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Factors associated with hand foot mouth disease among children in day care center, Chiang Rai, Thailand

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ABSTRACT

Objective: To determine the factors associated with hand foot mouth disease (HFMD) among children in day care center in Chiang Rai Province, Thailand.**Methods:** A community based case-control study was conducted to identify the factors associated with HFMD among the children under 6 years old who had been cared for in day care centers in Chiang Rai Province. A 47-item questionnaire had been developed and tested for validity and reliability before use. Index of item-objective congruence (IOC) method was used to evaluate the quality of the questionnaire. The items of questionnaire consisted of various aspects including age, sex, history of vaccination, history of breastfeeding, history of treatment, etc. Data were analyzed in the logistic regression model at alpha = 0.05 to identify the association between variables.**Results:** Totally, 380 subjects (125 cases and 255 controls) from 40 day care centers were recruited in the present study. Among the parents, 77.1% were female, 76.6% were aged 20–59 years old, 30.1% graduated at primary level, and 87.1% were Buddhist. Among the children, 53.8% were male, 58.7% were aged 3–4 years old, and 13.3% were overweight. After control for all possible confounding factors in the multiple logistic regression, two factors were associated with HFMD: children aged < 2 years old had a greater chance (6.35 times) to develop HFMD than those aged > 5 years old (95% CI = 1.37–29.38), and children who had been breastfed for less than 6 months had a greater chance (1.97 times) to develop HFMD than those who had a history of being breastfed ≥ 6 months (95% CI = 1.01–3.81).**Conclusions:** A specific prevention and control measure for HFMD should be developed and implemented. Breastfeeding young children for more than 6 months should be encouraged.

1. Introduction

Hand foot mouth disease (HFMD) is a communicable disease caused by enterovirus 71 and Coxsackie virus A16. It is transmitted by fecal-oral route and mostly common in children under 6 years old[1]. It occurs worldwide such as Hong Kong, Taiwan, Japan, and Thailand in Asia[2]. In Thailand, HFMD has been defined as new emerging disease that occurs every year and tends to rise in recent years[3]. The number has increased in raining season (June–August),

which is the period of beginning of the school semester[4]. In 2016, Northern Thailand had been reported as the most epidemic area especially the Chiang Rai Province[5]. In 2015, totally 1767 cases of HFMD (136.07 per 100000 persons) were reported in Chiang Rai Province, with the ratio of male to female at 1:1.24[6]. More cases had been reported in 2016 (3505 cases) in the same province[6].

The impacts of HFMD are not limited only to health but also in social and economic sectors. Northern Thailand is one of the tourist attraction areas in Thailand. Therefore, some economic sectors depend on the number of tourists visiting the area[7]. The occurrence of HFMD in this area is not preventable and it has numerous impact on tourist industry particularly visitors from western countries. There is no treatment available for HFMD yet[2]. The main characteristic of HFMD is high infectivity and quick spread[8]. However, most vulnerable population for the diseases is children under 6 years old[1].

Many published research papers reported that climatic factors

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including humidity, temperature, wind speed and rainfall amount are major contributors to the distribution of HFMD[9-11]. Northern Thailand has three seasons; raining, hot (summer), and cold (autumn). The geographical characteristic, mountainous areas, also supports the spread of the disease. Many people live far away from the city and have difficulty in accessing health care settings due to transportation problems. Therefore, outbreak of any disease including HFMD directly impacts on people's health and quality of life.

Day care centers take care of children under 6 years old during the daytime. Most parents prefer to leave their children in day care centers during daytime to have more time to work in their farm. Day care centers are operated under the administration of sub-district local administration office. In 2015, totally 499 day care centers were functioning in Chiang Rai Province. In 2015, totally 51 737 children aged 2–5 years old lived in Chiang Rai, and among them 19 526 were left at day care centers. However, there were totally 75 116 children aged less than 6 years old in Chiang Rai Province. Under the regulation of day care centers, only children aged 2–5 years old are allowed to stay at day care centers during daytime without charging[12]. But in reality, many children aged less than two years old are cared for in the day care center. Therefore, children in day care centers are composed of those aged less than 6 years old, the preschool age. This particular age group has specific characteristics that make them highly vulnerable to HFMD infection. Therefore, the objective of the present study was to investigate the factors associated with HFMD infection among children under 6 years old in day care centers in Chiang Rai Province, Thailand.

2. Materials and methods

2.1. Study design

A community-based case control study was conducted to identify factors associated with HFMD among children under 6 years old who lived in a day care center in Chiang Rai Province, Thailand.

2.2. Study area

There are 499 day care centers in Chiang Rai Province[13], and 40 day care centers were selected for the study from 15 districts in Chiang Rai Province: Paya-Meng Rai, Chiang Khong, Muang, Phan, Mae Suay, Pa-Dad, Khun Than, Chiang San, Theong, Mae Chan, Mae Sai, Mae Fah Luang, Mea Lao, Wiang Khan, and Wiang Chiang Rung districts.

2.3. Study population

The information of children under 6 years old who lived in day care centers in Chiang Rai Province in the present study was obtained from their parents.

2.4. Sample size estimation

The sample size was calculated using Schlesselman's formula[14]; at alpha value of 0.05, the power of test was set at 80%, and the ratio of case by control was 1:2, therefore, at least 375 children were required (125 cases and 250 controls).

2.5. Method of sample selection

The Chiang Rai Provincial Public Health Office was contacted to

get the list of all day care centers in Chiang Rai Province. The listed day care centers were divided into two different groups: the day care centers located in the high and low epidemic areas. The classification criteria for the high and low HFMD epidemic areas in the study was based on the median line of the number of HFMD cases three years ago (2012–2014), at 146:100 000 population[15]. Finally, there were 121 day care centers located in the high epidemic area, and another 378 in the low epidemic area. A simple random sampling was performed to get 20 day care centers from the high epidemic areas, and another 20 from the low epidemic areas.

2.6. Research instruments

A 47-item questionnaire was developed from the literature review from both medical textbooks and relevant research articles. Questionnaire had been evaluated for validity and reliability by three external experts (Index of Item-Objective Congruence; IOC)[16] and piloted in 15 samples that had characteristics similar to the study sample. In the step of IOC testing, only questions with a score > 0.5 were kept, and the remaining questions were deleted or improved before use. Cronbach's alpha was 0.78 in the attitude and practice parts. In the part of knowledge, only questions with Kuder's score (KR) > 0.5 were kept for use[17].

2.7. Process of data collection

There were 675 children in the list from day care centers located in the high epidemic areas, and 719 children in the list from day care centers in the low epidemic areas.

However, 23 children from the list of low epidemic areas had a history of HFMD in the year of 2015, and then they were excluded from the study. Therefore, only 696 children were eligible for selection into control group.

Meanwhile, 279 children from the list of the high epidemic area were diagnosed to have HFMD in 2016 at least once. They were eligible for selection into the case group.

After getting the lists both in the high and low epidemic areas, appointments were made to collect the information. The appointments had been made for both the care givers in day care centers and parents of selected children at day care centers. Parents were informed to bring their children together with logbook of their children on the interview date for collecting data on health development and history of vaccination of their children. All information of both children and their parents were collected. The information providers were the parents. A private and confidential room was prepared and used for interview. Participants were given all essential information of the research including objective, rights, etc., and the informed consent form was obtained before starting the interview. The interview lasted for 35 min each. Finally, 125 cases and 255 control were recruited into the study.

2.8. Data analysis

Data were double-entered and validated using Microsoft Excel. Data analysis was carried out 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 statistics (means, standard deviation, frequency, and percentage) were used to describe the general characteristics of the subjects.

Chi-square test and logistic regression were used for testing the associations between variables at $\alpha = 0.10$ in simple model, and 0.05

in the multiple model.

2.9. Ethical consideration

All research procedures and instruments had been approved by the Human Research Ethic Committee of Mae Fah Laung University, Chiang Rai, Thailand (Ref. No. REH-59024). All participants were given a small gift to appreciate their participation after finishing the interview.

3. Results

3.1. Characteristics of parents

A total of 380 subjects from 40 day care centers were recruited into the study. Among them, 20.5% were from Mae Suay District, 12.1% from Muang District, and 10.8% from Phan District. Among the parents participated, 77.1% were female, and average age was (36.6 ± 12.3) years old (range: 17–99); 84.1% were married; 87.1% were Buddhist; 30.1% were educated at a primary school level; 39.1% were farmers; 41.7% had income ≤ 5000 baht/month; 46.6% reported that mother was the major care giver; 67.3% had 4–6 family members; 42.4% had 2–3 children < 12 years old per family. 49.5% of the parents reported that they took their children to visit a medical doctor whenever they have an illness, and 61.1% visited a health promoting hospital staff while having health problem.

Regarding the knowledge, attitude and practice about HFMD, in case group, 63.9% parents had a high level of knowledge, 80.2% had a positive attitude on prevention and care for HFMD, and 92.9% could indicate correct practices for HFMD prevention and control.

Whereas, in control group, only 50.4% parents had a high level of knowledge on HFMD prevention and control, 77.0% had a positive attitude on prevention and care for HFMD, and 96.0% parents of the control group had a good practice on HFMD prevention and control.

Simple logistic regression model revealed that three factors were associated with HFMD: children whose parents were Buddhist had a greater chance (3.34 times) for infection than those whose parents were Christian (90% CI: 1.58–7.03); children who had parents that graduated with a bachelor degree had a greater chance for infection than those whose parents had no education (2.96 times) (90% CI = 1.14–7.73), and children who had parents with medium and high knowledge on HFMD had a greater chance [3.49 times (90% CI = 1.58–7.71) and 4.39 times (90% CI = 2.06–9.35) respectively] for infection than those with low knowledge (Table 1).

3.2. Characteristic of children

Among the participated children, 53.8% were male, 58.7% were 3–4 years old, 38.9% were underweight, 14.3% had a history of hospital admission, and 18.9% had been breastfed for less than 6 months from the birthdate.

In the case group, 57.3% were under 2 years old (mean = 1.46, SD = 0.57), 53.6% were female, 49.1% were underweight, 57.3% got infection while < 2 years old, 17.0% had a history of hospital admission, 5.7% had an underlying disease, 27.2% had been breastfed for less than 6 months.

Table 1

Characteristics of parents associated with HFMD in a simple logistic regression.

Characteristics	Total [n (%)]	Case [n (%)]	Control [n (%)]	OR	90% CI	P-value
Sex						
Male	80 (22.9)	26 (25.2)	54 (21.9)	1.21	0.77–1.89	0.493
Female	270 (77.1)	77 (74.8)	193 (78.1)	1.00		
Parent's age (years)						
< 19	9 (2.4)	2 (1.7)	7 (2.6)	1.00		
20–59	291 (76.6)	95 (82.6)	196 (74.0)	1.69	0.44–6.44	0.515
> 60	80 (21.1)	18 (15.7)	62 (23.4)	10.1	0.25–4.08	0.985
Marital status						
Single	59 (15.9)	17 (15.5)	42 (16.1)	1.00		
Married	312 (84.1)	93 (84.5)	219 (83.9)	1.05	0.63–1.76	0.878
Number of family member						
< 3	75 (20.3)	25 (22.1)	50 (19.5)	1.00		
4–6	249 (67.3)	78 (69.0)	171 (66.5)	0.91	0.57–1.44	0.743
> 7	46 (12.5)	10 (8.9)	36 (14.0)	0.53	0.24–1.15	0.179
Number of child < 12 years old per family						
1	197 (54.6)	67 (59.8)	130 (52.2)	1.80	0.88–3.67	0.175
2–3	153 (42.4)	41 (36.6)	112 (45.0)	1.64	0.88–3.08	0.195
> 3	11 (3.0)	4 (3.6)	7 (2.8)	1.00		
Religion						
Buddhist	325 (87.1)	105 (94.6)	220 (84.0)	3.34	1.58–7.03	0.008*
Christian	48 (12.9)	6 (5.4)	42 (16.0)	1.00		
Occupation						
Unemployed	36 (9.9)	11 (10.3)	25 (9.8)	1.00		
Merchant	51 (14.0)	16 (15.0)	35 (13.7)	1.03	0.47–2.25	0.935
Government officer	9 (2.5)	4 (3.7)	5 (2.0)	1.81	0.51–6.36	0.433
Farmer	142 (39.1)	33 (30.8)	109 (42.6)	0.68	0.34–1.35	0.365
Employee	114 (31.5)	39 (36.4)	75 (29.3)	1.18	0.60–2.32	0.685
Other	11 (3.0)	4 (3.7)	7 (2.7)	1.29	0.39–4.27	0.718
Income (baht/month)						
≤ 5000	118 (41.7)	34 (35.8)	84 (44.7)	1.21	0.44–3.32	0.751
5001–10000	104 (36.7)	42 (44.2)	62 (33.0)	2.03	0.74–5.55	0.246
10001–15000	24 (8.5)	6 (6.3)	18 (9.6)	1.00	0.29–3.40	0.100
15001–20000	21 (7.4)	9 (9.5)	12 (6.4)	2.25	0.68–7.43	0.264
≥ 20001	16 (5.7)	4 (4.2)	12 (6.4)	1.00		
Education						
No education	30 (8.1)	5 (4.5)	25 (9.6)	1.00		
Primary school	112 (30.1)	35 (31.2)	77 (29.6)	2.27	0.95–5.44	0.122
Lower secondary	72 (19.4)	23 (20.5)	49 (18.8)	2.35	0.95–5.81	0.122
Higher secondary	77 (20.7)	20 (17.9)	57 (21.9)	1.75	0.70–4.37	0.311
Vocational	38 (10.2)	13 (11.6)	25 (9.6)	2.60	0.97–6.95	0.110
Bachelor	43 (11.6)	16 (14.3)	27 (10.4)	2.96	1.14–7.73	0.050*
Care giver						
Father	41 (11.1)	10 (8.8)	31 (12.1)	1.00		
Mother	172 (46.6)	50 (44.2)	122 (47.7)	1.27	0.66–2.45	0.550
Father and mother	46 (12.5)	13 (11.5)	33 (12.9)	1.22	0.55–2.73	0.683
Relatives	110 (29.8)	40 (35.4)	70 (27.3)	1.77	0.90–3.50	0.167
Resident areas						
Rural	171 (45.0)	60 (52.2)	149 (60.2)	1.00		
Urban	209 (55.0)	55 (47.8)	166 (63.8)	1.18	0.81–1.70	0.466
Knowledge						
Low	53 (15.1)	6 (5.6)	47 (19.3)	1.00		
Medium	107 (30.4)	33 (30.6)	74 (30.3)	3.49	1.58–7.71	0.009*
High	192 (54.5)	69 (63.9)	123 (50.4)	4.39	2.06–9.35	0.001*
Attitude						
Neutral	79 (22.1)	21 (19.8)	58 (23.0)	1.00		
Positive	279 (77.9)	85 (80.2)	194 (77.0)	1.21	0.76–1.94	0.505
Practice						
Neutral	18 (5.0)	8 (7.1)	10 (4.0)	1.81	0.81–4.06	0.220
Good	344 (95.0)	105 (92.9)	239 (96.0)	1.00		

*: Significant at $\alpha = 0.10$.

In control group, 65.4% were aged 3–4 years old (mean = 1.82, SD = 0.56), 60.9% were male, 28.6% were underweight, 13.2% had a history of hospital admission, and 15.0% had been breastfed for less than 6 months.

Simple logistic regression model revealed that three factors had a significant association with HFMD: females had a greater chance (1.80 times) to develop HFMD than males (90% CI = 1.08–3.00); underweight children had a greater chance (3.50 times) to develop HFMD than those who were overweight (90% CI = 1.24–9.88); and children who had a history of being breastfed < 6 months had a greater chance (2.12 times) to develop HFMD than those who had a history of being breastfed ≥ 6 months (90% CI = 1.31–3.43) (Table 2).

Table 2

Characteristics of children associated with HFMD in simple logistic regression.

Characteristics	Total [n (%)]	Case [n (%)]	Control [n (%)]	OR	90%CI	P-value
Age (years)						
< 2	110 (34.2)	47 (57.3)	63 (26.2)	1.58	0.71–3.53	0.343
3–4	189 (58.7)	32 (39.0)	157 (65.4)	1.16	0.54–2.49	0.742
> 5	23 (7.1)	3 (3.7)	20 (8.3)	1.00		
Sex						
Male	92 (53.8)	39 (46.4)	53 (60.9)	1.00		
Female	79 (46.2)	45 (53.6)	34 (39.1)	1.80	1.08–3.00	0.058*
BMI						
Underweight	44 (38.9)	28 (49.1)	16 (28.6)	3.50	1.24–9.88	0.047*
Normal	54 (47.8)	24 (42.1)	30 (53.6)	1.60	0.58–4.38	0.443
Overweight	15 (13.3)	5 (8.8)	10 (17.9)	1.00		
History of hospital admission						
Yes	51 (14.3)	15 (17.0)	33 (13.2)	1.34	0.79–2.27	0.353
No	305 (85.7)	88 (83.0)	217 (86.8)	1.00		
Underlying disease						
Yes	18 (5.0)	6 (5.7)	12 (4.7)	1.00		
No	341 (95.0)	100 (94.3)	241 (95.3)	1.20	0.52–2.80	0.717
Taking medication regularly						
Yes	6 (1.7)	2 (1.9)	4 (1.6)	1.23	0.29–5.18	0.812
No	353 (98.3)	102 (98.1)	251 (98.4)	1.00		
Breast feeding (month)						
< 6	60 (18.9)	28 (27.2)	32 (15.0)	2.12	1.31–3.43	0.010*
≥ 6	257 (81.1)	75 (72.8)	182 (85.0)	1.00		

*: Significant level at α = 0.10.

In the multiple logistic regression model, after control for all possible factors, it was revealed that two factors were associated with HFMD in children: children aged less than 2 years old had a greater chance (6.35 times) to develop HFMD (95% CI = 1.37–29.38) compared with those aged > 5 years old; and those who had a history of being breastfed less than 6 months had a greater chance (1.97 times) to develop HFMD compared to those that had a history of being breastfed ≥ 6 months (Table 3).

Table 3

Factors associated with HFMD in multiple logistic regression.

Factors	OR	95% CI	P-value
Age (year)	< 2	6.35	1.37–29.38
	3–4	1.83	0.39–8.46
	> 5	1.00	
Breast feeding (month)	< 6	1.97	1.01–3.81
	≥ 6	1.00	

* Significant level at α = 0.05.

4. Discussion

The results show that children whose parents were Buddhist had a greater chance (3.34 times) to develop the HFMD than those whose parents were Christian in the simple model, but the significance was not found in the multiple model. This might not be directly related to religion but because some rural areas of Thailand have developed

their economy quickly[18]. The economic growth indicates that the parents have to leave their children in a day care center. Day care center is the center for taking care a preschool child during daytime which is organized by the local government. However, there was no previous report on the association between religion and HFMD. There are many children living together in day care center during the daytime, which is a contributing factor to the epidemic of HFMD. Samphutthanon *et al.*[19] reported that children who lived in crowded place had a high risk to expose and get infection of HFMD in China. The study of Navarro *et al.*[20] presented that the children who attended day care center had 14 times greater chance of getting HFMD infection than those who did not. Meanwhile the Thai National Disease Control Center reported that most of the HFMD outbreaks occurred in the day care center, and the risk factors were unregular hand washing of children and also limited knowledge on disease control and prevention among the caregivers in the day care center[21]. Huang *et al.* also reported that economy and population density were risk factors of HFMD[22].

In our study, the simple logistic regression revealed that girls had a greater opportunity to develop HFMD. This agrees with the study of Navarro *et al.*[20] which reported that the prevalence of HFMD was higher in girls. In our study we also found that children who were underweight had a greater opportunity (3.5 times) to get HFMD infection than those who were overweight. This agrees with the study of Chen *et al.*[23] which showed that underweight children had a greater risk for HFMD.

Regarding the multiple model, we found that younger age and sex are the important factors for HFMD infection in Chiang Rai, Thailand. This is similar with the meta analysis from the papers published in Asia which reported that age and being female were the major risk factors of HFMD[24]. Some studies[25-27] reported that age was the main risk factor for HFMD particularly age < 4 years old.

In the final model, we found that breastfeeding is a major factor for HFMD infection among children in Chiang Rai Province. The study of Lin *et al.*[28] supports this finding; children who had been breastfed for less than 6 months had a greater chance for HFMD infection than those who had been breastfed for more than 6 months. Zhang *et al.*[29] reported that in a case-control study in China, breastfeeding was presented as a major factor for HFMD infection among young children.

Children at early stage of life are the most vulnerable for the HFMD infection particularly those who are living in urban areas, and high socioeconomic group. Day care center is a setting for Thai parents to leave their children during day time, but it becomes a source of infection for young children. Due to economic constraints among Thai people, women in a family in rural area could not spare their time to breastfeed for six months, children then become vulnerable for HFMD.

A specific prevention and control measure for HFMD should be developed and implemented in day care centers in Northern Thailand, and breastfeeding young children for more than 6 months should be encouraged.

Conflict of interest statement

We declare that we have no conflict of interest.

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