

A mixed-effects model of the determinants of measles incidence: a nationwide study in Malaysia, 2018 to 2022

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ABSTRACT

Measles remains a significant global public health concern, particularly in Malaysia. Despite national vaccination coverage exceeding 90%, measles continues to persist, highlighting the need for a deeper understanding of the multifaceted factors influencing its transmission dynamics. This study aimed to explore the determinants of measles incidence in Malaysia, focusing on local demographic profiles, healthcare-related factors, and environmental factors at the district level from 2018 to 2022. Data for this study were collected from the e-measles database of Malaysia's Ministry of Health, including statistics on the number of cases reported in each district. Additionally, vaccination coverage data were obtained from the Malaysian Health Informatics Centre. Local demographic profiles, such as median household income, population density, and urbanisation, were sourced from the Department of Statistics Malaysia (DOSM). Data on the number of health and rural clinics were also extracted from DOSM. Environmental data, including relative humidity, temperature, and PM2.5 levels, were obtained from the Department of Environment (DOE). A negative binomial mixed-effects model was employed for data analysis using R software, and the results were interpreted to identify significant determinants of measles incidence. The analysis revealed that median household income (adjusted incidence rate ratio [aIRR] 1.02, 95% confidence interval [CI]: 1.01, 1.03) and the number of health and rural clinics (aIRR 1.02, 95% CI: 1.01, 1.04) were positively associated with measles incidence. Conversely, temperature (aIRR 0.85, 95% CI: 0.74, 0.99) and the year of observation (aIRR 0.51, 95% CI: 0.47, 0.56) were negatively correlated with measles incidence. These findings highlight the complex interplay between socioeconomic, healthcare, and environmental factors in measles transmission, underscoring the need for comprehensive public health strategies to maintain high vaccination rates and adapt to varying local conditions.

Key words:

measles, determinants, demographics, healthcare factors, environmental factors

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INTRODUCTION

Measles remains a major public health challenge globally, including in Malaysia, despite substantial progress in immunisation efforts. With vaccination coverage exceeding 90%, the persistence of measles underscores the need to understand the complex factors driving its transmission. The variability in measles incidence across different districts in Malaysia, with rates ranging from 24.5 to 225.6 per million, suggests that localised factors at the population or district levels significantly influence disease patterns.¹⁻³

In addition to individual-level factors such as age, vaccination status, contact history, and travel history, previous studies have identified broader determinants such as population density, urbanisation, and median household income as influential in measles transmission.⁴⁻⁸ However, these are not the only factors explaining the disparities in incidence observed across countries. Malaysia's healthcare infrastructure, primarily delivered through governmental health and rural clinics, may also affect disease detection and reporting.⁹ The association between access to healthcare services and the infectious disease burden further complicates the landscape of disease incidence.¹⁰

Environmental factors, including air quality and climate, have also been linked to measles transmission.¹¹ Virology studies have shown that high relative humidity decreases the survival time of the measles virus, resulting in longer survival at lower relative humidity.¹² An increase in PM2.5 levels has been associated with higher measles incidence.^{13,14} These environmental factors can exacerbate or mitigate the spread of the virus in regions with varying temperatures, humidity, and pollution levels. The influence of environmental factors on measles incidence

in Malaysia has not been thoroughly explored.

This study aims to address these gaps by identifying the determinants of measles incidence in Malaysia at the district level from 2018 to 2022, incorporating local demographics, healthcare access, and environmental factors from various sources. Understanding these multifactorial influences is crucial for developing targeted public health interventions to effectively control and prevent measles outbreaks.

METHODS

Study area

Malaysia is a Southeast Asian country located partly on the Asian mainland and partly on the northern third of Borneo. As of 2020, Malaysia has a diverse population of over 32 million and is known for its cultural heritage, vibrant cities, and lush landscapes. The country has a tropical rainforest climate heavily influenced by the annual southeast (from May to September) and northwest (from November to March) monsoons. The climate is characterised by high humidity and substantial rainfall, with average annual precipitation ranging from 2,000 mm to 2,500 mm. Temperatures generally remain constant throughout the year, averaging between 23°C and 32°C.¹⁵ Its geographic location and climate make Malaysia a hub of biodiversity and a popular destination for ecotourism.

Study design and data sources

Various governmental and institutional databases were used to obtain data for this study, focusing on district-level data to visualise variations in measles incidence and its determinants across different regions of Malaysia from 2018 to 2022. Data on confirmed measles cases in each district from 1 January 2018 to 31 December 2022 were aggregated annually from the e-measles database supplied by the Disease Control Division, Ministry of

Health Malaysia. The e-measles database standardises reporting, investigations, and findings at the district, state, and national levels for measles control and prevention.² All confirmed measles cases included in this study were defined based on the Case Definitions for Infectious Diseases in Malaysia.¹⁶ A confirmed measles case is either laboratory-confirmed or meets the clinical definition of measles and is epidemiologically linked to a laboratory-confirmed case.

Data on population count, land area in square kilometres, the annual median household income, and the number of health and rural clinics within each district from 1 January 2018 to 31 December 2022 were sourced from the Department of Statistics Malaysia. The annual population density for each district was calculated by dividing the total population by the land area in square kilometres. Measles vaccination coverage data for each district were provided by the Health Informatics Centre of the Ministry of Health Malaysia. Environmental data, including daily average PM2.5 ($\mu\text{g}/\text{m}^3$), daily average relative humidity (%), and daily average temperature ($^{\circ}\text{C}$) from all 65 air quality monitoring stations in Malaysia, were obtained from the Department of Environment, Malaysia. From these daily averages, the annual averages for PM2.5, relative humidity, and temperature were calculated. For districts with air quality monitoring stations, environmental data were derived directly from measurements taken at these stations. For districts lacking meteorological stations, data from the geographically closest stations were used to ensure the application of the nearest available meteorological information. The designation of each district as either urban or rural was determined by the local council.

Statistical analysis

The normal distribution of the determinants for each year was assessed using descriptive analysis. Determinants included population density, median household income, urbanisation, number of health and rural clinics, vaccination coverage, PM2.5 levels, relative humidity, and temperature. Non-normally distributed numerical data are presented as median (IQR), while categorical data are presented as frequencies (percentages).

The association between measles incidence and its determinants was initially assessed using simple Poisson regression. Variables with p -values < 0.25 and important factors were selected for multivariable analysis. An overdispersion test was used to detect overdispersion in the datasets. Due to overdispersion, a negative binomial regression was applied.¹⁷ A generalised linear mixed-effects model with residual maximum likelihood (REML) estimation was used to account for nested data, with yearly observations nested within districts. This approach also accounts for unobserved heterogeneity across districts. Model 1, a null model with the district as a random effect and no explanatory variables, served as a baseline for comparison and to establish variance attributed to random effects. Model 2 used a Poisson mixed-effects model adjusted for district as a random effect, with all determinants included as fixed effects. Model 3 applied a negative binomial mixed-effects model, adjusted for district as a random effect and included all determinants as fixed effects. Model 4 used a negative binomial mixed-effects model adjusted for district as a random effect, with significant variables included only as fixed effects along with an additional two-way interaction between significance variables. Model 5 used a negative binomial mixed-effects model adjusted for district as a random effect, with significant variables included only as fixed

effects and no additional two-way interactions.

Model fit was assessed using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and log-likelihood of the models. The Variance Inflation Factor (VIF) for the generalised linear model (GLM) was applied to test for multicollinearity. Statistical significance was defined as a p -value < 0.05 . All modelling was performed using R software version 4.3.1 in RStudio (version 2023.12.1+402).

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Human Research Ethics Committee of University Sains Malaysia (approval code USM/JEPeM/KK/23010094) and the Malaysia Medical Research and Ethics Committee (approval code NMRR-23-00290-E4U). Given the use of secondary data, we ensured compliance with data protection and privacy regulations.

RESULTS

There were 160 districts across Malaysia, each providing annual data on

population density, urbanisation, median household income, number of health and rural clinics, vaccination coverage, PM2.5 levels, relative humidity, and temperature over five years, yielding 800 district-year observations. However, 79 (9.8%) observations were excluded due to incomplete data, resulting in 721 complete district-year observations.

There was a notable decrease in PM2.5 levels in 2020 compared to the preceding years. Concurrently, there was an upward trend in population density and median household income. The number of health and rural clinics and vaccination coverage remained relatively constant, as did median temperature and relative humidity across the 5-year period (Table 1).

The intraclass correlation coefficient (ICC) value in Model 1 was 0.10, indicating that approximately 10% of the total variability in measles incidence was due to differences between districts, while the remaining 90% was attributable to individual differences. Model 5 was the final model and was well specified compared to the other models based on fit indices, as evidenced by the lowest AIC (2683.11), BIC (2715.18), and log-likelihood (-1331.6). The fitted models are listed in Table 2.

Table 1. Descriptive statistics of determinants of measles incidence in Malaysia from 2018 to 2022 (n=721).

Variables	2018 Median (IQR)	2019 Median (IQR)	2020 Median (IQR)	2021 Median (IQR)	2022 Median (IQR)
Population density	83.87 (208.09)	84.61 (215.79)	85.27 (236.43)	85.91 (244.69)	85.93 (232.35)
Urbanisation					
Rural*	85 (59.86)	86 (59.72)	86 (59.72)	86 (59.72)	89 (60.54)
Urban*	57 (40.14)	58 (40.28)	58 (40.28)	58 (40.28)	58 (39.46)
Median household income (RM)	3792.50 (1676.00)	4055.50 (2057.25)	4097.00 (2057.25)	4113.00 (2048.00)	4283.00 (1916.00)
Number of health and rural clinics	18.00 (19.00)	17.50 (19.00)	17.50 (19.00)	17.50 (19.00)	17.00 (19.50)

Variables	2018 Median (IQR)	2019 Median (IQR)	2020 Median (IQR)	2021 Median (IQR)	2022 Median (IQR)
National Vaccination Coverage (%)	83.67 (29.06)	92.39 (20.21)	92.48 (20.26)	93.57 (22.39)	93.43 (23.28)
PM2.5 ($\mu\text{g}/\text{m}^3$)	15.83 (5.60)	19.72 (7.41)	11.81 (6.25)	12.03 (6.94)	12.67 (6.27)
Relative humidity (%)	82.27 (3.46)	80.34 (3.97)	83.26 (4.27)	83.52 (4.80)	84.90 (3.90)
Temperature ($^{\circ}\text{C}$)	27.38 (1.00)	27.42 (0.96)	27.29 (0.83)	27.14 (0.75)	27.01 (0.74)

Data are presented as median (interquartile range) or *n(%)

Table 2. Determinants of measles incidence in Malaysia from 2018 to 2022 (n=721)

Variables	Model 1 ^a	Model 2 ^b [aIRR (95% CI)]	Model 3 ^a [aIRR (95% CI)]	Model 4 ^a [aIRR (95% CI)]	Model 5 ^a [aIRR (95% CI)]
<i>Fixed effect</i>					
Population density		0.98 (0.96,1.01)	0.99 (0.97,1.02)		
Median household income		0.97 (0.96,0.98)*	1.02 (1.01,1.04)*	1.02 (1.01,1.04)*	1.02 (1.01,1.03)*
Urbanisation					
Rural		1	1		
Urban		4.11 (2.22,7.61)*	0.96 (0.58,1.59)		
Number of health and rural clinics		1.00 (0.98,1.03)	1.02 (1.00,1.04)*	1.02 (1.00,1.04)*	1.02 (1.01,1.04)*
Vaccination Coverage		0.99 (0.99,0.99)*	1.00 (0.99,1.00)		
PM2.5		1.01(1.00,1.02)	1.03 (1.00,1.07)		
Relative humidity		0.88(0.85,0.91)	1.03 (0.98,1.09)		
Temperature		0.73 (0.67,0.80)	0.85 (0.73,0.98)*	0.98 (0.77,1.25)	0.86 (0.74,0.99)*
Observation year		0.6 (0.57,0.63)	0.52 (0.47,0.58)*	3.25 (0.22,47.88)	0.51 (0.47,0.56)*
Temperature X observation year				0.93 (0.85,1.03)	
<i>Random effect</i>					
ICC	0.10	0.17	0.08	0.08	0.08
AIC	2910.0	4005.29	2687.6	2683.30	2683.11

Variables	Model 1 ^a	Model 2 ^b [aIRR (95% CI)]	Model 3 ^a [aIRR (95% CI)]	Model 4 ^a [aIRR (95% CI)]	Model 5 ^a [aIRR (95% CI)]
BIC	2923.8	4055.68	2742.6	2719.95	2715.18
Log-likelihood	-1452.0	-1991.6	-1332.8	-1333.7	-1331.6

aIRR = adjusted incidence rate ratio, CI = confidence interval, ICC = intraclass correlation coefficient, AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion, * p -value<0.05, ^aNegative Binomial Mixed-Effect Model, ^bPoisson Mixed-Effect Model; Model 1 is a null model with the district as a random effect without explanatory variable; Models 2 and 3 are models with district as random effect adjusted for all explanatory variables; Model 4 is a model with district as random effect adjusted for year of study, median household income, number of health and rural clinics and temperature with interaction between observation year and temperature; and Model 5 is a model with district as random effect adjusted for year of study, median household income, number of health and rural clinics and temperature. No multicollinearity was detected.

DISCUSSION

This study examined the determinants of measles in Malaysia, specifically focusing on the local demographic profile, healthcare-related factors, and environmental factors at the district level from 2018 to 2022. Median household income, number of health and rural clinics, temperature, and year of observation were found to be associated with the incidence of measles.

The study observed a notable decrease in PM2.5 levels in 2020, as shown in Table 1. This decrease could be linked to factors related to the unique circumstances of the year, primarily connected to the global COVID-19 pandemic. In 2020, numerous countries, including Malaysia, implemented strict lockdown measures to curb the spread of COVID-19. These measures led to reduced industrial activity, fewer cars on the road, and a general slowdown in economic activity, all contributing to decreased air pollution. Consequently, emissions of particulates, including PM2.5, were significantly reduced during this period. A study conducted during the COVID-19 pandemic found that the air quality of major cities worldwide improved, with Bogota, as one of the cities with the most traffic in the world, experiencing the greatest reduction in PM2.5 at 57%, and New Delhi, the most polluted capital city, showing a 40% decrease in PM2.5.¹⁸ This reduction in air

pollution likely decreased pollution-related health issues, including respiratory diseases such as COVID-19, influenza, and measles. However, population density and median household income continued to rise. Increased population density reflects natural population growth over time and can facilitate the rapid spread of infectious diseases due to closer human contact and increased interaction rates.¹⁹

The study found a significant association between higher median household income and the incidence of measles (aIRR 1.02, 95% CI: 1.01, 1.03, p -value < 0.001). This finding is supported by a study in Germany, which found that areas with lower socioeconomic deprivation had a 1.58 times greater risk (95% CI: 1.32, 2.00) of measles than areas with higher socioeconomic deprivation. Deprivation was assessed using the German Index of Socioeconomic Deprivation, based on education, occupation, and household income. Essentially, the findings suggest that areas with higher household income, reflected by lower socioeconomic deprivation, are at an increased risk of measles.²⁰ In Malaysia, high-income families often have dual-working parents, leading to a greater dependence on daycare services for childcare.²¹ This reliance places children in often crowded daycare settings, raising the potential for the spread of infectious diseases such as measles. Additionally, demanding work schedules for both parents may result in delayed or

incomplete vaccination of their children.²² The lack of timely immunisation increases vulnerability to measles. High-income families are also more likely to travel internationally,²³ which may expose them to measles and other infectious diseases uncommon in their home country. If these travellers are not adequately vaccinated, they may contract measles abroad and bring it back to their community, increasing local incidence rates.

Generally, the presence of more health clinics indicates improved access to healthcare, leading to enhanced diagnostic accuracy, more effective treatment options, and higher vaccination rates, thereby facilitating more effective disease prevention measures and improved health outcomes. Conversely, limited access to healthcare may result in a higher incidence of diseases due to challenges in obtaining diagnoses, treatments, and vaccinations.^{10,24} However, this study found a significant association between the number of healthcare clinics and the incidence of measles (aIRR = 1.02, 95% CI: 1.01, 1.04, p -value = 0.021). Districts with more health clinics tended to have improved capabilities for detecting, reporting, and responding to disease cases. This enhanced surveillance system may result in an apparent increase in reported measles cases, not because the disease is more prevalent but due to more efficient identification and documentation processes. This does not indicate a deteriorating public health situation but highlights notable improvements in public health infrastructure and disease management capabilities. Additionally, an abundance of health clinics encourages more people to seek medical attention for various health concerns, including minor symptoms and health queries. A study conducted in Hong Kong suggested that ease of access to healthcare facilities encouraged individuals to seek medical attention more promptly.²⁵ These

behaviours can increase the likelihood of early disease detection, including asymptomatic and atypical cases, thus elevating reported incidence rates in these areas.

This study found a negative association between temperature and measles incidence, suggesting that environmental factors may influence disease transmission dynamics. This finding aligns with the characteristics of the measles virus, which is rapidly inactivated by heat and sunlight.²⁶ Similar findings were reported in China and Kazakhstan, which experience four seasons.²⁷⁻²⁹ Although Malaysia is situated in the equatorial region and does not experience four seasons, it experiences a monsoon season twice a year, characterised by heavy rainfall.¹⁵ During this period, most Malaysians tend to stay indoors, limiting outdoor activities. In colder weather, people spend more time indoors, resulting in indoor crowding, creating ideal conditions for the transmission of respiratory viruses such as measles, which spreads through respiratory droplets when an infected person coughs or sneezes.³⁰ Consequently, lower temperatures can contribute to heightened measles transmission dynamics within indoor settings such as households, schools, or healthcare facilities. Exposure to cold temperatures can impair immune function in the respiratory tract, affecting the body's defence against respiratory pathogens such as the measles virus. Research has shown that cold exposure may suppress the production of B-cell-activating factors (BAFF), leading to reduced IgA secretion in the bronchial epithelium and explaining the increased frequency of respiratory tract infections in cold weather.³¹

The negative association between the observation year and measles incidence signifies a downward trend in measles cases over time, suggesting that public health

measures, including vaccination in Malaysia, have yielded positive outcomes. The modification of the measles vaccination schedule in Malaysia in 2016, shifting the age of measles vaccination from 12 months and seven years to nine months and 12 months, has shown favourable results, as evidenced by a reduction in measles cases, indicating the effectiveness of these control strategies.³ Enhanced surveillance and reporting systems, such as *e-notifikasi* and *e-measles*, have led to more precise data collection and timely interventions, further contributing to the decline in measles occurrences.^{32,33}

STRENGTHS AND LIMITATION

This study has several strengths. It is comprehensive, providing a thorough examination of measles incidence in Malaysia by integrating data on socioeconomic factors, environmental conditions, and healthcare access. This multifactorial approach offers a detailed understanding of the determinants of measles transmission dynamics. The inclusion of data from 2018 to 2022 allows for the evaluation of recent trends and the impact of significant events, such as the COVID-19 pandemic and changes in vaccination schedules. This timely analysis ensures the relevance of the study's findings to current public health challenges. By employing a mix of negative binomial regression and mixed-effects models, this study addresses data overdispersion and accounts for variability across districts, enhancing the accuracy of the findings and the reliability of the conclusions.

However, our study has some limitations. Being a cross-sectional study, it limits the ability to establish causality between the identified factors and measles incidence. The reliance on secondary data sources may introduce biases related to data quality, completeness, and reporting

accuracy. Excluding incomplete observations may have led to the loss of potentially relevant information. The use of data from the nearest air quality monitoring stations in districts without their own stations may introduce inaccuracies in environmental exposure assessments. Additionally, using median household income as a proxy for socioeconomic status may not capture the full spectrum of socioeconomic factors influencing measles incidence, such as education level and specific community vulnerabilities.

CONCLUSION AND RECOMMENDATIONS

In conclusion, measles incidence is influenced not only by individual factors but also by socioeconomic, healthcare, and environmental factors. Therefore, integrated public health strategies should address healthcare accessibility and consider environmental and socioeconomic factors to control measles incidence. Targeted public health interventions are crucial for effectively controlling measles in Malaysia. The correlation between higher median household income and increased measles incidence indicates the need for awareness campaigns not only in low-income areas but also in high-income areas, emphasising the importance of timely vaccinations. Strengthening healthcare infrastructure is essential for improving disease detection and vaccination outreach, particularly in regions with fewer clinics. Environmental factors, such as temperature, should be incorporated into surveillance strategies with heightened measures implemented during conditions conducive to measles transmission, such as the monsoon season.

Future research should focus on exploring the impact of socio-cultural factors on vaccination uptake and measles transmission in Malaysia. Additionally, integrating advanced spatial analysis

techniques could enhance our understanding of local-level determinants, aiding in the development of targeted interventions to further reduce measles incidence.

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