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Characteristics of Tuberculosis Patients from A Single-Center Study in Kudus, Indonesia: Between Biological and Social Determinant

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ABSTRACT

Introduction: Tuberculosis is a major public health problem worldwide, with an estimated 10 million new cases annually and 1.4 million deaths reported in 2019 alone. Indonesia is currently the third-highest burden country and caused extremely high burden in economy. We aim to investigate the characteristics of TB patients especially those with comorbidities (HIV & Diabetes Mellitus) and to improve TB management and preventio at Kudus Regional Hospital. **Methods:** This study was an analytic observational study with a cross-sectional design. The population in this study were tuberculosis patients in Kudus Regional Hospital, based on medical records.

Results:

From a total of 409 samples, the population was dominated >19 years of age (78.5%) and male patients. 67.7% were low educated patients. Reactive HIV status was present among 7.2% of bacteriologically confirmed TB status and 16.2% clinically diagnosed of TB status. Positive DM status was present among 33% of patients with bacteriologically confirmed TB status and 21% with clinically diagnosed of TB status.

Conclusion:

Studying all the characteristics of the TB populations is essential for not only developing effective strategies to cotrol and prevent TB , but also to improve diagnostics, treatment and public health policies.

Keywords: *Tuberculosis, Demographic, Biosocial Determinant, Diabetes Mellitus, HIV*

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacterium Mycobacterium tuberculosis.[1,2] It is a major public health problem worldwide, with an estimated 10 million new cases annually[2] and 1.4 million deaths reported in 2019 alone. The highest incidence rates of TB are found in regions such as South-East Asia (44%), Africa (24%), and the Western Pacific (18%). Most TB cases occur in countries like India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), and Bangladesh (4%).[3]

TB is a significant public health issue in Indonesia, particularly in the Central Java region. Indonesia is currently the third-highest burden country and caused extremely high burden in economy.[3,4] The economic burden was about US$ 6.9 billion, of which lost productivity due to premature death was the largest contributor at about 86.6% or US$ 6.0 billion. Central Java is the fourth province in Java which have the highest TB prevalence, after Banten, West Java, and Jakarta.[5]

TB is curable and preventable, yet it remains a public health crisis due to the emergence of multidrug-resistant TB (MDR-TB).[3] TB is also a major problem among vulnerable populations such as the homeless, those with compromised immune systems, such as people with HIV-AIDS and individuals living in poverty. TB is the cause of 374,000 HIV-related deaths.[6] Management of TB requires certain strategic policy because TB is a complex disease with a wide range of social determinants that contribute to its incidence, progression, complications, and treatment outcomes. Social determinants are the conditions in which people are born, grow, live, work, and age, and they have a significant impact on health outcomes. Complications in TB with Diabetes Mellitus (DM) and HIV infection still become problem that cannot be underestimated.[7] Understanding these determinants is crucial for developing effective strategies to prevent and control TB.

In this study, we aim to investigate the characteristics of TB patients at Kudus Regional Hospital. Specifically, we will examine the demographic information of hospitalized TB patients and prove the correlation between TB-HIV and TB-DM. By analyzing these factors, we hope to gain a better understanding of the patient population affected by TB at this hospital and identify potential areas for improvement in TB management and prevention, especially from biomedical perspective and social aspects. This research has the potential to contribute to the development of more effective TB control strategies and improve patient treatment outcomes. Ultimately, our goal is to reduce the burden of TB on individuals and communities and work towards eradicating this devastating disease globally.

MATERIAL and METHODS

This study was an analytic observational with a cross-sectional design. The population in this study were TB patients in Kudus Regional Hospital, Central Java Province based on patient data recorded in medical records. The inclusion criteria of this study is TB patient from any age recorded in medical status. Incomplete data from medical record will be excluded. This study using consecutive sampling of 409 medical record patients with pulmonary TB from January to December 2023. In this study, univariate analysis aims to explain or describe the characteristics of each variable studied and is used to describe descriptively the frequency distribution and proportion of each variable studied. Meanwhile, bivariate analysis aims to explain the correlation between DM and HIV status to TB.

RESULTS

A total of 409 samples of patients with TB were obtained from the medical records according to the inclusion and exclusion criteria. The demographic and tuberculosis characteristics of the study samples are presented below.

Table 1. Demographic and tuberculosis characteristics of the study

Characteristics		**Subject (%) n= 409**
Sex		
	Male	245 (59.9)
	Female	164 (40.1)
Age (year, mean ± SD)		38.5 ± 20.9
Age Categorization (%)		
	Children (0-10 years)	59 (14.4)
	Adolescent (10-19 years)	29 (7.1)
	Adults (>19 years)	321 (78.5)
Education		
	Low Educated	277 (67.7)
	High Educated	132 (32.3)
TB Method of Diagnosis		
	Bacteriologically Confirmed	236 (57.7)
	Clinically Diagnosed	173 (42.3)
Anatomical Location		
	Pulmonary TB	342 (83.6)
	Extrapulmonary TB	67 (16.4)

Based on the results obtained, from a total of 409 patients, the mean age was 38.5 ± 20.9 years. The sample population was dominated by patients with an age category of >19 years 78.5%. Based on gender, male patients also dominated, at 59.7%. Based on the latest education, 67.7% of pulmonary TB patients received basic education (elementary school, junior high school). Based on TB characteristics, by TB status, the majority of the sample population were patients with bacteriological confirmed TB (57.7%) with the remainder (42.3%) being patients diagnosed with clinical TB. While from the anatomical location of TB, 83.6% were pulmonary TB.

Table 2. TB method of diagnosis and HIV status

TB Status	HIV Status		p-value
	Reactive (n%)	**Non-reactive (n%)**	
Bacteriologically Confirmed	13 (7.2%)	168 (92.8%)	0.018
Clinically Diagnosed	16 (16.2%)	83 (83.8%)	

Table 2 shows the HIV status in relation to the TB status. Reactive HIV status was present among 7.2% (n=13) of patients with bacteriologically confirmed TB status and 16.2% (n=16) of patients with clinically diagnosed of TB status, with a statistically significant difference between the groups (p=0.018)

Table 3. TB method of diagnosis and DM status

TB Status	DM Status		p-value
	Positive (n%)	**Negative (n%)**	
Bacteriologically Confirmed	63 (33%)	128 (67%)	0.021
Clinically Diagnosed	27 (21%)	101 (79%)	

Table 3 shows the DM status in relation to the TB status. Positive DM status was present among 33% (n=63) of patients with bacteriologically confirmed TB status and 21% (n=27) of patients with clinically diagnosed of TB status, with a statistically significant difference between the groups (p=0.021)

DISCUSSION

In terms of sex, it was found in this study that TB was more prevalent in male patients than female. These results are in line with several previous studies in Indonesia who conducted TB epidemiology research in Indramayu and found that 66.1% of pulmonary TB patients were male.[8] A similar percentage was obtained from the research in Kediri District (TB endemic

area) where 61.8% of TB patients were male.[9] A systematic review and meta-analysis taking data from low and middle income countries in 2016 concluded the similar finding of higher prevalence TB in male.[10] Gender differences in TB has been shown in prevalence rates, disease manifestation, disease progression, case fatality rates, response to treatment and along the continuum of TB pathogenesis and care.[10,11]

Biologically, sex is a crucial factor in determining health. This is because differences in genetics, hormones, and epigenetic regulation between sexes can affect the prevalence, manifestation, and treatment of diseases.[12] While taking into account in social determinant, men might have higher risk of behavioral factor. Behavioral factors such as smoking and alcohol use, which are more prevalent among men, can contribute to increased susceptibility to TB infection. There are also barriers faced by men in seeking or accessing healthcare which is demonstrated by the results indicating that men were less likely to participate in prevalence surveys. Furthermore, surveys that required participants to self-report signs or symptoms in initial screening procedures found relatively fewer cases among men.[10]

There is evidence that genetic susceptibility may play a role in the higher prevalence of tuberculosis (TB) in men compared to women. Several studies have identified genetic variants associated with susceptibility to TB, some of which may be more common in men than women. For example, a study found that the rs3764880 allele A (Met) was associated with susceptibility to TB in men, but this association was not observed in women. Another study found that variation in the X chromosome may be involved in the genetic predisposition to TB, from both Mendelian and complex genetic perspectives.[13]

However, it is important to note that these studies do not definitively prove that genetic susceptibility is the sole factor contributing to the higher prevalence of TB in men. Other factors, such as behavioral and environmental factors, may also play a role. For example, men are more likely to engage in high-risk behaviors, such as smoking and alcohol use, which can increase the risk of TB infection. Additionally, men may have higher exposure to TB due to occupational factors or other risk factors.[11,14,15] Men who smoke daily or occasionally are 47.3%, while women are only 1.2%.

In this study, the mean age of pulmonary TB patients at the Kudus Regional Hospital was 38.5±20.9 years, with 321 patients (78.5%) being adults (>19 years), followed by patients aged 0-10 years as many as 59 people (14.4%), and the last 10-19 years as many as 29 people (7.1%). Age is an important factor in the risk of developing tuberculosis (TB) and the severity of the disease. TB affects individuals of all ages, but certain age groups are more susceptible to the disease.

Children are at risk of developing TB due to their developing immune systems and exposure to the bacteria in their environment. Neonates and young children are more susceptible to severe forms of TB, such as meningeal and disseminated TB.[16,17] The elderly are at a higher risk of developing TB due to a weakened immune system, increased exposure to risk factors, and the presence of comorbidities such as diabetes and lung diseases. The elderly are also more likely to experience diagnostic difficulties, decreased completeness of treatment, and a higher risk of treatment failure.[18]

Age above 19 years is the productive age of humans. Similar results were also obtained by Hermansyah et al. in his research in Palembang.[19] It was found that the largest age group of TB patients was at a productive age. The result is also in line with a larger cohort in Indonesia. the prevalence of TB in the Indonesian population aged 15 years and over was 759 per 100,000. However, the highest TB prevalence was in the old age group (55 years and over) in the cohort.[20] Middle-aged adults are at an increased risk of developing TB due to a combination of factors, including increased exposure to risk factors and a higher likelihood of having underlying health conditions that weaken the immune system.[16,17] Productive age has a greater possibility of contact with TB due to work activities. A person suffering from TB at a productive age will result in disruption of work productivity and cause losses in the socio-economic aspect.

From educational background, 277 had low education (67.7%). Education level has been widely studied in relation to disease. Socio-economic determinants of health include the social, political, and economic conditions in which people are born, grow up, live, work, and age.[21,22] Globally, more than 90% of TB patients live in low- and middle-income countries, and cases remain concentrated in economically and socially disadvantaged groups.[23] When it comes to TB disease, many studies have found a link between TB and low education levels. Education level greatly influences a person's ability to absorb and receive information. With exposure to health information and education, a person will be careful not to be exposed to disease. Studies have shown that individuals with lower levels of education are more likely to have a higher risk of developing TB and may face challenges in accessing appropriate treatment and care. This is due to several factors, including lack of knowledge about TB, poorer health-seeking behaviors, and socioeconomic disadvantages that may limit access to healthcare services.[23,24] Research has shown that lower socioeconomic status is associated with higher TB rates. In South Korea, for example, there were substantial correlations between tuberculosis rates and socioeconomic status, with lower monthly household income and education level being linked to higher TB rates.[25] TB disproportionately affects low-income households and

those with limited financial resources. The financial burden of TB can be catastrophic, with costs including direct medical costs, direct non-medical costs, and indirect costs such as lost income. In many cases, the cost of TB treatment and care can exceed an individual's or household's income, leading to financial ruin or further impoverishment.[26]

In terms of the characteristics of TB found in this study, 236 (57.7%) were bacteriologically confirmed patients, while 42.3% were clinically diagnosed patients. Based on anatomical location, 342 patients (83.6%) were pulmonary TB patients. Meanwhile, 67 people (16.4%) were extrapulmonary TB cases. According to the 2022 European Centre for Disease Prevention and Control (ECDC) report, a total of 33,148 TB cases were reported in 2020. Of these cases, 73.1% were pulmonary TB cases, compared to 21.5% who were extrapulmonary TB cases.[27]

Studying the characteristics of TB populations in specific areas is crucial. By studying the prevalence, incidence, and distribution of TB cases in a particular area, researchers can gain insights into the severity of the disease and identify regions or populations that require more attention and resources for TB control and prevention. Studying TB populations may also help researchers identify factors that contribute to the spread of the disease, such as socioeconomic conditions, population density, and access to healthcare services.[20,28] This information can be used to develop targeted interventions to reduce the risk of TB transmission. Understanding the characteristics of TB populations help us to develop more effective diagnostic tools and treatment strategies tailored to the specific needs of the population. Furthermore, the findings from TB population studies can inform public health policies and resource allocation, ensuring that efforts to control and prevent TB are focused on the areas and populations most in need.

Understanding biological and social determinants is also crucial for developing effective strategies to prevent and control TB. Poverty is linked to other social determinants, such as lack of education and employment opportunities, which can further exacerbate the risk of TB infection and disease progression. Inadequate living and working conditions can also contribute to poor general health knowledge and lack of empowerment to act on health knowledge, increasing the risk of exposure to TB risk factors such as HIV, smoking, and alcohol abuse.[7,23] To address these social determinants, a more holistic approach is required, which continues to incorporate biomedical responses and also addresses the broader socio-economic determinants of TB. This includes pursuing overarching poverty reduction strategies, expanding social protection, reducing food insecurity, improving living and working conditions, addressing the social, financial, and health situation of migrants, and promoting healthy diets and lifestyles.

In this study show 29 had reactive HIV status, 13 (7.2%) with bacteriologically confirmed TB status and 16 (16.2%) with clinically diagnosed of TB status. HIV attack and weaken the immune system, broke the cell-adhesion within the airway epithelium and increases local inflammatory mediators.[29] After HIV infection, the risk of TB will increase eventhough CD4 count still high. This risk not always depend on lower CD4 count but also from the impairment of TB specific T cell. Infection of HIV limit the macrophage's capability to obstruct the growth of TB bacilli. [30] These consequences result in increased B cell activation, which impairs long-term serologic immunity, and a progressive loss of T cell functioning, including a reduced cytokine response to antigenic stimuli. These alterations take place in the lung as well as throughout the body, leading to serious pulmonary problems. [31] From research conducted in Uganda, increase rate of TB infection in line with increase HIV. Immune suppression plays an important role in TB with HIV. People with HIV have rapid progression to acute disease, estimated have 50% risk of developing TB.[32]

Our result showed the prevalence of diabetes mellitus among patient with bacteriologically confirmed TB status was 63 (33%) and 27 (21%) of patients with clinically diagnosed of TB status. Disturbance of immunological mechanisms related to DM explain the increased TB risk. High glucose broke the cell activation, phagocytic capacity, interfere the mechanisms of alveolar neutrophyls and macrophages, transmigration of leukocyte transmigration, delaying antigen presentation and weaken the mechanisms to fight against Mycobacterium tuberculosis.[33] Based on research conducted in China started from 2019 until 2021, the studies found that people with TB and DM may have some problems started from weight gain loss, prolonged fever, increased sweats, and dyspnea. These manifestation became worst related to severity lung involvement that caused of lesion in parenchymal lesion and cavities. Poor glycemic control will worsen the manifestation.[34] Active TB infection can make changes started from inflammation, increased free fatty acid levels and adipose tissue modulation which causes insulin resistance. This mechanism lead to development of type 2 diabetes if not handled properly. [35]

CONCLUSION

Studying the characteristics of TB populations is essential to understanding the disease burden, identifying risk factors, improving diagnostics, treatment, and monitoring disease trends. This information is crucial for developing effective strategies to control and prevent TB in specific areas, ultimately reducing its impact on public health. Moreover, genetic

susceptibility may contribute to the higher prevalence of TB in men compared to women, it is likely that a combination of genetic and environmental factors is responsible for this difference. Thorough DM and HIV screening programmes in nations where TB is still a major health concern, may help patients properly diagnosed and treated. Further holistic research in much larger scale is needed to better understand the complex interplay between these factors and to develop targeted interventions to reduce the burden of TB.

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