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HTLV infection in inmates with active tuberculosis in Mato Grosso do Sul, Brazil

Infecção pelo HTLV em privados de liberdade com tuberculose ativa em Mato Grosso do Sul, Brasil

Larissa Melo Bandeira^{1*} D, Marco Antonio Moreira Puga² D, Carolina Amianti¹ D, Maurício Antonio Pompílio¹ D, Ana Rita Coimbra Motta-Castro¹ D

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ABSTRACT

Human T-cell lymphotropic virus (HTLV) is a retrovirus with a worldwide presence that may influence tuberculosis (TB) pathogenesis, particularly in populations where both infections are prevalent. This cross-sectional study aimed to estimate the prevalence of HTLV-1/2 infection among inmates with TB in Mato Grosso do Sul (MS) State, Central Brazil. Male individuals with bacteriologically confirmed active TB were recruited from two major closed male penal institutions in MS State: Instituto Penal de Campo Grande (IPCG) and Estabelecimento Penal Jair Ferreira de Carvalho (EPJFC). Serum samples were screened for anti-HTLV-1/2 antibodies using enzyme-linked immunosorbent assay (ELISA), and positive samples were confirmed by HTLV-1/2 Western Blot (WB) assay. A total of 279 inmates participated in the study. Two participants (0.72%; 95% CI 0.18 – 2.84) initially tested positive for anti-HTLV by ELISA. One patient was confirmed to have HTLV-1 infection by WB, along with active syphilis, while the other showed an indeterminate WB result and tested positive for anti-HIV and anti-HCV. Although the overall HTLV prevalence in the sample was relatively low, this study underscores the potential for HTLV and TB co-infection in high-risk populations such as inmates.

Keywords. HTLV-1, Tuberculosis, Prevalence, Prisoners.

RESUMO

O Vírus Linfotrópico de Células T Humana (HTLV) é um retrovírus que apresenta distribuição mundial com potencial para impactar a patogênese da tuberculose (TB), especialmente em populações com alta prevalência de ambas as infecções. Este estudo transversal objetivou descrever a prevalência da infecção por HTLV-1/2 entre Pessoas Privadas de Liberdade (PPL) com TB ativa no estado de Mato Grosso do Sul (MS), Centro-Oeste do Brasil. Foram incluídos indivíduos do sexo masculino com confirmação bacteriológica (TB ativa) de duas instituições penais fechadas, Instituto Penal de Campo Grande (IPCG) e Estabelecimento Penal Jair Ferreira de Carvalho (EPJFC), de Campo Grande, MS. Amostras de soro foram triadas para anticorpos anti-HTLV-1/2 por ensaio imunoenzimático (ELISA) e os resultados reagentes foram submetidos à confirmação por Western Blot (WB). O estudo envolveu 279 indivíduos. Dois (0,72%; IC 95% 0,18-2,84) apresentaram resultado positivo na triagem para anti-HTLV por ELISA. Um caso foi confirmado para HTLV-1, com coinfecção por sífilis ativa, enquanto o outro teve resultado indeterminado por WB e sorologia positiva para anti-HIV e anti-HCV. Embora a prevalência para a infecção pelo HTLV tenha sido relativamente baixa, o estudo destaca o potencial de coinfecção por HTLV e tuberculose em populações de alto risco, como em PPL.

Palavras-chave. HTLV-1, Tuberculose, Prevalência, Pessoas Privadas de Liberdade.



¹ Laboratório de Imunologia Clínica, Universidade Federal de Mato Grosso do Sul, Campo Grande, MS, Brasil.

² Fundação Oswaldo Cruz, Fiocruz Mato Grosso do Sul, Campo Grande, MS, Brasil.

^{*}Corresponding author/Autor de correspondência: larissa.m.bandeira@ufms.br Received/Recebido: 05.02.2025 Accepted/ Aceito: 04.06.2025

INTRODUCTION

Human T-lymphotropic viruses 1 and 2 (HTLV-1/2) are retroviruses with tropism for T lymphocytes. HTLV-1 has been implicated in adult T-cell leukemia (ATL), HTLV-1-associated myelopathy (HAM), and various inflammatory diseases. This virus is globally distributed and is considered endemic in sub-Saharan Africa, South America, South Japan, the Caribbean islands, and Melanesia¹⁻³. In contrast, HTLV-2 does not exhibit a cosmopolitan distribution and is more prevalent among indigenous populations and individuals who use injecting drugs⁴. In Central Brazil, HTLV-1/2 infection has been documented in communities such as Quilombos, individuals living with HIV (PLHIV), and those with *Mycobacterium tuberculosis* (Mtb) infection⁵⁻⁷.

Tuberculosis (TB) is a public health concern and a principal cause of morbidity worldwide. Infection is caused by Mtb when aerosol droplets containing the bacillus settle in the lung, which is the leading site of infection⁸. HTLV-1 infection may induce immunological compromise, potentially leading to various coinfections, such as tuberculosis and strongyloidiasis, which can affect the natural course of both infections. Additionally, this virus may cause several clinical manifestations, including dermatitis and rheumatoid arthritis^{9,10}. In areas where both Mtb and HTLV-1 are endemic, there is a significant relationship between their co-infection and a higher incidence of tuberculosis in people living with HTLV-1¹¹⁻¹³.

Furthermore, incarcerated populations are at high risk of sexually transmitted infections (STIs) and tuberculosis disease¹⁴. In Mato Grosso do Sul (MS) state, HTLV-1 infection and tuberculosis (incidence and prevalence) have already been described in inmates^{15,16}. However, the prevalence of HTLV and active Mtb co-infections among prisoners has not been widely investigated.

Therefore, this study aimed to assess the prevalence of HTLV-1/2 infection and identify the main types of HTLV among this population vulnerable to tuberculosis.

MATERIAL AND METHODS

Study population

This cross-sectional study was conducted among inmates from two closed penal institutions, Instituto Penal de Campo Grande (IPCG) and Estabelecimento Penal Jair Ferreira de Carvalho (EPJFC), in Campo Grande, the capital of the state of Mato Grosso do Sul, Central Brazil. The study was conducted between March 2014 and March 2017. Male individuals diagnosed with active tuberculosis, defined as bacteriologically confirmed TB by at least one positive smear microscopy or solid culture for Mtb¹⁷. Participants were interviewed about their socioeconomic and behavioral characteristics, and blood samples were collected and stored at -20 °C until serological analysis¹⁷.

Serological tests

The stored serum samples were screened using a commercial enzyme-linked immunosorbent assay (ELISA) kit for the presence of anti-HTLV-1/2 antibodies (GOLD ELISA HTLV-I/II – REM) following the manufacturer's instructions. Positive samples were repeatedly tested and confirmed by HTLV-1/2 Western Blot (WB) assay (MP Diagnostics HTLV BLOT 2.4, Singapore). HTLV infection was defined as repeated



positive ELISA and WB results. The selected samples were also tested by electrochemiluminescence (ECL) for HIV (anti-HIV-1/2), HCV (anti-HCV), HBV (HBsAg, total anti-HBc, and anti-HBs), and ELISA for syphilis infection (anti-*T. pallidum*) as described by Puga et al¹⁷. ELISA-reactive samples for anti-*T. pallidum* were serially diluted to quantify Venereal Disease Research Laboratory (VDRL) titers. All the samples which tested positive for anti-HCV and anti-HIV antibodies were confirmed for HCV RNA detection using the qPCR assay (Abbott RealTime HCV), and for HIV infection using the Western blot assay (Immunoblot, Bio-Rad).

Data analysis

The variables were analyzed using the Stata software (version 13.0; Stata Corporation, College Station, TX, USA). Categorical variables were presented as absolute and percentage frequencies, and continuous variables were expressed as means and medians.

Ethics Statement

This study was approved by the Ethical Committee on Human Research of the Universidade Federal de Mato Grosso do Sul (protocol number CAAE: 67923923.7.0000.0021). At the time of sampling, all participants gave their written informed consent to participate in the study, which was performed according to relevant guidelines and regulations.

Data availability statement

All relevant and original data presented in the study are included in this article.

RESULTS

A total of 279 participants were enrolled in the study, comprising 204 (73.12%) individuals from the EPJFC and 75 (26.88%) from the IPCG, the two largest prison institutions in MS. All participants were men, aged 19-71 years, with a median age of 29. Most participants (n = 178) were from Mato Grosso do Sul. 211 (75.63%) participants had completed five or more years of education. Regarding ethnicity, most individuals identified themselves as multiracial (53.96%). 59.86% of participants reported not having a steady partner during the study (**Table 1**).

Two individuals (PTB-05 and PTB-263) tested positive for anti-HTLV antibodies by ELISA (0.72%; 95% CI 0.18 – 2.84). PTB-263 was confirmed as HTLV-1 positive by Western blot and reported a history of syphilis. PTB-05 tests exhibited an indeterminate result by Western Blot, displaying bands p24 and GD21. Performing a polymerase chain reaction (PCR) test was impossible due to the unavailability of whole blood and access to the participant to perform a new blood collection. Additionally, PTB-05 tested positive for anti-HIV-1 and anti-HCV antibodies and reported a history of blood transfusion before 1993. PTB-05 was from the IPCG, and PTB-263 was from EPJFC institutions. Both are related to being single, heterosexual, and irregular condom use. Participant PTB-05 discontinued both HIV and TB treatments and subsequently died (**Table 2**). The drugs used to treat both infections are free of charge in the Brazilian Public Health System.



Table 1. Characteristics of 279 inmates with active TB in the cross-sectional study

| Variable | N (Absolute number) | Percentage (%) |
|-----------------------------|---------------------|----------------|
| Ethnicity | | |
| White | 73 | 26.26% |
| Black | 51 | 18.35% |
| Asian | 4 | 1.44% |
| Mixed race | 150 | 53.96% |
| Marital Status | | |
| Steady partner | 112 | 40.14% |
| Without steady partner | 167 | 59.86% |
| Sexual orientation | | |
| Homosexual | 8 | 2.87% |
| Heterosexual | 267 | 95.70% |
| Bisexual | 4 | 1.43% |
| Education (years) | | |
| ≤ Four years | 69 | 24.73% |
| . ≥ Five years | 210 | 75.27% |
| Condom use | | |
| Always | 53 | 19.00% |
| Sometimes | 155 | 55.56% |
| Never | 71 | 25.45% |
| Share needle | | |
| No | 266 | 95.34% |
| Yes | 13 | 4.66% |
| Share sharp objects | | |
| No | 51 | 18.28% |
| Yes | 228 | 81.72% |
| History of <i>crack</i> use | | |
| No | 247 | 88.53% |
| Yes | 32 | 11.47% |
| History of cocaine use | | |
| No | 115 | 41.22% |
| Yes | 164 | 58.78% |
| History of marihuana use | | |
| No | 54 | 19.35% |
| Yes | 225 | 80.65% |
| | | |

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| Variable | N (Absolute number) | Percentage (%) |
|------------------------------|---------------------|----------------|
| History of heroin use | | |
| No | 276 | 98.92% |
| Yes | 3 | 1.08% |
| History of STIs | | |
| No | 216 | 77.42% |
| Yes | 63 | 22.58% |
| History of blood transfusion | | |
| No | 237 | 84.95% |
| Yes | 42 | 15.05% |
| Year of blood transfusion | | |
| After 1993 | 35 | 88.33% |
| Before 1993 | 7 | 16.66% |
| Type of tattoo | | |
| Unprofessional tattoo | 176 | 79.64% |
| Professional tattoo | 45 | 20.36% |
| Sex worker | | |
| No | 269 | 96.42% |
| Yes | 10 | 3.58% |
| Anti-HCV | | |
| Negative | 260 | 93.19% |
| Positive | 14 | 5.02% |
| Anti-HIV | | |
| Negative | 260 | 93.19% |
| Positive | 19 | 6.81% |
| HBsAg | | |
| Negative | 275 | 98.57% |
| Positive | 4 | 1.43% |
| Anti-T. pallidum | | |
| Negative | 251 | 89.96% |
| Positive | 28 | 10.04% |



Table 2. Descriptive characteristics of both inmates coinfected with TB/HTLV of the 279 participants with active TB of the cross-sectional study

| Characteristics | PTB-05 | PTB-263 |
|-------------------------------|-----------------------|-----------------|
| Serological HTLV status | Indeterminate | HTLV-1 |
| Age (years) | 42 | 49 |
| Marital status | Single | Single |
| Gender | Male | Male |
| Ethnicity | Multiracial | White |
| Education level | Elementary school | High school |
| Prison | IPCG | EPJFC |
| IDU history | No | No |
| Tattoo | Home tattooing | No |
| Blood transfusion before 1993 | Yes | No |
| Condom use | Irregular | Irregular |
| Sexual preference | Heterosexual | Heterosexual |
| Previous incarceration | Yes | No |
| Time in prison (months) | 192 | 12 |
| STI history | Yes (HPV) | No |
| Anti-HIV positive | Yes | No |
| Anti-HCV positive | Yes | No |
| HBsAg positive | No | No |
| Anti-HBs positive | No | No |
| Active syphilis | No | Yes |
| TB treatment | Abandonment treatment | Under treatment |

IPCG: Instituto Penal de Campo Grande; EPJFC: Estabelecimento Penal Jair Ferreira de Carvalho; IDU: injection drug use; STI: sexually transmitted infection

DISCUSSION

To our knowledge, this is the first study to investigate the prevalence of HTLV infection among inmates with active TB. Furthermore, the progression from latent tuberculosis infection (LTBI) to active tuberculosis is more commonly observed in individuals with pre-existing conditions, such as cancer, diabetes, immunodeficiency, organ transplantation, and viral infections, including HIV and HTLV-18.

The prevalence of HTLV-1 infection was 0.72% (95% CI 0.18 – 2.84), which is considered a low to medium prevalence¹⁸. This result is expected since active TB could be viewed as a predictable disease among people living with HTLV-1 (PLwHTLV-1)⁸ due to the significant relationship between these coinfections in countries like Brazil, which has a high burden of these pathogens. TB disease may present a chance almost three times greater in people living with HTLV-1 than among individuals without HTLV-1



infection¹¹. We could not provide additional insights regarding the prevalence uncovered since no existing literature has assessed this coinfection in this particular population group.

The PTB-05 case underscores the critical importance of adherence to treatment regimens for patients co-infected with TB and HIV. Nonadherence can lead to poor treatment outcomes, including increased mortality^{19,20}. The death of PTB-05 after abandoning HIV treatment is a stark reminder of the complexities and necessity of maintaining strict adherence to TB and HIV treatment protocols. Ensuring patients understand the importance of adherence and managing potential complications of combined treatment is essential for improving patient outcomes. Co-infections present significant clinical challenges, as treating one infection can interfere with the treatment of another. The participant reported a history of blood transfusion before 1993, when screening for HTLV-1/2 infection in Brazilian blood banks had not been mandatory yet²¹. Additionally, prisoners frequently exhibit low adherence to treatment regimens, leading to virologic failure²².

Participant PTB-05's initial screening test yielded a positive result, yet subsequent WB analysis produced an indeterminate result. WB could show up to 67% of the results as indeterminate; these results are common mainly in individuals co-infected with HIV/HTLV²³⁻²⁵. Indeterminate WB results may occur and could necessitate further testing with highly sensitive methods such as PCR to detect the presence of viral genomic material²⁶. However, the inability to perform polymerase chain reaction (PCR) testing due to the unavailability of whole blood precluded definitive confirmation of the participant's status.

PTB-263's recurring incarceration indicates a pattern of behavior that makes it challenging to monitor the treatment of these individuals within the correctional system. The instability associated with re-entry and the potential for recidivism can disrupt the continuity of care, which is crucial for effective infection management²⁷. Furthermore, incomplete adherence to prescribed antituberculosis therapy, often seen in correctional settings, is a known risk factor for multidrug-resistant TB, increasing the complexity of treatment in such populations²⁸.

Some limitations must be considered. Some risky behaviors could have been under-reported during the interviews due to a potential apprehension of stigma, leading to a possible underestimation of the risks among the studied group. Although only two prisons were included in this study – and may not fully represent the current epidemiological panorama of HTLV and TB co-infection in the broader prison population – they are the two largest male prisons in the MS state. Furthermore, the absence of a whole blood sample from PTB-05 with an indeterminate serological status for HTLV made it impossible to confirm the diagnosis of HTLV infection by molecular analyses.

CONCLUSION

Although the prevalence of HTLV infection identified in this study was relatively low, the presence of positive cases in this context, particularly among individuals with other STIs, highlights the ongoing necessity for healthcare programs that emphasize diagnosis and prevention. Despite the acknowledged impact of HTLV and tuberculosis (TB) in high-risk populations, there exists a substantial gap in the literature concerning their co-infection among incarcerated individuals. This paucity of data accentuates the significance of our findings and highlights the critical need to advance our understanding of HTLV-TB co-infection within this vulnerable group.



CONFLICT OF INTEREST

The authors declare that there are no conflicting interests.

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AUTHOR'S CONTRIBUTIONS

Conceptualization: Marco Antonio Moreira Puga, Ana Rita Coimbra Motta-Castro. Methodology: Larissa Melo Bandeira, Marco Antonio Moreira Puga, Maurício Antonio Pompílio. Analyzed the data: Carolina Amianti. Contributed reagents/materials/analysis tools: Ana Rita Coimbra Motta-Castro. Writing – original draft preparation, review, and editing: Larissa Melo Bandeira, Carolina Amianti, Marco Antonio Moreira Puga. Supervision: Ana Rita Coimbra Motta-Castro. All authors have read and agreed to the published version of the manuscript.

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