

## A retrospective analysis on incidence of hand, foot, and mouth disease in Kota Kinabalu, district of Sabah Malaysia

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### Article Info

#### Article history:

Received Sep 8, 2021

Revised Dec 31, 2021

Accepted Feb 19, 2022

#### Keywords:

Endemic

EV71

HFMD

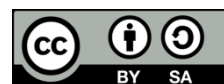
Kota Kinabalu

Sabah

### ABSTRACT

Malaysia is one of the most affected countries by hand, foot, and mouth disease (HFMD) outbreak. Sabah, as a state of Malaysia, has an incidence of 2,200 HFMD cases in 2018. Kota Kinabalu hits the highest records of HFMD cases compared to other districts. Given the marked increase in HFMD cases, HFMD become a public health concern which is associated with a substantial economic and social burden. From the perspective of public health, it is important to study the disease patterns and associated risk factors. This paper describes the incidence of HFMD and potential demographic risk factors in this understudied Kota Kinabalu District. A total of 3,327 HFMD cases from year 2013 to 2018 were obtained from the Kota Kinabalu Health Office. Cases were classified according to year of incidence, patient's gender, age, and ethnic. Incidence of HFMD and percentage of severe HFMD were calculated for each category. Odd ratio of severe HFMD for each category was assessed with logistic regression model. Chi-square tests were implemented to identify the association between the case characteristics and severe HFMD. This study found that male and Sabah indigenous group are predominant in HFMD incidence. Chi-square test indicated that severe HFMD is significantly associated with patient's age and ethnicity.

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## 1. INTRODUCTION

Hand, foot, and mouth disease (HFMD) is an endemic disease that occurs in many East and Southeast Asian countries. It is caused by a group of enteroviruses. The most common pathogenic agents include coxsackievirus A16 and enterovirus 71 (EV71) [1], [2]. HFMD can present as fever, a bullous rash on palms, soles of the foot, and mouth ulcer. This highly infectious disease is commonly transmitted to another person through direct contact with the saliva, nasal discharge, and other bodily fluid of HFMD patients [3]. HFMD is usually mild and self-limiting. Most HFMD cases do not require hospitalisation and only need to be treated at outpatient clinics. However, patients with severe HFMD may develop complications of the central nervous system, which could lead to hospitalisation [4], [5].

Globally, the HFMD outbreaks have been recorded for over four decades. The countries that have been affected included Japan, Malaysia, Singapore, Thailand, China, Hong Kong, Taiwan, Brunei,

Cambodia, Vietnam, Mongolia, and the Republic of Korea [6], [7]. Meteorological factors such as humidity, temperature, and precipitation strongly affect the spread of HFMD [8]–[11]. For instance, high humidity during the rainy season and warm temperature increases the spread of HFMD [3], [12]–[15].

In Malaysia, the worst and largest HFMD outbreak happened in 1997, whereby the EV71 strain caused 41 deaths among infants. Then, another HFMD outbreak occurred in late 2000, causing eight deaths [16]. Since then, the HFMD outbreaks take place almost every two to three years in Malaysia [17]. In 2019, HFMD recorded an incidence rate of 232.62 per 100,000 population, with a mortality rate of 1% [18]. A total of 2,200 HFMD cases were recorded in Sabah. Kota Kinabalu recorded 250 cases (26.6%), making it the district with the highest number of HFMD cases in Sabah. Most of the recorded cases were from kindergarten and nursery. Several precautionary measures were taken after the HFMD outbreak. These measures included the closure of schools, nurseries, and kindergartens. The economic and social burden of HFMD is a concern for public health authorities.

To date, studies in analysis on HFMD cases in Malaysia are scarce, particularly in Sabah. The impact and pattern of HFMD in Sabah is not well recognised even though there are increasing of HFMD cases in Sabah [19], [20]. It is crucial to understand the epidemiology patterns and the associated risk factors of HFMD in developing effective intervention options. Kota Kinabalu is the only city in Sabah and it is the district with the highest number of HFMD cases in Sabah. Therefore, this paper discussed the incidence of HFMD in Kota Kinabalu district of Sabah and the potential demographic risk factors of HFMD. It is hoped that this study can provide new insight to the relevant authorities in order to provide a scientific basis for the diagnosis, treatment, prevention and control of the disease for more effective implementation or policy on ameliorating the increasing HFMD cases in Kota Kinabalu, Sabah.

## 2. METHOD

### 2.1. Study population

Kota Kinabalu is the capital city of Sabah that is located at the northern area of Borneo, Malaysia (5.9804° North latitude and 116.0735° East longitude). Kota Kinabalu district has the highest population density in Sabah with nearly 500,000 people (1,397 people/km<sup>2</sup>). Apart from that, Kota Kinabalu has a tropical climate. Thus, the weather in Kota Kinabalu is hot and humid throughout the year, with temperature ranging from 30 to 32°C during the day and around 22°C at night. The temperature rarely goes up to 38°C. The rainy season usually occurs between October and March, while the dry season is between April and September

### 2.2. Data collection

HFMD cases between 2013 and 2018 were retrieved from the e-notification system at the Kota Kinabalu Health Office. The collected data comprised of HFMD cases reported from health centres located in Kota Kinabalu Central, Tanjung Aru, Sembulan, Kepayan, Luyang, Likas, Inanam, Menggatal, Sepanggar, and Telipok. Epidemiological variables including age, gender, locality of each HFMD case, and disease severity were obtained for this study. HFMD cases were diagnosed based on the clinical symptoms outlined by the Ministry of Health [21]. A case is classified as severe when patients show the following symptoms: i) unable to tolerate oral feeds, ii) a need for intravenous hydration, iii) clinically very ill or toxic-looking, iv) persistent hyperpyrexia, v) neurological complications, vi) myocarditis, and vii) requiring hospitalisation.

### 2.3. Statistical analysis

Firstly, HFMD cases were classified according to the following categories: i) year of incidence, ii) gender, iii) age, and iv) ethnic group. Incidence of HFMD and percentage of severe HFMD cases were calculated for each category. Odds ratio of severe HFMD for each category was assessed using the logistic regression model shown in (1):

$$\ln\left(\frac{\hat{p}}{1-\hat{p}}\right) = b_0 + b_1X_1 + b_2X_2 + \dots + b_kX_k \quad (1)$$

where  $\hat{p}$  is the expected probability of severe HFMD;  $X_1$  through  $X_k$  are the risk factors; and  $b_0$  through  $b_k$  are the regression coefficients. The antilog of the regression coefficient associated with a risk factor,  $\exp(b)$  was used to calculate the odds ratio adjusted for the risk factor. Lastly, Chi-square test was used to identify the association between the case characteristics and the number of severe HFMD cases.

## 3. RESULTS AND DISCUSSION

A total of 3,327 HFMD cases were notified in Kota Kinabalu from 2013 to 2018, with 134 severe cases, but no death was reported. A massive HFMD outbreak occurred in 2018 with the number of reported HFMD cases reaching 1,022. The same epidemic peak can be observed from the trending in whole Malaysia, as reported by the local news [22], [23]. Figure 1 shows that males were mostly affected by HFMD, as

highlighted by the previous studies [24], [25] that male is one of the risk factor of HFMD. Van Lunzen and Altfeld [26] state that males are prone to HFMD infections due to the regulation of immunity by the human X chromosome, such as toll-like receptor 7 (TLR7) that is responsible for detecting viral pathogens. Meanwhile, Figure 2 depicts the disease distribution among different ethnic groups in Sabah. The incidence of HFMD among Sabah indigenous was the highest in Kota Kinabalu. Ang *et al.* [24] suggests that gender and ethnic groups are associated with HFDM cases, but the reason remains unknown.

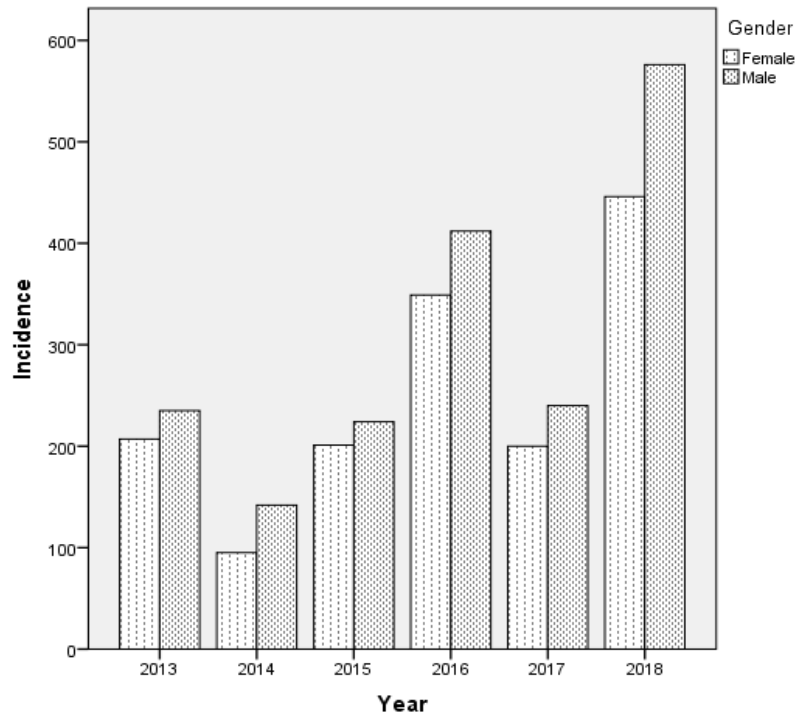


Figure 1. Incidence of HFMD in Kota Kinabalu by gender between 2013 and 2018

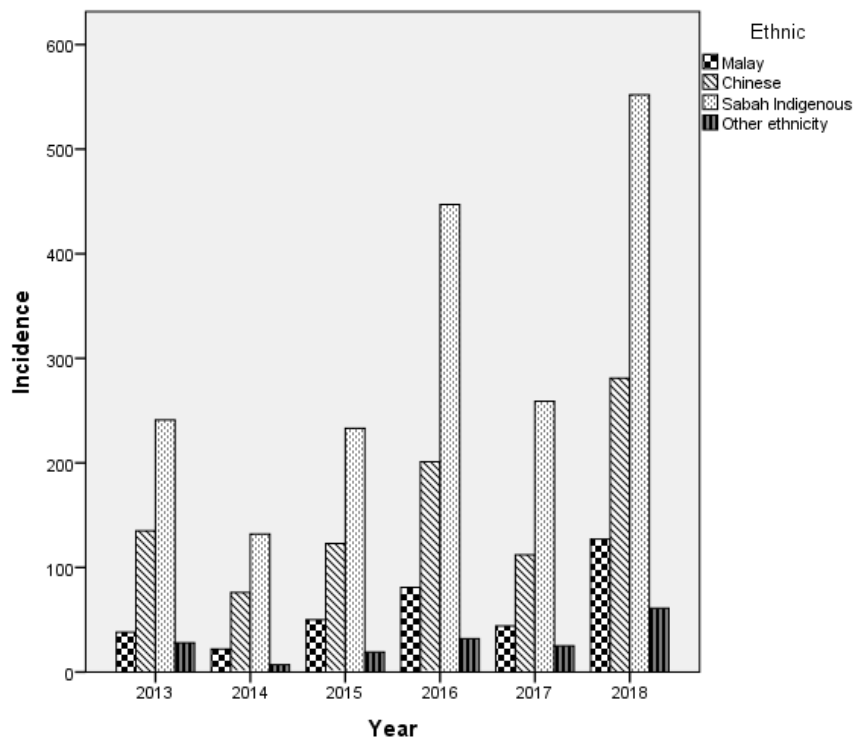


Figure 2. Incidence of HFMD in Kota Kinabalu by ethnic groups between 2013 and 2018

Children aged six years and below accounted for about 93% of the total case, with the highest incidence (29%) occurred among 1-year-old children as shown in Figure 3. This contagious illness is highly common in young children aged six years and below, as claimed in most of the previous studies [1], [8], [16], [27], [28]. The disease spreads among young children through close gatherings, such as in day care centres, nursery schools, and kindergartens [29]. The infectious virus is commonly present on toys and in public places. Water theme parks, shopping malls, and playgrounds are among other places where the HFMD virus spreads, as the virus is transmitted via direct physical contact or water droplets.

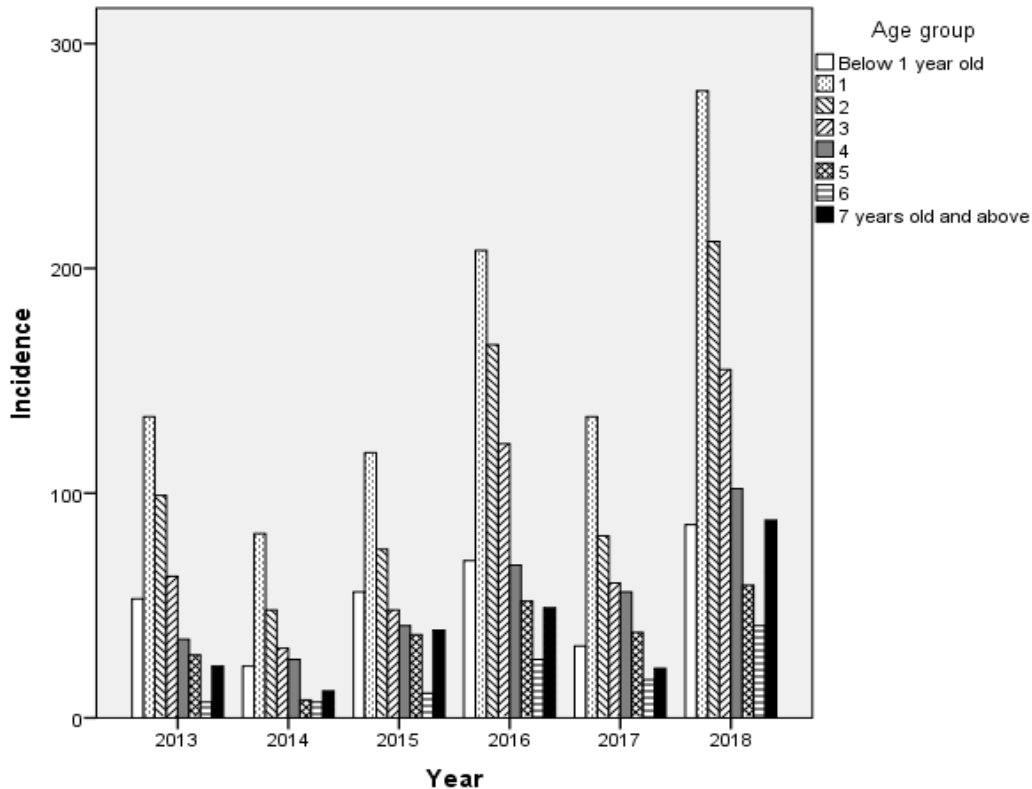


Figure 3. Incidence of HFMD in Kota Kinabalu by age between 2013 and 2018

Table 1 summarises the severe HFMD incidence in Kota Kinabalu from the year 2013 to 2018. Out of all HFMD cases reported over the six years, 4.0% were severe HFMD cases with an annual mean of 22 cases. The highest number of severe HFMD cases occurred in 2013 (6.6%), followed by in the year 2015 (5.4%), where the percentage dropped each year afterwards. Severe HFMD cases were more common in males (4.4%) than females (3.6%), where the odds of severe HFMD are 1.23 times higher among males as compared to females. However, Chi-square test result shows that the association between gender and severe HFMD is not significant ( $p=0.262$ ).

The highest social burden (7.5%) was reported in children aged below 1-year-old. The social burden decreased as age increased. The odds of severe HFMD cases were 8.06 times higher among children below 1-year-old than those aged above six years. Chi-square test revealed that the number of severe HFMD cases were significantly associated with patients' age ( $p<0.001$ ). Specifically, young patients had a higher risk of developing severe HFMD symptoms. A plausible reason is that the existing maternal antibodies in young patients may not be reliable in detecting viral pathogens [30].

As for the ethnic groups, most of the severe HFMD incidences occurred among the indigenous ethnic group. The other ethnic groups had less than 20 reported severe HFMD cases. The Sabah indigenous ethnic group also had a higher odd of severe HFMD as compared to the Malay and Chinese groups. Chi-square test result showed that the number of severe HFMD cases were significantly associated with patient's ethnic ( $p<0.001$ ).

Table 1. Summary of severe HFMD incidence in Kota Kinabalu for the year 2013 to 2018

	Number of severe HFMD incidences, n=134 (% among all HFMD cases)	Odds ratio of severe HFMD
<b>Year</b>		
2013	29 (6.6)	--
2014	5 (2.1)	0.307
2015	23 (5.4)	0.867
2016	35 (4.6)	0.722
2017	13 (3.0)	0.457
2018	29 (2.8)	0.446
<b>Gender</b>		
Male	80 (4.4)	1.233
Female	54 (3.6)	--
<b>Age (in years)</b>		
<1	24 (7.5)	8.058
1	58 (6.1)	6.700
2	26 (3.8)	4.250
3	15 (3.1)	3.731
4	3 (0.9)	1.064
5	4 (1.8)	1.958
6	2 (1.8)	2.221
>6	2 (0.9)	--
<b>Ethnic groups</b>		
Malay	15 (4.1)	--
Chinese	17 (1.8)	0.508
Sabah indigenous	92 (4.9)	1.263
Others	10 (5.8)	1.367

#### 4. CONCLUSION

In summary, this study discussed the incidence and severity of HFMD based on age, gender, and ethnic groups from 2013 to 2018 in Kota Kinabalu district of Sabah, Malaysia. This study has revealed that gender, age, and ethnicity are among the significant factors contributing to the infection on HFMD. The results also show that age and the ethnic group contributed significantly to the odds of severe HFMD cases. The findings from this study are overall consistent with previous studies in Malaysia as well as other countries affected with HFMD. To our best knowledge, this is the first analysis on HFMD disease in Sabah using logistic regression. The findings could shed a light on ways to the prevention of the disease. However, with the limitation on the variables available in the e-notification database, there could be missing cofounding factor which were not included in the study. Considering the increment of HFMD cases in Kota Kinabalu, more studies are warranted to understand the epidemiological factors causing HFMD.

#### ACKNOWLEDGEMENTS

This study was funded by Skim Geran Penyelidikan Universiti Malaysia Sabah (SGA0096-2019) with Malaysia Research Ethic Committee approval (NMRR-19-2601-49823). We would like to thank the Director-General of Health, Malaysia, for his permission to publish this paper.




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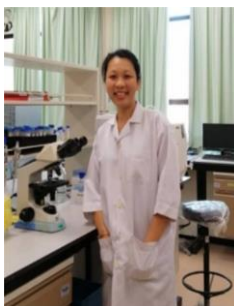
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**Chee Wei Yew**     is a senior lecturer and researcher in Biotechnology Research Institute, Universiti Malaysia Sabah, since 2015. He received his PhD in Biotechnology based on his thesis that worked on the genetic structure and molecular anthropology of the indigenous ethnic groups in Sabah, based on genome-wide DNA markers and whole genome sequences. Since then, molecular genetics studies on the indigenous ethnic groups in Sabah have been his primary research interest. Specifically, his research aims at deciphering the genomic variations of the people of Sabah. He believes that the differences at the DNA level could help to answer not only the fundamental questions on the manifestation of diseases, but also could serve as a key to unlock the current problems in medical genetics. As such, he is currently conducting a number of researches pertaining to hemophilia, thalassemia, genetic factors against malaria, adaptation of the Bajau Laut people to breath-hold diving, development of new COVID-19 testing method, network pharmacology of local herbal plants, surveillance and metagenomic analyses of zoonoses isolated from rodents and environmental samples. He wishes the outcome of the research could benefit the needs of the local people of Sabah. He can be contacted at email: cheewei.yew@ums.edu.my.








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