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Original Article

Resurgence of measles infection among children: findings from a surveillance-based population study

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Abstract

Background There has been a resurgence of measles infection in countries with high vaccination rates, including Malaysia. Understanding the geographical variation in measles resurgence and associated factors is important for measles prevention and control programs, especially where local information is scarce.

Objective To determine the incidence of laboratory-confirmed measles infection and associated factors in the state of Melaka, in the southern region of Malaysia.

Methods We obtained measles surveillance data for 4 years (January 2015 to December 2018) from the e-measles national database. A comparative cross-sectional study was carried out on these data involving children who had been selected through convenience sampling.

Results A total of 130 laboratory-confirmed measles cases and 213 non-measles cases were included in the study. Among the laboratory-confirmed cases, 56 (43.1%) had not been vaccinated against measles virus. Thirty-eight cases (51.4%) had received at least one dose of measles vaccine, while 36 cases (48.6%) had completed two doses of measles vaccination. There was a higher risk of contracting laboratory-confirmed measles among unvaccinated children (OR 19.39, 95%CI 8.82 to 42.6, P<0.001) and children aged 8-18 years (OR 0.40, 95% CI 0.21 to 0.76, P=0.005)

Conclusion Unvaccinated children and children aged 8-18 years have a higher risk of contracting laboratory-confirmed measles. The policy on routine immunization should be strengthened, the vaccine should be accessible to all children, and all children and adolescents should be given booster vaccinations. **[Paediatr Indones. 2023;63:162-8; DOI: https://doi.org/10.14238/pi63.3.2023.162-8]**.

Keywords: *measles; surveillance; vaccination; comparative cross sectional; Malaysia*

Measles, a highly contagious, vaccine-preventable disease, continues to be one of the top causes of childhood mortality, with an estimated 450 fatalities per day occurring globally.[1] Measles is caused by a respiratory virus that originated from the Paramyxoviridae family.[2] Measles virus is highly contagious and is one of the most common communicable illnesses.[1] It can be commonly transmitted by coughing or sneezing and inhaling small particles that contain the virus.[3] Fever, cough, coryza, conjunctivitis, and the emergence of a maculopapular rash are all symptoms of the measles infection, which can lead to serious complications like pneumonia, otitis media, and encephalitis.[1]

Measles has a 10-day incubation time before the onset of fever and a 14-day incubation period before the emergence of a rash. During this period, the measles virus replicates at its highest rate and becomes contagious when the symptoms of cough, coryza, and sneezing are severe.[3] One to two days

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prior to the onset of the rash, Koplik spots, small white lesions pathognomonic for measles infection, may appear on the buccal mucosa.[4] The erythematous and maculopapular rash is distinguished by its appearance on the face and behind the ears, followed by a centrifugal spread to the trunk and extremities. The rash lasts 3-5 days and begins to fade in the same given timeframe as it developed.[3]

Complications may occur in nearly half of patients, and they are more common and severe in the very young, very old, pregnant, immunocompromised, and malnourished[5]. Pneumonia is the most common cause of measles-associated death, especially among children.[6] Other reported complications include otitis media and gastrointestinal, ophthalmological, haematological, and neurological complications.[7] Spontaneous abortion, premature labor, low birth weight, intrauterine mortality, stillbirth, serious measles infection in neonates, and maternal death are all linked to measles during pregnancy.[5] Measles is a vaccine preventable disease a so the *WHO* recommends vaccinations for all susceptible children and adults.[8]

In terms of disease prevention, vaccination is the most cost-effective public health initiative.[9] It helps everyone in a population, not only by improving health and life expectancy, but also by improving social and economic consequences at the global, national, and local levels. It significantly lowers the global occurrences of vaccine-preventable diseases, disability, and mortality. The Western Pacific Region experienced a period of significantly low measles incidence in 2012, i.e., concurrently during the year of measles elimination. However, the region experienced a resurgence of measles transmission in 2013-2016.[10] Despite the accessibility of a safe and effective measles-mumps-rubella (MMR) vaccine, measles cases significantly increased by 57% in the Western Pacific Region alone in 2016, and most of the cases were among children aged <5 years10. Notably, Malaysia's measles incidence rate remains among the highest in the Western Pacific area, with 75.74 per 100,000 population between July 2017 and June 2018.[11] This re-emerging pattern occurred due to the presence of an immunity gap in the unimmunized age group and the inconsistency in terms of the age distribution of those who were not vaccinated in certain geographic areas, especially in densely populated countries.[12]

Similarly, the measles elimination initiative in Malaysia resulted in a significant decrease in measles incidence in 1980-2010.[13] The initiative included providing routine measles-containing vaccines (MCV1) to children at 9-12 months and 7 years (MCV2) of age. However, measles outbreaks occurred in 2010-2013 and 2015-2016 in Malaysia, where it predominantly affected children aged <7 years, and in particular, infants aged <1 year.[14] As a response, the routine immunization schedule was improved in 2016 when MCV1 (or MMR) was given at 9 months and MCV2 was offered again at 12 months, with a follow-up injection of an MCV dose (measles-rubella, MR) at 7 years of age.

Measles surveillance is an essential part of the Malaysia Measles Elimination Programme. Most reports on local measles epidemics were national level descriptive reports.[15,16] Cases that fulfilled the case definition of measles based on clinical symptoms and prior history of measles immunisation were strongly associated with laboratory-confirmed measles, according to a local study done in Malaysia's northern region.[15] Understanding the geographical variation in measles resurgence and associated factors is important for evidence-based decision-making in measles prevention and control program. The objective of our study was to determine the incidence of laboratory-confirmed measles infection and associated factors in the state of Melaka, in the southern region of Malaysia.

Methods

We conducted a cross-sectional study among all cases reported of suspected measles in the online measles surveillance database (e-Measles and e-notification) between January 1, 2015, and December 31, 2019. The three Melaka districts included were Alor Gajah, Melaka Tengah, and Jasin, with a total population of 940,000 in 2017.[17]

In Malaysia, measles surveillance is based on a case classification system. Any person with a fever, maculopapular (non-vesicular) rash, and one of the following symptoms is considered to have probable measles: cough, coryza, or conjunctivitis.[18] All cases of measles in Malaysian healthcare facilities must be reported.[18] *The Ministry of Health of Malaysia* has developed and manages both the e-notification and e-Measles systems. E-notification is an online notification system used by healthcare facilities to report to the district health office on all notifiable diseases.[19] The system is used to better control such diseases. Within 48 hours of receiving an e-notification, all cases of measles are investigated. According to WHO guidelines, laboratory confirmation of measles is done by detecting anti-virus IgM antibodies using an enzyme-linked immunosorbent test or real-time polymerase chain reaction (RT-PCR).[20] *The National Public Health Laboratory*, which has been designated as a WHO reference laboratory, received all of the specimens for this investigation. A "non-measles" case was defined as a case clinically suspected of measles and registered in the e-Measles system but with negative antibodies on laboratory confirmation.

We included all laboratory-confirmed cases reported to the Alor Gajah, Melaka Tengah and Jasin health districts and compared it with reported cases that had been clinically diagnosed but had negative laboratory results for measles infection. We compared the outcome of having measles infection with independent variables such as sociodemographic factors and MMR vaccination status. Cases with positive laboratory-confirmed measles infection occurring 21 days after MMR vaccination and those aged <9 months were excluded from this study.

The Malaysian Ministry of Health Medical Research and Ethics Committee and the Universiti Kebangsaan Malaysia Research Ethics Committee both gave their approval to this study. The sample size was calculated using *PS2* software considering 80% power to detect an odds ratio (OR) of >2 and 95% confidence interval (95%CI), assuming a measles prevalence of 72.3%. The minimum required sample size was 140 for each sex. Data were analysed using *SPSS version 23* (*IBM*, Armonk, New York). Statistical significance was set at P<0.05.

Results

A total of 130 measles and 213 non-measles cases were included in our study. Among the confirmed measles cases, 51.5% were male and 48.4% were female, while non-measles cases comprised 52.1% males and 47.9% females. The most affected age group was the 1-to-7-year group (40.8%). No deaths were reported and 93.8% of the measles cases occurred in Malay children. Most of the measles cases (75.4%) and non-measles cases (76.5%) were urban residents. Among the measles cases, 56 (43.1%) had not been vaccinated against measles virus, 38 (51.4%) had received one dose of the measles vaccine, while 36 (48.6%) had completed two doses of the measles vaccine (**Table 1**).

Table 1. Sociodemographic characteristics of the cases

Variables	Measles (n=130)	Non-measles (n=213)	Total (N=343)
Gender, n(%)			
Male	67 (51.5)	111 (52.1)	178 (51.9)
Female	63 (48.4)	102 (47.9)	165 (48.1)
Age, n(%)			
9-11 months	38 (29.2)	65 (30.5)	103 (30.0)
1-17 years	53 (40.8)	121 (56.8)	174 (50.7)
8-18 years	39 (30.0)	27 (12.7)	66 (19.2)
Ethnicity, n(%)			
Malay	122 (93.8)	189 (88.7)	311 (90.7)
Non-Malay	8 (6.2)	24 (113)	32 (9.3)
Residence, n(%)			
Urban	98 (75.4)	163 (76.5)	261 (76.1)
Rural	32 (24.6)	50 (23.5)	82 (23.9)
MCV dosages, n(%)			
MCV1	38 (51.4)	118 (57.8)	156 (56.1)
MCV2	36 (48.6)	86 (42.2)	122 (43.9)
Vaccination status, n(%)			
Vaccinated	74 (56.9)	205 (96.2)	279 (100)
Not vaccinated	56 (43.1)	8 (3.8)	64 (100)

The proportion of laboratory-confirmed measles cases did not significantly differ according to sex (95%CI 0.66 to 1.58, P=0.918). In addition, there was no association between ethnicity and laboratory-confirmed measles (95%CI 0.22 to 1.18, P=0.114). The type of location of residence was likewise found to be unrelated to laboratory-confirmed measles (95%CI 0.5 to 1.56, P=0.810). Furthermore, no difference was observed between measles and non-measles cases who had received MCV1 (95%CI 0.76 to 2.21 P=0.342,). Children who had not received any MMR vaccination had 19 times higher risk of contracting laboratory-confirmed measles infection compared to children who had received at least one dose of the MMR vaccine (95%CI 8.82 to 42.6, P<0.001). Age of 8 to 18 years was significantly associated with laboratory-confirmed measles (95%CI 0.21 to 0.76, P=0.005) (**Table 2**).

Discussion

There was a significantassociatione between the children's vaccination status and laboratory-confirmed measles infection in this study. This finding was consistent with our hypothesis and several other previous studies. Here, unvaccinated children had higher odds of contracting measles infection, which was similar to the previous reports.[21,22] A study showed that unvaccinated youngsters were responsible for the majority of measles infections at Disneyland in 2015.[23] Our findings also showed that 18.7% children of all ages were not vaccinated. This alarming figure calls for further in-depth research to understand the rationale or reasons for the low vaccination uptake among children. Furthermore, since we used secondary data from web-based surveillance, i.e., the e-measles database, the reasons these children were unvaccinated cannot be fully ascertained. Only 3.1% of the unvaccinated children were foreigners. Among the potential explanations for non-vaccination are refusal due to vaccination reactions, especially at the injection site,[24] low parental knowledge,[25] inadequate access to healthcare services,[26] and lower uptake of vaccination among healthcare workers.[27] Others have also shown that urbanization could also be a reason for the low immunization coverage in rural areas, due to young parents with small children migrating to urban areas seeking better employment opportunities.[22,28]

We also found a positive association between children aged 8-18 years and laboratory-confirmed measles infection. This conclusion was consistent with that of a Pakistani study, which found a higher incidence of measles cases and outbreaks among

Table 2. Association between sociodemographic characteristics and vaccination status with laboratory-confirmed measles cases (N=130)

Variables	n (%)	c2	Crude OR (95%CI)	P value
Gender, n(%)				
Male	67 (51.5)	0.011	1.02 (0.66 to1.58)	0.918
Female	63 (48.4			
Age, n(%)		16.366		<0.001
9-11 months	38 (29.2)		1.000	
1-7 years	53 (40.8)	1.21b	1.33 (0.79 to 2.23)	0.271*
8-18 years	39 (30.0)	7.83b	0.40 (0.21 to 0.76)	0.005*
Ethnicity				
Malay	122 (93.8)	2.49	0.51 (0.22 to 1.18)	0.114
Non-Malay	8 (6.2)			
Residence				
Urban	98 (75.4)	0.058	0.93 (0.56 to 1.56)	0.810
Rural	32 (24.6)			
Vaccination status				
Vaccinated	74 (56.9)	82.24	19.39 (8.82 to 42.6)	<0.001
Not vaccinated	56 (43.1)			
Dosage				0.342
MCV1	38 (51.4)	0.929	1.30 (0.76 to 2.21)	
MCV2	36 (48.6)			

*Wald

children and adolescents aged 10-19 years.[29] This may have been due to the difficulty of recognizing measles infection in this age group, including earliest possible quarantine, as most of them regularly attend school. A study in Malaysia revealed that children and adolescents had lower levels of measles immunity than adults,[30] which supports the importance of vaccinations for these individuals.

Unvaccinated children and reduced protective antibodies are the other factors that may have caused the significant number of measles cases in this study. Others have also mentioned secondary vaccine failure as the reason these children became susceptible to measles infection.[31,32] Primary vaccination failure is defined as a failure to create the antibodies required to protect against a disease, while secondary vaccine failure is defined as the creation of antibodies in response to a vaccination but the levels of these antibodies decrease and decline faster than expected. Gidding *et al.*[33] discovered that the vaccine-induced measles-specific antibodies waned compared to those attributed to natural measles infection. In terms of contracting laboratory-confirmed measles, we found no significant differences between the sexes. This is in accordance with a Chinese study of the general population.[34] However, it differs from that of a study among children aged 0-7 years, who found that boys had a significantly higher risk of contracting measles compared to girls.[35] Several studies have also found a discrepancy between ethnicity and measles infection.[36-38] A study showed that ethnicity and cultural background were strong predictors of MMR vaccine uptake.[36] These findings differed from our own, in that we found no link between ethnicity and laboratory-confirmed measles.

In our study, urban *vs.* rural residence showed no significant association with measles infection. In contrast, a previous study concluded that better socioeconomic status correlated with lower rates of measles infection. Urban residents are usually from a higher socioeconomic status. Furthermore, rural children had lower vaccination coverage compared to urban children, which can lead to an increased risk of developing vaccine-preventable diseases like measles.[28]

Our study had a few limitations. First, it was based on web-based surveillance data using the e-measles database. The laboratory-confirmed cases of measles were not representative of the general population. Furthermore, we could not validate how vaccination status was obtained. Second, the healthcare professionals who diagnose and notify the suspected measles cases are required to perform serology or virus isolation testing for confirmation. According to the *Centers for Disease Control and Prevention/World Health Organization*, up to 30% of tests for measles- and rubella-specific IgM may yield false negative results.[39] Specimens obtained on days of rash may be IgM-negative, and a repeat serum test may be needed. This could result in laboratory-confirmed measles cases being undetected if the negative result is not repeated.

Our findings showed that measles infection was associated with a large proportion of unvaccinated children in areas where healthcare service is accessible. The vulnerability of children in the older age group is reflected in their increased risk of developing measles infection. Routine immunization activities and other measles prevention strategies need to be strengthened. Schoolchildren should be the focus of enhanced immunization programs in Malaysia. Further studies should investigate the reasons for low vaccination uptake among the younger population to provide better understanding, subsequent better measles control, and the eventual elimination of measles in Malaysia.

Conflict of interest

None declared.

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