevalence study.

Materials and methods

Specimen ascertainment

We conducted an irreversibly-unlinked, anonymous seroprevalence surveillance study in eight HIV-PrEP clinics in England, including five in London. We used serum or EDTA plasma samples

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https://doi.org/10.1016/j.jinf.2023.01.033

where at least 500ul remained after testing for HIV, syphilis or viral hepatitis as part of standard care HIV-PrEP follow-up. Samples were identified (1) at clinic visit (prospective ascertainment) or (2) retrospectively from local laboratory archives by ascertaining current PrEP-user status from the national STI surveillance system, Genitourinary Medicine Clinic Activity Dataset (GUMCAD). Samples were available from September 2019 to November 2021. All specimens were labelled only with a unique Study Number and no patient identifiable information.

Limited demographic and clinical information for each individual were extracted from GUMCAD: date of sample collection, sex, age range, country of birth, ethnicity, any history of syphilis, and history of bacterial STI (chlamydia, gonorrhoea, or syphilis) within the previous 12 months. Countries of birth were grouped into HTLV-endemic and non-endemic categories according to criteria of the European Centres of Disease Control.[5] After data extraction and de-duplication, all identifiers were irreversibly deleted except for Study Numbers. Samples were transferred to the HTLV reference laboratory.

Testing

All testing was performed with the Abbott Architect rHTLV-I/II assay (Abbott Laboratories Weisbaden, Germany), a Chemiluminescent Microparticle Immunoassay (CMIA), according to the manufacturer's instructions.

To determine the pooling size for testing, a set of positive samples were serially diluted (2 fold) in normal human plasma (NHS Blood and Transplant) from neat to 1/128, with final volumes of 400uL. We included four anti-HTLV-1 reactive, three anti-HTLV-2 reactive, two dual reactive and three non-typeable reactive samples, with specimen Sample/Cut-off ratios at neat encompassing a range from 8.0 to 96.8. The lowest positive sample (anti-HTLV-2 reactive at 8.0 neat) remained positive (Sample/cut-off >1) at 1/8 but not at 1/16. Therefore, to ensure detection in pooled samples to at least the level of this lowest positive sample, pools of 5 were used.

The individual samples in any reactive pool were further tested by Abbott Architect rHTLV-I/II CMIA and reactivity was confirmed and typed by Western blot MP Diagnostics 2.2 according to the manufacturer's instructions.

Sample size

We estimated the sample size according to the ability to detect a change in HTLV-1 seroprevalence amongst HIV-PrEP users in serial surveys. Approximately 7% of HIV-PrEP users in England were born in an HTLV-1 endemic country (internal communication, PrEP Impact Trial investigators). If the observed HTLV-1 prevalence were 0% in individuals born in low prevalence countries, a sample size of 1,500 would give a 95% Confidence Interval (CI) of 0-0.27% around this prevalence. If the prevalence were 0.2%, then the 95% CI would be 0.04-0.61%. For assessing changes in prevalence in a subsequent survey of the same size, with 80% power and 5% significance level, for those born in low prevalence countries, 1,368 in each survey would allow a change from 0% to 0.7% to be detected, or from 0.2% to 1.2%. For those born in high prevalence countries, changes from 1% to 9% or 2% to 11% can be detected. Allowing for a proportion of stored samples being of poor quality for testing, we therefore aimed to test a minimum of 1500 specimens.

Statistical methods

The number of samples tested by age, sex, country of birth, ethnicity and bacterial STI history are described, and the overall prevalence as well as prevalence with those from an HTLV-endemic country given with a 95% exact confidence interval.

Table 1
Demographic characteristics of HIV-PrEP users.

	Number	%
Total	2015	
Gender	2007	
Male	1904	95
Female	103	5
Ethnicity	1655	
White	1265	76
Mixed/other	177	11
Black	108	7
Asian	105	6
Age (years)	1994	
<30	697	35
30-49	1091	54
>/=50	226	11
Country/region of birth	1732	
UK	1097	63
European Union	333	19
South America	66	4
Sub Saharan Africa	54	3
North Africa / Middle East	40	2
Australasia	35	2
North America	33	2
South Asia	26	2
East Asia	25	1
South East Asia	23	1
Other Europe	14	1
Caribbean	7	<1
Central America	5	<1
HTLV-1 endemic country	144	8
STI history	2015	
Any history of syphilis	193	10
Any bacterial STI in previous year*	791	39

* Chlamydia trachomatis, Neisseria gonorrhoeae or Treponema pallidum.

Ethics

This study was classified as surveillance permitting the collection of data without patient consent under section 251 of the UK National Health Service Act 2006 and Regulation 3 of the associated Health Service (Control of Patient Information) Regulations 2002. Ethical approval was provided by the UK Health Security Agency Research Ethics and Governance Group (Reference Number: NR0154).

Results

There were 2015 specimens from unique individuals matched via GUMCAD as HIV-PrEP users and with sufficient volume for testing. Demographic characteristics are shown in Table 1. Most individuals (95%) were male; 76% were of white ethnicity; 55% were aged 30-49 years and 82% were born in the UK or European Union. Overall, $n = 144/1732$ (8%) individuals were born in an HTLV-1 endemic country, with the five most frequent country of births being Brazil ($n = 41$, 2%), Nigeria ($n = 14$, 0.8%), Romania ($n = 11$, 0.6%), South Africa ($n = 10$, 0.6%) and Colombia ($n = 9$, 0.5%) . A bacterial STI, chlamydia, gonorrhoea or syphilis, had been diagnosed in the previous year in 39% of participants.

No specimen (0/2,015) was positive for HTLV antibodies by Abbott Architect CMIA. This gave a seroprevalence of 0%, 95% CI 0% – 0.18%. In relation to PrEP users born in HTLV-1-endemic countries, the 95% CI for 0/144 is 0% – 2.5%.

Conclusions

We found no cases of HTLV-1 or HTLV-2 in this HIV-PrEP-using population at high risk of a bacterial STI. This likely reflects the

demographic, with 76% being of white ethnicity and 92% born in a non-HTLV endemic country. These data are reassuring that HTLV is not circulating widely amongst current HIV-PrEP-users in England and are consistent with the low HTLV prevalence in the UK general population, estimated at 0.04% in pregnant women.[5] HTLV-1 seroprevalence was greater amongst UK HIV-positive individuals attending a South London hospital at 0.6% (5/777), likely reflecting the higher proportion of individuals of Afro-Caribbean heritage (50% versus 7%).[6]

To our knowledge, only one other study has described HTLV prevalence in HIV-PrEP-users. In Barbados, one HTLV-1 positive case was diagnosed amongst 134 (0.7%) people enrolled in a national PrEP program, 67% of whom were GBMSM.[7] This is consistent with the high HTLV-1 prevalence in the Barbados general population, at 4.3% (43/1,007) in pregnant women.[5]

Other studies in HTLV-endemic and non-endemic settings have shown that HTLV-1 seroprevalence amongst GBMSM may be increased compared to the general population.[8] HTLV-1 risk factors in GBMSM include HIV-coinfection, multiple partners, condomless receptive anal intercourse, syphilis, and HSV-2, a profile that overlaps with that of HIV-PrEP-users.[8]

Non-GBMSM HIV-PrEP-users may also be at increased risk for HTLV-1. In Kenya, Lesotho, and Tanzania, 50% of 47,352 PrEP-users were female sex workers (FSW), a group at high risk of HTLV-1 acquisition in much of Africa.[9,10] People who inject drugs (PWID) at high HIV risk are also recommended to take HIV-PrEP and are at risk of HTLV-1 particularly in endemic settings such as Brazil.[11]

HTLV-1 seroprevalence data are therefore needed for HIV-PrEP cohorts internationally, including GBMSM, FSW and PWID. This will permit ascertainment of the risk of HTLV-1 transmission to HIV-PrEP users, and inform country-specific public health interventions, such as an offer of HTLV testing at baseline and counselling on use of condoms for those infected. HTLV-1 incidence should also be measured in HIV-PrEP programs, together with the potential activity of tenofovir disoproxil-emtricitabine or tenofovir alafenamide-emtricitabine as HTLV-PrEP.[8] Evaluation of the injectable integrase strand transfer inhibitor cabotegravir as HTLV-PrEP should also be explored given its potent *in vitro* activity.[12] Unlike HIV, antiviral therapy to treat established HTLV is lacking, placing greater emphasis on transmission prevention.

Our finding of 8% of individuals within this high risk sexually active cohort having been born in an HTLV endemic country also supports the need for expanded HTLV testing in sexual health settings. In a previous UK report, most HTLV diagnoses (84%, 75/89) were made in secondary care, with almost no testing performed in sexual health, antenatal clinics or general practice.[13] Similarly, a recent report from Spain described a disproportionately high number of HTLV cases (22%, 96/428) diagnosed following symptomatic presentation and highlighted that late presentation of HTLV-1 in Europe could result from poor clinical suspicion, especially in individuals born in certain HTLV endemic regions such as Sub Saharan Africa, or with sex partners from these regions.[14] The authors called for expanded HTLV testing in sexual health and antenatal settings to identify asymptomatic carriers and thereby enable implementation of transmission prevention interventions.

Other notable findings include the lack of any sample with non-specific reactivity, which likely reflects the use of pooled testing. It has previously been shown that non-specific reactivity on the Abbott Architect rHTLV-I/II CMIA is usually at a level of OD/CO ≤ 4; therefore, any low level reactivity would become negative on pooling in a 1:5 ratio.[15] An important limitation of the study was the lack of information on history of injection drug use (IDU), which is a well-recognised route of HTLV transmission, particularly HTLV-2. Therefore, we were unable to assess the risk of HTLV transmission through IDU in this PrEP-using cohort.

In conclusion, we found no cases of HTLV amongst 2,015 HIV-PrEP-users at high bacterial STI risk in England. Our survey should be repeated in 3-5 years to assess for the early introduction of HTLV-1 in the PrEP-using population, and in the HIV-PrEP programs of other countries, particularly where HTLV-1 is endemic in the general population.

Declaration of Competing Interest

None

Acknowledgments

The authors wish to acknowledge the patients who contributed to this study. This work was supported by a grant from Gilead Sciences. The funder had no role in study design or conduct or in the analysis or presentation of study findings. All authors confirm that they do not have an association that might pose a conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2023.01.033.

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