

Prevalence and Risk Factors for Active Tuberculosis in HIV-Negative Individuals: A Retrospective Study on the Progression from Latent to Active Tuberculosis in Rwanda

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Abstract

➤ Background:

Tuberculosis is among the most widely spread and serious of all human infectious diseases. About one-third of the world's population is estimated to be infected by *Mycobacterium Tuberculosis*, in whom active Tuberculosis develops in nine million persons each year. This study aimed at identifying the associated factors to the progression of Latent Tuberculosis infection to Active Tuberculosis in HIV negative people and identifying the prevalence of Tuberculosis in HIV negative.

➤ Methods:

The factors were obtained by reviewing the files of patients who were Tuberculosis positive in the last two years from 2017 to 2018.

➤ Result:

The findings of this study showed that the factors that might be associated were: age, sex, being aged above 55 (0.9%), being in close contact with a Tuberculosis positive person (7.5%), collective housing (8.4%), drinking alcohol (7.1%), smoking (6.6%), living in Kigali district (4.7%), imprisonment (0.9%), some participants had more than two factors (2.8%), mostly drinking alcohol and smoking at the same time. Unfortunately, only 38.9% of the participants had a known factor that might have led to the activation of Tuberculosis and the remaining 61.1% of the cases had no specified factor. The association was found to be statistically significantly ($p < 0.005$). The prevalence of HIV negative with TB positive was found to be 68.8%.

➤ Conclusion:

The study recommended that the country should increase awareness of risk factors of Tuberculosis rather than HIV and set a specialized surveillance system even for HIV negative with TB positive.

Keywords: HIV Status, TB, LTBI, Prevalence, Risk Factors.

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I. INTRODUCTION

Tuberculosis (TB), a deadly airborne disease caused by *Mycobacterium tuberculosis* (MTB), is among the top ten global killers, with 3 million deaths annually, and exists in two forms which are latent infection (LTBI) and active disease (ATB)¹. LTBI is asymptomatic and non-contagious while active TB disease involves symptoms and the ability to spread the bacteria². According to the World Health Organization, around one-third of the global population has LTBI, with 5–15% at risk of reactivation when the immune system fails, leading to active TB^{3,4}. High-risk groups for reactivation include those recently exposed to TB, individuals with HIV, prisoners, the homeless, and people with immune-compromising conditions like diabetes or chronic renal failure³.

A study by Narasimhan *et al.* (2013) identified several risk factors for TB activation, including recent MTB infection, a history of untreated or poorly treated TB, immunosuppressive therapies, certain blood disorders like leukemia, lymphoma, cancers, prior gastrectomy or jejunoileal bypass, and children under five years old⁵. It is recommended to test all TB patients for HIV to ensure proper treatment; HIV-positive TB patients may require ARV adjustments for effective TB treatment, while HIV-negative TB patients begin treatment with further evaluation to identify risk factors for TB activation^{6,7}. A person with active TB has a significant number of bacteria in their body, may spread it to others, and experience symptoms like cough, fever, and weight loss⁸. Lab results for active TB include smear-positive, culture-positive, or molecular detection of MTB like GeneXpert system. These individuals may require respiratory⁹.

Millions of people worldwide continue to contract tuberculosis, with 10 million new cases each year, 90% of which are adults (aged ≥ 15 years), and 9% involving people living with HIV, particularly in Africa (72%). TB caused an estimated 1.3 million deaths in HIV-negative individuals and 300,000 deaths among HIV-positive TB patients. The TB epidemic's severity varies by country, with Rwanda reporting 7,000 new cases. Interestingly, TB-related deaths in Rwanda are lower among HIV-positive individuals was 320 deaths compared to HIV-negative individuals which were 600 deaths^{10,18}. The lack of systematic and regular screening for high-risk groups, including HIV-negative individuals, and the absence of specific surveillance systems for TB in groups like diabetics, undernourished people, and health workers, hinder effective diagnosis and prioritization¹¹. This study aims to identify additional clinical risk factors for TB activation and support better management and control of the disease.

II. MATERIAL AND METHOD

➤ Study Area

The study was conducted at Kibagabaga District Hospital located in Gasabo district. KDH serves as district hospital that provides the highest possible quality services in the health sector where it delivers healthcare service to

the general Population that comes from different Rwanda Health centers.

➤ Study Design

This was retrospective study collected data of two years from 1st January 2017 to 31st December 2018. Clinical conditions that are associated with progression of latent TB to active TB was assessed by reviewing clinical information of HIV negative patients whose TB results are positive via Laboratory information system and other records.

➤ Study Population

The retrospective study was conducted among 154 patients that attended KDH in the study period of 24 months.

➤ Inclusion Criteria

The study included all patient who attended KDH in the study period who were TB positive with a known HIV status.

➤ Exclusion Criteria

The study excluded all patient who attended KDH in the study period who were TB negative.

➤ Ethical Approvals

The proposal of this study was submitted at Ruhengeri Institute of applied sciences and Kibagabaga District Hospital's ethic committee. Both institutions approved this study to be conducted as proposed. Personal identifications of participants were kept confidential hence; anonymous presentation of data was used.

➤ Sample Size and Data Collection Technique

This study recruited 907 participants however, only 154 cases of TB progression were identified and analyzed together with associated risk factors in HIV-negative individuals. Clinical data were reviewed for HIV-negative patients with positive TB results. Information such as age, sex, address, and HIV status was collected from TB recording books. Each patient's record included a risk factor code, and if no risk factor was specified, additional details were retrieved from hospital archives.

➤ Laboratory Analysis of Sputum Sample

The GeneXpert system technology is an automated molecular tool for diagnosing TB by detecting TB bacteria DNA and resistance to Rifampicin through genetic mutations were used to analyse sputum samples. Additionally, the Auramine O stain was also used to visualize acid-fast bacilli like MTB by binding to mycolic acid in the cell walls, producing bright yellow or orange fluorescence against a green background under a fluorescent microscope.

➤ Statistical Analysis

After data collection, SPSS was used to organize and analyse data. The analysed data was presented using descriptive statistics, frequencies, percentages and graphs. Chi-square test was used to test for relationship between variables.

III. RESULTS AND DISCUSSION

This chapter presents the research findings. The results were interpreted according to the specific objectives as answers to the research questions checking the verification of hypotheses. The discussion is also made

by comparing the present study to other related ones carried out elsewhere near and far on the globe.

➤ Demographic Characteristic of Participants

The table below shows the demographic characteristics of participants, their frequencies and percentage

Table 1 Demographic Characteristic of Participants

Characteristics	Frequency	Percentage (%)
Gender		
Male	554	61.1
Female	353	38.8
TB Status		
Positive	154	17
Negative	753	83
HIV Status for TB Positive participants		
Positive	48	31.2
Negative	106	68.8
Age group for TB Positive participants		
Below 15	1	0.6
[16-25]	30	19.5
[26-45]	91	59.1
[45-60]	25	16.2
Above 60	7	4.6

The data are presented as frequency and percentage unless otherwise indicated. N=907.

This table shows the repartition of a total of 907 participants. The results show that the majority are men 5544 (61.1%) whereas women are 353 (98.9%). For TB positive participants the majority age group, including male and female, is 26-45 years with 91 (59.1) and the lowest age group is below 15 years (0.6%). These results are supported by Marcoa *et al.* (2018) noted that Men are more likely to be suspected and diagnosed with TB than

women men mostly because men are more likely to report risk factors associated with TB exposure¹². In addition, there is a study conducted by Dodd *et al.*, (2016) that also reported that higher rates of TB infection are seen in 25-40 age group¹³.

➤ Prevalence of HIV Status in TB Positive Participants

The table below shows the prevalence of HIV status participants with TB positive participants during the study period.

Table 2 Prevalence of HIV Negative Patients with TB Positive

Hiv status	Frequency	Prevalence (%)
Negative	106	68.8
Positive	48	31.2
Total	154	100

The data are presented as frequency and percentage unless otherwise indicated. N=154 for TB positive.

Table 2 shows the prevalence of HIV negative who were positive when tested for TB. HIV negative patients with TB have a prevalence of 68.8% which is higher than the prevalence of HIV positive with TB which is 31.2%. These results are supported by a study conducted by Fenner *et al.* (2012) in Swiss where it was found also that the number of HIV negative participants was greater than the number of HIV positive participants all with TB

positive¹⁴. Moreover, WHO report shows that in Rwanda, mortality rate of HIV-associated TB is lower than those in HIV negative people. Mortality in HIV negative is 600 deaths whereas mortality in HIV negative is 320 deaths¹⁰.

➤ Risk Factors of TB in HIV Negative Patients

The table below illustrates the risk factors that might be associated with progression of LTBI to ATB in HIV negative participants.

Table 3 The Risk Factors of TB in HIV Negative Patients

Factor	Frequency (%)
Aged above 55	1(0.9)
Close contact with TB positive	8(7.5)
Collective housing	13(8.4)
Drink alcohol	11(7.1)
Smoke	7(6.6)
TB positive in Kigali district	5(4.7)
Prisoner	1(0.9)
More than 2 factors	3(2.8)

The data are presented as frequency and percentage unless otherwise indicated.

The table shows different factors that are associated with TB activation in HIV negative participants. The factors include: being aged above 55 (0.9%), being in close contact with a TB positive person at 7.5%, collective housing at 8.4%, drinking alcohol at 7.1%, smoking at 6.6%, living in Kigali district at 4.7%, imprisonment at approximately 1%, and some participants had more than two factors at 2.8%, mostly drinking alcohol and smoking at the same time. Unfortunately, only 38.9% of the

participants had a known factor that might have led to the activation of TB and the remaining 61.1% of the cases had no specified factor. The factors are similar to those found by Narasimhan *et al.* (2013), along with malnutrition, young age, emerging variables such as diabetes, indoor air pollution, use of immunosuppressive drugs and cancer^{5,18,20}.

➤ Association of Different Factors with TB Status

The table below shows the association of age, sex, and the illustrated risk factors with TB status.

Table 4 Association of Different Factors with TB Status

		Value	DF	P value
Age	Pearson Chi square	15.578	4	0.004
Sex	Pearson Chi square	117.811	2	0.000
Risk Factors	Pearson Chi square	518.859	9	0.000

The p value of less than 0.05 was considered statistically significant.

The study has considered different risk factors that might play a role in the activation of TB in HIV negative such as drinking alcohol, smoking, collective housing, living in Kigali district, close contact with TB positive people, age and sex. Chi-squared was used to calculate P value and to ascertain the degree of association between these risk factors and the activation of TB by means of SPSS. The risk factors were found to be statistically significant in association with TB activation. Drinking alcohol and Smoking are among the factors that were found to be associated with TB activation in HIV negative people, this is in confirmation with studies conducted by Rehm *et al.* (2009) and Alavi *et al.* (2012) that both noted that these factors impact the body's immune system and make it more susceptible to TB infection^{14,15}. Age and sex are also found to be associated which is supported by Marcoa *et al.* (2018) that noted that men are more affected and stated that different factors have been proposed to explain this gender gap¹³. And also, for age, there elderly people and infants have a weak immune hence more exposed to TB activation^{16,21}.

Furthermore, living in Kigali district is considered a risk factor of TB since Kigali is high TB prevalence district in the country as reported by RBC. Other factors affecting TB in Kigali is the urban setting like crowding conditions in the capital city following rural population migration and access to diagnosis^{17,21}.

The factors such as collective housing, close contact and being in prison are in acceptance by a study conducted by Narasimhan *et al.* (2012) that noted that these factors increase the exposure to TB bacilli and the places have poor indoor air ventilation hence increasing the risk of TB infection to the people that live in the collective housing and prisons⁵.

IV. CONCLUSION

This study provides insights into the prevalence of TB in HIV-negative individuals and factors linked to the progression from latent TB (LTBI) to active TB (ATB). It highlights the role of age, sex, smoking, alcohol use, living conditions, and imprisonment in TB activation, with a 68.8% prevalence of TB among HIV-negative cases. While TB is a leading cause of death in people with HIV, it also significantly impacts HIV-negative individuals, a group often overlooked in existing research. The study calls for enhanced TB control measures, LTBI screening, and increased awareness among health workers and the public, aligning with global TB strategies focused on at-risk populations and proactive monitoring.

Future research should explore the progression from latent to active TB in HIV-negative individuals, focusing on immune and genetic influences. Identifying risk factors such as chronic diseases, malnutrition, and socioeconomic conditions can improve disease prevention.

- *Conflict of Interest:* The authors declare no conflicts of interest in conducting and publishing this article whether financial or non-financial
- *Source of Finding:* none
- *Consent for publication:* Not applicable.

• *Ethical Approvals*

The ethics and research committees at INES–Ruhengeri and Kibagabaga District Hospital approved this study.

• *Availability of Data and Materials*

The data supporting the findings of this study are available from the primary corresponding author upon reasonable request. However, the data are not publicly accessible due to privacy concerns and ethical restrictions related to the sensitive nature of the information collected from TB and HIV patients.

• *Funding Declarations:* not applicable

• *Contribution of Authors*

FU and SU conceptualized and initialized the study; SN, SU, DHG, LM, AU, and PN: data collection and analysis; JBM & FU: technical customization and original article manuscript writing. YLB, EB & JBM: Senior review of the project. All the authors contributed to the review and finalization of the original manuscript.

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