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Spatial Autocorrelation of Population Density, HIV/AIDS, and Diabetes Mellitus with Pulmonary Tuberculosis in Kupang, East Nusa Tenggara, Indonesia

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ABSTRACT

Background: The 2023 Global Tuberculosis (TB) Report ranks Indonesia second in the world for TB cases, with approximately 1,060,000 new cases and 134,000 deaths annually—equating to 17 deaths per hour. In East Nusa Tenggara (NTT) Province, pulmonary TB cases increased from 5,361 in 2020 to 5,184 in 2021, and significantly rose to 8,035 in 2022. Kupang Regency reported the highest number of TB cases in 2022. This study aimed to analyze the impact of risk factors, including population density, HIV/AIDS, and Diabetes Mellitus, on pulmonary TB cases using spatial analysis with the GeoDa application.

Subjects and Method: This ecological study, conducted in Kupang, Indonesia, between October and November 2024, uses secondary data from 2021 to 2023 as the research sample. The study includes all recorded pulmonary TB patients from the Kupang Health Office, with 441 cases in 2021, 785 cases in 2022, and 979 cases in 2023.

Results: The Local Indicator of Spatial Association (LISA) test results show a low-high spatial relationship between HIV and TB variables in the Maulafa district for 2022-2023. Additionally, the diabetes mellitus (DM) and TB variables exhibit a High-Low spatial pattern in 2021 and a Low-High pattern in 2022 within the district. Regarding population density in 2021, a clustered spatial autocorrelation was observed (p-value = 0.049 < 0.05; [I] = 0.051 > E[I] = -0.200; Mean = 0.116; SD = 0.120), with a High-Low pattern in the Kota Lama district and a Low-Low pattern in Maulafa. From 2022 to 2023, a Low-High spatial pattern was identified in the Maulafa district.

Conclusion: The results of this study indicate spatial autocorrelation between population density and pulmonary TB cases in Kupang City in 2021. However, from 2022 to 2023, no spatial autocorrelation was observed, and the same pattern was found for the Diabetes Mellitus and HIV/AIDS.

Keywords: diabetes mellitus, pulmonary tuberculosis, spatial autocorrelation

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BACKGROUND

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* (Indonesian Ministry of Health, 2020). The World Health Organization (WHO) estimates that a quarter of the

global population is infected with TB. In 2022, 55% of TB cases were in men, 33% in women, and 12% in children (aged 0–14 years) (WHO, 2023). TB primarily affects adults, with men being more commonly affected than women.

According to the 2023 Global TB Report, Indonesia ranks second globally for the highest number of TB cases, following India and ahead of China. The estimated annual TB cases in Indonesia is 1,060,000, with 134,000 deaths (17 deaths per hour). The 2024 First Quarter National TB Report recorded 821,200 confirmed TB cases and 23,858 TB-related deaths. Of the reported cases, 92% are pulmonary TB, while 8% are extra-pulmonary TB (Indonesian Ministry of Health, 2024).

Kupang City has the highest number of TB cases among the 21 districts and cities in NTT province. The city's TB case detection rate reached 64%, the highest in region. According to the Kupang Health Office, pulmonary TB cases have been steadily increasing: in 2021, there were 481 cases with a case notification rate (CNR) of 105 per 100,000 population; in 2022, the number rose to 785 cases; and in 2023, it increased further to 979 cases (Kupang Health Office, 2023). Pulmonary TB cases in Kupang are distributed across several sub-districts, including Alak, Kota Raja, Kota Lama, Oebobo, Maulafa, and Kota Lima (Kupang Health Office, 2023).

The TB elimination target for 2030 aims to reduce the TB incidence rate to 65 per 100,000 population and decrease the TB death rate to 6 per 100,000 population (Ministry of Health, 2020). In East Nusa Tenggara, the 2023 target for detecting new TB cases was 33%, well below the national target of 90%. Additionally, the TB treatment success rate in NTT province is 87%, falling short of the national target of 100% (Kupang Health Office, 2024).

TB is both a socially and environmentally influenced disease, with its incidence shaped by factors such as the surrounding environment, social interactions, and living conditions. The disease often exhibits spatial clustering, as many individuals with TB share similar social determinants and live in close proximity, increasing the risk of transmission. Population density is a key factor in accelerating TB spread, as denser populations facilitate faster transmission, especially for airborne diseases (Achmad, 2010). A previous study supported this, showing a positive autocorrelation between new TB cases and population density (Lestari et al., 2021). Additionally, approximately 60% of individuals with HIV develop active TB when infected with the TB bacteria. Chronic diseases, such as DM, also increase the risk of TB infection.

Patients with Diabetes Mellitus (DM) are three times more likely to develop TB due to their compromised immune function, which increases their susceptibility to infection. The cause of pulmonary TB in DM patients is linked to immune cell dysfunction, including the impairment of respiratory epithelial cells (Hartanto et al., 2019). TB is a region-based disease with spatial dependence, meaning its transmission is influenced by geographic factors. Geography, closely related to the environment, plays a key role in shaping public health conditions. Therefore, controlling pulmonary TB requires considering the spatial distribution of cases, which can be analyzed through spatial analysis (Leu et al., 2020).

This study aims to analyze the spatial influence of risk factors such as population density, HIV/AIDS, and Diabetes Mellitus on pulmonary TB cases using the GeoDa application.

SUBJECTS METHOD

1. Study Design

This study is an analytical observational research with an ecological study design, utilizing secondary data as the research sample. The study was conducted in Kupang, East Nusa Tenggara, Indonesia, from November to December 2024.

2. Population and Sample

The study population consisted of all individuals diagnosed with positive pulmonary TB who resided in Kupang between 2021 and 2023. In 2021, there were 441 cases, rising to 785 in 2022, and 979 in 2023. The sample includes the entire population of positive pulmonary TB cases in Kupang. Spatial analysis was conducted at the sub-district level, covering six sub-districts in Kupang. Secondary data on new TB cases, TB-HIV co-infection, and TB-DM cases were obtained from the Kupang Health Office, while population density data was sourced from the Kupang Central Statistics Agency.

3. Study Variables

The independent variables were population density and DM. The dependent variable was TB.

4. Operational Definition of Variables

Pulmonary tuberculosis (TB) is an infectious disease caused by an infection of the bacterium *Mycobacterium tuberculosis* in the lungs.

Population density is the ratio of the number of inhabitants to the area of a region.

HIV (Human Immunodeficiency Virus) is a disease that attacks the immune system. HIV can weaken the body's ability to fight infections and diseases.

Diabetes mellitus (DM) is a chronic disease characterized by high blood sugar levels.

5. Study Instruments

This study utilizes secondary data collected from various institutions, such as the Kupang Health Office and the Kupang Central Bureau of Statistics.

6. Data Analysis

The analysis technique in this study utilizes the GeoDa application to perform bivariate analysis through the global and local Moran's Index (LISA) test. The global Moran's Index test detects spatial autocorrelation by examining the p-value (<0.05) and assessing the spatial relationship pattern by comparing the Moran index ([I]) to the expected Moran index (I[E]). If I > E(I), the autocorrelation value is positive, indicating clustered data. If I = E(I), there is no spatial autocorrelation, and if I < E(I), the autocorrelation value is negative, suggesting dispersed data. Local Moran's or LISA is used to identify local autocorrelation by analyzing spatial correlations within each region. The results are presented as a cluster map, which includes the following patterns:

- (High-High): Locations with high observed values are surrounded by other locations with high observed values.
- (Low-High): Locations with low observed values are surrounded by locations with high observed values.
- (Low-Low): Locations with low observed values are surrounded by other locations with low observed values.
- (High-Low): Locations with high observed values are surrounded by locations with low observed values.
- In addition, there are areas classified as "not significant," where no spatial influence is detected between the location and its surrounding areas.

7. Research Ethics

This study has received ethical approval from the Research Ethics Committee of the Faculty of Public Health (FKM) at Nusa

Cendana University, Kupang, under approval number 002768/KEPK FKM UNDANA/2024.

RESULTS

1. Univariate Analysis

Figure 1 shows the spread of positive pulmonary TB cases across Kupang City in 2021. Maulafa District recorded the highest number with 109 cases, followed by Oebobo District with 96 cases, categorized as moderate. Other districts with lower case numbers included Alak (63 cases), Kelapa Lima (67 cases), Kota Lama (45 cases), and Kota Raja (61 cases). The distribution map reveals that no areas in Kupang City had very low case numbers (<34 TB cases) in 2021.

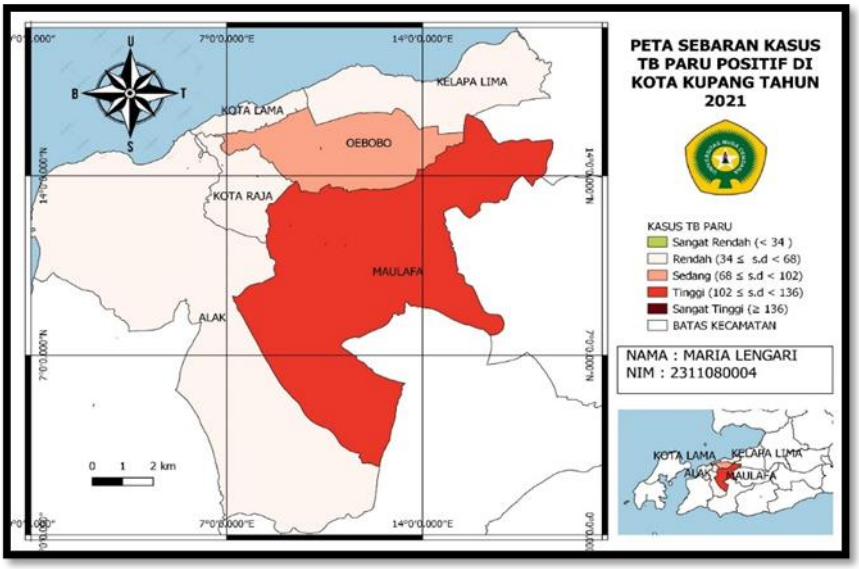


Figure 1. Spatial Distribution of Pulmonary TB Cases in Kupang City, 2021

The number of TB cases in 2022 saw a significant increase, with the distribution map revealing a clear clustering pattern. Adjacent areas tended to have similar case numbers. Oebobo and Maulafa Districts, both reporting more than 136 cases, were categorized as very high, with Oebobo recording 166 cases and Maulafa 167 cases. Alak and Kota Raja Districts fell into the high category (102–136 cases), with 130 cases in Alak and 129 cases in Kota Raja. Kelapa Lima District recorded 100 cases, while Kota Lama had 93, placing them in the medium category (68–102 cases) (see Figure 2).

The map of pulmonary TB case distribution in 2023 shows a continued significant increase. Most sub-districts in Kupang City now have high TB cases, ranging from 102 to 136 cases or more. Sub-districts in the very high TB case category (≥136 cases) include Oebobo District with 291 cases, Maulafa District with 185 cases, and Kelapa Lima District with 141 cases. Other districts, such as Kota Raja (132 cases), Kota Lama (107 cases), and Alak (123 cases), fall into the high category (see Figure 3).

TB cases have steadily increased over the past three years. In 2021, Maulafa District had the highest number of TB cases, with neighboring Oebobo, Alak, and Kota Raja districts also reporting significant numbers. By 2022, TB cases rose further,

with Oebobo joining Maulafa in the very high category, while Alak and Kota Raja moved to the high category. By 2023, Oebobo, Maulafa, Alak, and Kota Raja appeared to influence the spread of TB, resulting in Kota Lama and Kelapa Lima moving into the high and very high TB case categories. This trend emphasizes the need for heightened awareness and preventive measures in neighboring areas to avoid further spikes in TB and similar infectious diseases.

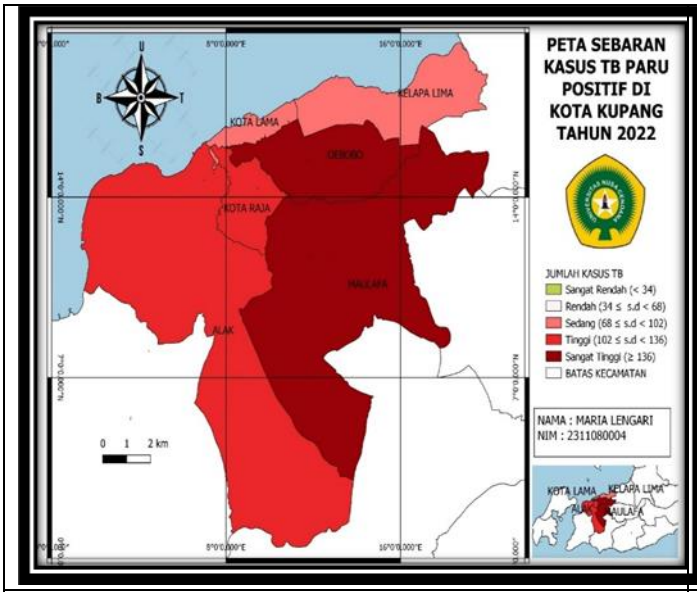


Figure 2. Pulmonary TB Case Distribution in Kupang, 2022

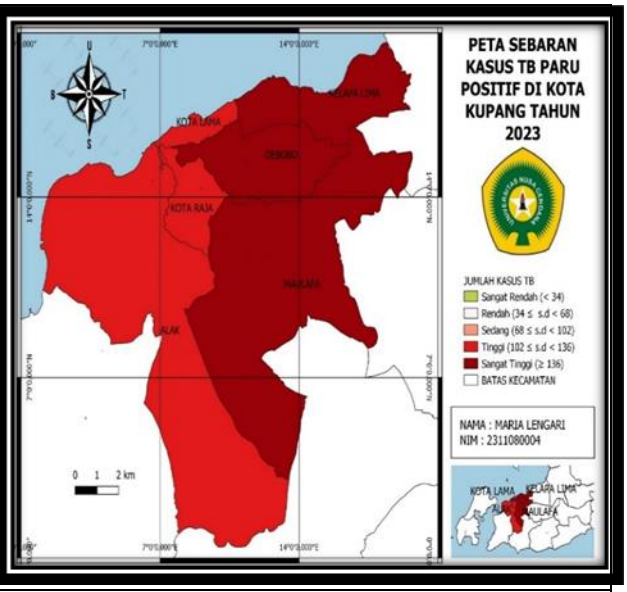


Figure 3. Pulmonary TB Case Distribution in Kupang, 2023

2. Bivariate Analysis

Weighting Matrix

The spatial weighting matrix defines the relationship between an observed area and its surrounding areas. In this study, the Queen method was used to identify the neighbors of each observation location. Below are the observation locations and their corresponding neighborhood details.

Table 1. Neighborhood Information

No	Observation Area	Neighbor
1	Alak	Kota Lama, Kota Raja, Maulafa
2	Kelapa Lima	Kota Lama, Maulafa, Oebobo
3	Kota Lama	Alak, Kelapa Lima, Kota Raja, Oebobo
4	Kota Raja	Alak, Kota Lama, Maulafa, Oebobo
5	Maulafa	Alak,Kelapa Lima, Kota Raja,Oebobo
6	Oebobo	Kelapa Lima, Maulafa, Kota Raja, Kota Lama

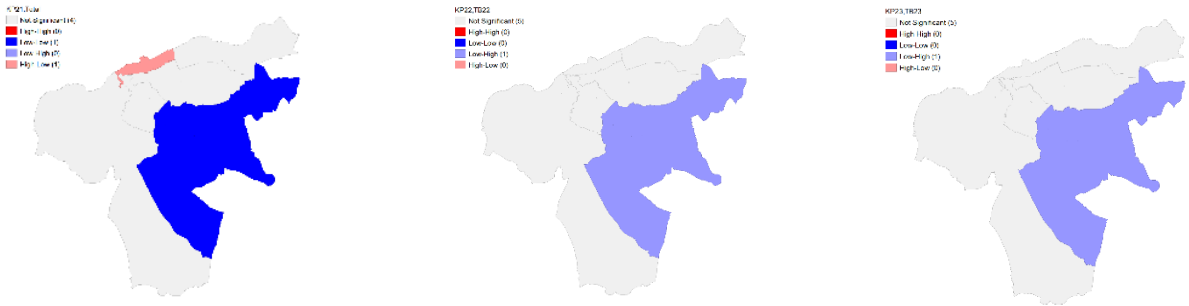
Autocorrelation of population density with positive Pulmonary TB

Table 3 presents the spatial autocorrelation of population density and pulmonary TB cases in Kupang City from 2021 to 2023. In 2021, there was a significant spatial autocorrelation between population density and positive pulmonary TB cases. The Moran's I value was 0.05, and the expected Moran's I (E[I]) was -0.20. Since I>E[I], with a mean of 0.12 (SD = 0.12), this indicates a positive autocorrelation, showing clustering of population density and TB cases. However, in 2022 and 2023, the spatial autocorre-

lation between population density and positive pulmonary TB cases was not significant.

Table 2. Spatial Autocorrelation of Population Density and Positive Pulmonary TB Cases in Kupang City (2021–2023)

No	Years	Mean	SD	Moran's index	E [I]	p
1.	2021	0.12	0.12	0.05	-0.20	0.049
2.	2022	0.08	0.13	0.02	-0.20	0.318
3.	2023	0.01	0.13	0.08	-0.20	0.353



1. 2021 **2. 2022** **3. 2023**

Figure 4. Cluster Map of Population Density and TB Cases in Kupang (2021-2023)

The cluster map in Figure 4 shows that in 2021, the Kota Lama District exhibited a significantly High-Low spatial relationship, indicating high population density but a low number of positive pulmonary TB cases. However, neighboring areas such as Oebobo District had relatively high TB case numbers. In contrast, Maulafa District showed a Low-Low spatial relationship pattern, suggesting both low population density and low TB cases. From 2022 to 2023, Maulafa District displayed a Low-High spatial relationship, indicating that while the population density remained low, the number of TB cases increased. The neighboring districts of Maulafa include Alak, Kelapa Lima, Kota Raja, and Oebobo.

Autocorrelation of TB-HIV with Positive Pulmonary TB Cases

Table 3. Spatial Autocorrelation of TB-HIV and Positive Pulmonary TB in Kupang (2021–2023)

No	Years	Mean	SD	Moran's index	E [I]	p
1.	2021	-0.13	0.14	0.06	-0.20	0.30
2.	2022	0.04	0.14	0.09	-0.20	0.29
3.	2023	-0.12	0.09	-0.03	-0.20	0.28

Table 3 presents data on the spatial autocorrelation between the HIV variable and the incidence of positive pulmonary TB in Kupang from 2021 to 2023. The results show that the p-values for the HIV variable were 0.303 in 2021, 0.29 in 2022, and 0.28 in 2023. These values indicate that there was no spatial autocorrelation between the TB-HIV variable and the incidence of

positive pulmonary TB in Kupang during the 2021–2023 period.

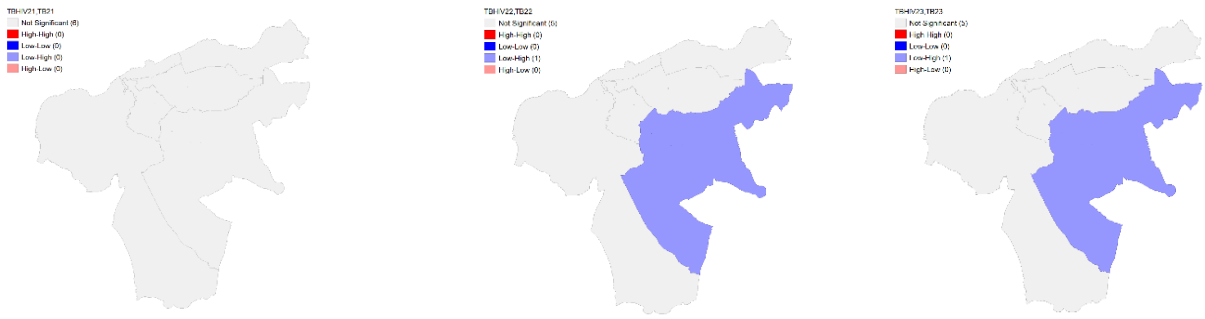


Figure 5. Cluster Map of TB-HIV and TB Cases in Kupang (2021-2023)

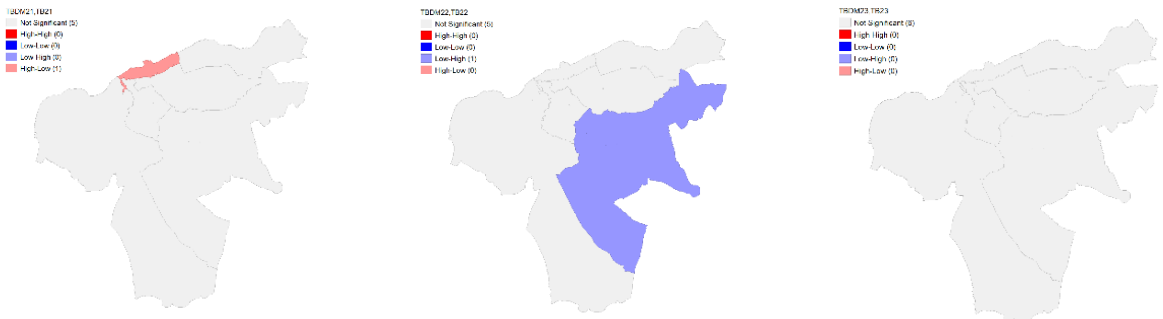
Figure 5 shows that in 2021, no sub-districts exhibited significant clustering. However, in 2022 and 2023, Maulafa District displayed a significantly Low-High spatial relationship, indicating that during this period, Maulafa District had low TB-HIV cases but high TB cases. Additionally, the surrounding neighboring areas of Maulafa, including Alak, Kelapa Lima, Kota Raja, and Oebobo, also had relatively high TB case numbers.

Autocorrelation of TB-DM with Positive Pulmonary TB Cases

Table 4 shows that in 2021, the p-value for the DM variable was 0.233. In 2022, the p-value for the DM variable was 0.456, and in 2023, it was 0.466. Since all p-values are greater than 0.05, this indicates that there was no spatial autocorrelation between the DM variable and the incidence of positive pulmonary TB in Kupang during the 2021–2023 period.

Table 4. Spatial Autocorrelation of TB-DM Variables and Positive Pulmonary TB Cases in Kupang (2021–2023)

No	Years	Mean	SD	Moran's index	E [I]	p
1.	2021	-0.10	0.14	-0.19	-0.20	0.23
2.	2022	0.10	0.14	0.07	-0.20	0.46
3.	2023	-0.13	0.13	-0.12	-0.20	0.47



1. 2021 **2. 2022** **3. 2023**

Figure 6. Cluster Map of TB-DM and TB Cases in Kupang City (2021-2023)

The TB-DM cluster map with TB cases in Kupang City from 2021 to 2023 shows that in 2021, the spatial relationship pattern formed in Kota Lama District was a High-

Low pattern. This indicates that Kota Lama Subdistrict had high TB-DM cases but low TB cases. However, the neighboring areas of Kota Lama District, such as Alak, Kelapa Lima, Kota Raja, and Oebobo, had high TB case numbers. In 2022, the map shows that Maulafa District exhibited a Low-High spatial relationship, indicating that Maulafa District had low TB-DM cases but high TB cases. Additionally, the surrounding areas of Maulafa District, including Alak, Kelapa Lima, Kota Raja, and Oebobo, also had high TB case numbers. In 2023, no sub-districts or regions showed a significant spatial relationship.

DISCUSSION

In 2021, a spatial autocorrelation was observed between population density and positive pulmonary TB cases in Kupang, showing a clustered pattern. Kota Lama District exhibited a significant high-low spatial relationship—indicating high population density but relatively low TB cases. Although high density can facilitate TB transmission, neighboring areas like Oebobo District reported notably higher TB cases.

Therefore, Kota Lama District warrants continuous monitoring to mitigate the risk of a potential increase in Tuberculosis (TB) cases. Maulafa District initially demonstrated a low-low spatial relationship, indicating both low population density and a low incidence of TB. However, between 2022 and 2023, this pattern shifted to a Low-High spatial relationship, characterized by low population density but a high number of TB cases. The increase in TB incidence within Maulafa District is primarily attributable to cases among the incarcerated population. Contributing factors include high housing density, inadequate ventilation, smoking, cohabitation with TB patients, the presence of workshops, extended detention periods, suboptimal physical environmental conditions (e.g., lighting, humidity, temperature), and high-risk behaviors such as coughing without covering the mouth and indiscriminate spitting. Supporting evidence from a study by Putri (2018) in Class I Semarang Prison identified poor lighting and inappropriate coughing behavior as significant contributors to the prevalence of TB. Additionally, the influence of adjacent districts should be considered in assessing TB transmission dynamics.

Maulafa District is bordered by the districts of Alak, Kelapa Lima, Kota Raja, and Oebobo. Kota Lama District has a population density of 10,966 people per square kilometer, while Oebobo District has a density of 7,231 people per square kilometer. These findings differ from those reported by Puteri (2020) in Jambi City, where a High-High spatial relationship between population density and TB cases was observed from 2015 to 2021 in subdistricts such as Beliung, Simpang IV Sipin, Paal Merah, Pasir Putih, and Mayang Mangurai (Puteri, 2022). Population density is defined by the number of individuals residing within a given land area. Elevated population density increases the potential for close and frequent contact between individuals with pulmonary TB and other household members, thereby facilitating disease transmission (Kenedyanti and Sulistyorini, 2017).

Previous studies have identified Jomblang Village as having the highest population density and the greatest number of TB cases, with 161 people per square kilometer within an area of only 108 km². In contrast, Jati Ngaleh Village, with a larger land area and smaller population, has a lower density of 58 people per square kilometer. These findings highlight that high population density is a key factor

contributing to the transmission of pulmonary Tuberculosis. Additional contributing factors include unfavorable socio-economic conditions, poor environmental quality, and inadequate nutritional status. Such conditions often lead to slum-like environments characterized by poor sanitation, which further facilitates TB transmission (Aditama and Suharyo, 2012). Supporting this, cities with a population density exceeding 80 people per square kilometer have been found to have a 4.18 times higher TB incidence compared to less densely populated cities ($p<0.001$). This is consistent with findings from Wates, where TB case clustering has been observed in areas with population densities above 900 people per square kilometer (Rohman, 2020).

In contrast, a study by Efendi and Darwis (2023) found that the distribution of TB patients in the service area of Pasar Rebo Hospital is not generally influenced by population density. Although certain districts have higher population densities, TB cases are not as widely distributed as in some less densely populated areas. For instance, Matraman District—one of the most densely populated areas in East Jakarta and among the top five in all of DKI Jakarta—reported only one TB case (Efendi & Darwis, 2023).

This pattern is likely influenced by other factors, such as individuals frequently traveling to or working in areas with high TB transmission, as well as underlying immune system vulnerabilities that increase susceptibility to infectious diseases like TB. Additionally, the expansion of infrastructure has led to increased employment opportunities, while improvements in educational facilities have contributed to population growth in Kupang City. These developments are considered key drivers of the city's rising population (Fernandez et al., 2023).

HIV is the strongest risk factor for the progression from latent to active Tuberculosis in infected individuals. HIV infection severely compromises the cellular immune system, rendering individuals highly susceptible to opportunistic infections such as TB. As a result, co-infected patients often experience severe illness and may face increased mortality. The rise in HIV cases is therefore closely associated with a corresponding increase in TB incidence and community transmission (Wijaya, 2019). Furthermore et al. (2020) highlight the role of *Mycobacterium tuberculosis* in evading immune responses through a key component known as lipoarabinomannan (LAM). LAM, a heteropolysaccharide complex composed of phosphatidylinositol, significantly modulates immunoregulatory mechanisms, thereby enhancing the pathogen's ability to persist within the host.

People living with HIV are 15-22 times more likely to develop TB than persons without. TB is the most common presenting illness among people living with HIV, including among those taking antiretroviral treatment, and it is the major cause of HIV-related deaths. Sub-Saharan Africa bears the brunt of the dual epidemic, accounting for approximately 84% of all deaths from HIV-associated TB in 2018 (WHO, 2025). In the present study, no subdistricts demonstrated a significant spatial relationship in 2021. However, in 2022 and 2023, Maulafa District exhibited a Low-High spatial pattern, characterized by low HIV/AIDS cases but relatively high TB incidence. Surrounding districts—including Oebobo, Alak, Kelapa Lima, and Kota Raja—also reported high numbers of positive pulmonary TB. Among these, Oebobo and Kota Lama are noted for relatively high population densities. According to Kevin et al. (2024), Kota Lama and Kota Raja are the most densely

populated sub-districts, with population densities ranging from 9,626 to 16,818 people per square kilometer, while Oebobo and Kelapa Lima fall within the moderate density range of 4,162 to 9,626 people/km^2.

Diabetes mellitus is a non-communicable disease characterized by chronic metabolic disturbances due to the body's inability to effectively utilize insulin, resulting in elevated blood glucose levels (hyperglycemia) (Indonesian Ministry of Health, 2018). In 2021, 22 of the 441 recorded TB cases involved individuals with both diabetes and tuberculosis, with the highest numbers reported in Maulafa and Oebobo sub-districts. By 2022, this number increased to 35 out of 785 TB cases, with Kota Raja recording the highest number of TB-DM comorbidities. In 2023, the figure rose significantly to 70 out of 979 TB cases, with Oebobo and Kota Raja again reporting the highest comorbidity rates.

A bivariate LISA analysis in 2021 identified a High-Low spatial relationship in Kota Lama, indicating a high number of TB-DM cases despite relatively low overall TB incidence. In contrast, neighboring sub-districts such as Alak, Kelapa Lima, Kota Raja, and Oebobo exhibited high TB incidence. In 2022, Maulafa displayed a Low-High spatial pattern, with low TB-DM comorbidity but high TB incidence, surrounded by neighboring districts—Alak, Kelapa Lima, Kota Raja, and Oebobo—that also reported high TB cases.

In addition to the pathological effects of tuberculosis associated with diabetes mellitus (DM), patients undergoing TB treatment while managing diabetes must carefully regulate their blood glucose levels. Rifampicin, a first-line anti-TB drug, reduces the efficacy of oral anti-diabetic medications like sulfonylureas, often requiring dosage adjustments. Furthermore, isoniazid inhibits the P450 enzyme, which can interfere with rifampicin's effectiveness. Studies have shown that diabetic patients undergoing TB treatment are more likely to experience treatment failure and increased mortality compared to non-diabetic TB patients (Iswahyuni et al., 2022). Consequently, close monitoring and appropriate dose adjustments for both anti-tuberculosis and anti-diabetic medications are essential for optimal therapeutic outcomes. Regular blood glucose monitoring and collaboration with healthcare providers are crucial in preventing complications. Additionally, lifestyle modifications, such as a balanced diet and consistent physical activity, can support blood sugar control while enhancing the efficacy of TB treatment.

The results of this study indicate spatial autocorrelation between population density and pulmonary tuberculosis (TB) cases in Kupang City in 2021. However, no spatial autocorrelation was observed from 2022 to 2023, including for the Diabetes Mellitus and HIV/AIDS variables. Based on these findings, researchers recommend increased vigilance in high-population-density areas to prevent further TB transmission and potential case surges. Additionally, maintaining strong immunity through clean and healthy living practices is essential to avoid preventable infectious diseases.

AUTHORS CONTRIBUTIONS

All authors contributed equally

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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