



# *HIV and Tuberculosis, coinfection in female transgenders in Managua between November 2017 and April 2018*

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## **ABSTRACT**

**H**IV positive transgender women face discrimination in health services, which leads to exclusion in access to prevention and treatment services, this represents higher rates of morbidity and mortality. This public health problem can be solved as deaths from pulmonary tuberculosis and latent tuberculosis can be avoided with low-cost prophylactic treatment.

In Latin America, there have been few studies of coinfection in transfeminine women, and in Nicaragua, there is a little history of scientific research that provides information for decision-making in the approach to this health problem.

This work was carried out in Managua from November 2017 to April 2018. Its purpose was to analyze the factors that affect access to health care for HIV-positive trans people in Managua. It adopted the quantitative paradigm, which included a survey of 61 HIV-positive trans women.

The results represent a scientific contribution to understanding the situation experienced by this population group of sexual diversity, to create awareness in national health authorities, the national and international scientific community, as well as society in general.

## **INTRODUCTION**

Data on HIV and TB co-infection among female transgender people are well documented worldwide. Tuberculosis coinfection enhances HIV acquisition and transmission. Globally, the prevalence of TB and HIV is higher among HIV-positive transgender women than in the general population, partly because of the low average CD4 cell counts. The leading cause of hospital admission and death among HIV-positive female transgenders is tuberculosis, which can be reduced through early diagnosis of HIV and rapid initiation of antiretroviral therapy and isoniazid preventive therapy.

Nicaragua has three official documents on HIV/TB co-infection, 1) “Guide of antiretroviral therapy for people with VIH”, issued by MINSa in 2015, 2) “Norms and Procedures for the Management of Tuberculosis” in 2014, 3) “Guidelines and protocol for the management of HIV co-infection and TB” 2010, where recommendations are made to apply them to HIV-positive female transgenders because this population is located among the key population. The health services do not comply with these recommendations for HIV-positive transgender women, according to the guidelines of the Ministry of Health (MINSa).

The situation of HIV-positive transgender women is extremely complex due to the stigma and discrimination affecting their right to health, Reisner et al. (2016)

The scientific literature highlights the lack of knowledge among both health personnel and the general population about the characteristics of HIV-positive transgender women (Baral, Poteat, Strömdahl, Wirtz, Guadamuz & Beyrer 2013). International scientific studies have found that HIV-positive transgender women consider health services to be incomplete and inadequate for their specific needs of gender affirmation and HIV status, Abayy et al. (2015)

HIV-positive transgender women do not access health services because of fear, ignorance, and mistreatment by health care providers, Reisner, et al. (2016), and they also consider health services incomplete and inadequate for their specific needs and HIV status. Tallada, Saleh-Ramirez, & Toro (2013). Lack of adherence to ART predisposes them to virological and immunological failure Winter, et al. (2016), and as a result, they have opportunistic infections

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such as tuberculosis, Wylie, et al. The Joint United Nations Programme on HIV/AIDS; UNAIDS (2016) and Garofalo, Kuhns, Reisner & Mimiaga (2016).

In 2016, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the WHO Global Health Workforce Alliance jointly launched the Agenda for Zero Discrimination in Health Care, which states that people around the world face barriers to accessing quality health services and enjoying the highest attainable standard of health, The Joint United Nations Programme on HIV/AIDS; UNAIDS (2016).

Stigma at the community level and discriminatory laws at the structural level also contribute to the high burden of HIV by limiting the provision and use of services. Regardless of geographic location, transgender women exist in social contexts that stigmatize them. Stigma is a powerful social determinant of health and a key driver of HIV disparities among transgender women. Besides, HIV infection is only one of many stigma-related health conditions that disproportionately affect transgender women. Syndemics have been defined as “the concentration and harmful interaction of two or more diseases or other health conditions in a population. This is the case with tuberculosis, which increases the risk of HIV and contributes to poor HIV treatment outcomes for transgender women. Existing evidence on syndemics suggests difficulties in successfully treating and preventing HIV infection in isolation from other social, behavioral, and medical conditions that occur together and interact to limit successful and sustained participation in medical care, Poteat et al. (2016)

The study conducted in the United States by Rebekah, et al. (2017), established that a syndemic framework should be used as a tool to recognize, investigate, evaluate, and implement integrated health programs, especially those that address multiple diseases such as HIV and tuberculosis. First, researchers and care providers must recognize how social and medical problems cluster and interact with certain populations. It is imperative to understand what social problems affect certain disease groups in geopolitical contexts and within specific regions and populations, Mendenhall et al. The application of the concept of syndromes is becoming increasingly apparent in the promotion of HIV treatment.

Another study by Ford et al (2015) in the United States found that the most common causes of hospital admission for HIV patients were diseases related to advanced HIV disease (AIDS) and bacterial infections. Within the category of AIDS-related illnesses, the main causes of hospital admission were tuberculosis. Pulmonary tuberculosis accounted for the majority of cases of tuberculosis-related hospital admissions (67%).

The high prevalence of pulmonary tuberculosis as a cause of hospital admission and mortality can be reduced by early diagnosis of HIV, rapid initiation of antiretroviral therapy, and preventive therapy with Isoniazid for latent tuberculosis. AIDS-related infections, particularly

tuberculosis and bacterial infections, have been identified as the leading causes of hospital admission and mortality in adults worldwide. This finding is explained in part by the low CD4 cell count of patients admitted to the hospital, with less than half of all HIV-positive patients on ART on admission attended, Ford et al (2015).

*Mycobacterium tuberculosis* and HIV, mutually reinforcing, accelerate the deterioration of immune functions and cause the progression of advanced HIV infection (AIDS) leading to premature death if not treated. HIV coinfection is the most important risk factor for developing active tuberculosis, increasing susceptibility to primary infection or reinfection, and also increasing the risk of reactivation of latent tuberculosis. The main feature of immunosuppression in patients with HIV is the loss of CD4 T cells, which contributes to an increased risk of developing active tuberculosis, Bruchfeld, Correia-Neves & Kallenius (2015).

The World Health Organization (WHO) recommends initiation of antiretroviral therapy for any HIV-infected patient who develops tuberculosis, regardless of CD4 T-cell count. Current treatment of patients with HIV-associated tuberculosis includes treatment for TB, administration of ART in conjunction with antifungals, prevention of HIV-related comorbidities, and prevention and treatment of the Immune Reconstitution Syndrome (IRIS) that can occur in HIV patients taking both treatments together. The number of people with HIV receiving preventive therapy for latent tuberculosis with Isoniazid was found to be a small fraction, Bruchfeld, Correia-Neves & Kallenius (2015).

The World Health Organization recommends the Three Rs (as in Spanish) strategy for active TB case finding in HIV-positive people: a) *intensified* case finding, b) *Isoniazid* preventive therapy, and c) *infection* control in health services should be implemented effectively, Bruchfeld, Correia-Neves & Kallenius (2015), and World Health Organization (2018).

Another meta-analysis in 2015 evaluated the effect of early initiation of antiretroviral therapy (ART) between the first two and four weeks after starting treatment for tuberculosis in patients co-infected with tuberculosis and HIV. It was concluded that there is a reduction in mortality of HIV-positive patients as a result of the early initiation of ART. This study also confirmed the high rate of tuberculosis and inflammatory immune reconstitution syndrome (IRIS) and death associated with this condition. Operational and implementation research is required to maintain the benefit of early initiation of ART and appropriate management of tuberculosis and IRIS, Abayy et al (2015).

The association of tuberculosis and HIV is a challenge to the survival of coinfecting patients. HIV complicates the presentation, diagnosis, and treatment of tuberculosis. Coinfecting patients have drug interactions, inflammatory immune reconstitution syndrome (IRIS), lower

plasma drug levels, and drug resistance during treatment despite adherence, Narendran G & Swaminathan S (2016).

Latent tuberculosis is a difficult diagnosis to make from HIV coinfection. Latent tuberculosis should be diagnosed in HIV-coinfected patients as early as possible before ART is initiated and preventive therapy with Isoniazid should be given for 6 to 9 months, regardless of the Tuberculin Skin Test (PPD), Gopalan, Chandrasekaran, Swaminathan & Tripathy (2016).

Advances in molecular technology have partially replaced conventional cultures, which has helped to make a rapid diagnosis of active TB, providing sensitive results in less time. The Tuberculin Skin Test (PPD) is used for the diagnosis of latent TB in HIV-positive populations. PPD is a strategic component of TB control that identifies high-risk populations such as female transgenders who are prone to developing pulmonary TB. There is a need for updated knowledge and awareness of Isoniazid Preventive Therapy (INH) among health professionals and policymakers for rapid implementation and for patients to gain the benefits of prophylaxis as it can be incorporated and monitored with the initiation of ART, Gopalan, Chandrasekaran, Swaminathan & Tripathy (2016).

The Xpert-MTB rif (GeneXpert) is the diagnostic option for tuberculosis in HIV-coinfected patients, providing results within two hours with a 45% increase in case detection rate compared to the microscopy of positive sputum smears and can also be used in patients with negative smears. It is endorsed by WHO for the rapid diagnosis of tuberculosis as well as early detection of rifampicin resistance among HIV-infected patients suspected of being co-infected with tuberculosis. The capture ELISA test is available to detect lipoarabinomannan (LAM) in urine samples. The sensitivity of LAM is significantly higher than sputum smear microscopy especially in advanced HIV infection where patients with CD4 counts of 100 or lower are found. The WHO from 2016 has now recommended the detection of LAM in urine samples in HIV-infected immunosuppressed patients as a complementary means to rapidly diagnose active TB disease, Gopalan, Chandrasekaran, Swaminathan & Tripathy (2016).

Patients living with HIV, with an unknown or positive Tuberculin Skin Test (PPD) should receive TB preventive treatment as part of a comprehensive treatment. Isoniazid monotherapy for 6 months is recommended for the treatment of latent tuberculosis in adults. World Health Organization (2018) Latent tuberculosis infection Updated and consolidated guidelines for programmatic management.

According to the 2018 World Health Organization report, there were 10 million cases of tuberculosis worldwide, with 12% (1.2 million) co-infected with human immunodeficiency virus (HIV); 37% of new TB cases were undiagnosed. The risk of developing TB among the 37 million people living with HIV is approximately 21 times greater than the risk for the rest of the world's

population. It is estimated that approximately 1.7 billion people, 23% of the world's population, have a latent TB infection and therefore are at risk of developing active TB disease during their lifetime. Deaths from TB and the disease itself can be prevented by preventive therapy with Isoniazid, but most people living with HIV who can benefit from it are not receiving it, World Health Organization, World TB Report 2018.

Tuberculosis is the most difficult infectious disease facing humanity and affecting impoverished communities in developing countries. It is the leading cause of death among high-risk populations, including HIV-positive transgender women. Concentrated epidemics of tuberculosis have been identified in vulnerable populations where tuberculosis and HIV are present. HIV-positive vulnerable populations include drug users, sex workers, and transgender women. Vulnerable or higher-risk populations co-infected with HIV and TB are bacillievers-negative, so sputum smears (BK) are negative. It is indicated to perform the Tuberculin Skin Test (PPD) or Xpert-MTB rif (GeneXpert), Peters et al (2019).

Most HIV-positive cases with exposure to tuberculosis lead to the development of asymptomatic latent tuberculosis, which is characterized by an immune response to the mycobacterial antigens used in tuberculin (PPD) that is defined as an asymptomatic disease without radiological or microbiological signs of disease, Bruchfeld, Correia-Neves, Kallenius, (2015). It is not clear whether HIV infection increases the risk of becoming infected with latent tuberculosis. Similarly, the risk of progression to active pulmonary tuberculosis also increases substantially in the presence of HIV coinfection according to Peters et al (2019).

## **MATERIALS AND METHODS**

The paper included two stages; in the first, a documentary review was carried out to learn about the state of art. The bibliographic review included the reading of all studies on transgender females in Nicaragua finding the Health Needs Diagnosis study and Available Services for Trans Women of Nicaragua, held in 2013, Morales-Miranda et al (2014) and the study Survey of Sexual Behavior Surveillance and Prevails of the HIV and syphilis in vulnerable populations at increased risk for HIV: men who have sex with men, transgender women, sex workers, injecting drug users, and people with HIV in Nicaragua, done in 2014, Sánchez, Ibarra, Tallada, & Saleh-Ramirez (2014), the trans-female interviewed was a mixed HIV positive and negative trans-female population and were included in the population of men who have sex with men (HSH).

In a second stage, primary source information was searched, to do so, this study adopted the paradigm of positivist research, having as a methodology for the collection of data the active search of cases from the identification of a key informant.

As there was no record of the universe of study, the method "Snowball" was used to apply a structured quantitative survey that consisted of 198 items to Managua's HIV-positive female trans, located on the streets at the meeting places where trans-women HIV-positive exerts commercial sexual work.

The information obtained was recorded in a database designed for that purpose, using the SPSS V25 statistical program. Also, the crosses of the main variables to exit specific objectives to facilitate analysis and interpretation of results.

## RESULTS

It was evidenced that HIV positive trans women who are on ART and those who are not on ART, in the health services they attend, are not receiving the follow-up tests for latent TB prophylaxis established in the "Antiretroviral Therapy for people with VIH", issued by MINSA in 2015, "Guidelines and Procedures for the Approach to Tuberculosis" in 2014 and Guidelines and Protocol for the Management of HIV and TB Coinfection 2010.

It was found that HIV-positive transgender women who participated in this study reported that only 34.4% were tested for sputum (BK), the remaining 65.6% were not tested for sputum (BK), nor were they given the Tuberculin Skin Test (PPD). 24.6% of them had sputum testing (BK) more than a year ago, 9.8% had less than a year of BK, and the rest had no BK testing in the same period. Regarding the results, 31.1% received the result of the BK tests and were negative, only one received a positive result for tuberculosis and complied with the treatment resolving tuberculosis after six months of shortened treatment. None of those who received a negative BK test result as well as those who did not receive a BK test result received Isoniazid prophylaxis for the treatment of latent tuberculosis.

A single HIV-positive female transgender person was diagnosed with pulmonary tuberculosis and received treatment for six months to resolve the tuberculosis problem. She was not on ART at the time of her HIV diagnosis. Latent tuberculosis should be diagnosed in HIV-coinfected patients as quickly as possible before starting ART and should be given preventive Isoniazid therapy for 6-9 months, regardless of the Tuberculin Skin Test (PPD), Gopalan, Chandrasekaran, Swaminathan &Tripathy (2016).

In the last twelve months, 44.3% of HIV-positive female transgenders had CD4 count tests done at the hospital and 9.8% at the health center. Only 26.2% know the results of the CD4 count tests. 21.3% of the participants never knew the result of the CD4 count tests. 8.2% received and remembered their CD4 test results stating that they were over 500 CD4s. 6.6% received and remembered a result of fewer than 350 CD4s, another 6.6% received and remembered a result

of fewer than 200 CD4s, and 3.3% received and remembered a result of fewer than 50 CD4s. It was found that 16.5% of HIV-positive female transgenders were found to be an immune failure.

In the last twelve months, 54.1% of HIV-positive transgenders have been tested for HIV viral load. 43.3% were tested at the hospital and 9.8% at the health center. It was found that 45.9% of HIV-positive female transgenders have had one viral load test in the last year, 8.2% have had two viral load tests, and 1.6% have had four viral load tests. It was determined that 32.8% of the female transgenders did not receive the results of their viral load tests, 13.1% received and recalled the result greater than 20 copies, and 9.8% received and recalled the result less than 20 copies. 13.1% of HIV-positive female transgenders are in virological failure.

Nicaraguan Department of Health (MINSA) registered 81 people with TB/HIV coinfection for the general population as of 2017, of which 89% are men, among whom it is presumed that HIV-positive trans-females are present since there is no disaggregation of the key population among which the trans-females are found. Twenty-nine percent have begun treatment for multi-drug resistant tuberculosis, not specifying how many men and women are included in this percentage. Ministry of Health-MINSA, HIV/AIDS Epidemiological Situation Report to March 2018, Nicaragua (2018).

For HIV and TB co-infection in HIV-positive transgender women, it was found that none of them received Isoniazid prophylaxis because their HIV-positive status made them vulnerable to acquiring latent TB. After all, their immune system is affected by the HIV that replicates and spreads in the T cells known as CD4 damaging the functions of CD4 cells so HIV-positive female transgenders are immunodeficient that over time develop advanced HIV infection (AIDS) that leads to the appearance of opportunistic infections such as active pulmonary tuberculosis causing death but they are given treatment with retrovirals (ART) in conjunction with antifungals, Ford et al (2015), why HIV-positive female transgenders should be given isoniazid treatment for nine months to prevent them from developing active pulmonary tuberculosis, Bruchfeld, Correia-Neves, Kallenius, (2015).

According to the guidelines of the Antiretroviral Therapy for Persons with HIV ("Handbook") of the Nicaraguan Department of Health (MINSA) December 2015, it is established that all persons who have a reactor/positive result for HIV tests are considered HIV positive patients and before starting ART they should be tested for CD4 count and viral load in addition to other serological and general chemistry tests, and then proceed to start retroviral treatment (ART). Among these tests before the initiation of ART are sputum smears (BK) and the Tuberculin Skin Test (PPD) for the diagnosis of tuberculosis. If both tests are negative, regardless of CD4 count and viral load, prophylaxis with Isoniazid should be initiated for nine months to treat latent tuberculosis and thus avoid the acquisition of pulmonary tuberculosis. Also, MINSA

in the “Standards and Procedures for Addressing Tuberculosis” in 2014 and “Guidelines and Protocol for the Management of HIV/TB Co-infection 2010” establishes the same algorithm for treating latent tuberculosis, which is not being followed.

Half of HIV positive transgender women are not on ART and do not access health services because they consider that health services do not have adequate conditions for their medical care, Reisner et al (2016) and Baral, et al (2013), although they know their HIV status, they do not have enough information regarding the prophylaxis of latent tuberculosis or negative complications for their health. This characteristic of HIV positive trans women from Managua has been found in scientific studies carried out internationally in HIV positive trans female population, The Joint United Nations Program on HIV / AIDS; UNAIDS (2016) and Garofalo, Kuhns, Reisner & Mimiaga (2016).

HIV positive trans females who are on ART share with HIV positive trans females who are not on ART, the lack of knowledge about latent tuberculosis and the importance of having the Tuberculin Skin Test (PPD) performed instead of the sputum smear (BK) because international studies established that HIV positive patients are smear-negative therefore sputum smears will be negative and the diagnosis of tuberculosis cannot be made, which is why it has been established that the Tuberculin Skin Test (PPD) is indicated, where there is access to GeneXpert it is the diagnostic option for tuberculosis in patients coinfecting with HIV, providing results within two hours, with an increase in the case detection rate of 45% compared to microscopy of sputum smears, it is endorsed by the WHO for the rapid diagnosis of tuberculosis, as well as the early detection of resistance to rifampicin among HIV-infected patients who are presumed to be co-infected with tuberculosis, especially in advanced HIV infection where patients with CD4 counts 100 or lower are found. In Nicaragua, GeneXpert is performed, but it is not available for HIV-positive trans-women, this test is indicated for other populations such as patients with multi-drug resistant tuberculosis, health workers, and others, Gopalan, Chandrasekaran, Swaminathan & Tripathy (2016).

Regardless of whether or not the Tuberculin Skin Test (PPD) is performed, the WHO established that all HIV-positive patients should be administered prophylaxis with Isoniazid for a minimum of six months for the treatment of latent tuberculosis. Of the participants of this study, none were administered this prophylaxis, World Health Organization (2018) Latent tuberculosis infection Updated and consolidated guidelines for programmatic management.

It was found that 16.5% of HIV positive trans females are in immune failure since all of them have a CD4 count lower than 350, it was also determined that they were tested for Viral Load and 13.1% had a higher result of 20 copies, this group is in virological failure, which

means that this group is at greater risk of developing active pulmonary tuberculosis and death, Bruchfeld, Correia-Neves & Kallenius, (2015) and Narendran & Swaminathan (2016).

Following the guidelines of the World Health Organization (2018)) Latent tuberculosis infection Updated and consolidated guidelines for programmatic management, MINSA has established in its Guidelines for Care for HIV-positive people and Standards for Tuberculosis and co-infection of tuberculosis and HIV that applies the strategy of the *Three Is* (as in Spanish) for the active search for tuberculosis cases in HIV positive people: a) *intensification* of the search for cases, b) preventive therapy with *isoniazid*, c) *infection* control in health services should be implemented in an effective. Health service providers are not applying them following MINSA's mandate.

It is estimated that approximately 1.7 billion people, 23% of the world's population, have a latent TB infection and are therefore at risk of developing active TB disease during their lifetime. Deaths from tuberculosis and the disease itself can be prevented with preventive therapy with isoniazid, but most people living with and who may benefit from it are not receiving it, World Health Organization (2018) Latent tuberculosis infection Updated and consolidated guidelines for programmatic management and World Health Organization World Tuberculosis Report 2018.

Noncompliance with World Health Organization recommendations (2018) Latent tuberculosis infection Updated and consolidated guidelines for programmatic management exposes female transgender people to increased risk of TB co-infection and thus increases the risk of death for transgender people, Baral, et al (2013). The lack of knowledge of health care providers in this regard can be considered an act of hostility Abayy et al (2015) may be the cause, lack of knowledge or discrimination that health care providers have against female transgender people as well as society in general, Ford, et al (2015) and World Health Organization World Tuberculosis Report (2018).

## CONCLUSIONS

The WHO-guided *Three Rs* strategy for actively seeking TB cases in HIV-positive people is not implemented by health care providers.

The diagnostic algorithm for latent TB guided by MINSA in the Antiretroviral Therapy for People with VIH", the "Guidelines and Procedures for the Management of Tuberculosis" and the "Guidelines and Protocol for the Management of HIV/TB Co-infection" is not implemented by health service providers.

The lack of knowledge of health care providers in the treatment of latent TB is considered an act of hostility toward HIV-positive transgender women and may be caused by lack of knowledge or discrimination by health care providers and society in general.

Sputum smears (BK) were performed on 34.4% of HIV-positive transgender women. These smears are not specific to the diagnosis of pulmonary tuberculosis because they are HIV-negative.

16.5% of the HIV-positive female transgenders are in immune failure because all of them have a CD4 count below 350.

13.1% of them had their viral load tested and had a result of more than 20 copies, they are in virological failure,

Deaths from pulmonary tuberculosis and latent tuberculosis can be avoided with Isoniazid prophylaxis, but the vast majority of HIV-positive female transgenders who can benefit from it are not receiving it. Sixty-five. 6% of HIV-positive female transgenders did not have sputum smears (BK), and only one of them was treated and the BK test became negative in six months, showing evidence of cure.

MINSA does not disaggregate by a population of higher risk the data of coinfection in HIV positive patients among which are HIV positive female transgenders

The WHO 2018 recommendations for treatment of latent tuberculosis are not implemented by health care providers.

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