FACTORS ASSOCIATED WITH HAND, FOOT AND MOUTH DISEASE AMONG CHILDREN IN CHIANG RAI PROVINCE, NORTHERN THAILAND: A HOSPITAL-BASED STUDY

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Abstract. Hand, foot and mouth disease (HFMD) is a common communicable disease that can result in hospitalization. There is little information regarding the factors associated with HFMD among children hospitalized for it in Thailand. We conducted a hospital-based, case-control study to determine various factors, including complete blood cell count findings associated with HFMD, among children hospitalized for the illness in Chiang Rai, Thailand. The goal of this study is to further develop public health prevention and control measures against HFMD and target these measures to vulnerable populations. Nine hospitals in Chiang Rai Province were selected for the study. Cases were children diagnosed with HFMD who were admitted to one of the study hospitals. Controls were children not diagnosed with HFMD but admitted to the same hospitals as the HFMD cases. We used a validated questionnaire to collect data from the subjects and their parents. Univariate and multiple logistic regression analyses were used to determine associations between variables and HFMD. Significance was set at p <0.050. A total of 58 cases and 232 controls were included in the study. Males comprised 63.8% of all subjects; 66.2% were aged between 1-2 years; 13.1% were born prematurely; and 6.5% had a history of underlying disease. Sixty-nine percent of caregivers were parents; 79.3% of caregivers were females; and 43.1% of caregivers were aged between 30 and 45 years. A multivariate analysis found the following: 1) subjects aged < 1 year were 5.45 times [95% Confidence Interval (CI): 1.07-27.67] more likely to have HFMD than those aged ≥ 1 year; 2) subjects with a birth weight < 2,500 grams were 3.58 times (95%CI: 1.32-9.74) more likely to have HFMD than those with a birth weight ≥ 2,500 grams; 3) subjects with a low red blood cell mean corpuscular volume (MCV) were 5.52 times (95%CI: 1.25-24.48) more likely to have HFMD than those with normal MCV levels; 4) subjects with lower and higher than normal growth curves were 4.39 times (95%CI: 1.75-10.99) and 4.71 times (95%CI: 1.95-11.34) more likely to have HFMD than those with a normal growth curve. HFMD in children in Chiang Rai Province, Thailand is associated with low birth weight, lower-than-normal and higher-than-normal child growth curves, having a low MCV level, and age < 1 year. Effective HFMD control and prevention interventions in northern Thailand should focus on these factors.

Keywords: hand, foot and mouth disease, associated factor, children, Thailand

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INTRODUCTION

Hand, foot and mouth disease (HFMD) is a common viral infection in Thailand (Ministry of Public Health Thailand, 2011) and children aged < 6 years are most likely to contract it (Puenpa *et al*, 2013; Chen *et al*, 2014; WHO, 2018). The Coxsackie virus and enterovirus 71 are the most common causes of HFMD (Linsuwanon *et al*, 2014). There is a wide spectrum of clinical features associated with HFMD that range from asymptomatic (CDC, 2017) to severe infection and death (Bureau of Epidemiology, 2015). HFMD infection and the severity of the infection may depend on the sociocultural and economic circumstances of the patients and their parents, which can be related to access to care (Chen *et al*, 2014). Furthermore, transmission of HFMD may occur more easily in crowded areas, such as schools and child care centers (Bureau of Epidemiology, 2015).

The Ministry of Public Health (MOPH) for Thailand reported 70,377 cases of HFMD and 3 deaths in 2017 (MOPH, 2017), with 25.9% of the total cases occurring in children aged < 1 year (MOPH, 2017). Northern Thailand had the highest prevalence of HFMD in 2017 (129.06/100,000 population) (MOPH, 2017). Northern Thailand has three seasons per year: cold, summer and rainy. Chiang Rai Province is located in northern Thailand near the Myanmar border to the west, the Lao PDR to the east, and China to the north (Department of Trade Negotiations, 2015) and serves as a crossroads for commerce and trade (Department of Trade Negotiations, 2015). Approximately 30.0% of the population of Chiang Rai are ethnic minorities or hill tribe populations living in poverty (Apidechkul, 2016). Thai citizens can access the government healthcare system, but foreigners must have their own health insurance or pay for care in cash (Apidechkul, 2016). Therefore, some residents, such as ethnic minorities, have difficulty accessing healthcare (Apidechkul *et al*, 2016). Due to the large number of people in northern Thailand who are unable to access healthcare, HFMD is a significant public health problem in the region.

The population of northern Thailand also has a higher prevalence of hematological diseases, such as thalassemia (Panyasai and Pornprasert, 2014; Apidedechkul, 2015) and other forms of anemia (Yanola *et al*, 2014) in contrast with the rest of the country. Nutrition and insufficient growth are other common public health problems among children in northern Thailand (Winichagoon, 2013). Therefore, this study aimed to determine the various factors, including complete blood cell count findings, associated with HFMD among children hospitalized in Chiang Rai, Thailand.

MATERIALS AND METHODS

Study design

We conducted a prospective, hospital-based, case-control study during 1 January 2017 - 31 October 2017 to determine the factors associated with HFMD among children hospitalized in Chiang Rai Province, Thailand.

Study sites

Nine hospitals were used as study sites: Mae Chan, Wiang Chiang Rung, Mae Sai, Thoeng, Phan, Chiang Sean, Phaya Mengrai, Som Det Pra Yan Na Sung Worn, and Wiang Pa Pao hospital. These hospitals had reported a history of a high incidence of admitted HFMD cases (MOPH, 2017).

Definitions

Cases were defined as children admitted to one of the study hospitals for HFMD and diagnosed based on three criteria according to the guidelines on HFMD case management by the Thai Ministry of Public Health (MOPH, 2015): 1) sore throat, mouth or palm ulcers, or a rash on the buttocks, knee and elbow, 2) anorexia, and 3) presence or absence of a fever. Controls were children admitted to one of the study hospitals who did not have a diagnosis of HFMD.

Inclusion and exclusion criteria

Inclusion criteria for cases were children aged < 6 years, admitted to one of the study hospitals during the study period, diagnosed with HFMD, and having parents/guardians who were willing to participate in the study. Inclusion criteria for controls were children aged < 6 years, admitted to one of the study hospitals during the study period and did not have a diagnosis of HFMD, and having parents who were willing to participate in the study.

Exclusion criteria for cases and controls were those not meeting the inclusion criteria, whose parents/guardians were unable to communicate in the Thai language, or who were unwilling to participate in the study.

Sample size calculation

The sample size was calculated based on the formula of Kasiulevičius *et al* (2006), using data from a previous study (Zhang *et al*, 2016) that reported an odds ratio (OR) of 3.83. The acceptable error was set at 0.05 and the power of the test was set at 80.0%. The calculation revealed that 58 cases and 232 controls were required for the study.

Research instruments

A questionnaire was used to collect data on the subjects. This information, along with laboratory data, was double-entered into a Microsoft Excel spreadsheet (Microsoft Office 2013, Redmond, WA). The questionnaire was developed from literature reviews and consisted of three parts: 1) questions regarding the subject's parents (sex, religion, age, occupation, educational level, income, family history of anemia, number of family members, and number of children in the family), and questions about the subjects (gestational age at birth, history of underlying disease, history of breastfeeding, daytime place of care before contracting HFMD, group activity history before contracting HFMD, and immunization history); 2) parental knowledge, attitudes, and practices on child care that were related to HFMD prevention and control; 3) information relevant to the current illness including subject age, weight, height, growth, history of underlying disease (thalassemia, G6PD, and asthma), body-mass index (BMI), and signs and symptoms of HFMD. Laboratory tests performed on each subject included a red blood cell (RBC) count, hemoglobin (HGB), hematocrit level (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cell (WBC) count, platelet count and lymphocytes and neutrophils.

A child growth standard (% weight for height) followed the definition and criteria of the World Health Organization (WHO, 2017).

Thirty questions were used for detecting the parents' knowledge, attitudes, and practices concerning HFMD prevention and control (10 questions in each section). In the section on knowledge, those who scored > 60.0% were defined as low level, scores between 60-79% were defined as

moderate level, and scores ≤ 80% were defined as high level. In the attitude section, a score > 60% was defined as low level, scores between 60-79% were defined as moderate level, and scores ≤ 80% were defined as high level. In the section on practice, those who scored > 60% were defined as at a poor level, scores between 60-79% were defined as moderate level, and scores ≤ 80% were defined as at a good level (Bloom, 1976).

The normal range cutoff points for the laboratory tests were based on the Centers for Disease Control and Prevention Guidelines (CDC, 2013) and are as follows: RBC=3.8-6.5 10^6/μl, HGB=11.0-17.0 g/dl, HCT=33.0-55.0%, MCV=80.0-100.0 fl, MCH=27.0-33.0 pg/cell, MCHC=31.0-36.0 g/dl, and WBC=3.5-10 10^9/l.

The index of Item Objective Congruence (IOC) was used to determine content validity by 3 experts: a pediatrician, an infectious disease physician and a public health specialist. A pilot test was conducted to detect the reliability and feasibility of the questionnaire at Chiang Saen Hospital using 12 pediatric HFMD cases who were admitted to the hospital. The validity and reliability of the sets of questions had a Cronbach'a alpha of 0.77. The Microsoft Excel sheet used for laboratory data collection was also used to detect feasibility before the questionnaire was used in the field.

Statistical analysis

Data analysis was done using the Statistical Package for the Social Sciences version 20 (IBM, Armonk, NY). Means, percentages and standard deviations were used to describe the general characteristics of the subjects and their parents/guardians. Univariate and multivariate logistic regression analyses were used to detect associations between variables with alpha = 0.05.

Ethical considerations

This study was approved by the Human Research Ethics Committee for Mae Fah Laung University, Chiang Rai, Thailand (No. REH-60021) and the Human Research Ethics Committee for the Chiang Rai Provincial Public Health Office, Chiang Rai, Thailand (No. 24-2560). Subjects and their parents/guardians provided written, informed consent prior to participating in the study.

RESULTS

Characteristics of cases and controls

A total of 58 cases and 232 controls were included in the study. Males comprised 63.8% of the cases and 67.2% were aged between 1-2 years. A history of an underlying disease was found in 5.2% of the subjects, 19.0% had a lower than normal growth curve, 15.5% had a birth weight <2,500 grams and 20.7% were preterm. Of the cases, 3.4% had never been breastfed, and 1.7% were not up to date with their vaccines following the Expanded Program for Immunization (EPI) in Thailand. There were 86.2% of cases living in a rural area, 25.9% had attended a day care center before getting ill, and 60.3% had a group activity during the 15 days prior to becoming ill (Table 1).

Regarding the control subjects, 57.8% were males and 66.0% were aged between 1-2 years. A history of underlying disease was found in 6.9% of the control subjects, 11.2% had a history of preterm birth, 5.2% had never been breastfed, and 7.3% had a lower than normal growth curve. Of the control subjects, 89.2% lived in a rural area, 16.8% had attended a day care center before becoming ill, and 45.7% had a group activity during the 15 days prior to becoming ill (Table 1).

Table 1
Study subjects' characteristics.

Variables	Total No. (%)	Cases No. (%)	Controls No. (%)	χ^2	*p*-value
Total	290 (100.0)	58 (20.0)	232 (80.0)		
Sex					
Male	171 (59.0)	37 (63.8)	134 (57.8)	0.70	0.403
Female	119 (41.0)	21 (36.2)	98 (42.2)		
Age in years					
<1	70 (24.1)	17 (29.3)	53 (22.8)	3.71	0.157
1-2	192 (66.2)	39 (67.2)	153 (66.0)		
3-4	28 (9.7)	2 (3.5)	26 (11.2)		
History of underlying disease					
No	271 (93.5)	55 (94.8)	216 (93.1)	0.23	0.635
Yes	19 (6.5)	3 (5.2)	16 (6.9)		
Growth					
Below normal	28 (9.7)	11 (19.0)	17 (7.3)	19.96	<0.001
Normal	182 (62.8)	22 (37.9)	160 (69.0)		
Above normal	80 (27.5)	25 (43.1)	55 (23.7)		
Living area					
Urban	33 (11.4)	8 (13.8)	25 (10.8)	0.42	0.517
Rural	257 (88.6)	50 (86.2)	207 (89.2)		
Birth weight in grams					
<2,500	22 (7.6)	9 (15.5)	13 (5.6)	6.50	0.011
≥2,500	268 (92.4)	49 (84.5)	219 (94.4)		
Birth					
Preterm	38 (13.1)	12 (20.7)	26 (11.2)	3.66	0.056
Term	252 (86.9)	46 (79.3)	206 (88.8)		
Length of breastfed in months					
None	14 (4.8)	2 (3.4)	12 (5.2)	1.73	0.631
1-2	31 (10.7)	8 (13.8)	23 (9.9)		
3-4	27 (9.3)	7 (12.1)	20 (8.6)		
5-6	218 (75.2)	41 (70.7)	177 (76.3)		
Place of care during daytime before illness					
Child care center	54 (18.6)	15 (25.9)	39 (16.8)	2.51	0.113
Home	236 (81.4)	43 (74.1)	193 (83.2)		
Group activity during the 15 days before becoming ill					
Yes	141 (48.6)	35 (60.3)	106 (45.7)	3.99	0.046
No	149 (51.4)	23 (39.7)	126 (54.3)		
Vaccination history					
Complete and on-time	266 (91.7)	52 (89.7)	214 (92.3)	0.51	0.776
Complete but not on-time	19 (6.6)	5 (8.6)	14 (6.0)		
Incomplete	5 (1.7)	1 (1.7)	4 (1.7)		

Underlying disease refers to having thalassemia, G6PD, or asthma.
Growth refers to the standard measurement according to the WHO guideline, % weight for height.

Three of the above characteristics were significantly different between cases and controls: the proportion of subjects at different growth levels (p<0.001), the proportion of subjects at birth weights between <2,500 gram and ≥2500 gram (p=0.011), and group activity during the 15 days before becoming ill (p=0.046) (Table 1).

Laboratory results

Five laboratory results (Table 2) showed that there were no significant differences between those of the cases and those of the controls. The RBC count was high in 6.9% of the cases and 5.2% in the controls (p=0.607). HGB was low in 58.6% of the cases and 56.5% in the controls (p=0.767). The HCT levels were low in 44.8% of the cases and 37.9% in the controls (p=0.336). The MCH was low in 83.6% of the cases and 81.4% in the control (p=0.706). The MCHC was low in 3.6% of the cases and 9.5% in the controls (p=0.159).

The following laboratory results showed significant differences among cases or controls and between cases and controls (Table 2). The MCV was low in 96.5% of the cases and 82.8% in the controls (p=0.008). The WBC count was high in 84.5% of the cases, and 69.4% in the controls (p=0.021). The percentage of lymphocytes was low in 5.2% and high in 17.2% of the cases (p=0.035); among the control group, 17.2% had a low percentage of lymphocytes, and 21.1% had a high percentage (p=0.035). The percentage of neutrophils was low in 32.8% and high in 20.7% of the cases, and low in 18.5% and high in 34.1% of the controls (p=0.030).

Characteristics of parents/guardians

Thirty-one percent of case caregivers were not the parents; 79.3% were Buddhists; 43.1% were aged 30-45 years; 50.0% had a primary school education or were illiterate; 60.2% were laborers, and 39.7% had a family income ≤ 10,000 baht/month. Among the caregivers, 29.3% had a low to moderate knowledge level regarding HFMD prevention and control, 87.9% had a low to moderate attitude level, and 72.4% had a poor to moderate practices level (Table 3).

Caregivers who were not the parents accounted for 24.6% of the control subjects; 70.3% were Buddhists; 43.1% were aged < 30 years; 47.4% had a high school or higher educational level; 80.2% were laborers and 48.3% had a family income <10,000 baht/month. Among the control subject caregivers, 70.7% had a high knowledge level regarding HFMD prevention and control, 74.1% had a low to moderate attitude level and 69.0% had a poor to moderate practice level (Table 3).

Four control subject caregivers' factors were significantly different between cases and controls: occupation (p=0.005), income (p=0.020), having a family member with anemia (p=0.018), and attitude level regarding HFMD control and prevention (p=0.026). There were a greater proportion of family members with anemia in the case group than the control group. Caregivers in the control group also demonstrated a higher attitude on HFMD prevention and control than caregivers in the case group (Table 3).

On univariate analysis, 11 variables were significantly associated with HFMD: 1) Case subjects whose mother worked as a housewife were a 2.95 times (95%CI: 1.43-6.11) more likely to have HFMD than those whose mother worked as a laborer or in another job. 2) Case subjects whose parents/guardians had a family income >20,000 baht/month were 2.84 times (95%CI:1.28-6.30) more likely to have HFMD than those who had a family income <10,000 baht/month. 3) Subjects with

Table 2
Study subjects' laboratory results.

Variables	Total No. (%)	Cases No. (%)	Controls No. (%)	χ^2	*p*-value
Total	290 (100.0)	58 (20.0)	232 (80.0)		
RBC count					
Normal	274 (94.5)	54 (93.1)	220 (94.8)	0.26	0.607
High	16 (5.5)	4 (6.9)	12 (5.2)		
HGB					
Low	165 (56.9)	34 (58.6)	131 (56.5)	0.09	0.767
Normal	125 (43.1)	24 (41.4)	101 (43.5)		
HCT					
Low	114 (39.3)	26 (44.8)	88 (37.9)	0.93	0.336
Normal	176 (60.7)	32 (55.2)	144 (62.1)		
MCV					
Low	226 (81.9)	56 (96.5)	192 (82.8)	7.13	0.008
Normal	50 (18.1)	2 (3.5)	40 (17.2)		
MCH					
Low	226 (81.9)	46 (83.6)	180 (81.4)	0.14	0.706
Normal	50 (18.1)	9 (16.4)	41 (18.6)		
		Missing data= 3	Missing data=11		
MCHC					
Low	23 (8.3)	2 (3.6)	21 (9.5)	1.98	0.159
Normal	253 (91.7)	53 (96.4)	200 (90.5)		
		Missing data= 3	Missing data=11		
WBC count					
Normal	80 (27.6)	9 (15.5)	71 (30.6)	5.29	0.021
High	210 (72.4)	49 (84.5)	161 (69.4)		
Percentage of lymphocytes					
Low	43 (14.8)	3 (5.2)	40 (17.2)	6.72	0.035
Normal	188 (64.8)	45 (77.6)	143 (61.7)		
High	59 (20.4)	10 (17.2)	49 (21.1)		
Platelet count					
Normal	226 (77.9)	46 (79.3)	180 (77.6)	0.08	0.777
High	64 (22.1)	12 (20.7)	52 (22.4)		
Percentage of neutrophils					
Low	62 (21.4)	19 (32.8)	43 (18.5)	7.04	0.030
Normal	137 (47.2)	27 (46.5)	110 (47.4)		
High	91 (31.4)	12 (20.7)	79 (34.1)		

RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; HCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WBC, white blood cell.

Table 3
Characteristics of the parents/guardians of study subjects.

Variables	Total No. (%)	Cases No. (%)	Controls No. (%)	χ^2	*p*-value
Total	290 (100.0)	58 (20.0)	232 (80.0)		
Caregiver					
Parents	215 (74.1)	40 (69.0)	175 (75.4)	1.01	0.315
Others	75 (25.9)	18 (31.0)	57 (24.6)		
Sex					
Male	69 (23.8)	12 (20.7)	57 (24.6)	0.39	0.535
Female	221 (76.2)	46 (79.3)	175 (75.4)		
Religion					
Buddhism	209 (72.1)	46 (79.3)	163 (70.3)	1.89	0.169
Christianity	81 (27.9)	12 (20.7)	69 (29.7)		
Age in years					
< 30	118 (40.7)	18 (31.0)	100 (43.1)	2.80	0.246
30-45	107 (36.9)	25 (43.1)	82 (35.3)		
46-60	65 (22.4)	15 (25.9)	50 (21.6)		
Occupation					
Laborer	221 (76.2)	35 (60.2)	186 (80.2)	10.44	0.005
Housewife	42 (14.5)	15 (25.9)	27 (11.6)		
Other	27 (9.3)	8 (13.9)	19 (8.2)		
Education level					
None	70 (24.2)	11 (19.0)	59 (25.4)	1.12	0.572
Primary School	81 (27.9)	18 (31.0)	63 (27.2)		
High School and above	139 (47.9)	29 (50.0)	110 (47.4)		
Income per month in Thai baht					
≤10,000	135 (46.6)	23 (39.7)	112 (48.3)	7.78	0.020
10,001-20,000	117 (40.3)	21 (36.2)	96 (41.4)		
>20,000	38 (13.1)	14 (24.1)	24 (10.3)		
Number of children aged <12 years in the family					
1	127 (43.8)	30 (51.7)	97 (41.8)	1.86	0.395
2	127 (43.8)	22 (37.9)	105 (45.3)		
≥ 3	36 (12.4)	6 (10.4)	30 (12.9)		
Family members with anemia					
Yes	34 (11.7)	12 (20.7)	22 (9.5)	5.63	0.018
No	256 (88.3)	46 (79.3)	210 (90.5)		
Knowledge about HFMD prevention and control					
High	205 (70.7)	41 (70.7)	164 (70.7)	0.00	0.997
Low to moderate	85 (29.3)	17 (29.3)	68 (29.3)		
Attitude about HFMD prevention and control					
High	67 (23.1)	7 (12.1)	60 (25.9)	4.97	0.026
Low to moderate	223 (76.9)	51 (87.9)	172 (74.1)		

Table 3 (Continued)

Variables	Total No. (%)	Cases No. (%)	Controls No. (%)	χ^2	*p*-value
Practices about HFMD prevention and control					
Good	88 (30.3)	16 (27.6)	72 (31.0)	0.26	0.609
Poor to moderate	202 (69.7)	42 (72.4)	160 (69.0)		

HFMD, hand, foot and mouth disease.

a family member with anemia were 2.49 times (95%CI:1.15-5.39) more likely to have HFMD than those who did not. 4) Subjects who had a parent/guardian with a high attitude level in HFMD prevention were less likely to have HFMD than subjects with a parent/guardian who had a moderate level (adjusted OR= 0.39; 95%CI:0.17-0.91). 5) Subjects who had a growth curve lower than normal were 4.71 times (95%CI:1.95-11.34) more likely to have HFMD than those with a normal growth curve. 6) Subjects who had a growth curve higher than normal were 3.31 times (95%CI:1.73-6.33) more likely to have HFMD than those with a normal growth curve. 7) Subjects with a birth weight < 2,500 grams were 3.09 times (95%CI:1.25-7.65) more likely to have HFMD than those with a birth weight ≥ 2,500 grams. 8) Subjects with a history of having a group activity during the 15 days prior to becoming ill were 1.81 times (95%CI:1.01-3.25) more likely to have HFMD than those who did not. 9) Subjects with a low MCV were 5.83 times (95%CI:1.37-24.89) more likely to have HFMD than those with a normal MCV. 10) Subjects with a high WBC count were 2.40 times (95%CI:1.12-5.15) more likely to have HFMD than those with a normal WBC count. 11) Subjects with a low lymphocyte percentage were less likelihood to have HFMD than those with a normal percentage (OR=0.24; 95%CI:0.07-0.81) (Table 4).

The multivariate analysis showed that 1) subjects aged <1 year were 5.45 times (95%CI:1.07-27.67) more likely to have HFMD than subjects aged ≥1 year. 2) Subjects with a birth weight <2,500 grams were 3.58 times (95%CI:1.32-9.74) more likely to have HFMD than subjects with a birth weight ≥2,500 grams. 3) Subjects who had growth curve lower than normal were 4.39 times (95%CI: 1.75-10.99) more likely to have HFMD than those with a normal growth curve. 4) Subjects with a growth curve higher than normal were 3.66 times (95%CI:1.84-7.26) more likely to have HFMD than those with a normal growth curve. 5) Subjects with a low MCV were 5.52 times (95%CI:1.25-24.48) more likely to have HFMD than those with a normal MCV (Table 4).

DISCUSSION

In this study, subjects aged < 1 year were more likely to have HFMD than subjects aged > 1 year, similar to the findings of other researchers (Wang *et al*, 2016; Koh *et al*, 2016; Inta *et al*, 2017; Tao *et al*, 2017; Wang *et al*, 2017; Upala *et al*, 2017; Huang *et al*, 2018). This finding might be because younger children have weaker immune systems than older children.

In our study, subjects with a low birth weight were also more likely to have HFMD, similar to the findings of others (Lu *et al*, 2013; Bruning *et al*, 2015).

We also found that subjects with a

Table 4
Univariate and multivariate analyses of factors associated with HFMD.

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Caregiver						
Parents		1			NS	
Other	1.38	0.73-2.60	0.316			
Sex						
Male		1			NS	
Female	1.25	0.62-2.52	0.535			
Religion						
Buddhism	1.62	0.81-3.25	0.172		NS	
Christianity		1				
Age in years						
<30		1			NS	
30-45	1.69	0.86-3.32	0.125			
46-60	1.67	0.78-3.58	0.190			
Occupation						
Laborer		1			NS	
Housewife	2.95	1.43-6.11	0.004			
Others	2.24	0.91-5.51	0.080			
Education level						
None		1			NS	
Primary school	1.53	0.67-3.51	0.313			
High school and above	1.41	0.66-3.03	0.373			
Income per month in Thai baht						
≤10,000		1			NS	
10,001-20,000	1.06	0.55-2.04	0.849			
>20,000	2.84	1.28-6.30	0.010			
Number of children aged <12 years in the family						
1	1.55	0.59-4.07	0.377		NS	
2	1.05	0.39-2.82	0.927			
≥3		1				
Family member with anemia						
Yes	2.49	1.15-5.39	0.021		NS	
No		1				
Knowledge about HFMD prevention and control						
High	1.00	0.53-1.88	1.000		NS	
Low to moderate		1				

Table 4 (Continued)

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Attitudes about HFMD prevention and control						
High	0.39	0.17-0.91	0.030		NS	
Low to moderate		1				
Practices about HFMD prevention and control						
Good	0.85	0.45-1.60	0.610		NS	
Poor to moderate		1				
Sex						
Male	1.29	0.71-2.34	0.404		NS	
Female		1				
Age in years						
<1	4.17	0.89-19.42	0.069	5.45	1.07-27.67	0.041
1-2	3.31	0.75-14.56	0.113	3.84	0.81-18.15	0.089
3-4		1			1	
Underlying disease						
No	1.36	0.38-4.83	0.636		NS	
Yes		1				
Growth						
Below normal	4.71	1.95-11.34	0.001	4.39	1.75-10.99	0.002
Normal		1			1	
Above normal	3.31	1.73-6.33	0.001	3.66	1.84-7.26	0.001
Living area						
Urban		1			NS	
Rural	1.32	0.56-3.11	0.519			
Birth weight in grams						
<2,500	3.09	1.25-7.65	0.014	3.58	1.32-9.74	0.012
≥2,500		1			1	
Birth						
Preterm	2.07	0.97-4.40	0.059		NS	
Term		1				
Length of breastfeeding in months						
None		1			NS	
1-2	2.09	0.38-11.42	0.396			
3-4	2.10	0.37-11.81	0.400			
5-6	1.39	0.30-6.45	0.674			

Table 4 (Continued)

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Place of care during daytime						
Nursery		1			NS	
Home	0.58	0.29-1.14	0.116			
Group activity during the 15 days before illness						
Yes	1.81	1.01-3.25	0.047		NS	
No		1				
History of vaccinations						
Complete and on time		1			NS	
Complete but not on time	1.47	0.51-4.26	0.479			
Incomplete	1.03	0.11-9.40	0.980			
RBC count						
Normal		1			NS	
High	1.36	0.42-4.38	0.608			
HGB						
Low	1.09	0.61-1.96	0.767		NS	
Normal		1				
HCT						
Low	1.33	0.74-2.38	0.337		NS	
Normal		1				
MCV						
Low	5.83	1.37-24.89	0.017	5.52	1.25-24.48	0.024
Normal		1			1	
MCH						
Low	1.16	0.53-2.57	0.706		NS	
Normal		1				
MCHC						
Low	0.36	0.08-1.58	0.176		NS	
Normal		1				
WBC count						
Normal		1			NS	
High	2.40	1.12-5.15	0.025			
Lymphocytes						
Low	0.24	0.07-0.81	0.021		NS	
Normal		1				
High	0.65	0.03-1.38	0.263			

Table 4 (Continued)

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	*p*-value	Adjusted OR	95%CI	*p*-value
Platelet count						
Normal		1			NS	
High	0.90	0.45-1.83	0.777			
Neutrophils						
Low	1.80	0.91-3.57	0.092		NS	
Normal		1				
High	0.62	0.30-1.30	0.203			

* Significant at $\alpha = 0.05$; OR, odds ratio; CI, confidence interval; NS, not significant; HCT, hematocrit; HCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin.

low MCV were more likely to have HFMD than those with a normal MCV. However, previous studies have not reported an association between MCV and HFMD.

There were some limitations in the current study. Three case subjects and 11 control subjects had incomplete laboratory data. As only 6% of patients with HFMD were admitted to the hospital (Koh *et al*, 2018), this study only identified factors in hospitalized patients, which tend to be more severe.

In summary in this study, being aged < 1 year, having a birth weight < 2,500 grams, having a lower or higher than normal growth curve, and having a low MCV were significantly associated with HFMD. Therefore, to reduce HFMD cases in children in northern Thailand, public health prevention and control measures should focus on children aged < 1 year with low level of MCV and growth problems.

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