

ARTICLE INFORMATION

Received: November, 27, 2025

Revised: March, 27, 2026

Available online: March, 28, 2026

at : <https://e-jurnal.iphorr.com/index.php/minh>

Analysis of multidrug-resistance tuberculosis distribution in Indonesia 2021–2023

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado

Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

Abstract

Background: Multidrug-resistant tuberculosis (MDR-TB) is a major obstacle to tuberculosis eradication worldwide. MDR-TB cases are a form of tuberculosis resistant to two main drugs, isoniazid and rifampin.

Purpose: To (1) determine trends in the pattern of changes in the number of MDR-TB cases, (2) identify the distribution of MDR-TB cases in Indonesia by time and region (province), and (3) identify clusters based on incidence rates and population density.

Method: An observational ecological study using aggregate provincial-level data. MDR-TB case data was obtained from the Indonesian Ministry of Health for 2021–2023. The analysis was conducted descriptively, spatially, and cluster-wise. The spatial epidemiology approach included the creation of thematic maps (choropleth maps), temporal trend analysis, Standardized Incidence Ratio (SIR), and hierarchical cluster analysis using the Ward method.

Results: There was an increase in MDR-TB cases in almost all provinces during 2021–2023. After adjusting for population (rate), the provinces with the highest risk were DKI Jakarta, North Maluku, Gorontalo, and North Sulawesi. Spatial analysis showed significant hotspots in West Java and Banten, while other provinces were classified as low risk. Based on clusters, DKI Jakarta formed a separate cluster with the highest rate and density. The distribution of MDR-TB in Indonesia is uneven, with an increase in national cases and concentration of risk in several regions.

Conclusion: A spatial-based approach is essential for planning more targeted interventions. These findings indicate that the distribution of MDR-TB in Indonesia is uneven, with an increase in national cases and concentration of risk in certain provinces, so these areas need to be prioritized in MDR-TB control.

Keywords: Cluster; Indonesia; MDR-TB; SIR; Spatial Distribution

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) is a major obstacle to the eradication of tuberculosis worldwide. MDR-TB cases are a specific form of tuberculosis that is resistant to drugs, specifically the two most effective anti-tuberculosis drugs used primarily when tuberculosis bacteria are resistant. This condition occurs when *Mycobacterium tuberculosis* bacteria can no longer be treated with first-line drugs, at least isoniazid and rifampicin, which are types of anti-tuberculosis drugs (Muhammad & Fadli, 2019; Maksum, Suhaili,

Amalia, Kamara, Rachman, & Rachman, 2018; Aristiana, Wartono, 2018).

Based on the Global Tuberculosis Report, the estimated number of MDR-TB cases in 2021 is around 450,000 cases. Indonesia is one of the 10 countries with the highest global burden of MDR-TB cases in the world, with an estimated 28,000 MDR-TB cases in Indonesia in 2021, or 10 per 100,000 people (Handari & Ronoatmodjo, 2024). MDR-TB in Indonesia also ranked 5th highest worldwide in 2022, with approximately 24,666 cases of MDR-TB, 50% of

which had not undergone second-line treatment. In 2023, there were approximately 30,000 recorded cases, and of that number, 73% of patients started treatment but only 55% completed the treatment (Ministry of Health of the Republic of Indonesia, 2024).

Globally, the World Health Organization (WHO) estimates that MDR-TB caused approximately 160,000 deaths in 2022 (World Health Organization, 2023). The number of people with MDR-TB each year was relatively stable between 2015 and 2020, and increased in 2021 by 3.1% from 2020. Indonesia is among the seven countries with the highest number of MDR-TB cases in the world (Handari & Ronoatmodjo, 2024).

Based on a 2019 report by the WHO, there were an estimated 9.96 million cases of tuberculosis worldwide, 465,000 of which were MDR-TB. Of these estimated MDR-TB patients, only 206,030 were successfully identified and 177,099 (86%) were treated, with a global treatment success rate of 57%. In the same year, it was estimated that 3.3% of new TB patients and 17.7% of previously treated TB patients were MDR-TB patients (World Health Organization, 2020).

Treatment for MDR-TB requires intensive monitoring and management of drug side effects. All side effects that occur as a result of treatment, whether mild or severe, require appropriate clinical management. If drug side effects are not addressed, they can cause congenital abnormalities in babies, permanent disabilities, life-threatening conditions, and even death. In addition, treatment side effects often require patients to be hospitalized, which can increase treatment costs. Therefore, intensive monitoring of anti-TB drugs side effects in MDR-TB patients must be carried out carefully, and immediate action must be taken to minimize side effects. This is expected to improve patient treatment adherence and prevent patients from discontinuing treatment (Ministry of Health of the Republic of Indonesia, 2020b).

Treatment for MDR-TB poses considerable challenges. One of these is that the drugs used can cause side effects that interfere with daily activities.

Many drug side effects range from mild symptoms such as dizziness, nausea, muscle pain, and visual and hearing impairment to severe side effects that can be life-threatening. Therefore, nurses must closely monitor the emergence of side effects and provide appropriate nursing care for their management. Proper and effective management of side effects is key to the success of treatment and minimizing patient discomfort (Ministry of Health of the Republic of Indonesia, 2020a).

RESEARCH METHODS

This research employed an observational ecological design to examine the spatial distribution of Drug-Resistant Tuberculosis (DR-TB), with a particular focus on Multi-Drug Resistant Tuberculosis (MDR-TB), across Indonesia using aggregated provincial data from 2021 to 2023. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure methodological rigor.

The variables analyzed included: (1) Province, treated as a categorical variable representing the geographical unit of analysis; (2) Reporting year (2021, 2022, and 2023); and (3) Number of MDR-TB cases, defined as the annual count of reported cases per province. Data processing utilized electronic tools and software, including QGIS and ArcGIS for spatial mapping, IBM SPSS Statistics version 29, and Microsoft Excel. These instruments facilitated the management and analysis of provincial-level aggregate data obtained from the official website of the Ministry of Health of the Republic of Indonesia.

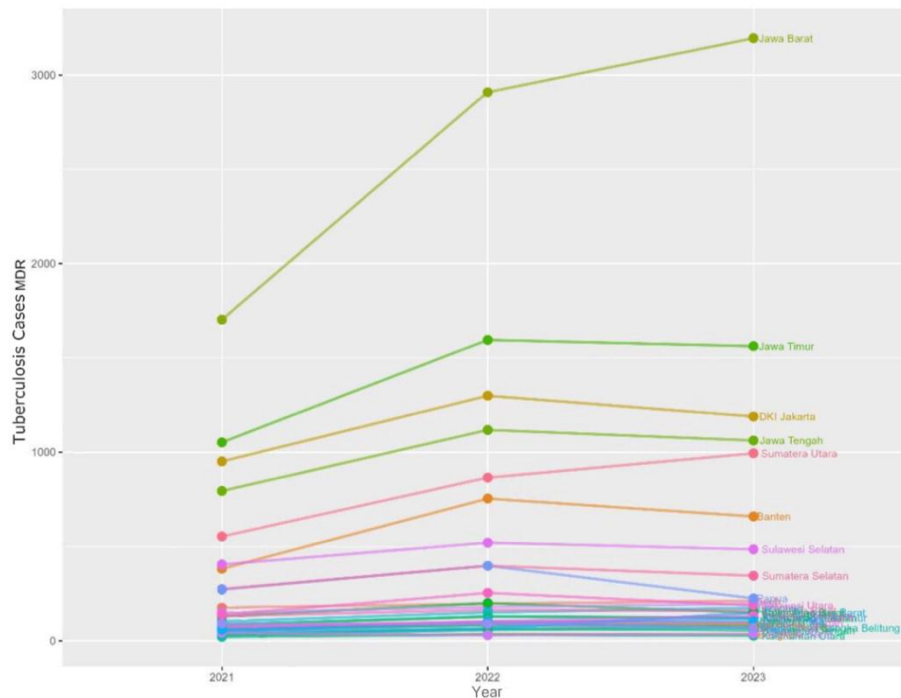
Analytical procedures were primarily univariate, aimed at describing the characteristics of MDR-TB case distribution. The analysis proceeded in three stages: (1) Trend analysis, to identify temporal changes in provincial case counts between 2021 and 2023; (2) Descriptive analysis, to present the distribution of MDR-TB cases by province and year through tabular summaries and thematic (choropleth) maps; and (3) Cluster analysis, to detect statistically significant groupings of provinces based on case burden.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

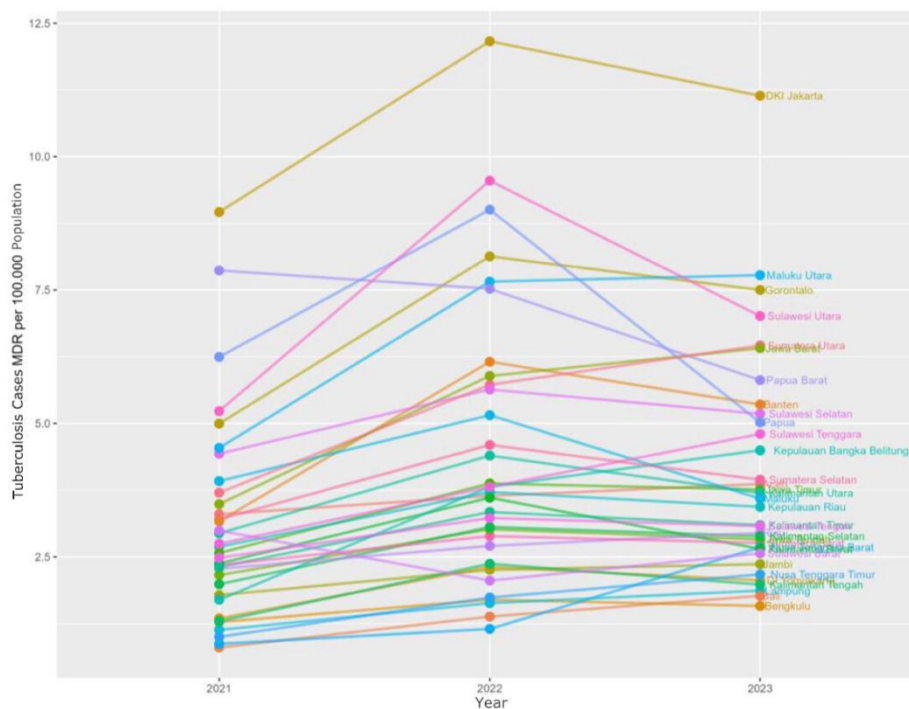
Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

RESEARCH RESULTS



(i) Cases



(ii) Rate

Figure 1. Slope chart of case distribution and MDR-TB rate, 2021-2023.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

Analysis of multidrug-resistance tuberculosis distribution in Indonesia 2021–2023

An increase in MDR-TB cases was observed in almost all provinces in Indonesia during the period 2021–2023. This is shown by the slope curve in Figure 1, which illustrates the change over time. In terms of absolute numbers, all provinces in Java (including DKI Jakarta) still rank highest.

However, after adjusting for population size, it appears that several provinces outside Java, such as North Maluku, Gorontalo, and North Sulawesi, actually have quite high MDR-TB rates and are only slightly below DKI Jakarta.

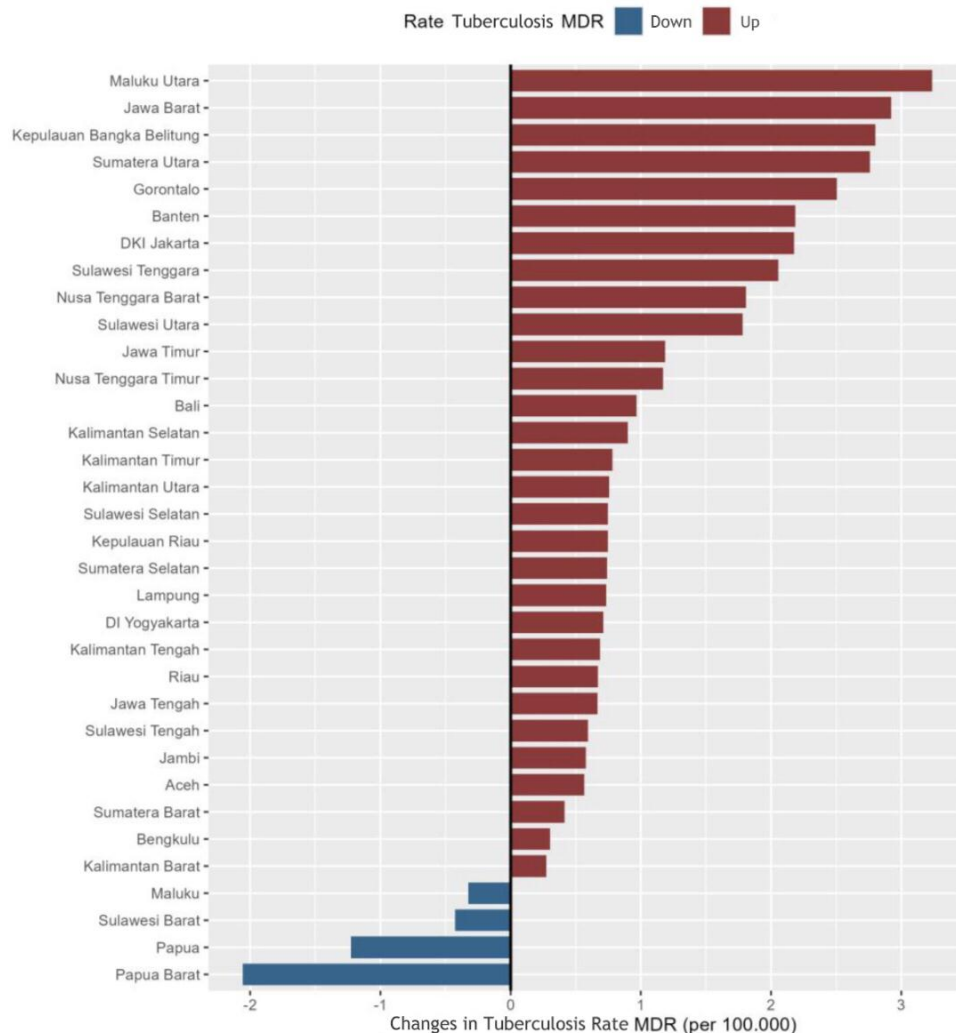


Figure 2. Changes in TB-MDR rates by province, 2021–2023.

The rate is the ratio between the number of cases and the population, so its value can illustrate the level of MDR-TB risk in each region. Changes in the MDR-TB rate throughout 2021–2023 are shown in Figure 2. Most provinces showed an increase in risk, with North Maluku, West Java, and Bangka Belitung Islands being the three provinces with the highest rate increases. North Sulawesi ranked tenth in the list of provinces with an increase in rates.

Conversely, there were four provinces that actually experienced a decrease in rates during the 2021–2023 period, namely West Papua, Papua, West Sulawesi, and Maluku. These findings indicate that although the national trend is increasing, the dynamics of MDR-TB risk are not uniform across Indonesia.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

Analysis of multidrug-resistance tuberculosis distribution in Indonesia 2021–2023

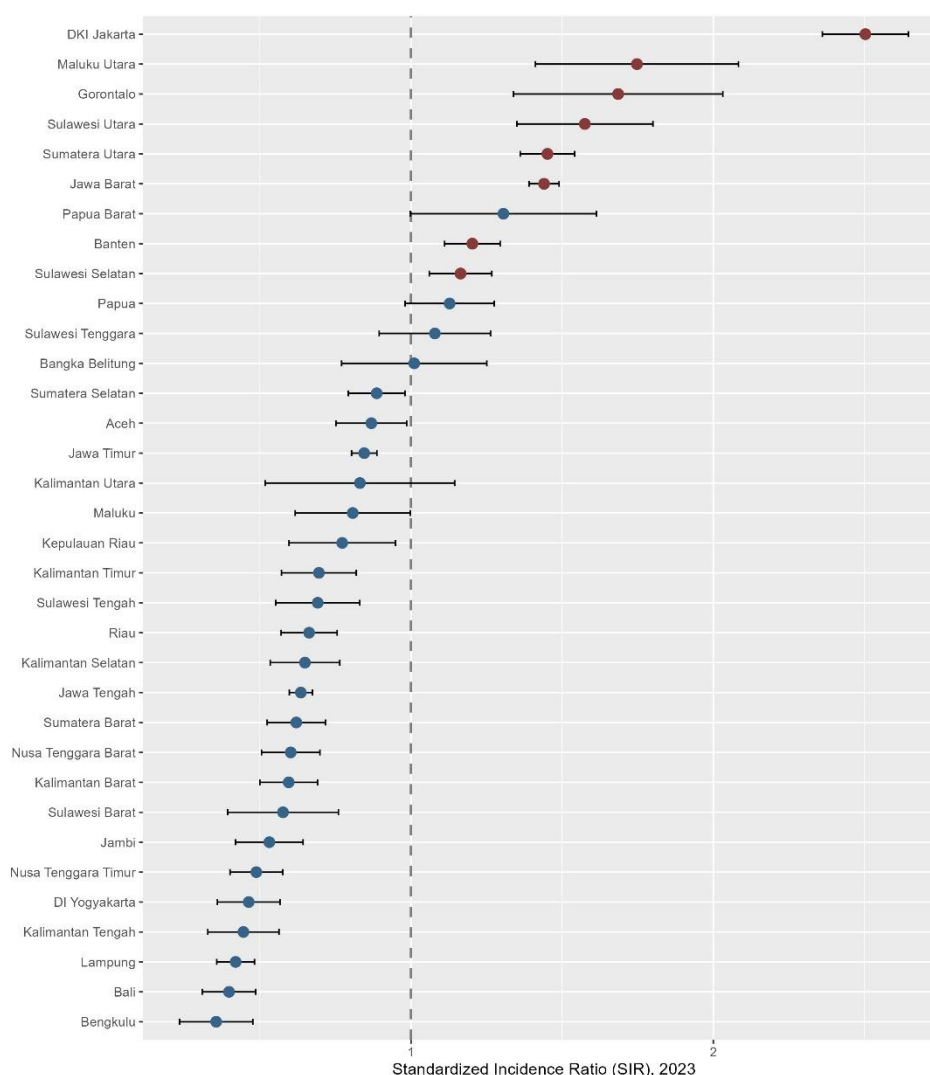


Figure 3. Standardized incidence ratios (SIR) with 95% confidence intervals for MDR-TB by province, 2023. Red dots indicate SIR estimates and 95% confidence intervals above 1, while blue dots indicate SIR ≤ 1.

An SIR value greater than 1 ($SIR > 1$) means that the province has a higher risk of MDR-TB than the national average. An SIR value less than 1 ($SIR \leq 1$) means that the province has a risk of MDR-TB that is equal to or lower than the national average. The provinces of DKI Jakarta, North Maluku, Gorontalo, North Sulawesi, West Sulawesi, Banten, and South Sulawesi were identified as areas with $SIR > 1$. This means that the number of MDR-TB cases occurring in these provinces is higher than the number of cases that should occur based on the national average rate and the population of each province.

For example, in DKI Jakarta in 2023, the expected number of cases is calculated as follows. Expected cases = (national average rate: 4.451×10^{-5}) $\times$ (population of DKI Jakarta: $10,672.1 \times 10^3$). This calculation results in approximately 475 expected cases after rounding. Meanwhile, the number of MDR-TB cases recorded according to observations was 1,189 cases. Thus, $SIR = 1,189/475$ or approximately 2.5, as shown in Figure 3. An SIR value greater than 1 indicates that a region has a higher risk of MDR-TB than the expected level based on the national pattern.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

Projection EPSG:23830 (UTM Zone 50N)

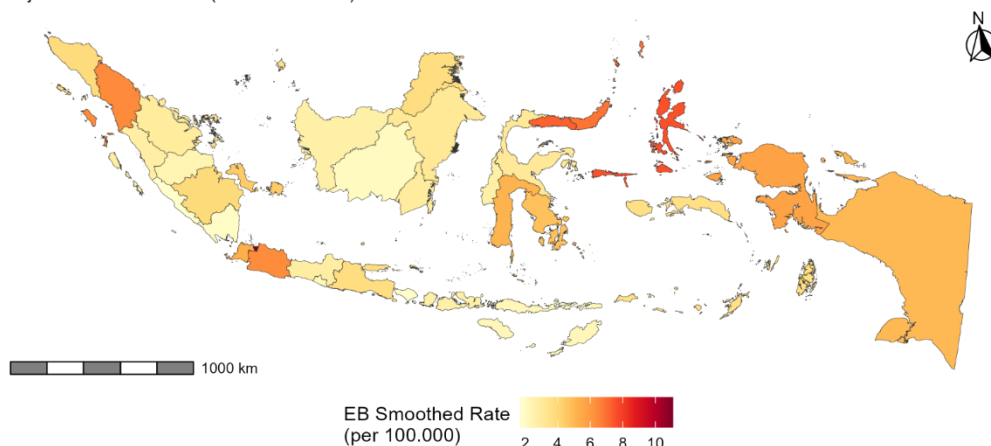
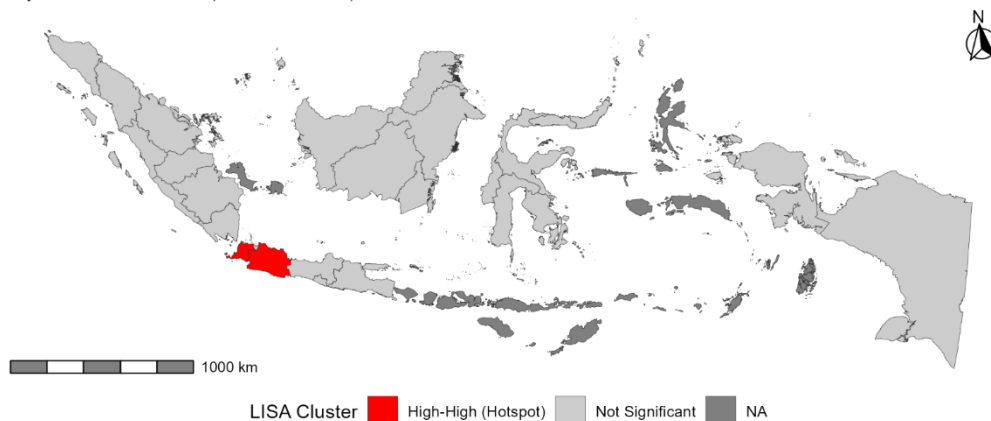


Figure 4. Map of TB-MDR risk using empirical Bayes (EB) smoothed rate, Indonesia 2023.

Projection EPSG:23830 (UTM Zone 50N)



Notes: LISA Local Indicators of Spatial Association

Figure 5. Local spatial cluster map of TB-MDR (Local Moran's I) for hotspot identification, Indonesia 2023.

Data from 2023 was used as the focus for spatial analysis of MDR-TB distribution. Figure 5 shows a map of MDR-TB risk distribution in Indonesia using empirical Bayes (EB) smoothed rates. EB rates were used because crude rates (number of cases divided by population) are often unstable, especially in provinces with small populations. With the EB method, the rate becomes more stable because it takes into account information from the national average, similar to the SIR calculation principle.

The results of the choropleth map in Figure 5 show that the provinces of DKI Jakarta, North Maluku, Gorontalo, North Sulawesi, North Sumatra,

and West Java have EB smoothed rates that are classified as very high or high. Provinces with a high risk level are Banten, West Papua, Papua, South Sulawesi, and Southeast Sulawesi. These areas are priority areas because they have a higher estimated risk of MDR-TB than other provinces, thus requiring further attention and intervention.

The next spatial analysis was conducted to group regions in Indonesia based on the SIR TB-MDR value for each province. The evaluation was conducted using Local Indicators of Spatial Association (LISA), a method that detects spatial autocorrelation based on Local Moran's I values.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

These statistics will help determine areas with higher than expected case numbers (hotspots) and lower than expected case numbers (coldspots). The LISA cluster map shown in Figure 6 indicates that the region covering West Java and Banten was detected as a hotspot cluster, signifying a high concentration of MDR-TB risk in the area. Meanwhile, other provinces did not show any spatial patterns and were considered statistically insignificant. Several provinces could not be evaluated because their land areas do not directly

border other provinces. In the map, these areas are marked with NA (not applicable). This condition is an important note. Spatial analyses such as LISA generally assume a single, continuous land system, which makes it difficult to assess archipelagic regions such as Indonesia. To overcome this, the analysis applies an ad hoc solution by assigning a spatial weight of zero to provinces that have no neighbors (zero policy), so that calculations can still be performed without ignoring the archipelagic geography of Indonesia.

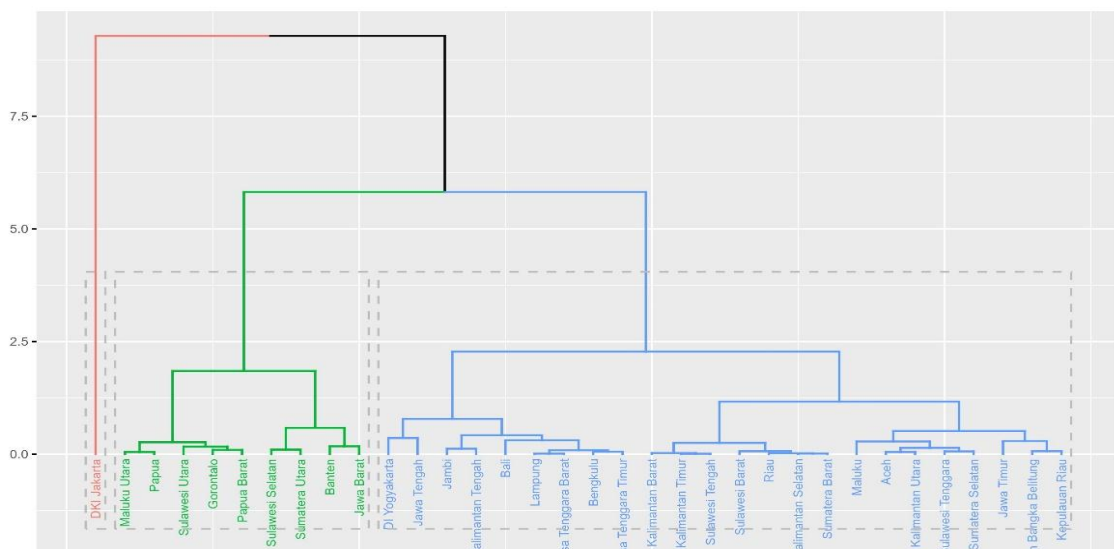


Figure 6. Hierarchical cluster dendrogram according to Ward's method. Province grouping follows risk profiles, namely MDR-TB rate vs. population density, 2021-2023.

Table 1. MDR-TB Risk Profile Clusters in Indonesia based on Rate vs. Population Density, 2021-2023

Province Profile Cluster	
1	Low TB-MDR rate, low population density Aceh, Bali, Bengkulu, DI Yogyakarta, Jambi, Central Java, East Java, West Kalimantan, South Kalimantan, Central Kalimantan, East Kalimantan, North Kalimantan, Bangka Belitung, Riau Islands, Lampung, Maluku, West Nusa Tenggara, East Nusa Tenggara, Riau, West Sulawesi, Central Sulawesi, Southeast Sulawesi, West Sumatra, South Sumatra
2	Moderate TB-MDR rate, low population density Banten, Gorontalo, West Java, North Maluku, Papua, West Papua, South Sulawesi, North Sulawesi, North Sumatra
3	High TB-MDR rate, high population density DKI Jakarta

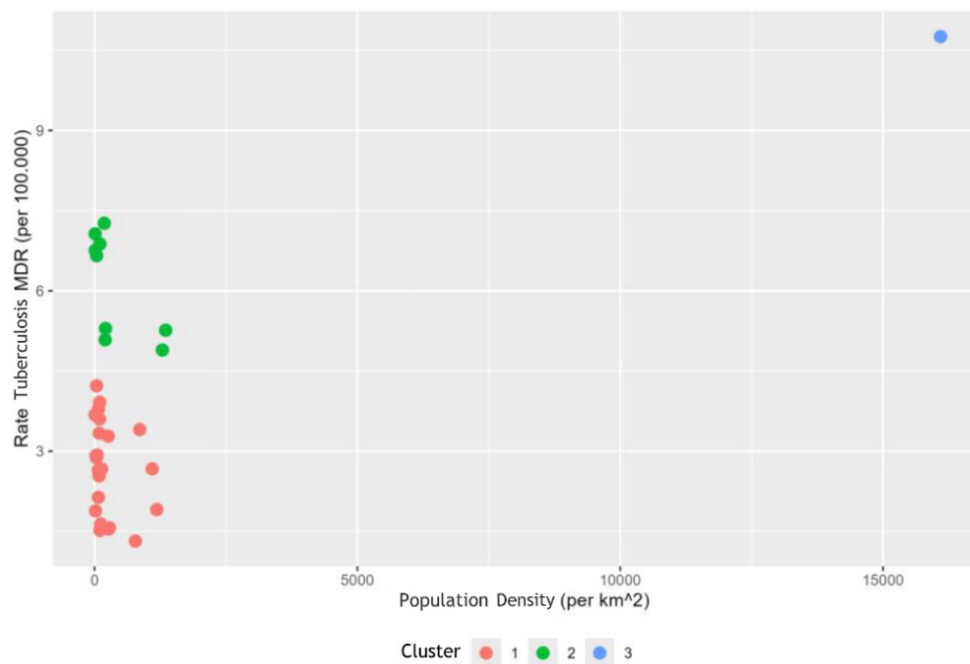
Note: The TB-MDR rate and population density are average values for 2021-2023. Median (min; max) MDR-TB rate (per 100,000) for clusters: (1) 2.7 (1.3; 4.2), (2) 6.7 (4.9; 7.3), (3) 10.8 (only one province).

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

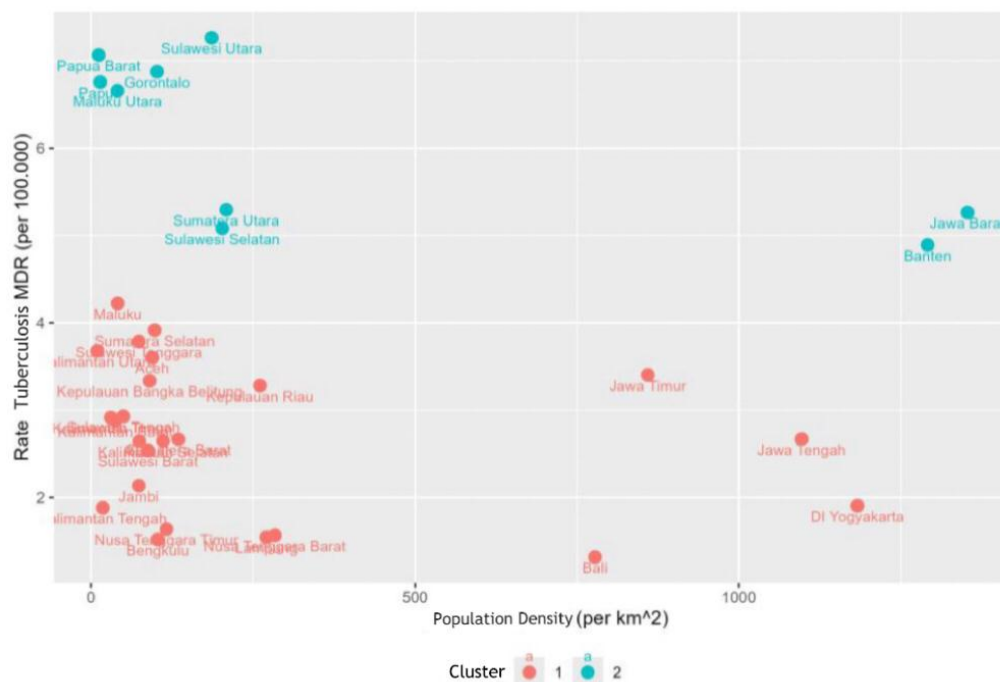
Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

Analysis of multidrug-resistance tuberculosis distribution in Indonesia 2021–2023



(i) All Clusters



(ii) Without Cluster 3 (DKI Jakarta)

Figure 7. Scatter plot of provincial classification based on MDR-TB rate vs. population density, 2021-2023

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugui21@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

Figures 6-7 and Table 1 present the results of TB-MDR risk profile classification in Indonesia according to the absolute number of cases, rate, and population density in each province from 2021 to 2023. This grouping was carried out through hierarchical cluster analysis using the Ward method. This multivariate technique identified three risk clusters in Indonesia. The first group consists of areas with low risk, where standard TB-MDR case management can be an adequate intervention. The other two groups are areas with moderate rates despite low population density, and DKI Jakarta as a separate cluster with very high rates. The latter two clusters clearly require interventions that exceed the national standard for TB-MDR case management.

DISCUSSION

This study identified temporal and spatial patterns of multidrug-resistant tuberculosis (MDR-TB) in Indonesia during the period 2021-2023 using a spatial epidemiology approach and cluster analysis. The findings showed an almost uniform increase in MDR-TB cases across all provinces, with the identification of hotspot areas requiring priority intervention, as well as the classification of provinces based on different risk profiles.

Temporal analysis results show a consistent increase in MDR-TB cases in almost all Indonesian provinces during the observation period. These findings are in line with global trends that confirm that MDR-TB cases remain a major public health challenge worldwide (World Health Organization, 2024). Indonesia is one of the eight countries with the highest burden of MDR-TB in the world and requires special attention in controlling this disease (Soeroto, Pratiwi, Santoso, & Lestari, 2021).

The observed increase in the absolute number of cases may indicate several possibilities: an increase in active transmission of MDR-TB at the community level, improvements in the case detection, diagnosis, and reporting systems leading to more cases being identified, or a combination of both factors.

The use of rates adjusted based on population size provides a more accurate perspective on the actual risk in each province than if only absolute numbers were used. The finding that provinces such as North Maluku, Gorontalo, and North Sulawesi have high MDR-TB rates even though the absolute number of cases is not as high as in the provinces

on Java Island underscores the importance of rate standardization in epidemiological analysis. This is consistent with the basic principle of epidemiology which states that comparisons between regions with different population characteristics must take into account the size of the population at risk (Clayton & Kaldor, 1987).

The identification of DKI Jakarta as the province with the highest standardized incidence ratio (SIR around 2.5) provides strong evidence that this region has a TB-MDR burden that far exceeds the national average after controlling for population size. An SIR above one indicates that the number of observed cases exceeds the number of cases expected based on the national rate, suggesting the presence of local factors that facilitate transmission or more intensive case detection (Rothman & Boice, 1982). This phenomenon can be attributed to the urban characteristics of DKI Jakarta, which include high population density, intensive population mobility, and the possibility of high-risk population concentrations.

The relationship between population density and tuberculosis transmission has been well documented in the literature. Research shows that urbanization has a dual impact on tuberculosis epidemiology: on the one hand, it can improve access to health services and sanitation conditions, but on the other hand, it increases the risk of transmission through more frequent contact between individuals in densely populated environments (Neiderud, 2015; Prasad, Ross, Rosenberg, & Dye, 2016; Bawonte, Mambo, & Masengi, 2021). The findings of this study, which identify DKI Jakarta as a separate cluster with a high rate and high population density, are in line with this paradigm.

Provinces in Cluster 2 that show moderate MDR-TB rates despite low population density deserve special attention. Regions such as North Maluku, Gorontalo, Papua, and West Papua may face unique challenges related to access to health services, delayed diagnosis, and infrastructure limitations that can exacerbate local transmission despite their lower population density compared to urban areas (Shaweno, Karmakar, Alene, Ragonnet, Clements, Trauer, & McBryde, 2018). Studies in China indicate that urbanization factors such as GDP, environmental quality, and healthcare service availability may have different associations with tuberculosis incidence depending on the regional

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

context (Wang, Liu, Li, Liu, Wang, Zhang, & Zhao, 2025).

The geographical concentration of MDR-TB cases in urban areas, as observed in this study, is consistent with findings from other countries. Research in Nanchang, China, shows that rapid urbanization can affect the dynamics of tuberculosis transmission through environmental changes and population movements (Yang, Gao, Luo, Liu, Lei, & Zhang, 2019). Similarly, a study in Vietnam identified large cities as predicted tuberculosis hotspots due to intensive migration and urbanization (Dao et al., 2022).

The use of the empirical Bayes method for smoothing rates provides more stable estimates than crude rates, especially for provinces with small populations. This method addresses the high variability that often occurs in data with small samples by shrinking extreme values towards the global or local mean (Berke, 2004; Marshall, 1991). The resulting chlorophyll map provides a clear visualization of the spatial distribution of TBMDR risk in Indonesia, facilitating the identification of geographical intervention priorities.

Spatial autocorrelation analysis using Local Moran's I identified West Java and Banten as statistically significant hotspot clusters. This finding indicates that the high SIR values in these regions are not merely random variations, but rather reflect a consistent spatial pattern in which regions with high rates are surrounded by other regions with high rates (Shaweno et al., 2018; Lestari, Makful, & Okfriani, 2023). This clustering pattern may indicate intensive local transmission or shared risk factors between neighboring regions.

The Local Indicators of Spatial Association (LISA) method has been widely used in spatial epidemiology of tuberculosis to identify transmission hotspots. A systematic review of spatial analysis methods for tuberculosis shows that Kulldorff's spatial scan statistic and Local Moran's I are the two most frequently used methods, although the results of cluster identification may differ depending on the method chosen (Shaweno et al., 2018). In the context of Indonesia, which is an archipelagic country, special challenges arise because many provinces do not directly border other provinces, so the assumption of spatial continuity in LISA analysis is not always met.

The methodological decision to assign a spatial weight of zero (zero policy) to areas without neighbors is a pragmatic approach that has been used in various studies, although it has limitations in capturing potential spatial relationships through transportation routes or maritime migration (Dao, Hoang, Nguyen, Huynh, Pham, Nguyen, & Bui, 2022). Future research may consider the use of spatial weights based on distance or transportation connectivity as an alternative to land-based proximity.

An interesting finding from this study is the decline in the rate of TB-MDR in four provinces (West Papua, Papua, West Sulawesi, and Maluku) during the period 2021-2023. This phenomenon can be interpreted from several perspectives. First, this decline may reflect the success of tuberculosis control interventions in the region, including improvements in case detection, adherence to treatment, and prevention programs. Second, this apparent decline may be influenced by changes in the surveillance or case reporting system. Third, in the context of the COVID-19 pandemic that occurred during the study period, there may have been underdiagnosis or underreporting due to disruptions in the health system (Iskandar, Suwantika, Pradipta, Postma, & van Boven, 2023). It is important to note that although the rate has declined, this does not necessarily indicate the elimination of MDR-TB in the region. Further analysis is needed to understand the factors contributing to this decline and whether this positive trend can be sustained in the long term. Evaluating the quality of surveillance data and validating the findings through additional studies would be very useful.

Classifying provinces into three risk clusters provides a practical framework for resource allocation and intervention prioritization. Provinces in Cluster 3 (DKI Jakarta) and Cluster 2 (including Banten, Gorontalo, West Java, North Maluku, Papua, West Papua, South Sulawesi, North Sulawesi, and North Sumatra) require intensification of MDR-TB control programs that exceed national standards. This may include increasing molecular diagnostic capacity, expanding access to more effective treatment regimens, strengthening directly observed therapy (DOT) programs, and stricter drug resistance surveillance (Soeroto et al., 2021).

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

For high-density urban areas such as DKI Jakarta, interventions must consider aspects of urban planning that can influence tuberculosis transmission, including improving housing quality, ventilation, and reducing overcrowding (Prasad et al., 2016). Research shows that careful urban planning can influence the physical and social environment, which in turn affects the transmission of infectious diseases (Neiderud, 2015).

The identification of spatial hotspots in West Java and Banten indicates the need for a geographic-based approach to controlling MDR-TB. Targeted interventions in these areas, including active case finding, contact screening, and community education, can be more cost-effective than a uniform approach across the entire region (Shaweno et al., 2018). The use of Geographic Information Systems (GIS) and spatial analysis can facilitate the identification of specific locations for mobile screening units or the intensification of primary health care services.

The findings of this study are generally consistent with the global literature on MDR-TB epidemiology. The association between high population density and higher MDR-TB rates has been documented in various settings, including China, India, and African countries (Neiderud, 2015; Wang et al., 2025). The spatial heterogeneity in the distribution of tuberculosis observed in this study is also in line with the findings of a systematic review showing that tuberculosis always exhibits heterogeneous spatial patterns in all studies reviewed (Shaweno et al., 2018).

The results of this study also align with the findings of a research showing that the detection rate of pulmonary TB cases in Indonesia during the 2015–2018 period varied between provinces (Tangkilisan, Langi, & Kalesaran, 2020). In this study, some provinces had high CNRs and others had lower CNRs, reflecting the unequal TB burden at the national level. The pattern of interregional variation supports the findings of this study, which suggests that the distribution of MDR-TB in 2023 will also be uneven and will show differences between provinces. The WHO Global Tuberculosis Report of 2023 also confirms that unequal TB distribution is a common epidemiological pattern found in various countries, including Indonesia. Regions with high

detection capacity tend to report higher case numbers (World Health Organization, 2023).

The use of standardized incidence ratios in the Indonesian context can be compared with their application in other countries. A study in South Africa identified clusters with SIRs up to 20 times higher in certain urban areas, indicating significant transmission hotspots (Kapwata, Breetzke, Wright, & Marcus, 2024). Although the magnitude of SIR in Indonesia is not as high, the basic pattern where urban areas show higher SIR remains consistent.

The increase in MDR-TB cases in Indonesia also reflects global challenges in controlling antimicrobial resistance. A study in West Java showed that factors such as previous tuberculosis treatment history, slow culture conversion, and certain comorbidities are associated with MDR-TB treatment outcomes (Soeroto et al., 2021). This emphasizes the importance of not only focusing on detecting new cases, but also on effective case management to prevent treatment failure and acquired resistance.

This study makes several important contributions to the literature on MDR-TB epidemiology in Indonesia. First, it is one of the first comprehensive studies to systematically use a spatial epidemiology approach to analyze the distribution of MDR-TB across all provinces in Indonesia. The use of a combination of visualization methods (slope charts, forest plots, choropleth maps), spatial autocorrelation analysis (Local Moran's I), and hierarchical cluster analysis provides a multidimensional understanding of the geographical and temporal patterns of the disease. Second, the application of empirical Bayes smoothing to stabilize rate estimates in Indonesia, a country with large variations in population size between provinces, is an appropriate methodological approach and could serve as a model for surveillance of other diseases. Third, the identification of risk clusters based on a combination of MDR-TB rates and population density provides a practical framework for prioritizing interventions that can be adopted by national tuberculosis control programs. Fourth, systematic documentation of the geographic heterogeneity of MDR-TB in Indonesia during the 2021–2023 period, which includes the COVID-19 pandemic era, provides an important baseline for monitoring future trends. This period was a critical phase in which the

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

health system faced the dual pressures of COVID-19 and endemic diseases such as tuberculosis, and documenting its impact on MDR-TB surveillance is important for planning future responses.

This study has several significant methodological strengths. The use of national surveillance data covering all 34 provinces of Indonesia provides a comprehensive representation of the MDR-TB situation at the national level. The combination of temporal and spatial analysis allows for the identification of not only where but also when interventions are most needed. The application of multiple analytic approaches (rate calculation, SIR, empirical Bayes smoothing, spatial autocorrelation, cluster analysis) provides convergent validity to the findings and a more robust understanding of epidemiological patterns.

The use of standardized incidence ratios controlled for population structure is an important strength because it addresses confounding from variations in population size between provinces. This allows for the identification of genuine excess risk that is not merely a reflection of large population denominators. Data visualization through multiple graphic approaches (slope charts for temporal trends, choropleth maps for spatial distribution, dendrograms and scatter plots for classification) facilitates the interpretation of complex findings and communication of results to health policy stakeholders.

The three-year study period (2021–2023) is sufficient to identify consistent trends while remaining relevant for short-term intervention planning. The incorporation of population density data into cluster analysis provides an important additional dimension given the well-established relationship between urbanization, density, and tuberculosis transmission.

Although it has several strengths, this study also has limitations that need to be acknowledged. First, the use of passive surveillance data means that findings depend on the quality of case detection and reporting systems in each province. Variations in diagnostic capacity, particularly access to GeneXpert and drug susceptibility testing, can affect the ascertainment rate and lead to underestimation of cases in some areas (Iskandar et al., 2023). Underreporting remains a significant issue in Indonesia, with estimates that up to 41% of

tuberculosis cases are not reported, particularly from the private health care sector (Suryanti, & Ahmed, 2025). Second, the ecological design of this study does not allow for causal inference at the individual level. The observed association between population density and MDR-TB rates at the provincial level cannot be directly translated into a causal relationship at the individual level due to ecological fallacy (Wang et al., 2025). Individual factors such as HIV status, diabetes, previous TB treatment history, and other sociodemographic factors known to be associated with MDR-TB cannot be analyzed in this design. Third, the definition of spatial neighbors based on land proximity has significant limitations for Indonesia as an archipelagic country. Provinces that are geographically separated but connected by intensive maritime or air transportation routes cannot be adequately captured in traditional spatial autocorrelation analyses. The zero policy solution applied to provinces without neighbors, although pragmatic, can result in the loss of information about potential spatial spillover effects through non-contiguous routes. Fourth, the study period coinciding with the COVID-19 pandemic may influence the interpretation of the findings. Disruptions to the health system during the pandemic can result in diagnostic delays, treatment interruptions, and changes in health-seeking behavior patterns, which in turn can affect the case detection rate (Iskandar et al., 2023). Whether the observed increase in cases reflects a genuine increase in incidence or a catch-up from a backlog of cases missed during the lockdown period cannot be ascertained without additional data. Fifth, the analysis does not take into account intra-provincial heterogeneity. Provinces in Indonesia are geographically large with significant variations in urban-rural characteristics, health access, and sociodemographic risk factors. Analysis at a more granular level (district/city) would provide more detailed insights for targeted interventions. Sixth, the study lacks data on molecular strains or specific resistance patterns (resistance beyond MDR, such as pre-XDR or XDR tuberculosis), which could provide additional information about transmission versus acquired resistance. Seventh, the unavailability of data on the coverage of MDR-TB program management, treatment outcomes, and loss to follow-up at the provincial level limits the

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

interpretation of whether geographical differences in MDR-TB rates reflect differences in incidence, detection, or both. Finally, temporal cross-sectional analysis does not allow for the evaluation of the impact of specific interventions or the identification of turning points in epidemiological trends with high precision.

Several research directions can be recommended based on the findings and limitations of this study. First, studies with more granular units of analysis (districts/cities or even subdistricts) would provide a more detailed understanding of micro-geographic variation in MDR-TB risk. Second, qualitative investigations in identified hotspots could explore context-specific factors that facilitate high transmission, including housing conditions, health-seeking behaviors, and barriers to treatment access. Third, prospective cohort studies that follow MDR-TB patients from diagnosis to completion of treatment in various geographic settings could provide insights into treatment outcomes and factors that influence success rates. Fourth, molecular epidemiology studies that combine genotyping data with geographic information can distinguish between ongoing transmission clusters versus reactivation from latent infection, information that is crucial for targeted interventions (Shaweno et al., 2018). Fifth, investigations into the influence of population mobility and migration patterns on the spatial spread of MDR-TB, using data from population information systems or mobile phone data, can help to understand connected risks outside of traditional spatial continuity. Sixth, modeling studies that estimate the impact of various intervention scenarios (enhanced case finding, improved treatment adherence, novel regimens) in hotspot versus nonhotspot areas can inform optimal resource allocation strategies. Seventh, operational research on the implementation and effectiveness of GIS-guided screening or community-based active case finding in hotspot clusters can evaluate the feasibility and cost-effectiveness of geographically targeted intervention approaches. Finally, longitudinal surveillance with higher temporal resolution can facilitate early detection of new clusters and rapid response.

CONCLUSION

The study provides empirical evidence of significant geographic heterogeneity in the distribution of MDR-TB in Indonesia and the importance of a spatial approach to disease surveillance and control. The combination of temporal analysis, spatial autocorrelation, and cluster analysis provides comprehensive information for evidence-based policy on MDR-TB control in Indonesia.

REFERENCES

- Aristiana, C. D., & Wartono, M. (2018). Faktor-faktor yang mempengaruhi kejadian multi drug resistance tuberculosis (MDR-TB). *Jurnal Biomedika Dan Kesehatan*, 1(1), 65-74.
- Bawonte, T. G., Mambo, C. D., & Masengi, A. S. (2021). Faktor-faktor yang mempengaruhi tuberculosis multidrug resistance (TB MDR). *Jurnal e-Biomedik*, 9(1), 117-125. Retrieved from: <https://ejournal.unsrat.ac.id/v3/index.php/ebiome/dik/article/view/31949>
- Berke, O. (2004). Exploratory disease mapping: kriging the spatial risk function from regional count data. *International journal of health geographics*, 3(1), 18.
- Clayton, D., & Kaldor, J. (1987). Empirical Bayes estimates of age-standardized relative risks for use in disease mapping. *Biometrics*, 671-681.
- Dao, T. P., Hoang, X. H. T., Nguyen, D. N., Huynh, N. Q., Pham, T. T., Nguyen, D. T., & Bui, H. M. (2022). A geospatial platform to support visualization, analysis, and prediction of tuberculosis notification in space and time. *Frontiers in Public Health*, 10, 973362.
- Handari, R. D., & Ronoatmodjo, S. (2024). Prevalensi dan Faktor Risiko Kejadian Efek Samping Obat pada Pasien TB-MDR: Literature Review. *Media Publikasi Promosi Kesehatan Indonesia (MPPKI)*, 7(3), 506-517.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

- Iskandar, D., Suwantika, A. A., Pradipta, I. S., Postma, M. J., & van Boven, J. F. (2023). Clinical and economic burden of drug-susceptible tuberculosis in Indonesia: national trends 2017–19. *The Lancet Global Health*, 11(1), e117-e125.
- Kapwata, T., Breetzke, G., Wright, C. Y., & Marcus, T. S. (2024). The identification and spatial distribution of hotspots of tuberculosis occurrence in South Africa. *BMC Research Notes*, 17(1), 364.
- Lestari, A. A., Makful, M. R., & Okfriani, C. (2023). Analisis spasial kepadatan penduduk terhadap kasus tuberculosis di Provinsi Jawa Barat 2019–2021. *Jurnal Cahaya Mandalika*, 3(2), 577–584.
- Maksum, I. P., Suhaili, S., Amalia, R., Kamara, D. S., Rachman, S. D., & Rachman, R. W. (2018). PCR Multipleks untuk identifikasi Mycobacterium tuberculosis resisten terhadap isoniazid dan rifampisin pada galur lokal Balai Laboratorium Kesehatan Provinsi Jawa Barat. *Jurnal Kimia Valensi*, 107–118.
- Marshall, R. J. (1991). Mapping disease and mortality rates using empirical Bayes estimators. *Journal of the Royal Statistical Society Series C: Applied Statistics*, 40(2), 283–294.
- Ministry of Health of the Republic of Indonesia. (2020a). *Petunjuk Teknis Penatalaksanaan Tuberculosis Resistensi Obat di Indonesia*. Retrieved from: <https://repository.kemkes.go.id/book/1283>
- Ministry of Health of the Republic of Indonesia. (2020b). *Petunjuk Teknis Pendampingan Pasien TBC Resistensi Obat oleh Komunitas*. Retrieved from: <https://www.scribd.com/document/505556634/JUKNIS-PENDAMPINGAN-TB-RO>
- Ministry of Health of the Republic of Indonesia. (2024). *Laporan Program Penanggulangan Tuberculosis 2023*. Direktorat Jenderal Pencegahan dan Pengendalian Penyakit. Direktorat Pencegahan dan Pengendalian Penyakit. Diakses dari: <https://www.scribd.com/document/850503586/Laporan-Program-Penanggulangan-TBC-2023-Final>
- Muhammad, M., & Fadli, F. (2019). Analisis Faktor Penyebab Multi-Drug Resistance (Mdr) Pada Penderita Tuberculosis. *Jurnal Publikasi Kesehatan Masyarakat Indonesia*, 6(2), 62–67.
- Neiderud, C. J. (2015). How urbanization affects the epidemiology of emerging infectious diseases. *Infection ecology & epidemiology*, 5(1), 27060.
- Porta, M., Greenland, S., Hernán, M. M., Silva, I. D. S., & Last, J. M. (2014). *A Dictionary of Epidemiology. Sixth Edition*. Oxford University Press. Retrieved from: <https://books.google.co.id/books?id=3ckVDAAAQBAJ&printsec=frontcover&hl=id#v=onepage&q&f=false>
- Prasad, A., Ross, A., Rosenberg, P., & Dye, C. (2016). A world of cities and the end of TB. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 110(3), 151–152.
- Rothman, K. J., & Boice Jr, J. D. (1982). *Epidemiologic analysis with a programmable calculator* (Vol. 79, No. 1649). Kenneth Rothman.
- Shaweno, D., Karmakar, M., Alene, K. A., Ragonnet, R., Clements, A. C., Trauer, J. M., & McBryde, E. S. (2018). Methods used in the spatial analysis of tuberculosis epidemiology: a systematic review. *BMC medicine*, 16(1), 193.
- Soeroto, A. Y., Pratiwi, C., Santoso, P., & Lestari, B. W. (2021). Factors affecting outcome of longer regimen multidrug-resistant tuberculosis treatment in West Java Indonesia: A retrospective cohort study. *PloS one*, 16(2), e0246284.
- Suryanti, S., & Ahmed, I. A. (2025). Recent Review Tuberculosis in Indonesia: Burden and the Challenge of Under-Reporting. *Iranian journal of public health*, 54(2), 445–446.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>

- Tangkilisan, J. R. A., Langi, F. L. F. G., & Kalesaran, A. F. C. (2020). Angka penemuan kasus tuberkulosis paru di Indonesia tahun 2015-2018. *Jurnal KESMAS*, 9(5), 1-9. Retrieved from: <https://ejournal.unsrat.ac.id/v3/index.php/kesmas/article/view/30330>
- Wang, Y., Liu, X., Li, Y., Liu, M., Wang, Y., Zhang, H., & Zhao, Y. (2025). Association of urbanization-related factors with tuberculosis incidence among 1992 counties in China from 2005 to 2019: a nationwide observational study. *Infectious Diseases of Poverty*, 14(1), 30.
- World Health Organization. (2020). Global Tuberculosis Report 2020. Retrieved from: <https://www.who.int/publications/i/item/9789240013131>
- World Health Organization. (2023). Global Tuberculosis Report 2023. Retrieved from: <https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2023>
- World Health Organization. (2024). Global Tuberculosis Report 2024. Geneva: World Health Organization. Retrieved from: <https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2024>
- Yang, S., Gao, Y., Luo, W., Liu, L., Lei, Y., & Zhang, X. (2019). Spatiotemporal distribution of tuberculosis during urbanization in the new urban area of Nanchang City, China, 2010–2018. *International journal of environmental research and public health*, 16(22), 4395.

Avinia Kapugu*, Fima Lanra Fredrik Gerarld Langi, Angela Fitriani Clementine Kalesaran

Fakultas Kesehatan Masyarakat, Universitas Sam Ratulangi, Manado
Corresponding author: *E-mail: aviniakapugu121@student.unsrat.ac.id

DOI: <https://doi.org/10.33024/minh.v9i1.1909>