IJSCIA

International Journal of Scientific Advances
ISSN: 2708-7972
Volume: 5 | Issue: 1 | Jan – Feb 2024 Available Online: www.ijscia.com
DOI: 10.51542/ijscia.v5i1.7

Profile of Prisoners with Latent Tuberculosis Infection (LTBI) In Correctional Institution Level IIA Kerobokan, Badung, Bali

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ABSTRACT

Background: Prisoners have a high risk of being infected with latent Mycobacterium tuberculosis (LTBI). Crowded living conditions, poor ventilation, and inadequate facilities lead to a high risk of Mycobacterium tuberculosis (M.tb) transmission in correctional institutions (CI). TB disease causes a decline in the health of prisoners so it affects the quality of life while serving in prison. For this reason, it is necessary to conduct research on the profile of prisoners with LTBI. The results can later be used as a consideration for improving the health status of CI. This study was conducted in July 2023 in Level IIA prison, Kerobokan, Badung, Bali with variables in the form of characteristics of prisoners with positive LTBI status. ***Methods:*** Sample collection using cluster sampling by taking all prisoners in 1 block who have active TB patients. Prisoners underwent Tuberculin Skin Tests to determine LTBI status. ***Results:*** Prisoners with LTBI were found with the following characteristics: female gender (56.67%), aged <60 years (93.3%), smoking history (70%), length of stay in prison ≥12 months (73.3%), drug users (36.67%), history of alcohol consumption (50%). ***Conclusion:*** This study provides an overview of the profile of prisoners with LTBI in level IIA Kerobokan prison, Badung, Bali. Latent TB infection was more prevalent among female prisoners with female gender, young age, active smokers, drug and alcohol consumption, and length of stay in prison more than 12 months.

Keywords: latent tuberculosis infection; tuberculin skin test; correctional institutions; prisoners

INTRODUCTION

Tuberculosis (TB) is an important health problem in Indonesia caused by *Mycobacterium tuberculosis* (M.tb). Indonesia is a high TB burden country, where in 2022 WHO reported pulmonary TB caused 1.3 million deaths. Indonesia became the second highest contributor to tuberculosis cases after India with the incidence of India at 28%, Indonesia at 9.2%, China at 7.4%, Philippines at 7%, and Pakistan (at 5.8%) respectively [1].

Latent *Tuberculosis Infection* (LTBI) is a condition where the immunity of an individual infected with *Mycobacterium tuberculosis* (Mtb) is unable to eliminate Mtb from the body completely but can still control the development of Mtb so that TB disease does not occur. According to WHO, LTBI is defined as a status characterized by the presence of an immune response to Mtb but without clinical evidence of active TB.

LTBI can progress to TB disease when the patient's immune system declines to fight Mtb. Without appropriate management, 5-10% of LTBI will progress to TB disease and approximately 50% progress to TB disease within two years [2,3]

In 2022, there were an estimated 10.6 million people with active TB cases and a total of 1.3 million deaths. Nearly a quarter (23%) of the world's population of 1.7 billion subjects is estimated to have LTBI [1,4]. Several studies have shown that, on average, 5–10% of LTBI will develop active TB disease, usually within the first 5 years after initial infection. Based on the latest WHO guideline, the global burden of LTBI in 2014 was estimated at 1,700,000,000 individuals [5]. Of the total number, 35% of sufferers come from the Southeast Asian region, especially Indonesia.

Meanwhile, the *End TB Strategy* target to *be* achieved by 2035 combines efforts to effectively treat TB disease and prevent TB disease through the administration of Tuberculosis Preventive Therapy (TPT) in LTBI cases. Minister of Health Regulation No. 67/2016 on TB Control has set targets for the national TB Control program in Indonesia, namely elimination according to the *End TB strategy target* in 2035 and TB disease-free in 2050 [4,6,7]. In addition, the TPT coverage target reported in the 2020-2024 period by the Ministry of Health data is 2,922,056 household contacts of individuals with bacteriologically confirmed TB disease, 258,960 People Living With HIV/AIDS, 290,966 other risk groups where prisoners are included. [3]

Tuberculin Skin Test (TST) examination is one of the LTBI examinations recommended by WHO [4,8]. The TST examination is still the first choice for LTBI diagnosis because this modality is cheap, practical, does not require specialized skilled personnel, and is widely available compared to the IGRA examination. Identifying people with LTBI is important for TB control and elimination because LTBI treatment can prevent infected people from developing TB disease and stop the further spread of TB. [6]

Globally, the prevalence of TB has been reported to be higher among prisoners in correctional institutions than among the general population. The crowded conditions and inadequate facilities in prisons are thought to be favorable conditions for TB transmission among prisoners. Factors influencing this include conditions in CI.

Such as poor ventilation, overcrowding, poor nutritional status, difficult access to health services, suboptimal management, and poor immunity of prisoners. This situation, especially in Kerobokan Level IIA Prison, Badung, Bali, is suspected to have contributed to the increased vulnerability of prisoners to TB transmission.

Kerobokan Class IIA Correctional Institution located in Badung Regency, Bali Province, has 1,022 prisoners. Kerobokan Level IIA prison has a 1 TB isolation block with 6 TB patients in 2022. Suspected TB cases in Kerobokan Level IIA Prison were assessed clinically and then diagnosed based on sputum TCM results.

There was an increase in suspected TB cases at LP IIA Kerobokan, namely 38 people in 2021 and 48 people in 2022. Measurement of the prevalence rate of LTBI in Kerobokan Level IIA prison has never been carried out so steps to prevent active TB cases cannot be carried out comprehensively. Based on the various problems above, the author is interested in further researching the profile of prisoners with LTBI in Level IIA Kerobokan Prison, Badung, Bali.

METHODS

This study is descriptive using a *cross-sectional* research design to determine latent TB infection in prisoners at Level IIA Kerobokan Prison, Badung, Bali. Inclusion criteria include cooperative patients and willingness to become research subjects. Exclusion criteria: 1) Having TB symptoms such as cough ≥ 2 weeks, shortness of breath, night sweats, and weight loss in the past month; 2) Currently undergoing TB treatment; 3) Have ever suffered from TB and have a history of TB treatment in the last 2 years. Data analysis will be carried out with *statistical software* through analytical statistical analysis, namely 1). Descriptive analysis to determine the demographic characteristics of the subject; 2). Determination of *cut-off* age using the median value; 3) Viewing the profile of prisoners with LTBI in Level IIA Kerobokan prison, Badung, Bali; 4) Viewing the description of characteristics (smoking status, length of stay, age, diseases suffered) in prisoners with LTBI and not using *chi-square* analysis.

RESULTS

This study obtained a total of 100 samples of prisoners in Kerobokan prison who met the inclusion and exclusion criteria. The basic characteristics of the sample were found to be mostly female (70%), with an average age of 36 years, most samples had no history of the disease (75%), most samples had no history of allergies (85%), most samples smoked (69%) with an average of 12 years of smoking, the average sample had lived in prison for 26.8 months, most samples had a history of drinking alcohol (51%) with an average of 5.19 years of consumption, most samples consumed drugs (51%) with an average of 9.8 years of use, most of the HIV test results were negative (91%). The results of the basic characteristics of the sample can be seen in Table 1.

TABLE 1: Basic Clinical Characteristics of Patients.

Variables	Total (n=100)
Gender	
Male	30%
Female	70%
Disease History	
None	75%
Asthma	4%
DM	4%
TB	1%
HT	5%
Hepatitis	1%
HIV/AIDS	8%
Heart	2%
Breast Cancer	1%
Kidney failure	1%

Variables	Total (n=100)
Allergy History	
None	85%
Amoxicillin	8%
Powder	1%
Dust	1%
Seafood	5%
Smoking	
Yes	69%
No	31%
History of Drug Use	
There is	51%
No	49%
HIV Status	
Yes	8%
No	92%
History of Contact with TB Patients	
Yes	100%
No	0
Age (Average)	36,3
Length of smoking (average)	12,1
Length of time in prison (average)	26,8
Length of alcohol consumption (average)	5,19
Drug Duration (average)	9,80

Based on the characteristics of the TST examination (Table 2), it was found that most of the 99% TST examinations had been carried out, only 1% were not due to positive sputum TCM results. For TCM sputum was examined in all samples 100%, and for latent TB examination results obtained 69% negative.

TABLE 2: Characteristics based on Latent TB examination.

Variables	Total (n=100)
TST examination	
Done	99%
No	1%
TCM Sputum Examination	
Done	100%
TCM Sputum	
Positive	1%
Negative	99%
Latent TB	
Positive	30,3%
Negative	69,7%
Pulmonary TB	1%

Based on the characteristics of samples with TST examination results (table 3), 30.3% of samples were infected with latent TB with female gender more than male. A total of 8.08% of samples with positive latent TB infection had comorbid diseases. Samples with positive latent TB infection mostly had a history of smoking (21.21%). All samples had a history of contact with TB patients during their detention.

TABLE 3: Characteristics based on Samples infected with LTBI.

Variables	Positive Latent TB Infection (n= 30)	Latent TB Infection Negative (n=69)	Total (n=99) *
Gender			
Male	13.13% (13)	16.16% (16)	29.3% (29)
Female	17.17% (17)	53.53% (53)	70.7% (70)
Age			
< 60 years	28.28% (28)	66.66% (66)	94.94% (94)
≥ 60 years	2.02% (2)	3.03% (3)	5.05% (5)

Variables	Positive Latent TB Infection (n= 30)	Latent TB Infection Negative (n=69)	Total (n=99) *
Comorbid Diseases			
No	22.22% (22)	53.53% (53)	75.75% (75)
Yes	8.08% (8)	16.16% (16)	24.24% (24)
HIV-AIDS	3	5	8
Hypertension	2	2	4
Diabetes Mellitus	1	3	4
Breast Cancer	0	1	1
Chronic Renal Failure	0	1	1
Hepatitis	1	0	1
Asthma	2	2	4
Heart	0	2	2
Smoking History			
Positive	21.21% (21)	46.46% (46)	67.67% (67)
Negative	9.09% (9)	23.23% (23)	32.32% (32)
Length of stay in prison			
< 12 months	7.07% (7)	22.22% (22)	29.29% (29)
12-24 months	11.11% (11)	25.25% (25)	36.6% (36)
> 24 months	12.12% (12)	22.22% (22)	34.4% (34)
Drug users			
Yes	11,11% (11)	35.5% (35)	46.46% (46)
No	19.19% (19)	34.34% (34)	53.53% (53)
History of Alcohol Consumption			
Yes	15.15% (15)	36.36% (36)	51.51% (51)
No	15.15% (15)	33.33% (33)	48..48% (48)
History of Contact with TB Patients			
Yes	30.30% (30)	69.70% (69)	100% (99)
No	0	0	0

* : 1 out of 100 samples were found to be positive in TCM sputum examination and were therefore excluded.

DISCUSSION

In this study, a total of 100 samples of prisoners in Kerobokan prison were examined. The basic characteristics of the samples were found to be mostly female (70%). Of the total 100 samples, one sample was excluded from data analysis due to positive sputum TCM results. Based on the results of the existing study, the male gender was predominant in active tuberculosis. Gender inequality in socio-cultural status is often cited as a contributing factor to gender differences in active TB patients. In this study, residents with LTBI were found to be female (17 people). This result may be due to the fact that there were more female samples (n=70) than male samples (n=29). Gender differences in the prevalence of LTBI have rarely been studied and need to be clarified. In a *cross-sectional* study conducted in a TB-endemic area, Ting WY et al evaluated patients at high risk of LTBI and progression from LTBI to active TB from 2011 to 2012. Sex differences in the prevalence of LTBI and clinical predictors for LTBI were investigated. Associations between age, smoking status, and sex disparities in LTBI were also analyzed. A total of 1,018 high-risk individuals were included for analysis, including 534 men and 484 women. The proportion of ILTB was significantly higher in males compared to females (32.6% vs 25.2%, p = 0.010). The difference in LTBI proportion between genders was most prominent in older patients (age ≥55 years). Male gender was not an independent factor for LTBI (p = 0.88). In conclusion, although the proportion of LTBI was higher in males, there were no significant sex differences in LTBI among high-risk individuals after adjusting for age, smoking status, and other clinical factors [9].

The average age of the sample was 36 years. Most of the sample was less than 60 years old. This is due to the average age of the inmates who occupy Kerobokan IIA Correctional Institution is younger. Among the 94.94% of samples aged <60 years, 28.28% of them had positive TST results. Of the 30 prisoners with LTBI, two samples were more than 60 years old, one of whom had comorbid diseases of hypertension and chronic renal failure. Based on the age of LTBI occurrence, the LTBI rate in people aged 15 years and over was 20.3% and the infection rate also increased with age (Gao et al., 2022). Several multicenter studies have reported that the LTBI burden and annual Mtb infection rate are both significantly higher in elderly people compared to younger people in rural areas in China [10].

Most of the samples had no history of disease (75%). Of the 30 samples with LTBI infection, only eight had comorbid diseases. Three samples had HIV-AIDS, two samples had hypertension, one sample with diabetes mellitus (DM), one sample with hepatitis, and two samples with asthma. The association of DM with the occurrence of LTBI, due to the condition of hyperglycemia, insulin resistance, macrophage and lymphocyte function, and abnormal levels of homeostatic cytokines such as type 1 and type 17 cytokines, DM patients are more susceptible to TB infection. In addition, in LTBI patients, DM may reduce protective CD4+ and CD8+ T cell responses. These T cells can produce IFN-γ, TNF-α, and IL-2, which have been shown in previous studies to have important functions during M. tb infection. In DM patients, lower frequencies of myeloid and plasmacytoid dendritic cells (DCs), and classical and intermediate monocytes, as well as significantly higher frequencies of non-classical monocytes were also observed in other studies, compared to individuals without DM, resulting in an increased risk of developing LTBI [11,12].

Meanwhile, hypertension was present in two residents with positive TST. Chronic inflammatory conditions in hypertensive patients are generally found to have increased *Reactive Oxidative Stress* (ROS), and decreased levels of T lymphocytes and Interleukin. This is associated with hypertensive patients being more susceptible to infection (Sadik et al., 2022). The prevalence of hypertension was higher in the LTBI group (58.5%, 95%CI 52.4-64.5) than without LTBI (48.3%, 95%CI 44.5-52.1) (prevalence ratio [PR]=1.2, 95%CI 1.1-1.3) [13].

There were three HIV-positive prisoners with latent TB infection. HIV-positive individuals have an increased risk of contracting TB and progressing to active disease through reactivation of LTBI. Analysis of TB incidence rates in an HIV-positive cohort study in the UK showed high rates in black Africans, those with low blood CD4 counts, and higher rates in whites than in the HIV-negative white population. This is despite widespread access to and use of antiretroviral (ARV) therapy. The WHO's increasing push to identify and treat LTBI in HIV-positive people as part of TB control, particularly in high HIV prevalence/low-income settings, is supported by a Cochrane meta-analysis which found that LTBI treatment in this group reduced the risk of active TB by 32%.5 HIV/TB mortality remains high in the UK. Currently, LTBI screening in HIV-positive people is recommended by the *British* HIV *Association* (BHIVA) and the *National Institute for Health and Care Excellence* (NICE). The NICE guidelines in place at the time of this evaluation began in 2011. BHIVA recommends screening with the IGRA test which relies on a combination of criteria including region of origin, duration of ARV receipt, and CD4 count. NICE recommends screening all people with CD4 counts of 200-500 cells/mm3 with IGRAs plus the additional option of tuberculin skin test (TST), with a definitive recommendation of IGRAs plus TST in those with CD4 counts <200 cells/mm3 [14].

Most of the samples smoked (69%) with an average of 12 years of smoking. Of the 30 samples with LTBI, 21 had a history of smoking. Studies have shown that smoking increases the risk of respiratory infections, such as TB, and therefore has an adverse impact on respiratory immune function. Smoking is also associated with a negative prognosis for TB. The ciliary dysfunction and hormonal effects of smoking facilitate TB infection. Smoking can also increase the risk of relapse, by aiding the persistence of Mycobacterium tuberculosis (M.tb) infection after treatment. Once infected, TB bacteria may remain dormant in the body, in a dormant or latent form. Data from several studies suggest that one-third of people worldwide suffer from LTBI. LTBI is a state in which the body's immunity can control the infection but is unable to eradicate M.tb completely. WHO emphasizes the prevention of frequent TB risk factors as a TB control strategy. In addition, several studies confirm evidence of an association between smoking and LTBI. Therefore, WHO recommends tobacco cessation as part of TB control programs. It has previously been observed that awareness and treatment of LTBI, especially in high-risk individuals, can improve TB control and elimination. Individuals with respiratory symptoms and those with possible exposure to TB are considered a high-risk group for expanding LTBI into active TB and should be considered for ILTB evaluation and treatment [15,16].

Most samples had a history of drinking alcohol (51%) with an average of 5.19 years of consumption. Of the 51 samples who consumed alcohol, 15 had LTBI. The increased risk of TB disease due to alcohol use is well known. A systematic review found that low to moderate alcohol intake was not associated with TB disease risk, but excessive alcohol use (≥40 g/day) increased the odds of TB disease 2.9-fold. In a more recent meta-analysis, alcohol intake ≤60 g/day had no effect on TB disease risk, but consumption >60 g/day was associated with a 68% higher risk compared to no alcohol use and showed a dose-response relationship with increasing levels >60 g/day [17,18].

The mechanisms underlying the association between higher levels of alcohol use and LTBI are thought to be due to abnormalities in biological, structural, and social behavioral pathways and are likely multifactorial. Chronic alcohol use impairs the innate and adaptive immune system, which may increase susceptibility to TB infection. Alcohol inhibits interferon-gamma production, suppresses alveolar macrophage function, and impairs antigen-specific T-cell activation and proliferation. Individuals with *Alcohol Use Disorder* (AUD) have a higher risk of LTBI due to frequent exposure to environments with high M. tb transmission (crowded and enclosed population spaces). From a structural standpoint, people involved in alcohol use may spend more time in congregate locations with increased TB transmission, such as bars, prisons, or homeless shelters.

From a social behavioral standpoint, they may be more likely to socially associate with others involved in alcohol use, who have higher rates of TB disease, and are more likely to have BTA-positive pulmonary TB, thus increasing infection [19,20].

Most of the sample consumed drugs (51%) with an average use of 9.8 years. 11.11% of the sample consumed alcohol and were positive for the tuberculin test. Drug use has been associated with a higher prevalence of LTBI and a higher incidence of TB. Several studies have shown that duration of injection drug use and older age is most commonly associated with LTBI. Studies comparing the prevalence of LTBI in injecting drug users with non-injecting drug users have yielded mixed results, suggesting that these groups are at equal risk of developing LTBI. The high prevalence of LTBI and longer periods of transmission may contribute to increased TB transmission rates among drug users. Evidence from contact investigations and molecular epidemiology studies suggests that the disproportionate incidence of TB disease among drug users is due to TB transmission, with identical DNA patterns ("clusters") among TBs. Cluster analysis has been used to identify outbreaks of drug-resistant TB among drug users in the UK and multidrug-resistant TB (MDR-TB) in Thailand, Argentina, Latvia, and Portugal. In the US, a TB outbreak occurred in a methadone treatment program, with one patient subsequently becoming the source of a hospital case of MDR-TB. TB outbreaks among non-injecting drug users are also caused by sharing drug equipment or cramped and poorly ventilated conditions [21].

The average length of stay in prison ranged from 12-24 months (36.6%) and >24 months (34.4%). Most of the sample with latent TB had been in prison for >12 months (n=23). Longer prison terms lead to a higher risk of LTBI. Many prisoners come from populations at high risk of TB infection and active TB disease (alcohol or drug users and people living with HIV) [22]. Structural and institutional factors that contribute to TB transmission in prisons include poor ventilation, overcrowding, delayed diagnosis, and inadequate treatment [23].

CONCLUSION

From this study it can be concluded:

- Latent TB infection was more prevalent among female prisoners with female gender, young age, active smokers, drug and alcohol consumption, and length of stay in prison more than 12 months.

- 100 of the asymptomatic prisoners who had close contact with active TB cases had undergone sputum TCM examination. Sputum TCM was found positive in 1% of cases. TST examination was done in 99 subjects, Examination results obtained 30,3% of subjects had LTBI.

ACKNOWLEDGMENTS

All patients, all authors, and all support in the paper

DECLARATIONS

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by Udayana University

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