ปัจจัยที่มีความสัมพันธ์ต่อโรคมือ เท้า ปาก ของเด็กที่อยู่ในศูนย์พัฒนาเด็กเล็ก จังหวัดเชียงราย ประเทศไทย

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บทคัดย่อ

การศึกษานี้เป็นแบบ Case-control design มีวัตถุประสงค์เพื่อประเมินปัจจัยที่สัมพันธ์กับการเกิดโรคมือ เท้า ปาก ของเด็กอายุต่ำกว่า 6 ปีที่อยู่ในศูนย์พัฒนาเด็กเล็ก จำนวน 40 แห่ง ในจังหวัดเชียงราย กลุ่มตัวอย่างสุ่มจากเด็กที่อยู่ในศูนย์เด็กเล็กทั้งหมด 380 ราย (115 เป็นกลุ่มผู้ป่วย และ 265 เป็นกลุ่มควบคุม) แบบสอบถามเก็บข้อมูลจากผู้ปกครองเด็ก ครูผู้ดูแลเด็กที่ศูนย์เด็กเล็ก และสิ่งแวดล้อมศูนย์เด็กเล็ก สถิติถดถอยโลจิสติกส์ใช้ในการวิเคราะห์ข้อมูลที่ระดับนัยความผิดพลาดที่ยอมรับได้ที่ 0.05 ผลการศึกษาพบว่า เด็กที่อาศัยอยู่ในศูนย์เด็กเล็กที่มีอากาศถ่ายเทไม่ดีมีโอกาสเป็นโรคมือ เท้า ปาก มากกว่าเด็กที่อาศัยอยู่ในศูนย์เด็กเล็กที่มีอากาศถ่ายเทสะดวก (OR_{adj} = 3.11, 95%CI = 1.32-7.32) เด็กที่อาศัยอยู่ในศูนย์เด็กเล็กที่ไม่มีสบู่ในห้องน้ำมีโอกาสเป็นโรคมือ เท้า ปาก มากกว่าเด็กที่อาศัยอยู่ในศูนย์เด็กเล็กที่มีสบู่ในห้องน้ำ (OR_{adj} = 2.84, 95%CI = 1.33-6.07) และเด็กที่มีพฤติกรรมไม่ล้างมือก่อนและหลังการใช้ห้องน้ำมีโอกาสเป็นโรคมือ เท้า ปาก มากกว่าเด็กที่ล้างมือก่อนและหลังใช้ห้องน้ำ (OR_{adj} = 3.74, 95%CI = 1.61-8.70) ดังนั้น การพัฒนาสุขาภิบาลสิ่งแวดล้อมเป็นมาตรการที่สำคัญในการป้องกันและควบคุมการเกิดโรคมือ เท้า ปาก ในศูนย์เด็กเล็ก

คำสำคัญ: โรคมือ เท้า ปาก ศูนย์พัฒนาเด็กเล็ก ปัจจัยที่มีความสัมพันธ์ เด็ก

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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

This is a community-based case control study that aimed to identify the factors associated with hand foot mouth disease (HFMD) among children under 6 years old in 40 day care centers (DCCs) in Chiang Rai Province, Thailand. A total of 380 subjects were randomly recruited (115 cases and 265 controls). Data were analyzed using the logistic regression model at alpha = 0.05 to identify the association between variables. The results revealed that the children who stay in a poorly ventilated DCCs had a greater chance of HFMD infection than those who lived in well ventilated DCCs (OR_{adj} = 3.11, 95%CI = 1.32-7.32). The children who lived in DCCs that did not provide a soap in toilet had a greater chance of HFMD infection than those who lived in DCCs that provide a soap in toilet (OR_{adj} = 2.84, 95%CI = 1.33-6.07). The children who did not wash their hands before and after using the toilet had a greater risk for HFMD infection than those who usually wash their hands before and after using the toilet (OR_{adj} = 3.74, 95%CI = 1.61-8.70). Improving environmental sanitation of a DCC is significant for prevention and control of HFMD infection in children.

Keywords: hand foot mouth disease, day care center, associated factors, children

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Introduction

Hand foot mouth disease (HFMD) is a common communicable disease caused by enteroviruses; Enterovirus 71 and Coxsackie virus A16. Fecal-oral route is a common route of transmission. Children aged below 6 years old[1] is a major venerable population for infection. It has been reported from all countries in tropical zone including Taiwan, Japan, and Thailand[2]. Health professionals in Thailand define the HFMD as new emerging disease that has been reported from all health institutes along the country in whole year[3]. The main characteristic of HFMD in Thailand is being reported in high numbers in the season (June-August). This time is concurrent with the beginning of the school semester[4]. In 2016, northern Thailand had been reported as the highest epidemic area especially in Chiang Rai Province[5]. In 2015, 1,767 cases of HFMD (136.07 per 100,000 persons) were reported throughout the surveillance system in Chiang Rai Province, the ratio of male to female was 1:1.24[6], and another 3,505 cases had been reported in 2016[6].

HFMD impacts are not limited only to human health but also in family, community, and economic sectors. Normally, northern Thailand is tourist attraction area, and a number of tourists visit Chiang Rai province. Approximately 25-30% of the province's economic growth depended on the number of visitors[7]. HFMD is non-treatable disease[1], but has a high infectivity and a high incident rate[8]. However, most vulnerable populations for the disease are children aged under 6 years old[1].

The weather is a major influence in the incidence rate of HFMD[9-11]. Northern Thailand has a unique weather in three different seasons; rainy, hot (summer) and cold (winter). Geographical area, mountainous areas, enhances the infectivity rate of the disease. A number of people are living in the very remote and rural areas in Chiang Rai province, resulting in limited access to health care. Any epidemic episode of HFMD directly impacts the health of the people in this area.

DCCs are the centers that take care of children aged below 6 years during the daytime. Most parents prefer to leave their children there while working on their farms at daytime. DDCs operate under the support of sub-district local administration office. Four hundred and ninety-nine DCCs are operating in Chiang Rai Province. There were 19,526 children left at DCCs in Chiang Rai province in 2015. Under the regulation of DDC, only children aged 2-5 years old are allowed to stay at DCCs in daytime without charge[12], however, many children aged below 2 years old are also attending DCCs. This is because the parents have no choice but to leave their child during the day while working in their farm. A number of the vulnerable populations for HFMD are staying in the same place with limited room in DCCs. This might support the spreading of the disease. Therefore, the objective of the study was to investigate the factors associated with HFMD

infection among children aged below 6 years old in DDCs in Chiang Rai Province, Thailand.

Materials and Methods

Study design

A community-based case-control study was carried out to identify factors associated with HFMD infection in children aged below 6 years old who are attending DCCs in Chiang Rai Province, Thailand.

Study area

Four hundred and forty nine DCCs in Chiang Rai province were the study targeted centers[13]. Forty DCCs were selected for collecting the data. There were 15 districts in Chiang Rai Province defined as the study settings; Pa Ya Meng Rai, Chiang Khong, Muang, Phan, Mae Suai, Pa Dad, Khun Than, Chiang San, Theong, Mae Chan, Mae Sai, Mae Fah Luang, Mea Lao, Wiang Khan, and Wiang Chiang Rung districts.

Study population

The parents and care givers in DCCs were the study populations. Parents and care givers in DCCs were asked to provide the necessary information by validated questionnaires.

Sample size estimation

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

Method of sample selection

The lists of DCCs were classified into two groups; list of DCCs in the high epidemic areas, and the list of DCCs in low epidemic areas. Simple random sampling was used to select 20 DCCs from the high epidemic areas, and another 20 DCCs from the low epidemic areas.

All children who had been diagnosed with HFMD in 2015 were listed from the DCCs in the high epidemic areas, and a simple random sampling was used again to get 125 cases of HFMD. Meanwhile, children who were not diagnosed with HFMD in 2015 were listed from 20 DCCs in low epidemic areas, and then, a simple random sampling was used to select the 250 controls.

Research instruments

A 47-item questionnaire was developed from the literature review from all sources of information including research articles. Questionnaire was reviewed by three external experts by the Index of Item-Objective Congruence technique (IOC)[15]. A pilot test was done with 15 samples that had a similar characteristic to examine the feasibility of the questionnaire. In the step of IOC testing, only questions with a score of score > 0.5 were kept and used in the study. A Cronbach's alpha was obtained at 0.78 in the attitude and practice parts. Kuder's score (KR) > 0.5 was kept for use in the questions regarding knowledge[16].

The standard of DCCs environment developed by the Ministry of Public Health[17] was used as the instrument for detecting the environmental factors of a DCC.

Process of data collection

The Chiang Rai Provincial Public Health Office was contacted to get the list of all DDCs in Chiang Rai province. After getting the list of DCCs, it was divided into two different groups; the high epidemic DCCs and the low epidemic DCCs. The median line of HFMD in previous three years (2012-2014) was used to classify the high and low epidemic areas at 146:100,000 populations[18]. Finally, 121 DCCs were listed as the high epidemic areas, and 378 DCCs were listed as the low epidemic areas.

A simple random sampling method was used to select 40 DCCs as the study sites; 20 DCCs from the low epidemic areas, and 20 DCCs from the high epidemic areas. Six hundred and seventy-five children attended the high epidemic DCCs, and 719 children attended the 20 low epidemic DCCs at the time of collecting data.

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

Meanwhile, only 279 children from the list of children in the high epidemic area were diagnosed with HFMD in 2016 at least once. These met the eligible criteria for the case group.

After getting all the lists both in the high and low epidemic areas, appointments were made to collect the information. The appointments had been made ahead for both the care givers in DCCs and selected children's parents at DCCs. Parents were informed to bring the logbook of their children together with them on the interview date. This was for collecting data on health development and history of vaccination of their children.

All information from both children and their parents were collected. Parents and care givers from the DCCs were asked for the information. A private and confidential room was prepared and used for the interview. Participants were given all essential information of the research process including objective, rights, etc., and obtained the informed consent form before starting the interview. The interview lasted for 35 minutes each.

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) was used to describe the general characteristics of the subjects. Chi-square and logistic regression were used for testing the associations between variables at the alpha value of 0.10 for a univariate

analysis, and alpha at 0.05 in the multivariate analysis. Characteristics of parents, children's characteristics, care givers characteristics, and environmental characteristics were tested for association with HFMD in the univariate analysis. All the factors that were found to be associated with HFMD in the univariate analysis were further tested for association in the multivariate analysis.

Ethical consideration

All research procedures and instruments had been approved by the human research ethic committee of Mae Fah Laung University, Chiang Rai, Thailand (No.REH-59024).

Results

Characteristics of parents

A total of 380 subjects from 40 DCCs were recruited into the study. Majority had resident in Mae Suai district (20.5%) followed by Muang district (12.1%) and Phan district (10.8%). 77.1% were females, average age was 36.6 years old (SD=12.3, min=17, max=99), 84.1% were married, 87.1% were Buddhist, 30.1% graduated a primary school, 39.1% were farmers, and 41.7% had income <5,000 baht/month. 46.6% had a mother as the major care giver in their family, 67.3% had a family member of 4-6 persons, and 42.4% had children less than 12 years old at 2-3 persons/family. 49.5% of parents reported that they took their children to see a medical doctor whenever their children had health problem, and 61.1% favored to visit a health promoting hospital.

Regarding the knowledge, attitude and practice about HFMD; in non-disease group, 63.9% had a high level of knowledge, 80.2% had a positive attitude on prevention and care for HFMD, and 92.9% could indicate preventive practices for HFMD prevention and control correctly.

Among disease group; only 50.4% 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% had a good practice on HFMD prevention and control.

Three factors were associated with HFMD in univariate analysis; children who had parents who were Buddhist had a greater chance of contracting HFMD than those whose parents were Christian (OR = 3.34, 90%CI = 1.58-7.03). Children whose parents graduated with a university degree had a greater chance of HFMD infection than those who had parents with no-education (OR = 2.96, 90%CI = 1.14-7.73). Children who had parents with high knowledge on HFMD had a greater chance of HFMD infection than those in the low knowledge group (OR = 4.39, 90%CI = 2.06-9.35), and median knowledge group (OR = 3.49, 90%CI = 1.58-7.71) (Table1).

Table 1 Univariate analysis of parents' characteristics and HFMD in children

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
Family members (persons)						
<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 children <12 years in family (persons)						
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)						
≤5,000	118 (41.7)	34 (35.8)	84 (44.7)	1.21	0.44-3.32	0.751
5,001-10,000	104 (36.7)	42 (44.2)	62 (33.0)	2.03	0.74-5.55	0.246
10,001-15,000	24 (8.5)	6 (6.3)	18 (9.6)	1.00	0.29-3.40	0.100
15,001-20,000	21 (7.4)	9 (9.5)	12 (6.4)	2.25	0.68-7.43	0.264
≥20,001	16 (5.7)	4 (4.2)	12 (6.4)	1.00		

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	*p*-value
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 (2.05)	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*
Major care giver at home						
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
Residential areas						
Rural	171 (45.0)	60 (52.2)	149 (0.2)	1.00		
Urban	209 (55.0)	55 (4.78)	166 (43.8)	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 level at α=0.10

Characteristic of children

The proportion of children that participated in the study was mostly equal between sexes. Majority were aged at 3-4 years old, one-third (38.9%) were underweight, less than one-fifth (14.3%) had a history of hospital admission, and close to one-fifth (18.9%) had a history of breastfeeding less than 6 months from the birthdate.

Specific characteristics among case group; 60.4% were aged 3-4 years old (mean = 1.46, SD = 0.57), 53.6% were females, 49.1% were underweight, 57.3% got infection while < 2 years old, 17.0% had a history of hospital admission, 5.7% had a medical condition, 27.2% had breastfeeding less than 6 months.

In control group; 65.4% were aged 3-4 years (mean = 1.82, SD = 0.56), 60.9% were males, 28.6% were underweight group, 13.2% had a history of hospital admission, and 15.0% had breastfeeding less than 6 months.

In the univariate analysis, it was found that three factors had a significant association with HFMD. Female children had a greater chance to develop HFMD than males (OR = 1.80, 90%CI = 1.08-3.00), underweight children had a greater chance to develop HFMD than those who were overweight (OR = 3.50, 90%CI = 1.24-9.88), and children who had a history of breastfeeding < 6 months of age had a greater chance to develop HFMD than those who had a history of breastfeeding ≥ 6 months of age (OR = 2.12, 90%CI = 1.31-3.43) (Table 2).

Table 2 Univariate analysis of children characteristics and HFMD

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		
Medical condition						
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

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	*p*-value
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

Characteristics of care givers

Majority were aged 30-39 years old, were female, married, and graduated with a university degree. While looking at the two different groups, it was found that majority had average working experience of 10-19 years and had high level of KAP about the HFMD prevention and control in the case group. While in the control group, majority had average working experience of 10-19 years, and low to medium level of knowledge in HFMD prevention and control.

Five factors showed significant association with HFMD in the univariate analysis; care givers aged 30-39 (OR = 0.09, 90%CI = 0.04-0.79) and 40-49 years old (OR = 0.45, 90%CI = 0.27-0.90) showed as a protective factor for HFMD in their children compared to those aged 50-59 years old. Children whose care givers were Buddhists had a greater chance to develop HFMD than children whose care givers were Christians (OR = 5.38, 90%CI = 2.68-10.77). Children whose care giver had a work experience of 10-19 years (OR = 5.94, 90%CI = 2.59-13.62), and ≥ 20 years (OR = 7.62, 90%CI = 3.15-18.47) had a greater chance to develop HFMD than those who had a work experience of 0-9 years. Care givers who had a high attitude in HFMD control and prevention had a greater chance of HFMD in their children than those with a medium level of attitude (OR = 9.40, 90%CI = 3.19-27.77), and those with a high level of practice had a greater chance of HFMD in their children than those who were in the medium practice group (OR = 1.95, 90%CI = 1.12-3.38) (Table 3).

Table 3 Univariate analysis of care giver characteristic and HFMD

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	*p*-value
Age (years)						
20-29	12 (4.7)	5 (6.8)	7 (3.9)	0.52	0.17-1.60	0.337
30-39	112 (44.1)	12 (16.4)	100 (55.2)	0.09	0.04-0.79	0.001
40-49	99 (39.0)	38 (52.1)	61 (33.7)	0.45	0.27-0.90	0.056
50-59	31 (12.2)	18 (24.7)	13 (7.2)	1.00		
Sex						
Male	33 (11.6)	9 (10.7)	24 (11.9)	1.00		
Female	252 (88.4)	75 (89.3)	177 (88.1)	1.13	0.57-2.23	0.768
Status						
Single	62 (21.8)	18 (21.4)	44 (21.9)	0.97	0.58-1.63	0.931
Married	223 (78.2)	66 (78.6)	157 (78.1)	1.00		
Religion						
Buddhist	212 (74.4)	77 (91.7)	135 (67.2)	5.38	2.68-10.77	0.001
Christian	73 (25.6)	7 (8.3)	66 (32.8)	1.00		
Education						
<Bachelor	67 (23.5)	22 (26.2)	45 (22.4)	1.00		
≥Bachelor	218 (76.5)	62 (73.8)	156 (77.6)	0.81	0.50-1.33	0.491
Work experience						
0-9 Years	63 (26.0)	5 (7.2)	58 (33.6)	1.00		
10-19 Years	121 (50.0)	41 (59.4)	80 (46.2)	5.94	2.59-13.62	0.001
>20 Years	58 (24.0)	23 (33.4)	35 (20.2)	7.62	3.15-18.47	0.001
Knowledge						
High	85 (36.8)	31 (44.9)	54 (33.3)	0.57	0.35-1.00	0.106
Medium	102 (44.2)	26 (37.7)	76 (46.9)	0.65	0.33-1.27	0.295
Low	44 (19.0)	12 (17.4)	32 (19.8)	1.00		
Attitude						
Very high	95 (35.2)	58 (69.0)	37 (19.9)	9.40	3.19-27.77	0.001
Medium	154 (57.0)	23 (27.4)	131 (70.4)	1.05	0.35-3.13	0.937
Low	21 (7.8)	3 (3.6)	18 (9.7)	1.00		
Practice						
Very high	195 (72.5)	61 (81.3)	134 (69.1)	1.95	1.12-3.38	0.046
Medium	74 (27.5)	14 (18.7)	60 (30.9)	1.00		

* Significant level at α=0.10

Characteristics of DCCs' environment and relevant behaviors

Regarding environment, it was found that more than half of DCCs did not meet the standard criteria of Thai DCC in the aspects of; a) the proportion of care givers and children under care, b) the density of room per child, c) quality and quantity of the inside room lighting, d) number of windows and doors in DCC, e) having infirmary in DCC.

Characteristics of DCCs environment and behaviors in the high epidemic area; 69.6% did not have washing basin in rest room, 2.0% had no soap in rest room, 19.5% of children did not wash their hands before and after lunch, 78.0% of children did not wash their hands before and after using the toilet, 87.8% of children did not wash their hands before and after playing with toys, and 89.0% of children did not have a personal cup.

Characteristics of DCCs environment and behaviors in the low epidemic area; 68.2% had not enough rest room, 77.2% did clean toys twice a week with hygienic practices.

Univariate analysis found that five factors had a significant association with HFMD. Those DCCs that did not have enough number of doors and windows per child had a greater chance of HFMD occurrence than those DCCs had enough number of doors and windows per child (OR = 2.61, 90%CI = 1.53–4.47). DCCs with bad airflow had a greater chance to develop HFMD than DCCs with good airflow DCCs (OR = 3.06, 90%CI = 1.69-5.55). DCCs with infirmary had a greater chance with HFMD occurrence than DCCs that did not have (OR = 2.21, 90%CI = 1.44-3.40). DCCs that did not have washbasin in restroom had a greater chance of HFMD occurrence than those that had washbasin (OR = 3.20, 90%CI = 1.93-5.30). DCCs without soap in restroom had a greater chance of HFMD occurrence than those that have (OR = 3.61, 90%CI = 1.97-6.61).

Moreover, those children who did not wash their hands before and after having lunch had a greater chance to develop HFMD than those who frequently washed hands (OR = 2.25, 90%CI = 1.12-4.50). Those children who did not wash their hands before and after using the toilet had a greater chance to develop HFMD than those who frequently washed hands (OR = 1.87, 90%CI = 1.08-3.23). Those children who did not have individual cups for daily use had a greater chance to develop HFMD than those who had individual cups for daily use (OR = 4.27, 90%CI = 2.20-8.32) (Table 4).

Table 4 Univariate analysis on environment characteristic and relevant behaviors and HFMD

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	*p*-value
Number of care giver per children (1:10)						
Not enough	194 (64.0)	66 (68.0)	128 (62.1)	1.30	0.84-2.00	0.318
Enough	109 (36.0)	31 (32.0)	78 (37.9)	1.00		
Space per children (1:2)						
Not enough	129 (42.9)	47 (49.5)	82 (39.8)	1.48	0.98-2.23	0.116
Enough	172 (57.1)	48 (50.5)	124 (60.2)	1.00		
Lighting inside room						
Good	148 (50.9)	52 (57.1)	96 (48.0)	1.08	0.62-1.89	0.812
Moderate	89 (30.6)	21 (23.1)	68 (34.0)	0.62	0.33-1.16	0.207
Not enough	54 (18.6)	18 (19.8)	36 (18.0)	1.00		
Number of window and door in DCC						
Not enough	46 (15.4)	23 (24.7)	23 (11.2)	2.61	1.53-4.47	0.003*
Enough	253 (84.6)	70 (75.3)	183 (88.8)	1.00		
Bad smelling						
Yes	17 (5.7)	11 (11.8)	6 (2.9)	4.47	1.89-10.59	0.004*
No	282 (94.3)	82 (88.2)	200 (97.1)	1.00		
Air ventilation						
Well	258 (87.8)	69 (78.4)	189 (91.7)	1.00		
Poor	36 (12.2)	19 (21.6)	17 (8.3)	3.06	1.69-5.55	0.002*
Having infirmary						
No	147 (48.5)	38 (39.2)	109 (52.9)	1.00		
Yes with not meet the standard	32 (10.6)	5 (5.2)	27 (13.1)	0.53	0.22-1.25	0.226
Yes with meet the standard	124 (40.9)	54 (55.7)	70 (34.0)	2.21	1.44-3.40	0.002*
Number of toys per children						
Enough	258 (89.0)	81 (90.0)	177 (88.5)	1.17	0.59-2.31	0.706
Not enough	32 (11.0)	9 (10.0)	23 (11.5)	1.00		

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	*p*-value
Having a personal belonging						
Clearly visible of identification symbol	247 (81.5)	71 (73.2)	176 (85.4)	N/A		
No identification symbol	8 (2.6)	8 (8.2)	0 (0.0)	N/A		
Mixed use	28 (9.2)	16 (16.5)	12 (5.8)	N/A		
No	20 (6.6)	2 (2.1)	18 (8.7)	N/A		
Number of rest room						
Enough	189 (65.4)	58 (59.8)	13 (68.2)	0.69	0.45-1.06	0.155
Not enough	100 (34.6)	39 (40.2)	61 (31.8)	1.00		
Having washing basin in restroom						
Yes	91 (46.7)	25 (30.5)	66 (58.4)	1.00		
No	104 (53.3)	57 (69.6)	47 (41.6)	3.20	1.93-5.30	<0.001*
Having soap in restroom						
Yes	137 (71.0)	58 (85.0)	69 (61.1)	1.00		
No	56 (29.0)	12 (15.0)	44 (38.9)	3.61	1.97-6.61	<0.001*
Garbage management						
Every day	79 (43.9)	35 (42.7)	44 (44.9)	0.91	0.56-1.50	0.763
Not every day	101 (56.1)	47 (57.3)	54 (55.1)	1.00		
Drinking water						
Sanitized	292 (96.4)	97 (100.0)	195 (94.7)	N/A		
Non-sanitize	11 (3.6)	0 (0.0)	11 (5.3)	N/A		
Frequency of DCC cleaning						
Everyday	235 (77.6)	79 (81.4)	156 (75.7)	1.00		
Twice a week	48 (15.8)	4 (4.1)	44 (21.4)	0.18	0.07- 0.44	0.001*
Once a week	20 (6.6)	14 (14.4)	6 (2.9)	4.60	2.00-10.61	0.003
Frequency of clean hankie						
Every day	61 (20.9)	31 (32.0)	30 (15.4)	2.24	1.36-3.70	0.008*
Twice a week	60 (20.5)	12 (12.4)	48 (24.6)	0.54	0.30-0.99	0.091
Once a week	171 (58.6)	54 (55.7)	117 (60.0)	1.00		
Frequency of clean bed sheet						
Once a week	303 (100.0)	97 (100.0)	206 (100.0)	N/A		
Method of cleaning toys						
Hygienic	276 (91.1)	90 (92.8)	186 (90.3)	1.38	0.65-2.93	0.479
Not hygienic	27 (8.9)	7 (7.2)	20 (9.7)	1.00		

Characteristics	Total n (%)	Case n (%)	Control n (%)	OR	90%CI	*p*-value
Frequency of cleaning toys						
Every day	14 (4.6)	7 (7.2)	7 (3.4)	1.00		
Twice a week	205 (67.7)	46 (47.4)	159 (77.2)	0.29	0.11-0.73	0.027*
Once a week	59 (19.5)	32 (33.0)	27 (13.1)	1.18	0.44 -3.15	0.775
Once a month	25 (6.6)	12 (12.4)	13 (6.3)	0.92	0.31-2.77	0.905
Frequency of cleaning floor						
Everyday	290 (95.7)	97 (100.0)	193 (93.7)	N/A		
Twice a week	13 (4.3)	0 (0.0)	13 (6.3)	N/A		
Cleaning solution						
Appropriate	297 (98.0)	97 (100.0)	200 (97.1)	N/A		
Not appropriate	6 (2.0)	0 (0.0)	6 (2.9)	N/A		
Washing hands before and after lunch						
Yes	168 (86.2)	66 (80.5)	102 (90.3)	1.00		
No	27 (13.8)	16 (19.5)	11 (9.7)	2.25	1.12-4.50	0.050*
Washing hands before and after use toilet						
Yes	57 (29.2)	18 (22.0)	39 (34.5)	1.00		
No	138 (70.8)	64 (78.0)	74 (65.5)	1.87	1.08-3.23	0.049*
Washing hand before and after play toys						
Yes	27 (13.8)	10 (12.2)	17 (15.0)	0.78	0.39-1.59	0.570
No	168 (86.2)	72 (87.8)	96 (85.0)	1.00		
Having a personal cup and not use with another people						
Yes	48 (24.6)	9 (11.1)	39 (34.5)	1.00		
No	147 (75.4)	73 (89.0)	74 (65.5)	4.27	2.20-8.32	<0.001*

* Significant level at α=0.10

In the multivariate analysis, after control for all possible variables including the characteristics of children, characteristics of parents, characteristics of care givers, and DCCs' environment characteristics and relevant behaviors, three factors were found to be associated with HFMD in children. Children who lived in poorly ventilated DCCs had a greater chance of HFMD development than those who lived in well ventilated DCCs (OR_{adj} = 3.11, 95%CI = 1.32-7.32). Children that lived in DCCs that did not provide a soap in toilet had a greater chance of HFMD development that those who lived in DCCs that provided a soap in toilet (OR_{adj} = 2.84, 95%CI = 1.33-6.07). Children that did not wash hands before and after toilet use had a greater chance to develop HFMD than those who usually wash hands before and after toilet use (OR_{adj} = 3.74, 95%CI = 1.61-8.70) (Table 5).

Table 5 Multivariate analysis of factors associated with HFMD

Factors	OR_{adj}	95%CI	*p*-value
Air ventilation			
Well	1.00		
Poor	3.11	1.32-7.32	0.009*
Having a soap in rest room			
Yes	1.00		
Not	2.84	1.33-6.07	0.007*
Washing hand before and after use toilet			
Yes	1.00		
No	3.74	1.61-8.70	0.002*

* Significant level at α=0.10

Discussion

A total of 380 children from 40 DCCs in 15 districts in Ching Rai province recruited into the study. The number of children who participated in the study was proportionate between both sex. However, the data were elicited from parents, care givers in DCCs, and DCCs' environmental sanitations. The case-control study design was used to identify the associations of possible risk factors and HFMD in children. One year history of previous HFMD occurrence was used as the identification tool for a case and a control. We did four univariate models, and one multivariate model to test the association between variables at different alpha value. In the parents' characteristics and HFMD in children model, it was found that increasing knowledge and education level of parents were associated with HFMD in their children. In the model of children's characteristics and HFMD, we found that overweight and length of breastfeeding were associated with HFMD. Age, religion, working experience, having high attitude and practice in HFMD prevention and control in care givers in DCCs were found to be associated with HFMD in children. Air ventilation and air flow, infirmary, washbasin, soap availability, frequency of hand washing before and after toilet use and lunch, personal cup for daily use were factors found to be associated with HFMD in children from the environmental model. However, in the final multivariate model, it was found that only quality of air-ventilation, availability of soap in toilet, and behavior of washing hands after use of toilet were associated with HFMD in children under 6 years old in northern Thailand.

There were some limitations in the study. Four selected DCCs were excluded from the study due to the difficulty of transportation in rainy season. Thirteen parents could not provide complete information due to Thai language barrier; they were the hill tribe people. However, during the study period, we got a great

collaboration from all selected care givers in DCCs and the local government officers in providing all necessary information.

Some information on their children such as the history of possible HFMD with hospital admission could possibly be inaccurate because some proportion of HFMD were at the mild stage with no need to attend a hospital[1,2]. This might impact the outcome of the study. One important point that might interfere with the association between variables is the limitation of the study design, since in this study we classified a case and control by history of HFMD with medical diagnosis in the previous year. There are two possible errors in this manner; one is error based on the natural history of disease, since HFMD could happen more than once in a lifetime; some of the children could have developed the HFMD in the previous year not before the year of the study. Second, with the natural history of HFMD[1,2], some of the HFMD cases could have a mild clinical sign leading to a lack of medical attention and diagnosis. It could be misclassification error in the study. The last limitation that could impact the study is the slight difference in the effect size between case and control groups. This was because DCCs in high epidemic and low epidemic areas are located in the same areas and under the same operation procedures from the same local government. Thus, this made the characteristics or frequency of risk factors between case and control not different and required a larger numbers of participants before the power (1-B) of the statistic could detect the associations.

In our study, Buddhism was found as a risk factor of HFMD in the univariate model, but it was not significant in the final model. Buddhists and Christians living in rural Thailand have different levels of economic growith[19], and economic status was related to environmental sanitary improvement, and it impacts HFMD occurrence. However, there was no previous report on the association between religion and HFMD.

Feng, et al.[20] reported that children who lived in crowded place had a higher opportunity to expose and get infection of HFMD in China. The study of Mareno et al.[21] presented that those children who attended DDCs had 14 times chances of HFMD infection than those who did not. Moreover, the Thai National Disease Control Center reported that most of the HFMD outbreak occurred in the DCCs. The same study showed that irregular hand washing of children and limited knowledge on disease control and prevention among the care givers in DCCs were associated with HFMD in central Thailand[22]. Jixia et al. also supported that economic status and population density were risk factors of HFMD in China[23]. These findings coincide with our study.

Moreno, et al.[21] also reported that girls and underweight children had a greater chance of HFMD infection. Chao-Ming et al.[24] reported that underweight children had a greater risk for HFMD. This is similar with the meta analysis which included all papers

conducted in Asia and reported that age and being female were major risk factors of HFMD[25]. Studies[26-28] reported that age was the main risk factor for HFMD particularly among < 4 years old. This supported our study that underweight children had a greater chance of HFMD infection than those with normal weight in univariate model.

In our study we found that breastfeeding was a major important factor for HFMD infection among children. Hualiang, et al.[29] and Dingmei, et al.[30] reported children who had breastfeeding less than 6 months had a greater chance for HFMD infection than those children who had breastfeed more than 6 months significantly.

Limei et al.[31] reported that hand washing behavior among children was the significant factor associated with HFMD in China. Jinyan et al.[32] reported that living environmental sanitation was a factor associated with HFMD infection in children. These two studies supported our findings which found environmental sanitations were key factors contributing to HFMD in children. However, we need more studies to test the associations between personal hygiene of children and environmental sanitation of DCCs and HFMD infection.

Conclusion

Many characteristics of children, parents, and care givers in DCCs and environmental sanitation in DCCs are associated to HFMD infection among children less than 6 years old in northern Thailand. Knowledge and attitude of the parents are associated with the occurrence of HFMD in their children. Despite the limitations of the study, it shows very significant determinants or possible risk factors for HFMD infection among children less than 6 years old in DCCs northern Thailand. The study shows very strong associations between variables with low confidence interval (CI) in the final model. This suggests that DCCs' environmental sanitations are playing a role as key factors that contribute to the occurrence of HFMD in DCCs in northern Thailand. Collaborations between health agencies and local governments should be promoted in all sections. New policy creation in particularly HFMD control and prevention measures among the relevant agencies is required to stop HDMD epidemic in DCCs.

Conflict of interest statement

We declare that we have no conflict of interest.

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