International Journal of Public Health Science (IJPHS)
Vol. 14, No. 3, September 2025, pp. 1119~1128
ISSN: 2252-8806, DOI: 10.11591/ijphs.v14i3.25223

Incidence rate and spatial clustering of measles cases in Malaysia, 2018–2022

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Article Info

Article history:

Received May 27, 2024
Revised Nov 19, 2024
Accepted Dec 13, 2024

Keywords:

Hotspot
Incidence rate
Measles
Moran
Spatial clustering

ABSTRACT

The distribution of measles varies worldwide. Malaysia has seen fluctuating incidence rates of measles across its districts, highlighting the persistent challenge of measles control despite national vaccination efforts. This study aimed to map the incidence rates of measles and identify hotspots areas of measles in Malaysia between 2018 and 2022. The study utilized secondary data from the Disease Control Division, Ministry of Health Malaysia, and was analyzed through spatial autocorrelation techniques. Choropleth map applied to the incidence rate of measles and Global Moran's I statistics quantified spatial autocorrelation, supplemented by local indicators of spatial association (LISA) for localized analysis. The measles incidence rate exceeded 500 per million population in Bintulu, Marudi, and Miri, Sarawak in 2018 and in Gua Musang, Kelantan in 2019. There is a downward trend in the incidence rate across the districts in Malaysia. The Global Moran's I statistic revealed significant positive spatial autocorrelation of measles cases in Malaysia from 2018 to 2022. Districts, specifically in Klang Valley, have been identified as persistent hotspot areas. There is a need for continuous surveillance, adequate vaccination coverage, and supplementary public health measures, especially in identified hotspot areas, in order to achieve measles elimination goals in Malaysia.

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1. INTRODUCTION

Measles is a vaccine-preventable disease that is characterized by fever, cough, runny nose, conjunctivitis, and maculopapular rashes. It remains a significant challenge to global health due to its highly infectious nature and the potential for severe outbreaks despite the availability of vaccines. Numerous countries have implemented measles elimination programs, aiming to eliminate the disease within their borders. Measles is considered eliminated in a country if it can maintain interrupted transmission for at least 36 months, with an incidence rate falling below one case per million population [1]. Eighty-three countries, accounting for 43% of all countries worldwide, have been verified to have achieved or maintained measles elimination status. However, at the regional level, no region has yet been declared to have eliminated measles [2].

Globally, there has been a significant reduction in measles cases, dropping from 3.9 million in 2000 to under 400,000 by 2018, as reported by Patel *et al.* [3]. Despite this global reduction of cases, the incidence rate of measles infections still shows variation across different countries or regions, particularly in those that have not achieved measles elimination [4]–[6]. Local studies in Malaysia show that the incidence rates across different states and districts do not align with the national incidence rate. The incidence rate in 2019 varied widely from as low as 24 per million population and as high as 101.9 per million population [7]–[9]. Thus, this study aims to determine the incidence rates of measles infections across districts in Malaysia from 2018 to 2022, providing an updated overview of the disease's epidemiology in the country and determining the hotspot areas of measles in Malaysia. The findings may contribute to understanding measles epidemiology in Malaysia and assist in creating targeted approaches for disease prevention and control, aiding the global effort to eliminate measles.

2. METHOD

Malaysia is a country in Southeast Asia that covers an area of approximately 329,847 km^2. It spans roughly between latitudes 1° and 7°N and longitudes 100° and 119°E. Malaysia is divided into two distinct regions, which are Peninsular Malaysia, a land connected to mainland Asia, and East Malaysia, the northern part of the island of Borneo. There are 13 states and 3 federal territories in Malaysia, which are further divided into 160 districts, spreading across its diverse geographic area [10].

This study was conducted using retrospective secondary data of measles cases from 2018 to 2022 from the e-measles database provided by the disease control division, Ministry of Health Malaysia. E-measles is a system that standardizes reporting of measles cases, investigations, and findings at the district, state, and national levels for measles control and prevention [9]. This study included all confirmed measles cases identified during the specified study period. A confirmed measles case in Malaysia is determined based on the case definitions for infectious diseases in Malaysia. A confirmed case includes any case that is laboratory-confirmed by detecting measles-specific IgM antibodies or isolating the measles virus using culture or molecular techniques. Additionally, a case can be a confirmed case if the case clinically has a fever and maculopapular rash along with either cough or coryza, or conjunctivitis, and has an epidemiological link to a laboratory-confirmed case [11]. The estimated population for each district in Malaysia was obtained online from the Department of Statistics Malaysia. The incidence rate of measles for each district was calculated by dividing the number of confirmed measles cases in a specific year with the estimated population for each district in that year. It was expressed as the number of cases per 1,000,000 population. A series of incidence rate choropleth maps was created using the tmap package of R software version 4.3.1 and RStudio version 2023.12.1+402 [12].

Spatial analysis in epidemiology has emerged as a tool for understanding the dynamics of disease spread and the identification of geographical areas at increased risk of infectious diseases such as dengue, tuberculosis, mumps, and measles [13]–[16]. Spatial autocorrelation is a technique used in spatial analysis that enables epidemiologists to explore the distribution of disease across specific areas and identify correlations between the incidence rates in adjacent regions [17]. Spatial autocorrelation can determine whether diseases are spatially clustered, randomly distributed, or dispersed which may help in detecting areas of disease hotspots. This is essential in the public health field as it can provides valuable insight into devising effective intervention and prevention strategies, including public health resource allocation based on local disease patterns and ultimately aiming to protect the health of the communities. In this study, we used Global Moran's I to determine whether there is a global spatial autocorrelation between 160 districts. Spatial autocorrelation is able to assess the degree of similarity observed among a certain location and its neighboring unit. The value of Global Moran's I range between -1 and 1. A positive value of Global Moran's I that is close to 1 indicates that districts with a high number of cases are clustered together, whereas a negative value closer to -1 indicates districts with a high number and a low number of cases are interspersed. Global Moran's I value of 0 means that there is no spatial clustering and the data are randomly distributed [18]. Z-score and p-value were calculated to evaluate the significance of Global Moran's I. This analysis was done using spdep package in R software.

Local indicators of spatial association (LISA) are statistical measures used to identify clusters of similar values or spatial outliers within geographic data. In contrast to Global Moran's I, which evaluates spatial autocorrelation across an entire dataset, LISA focuses on the local level to determine if similar values form clusters in particular areas. Based on LISA values, there are 4 types of clusters, which are high-high, low-low, high-low, and low-high. High-high clusters refer to districts with a high number of cases surrounded by other districts which also have a high number of cases. It indicates a hot spot where the number of cases is significantly higher than average, both for the district and its immediate geographic vicinity. Low-low clusters are districts with a low number of cases that are surrounded by other districts that also have a similarly low number of cases. Low-low cluster represents a cold spot. High-low and low-high clusters are identified as spatial outliers. High-low clusters are districts with a high number of cases surrounded by other districts with a low number of cases, whereas low-high clusters are described as districts with a low number of cases surrounded by districts with a high number of cases. The difference in attributes of interest compared to the surrounding area makes it a spatial outlier. This analysis was done using spdep package in R software.

3. RESULTS AND DISCUSSION

3.1. Results

There were 3,850 confirmed measles cases in Malaysia reported from 2018 to 2022. The distribution of measles incidence at the district level across Malaysia, expressed per 1,000,000 population, was displayed in Figure 1. The maps show that in 2018, the highest rate of measles incidence, depicted in red, was observed in the districts of Bintulu, Miri, and Marudi in Sarawak. A similar high incidence of more than 500 per million population was observed in Gua Musang district, Kelantan and Hulu Terengganu district, Terengganu, in 2019. From 2018 to 2022, a clear downward trend in incidence rates can be seen across districts in Malaysia, as evidenced by more light orange and yellow shade areas, with the most significant decline visible by 2021. Districts within Sabah and Sarawak showed the most pronounced decrease, with many maintaining a zero-incidence rate over the last three years. Most districts in Selangor reported persistent infection of measles, with incidence rates ranging from 5 to 500 cases per million population throughout the five years. Overall, districts in Peninsular Malaysia have seen a downward trend in measles incidence rates since 2018, although the rate fluctuates in the years 2021 and 2022, ranging from 0 to 50 per million population.

The Global Moran's I statistic revealed significant positive spatial autocorrelation, indicating that measles cases were spatially clustered in Malaysia from 2018 to 2022. Annual values of Moran's I statistics and its p-value are presented in Table 1. The LISA map shown in Figure 2 illustrates a dynamic pattern of measles infection hotspots in Malaysia. Initially, in 2018, Bintulu district in Sarawak was identified as a hotspot. In the following year, 2019, the hotspot regions shifted to Gua Musang district in Kelantan, as well as Hulu Terengganu, Kuala Terengganu, and Kuala Nerus in Terengganu, and also to Kunak, Semporna, and Tawau districts, with Bintulu returning as a cold spot. The year 2020 saw the emergence of Kuantan and Maran in Pahang, alongside Tumpat, Kota Bharu, and Bachok as areas of hotspots. By 2021, Kuala Nerus in Terengganu was highlighted as a hotspot. Throughout this period, the central region of Malaysia, particularly districts within the state of Selangor and the federal territories of Kuala Lumpur, consistently manifested as hotspots, indicating a persistently high number of measles cases over several years. Initially, the number of low-low districts, known as cold spot areas, decreased but later experienced a steady increase over the years. The majority of these cold spot districts were located in Sabah and Sarawak. On the other hand, the districts exhibiting a high-low pattern, indicating they were high-incidence areas surrounded by low-incidence neighbors, displayed variability in their numbers. These fluctuating high-low areas primarily consisted of districts in Kelantan, Terengganu, Pahang, and Johor.

3.2. Discussion

This study examines the distribution and incidence rate of measles infection across various districts in Malaysia, aiming to detect spatial clustering and identify hotspots areas of measles. Despite efforts to eliminate measles through a national elimination program, Malaysia continues to face challenges in combating the disease. Overall, the trend of measles incidence rates across Malaysia shows a decline. However, there are fluctuations in rates by district up to 2022, suggesting that measles transmission still persists in the country.

Table 1. Global Moran's I spatial autocorrelation analysis of measles infection in Malaysia from 2018 to 2022

Year	Moran's I statistics	p-value*
2018	0.48	<0.001
2019	0.22	<0.001
2020	0.27	<0.001
2021	0.16	<0.001
2022	0.51	<0.001

*p-value for Global Moran I statistic

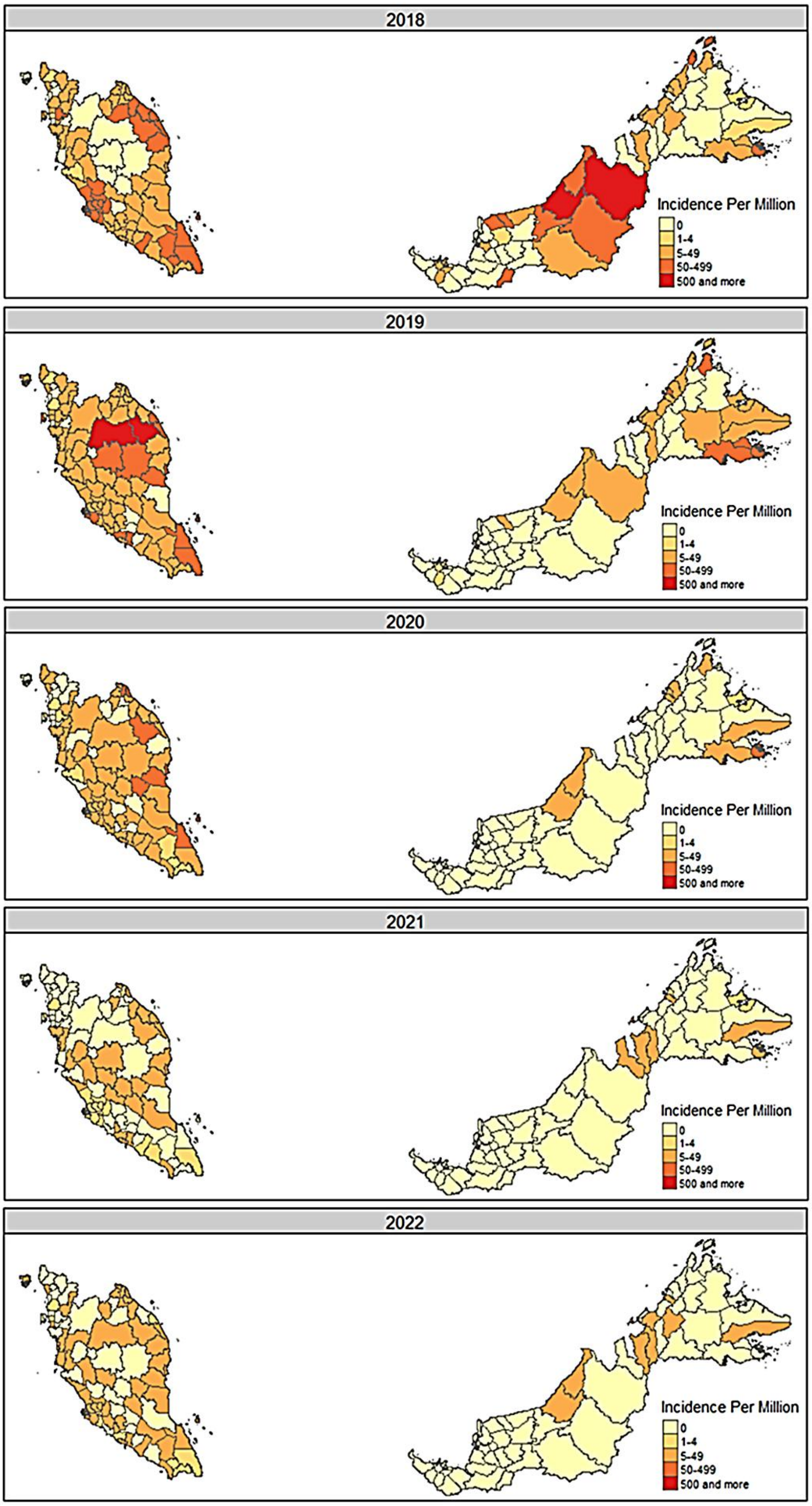

Figure 1. The incidence rate of measles infection in Malaysia from 2018 to 2022

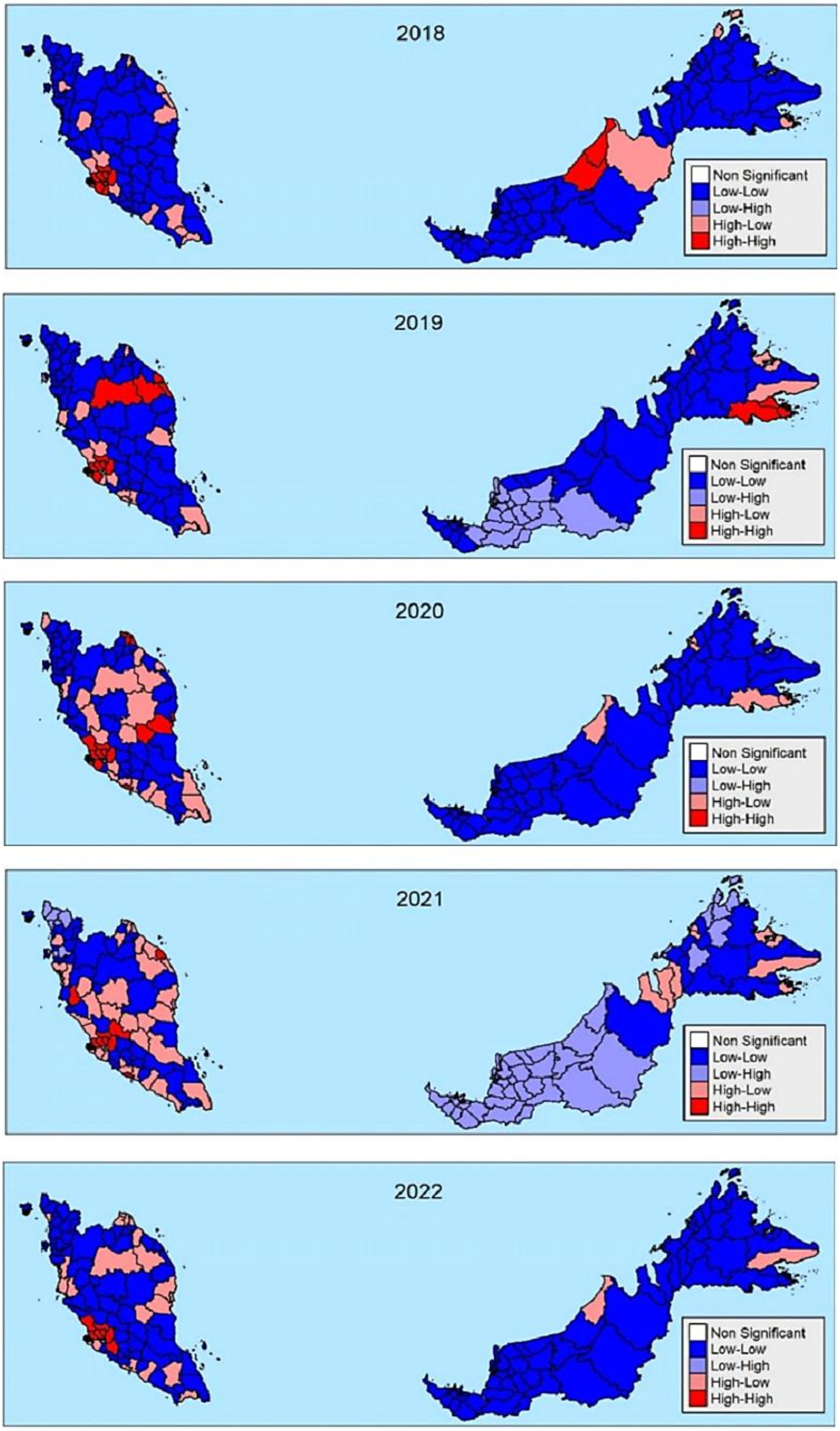

Figure 2. Map of local indicator of spatial autocorrelation (LISA) analysis of measles cases at district level in Malaysia from 2018 to 2022

In 2018, Bintulu district experienced a notable rise in cases of measles with 58.6 cases per 100,000 population primarily contributed by 81.6% of cases occurring in residential areas including housing areas, villages, long houses, and government quarters compared to 11.2% occurring at workplace [19]. Among the cases detected in Bintulu, more than half of them had unknown immunization status. Supplementary immunization activities (SIAs) involving children aged 6 months to 15 years old were implemented in Bintulu to curb the spread of disease. SIAs deliver vaccination to all targeted individuals regardless of their vaccination status and prior history with the aim to rapidly raise population level immunity and reduce the number of susceptible individuals. This campaign results in a reduction of measles cases in Bintulu in the subsequent years [20]. An outbreak was also reported in 2018 involving Marudi district with visitors from Miri district identified as the primary source of infection. This outbreak spread during a funeral in a rural village in Marudi district. However, the transmission was limited only to the attendees and did not affect the wider village population. This containment was attributed to the herd immunity present among children in the rural village and thus highlighting the importance of reaching herd immunity in a community [21].

In 2019, a large-scale outbreak involving predominantly unvaccinated individuals occurred in Gua Musang district and Hulu Terengganu district causing a spike of incidence rate in both areas. The outbreak was responsible for 110 confirmed measles cases including 11 deaths. The outbreak occurs among Bateq tribe individuals in Gua Musang, a tribe with nomadic habits whose movements to neighboring district facilitated the spread of the disease to Hulu Terengganu [8]. The outbreak highlights the critical role of population mobility in transmitting measles and heightened the disease risk associated with being unvaccinated. Therefore, public health approaches should account for the living conditions and behaviors of populations to ensure inclusivity and no one is left behind particularly in vaccination program. This is critical to prevent pockets of vulnerable populations to exist.

Between 2018 and 2022, Malaysia experienced a notable decline in the incidence rate of measles, a trend largely attributable to the effectiveness of public health policies and initiatives. This period witnessed the effect of modification in health policy regarding vaccination schedules in 2016 and the intensification of nationwide vaccination strategies. Previously, vaccinations were administered at 12 months and 7 years of age. Starting in 2016, the policy was amended to provide vaccinations at an earlier age, specifically at 9 and 12 months [22], [23]. This change led to earlier protection of children against measles and thus facilitated the earlier establishment of herd immunity, resulting in a reduced risk of disease transmission and, subsequently decrease in the incidence rate of measles in Malaysia. Widespread promotion of immunization activities across Malaysia through mass media, campaigns and health education in health facilities and promotion via social media had contributed to the increase in vaccination coverage. According to a report by the World Health Organization, the coverage for the first dose of measles-containing vaccine has increased by year from 92% in 2014 and consistently maintained above 95% since 2018 [24].

The fluctuation in measles incidence rates across districts, particularly in 2021 and 2022, can be directly linked to the global disruptions caused by the COVID-19 pandemic, which had a dual impact on measles by both reducing and increasing them under different circumstances. In Malaysia, measures to counteract COVID-19, such as lockdowns, hygiene practices, and physical distancing, inadvertently contributed to a decrease in measles cases. The enforcement lockdown orders, the closure of educational institutions, including schools and kindergartens and the implementation of work-from-home policy may lower the risk of measles transmission by limiting interpersonal interactions [25]. Conversely, the pandemic precipitated widespread interruptions in routine immunization services, as healthcare systems were overburdened with managing COVID-19 cases. This situation was compounded by the diversion of healthcare resources to address the pandemic, sidelining preventive services like measles vaccination campaigns and delaying immunizations, which could potentially elevate the risk of measles spread. Additionally, the fear of contracting COVID-19 discouraged individuals from seeking healthcare for non-COVID-related health issues, including measles, thereby hindering efforts to control and mitigate the spread of this highly infectious disease [25], [26]. These conditions highlight the need for sustained vigilance and the maintenance of adequate measles vaccination coverage despite the challenges posed by the pandemic. The pandemic illustrates the critical balance between managing immediate public health crises and maintaining routine health services to prevent outbreaks of vaccine-preventable diseases such as measles. This delicate equilibrium necessitates strategic planning and resource allocation to ensure the continuation of essential health services, including immunization programs, even during global health emergencies.

Global Moran I statistic was utilized in the study to detect the presence of spatial autocorrelation of measles infections in Malaysia. There was a significant clustering of similar values, of either high values or low values between neighboring districts in Malaysia, as indicated by the positive Global Moran's I statistic with a p-value of less than 0.001. This finding aligns with previous research from other countries, indicating that measles transmission occurs in spatial clusters [27], [28]. Another study in China also reported spatial clustering of measles, although the study involves a larger polygon size of province-level [29].

The selection of the district as the unit for observation in this study was appropriate given the role of the district health office in coordinating measures to prevent and control measles, addressing both individual cases and outbreaks.

Further analysis was done using a LISA map to identify the location of spatial clustering in Malaysia. There was a temporary shift to high-high (H-H) cluster areas for a year observed in Bintulu and Miri in Sarawak in 2018 and Gua Musang in Kelantan and Hulu Terengganu district in Terengganu in 2019. These occurrences may be the result of large-scale outbreaks in these districts, as discussed earlier. Kuala Lumpur and major districts in Selangor have consistently been identified as H-H areas or hotspots for measles over five consecutive years, indicating the presence of underlying factors that contribute to this trend. These districts are characterized by their industrialized urban area and a significant presence of migrant workers, leading to areas of high population density [30]. Such conditions facilitate widespread transmission of the virus, especially in settings where close contact is common, including public transportation, educational institutions like schools and kindergartens, and densely populated residential settings such as high-rise apartments. Therefore, additional public health measures should be implemented in hotspot districts. Deployment of mobile teams from non-hotspot districts and conducting supplementary immunization activities in hotspot zones can serve as complementary strategies to augment existing measles prevention and control efforts in Malaysia. There was a noticeable increase in the number of low-low (L-L) areas or cold spots, suggesting that measles vaccination efforts have been successful in the majority of districts across the country. The escalating occurrence of high-low (H-L) districts is a concern in Malaysia. These H-L districts possess the potential to transform into hotspots in the future if there are no effective prevention and control measures in these districts.

A notable strength of this research is its utilization of extensive, nationwide data from across Malaysia, enabling a thorough exploration of the disease's distribution throughout the nation. By drawing on data that spans the entire country, the study benefits from a comprehensive perspective, encompassing all regions and thereby providing a detailed overview of measles distribution patterns. The study's methodology is notably strengthened by the use of confirmed measles case reports sourced from the e-measles database which is managed by the Disease Control Division of the Ministry of Health Malaysia. The Ministry of Health Malaysia, being the primary body responsible for the collection and oversight of measles data in this country, provides a highly credible foundation for this study. The reliance on this official, authoritative source ensures that the analysis is based on dependable data, essential for drawing accurate conclusions about the spatial distribution of measles. However, the study faces limitations related to the nature of secondary data and the potential of incompleteness of the data and underreporting, particularly in remote areas where access to healthcare and reporting mechanisms may be limited. This could affect the accuracy of incidence rate calculations and hotspot identification.

4. CONCLUSION

In conclusion, the fluctuating incidence of measles in Malaysia from 2018 to 2022, despite national immunization efforts, underscores the persistent threat of transmission, particularly in identified hotspot areas. The study's spatial analysis revealed significant clustering of cases, highlighting the need for targeted public health interventions. Continuous surveillance and tailored vaccination campaigns are critical to achieving measles elimination. Future research should explore the socio-economic, cultural, and environmental factors that contribute to sustained transmission in hotspot areas to inform more effective prevention strategies. This should includes an assessment of the current vaccination strategies' effectiveness, particularly within hotspot areas.

ACKNOWLEDGMENTS

We would like to express our gratitude to the Director-General of Health, Ministry of Health, for granting permission to publish this study and extend our thanks to all who directly or indirectly contributed to this research.

FUNDING INFORMATION

This study has no funding involved.

AUTHOR CONTRIBUTIONS STATEMENT

This journal uses the Contributor Roles Taxonomy (CRediT) to recognize individual author contributions, reduce authorship disputes, and facilitate collaboration.

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C : **C**onceptualization	I : **I**nvestigation	Vi : **Vi**sualization
M : **M**ethodology	R : **R**esources	Su : **Su**pervision
So : **So**ftware	D : **D**ata Curation	P : **P**roject administration
Va : **Va**lidation	O : Writing - **O**riginal Draft	Fu : **Fu**nding acquisition
Fo : **Fo**rmal analysis	E : Writing - Review & **E**diting	

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

INFORMED CONSENT

This study uses aggregated data and permission to access the data was obtained from the Head of Information and Documentation Sector, Disease Control Division, Ministry of Health Malaysia. No individual data were obtained in this study.

ETHICAL APPROVAL

Ethical approvals for the study were obtained from the Human Research Ethics Committee, Universiti Sains Malaysia (USM/JEPeM/KK/23010094) and the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR ID-23- 00290-E4U (IIR)) prior to this study. This study adhered to the ethical principles outlined in the Declaration of Helsinki.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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