

# Factors Influencing the Occurrence of Hand Foot and Mouth Disease Among Children in Day Care Centers in Northern Thailand

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## ABSTRACT

**Objective:** Hand-foot-and-mouth disease (HFMD) is crucial and has a large-scale impact on worldwide healthcare systems in terms of expenses especially in the population of young children.

**Methods:** A community-based, case-control study was conducted to identify the factors influencing the occurrence of HFMD among children in day care centers (DCC). The study was conducted in three provinces in Northern Thailand including Chiang Rai, Chiang Mai, and Pha Yao. DCC and study samples were selected by a simple random method. A validated questionnaire was developed and used for collecting data after an index of item-objective congruence (IOC) method has been used to improve the quality of the questionnaire and piloted. Logistic regression was used to detect the associations between variables at the  $\alpha = 0.05$ .

**Results:** In total, 1,022 subjects were recruited into the analysis. Regarding parents' characteristics, 77.3% of the subjects were female, the average age was 33.9 years, 85.3% were married and 92.2% were Buddhist, 30.4% earned 5,001- 10,000 baht a month, and 49.9% had 1-3 family members. 17.9% had a low level of knowledge, 49.3% had a neutral attitude, and 96.7% had good practice for HFMD prevention and control. 34.2% of the children were aged  $\leq 2$  years, 54.9% were male, 50.4% were overweight and 21.1% had been breastfed. Three associated factors were found statistically significant with the occurrence of HFMD; children aged  $\leq 2$  years (OR=7.05, 95%CI=3.25–15.28), the number of household members (OR=1.43, 95%CI=1.04–1.97), and parents' knowledge (OR=2.35, 95%CI= 1.47–3.77).

**Conclusion:** Improving knowledge of HFMD among the parents, particularly those having many household numbers, is essential in order to reduce the incidence of the disease.

**Keywords:** Hand foot mouth disease; day care center; associated factors; children (Siriraj Med J 2020; 72: 151-158)

## INTRODUCTION

Hand foot and mouth disease (HFMD) is a common infectious disease<sup>1,2</sup> which is often reported in children under 6 years old particularly in tropical zones including Thailand.<sup>3</sup> HFMD is known to be a viral disease with limited specific treatment, but the number of infections has impacts on a global scale<sup>4,5</sup> and has defiantly become

a public health challenge due to the cost of care, prevention, and control measures.<sup>6,7</sup> Most of HFMD infected patients come with mild signs and symptoms; however, some of them are in a severe stage of infection with brain and nervous systems complications.<sup>2,8</sup>

In Thailand, 70,077 cases were reported in 2017 (morbidity rate 107.57 per 100,000 pop.), and the three cases

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of reported death, were mostly children aged between 0-6 years<sup>9,10</sup> Northern region of Thailand had been announced as the highest epidemic area.<sup>11</sup> Meanwhile, Chiang Rai, Chiang Mai, and Pha Yao were ranked in top HFMD epidemic area in 2015.<sup>12</sup>

Health promoting hospitals are the peripheral health care center under the health care system of Thailand. A center is in a sub-district and responsible for more than 5,000 inhabitants.<sup>3</sup> These health care centers are delivering care by 2-3 health care professionals who are, for example, nurse, public health professional, etc. There are a few health care centers that have a medical doctor.<sup>10</sup> The limitation of the operation is that some of the centers are located far away from the city and received limited recourse each year. Therefore, the main duty of these centers is to treat their patients. A small budget is provided in health promotion and disease prevention including the control of HFMD outbreaks.

Chiang Rai, Chiang Mai, and Pha Yao are located in Northern Thailand which their typical mountainous characteristics, with lower average temperatures than other regions in Thailand for a whole year.<sup>13</sup> There are some hill tribe populations living in these areas with low economic status.<sup>14</sup> For this reason, in daytime, most parents leave their children in a day care center where care givers take care of the children. Many studies have shown that HFMD is associated with economic status.<sup>15,16,17</sup>

DCC, operated by the local government, is a place where children under 6 years are taken care of during the daytime.<sup>11</sup> Many people in rural area of Thailand prefer to leave their children at the DCC before going to the farm during the daytime. The numbers of children receiving care in some DCCs are higher than the standard of the Ministry of Public Health<sup>3</sup> and some DCCs became overcrowded.

There are several guidelines for HFMD control and prevention in Thailand and many health implementations have also been conducted under the supervision of the Ministry of Public Health of Thailand. However, there were many episodes of outbreaks reported throughout Thailand during the past years especially in Chiang Rai, Chiang Mai, and Pha Yao provinces. The study aimed to investigate the factors influencing HFMD in DCCs. The information might help develop the proper prevention and control measures to reduce the number of HFMD outbreaks in Northern Thailand.

## MATERIALS AND METHODS

### Study design

A community-based, case-control study was conducted to reveal the factors influencing HFMD among children

under 6 years old who stayed in day care centers in Chiang Rai, Chiang Mai, and Pha Yao, Thailand.

### Study site

The day care centers located in Chiang Rai, Chiang Mai, and Pha Yao were the study settings. In 2015, 1,345 DCCs in three provinces (Chiang Rai=499 DCCs, Chiang Mai=645 DCCs, and Pha Yao=199 DCCs) were examined. Using the median line of three years prior to 2015 (2012-2014) [Ministry of Public Health, 2016], 438 DCCs were marked as the high epidemic area, and 907 DCCs were marked as the low epidemic area.

### Study population

The study population was the children aged less than 6 years and attended any DCC in 2015. However, the data was collected from their parents.

### Study sample and sample size estimation

Case were children who were less than 6 years old and had been diagnosed with HFMD (ICD- 10: B08.4) in DCC by a medical doctor in 2015. The confirmation of the diagnosis was reviewed based on the medical record after obtaining the verbal approval from their parents. The selected samples that did not have the medical record on their diagnosis were excluded from the study. Controls were selected by a random method, from children who were less than 6 years old and had not been infected by HFMD in 2015 in the low epidemic DCC with a 1:2 ratio of the cases to controls.

The sample size was calculated using Schlessel man's formula<sup>18</sup> at alpha value 0.05, the power of test was set at 80%, and the ratio of cases to controls was 1:2, probability of exposure in case at 4.5%.<sup>19</sup> The ratio of the cases to controls was 1:2; therefore, 332 cases and 690 controls were required after adding 10% for any possible errors in the study.

### Research instruments

The questionnaire was developed from reviewing the literature from all relevant sources of information. It consisted of three sections; general information, identification of infection risks, and assessment of knowledge, attitude, and practice (KAP). There were eighteen items for the general information section and 23 items for the identification of HFMD infection risks. In the KAP section, there were 10 items for knowledge, 10 items for attitude, and 10 items for practice.

The questionnaire had been tested for the validity and reliability by three external experts who had a relevant knowledge and experience in the field.<sup>20,21</sup> The quality

of the questionnaire also had been improved by being piloted with 20 selected samples from Mae Fah Luang University Hospital who had similar characteristics with the subjects in the study. Cronbach's alphas were calculated and found at 0.77 and 0.73 for attitude and practice respectively.

### Process of data collection

The lists of DCCs were classified into two different groups; the high epidemic area and the low epidemic area by using the median of cases reported during 2012-2014. A list of DCCs were inserted into the same work-sheet and labeled with numbers.

A simple random method was applied to select the targeted DCCs for the high and low epidemic areas. There were 62 DCCs from the high epidemic area and 47 DCCs from the low epidemic area.

Cases were all the selected children who met the criteria, and controls, chosen by a simple random method, were the children from the same DCC where the cases were found but did not have HFMD.

The parents whose children had been selected as case or control were invited to the interview. A private room was prepared and used for the interview. The participants were given all essential information of the research including objective, rights, etc. Signed informed consent forms were obtained from each participant before the one-to-one interview which lasted 35 minutes.

### Data analysis

The analyses were performed by using SPSS version 20, 2014 (SPSS, Chicago, IL), and Epi-Info version 6.04d (US Centers for Disease Control and Prevention, Atlanta, GA). Descriptive and inferential statistics were used to explain the characteristics and to answer the objective of the study. Logistic regression was employed to identify the associations between variables at the significant level  $\alpha = 0.05$ .

### Ethical consideration

All study protocols were reviewed and approved by Mae Fah Laung University Ethics Committee on Human Research by No. REH-59024. Permissions to access the DCCs were granted by the director of the local administration office. Prior to the process of data collection, the written information about the research project was delivered to the participants along with verbal information. After they agreed to take part in the study, a written informed consent form was contributed to each participant for their signature. All participants

were given a small gift as a token of appreciation for their participation after finishing the interview.

## RESULTS

### A) Characteristics of parents

There were 1,022 participants from 109 DCCs suitable for the analysis. 37.2% were from Chiang Rai, 33.9% were from Phayao and 29.0% were from Chiang Rai. 77.3% were female, the average age was 33.9 years old ( $SD=10.9$ ,  $min=17$ ,  $max=75$ ), 85.3% were married, 92.2% were Buddhist, 36.2% had educational attainment at primary school level, and 30.4 % made 5,001-10,000 baht a month. 46.5% of the mothers were the major care giver, and 49.9% of the participants had 1-3 members in their household.

Case group: 12.1% had a low level of knowledge, 48.0 % had a neutral attitude, and 96.2% had good practice for HFMD prevention and control.

Control group: 38.5% had a high level of knowledge, 52.0% had a positive attitude, and 96.9% had good practice on HFMD prevention and control.

Simple logistic model revealed that there were three factors associated with HFMD. Firstly, the children whose parents were Buddhist had a 1.96 times greater chance of infection than those with Christian parents ( $90\%CI=1.23-3.18$ ). Next, the children whose parents earned bachelor's degree had a 2.29 times greater chance of infection than those with illiterate parents ( $90\%CI=1.23-4.27$ ). Lastly, the children whose parents had a high level of knowledge on HFMD prevention and control had a 1.81 times greater chance of infection than those whose parents had low level of knowledge ( $90\%CI=1.28-2.57$ ) and 2.01 times greater than those whose parents had neutral knowledge ( $90\%CI=1.42-2.85$ ) (Table 1).

### B) Characteristic of children

54.9% were male, 56.9% were 3-4 years old, 50.4% were underweight, 15.4% had been admitted to the hospital, and 21.1% had been breastfed for less than 6 months since their birth.

Case group: 55.3% were aged less than 2 years old ( $mean=2.94$ ,  $SD=1.02$ ), 57.0% were male, 48.3% were underweight, 18.1% had been admitted to the hospital, 5.6% had a medical condition, and 26.0% had been breastfed for less than 6 months.

Control group: 62.8% were aged 3-4 years ( $mean=2.94$ ,  $SD=1.02$ ), 53.7% were male, 51.7% were underweight, 14.1% had been admitted to the hospital, and 81.1% had been breastfed for less than 6 months.

Simple logistic regression model revealed the

**TABLE 1.** Parents' characteristic and HFMD in a simple logistic regression (1,022).

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	P-value
<b>Total</b>	1022(100.0)	322 (32.4)	690(67.6)	NA		
<b>Sex</b>						
Male	224 (22.7)	73 (22.9)	151 (22.6)	1.00		
Female	762 (77.3)	246 (77.1)	516 (77.4)	1.01	0.77 – 1.39	0.931
<b>Parent's age (years)</b>						
<19	20 (2.2)	4 (1.3)	16 (2.6)	1.00		
20-59	847 (92.7)	288 (93.8)	559 (92.1)	2.06	0.82 – 5.21	0.200
>60	47 (5.1)	15 (4.9)	32 (5.3)	1.87	0.65 – 5.38	0.326
<b>Marital status</b>						
Single	54 (5.4)	16 (5.0)	38 (5.6)	1.00		
Married	854 (85.3)	272 (84.5)	582 (85.7)	1.11	0.67 – 1.84	0.734
Divorce	93 (9.3)	34 (10.6)	59 (8.7)	1.37	0.75 – 2.50	0.393
<b>Family member (person)</b>						
1-3	220 (49.9)	120 (30.4)	210 (36.1)	0.77	0.59 – 1.01	0.068
≥ 4	692 (50.1)	212 (69.6)	480 (63.9)	1.00		
<b>Number of child &lt;12 years in family (persons)</b>						
1	564 (56.7)	206 (63.4)	358 (35.5)	1.00		
2-3	404 (40.6)	111 (34.2)	293 (43.8)	0.65	0.52 – 0.83	0.003*
> 3	28 (2.6)	8 (2.5)	18 (2.7)	0.72	0.38 – 1.58	0.552
<b>Religion</b>						
Buddhist	933 (92.2)	312 (95.1)	621 (90.8)	1.98	1.23 – 3.18	0.018*
Christian	79 (7.8)	16 (4.9)	63 (9.2)	1.00		
<b>Occupation</b>						
Unemployed	72 (7.2)	29 (9.0)	43 (6.4)	1.00		
Merchant	416 (41.6)	140 (43.5)	276 (40.8)	0.75	0.49 – 1.16	0.276
Government Officer	42 (4.2)	21 (6.5)	21 (3.1)	1.48	0.78 – 2.82	0.314
Farmer	324 (32.4)	83 (25.8)	241 (35.6)	0.51	0.33 – 0.80	0.013
Employee	114 (11.4)	39 (12.1)	75 (11.1)	0.77	0.46 – 1.29	0.403
Other	31 (3.1)	10 (3.1)	21 (3.1)	0.71	0.34 – 1.49	0.442
<b>Income (baht/month)</b>						
≤ 5,000	258 (29.3)	87 (29.4)	171 (29.2)	1.09	0.77 – 1.53	0.681
5,001–10,000	303 (30.4)	111 (37.5)	192 (32.8)	1.24	0.89 – 1.72	0.287
10,001–15,000	101 (11.5)	27 (9.1)	74 (12.6)	0.78	0.50 – 1.23	0.371
15,001–20,000	40 (4.5)	14 (4.7)	26 (4.4)	1.52	0.63 – 2.11	0.700
≥ 20,001	179 (20.3)	57 (19.3)	122 (20.9)	1.00		
<b>Education</b>						
Illiterate	48 (4.8)	12 (3.7)	36 (5.3)	1.00		
Primary school	365 (36.2)	125 (38.2)	240 (35.3)	1.56	0.88 – 2.78	0.204
Lower secondary	193 (19.2)	154 (16.5)	139 (20.4)	1.16	0.63 – 2.14	0.679
Higher secondary	236 (23.4)	68 (20.8)	168 (24.7)	1.21	0.67 – 2.20	0.593
Vocational	38 (3.8)	13 (4.0)	25 (3.7)	1.56	0.71 – 3.42	0.352
Bachelor	127 (12.6)	55 (16.8)	72 (10.6)	2.29	1.23 – 4.27	0.028*
<b>Care giver</b>						
Father	92 (9.3)	21 (6.4)	71 (10.7)	1.00		
Mother	462 (46.5)	151 (46.2)	311 (46.8)	1.64	1.06 – 2.55	0.064
Father and Mother	105 (10.6)	35 (10.7)	70 (10.5)	1.69	0.99 – 2.88	0.104
Relatives	333 (33.6)	120 (36.7)	213 (32.0)	1.90	1.21 – 2.99	0.018
<b>Knowledge</b>						
Low (0-6)	172 (17.9)	38 (12.1)	134 (20.7)	1.00		
Medium (7-8)	398 (41.4)	135 (42.9)	263 (40.7)	2.01	1.42 – 2.85	0.001*
High (9-10)	391 (40.7)	142 (45.1)	249 (38.5)	1.81	1.28 – 2.57	0.005*
<b>Attitude</b>						
Neutral (1-3)	476 (49.3)	161 (51.9)	315 (48.0)	1.00		
Positive (4-5)	490 (50.7)	149 (48.1)	341 (52.0)	0.86	0.68 – 1.07	0.256
<b>Practice</b>						
Neutral (1-3)	32 (3.3)	12 (3.8)	20 (3.1)	1.00		
Good (4-5)	936 (96.7)	301 (96.2)	635 (96.9)	0.79	0.43 – 1.46	0.526

\*Significant level at  $\alpha=0.10$

**TABLE 2.** Children characteristic and HFMD in simple logistic regression.

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	P-value
<b>Age</b>						
≤ 2	325 (34.2)	147 (55.3)	178 (26.0)	7.94	4.20-15.04	<0.001*
3-4	541 (56.9)	111 (41.7)	430 (62.8)	2.48	1.32-4.69	0.019*
>4	85 (8.9)	8 (3.0)	77 (11.2)	1.00		
<b>Sex</b>						
Male	403 (54.9)	150 (57.0)	253 (53.7)	1.00		
Female	331 (45.1)	113 (43.0)	218 (46.3)	0.87	0.68-1.13	0.386
<b>BMI</b>						
Underweight	234 (50.4)	83 (48.3)	151 (51.7)	1.29	0.73-2.29	0.455
Normal	183 (39.4)	75 (43.6)	108 (37.0)	1.63	0.92-2.92	0.162
Overweight	47 (10.1)	14 (8.1)	33 (11.3)	1.00		
<b>History of hospital admission</b>						
Yes	151(15.4)	57 (18.1)	94 (14.1)	1.34	0.99-1.82	0.110
No	829(84.6)	258 (81.9)	571 (85.9)	1.00		
<b>Medical condition</b>						
Yes	53 (5.3)	18 (5.6)	35 (5.2)	1.00		
No	938 (94.7)	302 (94.4)	636 (94.8)	0.92	0.56-1.50	0.789
<b>Breast feeding (month)</b>						
< 6	145 (21.1)	55 (26.0)	90 (18.9)	1.52	1.10-2.10	0.031*
≥ 6	542 (78.9)	155 (73.8)	387 (81.1)	1.00		

\* Significant level at  $\alpha=0.10$ **TABLE 3.** Factors associated with HFMD in multiple logistic regression.

Factors	OR	95%CI	P-value
<b>Age (year)</b>			
≤ 2	7.05	3.25 – 15.28	<0.001*
3-4	2.09	0.97 – 4.51	0.061
>5	1.00		
<b>Family member (person)</b>			
1-3	1.43	1.04 – 1.97	0.028*
≥ 4	1.00		
<b>Knowledge</b>			
Low (0-6)	1.00		
Medium (7-8)	2.35	1.47 – 3.77	<0.001*
High (9-10)	1.61	1.00 – 2.59	0.051

\* Significant level at  $\alpha=0.05$



factors significantly associated with HFMD. Firstly, the children aged  $\leq 2$  years had a 7.94 times greater chance of acquiring HFMD than those aged more than 4 years (90%CI=4.20-15.04) and 2.48 times greater than those aged 3-4 years (90%CI=1.32-4.69). Besides, the children who had been breastfed for less than 6 months had a 1.52 times greater chance to having HFMD than those who had been breastfed for 6 months or more (90%CI=1.10-2.10).

After all possible factors were controlled; it was found that three factors were associated with HFMD in the children. The children aged  $\leq 2$  years old had a 7.05 times greater chance of HFMD infection than those children aged more than 5 years old (95%CI=3.25-15.28). Furthermore, the children from the family with 1-3 members had a 1.43 times greater chance of acquiring HFMD than those from the family with  $\leq 4$  members.

## DISCUSSION

The results from the simple model showed that the children whose parents were Buddhist had a 1.98 times greater chance of having HFMD than those with Christian parents; however, the significance was not found in the multiple model. HFMD might not be directly connected to religions, but some rural areas of Thailand have had a quicker economic growth.<sup>22</sup> The economic growth makes the parents from those rural areas, where one religion might be predominate than others leave their children at a day care center so they can go to work. Day care centers organized by the local government take care of preschool children during daytime. However, there was no previous report on the association between religions and HFMD.

In this study, the children aged  $\leq 2$  years old had a 7.05 times greater chance of HFMD infection than those aged more than 5 years old. According to the report of HFMD assessment in Thailand, the age group with high morbidity was mainly the children aged 0-2 years old who were immunosuppressed.<sup>5</sup> This is also consistent with Liu's study.<sup>23</sup> In Taiwan, it was found that patients with HFMD were often children aged less than 3 years old, similarly in Vietnam and China, the occurrences of HFMD were found in children younger than 3 years old. Another study by Chan et al.<sup>24</sup> also found that most patients were the children aged from 1 to 2.9 years old. In terms of household members, the households with 1-3 members had a 1.43 times greater chance of HFMD infection than those with  $\geq 4$  members. It could be that the current population characteristic of Northern Thailand is mostly a single family with few members as most families in the rural areas often have only 1-2 children.

The number of family members may contribute to the prevention of HFMD due to the number of members who had to keep clean. The results of this study support the study of YIN and et al.<sup>25</sup> indicating that families with children who had a history of HFMD infection was one of the factors contributing to HFMD.

Regarding the knowledge of HFMD, the parents with moderate level of knowledge had a 2.36 times greater chance of HFMD infection in their children than those with low level of knowledge. This study had been conducted to investigate HFMD infection since the past few years. After that, these groups of parents had more experience in children's care and learned more about HFMD. However, knowledge is important because the correct knowledge leads to appropriate practice in HFMD prevention and control.<sup>16,26</sup>

Generally parents or care givers at home with knowledge, good attitude and good practices of personal and environmental hygiene should have children who are less susceptible to HFMD. It is necessary to find out why children whose parents had moderate knowledge of HFMD turn to have a higher chance of contracting HFMD. May be having knowledge alone is not enough and parent and care givers at home, need knowledge of good practice and preventive measures of HFMD.<sup>4</sup>

Day care center is the place that often found and report HFMD cases as it is a crowded place where a lot of children are living together<sup>11</sup> and the children are usually under 5 years old with low immune system and lack of personal healthcare.<sup>22</sup> Moreover, care givers with deficient knowledge might misunderstand how to prevent and control HFMD.<sup>27</sup> Although the Ministry of Public Health has released the annual health measure for HFMD control in children's care centers, there are still HFMD outbreaks every year. Although this study did not focus on care givers at DCC, it is clear from other reports, that care givers are very crucial in the prevention and control of HFMD, since they spend more time during the day with a lot of children in a crowded place. Their knowledge and practices of safe and simple personal and environmental hygiene is vital to the prevention and control of HFMD<sup>2</sup> in their study of the knowledge and practice in prevention control of HFMD stated that, care givers at DCC have enough knowledge of HFMD but their knowledge of prevention of HFMD is not enough and simple practices such as screening of children at the entrance of the DCC before admission every morning may be the most efficient method of prevention of HFMD. Further studies may be needed in the HFMD preventive practices knowledge of care givers.<sup>3</sup>

There are several factors influencing HFMD such as the parents being Buddhist, the duration of breastfeeding, the parents' knowledge on prevention and control of HFMD, and importantly, how to keep day care center's environment clean. Interestingly, HFMD prevention in day care centers involves indoor and outdoor environment conditions of the centers, for instance, cleaning the contaminated surfaces with effective disinfection agent.<sup>26</sup> Another interesting issue is the guideline for HFMD prevention and control. Even though Thailand had issued the measure of HFMD prevention and control in day care centers, outbreaks are still present. Thus, it is essential to develop a proper guideline for HFMD prevention and control which can effectively and practicably help control the disease. It is obvious that whichever measures are adopted, care givers both at home and at DCC should be educated and well informed of the useful preventive measures to support each other in the prevention and control of HFMD.<sup>4</sup>

## CONCLUSION

This study found that the factors including children aged less than 2 years old, 2-3 family members per household, and parents' knowledge of HFMD prevention and control are related to HFMD in upper Northern Thailand. Therefore, Thailand should concentrate on children at an early age with low immunity and the number of members in each family and promote the importance of knowledge and understanding of HFMD prevention and control among parents and care givers because these all play crucial roles in HFMD prevention and control.

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## REFERENCES

1. Qiaoyun F, Xiongfei J, Lihuan L, Angao X. Epidemiology and etiological characteristics of hand, foot and mouth disease in Huizhou City between 2008 and 2011. *Arch Virol* 2012;158: 895-9.
2. World health organization [WHO]. Hand, Foot and Mouth Disease. [Cited 2017 Feb 16]. Available from: [http://www.wpro.who.int/mediacentre/factsheets/fs\\_10072012\\_HFMD/en/](http://www.wpro.who.int/mediacentre/factsheets/fs_10072012_HFMD/en/).
3. Bureau of Epidemiology. Guideline of surveillance, investigation and reported case of hand foot mouth disease. 2016. [Cited 2016 August 24]. Available from: [http://thaigcd.ddc.moph.go.th/uploads/pdf/baby/13.7.58/Measure\\_HFM.pdf](http://thaigcd.ddc.moph.go.th/uploads/pdf/baby/13.7.58/Measure_HFM.pdf).
4. Chen CT, Chang HL, Wang ST, Cheng YT, Yang JY. Epidemiologic features of hand-foot mouth disease and herpangina caused by enterovirus 71 in Taiwan, 1998-2005. *Pediatrics* 2007;120: e244-52.
5. Wang H, Du Z, Wang X, Liu Y, Yuan Z, Liu Y, et al. Detecting the association between meteorological factors and hand, foot, and mouth disease using spatial panel data models. *Int J Infect Dis* 2015;34:66-70.
6. Zhang Z, Xie X, Chen X, Li Y, Lu Y, Mei S, et al. Short-term effects of meteorological factors on hand, foot and mouth disease among children in Shenzhen, China: Non-linearity, threshold and interaction. *Sci Total Environ* 2016;539:576-82.
7. Ruan F, Yang T, Ma H, Jin Y, Song S, Fontaine RE, et al. Risk Factors for Hand, Foot, and Mouth Disease and Herpangina and the Preventive Effect of Hand-washing. *Pediatrics* 2011;127: e898-904.
8. Yang T, Xu G, Dong H, Ye M, He T. A case-control study of risk factors for severe hand-foot-mouth disease among children in Ningbo, China, 2010-2011. *Eur J Pediatr* 2012;171:1359-64.
9. Department of Disease Control. Situation of hand foot mouth disease in Thailand. [Cited 2018 May 10]. Available from: <http://27.254.33.52/healthypreschool/uploads/file/HFM%20wk%2060/HFM%20WK%2053.pdf>.
10. Bureau of general communicable disease. Surveillance Data of Hand foot mouth disease situation from bureau of epidemiology 2015 on 31 December 2015 (Week 52). Ministry of public Health; 2015. [Cited 2016 Jun 16]. Available from: <http://27.254.33.52/healthypreschool/contents/view/information/138>.
11. Centers for Disease Control and Prevention. Hand, Foot, Mouth Disease. 2017. [Cited 2017 Feb 16]. Available from: <https://www.cdc.gov/hand-foot-mouth/about/transmission.html>.
12. Office of Disease Prevention and Control 10th, Chiang Mai. Hand foot mouth prevention and control in Upper Northern part, Thailand: Annual communicable report, 2014. [Cited 2016 August 16]. Available from: <http://odpc1.ddc.moph.go.th/index01.html>.
13. Center for Disease Control and Prevention. Guideline for disinfection and sterilization in healthcare facilities. 2015. [Cited 2016 August 26]. Available from: <https://www.riskcomthai.org/th/media/infographic/all-detail.php>.
14. Somkit K, Saowapak H. Epidemiology of hand foot mouth disease and Enterovirus infection in Thailand 2013. Ministry of public Health; 2014. [Cited 2016 Jun 16];45(7):97-105. Available from: [http://www.boe.moph.go.th/files/report/20150106\\_66194901.pdf](http://www.boe.moph.go.th/files/report/20150106_66194901.pdf).

15. Koh WM, Bogich T, Siegel K, Jin J, Chong EY, Tan CY, et al. The Epidemiology of Hand, Foot and Mouth Disease in Asia: A Systematic Review and Analysis. *Pediatr Infect Dis J* 2016;35: e285-300.
16. Pan H, Zheng Y, Mao S, Hu J, Zheng Y, Li J, et al. A case-control study on risk factors that associated with severe hand-foot-mouth disease in Shanghai. *Zhonghua Liu Xing Bing Xue Za Zhi* 2012;33:763-7.
17. Li Y, Dang S, Deng H, Wang W, Jia X, Gao N, et al. Breastfeeding, previous Epstein-Barr virus infection, Enterovirus 71 infection, and rural residence are associated with the severity of hand, foot, and mouth disease. *Eur J Pediatr* 2013;172:661-6.
18. Schlesselman JJ. *Case-Control Studies*. New York: Oxford University Press, 1982.
19. Sun L, Lin H, Lin J, He J, Deng A, Kang M, et al. Evaluating the transmission routes of hand, foot, and mouth disease in Guangdong, China. *Am J Infect Control* 2016;44:e13-4.
20. Waltz CF, Strickland OL, Lenz ER. *Measurement in Nursing and Health Research*. 5<sup>th</sup> ed. New York: Springer Publishing company, LLC; 2017.
21. Lehman A, O'Rourke N, Hatcher L, Stepanski EJ. *JMP for basic Univariate and Multivariate Statistic: Methods for Research and Social Scientists*. 2<sup>nd</sup> ed. United States of America: SAS Institute Inc, 2013.
22. Somkit K, Saowapak H. Hand foot mouth disease situation report, Thailand, 2014 (From R506 weekly 28: 19 July 2014. Ministry of public Health; 2014. [Cited 2016 Jun 16]. Available from: [http://www.boe.moph.go.th/files/report/20140729\\_43933995.pdf](http://www.boe.moph.go.th/files/report/20140729_43933995.pdf)
23. Liu CC, Tseng HW, Wang SM, Wang JR, Su IJ. An outbreak of enterovirus 71 infection in Taiwan, 1998: Epidemiologic and clinical manifestations. *J Clin Virol* 2000;17:23-30.
24. Wang Y, Feng Z, Yang Y, Self S, Gao Y, Longini IM, et al. Hand, foot and mouth disease in China: patterns of spread and transmissibility. *Epidemiology* 2011;22:781-92.
25. Yin XG, Yi HX, Shu J, Wang XJ, Wu XJ, Yu LH. Clinical and epidemiological characteristics of adult hand, foot, and mouth disease in northern Zhejiang, China, May 2008-November 2013. *BMC Infect Dis* 2014;14:251.
26. Chang LY, King CC, Hsu KH, Ning HC, Tsao KC, Li CC, et al. Risk factors of enterovirus 71 infection and associated hand, foot, and mouth disease/herpangina in children during an epidemic in Taiwan. *Pediatrics* 2002;109:e88.
27. Ministry of Public Health. Report: Hand foot mouth situation in Thailand in 2016. [Cited 2017 Feb 28] Available from: [http://www.amno.moph.go.th/amno\\_new/attachments/3958\\_disease%20.pdf](http://www.amno.moph.go.th/amno_new/attachments/3958_disease%20.pdf).