An investigation of geographical clusters of leptospirosis during the outbreak in Pangandaran, West Java, Indonesia

Mutiara Widawati,[1] Pandji Wibawa Dhewantara,[1] Raras Anasi,[2] Tri Wahono,[1] Rina Marina,[1] Intan Pandu Pertiwi,[3] Agus Ari Wibowo,[3] Andri Ruliansyah,[4] Muhammad Umar Riandi,[4] Dyah Widiastuti,[1,5] Endang Puji Astuti[1]

[1]Vector-borne and Zoonotic Diseases Research Group, Research Center for Public Health and Nutrition, National Research and Innovation Agency, Cibinong, Bogor, West Java; [2]Health Development Policy Agency, Ministry of Health of Indonesia, Jakarta; [3]Environmental Health Technology and Disease Control Agency, Ministry of Health of Indonesia, East Jakarta, DKI Jakarta; [4]Pangandaran Public Health Laboratory, Ministry of Health of Indonesia, Pangandaran, West Java, Indonesia; [5]School of Postgraduate Studies, Gadjah Mada University, Yogyakarta, Indonesia

Correspondence: Pandji Wibawa Dhewantara, Vector-borne and Zoonotic Diseases Research Group, Research Center for Public Health and Nutrition, National Research and Innovation Agency, Cibinong, Bogor, West Java 16911, Indonesia. E-mail: pand004@brin.go.id

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Abstract

Leptospirosis is neglected in many tropical developing countries, including Indonesia. Our research on this zoonotic disease aimed to investigate epidemiological features and spatial clustering of recent leptospirosis outbreaks in Pangandaran, West Java. The study analysed data on leptospirosis notifications between September 2022 and May 2023. Global Moran *I* and local indicator for spatial association (LISA) were applied. Comparative analysis was performed to characterise the identified hotspots of leptospirosis relative to its neighbourhoods. A total of 172 reported leptospirosis in 40 villages from 9 sub-districts in Pangandaran District were analysed. Of these, 132 cases (76.7%) were male. The median age was 49 years (interquartile range [IQR]: 34-59 years). Severe outcomes including renal failure, lung failure, and hepatic necrosis were reported in up to 5% of the cases. A total of 30 patients died, resulting in the case fatality rate (CFR) of 17.4%. Moran's *I* analysis showed significant spatial autocorrelation (I=0.293; p=0.002) and LISA results identified 7 High-High clusters (hotspots) in the Southwest, with the total population at risk at 26,184 people. The hotspots had more cases among older individuals (median age: 51, IQR: 36-61 years; p<0.001), more farmers (79%, p=0.001) and more evidence of the presence of rats (p=0.02). A comprehensive One Health intervention should be targeted towards these high-risk areas to control the transmission of leptospirosis. More empirical evidence is needed to understand the role of climate, animals and sociodemographic characteristics on the transmission of leptospirosis in the area studied.

Introduction

Leptospirosis is one of the zoonotic diseases of public health significance commonly reported in tropical and subtropical countries. It is caused by pathogenic bacteria belonging to the genus *Leptospira*. There are approximately more than one million cases and over 58,000 mortalities every year worldwide (Costa *et al*., 2015). Severe outcomes (Weil's syndrome) can lead to multi-organ failure and death. Leptospirosis transmission occurs in a variety of epidemiological contexts. In urban areas, people who live in poor settlements with limited access to adequate basic services such as clean water, sanitation, waste disposal, and health-

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care, especially those in flood-prone areas, are at a higher risk of exposure. In rural areas, leptospirosis is frequent among farmers who work in forestry, rice farming and animal husbandry (Barcellos & Sabroza, 2000; Haake and Levett, 2015; Mwachui *et al*., 2015; Sakundarno *et al*., 2014). Leptospiral infection occurs through contact with water or soil contaminated by urine of infected host animals. A direct infection can also occur through contact with urine or tissue of infected animals. The bacteria enter the human body through wounds, mucosal membranes or ingestion. Rodents play a major role in the transmission, but other animals such as livestock, domestic animals, and wildlife can also host *Leptospira* (Adler & de la Peña Moctezuma, 2010; Dietrich *et al*., 2018; Javati *et al*., 2022; Levett, 2001; Sprißler *et al*., 2019).

A large outbreak has been reported in the city of Jakarta after the severe flooding event in 2002 (Laras *et al*., 2002). The incidence of leptospirosis has also been reported elsewhere across Indonesia and the trend of leptospirosis outbreaks have tended to increase in the past few years (Ministry of Health of Indonesia, 2022; Setyaningsih *et al*., 2022). A total of 9,889 cases and 1,102 deaths due to leptospirosis was reported during over 2011-2022 with case fatality rates (CFR) ranging from 7.5% to 16.8% (Ministry of Health of Indonesia, 2022). The actual incidence remains unknown due to poor awareness and limited diagnostic capacity (Gasem *et al*., 2020). Evidence has shown the existence of *Leptospira* in host animals in several places in Indonesia (Sunaryo & Priyanto, 2022; Widiasih *et al*., 2021), which suggests the potential of *Leptospira* transmission in the population.

The first case of leptospirosis in Pangandaran District, West Java was discovered at the final quarter of 2022 (Environmental Health Technology and Disease Control Agency - Ministry of Health of Indonesia, 2023). There had never been any known occurrences of leptospirosis in this area previously, but there has been a rapid surge of human cases since then. Total of 158 leptospirosis cases and 28 deaths were reported until December 2022. A local epidemiological investigation identified three patients of laboratory-confirmed cases based on microscopic agglutination test (MAT), presence of seropositive rats (*Rattus tanezumi*) and *Leptopira*-contaminated water (Environmental Health Technology and Disease Control Agency - Ministry of Health of Indonesia, 2023). To date, there is no evidence describing the distribution pattern of leptospirosis cases in Pangandaran. Further investigations are needed to explore and characterise the epidemiology and distribution of leptospirosis in this location.

The use of spatial approaches in disease control and surveillance has been increasing in the past decades, including its use for leptospirosis investigations in human or animals (Barcellos & Sabroza, 2000; Dhewantara *et al*., 2019a; Dhewantara *et al*., 2019b; Luenam & Puttanapong, 2019; Nardoni Marteli *et al*., 2022; Taylor *et al*., 2021). Nardoni Marteli *et al*. (2022) applied spatial clustering analyses to reveal geographic variation in leptospirosis notifications over 11 years in Brazil. In Great Britain, Taylor *et al*. (2021) used several spatial techniques to understand spatial and temporal patterns of leptospirosis in dogs across the country and its drivers. Spatial analytical techniques can be integrated into current surveillance programmes to improve disease control strategies and re-allocation of the resources needed. We analysed demographic, clinical presentation and exposure data collected during the surge period of leptospirosis in Pangandaran to characterise the epidemiology. We also applied spatial analytical approaches to analyse the geographical patterns of leptospirosis to locate high-risk areas for leptospirosis to help local authorities to design necessary interventions appropriately and to improve surveillance and responses to cope with the current and future outbreak.

Materials and Methods

Study site

The study was set in Pangandaran District, West Java, Indonesia situated around coordinates 7.615S and 108.498E (Figure 1). The district comprises 10 sub districts and 93 villages with a total area of 1,011 km^2. The total population of 423,670 people, ranged from 1,641 people in Mekarwangi village to 12,365 people in Babakan village (Central Bureau of Statistics, 2022).

Data collection

We analysed all cases (suspected, probable and confirmed) of human leptospirosis reported during the period of September 2022 – May 2023 obtained from the District Health Agency of Pangandaran. The notification data contained information on age, gender, occupation, address (village name), date of onset illness, clinical presentation and exposure history. Population data and population density (person per km^2) for each village were collected from the local Bureau of Statistics (https://pangandarankab.bps.go.id/).

Spatial analysis of incidence

The village (n=93) was used as the spatial unit of analysis. All leptospirosis cases were linked with village polygons by using QGIS Version 3.2.0-Bonn. Village-level polygons (shapefile) were obtained from the Statistical Services Information System of National Bureau of Statistics (*Sistem Informasi Layanan Statistik*) (https://silastik.bps.go.id/v3/index.php/site/login/)

Cumulative incidence (per 10,000 people) of leptospirosis during the period studied was estimated and mapped. Map of incidence at the village level was created by using QGIS Version 3.2.0-Bonn. Moran's *I* statistics (Moran, 1950) was conducted to examine spatial autocorrelation of the incidence of leptospirosis. Queen-based spatial contiguity matrix was used when determining the spatial weight. The values of the Moran's *I* range from -1 to 1, with positive values indicating positive autocorrelation and negative values negative autocorrelation. To detect high-risk (indicated by High-High or HH) and low-risk (indicated by Low-Low or LL) leptospirosis clusters, local indicator spatial association (LISA) analysis was conducted (Anselin, 1995). Further, comparative analysis was conducted to profile epidemiological characteristics of HH clusters relative to the other neighbourhoods. The case characteristics (age median, proportion of gender, proportion of occupation, environmental risk factors) and the proportion of the outcomes (severity and fatality rate) of the HH clusters were compared to other neighbourhoods. The *t*-test (for continuous variables) or Fisher's Exact/Chi-square (for categorical variables) or Mann-Whitney U test was performed when appropriate. Levels of significance were set at 5%. All spatial analyses were performed using GeoDA v.1.8 software.

Statistical data analysis

Descriptive analyses were performed using STATA 15 (StataCorp LLC, Texas, USA). The distribution of case characteristics by age, gender, occupation, and week was summarised. Clinical presentation and exposure history were also summarised.

Results

Demographic characteristics and clinical outcomes cases

Table 1 shows the summary of the demographic, symptoms, and outcome of notified leptospirosis cases. A total of 172 cases were reported in 40 villages from 9 sub-districts in Pangandaran District between week 38, 2022 and week 17, 2023. Of these, 132 cases (76.7%) were male. One sub-district (Sidamulih) did not report any leptospirosis cases.

The median age was 49 years (interquartile range [IQR]: 25 years). The greatest number of cases were observed among people aged 45-59 years (n=56; 32.6%). Based on occupation, farmers accounted for the largest proportion of leptospirosis cases (n=122; 70.9%). Most patients experienced fever (n=138; 80.2%), headache (n=105; 61.1%) and myalgia (n=130; 75.6%). Renal dysfunction, lung dysfunction, and hepatic necrosis was reported in around 2% to 5% of the cases. A total of 30 patients died, resulting in a case fatality rate (CFR) of 17.4%.

Temporal and geographical analysis

The number of leptospirosis cases began to increase in the early fourth quarter (Q4) of 2022 (Figure 2). The highest number of weekly cases occurred in week 50, 2022 (25 cases). The number of cases diminished significantly in the first quarter (Q1) of 2023. In general, the cumulative leptospirosis incidence was spatially heterogeneous at the village level (Figure 3). The highest cumulative incidence (per 10,000 people) was observed in Cibanten (111.1 per 10,000 people). According to the distribution maps, leptospirosis incidence was generally higher in the south-western counties. The distribution maps showed changes in leptospirosis

Table 1. Demographic characteristics of persons with leptospirosis in Pangandaran in the period September 2022-April 2023.

Characteristic	Frequency n (%)
Age, median (IQR)	49 (25)
Year group	
5-14	5 (2.9)
15-29	27 (15.7)
30-44	42 (24.4)
45-59	56 (32.6)
≥60	42 (24.4)
Gender	
Male	132 (76.7)
Female	40 (23.3)
Occupation	
Farmer	122 (70.9)
Fisher	2 (1.2)
Labour	15 (8.7)
Other	21 (12.2)
Not working	12 (7)
Clinical presentation	
Fever	138 (80.2)
Headache	105 (61.1)
Myalgia	130 (75.6)
Conjunctival suffusion	37 (21.5)
Malaise	51 (29.7)
Jaundice	93 (54.1)
Renal dysfunction	4 (2.3)
Lung dysfunction	9 (5.2)
Hepatic necrosis	4 (2.3)
Outcome	
Death	30 (17.4)
Recovery	142 (82.6)

Total number (n) of cases; IQR=interquartile range.

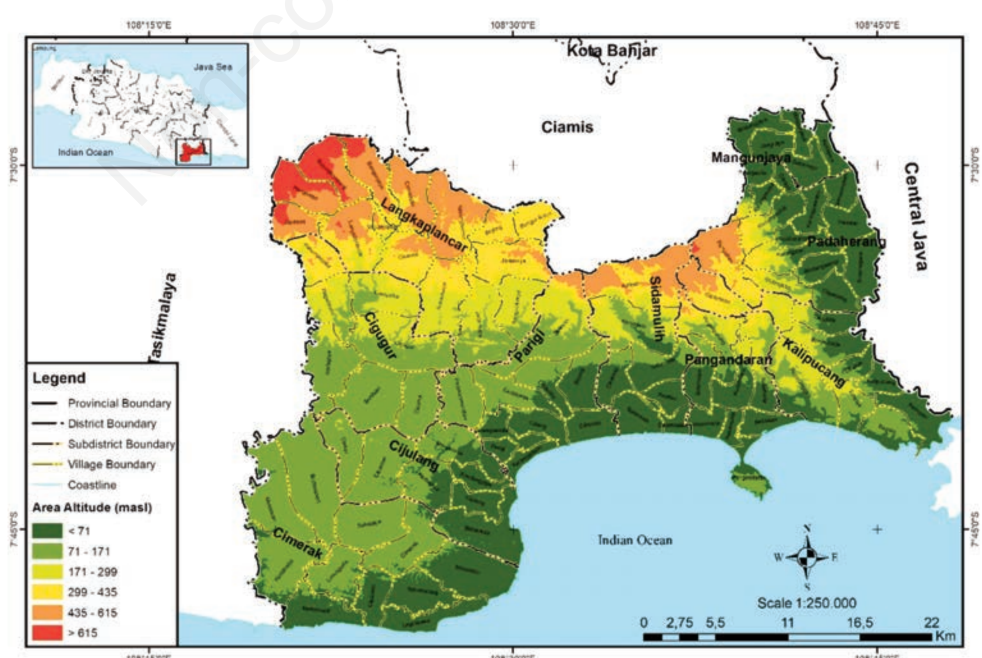

Figure 1. The study site in Pangandaran District, West Java, Indonesia.

incidence by every four-week period from week 38, 2022 until week 17, 2023 (Figure 4). The first leptospirosis case was reported in Ciakar village. A significant expansion was observed during weeks 42-45 and weeks 46-49. Cibanten and Ciakar were consistently reported to have a high incidence during these periods. A total of 27 villages were affected by leptospirosis during weeks 46-49 in 2022 with most of these villages belonging to the Cimerak sub-district. The maps also show a sporadic emergence of leptospirosis in the eastern villages. Interestingly, there was a significant reduction in the incidence and the number of counties reporting leptospirosis after week 1, 2023.

Spatial autocorrelation and hotspot detection

As indicated by Moran's I, the incidence of leptospirosis was significantly clustered (I=0.293; p=0.002). Furthermore, based on LISA results, we identified 7 HH clusters in the Southwest, including the villages Sukajaya, Legokjawa, Cimerak, Ciakar, Cibanten, Kertayasa and Margacinta, with total population at risk estimated at 26,184 people (Figure 5, Table 2). Two sets of LL clusters were found in the North (Karangkamiri, Cisarua, and Langkaplancar) and in the centre (Sidomulih, Wonoharjo, Purbahayu, and Pagergunung).

Characteristics of leptospirosis hotspots

We compared the case characteristics between those cases reported in HH clusters and outside these clusters (Table 3). Compared to other clusters, leptospirosis cases in the HH clusters

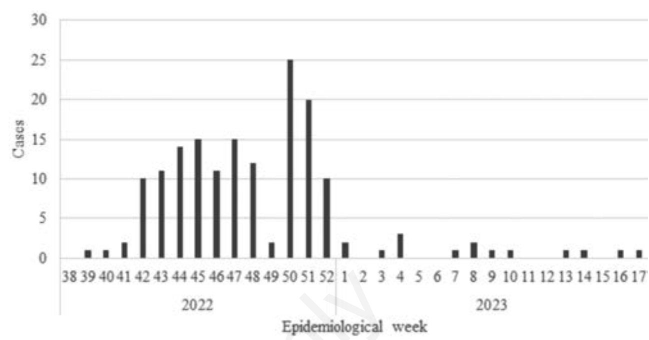

Figure 2. The trend of weekly leptospirosis notifications, Pangandaran from September 2022 to May 2023.

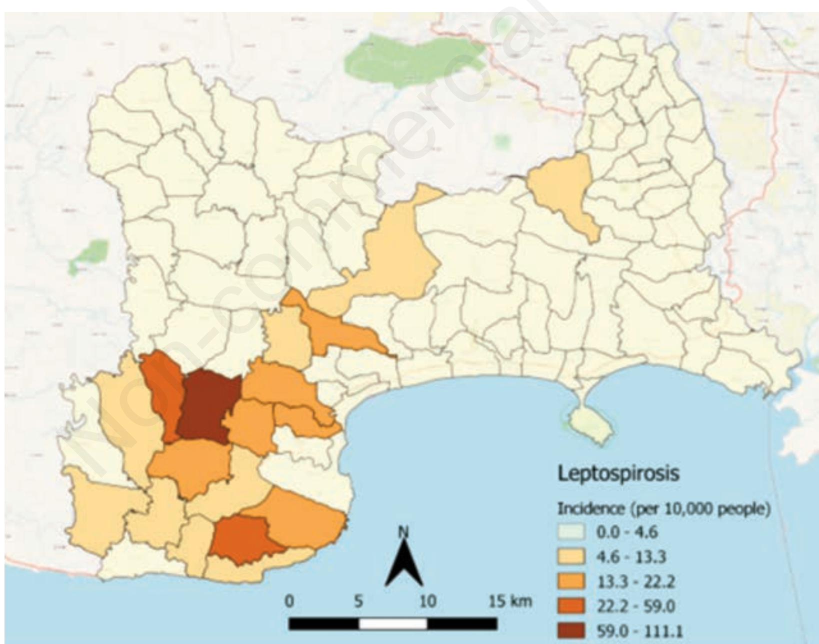

Figure 3. Cumulative incidence of leptospirosis at the county level, Pangandaran from September 2022 to May 2023.

Table 2. Characteristics of spatial clusters of leptospirosis as detected by LISA, Pangandaran, West Java.

Cluster	Village count (n)	Village name	Case count (n)	Population at risk
High-High	7	Sukajaya, Legokjaya, Cimerak, Ciakar, Cibanten, Kertayasa, Margacinta	81	26,184
Low-Low	7	Sidamulih, Karangkamiri, Cisarua, Langkaplancar, Purbahayu, Pagergunung, Wonoharjo	1	36,335
Low-High	2	Bunisari, Cimindi	0	7,256

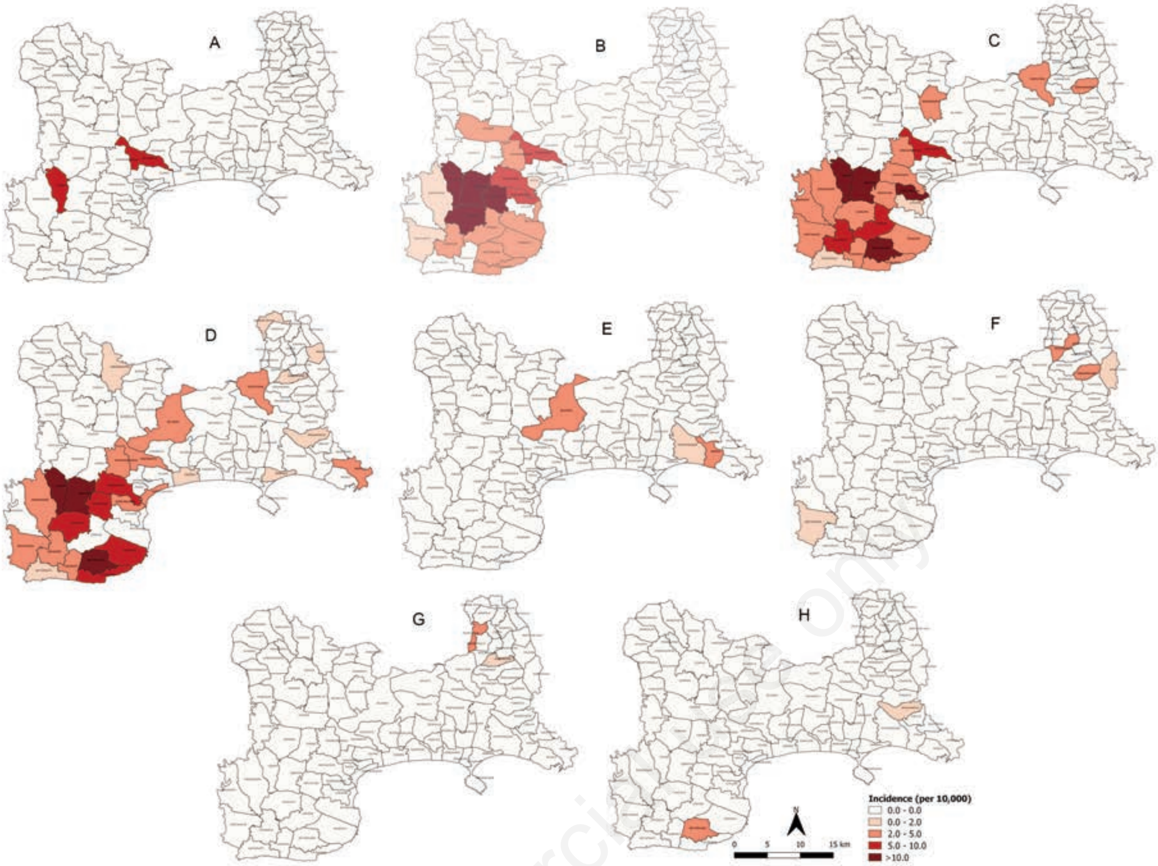

Figure 4. Spatial-temporal distribution of leptospirosis incidence at the village level in Pangandaran from September 2022 to May 2023. A) Week 38-41, B) Week 42-45, C) Week 46-49, D) Week 50-1, E) Week 2-5, F) Week 6-9, G) Week 10-13, Week H) 14-17.

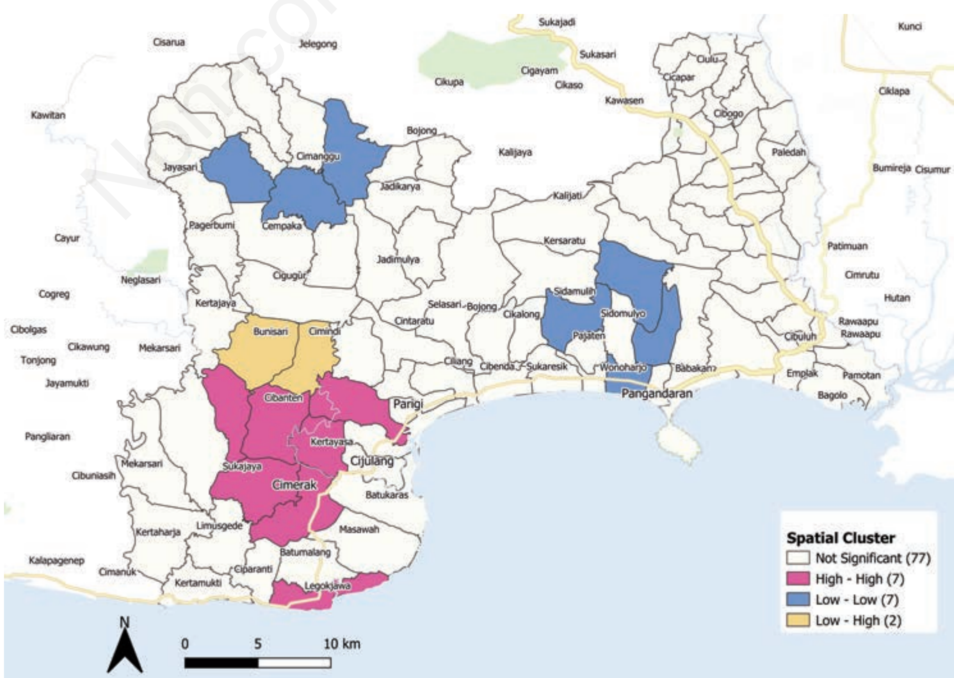

Figure 5. Spatial clusters of the incidence of leptospirosis in Pangandaran.

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included older individuals with a median age of 51 (IQR=36-61) years (p<0.001). Yet, there was no difference in the proportion of cases by group of age and gender (p>0.05) between clusters. The HH clusters had more farmers (79%, p=0.001) compared to other neighbours. Based on the potential environmental exposure, there was a higher proportion of patients residing in the HH clusters and reported presence of rats (55.6%, p=0.02) in their surroundings compared to those residing outside these clusters. Based on the outcome of infection, there was no difference in the proportion of severe cases between the inside and outside of the HH clusters (p=0.09). Yet, while it is not statistically significant, severe cases were much greater reported outside the HH clusters. However, the fatality rate was much higher (19.8%) in these clusters compared to the outside although again not statistically significant (p=0.451).

Discussion

Leptospirosis is one of the important zoonotic diseases in Indonesia, yet the epidemiology and its true burden in communities remain unclear. This study analysed recent human leptospirosis notification data obtained during the leptospirosis outbreak in Pangandaran, West Java, aiming to describe the epidemiological features and to reveal geographical patterns of leptospirosis cases over 32 weeks of observation. The significant clustering in the leptospirosis incidence observed highlight a strong existence of specific drivers and circulating *Leptospira* in this specific environment. Moreover, our analysis identified seven significant high-risk clusters in the Southwest, which should help local health authorities to specifically design intervention in these identified hotspots.

Farming is one of the known risk factors associated with leptospirosis infection (Dung *et al*., 2022; Hinjoy *et al*., 2019; Mwachui *et al*., 2015; Sakundarno *et al*., 2014;). Our finding of this infection in older males and those who engage in farming is consistent with studies elsewhere (Hinjoy *et al*., 2019; Ridzuan *et al*., 2016). In Pangandaran, farming activities including harvesting paddy crops, ploughing, raising cattle, and working in the forest are more likely done by men. The simultaneous peak of incidence of leptospirosis found and the rainy season during November-December 2022 indicates favourable environmental conditions for rodent populations to reproduce and actively migrate, increase human exposure. Presence of rodents and flooded land are some of environmental exposures reported by many patients during the outbreak. Further supporting evidence comes from local reports of seropositive rodents (*Rattus tanezumi*) and bacteria-contaminated water and paddy fields (Environmental Health Technology and Disease Control Agency - Ministry of Health of Indonesia, 2023).

Even if the CFR rate of leptospirosis was found to be high (17.4%) in this study compared to elsewhere, such as the 14.1%) reported in New Caledonia (Tubiana *et al*., 2013), it may lead to an underestimation the actual burden in the population investigated. Some of the infected individuals in this study presented severe outcomes (Weil's syndrome) leading to multi-organ failure such as renal failure and lung failure. The severity and fatality due to leptospirosis found in this study can be linked to several factors including individual underlying conditions, epidemiological set-

Table 3. Case characteristics observed in the high-risk clusters in Pangandaran relative to other neighbourhoods.

Characteristic	High-risk cluster (n=81)	Outside cluster (n=91)	$t/\chi^2/U$	p
Age, median (IQR)	51 (36-61)	48 (32-57)	17.79	<0.001***
Year group			4.95	0.31
5-14	1 (1.2)	4 (4.40)		
15-29	10 (12.3)	17 (18.7)		
30-44	23 (28.4)	19 (20.9)		
45-59	24 (29.6)	32 (35.2)		
≥60	23 (28.4)	19 (20.9)		
Gender			0.176	0.72
Male	61 (75.3)	71 (78)		
Female	20 (24.7)	20 (22)		
Occupation			17.15	0.001*
Farmer	64 (79)	58 (63.7)		
Fisher	-	2 (2.2)		
Labour	5 (6.2)	10 (11)		
Other	3 (3.7)	18 (19.8)		
Not working	9 (11.1)	3 (3.3)		
Environmental exposure				
Presence of rats	45 (55.6)	34 (37.4)	5.71	0.02*
Presence of animals	3 (3.7)	8 (8.8)	1.85	0.22
Flooded/inundated	15 (18.5)	16 (17.6)	0.02	0.87
Near forest or paddy field	2 (2.5)	7 (7.7)	2.35	0.17
Outcome			2.98	0.09
Mild	39 (48.1)	32 (35.2)		
Severe	42 (51.9)	59 (64.8)		
Fatality rate (%)	19.8	15.4	0.75	0.451

Number (n) of leptospirosis cases (81) as detected by LISA; IQR=interquartile range; $t/\chi^2/U$, t statistics (*t*-test), Chi-squared statistics, Mann-Whitney test statistics, respectively. *p<0.05, **p <0.01, ***p <0.001.

tings, disease awareness, and case management, e.g., diagnosis and treatment (Gasem *et al*., 2020; Pongpan *et al*., 2023; Tubiana *et al*., 2013). A rapid epidemiological investigation following the outbreak in October 2022 found various *Leptospira* serovars among patients, including Canicola, Pomona, Australis, Autumnalis, Ballum, Djasiman, Javanica and Icterohaemorrhagiae (Environmental Health Technology and Disease Control Agency - Ministry of Health of Indonesia, 2023). Such a diverse *Leptospira* serovars found in humans makes one wonder of the reservoir hosts in the area, including rodents, dogs, and livestock animals. Some *Leptospira* serovars have been linked to specific maintenance hosts. The findings from a survey conducted by the local epidemiological unit found four potential rodent species including *R. tanezumi*, *R. tiomanicus*, *R. argentiventer* and *Niviventer spp*., out of which 12.5% of *R. tanezumi* were positive for the bacteria, suggesting an important role for rodents, at least in the recent outbreak. The result was higher than that recently reported in Yogyakarta, which found 4.8% of *R. tanezumi* samples positive for *Leptopira* (Sunaryo & Priyanto, 2022). To date, evidence is lacking with regard to *Leptospira* species and serogroups circulating in the other domestic and livestock animals in this area.

The kind of a clustered pattern of leptospirosis incidence discovered in this study has also been reported in other endemic regions (Dhewantara *et al*., 2018; Luenam & Puttanapong, 2019; Nardoni Marteli *et al*., 2022). Our analysis indicates the incidence was found to be concentrated in certain villages, with localised clusters indicating found high-risk areas. This pattern suggests the existence of local factors driving the transmission of leptospirosis, which requires further investigation. To understand the profile of the identified hotspot and its difference with other areas, we compared the case characteristics between those cases reported in high-risk clusters and outside the high-risk clusters. Moreover, our result found the proportion of patients who reported presence of rats in their dwelling to be much higher among those who resided in the high-risk villages than in others. While self-reporting is prone to subjectivity and may not explain the true density of rodents in the environment, the evidence provided by the patients confirms the potential role of rodents on the disease transmission so that necessary actions can be targeted towards these hotspots of leptospirosis.

The current study found a considerable shift in the geographical pattern of leptospirosis incidence throughout the period of study. Our finding showed a significant expansion of the distribution of notified leptospirosis cases was observed in the Southwest at the end of 2022. However, the incidence was then randomly spread in a small number of villages in early 2023. These changes may partly be explained by several factors. First, there has been an indication of lack of diagnostics. A limited availability of rapid detection test (RDT), the only available and easy-to-use first-line test for leptospirosis in the primary level in the district, might have affected physicians to promptly detect all suspect cases in the primary healthcare (*Puskesmas*) during early 2023. Second, some people may avoid visiting healthcare due to some reasons after knowing there was an outbreak and fatalities. Poor awareness of illness or believes illness is a common fever or flu, and fear of a diagnosis may be some of psychological factors driving people to not seek medical treatment (Taber *et al*., 2015). Lastly, change in rainfall intensity or dry condition during the early weeks of 2023 might have reduced the human exposure to rodents and waters, thus lessen the number of infections.

The findings of this study have to be seen in light of some limitations. First, our study analysed data collected from routine facility-based data which is mainly based on passive case surveillance, so that there may be under-reporting that influences the accuracy of the data. The result presented in this study may not reflect the actual incidence in the community. Many people are likely not aware and seek treatment since most leptospirosis cases (approximately 90% of cases) could be asymptomatic or lacking pathognomonic symptoms. Future studies may use a combination of data from both routine and population-based survey sources to improve the burden estimates of leptospirosis in Pangandaran. In addition, while there has been a standardised guideline for leptospirosis detection and management, the readiness and capacity among healthcare providers to diagnose or detect leptospirosis might be limited so that it also likely affects our present results. In the future, we recommend improvement in disease surveillance by equipping healthcare providers and local laboratories with capacity to detect leptospirosis. Second, our present study used ecological approach that does not aim to draw causal links for the emergence of leptospirosis infection in the study area. A population-based study is required to understand the drivers of the emergence of leptospirosis in the study area. A study aimed at investigating the connection of animals and human infection is important as it would help improve our understanding on the epidemiology of leptospirosis which could help design a better ‘One Health’ surveillance for leptospirosis control in the studied area.

Conclusions

The current study discovered a spatial heterogeneity of leptospirosis incidence in Pangandaran, with high-risk areas predominantly situated in the south-western villages. Spatial analytical approaches can be used to help identify areas at higher risk so that resources can be effectively allocated. The present findings highlight the need to improve capacity to detect leptospirosis and to increase people’s understanding towards this infection to better mitigate future outbreaks. Comprehensive and multi-sectoral-based interventions should be targeted towards the identified high-risk areas to control the transmission of leptospirosis.

The drivers of the emergence of leptospirosis in Pangandaran remain unknown. The role of climate, animals, and host socio-demographic characteristics on transmission as well as the factors associated with severity and deaths of leptospirosis need further investigation. In addition, the causal relationship of rodents, environment and leptospirosis incidence in this area should be further explored and so should the molecular epidemiology of leptospirosis in animal hosts to better understand the importance of the circulating serovars and animals in the community.

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