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Original Article

Epidemiology of Tuberculosis in Aceh, Indonesia, 2016–2021: An Ecological Study of Regional Surveillance Data

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ABSTRACT

Background: Aceh Province reported the lowest tuberculosis (TB) treatment coverage in Indonesia in 2020; however, the distribution of TB across its 23 districts and cities has not been described using spatial methods. **Objective:** To describe the temporal and spatial distributions of TB notifications, case fatalities, and treatment outcomes in Aceh from 2016–2021 and to explore their ecological associations with district demographic characteristics. **Methods**: This ecological study used aggregated annual district-level data from the Aceh Provincial Health. Case notification rates (CNRs) and case fatality ratios (CFRs) were analyzed using negative binomial mixed models. Associations with population density, growth rate, and sex ratio were explored using Spearman correlation and negative binomial regression. Districts were grouped using K-means clustering, and spatial autocorrelation was assessed using global and local Moran's I. **Results**: Notifications rose in 2016 to 2019, decreased by 30.7% in 2020, and recovered only partly in 2021 (133.8). The CFR increased from 1.08% in 2019 to 2.18% in 2020 and 3.58% in 2021, a 3.3-fold increase relative to the 2016–2019 rate. Treatment success reached 90% only in 2016 and 2017, whereas the cure rate decreased from 80% to 30%. No demographic covariates showed a consistent association with the CNR. The cluster structure was weak (mean silhouette = 0.41). The global Moran's I was negative (−0.35; p = 0.039), reflecting high-CNR cities surrounded by lower-CNR regions, and this pattern was not robust to an alternative neighborhood definition. **Conclusion**: The TB in Aceh showed an urban-enclave pattern without contiguous hotspots. Restoring active case findings and bacteriological follow-up and improving the quality of district surveillance data should be priorities for TB elimination in Aceh.

KEYWORDS

Tuberculosis, epidemiology, public health surveillance, spatial analysis, case fatality, Indonesia

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INTRODUCTION

Tuberculosis (TB) is an infectious disease that continues to pose a hazard to people worldwide, including those in Indonesia [1]. TB is caused by *Mycobacterium tuberculosis* and is transmitted through airborne particles expelled when a person with pulmonary TB coughs, sneezes or talks. Smoking increases the risk of infections and diseases [2–4]. According to the 2019 Global Tuberculosis Report, an estimated 10 million people developed TB in 2018, and 30 high-burden countries accounted for 87% of all cases [5]. In 2021, Indonesia accounted for 9.2% of global TB cases, second only to India [6].

Over the past decade, Indonesia has made progress in reducing the incidence of tuberculosis (TB) and improving treatment efficacy. However, there are still considerable obstacles to national TB eradication [7]. There is not enough appropriate health services or access to high-quality, patient-centered TB care in every region of Indonesia, which contributes to the high morbidity and mortality rates of tuberculosis. Inadequate services involve delayed early screening and limited support for TB survivors and their communities. During the COVID-19 pandemic, which continued through 2022 [8], Indonesia reported a marked decrease in notified TB cases. In 2020, 351,936 cases were reported nationally, a reduction from 568,987 cases in 2019 [9]. Globally, notifications fell by 18% between 2019 and 2020 and by 31% in Indonesia, while TB deaths increased for the first time in more than a decade [10]. In addition, treatment coverage (TC) during the pandemic did not reach the national target of at least 80%. The province with the lowest TC concentration was reported to be Aceh, at 32.6% [9].

A reanalysis of national survey data revealed that the bacteriologically confirmed TB incidence in Sumatra (913 per 100,000) exceeded that in Java–Bali (593 per 100,000) [11]. Within Aceh, many districts contributed disproportionately high numbers of TB cases, and the case notification rate (CNR) was much lower than the objective [12]. During the pandemic, low contact tracing and large-scale social restrictions in Aceh may have impeded TB care, as health services prioritized COVID-19 [13–15], and overlapping symptoms led to a misdiagnosis between COVID-19 and pulmonary TB [16–19].

In a country with a high TB caseload, namely, Pakistan, COVID-19 decreased health services, including regular monitoring efforts [20]. As a result of routine surveillance activities that are categorized as low, the number of cases has not been recorded, treatment has been delayed, and spread and prevention have not been carried out on time or target, resulting in an increase in cases throughout the year [21]. Aceh was chosen because it combines the lowest provincial TC in 2020 [9], a regional prevalence higher than the national average [11], and a lack of province-wide district-level analysis. The only spatial study we identified in the province involved the subdistricts of North Aceh from 2019–2021 [22]. The period 2016–2021 covers the six most recent annual health profiles available when the data were collected (October–December 2022), comprising four pre-pandemic years and two pandemic years.

This study therefore aimed (1) to describe the annual distribution of TB notifications, deaths, and treatment outcomes in Aceh during 2016–2021 at the provincial and district levels, including changes during the COVID-19 pandemic; (2) to explore the ecological association of district population density, growth rate, and sex ratio with the case notification rate; and (3) to identify the groupings and spatial clustering of districts using K-means clustering and spatial autocorrelation statistics. The findings are intended to inform the acceleration of TB elimination in Aceh by 2030.

MATERIALS AND METHODS

Study design

This research is an ecological study with descriptive and exploratory analytical components and is based on routinely collected surveillance data aggregated at the district/city level [23]. Reporting follows the REporting of Studies Conducted using Observational Routinely Collected Health Data (RECORD) statement [24]. The data source was the 2016–2021 Health Profiles of Aceh Province, obtained through https://dinkes.acehprov.go.id. Data were collected over three months (October–December 2022).

Data sources, completeness, and quality

The official website of the Aceh Provincial Health Office was used to collect yearly TB statistics contained in the Aceh Province Health Profile from 2016 to 2021, as well as population data from the Aceh Province Central Statistics Agency (BPS) [25]. All the data were aggregated annual counts per district or city. No individual-level records were available. For each of the 23 districts/cities and each year, we extracted the number of notified TB cases, the number of TB deaths, and the number of patients cured and completing treatment. The 2020 census population, sex ratio, and 2010–2020 annual population growth rate were also extracted. District boundaries were obtained from the 1:50,000 administrative boundary dataset of the Indonesian Geospatial Information Agency (BIG) [26].

Data completeness and internal consistency were checked before the analysis. All 138 district-year records (23 districts × 6 years) were complete. For every year, the district totals of cases, deaths, population, and area equaled the provincial totals, and all rates recalculated from the counts reproduced the values in the source spreadsheet. Year-on-year changes larger than three times were flagged as potential reporting artifacts. These were Aceh Barat Daya in 2017 (18 to 146 cases) and 2018 (146 to 484), Aceh Utara in 2017 (175 to 1,282), Kota Sabang in 2017 (12 to 48), and Pidie Jaya in 2020 (199 to 65). They were retained as officially reported. In the district treatment–outcome tables, the 2016–2018 values for treatment success were recorded as percentages, whereas those for 2019–2021 were counts. Treatment-outcome analyses were therefore restricted to the provincial percentages published in the profiles.

Variables and operational definitions

Area represents the land area under the jurisdiction of each district or city (km^2). The total population was the number of male and female residents in the 2020 census (persons), and the population density was the population divided by the area (persons/km^2); the sex ratio is the ratio of the male population to the female population in a certain area and at a certain time expressed as males per 100 females. Population growth was the 2010–2020 average annual growth rate (% per year).

The case notification rate (CNR) was the number of notified TB cases divided by the population and expressed per 100,000. Because the source profiles report notifications rather than true incidence, CNR replaces the term incidence rate (IR) used in the original submission. Annual district populations were estimated using geometric projection from the 2020 census, using each district's 2010–2020 growth rate, $P_t = P_{2020} \times (1 + r)^{(t - 2020)}$. A sensitivity analysis used the constant 2020 census population, which was the denominator applied in the original submission. The mortality rate was the number of TB deaths per 100,000 population. The case fatality ratio (CFR) was the number of TB deaths reported in a year divided by the number of TB cases reported in the same year and multiplied by 100. Treatment outcomes followed the national definitions, which are consistent with those of the World Health Organization [27].

The cure rate is the percentage of bacteriologically confirmed pulmonary TB patients in the treatment cohort who were cured. The completion rate is the percentage of all TB patients in the cohort who completed treatment without bacteriological evidence of cure. The treatment success rate is the percentage of all patients in the cohort who were cured or completed treatment. Mortality during treatment is the percentage of all patients in the cohort who died from any cause during treatment. A CNR of at least 40 per 100,000 was used to denote a high-incidence setting [28], and a treatment success rate of at least 90% was used as the End TB Strategy target [29].

Statistical analysis

All analyses were performed using R version 4.3.3 [30]. Annual provincial CNR and mortality rates are presented with exact Poisson 95% confidence intervals (CIs), and CFR is presented with exact binomial 95% CIs. Temporal changes in notifications were modeled using a negative binomial generalized linear mixed model (GLMM). The model included year as a categorical fixed effect (reference 2019), the logarithm of the projected population as an offset, and a random intercept for district and was fitted with glmmTMB [31]. Deaths were modeled with the logarithm

of notified cases as the offset and period (2016–2019, 2020, 2021) as the exposure so that exponentiated coefficients could be used to estimate the CFR ratios.

The Poisson and negative binomial specifications were compared using the Akaike information criterion. Residual dispersion was checked with simulated residuals using the DHARMa package [32]. Ecological associations between the mean CNR for 2016–2021 and $\log_{10}$ population density, growth rate, sex ratio, $\log_{10}$ population, and $\log_{10}$ area were assessed with Spearman's correlation, using Holm-adjusted p values and bootstrap 95% CI from 2,000 resamples. These covariates were then entered as standardized variables (per 1 SD) into a negative binomial GLMM with year fixed effects. Multicollinearity was checked using variance inflation factors. Two sensitivity analyses were performed: one restricted to the 18 regencies and one using a cross-sectional negative binomial regression of total cases for 2016–2021 [33].

Districts were grouped by K-means clustering [34] using three standardized indicators: the logarithm of the 2016–2019 CNR, the logarithm of the 2020–2021 CNR, and the pooled CFR. The algorithm uses 100 random starts. The number of clusters (k = 2–6) was selected by the mean silhouette width [35], and the gap statistic with 500 bootstrap samples was reported as a check [36]. Spatial autocorrelation was assessed using global Moran's I [37].

Its empirical Bayes adjustment for rates was also computed [38]. Local indicators of spatial association (LISA) [39] and the Getis–Ord Gi* statistic [40] were calculated using the spdep package [41] with 9,999 conditional permutations and two-sided tests. The primary spatial weights were row-standardized queen contiguity weights. The two island districts without contiguous neighbors (Simeulue and Kota Sabang) were linked to their nearest neighbor by centroid distance so that the network formed a single connected component. A four-nearest-neighbor matrix was used for the sensitivity analysis.

Local p values were also adjusted by the false discovery rate. All tests were two-sided with α=0.05, and the random seed was fixed at 2026. Maps were produced in R with the sf, ggplot2, and ggspatial packages [42] on the BIG boundaries in geographic coordinates (WGS 84). Each map includes a legend, a north arrow, and a scale bar. The demographic variables were classified into quantile classes. The CNR maps used one fixed classification for all years (0–50, 50–100, 100–150, 150–200, 200–300, and 300–400 per 100,000, upper limits inclusive) to allow comparison over time. The figures were exported at 600 dpi. The dataset and complete R script are provided in the Supplementary.

Ethical considerations

The Health Research Ethics Committee, Faculty of Medicine, Airlangga University, declared this research ethically feasible (number 2/EC/KEPK/FKUA/2023).

RESULTS

Overview of Aceh province

Aceh Province is in the western part of Sumatra Island, with a land area of 57,956 km^2, and is located between 01° 58′ 37.2" and 06° 04′ 33.6" north latitude (N) and 94° 57′ 57.6" and 98° 17′ 13, 2" east longitude (E), with four regional boundaries covering the north and east (Strait of Malacca), south (North Sumatra Province), and west (Indian Ocean) [25]. Aceh Province has 18 regencies and five cities with a 2020 census population of 5,274,871 persons, an average population density of 91 persons/km^2, an average annual population growth rate of 1.56% during 2010–2020, and an average male to female population ratio of 101, which indicates that the male population is greater than the female population. The population density ranged from 17.4 persons/km^2 in Gayo Lues to 4,145.9 persons/km^2 in Kota Banda Aceh. The area, total population, population density, sex ratio, and population growth rate of each region/city in Aceh Province are shown in Figure 1.

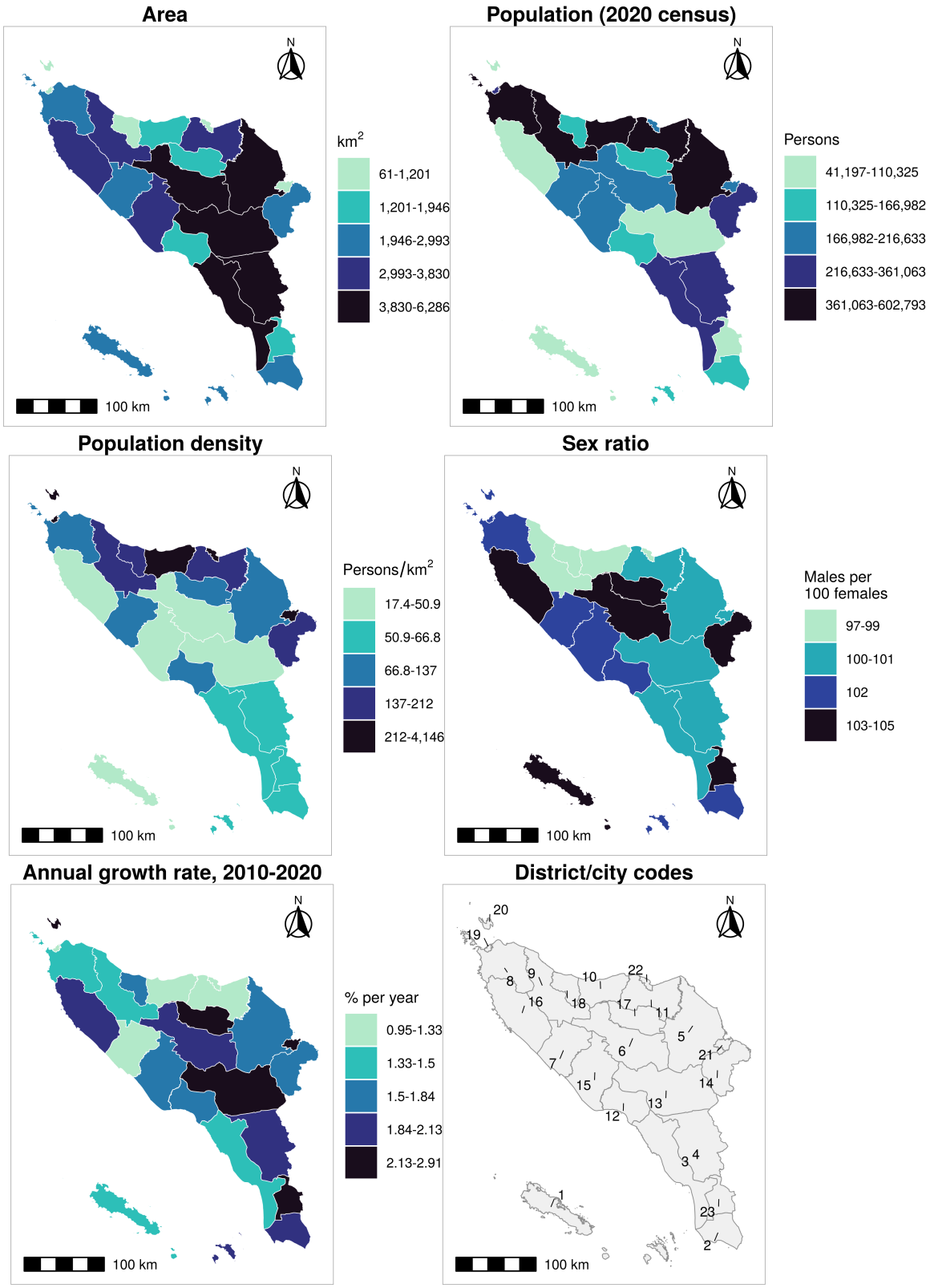


Figure 1. Area, 2020 census population, population density, sex ratio (males per 100 females), and annual population growth rate (2010–2020) of the 23 regencies and cities of Aceh Province, with a reference map of the district codes. Quantile classes. Boundaries: Indonesian Geospatial Information Agency (BIG) at 1:50,000 (2022). Codes: 1 Simeulue, 2 Aceh Singkil, 3 Aceh Selatan, 4 Aceh Tenggara, 5 Aceh Timur, 6 Aceh Tengah, 7 Aceh Barat, 8 Aceh Besar, 9 Kandaie, 10 Bireuen, 11 Aceh Utara, 12 Aceh Barat Daya, 13 Gayo Lues, 14 Aceh Tamiang, 15 Nagan Raya, 16 Aceh Jaya, 17 Bener Meriah, 18 Pidie Jaya, 19 Kota Banda Aceh, 20 Kota Sabang, 21 Kota Langsa, 22 Kota Lhokseumawe, 23 Kota Subulussalam.

Epidemiology of tuberculosis in Aceh province during 2016–2021

A total of 42,792 TB cases were reported in Aceh Province between 2016 and 2021. Annual notifications increased from 5,072 in 2016 to 7,342, 8,471, and 8,647 in 2017–2019, respectively. They then decreased to 6,090 in 2020 and partly recovered to 7,170 in 2021 (Table 1). Banda Aceh city contributed the most TB cases in 2016 (581 cases) and 2019 (997 cases), North Aceh District in 2017 (1,282 cases), 2018 (1,247 cases), and 2020 (762 cases), and Bireuen in 2021 (729 cases). The lowest number was reported by Kota Sabang every year except in 2018, when Bener Meriah reported the fewest cases (23).

Table 1. Tuberculosis notifications, deaths, and treatment outcomes in Aceh, 2016–2021

Indicator	2016	2017	2018	2019	2020	2021
Notified cases (n)	5,072	7,342	8,471	8,647	6,090	7,170
Projected population	4,956,387	5,034,018	5,112,960	5,193,236	5,274,871	5,357,889
CNR per 100,000 (95% CI)	102.3 (99.5–105.2)	145.8 (142.5–149.2)	165.7 (162.2–169.2)	166.5 (163.0–170.1)	115.5 (112.6–118.4)	133.8 (130.7–137.0)
CNR, constant 2020 denominator	96.2	139.2	160.6	163.9	115.5	135.9
IRR vs 2019 (95% CI)[a]	0.69 (0.57–0.85)	0.90 (0.74–1.11)	0.99 (0.81–1.21)	1 (ref.)	0.69 (0.56–0.84)	0.77 (0.63–0.94)
TB deaths (n)	95	83	59	93	133	257
Mortality per 100,000 (95% CI)	1.92 (1.55–2.34)	1.65 (1.31–2.04)	1.15 (0.88–1.49)	1.79 (1.45–2.19)	2.52 (2.11–2.99)	4.80 (4.23–5.42)
CFR, % (95% CI)	1.87 (1.52–2.28)	1.13 (0.90–1.40)	0.70 (0.53–0.90)	1.08 (0.87–1.32)	2.18 (1.83–2.58)	3.58 (3.17–4.04)
Cure rate, %	80.0	73.0	72.0	71.8	58.4	30.0
Completion rate, %	13.0	17.0	16.0	59.0	55.4	74.8
Treatment success rate, %	93.0	91.0	88.0	89.5	83.8	89.4
Mortality during treatment, %	2.41	2.36	1.88	5.70	1.58	3.73

CNR, case report rate; CFR, case fatality ratio; CI, confidence interval; IRR, incidence rate ratio. Projected population: geometric projection from the 2020 census with district growth rates. [a] Negative binomial mixed model with district random intercept. Compared with that in 2016–2019, the CFR ratio was 1.71 (1.11–2.65) in 2020 and 3.32 (2.16–5.09) in 2021.

The provincial CNR was 102.3 (95% CI 99.5–105.2) per 100,000 in 2016, which rose to 166.5 (163.0–170.1) in 2019, fell to 115.5 (112.6–118.4) in 2020, and reached 133.8 (130.7–137.0) in 2021 (Table 1, Figure 3A). With the constant 2020 denominator of the original submission, the corresponding values were 96.2, 139.2, 160.6, 163.9, 115.5, and 135.9 per 100,000. In the mixed model, the notification rate in 2020 was 31% lower than that in 2019 (incidence rate ratio [IRR] 0.69; 95% CI 0.56–0.84). The rate in 2021 remained 23% lower (IRR 0.77; 0.63–0.94), and the rate in 2016 was also lower than that in 2019 (IRR 0.69; 0.57–0.85).

The negative binomial model fit far better than the Poisson model (AIC 1,666 versus 4,144) and showed no residual dispersion (DHARMa $p = 0.53$). The CNR fell between 2019 and 2020 in 19 of the 23 districts, and by 2021, only six districts had returned to or exceeded their 2019 level. Every year, 20–23 districts had a CNR of at least 40 per 100,000. From 2016–2021, the mean CNR was highest in Kota Banda Aceh (272.4), Kota Lhokseumawe (255.5), and Kota Subulussalam (185.6) and lowest in Bener Meriah (41.3), Aceh Tenggara (62.2), and Kota Sabang (62.8) per 100,000 (Figure 2).

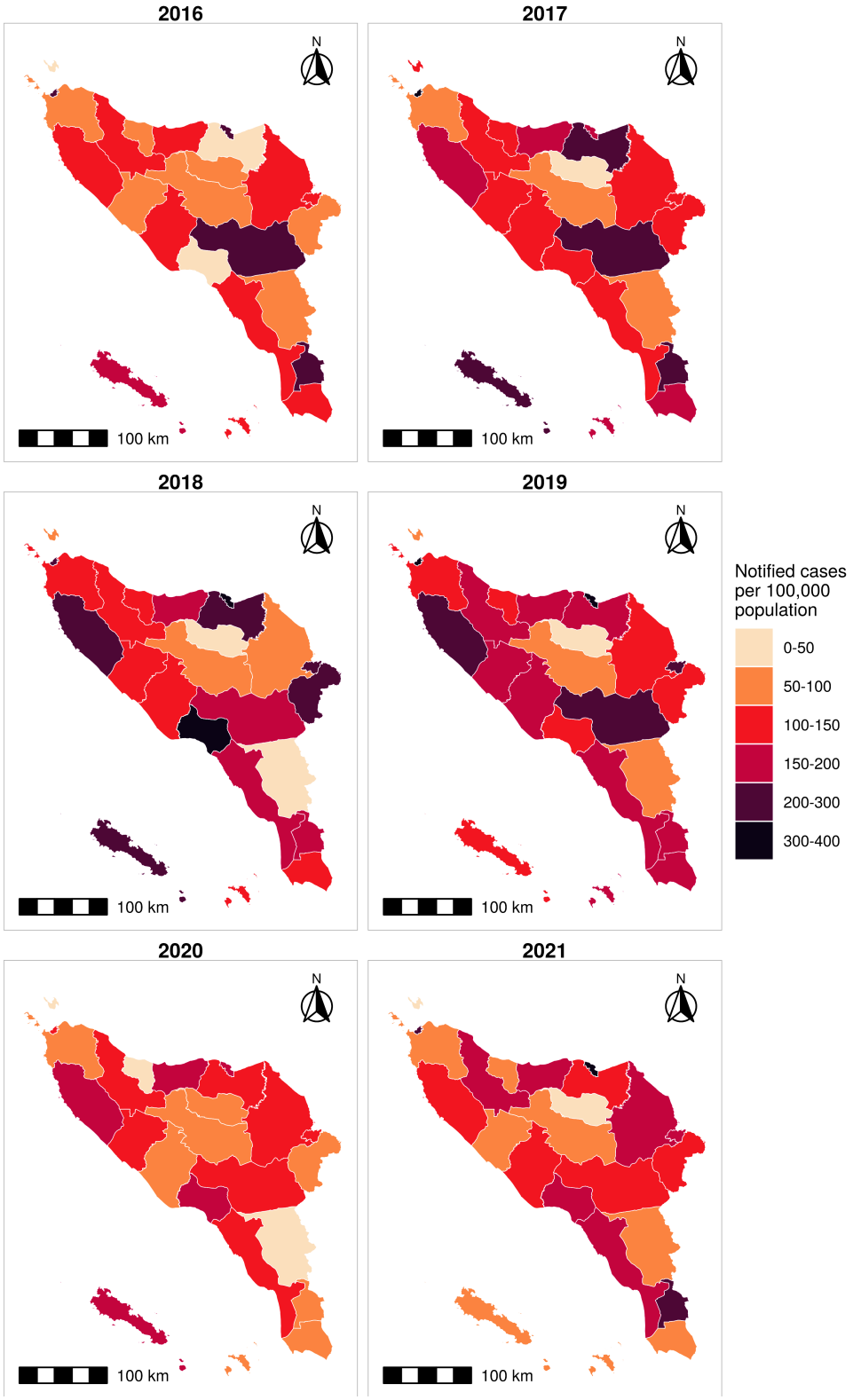


Figure 2. Tuberculosis case notification rate (notified cases per 100,000 projected population) by region and city in Aceh Province, 2016–2021. A common fixed classification was used for all years (upper class limits included).

TB death and case fatality rates were reported separately from notifications because the two indicators have different denominators. Reported TB deaths numbered 95, 83, 59, 93, 133, and 257 in 2016–2021, corresponding to mortality rates of 1.92, 1.65, 1.15, 1.79, 2.52, and 4.80 per 100,000 population, respectively. The CFR decreased from 1.87% (95% CI 1.52–2.28) in 2016 to 0.70% (0.53–0.90) in 2018. It was 1.08% (0.87–1.32) in 2019 and then increased to 2.18% (1.83–2.58) in 2020 and 3.58% (3.17–4.04) in 2021 (Table 1, Figure 3B). Compared with that in 2016–

2019, the CFR ratio was 1.71 (95% CI 1.11–2.65) in 2020 and 3.32 (2.16–5.09) in 2021. Between two and nine districts reported no deaths in a given year; therefore, district-level CFRs based on small numbers were unstable. An example is Aceh Tengah, whose reported 20 deaths among 147 cases in 2021 (13.6%).

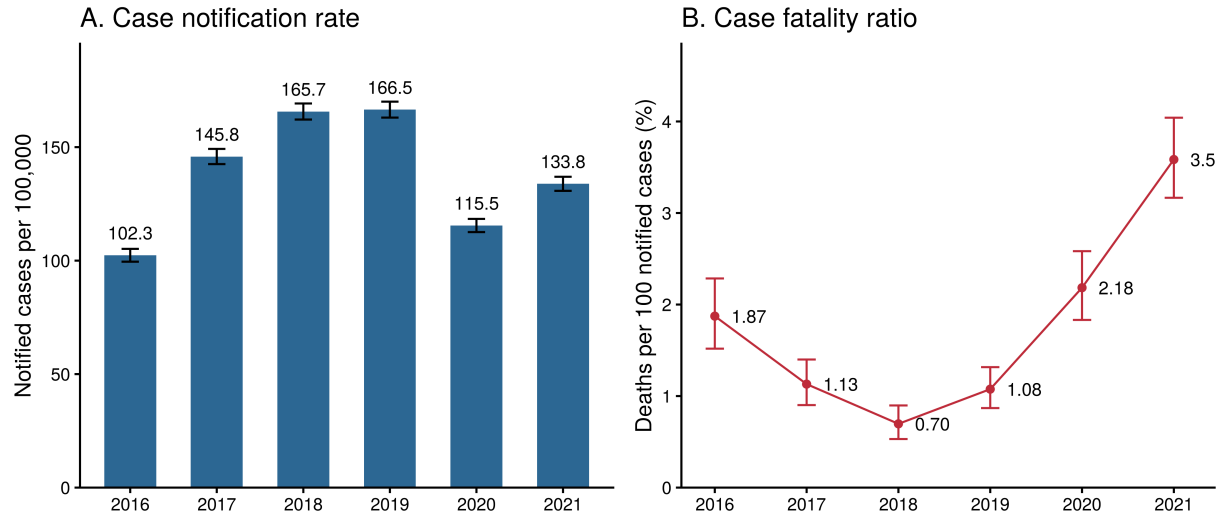


Figure 3. (A) Tuberculosis case notification rate per 100,000 people and (B) case fatality ratio (number of deaths per 100 notified cases) in Aceh Province, 2016–2021. The error bars show the exact 95% confidence intervals. The two indicators are plotted on separate axes because they have different denominators.

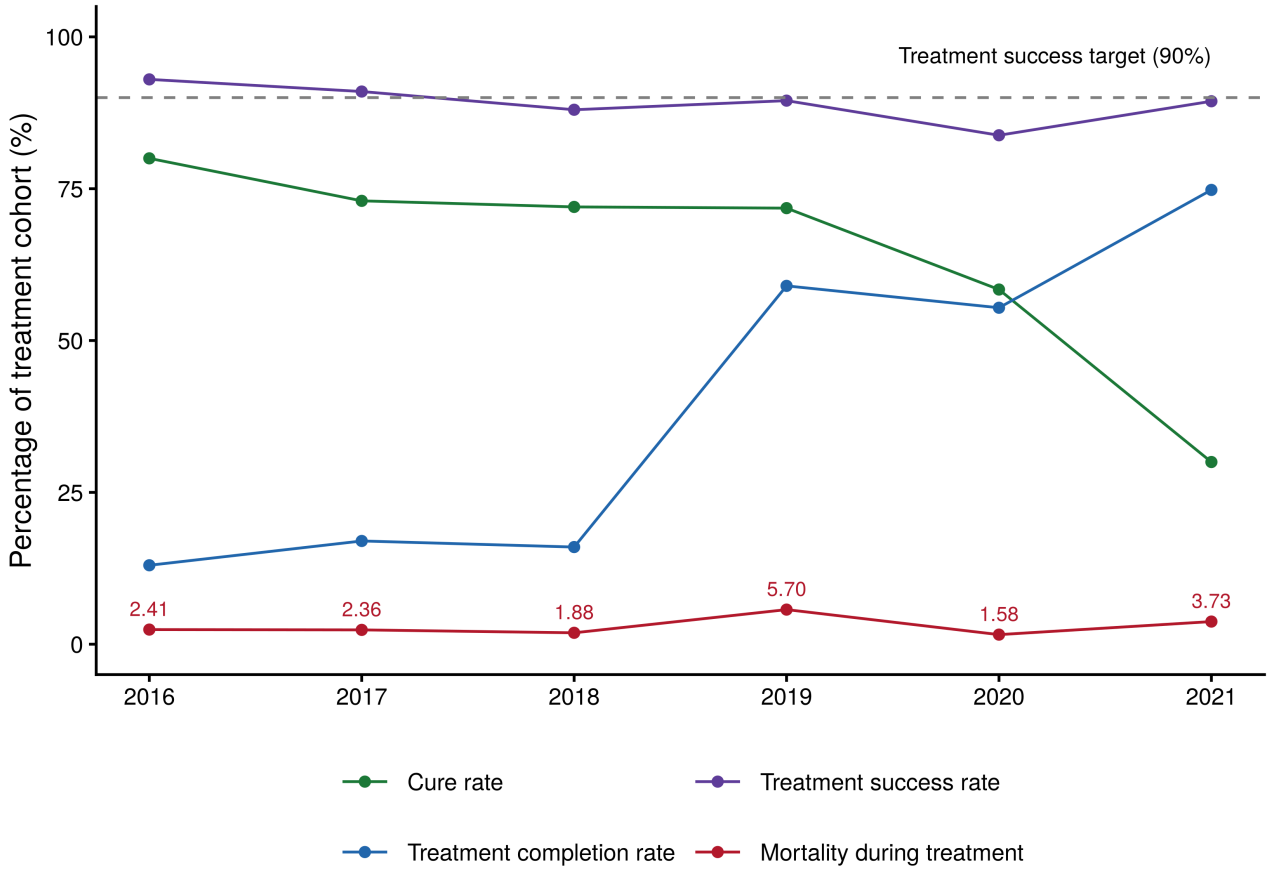


Figure 4. Cure rate, treatment completion rate, treatment success rate, and mortality during treatment among tuberculosis treatment cohorts in Aceh Province, 2016–2021 (provincial values from the health profiles). The dashed line indicates the 90% treatment success target. From 2019 onward, the cure rate was calculated for bacteriologically confirmed patients, and the other indicators were calculated for all patients.

The provincial TB cure rate decreased between 2016 and 2021 (Figure 4). It was the highest in 2016 (80%) and the lowest in 2021 (30%). The treatment completion rate increased from 13% in 2016 to 74.8% in 2021, with the largest step occurring between 2018 (16%) and 2019 (59%). The treatment success rate averaged 89.1% over the six years and reached the 90% target only in 2016 (93%) and 2017 (91%). For 2019–2021, the sum of the cure and completion rates exceeded 100%, which indicates that the cure rate was calculated on the bacteriologically confirmed subset of the cohort, while completion and success were calculated on all patients. The mortality rate during treatment fluctuated between 1.58% (2020) and 5.70% (2019) and was 3.73% in 2021.

Ecological associations and spatial patterns

None of the demographic covariates were correlated with the mean CNR (Spearman ρ = 0.17 for log density, −0.30 for growth rate, and −0.13 for sex ratio; all Holm-adjusted p > 0.8). In the negative binomial mixed model (variance inflation factors ≤ 1.27), each 1-SD increase in the growth rate was associated with an 18% decrease in the notification rate (IRR 0.82; 95% CI 0.69–0.97). Density (IRR 1.09; 0.93–1.28) and sex ratio (IRR 1.04; 0.88–1.23) were not associated with notification rates. In the cross-sectional sensitivity model, the association with the growth rate was not significant (IRR 0.87; 0.73–1.03). When the analysis was restricted to the 18 regencies, both density (IRR 0.66; 0.53–0.81) and growth rate (IRR 0.67; 0.57–0.78) were inversely associated with the CNR. Because the direction and significance changed across specifications, no robust demographic associations were identified (Table 2).

Table 2. Ecological association and spatial analysis of the tuberculosis case notification rate

Analysis	Estimate (95% CI)	p
Spearman ρ, $\log_{10}$ density	0.17 (−0.39 to 0.61)	0.45[a]
Spearman ρ, growth rate	−0.30 (−0.74 to 0.25)	0.17[a]
Spearman ρ, sex ratio	−0.13 (−0.53 to 0.28)	0.55[a]
NB GLMM, IRR per 1 SD log density	1.09 (0.93–1.28)	0.28
NB GLMM, IRR per 1 SD growth rate	0.82 (0.69–0.97)	0.019
NB GLMM, IRR per 1 SD sex ratio	1.04 (0.88–1.23)	0.65
Regencies only (n = 18), IRR log density	0.66 (0.53–0.81)	<0.001
Regencies only (n = 18), IRR growth rate	0.67 (0.57–0.78)	<0.001
Cross-sectional NB, IRR growth rate	0.87 (0.73–1.03)	0.097
Global Moran's I, mean CNR (queen + island link)	−0.353	0.039
Global Moran's I, mean CNR (4 nearest neighbors)	−0.182	0.21
Empirical Bayes Moran's I, mean CNR	−0.352	0.039
Global Moran's I, pooled CFR	0.008	0.74
LISA, significant districts (p < 0.05)	Kota Sabang (low–high)	0.047 (FDR 0.71)
K-means, k selected by silhouette	k = 2; mean silhouette 0.41	—

NB GLMM, negative binomial generalized linear mixed model with year fixed effects and district random intercept; IRR, incidence rate ratio; LISA, local indicator of spatial association; FDR, false discovery rate. [a] Unadjusted; all Holm-adjusted p > 0.8. Moran's I expected value under no autocorrelation = −0.045; p values from 9,999 permutations.

K-means clustering favored two clusters by silhouette width (0.41), whereas the gap statistic favored a single cluster, indicating a weak cluster structure (Figure 6). Cluster 2 (14 districts) had higher median CNRs (172.8 per 100,000 in 2016–2019 and 147.9 in 2020–2021) and a lower median CFR (1.55%). Cluster 1 (nine districts) had a lower CNR (101.9 and 63.4 per 100,000) and a higher CFR (2.34%) (Figure 5A). Population density did not differ between the clusters (Kruskal–Wallis p = 0.71). The global Moran's I for the mean CNR was negative (I = −0.353; expected −0.045; p = 0.039), and the empirical Bayes estimate was similar (I = −0.352; p = 0.039). Negative autocorrelation was also observed for 2016, 2019, 2021, and 2020–2021 (p = 0.006–0.023), but none of these estimates were significant with four-nearest-neighbor weights (all p ≥ 0.13). CFR showed no spatial autocorrelation (I = 0.008; p = 0.74). Locally, only Kota

Sabang formed a significant low–high outlier (p = 0.047; FDR-adjusted p = 0.71). No district formed a high–high or low–low cluster, and no Gi* hotspot of the CNR was detected (Figure 5B).

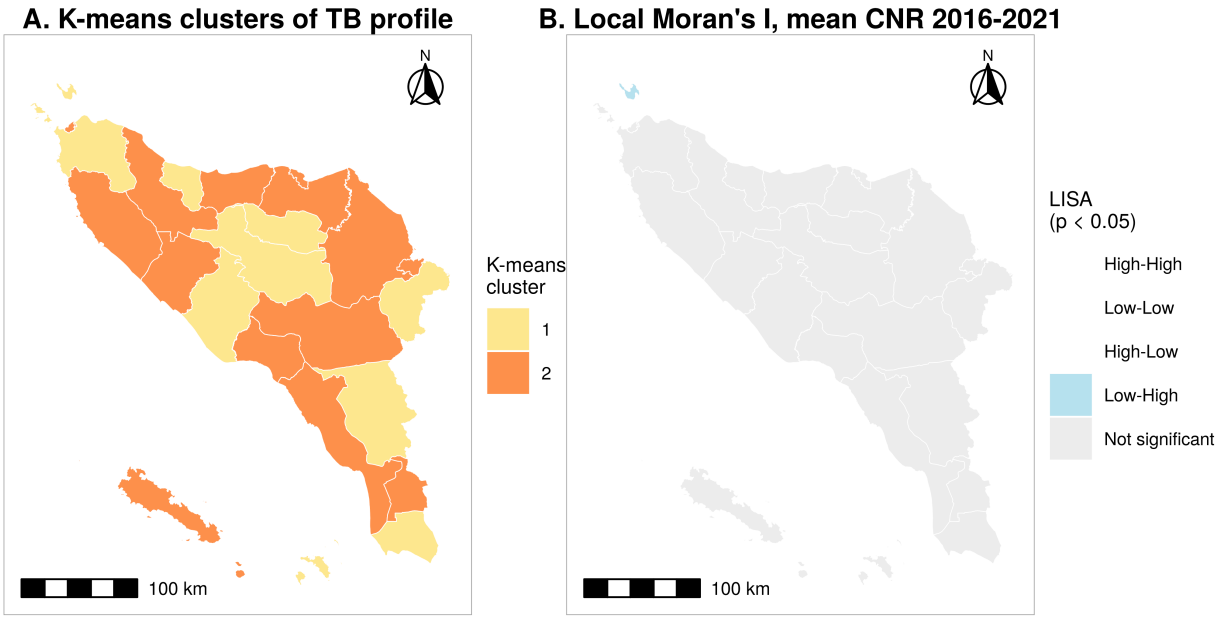


Figure 5. (A) K-means clusters (k = 2) of district TB profiles based on the 2016–2019 and 2020–2021 case notification rates and pooled case fatality ratios. (B) Local Moran's I (LISA) of the mean case notification rate, 2016–2021 (queen contiguity with island links, 9,999 permutations, p < 0.05).

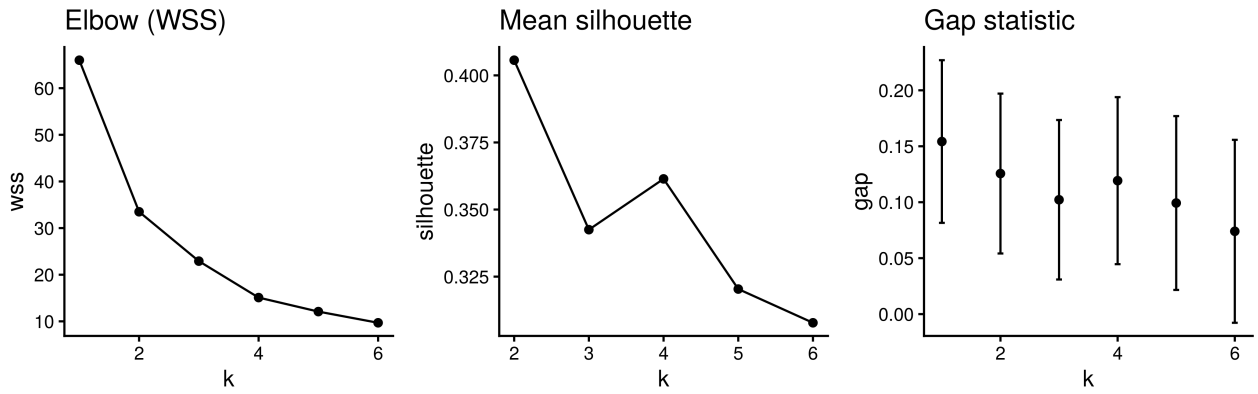


Figure 6. Selection of the number of K-means clusters: within-cluster sum of squares, mean silhouette width, and gap statistic (500 bootstrap samples).

DISCUSSIONS

This study provides district-level, spatially explicit evidence on TB in Aceh over a period that spans the COVID-19 pandemic. Three findings stand out. Notifications fell sharply in 2020, while case fatality doubled, and both indicators did not return to pre-pandemic levels by 2021. Treatment outcomes shifted from bacteriologically confirmed cure to complete cure without confirmation. The spatial pattern was dominated by high-notification cities embedded in lower-notification regencies rather than contiguous hotspots. In the paragraphs below, statements derived from our data are distinguished from explanations drawn from previous studies, which our aggregated data cannot test.

Our data show that notifications increased during 2016–2019, whereas the CFR decreased until 2018. This combination is compatible with intensified case findings, in which more and milder cases are detected, although our data cannot confirm this mechanism. The 31% decrease in notifications in 2020 was the same magnitude as the national decline [10] and occurred in 19

of the 23 districts, which argues against a local reporting artifact. Because TB transmission does not fall abruptly within a year, the simultaneous rise in the CFR suggests that the decline reflects missed or delayed diagnosis rather than a true decrease in incidence. Previous studies have attributed such declines to reduced contact tracing, underreporting, diagnostic disruption during large-scale social restrictions, and fear of attending health facilities [43,44]. Comparable pandemic-period falls in notifications were reported in Malawi and other high-burden settings [45–47], and similar shifts in the notification of other infectious diseases were observed in Indonesia [48].

Several explanations for the higher CFR in 2020–2021 have been proposed in the literature, and these are hypotheses in the context of this study. Late presentation can lead to more advanced disease at diagnosis. Coinfection with SARS-CoV-2 and comorbidities such as HIV, diabetes mellitus, and cardiovascular disease worsen prognosis and disrupt treatment [1,49,50]. In a Philippine cohort, COVID-19 patients with TB had a 2.17-fold higher risk of death and a 25% lower probability of recovery [51]. Coinfection is common among hospitalized COVID-19 patients, and its outcomes have been described in global cohorts and reviews [15,52–60]. Misdiagnosis and limited access to drugs may also contribute [18,61]. Our data cannot separate these mechanisms because deaths were not linked to individual patients or to COVID-19 status. The CFR used here also relates deaths reported in a year to cases reported in the same year rather than following a cohort; thus, a decrease in the denominator alone increases the ratio. However, the absolute number of deaths also increased, from 93 in 2019 to 257 in 2021; thus, the increase in the CFR is not an artifact of fewer notifications alone. This pattern is consistent with modeling studies that predicted excess TB deaths because of pandemic-related disruption [62–64].

The decrease in the cure rate was accompanied by a rise in the completion rate; therefore, treatment success changed little. A cure requires a negative sputum result at the end of treatment, whereas completion does not [27]. The shift therefore suggests that follow-up bacteriological examinations were not performed or not recorded rather than that more patients failed treatment. The change in denominators from 2019 onward, described in the Results, means that the cure rates before and after 2019 are not directly comparable. Disruption of sputum follow-up and laboratory services during the pandemic has been reported elsewhere [65].

Treatment success remained below 90% from 2018 onward [29], in line with the global pooled success rate of approximately 80% for drug-sensitive TB, which is influenced by age, HIV status, alcohol use, and early sputum conversion [66]. Mortality during treatment peaked in 2019 (5.70%) rather than during the pandemic years; therefore, this indicator did not monotonically increase. Studies from other settings have linked death during or after TB treatment to HIV, malnutrition, older age, bacteriologically unconfirmed diagnosis, and poor living conditions [67–70]. These factors could not be examined with the present data. The redirection of TB health workers to COVID-19 control, changes in care seeking during social restrictions, fear of infection, and inadequate follow-up have been described as drivers of poor treatment outcomes during the pandemic [1,7,44]. Such disruption may also favor the emergence of rifampicin-resistant and multidrug-resistant TB [44,64].

A negative global Moran's I indicates that neighboring districts tended to have dissimilar rather than similar CNRs. This pattern arises when cities with high notification rates, such as Kota Banda Aceh, Kota Lhokseumawe, and Kota Langsa, are surrounded by regencies with lower rates (Figure 2). Two explanations from the literature are plausible, but our data cannot distinguish between them. Diagnostic and referral facilities are concentrated in cities, so patients from surrounding regions may be notified where they are diagnosed rather than where they live. Crowding and poor ventilation in urban households also increase transmission [4,71,72]. The absence of high–high clusters at the district level contrasts with the space–time clusters found among the subdistricts of North Aceh [22] and in Bandar Lampung [73]. This difference is expected because clusters that exist at finer spatial scales are diluted when data are aggregated to large units.

The demographic covariates showed no consistent association with the notification rate. Previous studies have reported that behavior, density, and poor sanitation are risk factors for TB in Indonesia [74], that TB incidence varies across regions partly according to the diagnostic

approach used [11], and that most TB in Indonesia occurs in poor, densely populated urban areas [75]. Our inverse association between the growth rate and the CNR in some models should not be interpreted as protective. At the ecological level, associations can be confounded by access to diagnosis and do not necessarily apply to individuals [76]. Individual-level determinants such as malnutrition, diabetes, HIV, smoking, and alcohol use [3,4,71] were not available in the profiles. The K-means grouping was weak, and it should be read as a descriptive summary of two broad profiles rather than as evidence of distinct epidemiological zones.

Implications for TB elimination in Aceh

Eliminating tuberculosis (TB) in Aceh Province is challenging. Apart from requiring compliance with the standards and provisions set nationally, the elimination of TB requires many related sectors to support it in increasing the speed and success of the elimination program in 2030. The national target for 2030 is an incidence of 65 and a TB mortality rate of 6 per 100,000 population [77]. In Aceh, the number of notifications alone reached 133.8 per 100,000 in 2021, while the true incidence is likely higher because of undernotification. Our data identify three priorities: incomplete recovery of case findings after 2020, a cure rate that declined during the study period, and increasing case fatality. Previous studies in Indonesia have added inadequate management of drug side effects, poor adherence, and limited drug availability as barriers to successful treatment [61,78].

Other challenges for TB control in Aceh include low coverage of close-contact tracing, suboptimal use of rapid molecular testing (TCM) in high-incidence areas, and low coverage of TB preventive treatment (TPT) for household contacts and people with latent infection. Programmatic management of drug-resistant TB is limited, collaborative TB/HIV activities need to be expanded, and video-observed therapy (VOT) and other types of adherence support remain underused [79,80]. Routine surveillance at community health centers and district health offices also needs to be strengthened. The implausible year-on-year jumps and mixed recordings of treatment outcomes identified in this study show that data quality checks should be part of routine reporting. Surveillance results should be updated in real time, and people in affected areas should always be told to take precautions at home and be educated about how to control TB. Routine spatiotemporal analysis of surveillance data, at the subdistrict level where possible, would help target these efforts [22,73,81].

Combining national and regional programs can be a strategy to stop the spread of TB in Aceh Province. Community-based policies can accelerate expected control efforts [80,82]. The utilization of village human resources, such as youth, village cadres, cadet groups, and family welfare empowerment groups, can accelerate the reduction of household-based infectious diseases [83]. On the other hand, the strategy launched by the Government of the Republic of Indonesia through the Ministry of Health for TB control strategy in 2030 includes six commitments, including the government trying to improve and strengthen government leadership from the district/city level to the central government level; increasing access to high-quality, patient-centered TB diagnostic and treatment services; TB infection control and optimization of TB prevention therapy (TPT); increasing utilization of research findings on screening technology, diagnostics, and treatment regimens; increasing the participation and contribution of the community, partners, and other multisector actors, including universities, in efforts to control TB; and strengthening program management by strengthening the health system as a whole [84]. Aligning provincial action with these national commitments could improve the prospects of TB elimination in Aceh by 2030.

Multisectoral disease control is needed to accomplish all-encompassing health promotion. With a community-based strategy and the participation of local health workers, diagnosis and treatment success rates for tuberculosis (TB) can increase, leading to a decrease in TB-related mortality and transmission within the community. After the COVID-19 pandemic, it is important to increase knowledge, awareness, and community participation to detect active TB cases, including routine household-based surveillance with a spatial-temporal approach, to minimize transmission in the community and reduce TB infection cases in endemic areas. The district-level

estimates and reproducible analysis code provided in this study can be updated each year to monitor progress in Aceh Province.

Limitations

The data were aggregated annual counts; thus, associations apply to districts rather than individuals, and individual risk factors, HIV status, COVID-19 coinfection, and drug resistance could not be analyzed. Notifications reflect both disease occurrence and case detection; therefore, the CNR is not a measure of true incidence. Cases may also be recorded where patients are diagnosed rather than where they live. Deaths were not linked to treatment cohorts; therefore, the CFR is a crude ratio of deaths to same-year notifications. Annual populations were projected from a single census with constant growth rates, although the sensitivity analysis with the 2020 denominator yielded consistent results. The number of districts (n = 23) limits the statistical power of the ecological and spatial analyses, and the results may depend on the spatial scale and the choice of neighborhood matrix. Official BPS areas differed from the areas computed from the BIG polygons by a median of 10.8%, and the official figures were retained for density. Finally, several district-years showed implausible jumps that could not be verified against primary registers.

CONCLUSIONS

From 2016–2021, TB notifications in Aceh rose until 2019, decreased by 31% in 2020, and recovered only partially in 2021. Simultaneously, the case fatality ratio more than tripled relative to 2016–2019. Together with the shift from a bacteriologically confirmed cure to treatment completion, these findings indicate that the pandemic disrupted TB diagnosis and follow-up rather than reducing transmission. Notification rates were highest in the cities, and the spatial pattern was characterized by urban enclaves rather than contiguous hotspots. Population density, growth rate, and sex ratio did not consistently correlate with notification rates. Priorities for TB elimination in Aceh include catch-up active case finding, restoration of sputum follow-up, investigation of deaths among notified patients, and routine quality checks of district surveillance data. Further studies should use individual-level and subdistrict data to examine socioeconomic and clinical determinants.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization, DSE, IMDMA, and BU; methodology, DSE; software, IMDMA; validation, BU, NMM, and IMDMA; formal analysis, IMDMA; investigation, NMM, MRAE; resources, MRAE, MFS; data curation, DSE, BU; writing—original draft preparation, DSE, BU, IMDMA; writing—review and editing, BU, NMM, IMDMA; visualization, IMDMA; supervision, BU, NMM; project administration, MFS, LHMS; funding acquisition, MFS, LHMS. All the authors have read and agreed to the published version of this manuscript.

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PT Mega Science Indonesia, who helped to improve the quality of the language and check the substance of the articles.

DATA AVAILABILITY STATEMENT

The authors would like to thank all the parties who helped in this research, the health administration and data department of Aceh Province, who facilitated the collection of data, and PT Mega Science Indonesia, who helped to improve the quality of the language and check the substance of the articles.

DECLARATION OF ARTIFICIAL INTELLIGENCE USE

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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