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Epidemiological Description of Tuberculosis in PKU Muhammadiyah Bantul Hospital in 2021-2023

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ABSTRACT

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Tuberculosis is an infectious disease caused by the Mycobacterium tuberculosis germ, which is easily transmitted through the air when an infected patient coughs, sneezes, or talks. Indonesia is one of the countries with a high burden of tuberculosis. The number of tuberculosis cases reported in Bantul Regency in 2022 was 732 cases. The objective of this study is to determine the epidemiological picture of tuberculosis in PKU Muhammadiyah Bantul Hospital in 2023. The research method of this study was an observational method with cross-sectional studies. The number of tuberculosis cases at PKU Muhammadiyah Bantul Hospital between 2021 and 2023 exhibited fluctuations. In terms of gender, males accounted for the majority of cases, comprising 54% of the total. The highest number of tuberculosis patients fell within the age group of 55-64 years, constituting 86% of all patients. Pulmonary tuberculosis was the most prevalent form, accounting for 72% of cases. Additionally, 17% of tuberculosis patients had diabetes mellitus, while 2% were confirmed to be HIV positive. The study concluded that the majority of patients at PKU Muhammadiyah Bantul Hospital were male, aged between 55-64 years. Most patients resided in Bantul and had pulmonary tuberculosis. The thoracic examination results were mostly positive. Additionally, there were fewer patients with diabetes mellitus and fewer cases of tuberculosis in patients who were HIV-positive.

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INTRODUCTION

Tuberculosis remains a significant public health issue in both Indonesia and globally¹. Tuberculosis is an infectious disease caused by the Mycobacterium tuberculosis bacteria. It is a

major cause of mortality worldwide, ranking among the top 10 leading causes of death. Individuals with tuberculosis can transmit the disease through the air when they cough or sneeze, releasing bacteria in the form of splashes ^{2,3}.

Various studies have revealed that many factors influence the incidence of tuberculosis disease⁴. Factors that cause tuberculosis include a history of previous tuberculosis⁵, age⁶, gender⁷ (in this case men are more at risk), socioeconomics⁸, and environment ⁹ (consisting of physical and non-physical environments). The findings of this study present convincing evidence that a polluted household environment amplifies the susceptibility to Tuberculosis in India¹⁰. Promoting a clean environment is crucial for eliminating TB, which remains a major contributor to mortality rates in India. The study identified environmental risk factors associated with tuberculosis (TB), including indoor smoke exposure, the type of cooking fuel used, the presence of a separate kitchen space, the materials used for the floor, walls, and roof, the number of individuals sleeping in a room, the sharing of toilets with other homes, and the absence of access to safe drinking water¹⁰.

Additional risk factors encompass the state of the body's immune system and the practice of smoking¹¹. Smoking has a significant impact on various organ systems, but it causes the most severe damage to the lungs. Smoking causes harm to the lungs and weakens the body's immune system, increasing the vulnerability of smokers to tuberculosis infection¹². Smoking may also lead to secondary consequences such as mechanical disruption of cilia function and hormonal changes ^{11,12}. Thus, all of these characteristics can contribute to an individual's heightened vulnerability to developing a TB infection.

Indonesia is one of the countries with the highest burden of tuberculosis among 8 other countries, namely India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%), and South Africa (3%)¹³. The prevalence of tuberculosis in Indonesia stands at 4.0% with Banten and Papua provinces topping the list with a prevalence of 8.0%, followed by West Java province with a prevalence of 5.0%, followed by Aceh, South Sumatra, DKI Jakarta, North Kalimantan, and West Papua provinces. The provinces of Bali and Bangka Belitung have the lowest prevalence in Indonesia at 1.0%, followed by the provinces of Yogyakarta and Riau with a prevalence of 2.0%¹³.

In 2022 the number of tuberculosis cases in Bantul Regency was recorded at 732 cases, this number decreased from 2021 when there were 739 tuberculosis cases. This number has increased compared to 2020, when there were 691 cases of tuberculosis in Bantul Regency. Based on gender, the number of male cases of tuberculosis in Bantul Regency is higher than female cases¹⁴.

PKU Muhammadiyah Bantul Hospital is a private hospital located in the city of Bantul. The services provided in this hospital are quite complete so it has become a referral hospital for many

health facilities in Bantul Regency. The study aimed to determine the epidemiological picture of tuberculosis in PKU Muhammadiyah Bantul Hospital in 2021-2023.

METHODS

This research is an observational study with a cross-sectional research design. The study's population consisted of all tuberculosis patients from all categories who received treatment at PKU Muhammadiyah Bantul Hospital between 2021 and 2023. The entire sample was utilized as the sampling approach. The study's sample consisted of 273 outpatient TB patients who met the inclusion and exclusion criteria, using medical data from the years 2021-2023. The study's sample was selected based on the inclusion criteria of having complete medical records, being newly diagnosed with tuberculosis at PKU Muhammadiyah Bantul Hospital between 2021 and 2023, and being older than 18 years old. The study's sample was selected based on the exclusion criteria of deceased patients.

The data analysis approach used in this study is univariate analysis, which examines the features of each research variable by generating a frequency and percentage distribution. After processing all the data, a frequency distribution table is generated, displaying the data in the form of percentages.

RESULTS

The characteristics of tuberculosis patients at PKU Muhammadiyah Bantul Hospital in 2021-2023 are presented in the form of diagrams. Variables related to the characteristics of tuberculosis patients are related to the number of tuberculosis patients, patient gender, age group, patient residence, anatomical location of the disease, thoracic photo examination, history of diabetes mellitus, and HIV history.

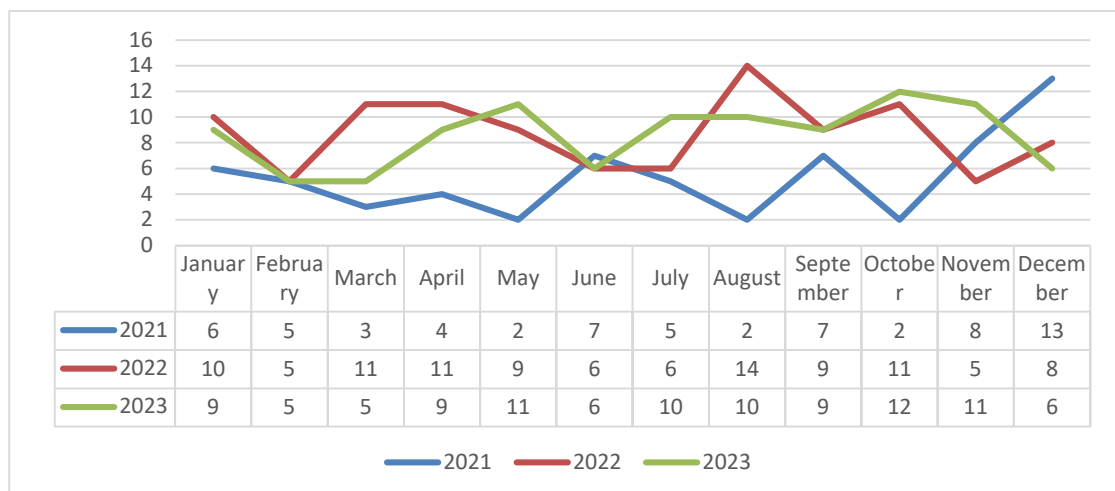


Figure 1. Trend of Tuberculosis Cases at PKU Muhammadiyah Bantul Hospital in 2021-2023

Figure 1 shows that the number of tuberculosis patients in PKU Muhammadiyah Bantul Hospital from 2021 to 2023 was the highest in 2022 with 105 cases, compared to 2021 where there were 64 cases, and in 2023 there were 103 tuberculosis cases in PKU Muhammadiyah Bantul Hospital.

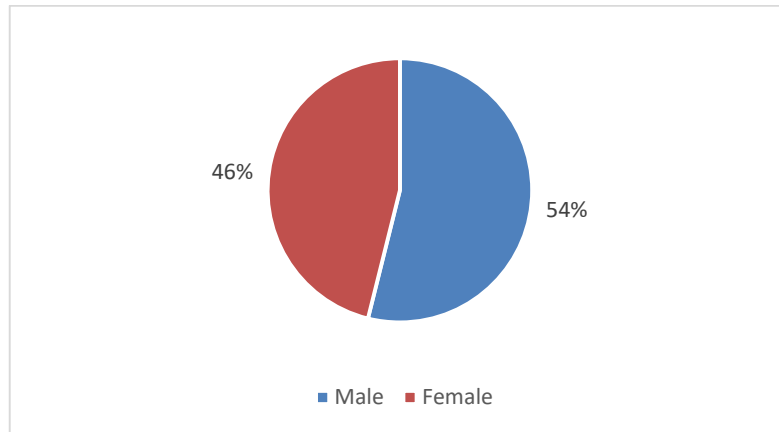


Figure 2. The proportion of tuberculosis cases based on gender at PKU Muhammadiyah Bantul Hospital 2021-2023

According to Figure 2, the cumulative data from 2021 to 2023 at PKU Muhammadiyah Bantul Hospital shows that tuberculosis is more prevalent in men. Specifically, there were 146 cases, accounting for 54% of the total, compared to 126 cases in women, which accounted for 46%.

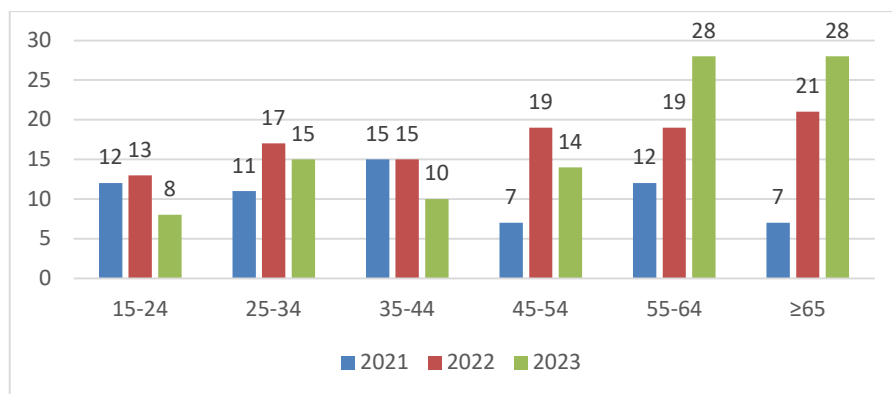


Figure 3. Frequency distribution of tuberculosis based on age classification at PKU Muhammadiyah Bantul Hospital in 2021-2023.

Figure 3 shows that in PKU Muhammadiyah Bantul Hospital in 2021-2023, cumulatively, tuberculosis was more prevalent in the 55-64 age group, with a total of 59 cases, whereas Figure 4 shows that 86% of tuberculosis patients in PKU Muhammadiyah Bantul Hospital in 2021-2023 come from or reside in Bantul Regency.

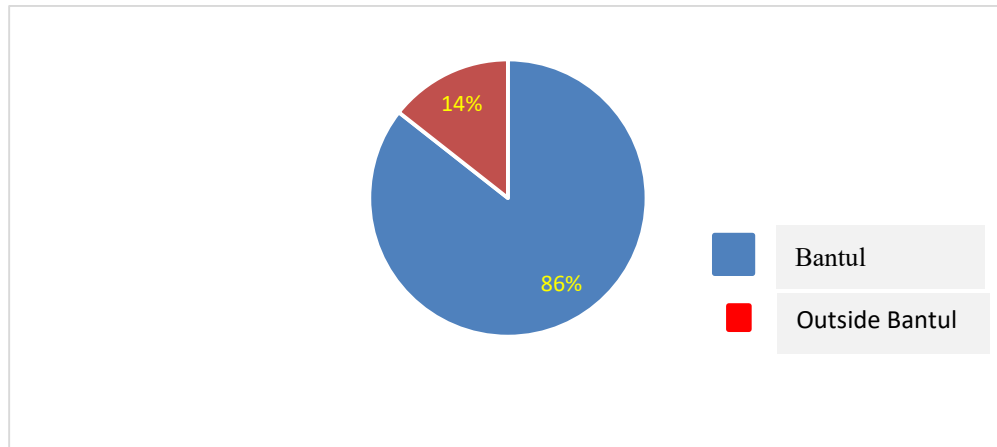


Figure 4. The proportion of tuberculosis cases based on place of residence at PKU Muhammadiyah Bantul Hospital in 2021-2023.

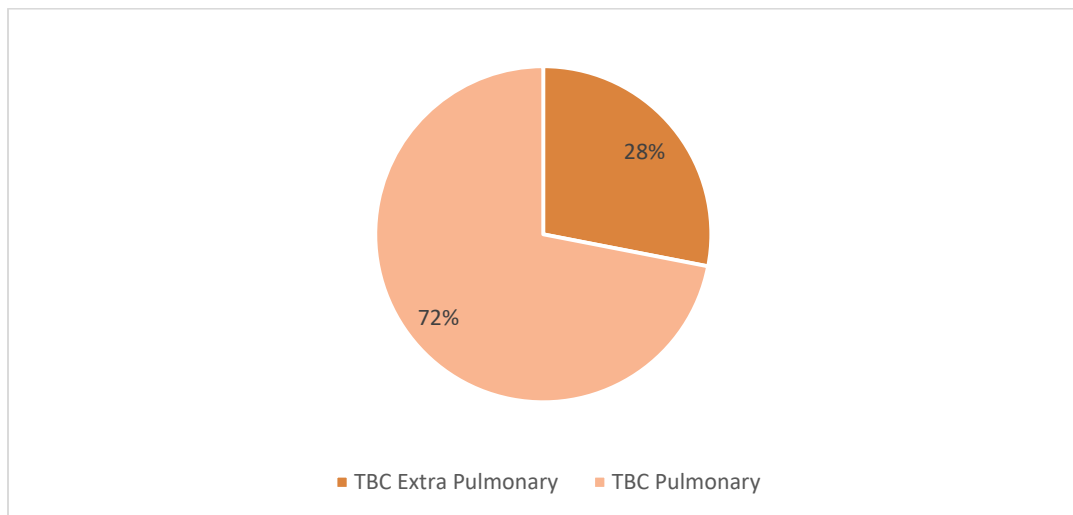


Figure 5. The proportion of tuberculosis cases based on the anatomical location of the disease at PKU Muhammadiyah Bantul Hospital in 2021-2023.

Figure 5 shows that tuberculosis patients at PKU Muhammadiyah Bantul Hospital in 2021-2023 cumulatively based on the anatomical location of the disease are more likely to suffer from pulmonary tuberculosis, namely 72% of cases, when compared to patients with extrapulmonary tuberculosis, which is 28%. Figure 6 shows that 68% of tuberculosis patients at PKU Muhammadiyah Bantul Hospital in 2021-2023 were positive for tuberculosis based on the results of the thorax photo.

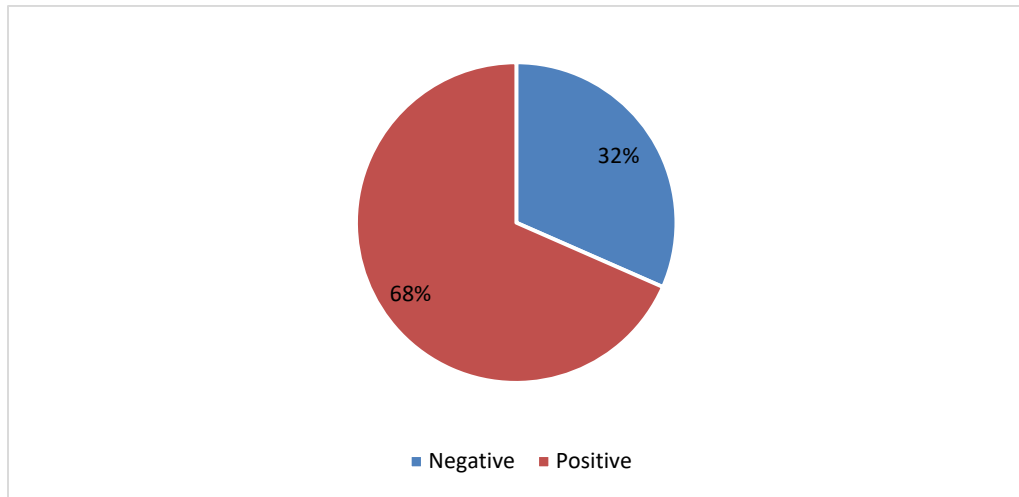


Figure 6. The proportion of tuberculosis cases based on the results of thorax photo at PKU Muhammadiyah Bantul Hospital in 2021-2023.

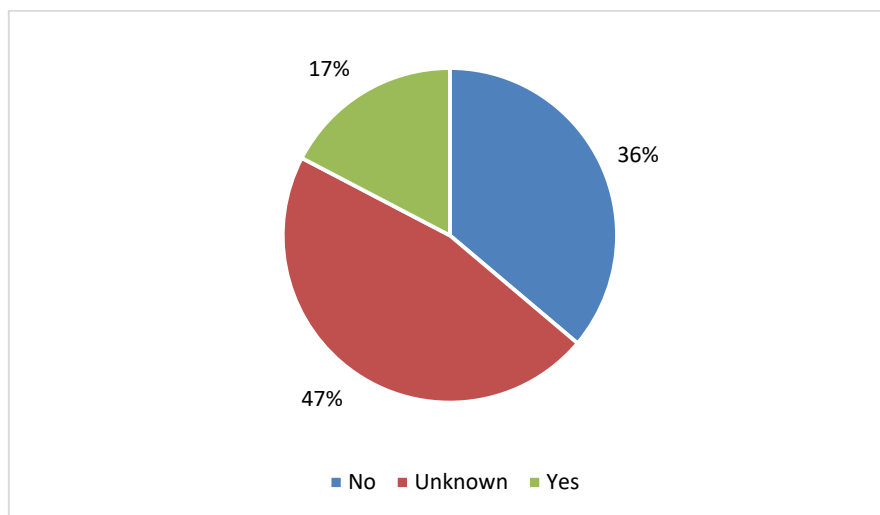


Figure 7. Proportion of tuberculosis cases based on history of diabetes mellitus at PKU Muhammadiyah Bantul Hospital in 2021-2023.

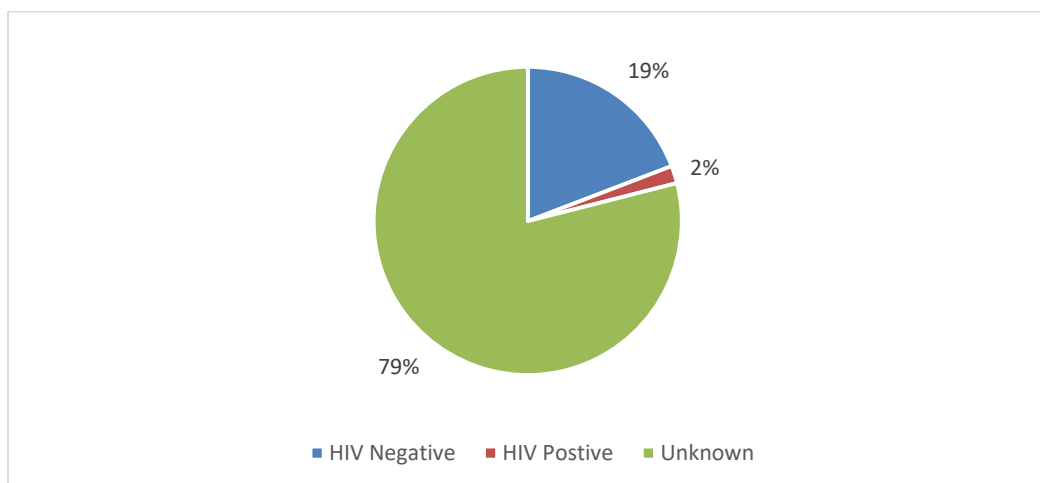


Figure 8. The proportion of tuberculosis cases based on HIV status at PKU Muhammadiyah Bantul Hospital in 2021-2023.

Figure 7 shows that 17% of tuberculosis patients at PKU Muhammadiyah Bantul Hospital in 2021-2023 had a history of diabetes mellitus, while 36% of tuberculosis patients did not have a history of diabetes mellitus. Figure 8 shows that tuberculosis patients at PKU Muhammadiyah Bantul Hospital in 2021-2023 are 2% HIV positive, while 19% are HIV negative and 79% are unknown.

DISCUSSION

Trend in the incidence of tuberculosis cases at PKU Muhammadiyah Bantul Hospital in 2021-2023

Based on the results of the analysis, it is known that the incidence of tuberculosis cases at PKU Muhammadiyah Bantul Hospital in 2021-2023 fluctuated every year, and cumulatively the incidence of tuberculosis cases occurred more in 2022, reaching 105 cases. Then in 2023, the incidence of tuberculosis decreased by two numbers to 103 cases, but this figure is still relatively high compared to the tuberculosis cases in 2021 which were only found in 64 cases.

Bantul Regency Health Office (2023) stated that until November 2023 there were 1144 cases of tuberculosis found. This number is still 58.67% of the predicted 1950 tuberculosis cases in 2023 in Bantul Regency. In 2022 the number of tuberculosis cases recorded in Bantul regency was 732 cases. This number has decreased compared to 2021, when there were 739 cases¹⁴.

The incidence of tuberculosis can be influenced by several factors. The first factor that can cause the incidence of tuberculosis is age because the highest incidence of tuberculosis disease occurs in adulthood, it is estimated that 75% of tuberculosis patients in Indonesia are in the productive age group. The second factor is gender, with tuberculosis affecting more males than females. The third factor is smoking, which can cause a decrease in the body's immune system, making the body vulnerable to disease. The fourth factor is environmental factors, *Mycobacterium tuberculosis* germs can live in dark buildings and do not get sunlight¹⁵.

The number of tuberculosis patients in 2021 is quite low compared to 2022 and 2023, probably due to the Covid-19 epidemic. This is consistent with several previous studies indicating that people with tuberculosis may be misdiagnosed as having COVID-19¹⁶. Furthermore, there is a possibility of an interaction between the two diseases, which could increase the mortality risk for TB patients who get COVID-19. There was a potential reduction in reported TB mortality due to the misclassification of certain patients who died from COVID-19 rather than TB, as numerous highly TB-infected patients died from COVID-19¹⁷. A study from China found similar results as well, that both TB incidence and mortality decreased immediately at the start of the COVID-19 pandemic¹⁸.

▪ **The proportion of tuberculosis cases based on gender at PKU Muhammadiyah Bantul Hospital in 2021-2023.**

The results of the analysis showed that the incidence of tuberculosis was more prevalent in the male group, with 146 cases, 54% of the total tuberculosis cases found in PKU Muhammadiyah Bantul Hospital from 2021 to 2023. During 1995-2022, the highest proportion of tuberculosis patients in Indonesia by gender was male with a range between 51.3%-59.6% compared to females with a range of 40.4%-48.7%. In 2022, the proportion of male tuberculosis patients reached 57.8%, higher than the proportion of female tuberculosis patients at 42.2%¹⁹.

Tuberculosis disease tends to be more prevalent among men than women³. Men are more susceptible to tuberculosis because men have heavy workloads and unhealthy lifestyles such as smoking²⁰. The impact of lifestyle behaviors in the spread of Mycobacterium TB infection is believed to be influenced by differences between men and women²¹. Nevertheless, Rhines stated in his research that there is a clear likelihood of an epidemiological sex bias in TB²¹. Whether the presence of a sex bias is caused by biological reasons, cultural factors, or a combination of both, it would have significant consequences in a contemporary demographic setting²¹. Although studies indicate that there are likely many undiagnosed instances of tuberculosis (TB) among women in impoverished countries, the existence of undetected TB among women does not necessarily prove that men and women have an equal susceptibility to TB²¹. This suggests that epidemiological models should consider the differences in TB prevalence and transmission based on sex²¹.

Frequency distribution of tuberculosis by age group at PKU Muhammadiyah Bantul Hospital in 2021-2023.

The analysis reveals that the prevalence of tuberculosis at PKU Muhammadiyah Bantul Hospital from 2021 to 2023 is highest in the age range of 55-64, with a total of 59 cases. The year with the highest number of instances was 2023, with 28 cases each in the age ranges of 55-65 and ≥65. Tuberculosis is a disease that can affect all age groups⁶. Older age groups are more susceptible to tuberculosis because at that age, the body's organs have decreased function, resulting in a weakened ability to fight germs, so Mycobacterium tuberculosis will easily enter the body⁵. In the productive age period of 15-59 years, a person has 5-6 times the susceptibility to suffer from tuberculosis, this is because in the productive age group, a person will tend to carry out higher activities, and the possibility of being exposed to Mycobacterium tuberculosis germs is also higher²².

The aged population is more vulnerable to tuberculosis (TB) illnesses and mortality due to several variables, including waning immunity, underlying disorders known as co-morbidities, and sensitivity to severe medication effects¹. Positive TB treatment outcomes and diagnosis are difficult to achieve in older people. For example, elderly people tend to have fewer classic TB

symptoms (such as cough, fever, night sweats, and weight loss), or TB lung lesions are commonly misdiagnosed as pneumonia. The difficulties in diagnosing and treating tuberculosis (TB) in the elderly have led researchers to suggest that (1) mechanisms to lower inflammation levels at the right time to prevent TB progression should be the focus of attention, and (2) strategies to prevent adverse drug effects should be the focus of attention to ensure successful TB treatment outcomes in this vulnerable and compromised population¹.

The proportion of tuberculosis cases based on place of residence in PKU Muhammadiyah Bantul Hospital in 2021-2023.

The analysis reveals that 86% of tuberculosis cases at PKU Muhammadiyah Bantul Hospital from 2021 to 2023 are concentrated in Bantul Regency. This can be attributed to the hospital's geographical location within Bantul Regency, which facilitates easier access for residents seeking treatment and is closer to their residential addresses.

The primary factor contributing to the persistently high tuberculosis (TB) rate in Bantul is the presence of social stigma²³. Environmental factors, such as the stigma surrounding tuberculosis sufferers, can influence medication adherence in patients^{23,24}. Tuberculosis patients often face social stigma due to the ease and speed of disease transmission. This environmental stigma leads to self-stigma among tuberculosis sufferers, resulting in a lack of confidence, shame, fear, and stress in their surroundings^{23,24}. Consequently, they may avoid social interactions, which can negatively impact their treatment process²³.

The proportion of tuberculosis cases based on the anatomical location of the disease at PKU Muhammadiyah Bantul Hospital in 2021-2023.

The analysis reveals that the prevalence of tuberculosis patients at PKU Muhammadiyah Bantul Hospital from 2021 to 2023 is higher in individuals with pulmonary tuberculosis, accounting for 72% of cases, as opposed to extra-pulmonary tuberculosis, which accounts for 28% of cases. In Indonesia, there is a significant prevalence of extrapulmonary tuberculosis in addition to the rising incidence of pulmonary tuberculosis. In 2014, there were 324,539 cases of pulmonary tuberculosis, which climbed to 511,873 cases in 2018¹³. According to WHO in 2018¹ there were 15% of the 7 million extra-pulmonary tuberculosis cases reported in 2018 in the West Pacific and East Mediterranean regions.

Pulmonary tuberculosis is a case of tuberculosis involving the lung or tracheobronchial parenchyma, while extra-pulmonary tuberculosis is a case of tuberculosis involving organs outside the lung parenchyma such as the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, and brain membranes. Patients with both pulmonary and extra-pulmonary

tuberculosis should be classified as pulmonary tuberculosis cases²⁵. Pulmonary tuberculosis cases are more common, this is because the *Mycobacterium tuberculosis* germ is aerobic where the germ prefers oxygen-rich tissues²⁶.

The proportion of tuberculosis cases based on the results of thoracic photo examination at PKU Muhammadiyah Bantul Hospital in 2021-2023.

Chest X-ray (CXR) is one of the screening efforts used in finding tuberculosis cases, screening with thoracic photo examination can be done both actively and passively²⁷. The analysis showed that the proportion of TB cases based on CXR at PKU Muhammadiyah Bantul Hospital in 2021-2023 was 68% positive for tuberculosis. Historically, one of the main methods for identifying TB, particularly pulmonary TB, has been CXR. With its high sensitivity for pulmonary TB, CXR is a useful diagnostic tool for patients to rule out TB, particularly when the X-ray is interpreted to look for any abnormalities that would be suggestive of TB. Nevertheless, CXR has low specificity; while certain abnormalities on the scan are highly specific to pulmonary tuberculosis (e.g., cavities), many other lung pathologies also exhibit CXR abnormalities that are consistent with pulmonary tuberculosis and, thus, may be indicative of other pathologies in addition to TB²⁸.

Furthermore, there exist notable differences in the interpretation of CXRs across and among observers. Both overdiagnosis and underdiagnosis result from basing tuberculosis diagnosis solely on CXR. A TB diagnosis should always be rigorously supported by bacteriological confirmation (sputum-smear microscopy, culture, or molecular testing)²⁸.

Latent tuberculosis cannot be detected by CXR, although active TB can usually be found by CXR. To confirm the diagnosis, a sputum test is required in both situations. If the CXR result shows positive TB but the TCM or BTA result is negative, it is diagnosed as clinical pulmonary TB²⁹. Both latent and active tuberculosis can be treated, although the approaches taken are slightly various. The goal of treating latent TB is to stop it from becoming active. Typically, this is done by taking one medication for a few months at a time^{30,31}. When treating active tuberculosis, treatment is typically more rigorous, involving the use of several medications (usually four in total), and taking longer³².

The proportion of tuberculosis cases based on history of diabetes mellitus at PKU Muhammadiyah Bantul Hospital in 2021-2023

The results of the analysis showed that the proportion of tuberculosis cases based on a history of diabetes mellitus at PKU Muhammadiyah Bantul Hospital in 2021-2023 was 17% with a history of diabetes mellitus, while 36% did not have a history of diabetes mellitus and 47% were unknown. Individuals diagnosed with diabetes mellitus (DM) are three times more likely to get tuberculosis (TB) and there is a notable connection between DM and TB, indicating that DM not

only influences the risk of TB but also impacts the way TB is presented, the response to therapy, and the final prognosis³³. Diabetes mellitus is a risk factor for the development of tuberculosis. This is because individuals with diabetes mellitus experience a weakened immunological response, leading to decreased body resistance. The immune system's impact on susceptibility to tuberculosis disease is significant, as the disease tends to manifest when the immune system is weakened⁵. Exposure to unhealthy lifestyles, decreased immune status and uncontrolled hyperglycemia contribute to the incidence of tuberculosis-diabetes mellitus³⁴.

The high incidence of diabetes mellitus will affect the incidence of tuberculosis. Diabetes mellitus is associated with decreased cellular immunity. Patients with diabetes mellitus have fewer T lymphocytes and decreased neutrophils. Reduced levels of T-helper 1 (Th 1) cytokine response, TNF alpha production, and IL-1 beta and IL-6 production are also seen in people with diabetes mellitus with tuberculosis compared to people without diabetes mellitus. Th 1 cytokines are very important in the control and inhibition of Mycobacterium tuberculosis germs. The decreased number and function of T lymphocytes are responsible for the susceptibility of people with diabetes mellitus to tuberculosis^{4,5,34}. Macrophage function is also impaired in individuals with diabetes mellitus. The combination of these dysfunction processes contributes to the increased risk of tuberculosis in people with diabetes mellitus³⁵.

The proportion of tuberculosis cases based on HIV history at PKU Muhammadiyah Bantul Hospital in 2021-2023

Based on the results of the analysis, the proportion of tuberculosis cases based on HIV status at PKU RS Muhammadiyah Bantul in 2021-2023 was 2% of tuberculosis patients confirmed as HIV positive, while 19% were HIV negative. There were 79% of patients with unknown HIV history, this could occur because HIV testing was not carried out on these patients. The trend of HIV-positive tuberculosis patients in Indonesia from 2017 to 2022 is increasing, due to several factors such as the establishment of a policy requiring tuberculosis patients to undergo HIV testing and increasing access to HIV testing in healthcare facilities and in the community. In 2017, the rate of TB patients knowing their HIV status was 17% and in 2022 it was 56%¹⁹.

HIV weakens the body's immune system, so if a person has HIV and latent tuberculosis, it is possible to develop active tuberculosis. Latent tuberculosis is more likely to develop into active tuberculosis in people with HIV^{36,37}. The prevalence of tuberculosis in HIV-positive patients is often 29-37 times higher than that of HIV-negative tuberculosis cases³⁸. Early detection of tuberculosis in HIV patients and early detection of HIV in tuberculosis patients need to be carried out and given immediate treatment according to appropriate management³⁹.

CONCLUSION

According to the research conducted at PKU Muhammadiyah Bantul Hospital on the epidemiological status of tuberculosis from 2021 to 2023, it can be inferred that the number of tuberculosis cases at the hospital varies annually. Men have a higher tuberculosis infection rate of 54%, whereas women have a lower rate of 46%. The age group most impacted by tuberculosis cases is individuals between the ages of 55 and 64. In total, there were 59 cases reported between the years 2021 and 2023. A total of 86% of tuberculosis patients treated at PKU Muhammadiyah Bantul Hospital were residents of Bantul Regency.

According to the anatomical location classification, pulmonary tuberculosis had a higher prevalence at PKU Muhammadiyah Bantul Hospital from 2021 to 2023, accounting for 72% of cases. In contrast, extrapulmonary tuberculosis was less common, with only 28% of patients affected. Based on the DM data, 17% of patients were diagnosed with tuberculosis in addition to DM, whereas 36% did not have DM, and the remaining 47% had an indeterminate DM status. Based on the HIV records, 2% of patients were identified as HIV positive, 19% were identified as HIV negative, and the HIV status of 79% of patients was undetermined.

REFERENCES

1. World Health Organization. Global Tuberculosis Report 2019. 2019. https://reliefweb.int/report/world/global-tuberculosis-report-2019?gad_source=1&gclid=CjwKCAjwuj2xBhA3EiwAMVjkVEheQ0hMAB9yqjM5tBN9hkUJ_xO_VWwMHODy80apXE57Gdd4OVUrBoCHZ8QAvD_BwE
2. Patterson B, Wood R. Is cough really necessary for TB transmission? *Tuberculosis (Edinb)*. 2019;117:31-35. doi:10.1016/j.tube.2019.05.003
3. World Health Organization. Tuberculosis. https://www.who.int/health-topics/tuberculosis#tab=tab_1
4. Millet J-P, Moreno A, Fina L, et al. Factors that influence current tuberculosis epidemiology. *Eur spine J Off Publ Eur Spine Soc Eur Spinal Deform Soc Eur Sect Cerv Spine Res Soc*. 2013;22 Suppl 4(Suppl 4):539-548. doi:10.1007/s00586-012-2334-8
5. Narasimhan P, Wood J, Macintyre CR, Mathai D. Risk factors for tuberculosis. *Pulm Med*. 2013;2013:828939. doi:10.1155/2013/828939
6. Olmo-Fontánéz AM, Turner J. Tuberculosis in an Aging World. *Pathog (Basel, Switzerland)*. 2022;11(10). doi:10.3390/pathogens11101101
7. Marçôa R, Ribeiro AI, Zão I, Duarte R. Tuberculosis and gender-Factors influencing the risk of tuberculosis among men and women by age group. *Pulmonology 2018 May-Jun; 24 199-202* doi:10.1016/j.pulmoe.2018.03.004. Published online 2018.
8. Hargreaves JR, Boccia D, Evans CA, Adato M, Petticrew M, Porter JDH. The social determinants of tuberculosis: from evidence to action. *Am J Public Health*. 2011;101(4):654-662. doi:10.2105/AJPH.2010.199505
9. Jannah RZ, Azizah R, Jalaludin JB, Sulistyorini L, Lestari KS. Meta-Analysis Study: Environmental Risk Factors of Tuberculosis (TB). *J Environ Health*. 2023;15(2).
10. Singh SK, Kashyap GC, Puri P. Potential effect of household environment on prevalence of tuberculosis in India: evidence from the recent round of a cross-sectional survey. *BMC Pulm Med*. 2018;18:1-10.
11. Wang EY, Arrazola RA, Mathema B, Ahluwalia IB, Mase SR. The impact of smoking on tuberculosis treatment outcomes: a meta-analysis. *Int J Tuberc Lung Dis Off J Int Union against Tuberc Lung Dis*. 2020;24(2):170-175. doi:10.5588/ijtld.19.0002

12. Alavi-Naini R, Sharifi-Mood B, Metanat M. Association between tuberculosis and smoking. *Int J high risk Behav Addict*. 2012;1(2):71-74. doi:10.5812/ijhrba.5215
13. Kementerian Kesehatan Republik Indonesia. Data dan Informasi Profil Kesehatan Indonesia Tahun 2018.
14. Dinkes Kabupaten Bantul. *Profil Kesehatan Kabupaten Bantul 2022.*; 2023.
15. Koh GCKW, Hawthorne G, Turner AM, Kunst H, Dedicoat M. Tuberculosis incidence correlates with sunshine: an ecological 28-year time series study. *PLoS One*. 2013;8(3):e57752. doi:10.1371/journal.pone.0057752
16. Kadota JL, Reza TF, Nalugwa T, et al. Impact of shelter-in-place on TB case notifications and mortality during the COVID-19 pandemic. *Int J Tuberc Lung Dis*. 2020;24(11):1212-1214.
17. Sy KTL, Haw NJL, Uy J. Previous and active tuberculosis increases risk of death and prolongs recovery in patients with COVID-19. *Infect Dis (Auckl)*. 2020;52(12):902-907.
18. Zhang Y, Zhang L, Gao W, et al. The impact of COVID-19 pandemic on reported tuberculosis incidence and mortality in China: An interrupted time series analysis. *J Glob Health*. 2023;13:6043. doi:10.7189/jogh.13.06043
19. Kementerian Kesehatan RI. 2022. Laporan Program Penanggulangan Tuberkulosis Tahun 2022.
20. Teshima A, Shatnawi AA, Satyanarayana S, Khader YS, Maia IF, Wilson NC. High prevalence of current tobacco smoking among patients with tuberculosis and people living with HIV in Jordan: A cross-sectional survey. *Tob Induc Dis*. 2023;21.
21. Rhines AS. The role of sex differences in the prevalence and transmission of tuberculosis. *Tuberculosis*. 2013;93(1):104-107.
22. de Martino M, Lodi L, Galli L, Chiappini E. Immune Response to Mycobacterium tuberculosis: A Narrative Review. *Front Pediatr*. 2019;7:350. doi:10.3389/fped.2019.00350
23. Sofiana L, Ayu SM, Amelia D, et al. Medication Adherence of Tuberculosis Patients in Yogyakarta: A Cross Sectional Study. *J Heal Educ*. 2022;7(2):95-106.
24. Courtwright A, Turner AN. Tuberculosis and stigmatization: pathways and interventions. *Public Health Rep*. 2010;125(4_suppl):34-42.
25. Niu T, He F, Yang J, et al. The epidemiological characteristics and infection risk factors for extrapulmonary tuberculosis in patients hospitalized with pulmonary tuberculosis infection in China from 2017 to 2021. *BMC Infect Dis*. 2023;23(1):488.
26. Sharma D, Sarkar D. Pathophysiology of tuberculosis: An update review. *PharmaTutor*. 2018;6(2):15-21.
27. Bhalla AS, Goyal A, Guleria R, Gupta AK. Chest tuberculosis: Radiological review and imaging recommendations. *Indian J Radiol Imaging*. 2015;25(3):213-225. doi:10.4103/0971-3026.161431
28. Organization WH. *Chest Radiography in Tuberculosis Detection: Summary of Current WHO Recommendations and Guidance on Programmatic Approaches*. World Health Organization; 2016.
29. Piccazzo R, Paparo F, Garlaschi G. Diagnostic accuracy of chest radiography for the diagnosis of tuberculosis (TB) and its role in the detection of latent TB infection: a systematic review. *J Rheumatol Suppl*. 2014;91:32-40.
30. Zenner D, Beer N, Harris RJ, Lipman MC, Stagg HR, Van Der Werf MJ. Treatment of latent tuberculosis infection: an updated network meta-analysis. *Ann Intern Med*. 2017;167(4):248-255.
31. Tang P, Johnston J. Treatment of latent tuberculosis infection. *Curr Treat options Infect Dis*. 2017;9:371-379.
32. Haas MK, Belknap RW. Updates in the treatment of active and latent tuberculosis. In: *Seminars in Respiratory and Critical Care Medicine*. Vol 39. Thieme Medical Publishers; 2018:297-309.
33. Huber FG, Kristensen KL, Holden IK, et al. The prevalence of diabetes among tuberculosis patients in Denmark. *BMC Infect Dis*. 2022;22(1):64.
34. Restrepo BI. Diabetes and tuberculosis. *Underst host immune response against mycobacterium Tuberc Infect*. Published online 2018:1-21.
35. Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis*. 2009;9(12):737-746.
36. Mutyambizi C, Dunlop J, Maluleke C, et al. Effect of COVID-19 on HIV, tuberculosis, and prevention of mother-to-child transmission of HIV indicators in Mopani district, South Africa. *S Afr Med J*. 2021;111(12):1181-1189. doi:10.7196/SAMJ.2021.v111i12.15822
37. Pawlowski A, Jansson M, Sköld M, Rottenberg ME, Källenius G. Tuberculosis and HIV co-infection. *PLoS Pathog*. 2012;8(2):e1002464.

- 38. Liu E, Makubi A, Drain P, et al. Tuberculosis incidence rate and risk factors among HIV-infected adults with access to antiretroviral therapy. *AIDS*. 2015;29(11):1391-1399. doi:10.1097/QAD.0000000000000705
- 39. Sullivan A, Nathavitharana RR. Addressing TB-related mortality in adults living with HIV: a review of the challenges and potential solutions. *Ther Adv Infect Dis*. 2022;9:20499361221084164.