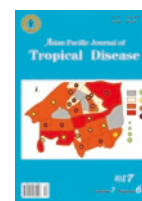


Asian Pacific Journal of Tropical Disease

journal homepage: <http://www.apjtdm.com>Original article <https://doi.org/10.12980/apjtd.7.2017D7-43>

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Epidemiology of hand foot mouth disease in Northern Thailand in 2016: A prospective cohort study

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ARTICLE INFO

Article history:

Received 5 Mar 2017

Received in revised form 5 May 2017

Accepted 24 May 2017

Available online 28 May 2017

Keywords:

Hand foot mouth disease

Meteorology

Epidemiology

Children

Cohort study

ABSTRACT

Objective: To determine the correlations between the meteorological data and the number of hand foot mouth disease (HFMD) cases in 2016 in Northern Thailand, and to estimate the medical costs.

Methods: A prospective cohort study was conducted. Data on numbers of HFMD cases were collected from 49 hospitals in three different provinces in Northern Thailand: 16 hospitals from Chiang Rai Province, 7 hospitals from Pha Yao Province, and 26 hospitals from Chiang Mai Province. A questionnaire had been developed and tested for validity and reliability before used. The specific form for collecting meteorological data was developed and used in the field. All information was recorded in the same data spread sheet before analysis. *Chi-square* and correlation tests were used for explaining the epidemiology of HFMD in the areas. An alpha error at 0.05 was used to determine the statistical significance level.

Results: A total of 8261 cases were analyzed in the study. 56.0% were males, 97.5% aged less than 6 years, 82.6% were out-patient department (OPD) cases, 75.5% were reported in raining season, and 43.2% were from Chiang Mai Province. The number of HFMD cases had statistically significant correlations with temperature, air pressure, relative humidity, and rainfall amount. Averagely, 216 baht and 3678 baht per case per visit had to be expended for medical cost in OPD and IPD cases, respectively. Most of the cases had been reported in the border areas: Thai-Myanmar, and Thai-Lao.

Conclusions: Thailand health care system should provide a concrete schedule for taking care of HFMD patients during raining season, and should develop an effective preventive and control program for HFMD particularly among children less than 6 years.

1. Introduction

Hand foot mouth disease (HFMD) has been classified as a major and common viral infection among children under 10 years old and can occur in adults, but it is most commonly seen in children under 5 years old particularly those who live in a tropical area[1]. Among the HFMD cases reported, younger children tended to have worse symptoms and complications[1]. Some cases had severe complications particularly in the nervous system[2,3]. However, there are no specific antiviral drugs or vaccine available against enteroviruses causing HFMD[4,5]. Moreover, a lot of public health resources including money were spent for treatment, care, and

control and prevention each year around the world[1].

In 2017, World Health Organization (WHO) reported that most of the HFMD cases were reported from the Western Pacific Region[6]. A total of 2468174 cases of HFMD including 220 deaths were reported from China, and during the same period, 69121, 42147 and 48866 cases were reported in Japan, Singapore and Vietnam, respectively. It has been termed as the most common disease among children under five years old from many countries. The main and specific characteristic of the HFMD is quickly spreading throughout the city, country, and region within a short period especially under proper environmental conditions including temperature, relative humidity, amount of rain, and human mobility rate[5].

In Thailand, several HFMD outbreaks were reported under the surveillance system of Thai Ministry of Public Health every year[7]. In 2015, Ministry of Public Health reported that 40417 cases (prevalence rate = 62.21/100000 people) were diagnosed as HFMD under the system of Thai health institutes in the country. It ranked 3rd among all communicable diseases in Thailand. Northern

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Foundation Project: Supported by the National Research Council of Thailand (NRCT), and Mae Fah Luang University, (Grant No. 5911).

The journal implements double-blind peer review practiced by specially invited international editorial board members.

Thailand was reported as the area with the highest prevalence of HFMD. In the first three months of the year of 2016 (January–March 2016), totally 8 973 cases of HFMD were reported through the system. Majority of the cases were under 5 years old, and there was no different proportion between sexes[8]. A lot of public health resources had been spent for treatment, care and prevention program for HFMD in Thailand[9].

Northern region of Thailand has its own specific geographical characteristics, which consists of 70% mountainous area[10]. This leads to variation of seasons: raining, hot (summer), and cold (autumn). Three provinces, Chiang Rai, Chiang Mai, and Pa Yao provinces, have specific and similar characteristics. These provinces have borders with Myanmar, China, and Lao. These countries have different health care systems and services. However, there are many people crossing borders every single day. The opportunity of spread of any specific diseases is high in these areas. Most of the public health staff who are working on disease control and prevention in border areas mainly focus on control of disease which is related to raw food and food product contamination[11].

Several researches presented the association between meteorological data and the occurrence of HFMD, but there is no research done in these particular settings. The aim of the study was to detect the association between the characteristics of HFMD including the number of the cases reported through the health institutes in Northern Thailand and the information from three meteorological stations.

2. Materials and methods

2.1. Study design

We conducted a prospective cohort study in Chiang Rai, Chiang Mai and Pha Yao provinces to explain the epidemiology of HFMD and its association with meteorological data in 2016.

2.2. Study sites

Data on HFMD were collected from 49 hospitals: 16 hospitals from Chiang Rai Province, 7 hospitals from Pa Yao Province, and 26 hospitals from Chiang Mai Province (Figure 1). The meteorological data were obtained from three different meteorological stations, or one station in each province, while the meteorological data were recorded from three meteorological stations, one station from each province.

2.3. Study sample

Totally, 8 261 cases of HFMD were reported and data were collected from the 49 targeted hospitals from January 1, 2016 to December 31, 2016. All of the cases were suitable for analysis. The information of wind speed, temperature, rainfall amount, air pressure, and relative humidity in the same period as HFMD reported was recorded from the three meteorological stations in Chiang Rai,

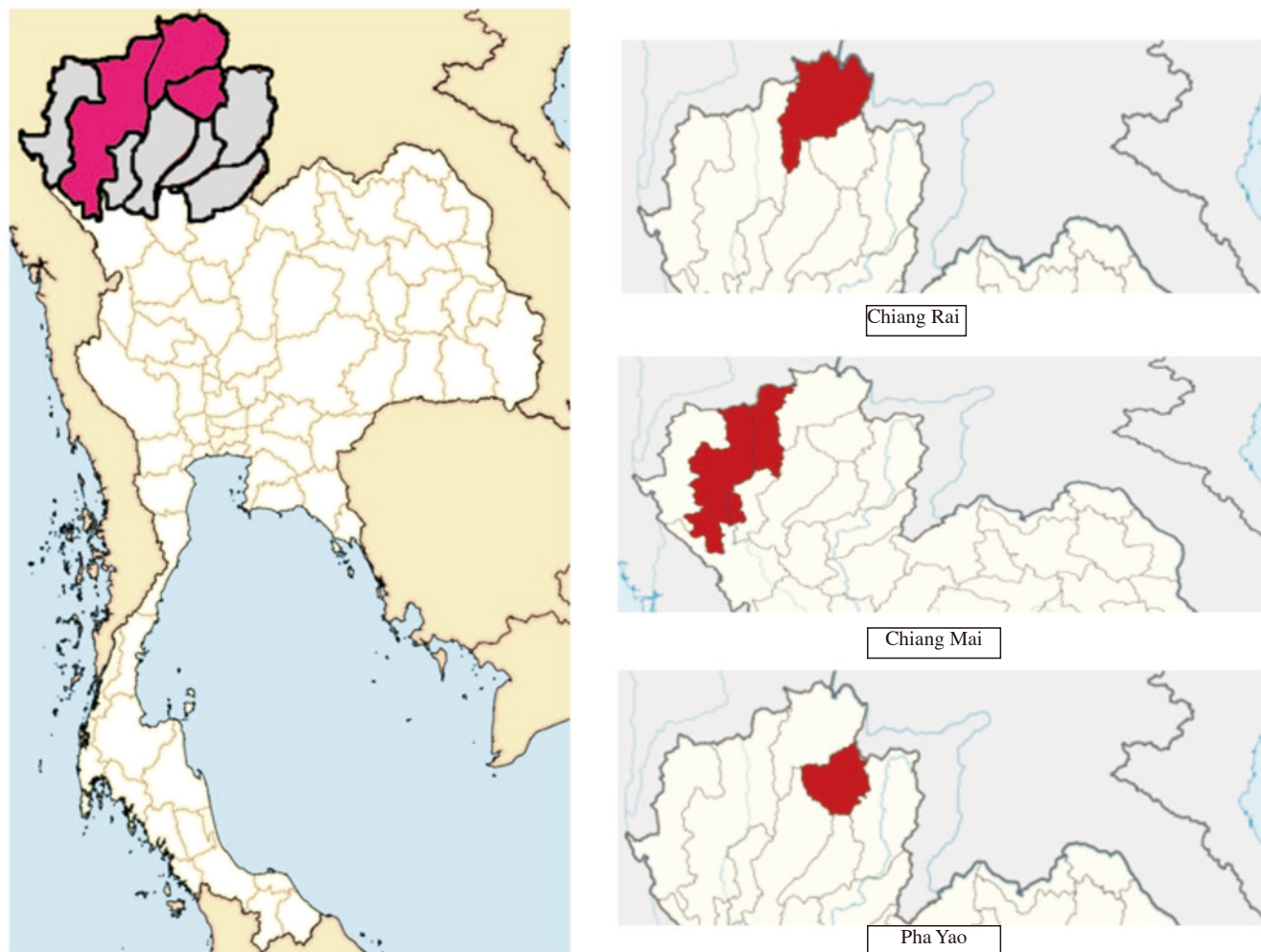


Figure 1. Location of the study area, Chiang Rai, Chiang Mai, and Pha Yao provinces in Northern Thailand.

Chiang Mai, and Pa Yao provinces.

2.4. Research instruments

A specific questionnaire developed for data collection regarding the HFMD from 49 hospitals was used. Questionnaire was tested for validity and reliability by three external experts [item-objective congruence technique (IOC)], and also a pilot study was done in a similar population before the questionnaire was used. Information such as age, sex, in patient or out patient case, residential area, date of seeking medical care, date of receiving treatment, treatment outcome, treatment cost, *etc.* was required.

The spread sheet was also developed for specific purpose on collecting the meteorological data. The form had been reviewed for feasibility test before starting the process of data collection in the three meteorological stations.

2.5. Procedure of data collection

Before the process of data collection in 49 hospitals, the hospital directors and the hospital staff who worked in Department of Diseases Investigation were invited to participate in the meeting. In the meeting, we provided all essential research information including information required from the HFMD patients. The system of reporting between researcher and hospitals had been created. Once the HFMD was detected by the medical doctor, the staff of Department of Disease Investigation was alerted. The personal and relevant information of HFMD patients was investigated by using the questionnaire. All information was sent to the research center afterward. All information of the HFMD patients from 49 hospitals was directly reported to the research center within 24 h.

The meteorological data were requested for every month from three meteorological stations in Northern Thailand. The data were entered into the spread sheet provided. The sheets were sent to the research center in the early weeks of every month. The meteorological data regarding environmental temperature, air pressure, relative humidity, wind speed, and rainfall amount were recorded on daily basis. The daily meteorological data were calculated to get the representative data of a week. Weekly data were used for forecasting the model and analysis.

Before starting the process of data analysis, two data sources were merged into the same file and stored.

2.6. Statistical analysis

Data were double-entered and validated by using Microsoft Excel. Data analysis was carried out by using SPSS version 24, 2016 (SPSS, Chicago, IL). Descriptive statistics (mean, maximum, minimum, standard deviations, frequencies and percentages) were used to describe the general characteristics of the patients. *Chi-square* and correlation tests were used to detect the association between variables at $\alpha = 0.05$. Specific graphs and maps were developed for explaining the epidemiology of HFMD.

2.7. Ethical considerations

All study procedures were approved by the Mae Fah Luang University Research Ethics Committee on Human Research (No. 027/2559). Permission of performing the study was also obtained

from Chiang Mai, Chiang Rai, and Pa Yao Provincial Chief of Public Health Offices. All participants had been given essential information including the objective of the study, and the informed consent was obtained before commencing the project.

3. Results

A total of 8 261 cases of HFMD were diagnosed from three provinces and recruited into the study; 56.0% were males (Table 1), 97.5% were aged ≤ 6 years old, 82.6% were identified as out-patient department (OPD) cases, and 43.2% were in Chiang Mai Province.

Table 1

General characteristic of the subjects ($n = 8\ 261$).

Characteristic	<i>n</i>	%	
Sex	Male	4628	56.0
	Female	3633	44.0
Type of patient	Out-patient	6822	82.6
	In-patient	1439	17.4
Age (year)	≤ 6	8053	97.5
	> 6	208	2.5
Season	Summer	1 105	13.4
	Raining	6239	75.5
	Winter	917	11.1

Four meteorological factors correlated with the number of HFMD cases in Chiang Rai Province: environmental temperature ($r = 0.283$, $P = 0.042$), air pressure ($r = -0.505$, $P < 0.001$), relative humidity ($r = 0.454$, $P = 0.001$), and rainfall amount ($r = 0.442$, $P = 0.001$) (Table 2).

Table 2

Pearson's correlation between meteorological data and the number of HFMD cases, 2016.

Area	Meteorological data	No. of cases	<i>r</i>	<i>P</i> -value
Chiang Rai	Temperature	3505	0.283	0.042*
	Air pressure		-0.505	< 0.001*
	Relative humidity		0.454	0.001*
	Wind speed		-0.084	0.552
	Rainfall amount		0.442	0.001*
Chiang Mai	Temperature	3 566	0.088	0.536
	Air pressure		-0.517	< 0.001*
	Relative humidity		0.575	< 0.001*
	Wind speed		0.048	0.737
	Rainfall amount		-0.438	0.001*
Pha Yao	Temperature	1 190	0.005	0.971
	Air pressure		0.135	0.339
	Relative humidity		-0.375	0.006*
	Wind speed		0.322	0.020*
	Rainfall amount		0.101	0.478

*: Significant level at $\alpha = 0.05$.

Three meteorological factors correlated with the number of HFMD cases in Chiang Mai Province: air pressure ($r = -0.517$, $P < 0.001$), relative humidity ($r = 0.575$, $P < 0.001$), and rainfall amount ($r = -0.438$, $P = 0.001$). Two meteorological factors correlated with the number of HFMD cases in Pha Yao Province: relative humidity ($r = -0.375$), and wind speed ($r = 0.322$, $P = 0.020$).

The number of HFMD cases significantly increased in raining season. A large proportion of HFMD cases in raining reason were

severe cases and were admitted in a hospital (Table 3). In 2016, the incidence of HFMD per 1000 people were 3.91, 2.68, and 2.94 in Chiang Rai, Chiang Mai, and Pa Yao provinces, respectively. Regarding the medical cost, the result found that averagely, 216 baht per visit to outpatient department (OPD) and 3678 baht per case for inpatient-department (IPD) per admission were spent respectively. A few cases of HFMD patients had a complication. The major complications were encephalitis, pulmonary edema, and hemorrhage. Therefore, in total 1473552 baht (50000 US dollar), and 7775292 baht (260000 US dollar) was spent for treatment for OPD and IPD respectively in the year 2016 in three provinces.

Table 3
Associations between types of patient with sex, season, and age.

Factors	Types of patient		χ^2	P-value	
	Out-patient	In-patient			
Sex	Male	3807	821	0.752	0.386
	Female	3051	618		
Season	Summer	940	165	20.309	< 0.001*
	Raining	5086	1152		
	Winter	795	122		
Age (years)	≤ 6	6645	177	0.938	0.333
	> 6	1408	31		

*: Significant level at $\alpha = 0.05$.

Figure 2 shows the distribution of HFMD cases in three different provinces in the year 2016. In Chiang Rai Province, most of the cases were reported from the central districts, followed by the eastern areas bordering Myanmar. In Chiang Mai Province, the disease distributed all over the province and many cases had been reported from the districts along Thai-Myanmar borders. In Pa Yao, most of the cases had been reported from Thai-Lao border areas particularly in the central district.

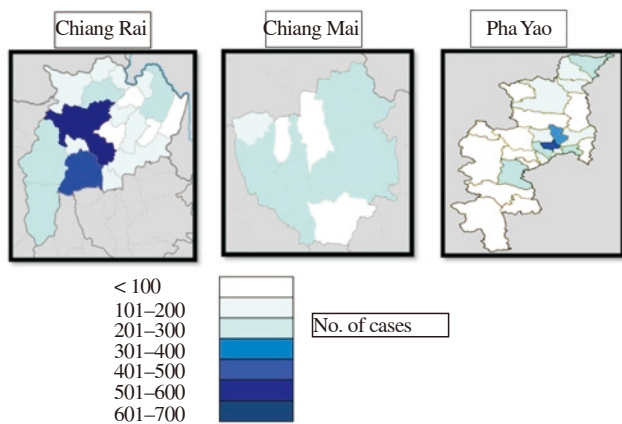


Figure 2. Number of HFMD cases in Chiang Rai, Chiang Mai, and Pha Yao provinces, 2016.

Figure 3 shows that in Chiang Rai Province, there were some cases reported in summer particularly in the central district, and high incidence occurred during the raining season. In Chiang Mai and Pha Yao provinces, most of the cases were reported in raining season; however, a few cases were reported in summer and winter.

4. Discussion

The major finding from the study indicated that humidity is strongly correlated with the number of HFMD cases; whereas, air pressure and rainfall amount are also correlated with the number of

HFMD cases in some areas. Most of the HFMD patients who visited a hospital were diagnosed in outpatient department, and there was no difference in ratio between sexes. However, most of the patients were aged less than 6 years at the time of diagnosis. It reflects that the most vulnerable population for HFMD is young children. This is supported by the study of Sun *et al.*[12] which reported that the major route of transmission of HFMD was close contact and un-washing hands instead of respiratory transmission. Yang *et al.*[13] reported that the major vulnerable population for HFMD was young children aged 0–4 years old.

The Thai government has to spend a lot of money for treatment of HFMD patients each year since there are a large number of visits to the hospitals. Most of the infected patients were asymptomatic and a few cases presented clinical and severe symptoms needed to get treatment and the severity was related to the genotype of the virus[14]. This implied that there were numbers of infected patients in the community but a few of them needed to attend a hospital to get treatment in Northern Thailand. To investigate the real epidemiology of the disease, we need to develop a proper method for investigation.

The complications of HFMD were mainly found in the respiratory tract and cardiopulmonary system. This coincides with the study of Li and Lao *et al.*[15] which found that some HFMD patients had a complication of encephalitis and pulmonary edema. The complication of HFMD was related to the genotype of virus and had been detected and confirmed in South East Asia including Thailand[16-19].

Wang *et al.*[20] performed a meta-analysis on HFMD in China which extracted the information from various published articles in different journals on the topic of HFMD in China during 2006–2015 and found that males were more susceptible to infection of HFMD than females (1.63 times more than females). This is different from the findings of our study which revealed that male and female had the same opportunity to get infected. However, in terms of age, the results had same direction that most of the HFMD cases occurred in children less than 5 years old; the number of HFMD cases will decrease as age increases.

In our study, we found that humidity was the most influencing factor to the number of HFMD cases but the environmental temperature had an impact on increase in the number of HFMD cases in some areas. This was consistent with the study of Yang *et al.*[13] which reported a few increases in number of cases while the humidity changed. Xu *et al.*[21] also reported that the temperature change between days had direct effect on the number of HFMD cases in children and it was a major factor for increase of the number of HFMD cases.

However, the study of Huong *et al.*[22] in Mekong Delta Region, Vietnam revealed that temperature was the major climatic factor influencing the number of HFMD cases; whereas the humidity had a little impact on the number of HFMD cases. This is supported by the study of Zhang *et al.*[23] which found that the environmental temperature was the largest contributor to the number of HFMD cases followed by humidity factor. However, the study of Xiao *et al.*[24] reported that the temperature was not a constant factor impacting the number of HFMD cases but the relation was shown in the V-shape pattern.

In our study, we also found that most of epidemic cases occurred in the borders with both Thai-Myanmar and Thai-Lao. A study in Ethiopia had presented that the major and common risk factor of occurrence of HFMD was geographical factor particularly in border areas[25]. This is concurrent with our study which found that most



Figure 3. Number of HFMD by seasons in three provinces Chiang Rai, Chiang Mai, and Pha Yao provinces, 2016

of the HFMD cases occurred in the Thai-Myanmar, and Thai-Lao border areas. It might be the impact of inaccessibility of the public health intervention in the areas.

Young children aged under 5 years old are the most vulnerable for HFMD infection. Thailand has spent a large amount of money for treatment and care particularly in Northern Thailand. The border areas, Thai-Myanmar and Thai-Lao, are most significant areas having outbreak of HFMD in Thailand. A specific public health intervention is needed for reducing the number of HFMD cases particularly in raining season.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The researchers would like to thank all 49 hospital directors in Chiang Rai, Chiang Mai, and Pha Yao provinces for their cooperation in providing essential information. We also would like to thank the director of meteorological stations in Northern

Thailand. Special thanks to the Center of Excellence for the Hill tribe Health Research and Mae Fah Luang University, Thailand for support in form of grant. This study was also supported by the National Research Council of Thailand (NRCT), and Mae Fah Luang University, (Grant No. 5911).

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