RELATED FACTORS TO THE SEVERITY OF HAND, FOOT AND MOUTH DISEASE IN CHILDREN TREATED AT CAN THO CHILDREN'S HOSPITAL 2022-2023

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ABSTRACT

Background*: Hand, foot, and mouth disease (HFMD) is an acute infectious disease caused by an intestinal virus with typical clinical manifestations: bullous rash on the hands, feet, buttocks, or mouth ulcers. The disease can spread very quickly from one child to another through two fecal-oral and respiratory routes. Hand, foot, and mouth disease is one of the most common acute infectious diseases in Vietnam. Most cases of the disease are mild. However, the disease can become severe and cause dangerous complications leading to death if not detected early and treated promptly.* ***Objectives:*** *1) To describe the clinical and paraclinical characteristics of hand, foot, and mouth disease in children treated at the Infection Department of Can Tho Children's Hospital. 2) To analyze factors related to the severity of hand, foot, and mouth disease in children treated at the Infection Department of Can Tho Children's Hospital.* ***Materials and methods****: A cross-sectional descriptive study with analysis.* ***Results:*** *General characteristics for men (60.5%), age group 12-24 months 43.5%, the reason for hospitalization is fever (95.5%), mouth ulcers (66.5%), rash, acne water (39%). The severity of hand, foot, and mouth disease is statistically significantly related to white blood cell count >=16x1G/l (p=0.0001) and platelet count >=400x109/l (p=0.0001). There is no relationship between hand, foot, and mouth severity with gender characteristics (p=0.980), age group (p=0.259), diet in the first 6 months (p=0.566), and education level (p=0.293), place of*

residence (p=0.948), number of days of onset before admission (p=0.171) and initial management (p=0.701). ***Conclusion:*** *Factors such as white blood cell count (p = 0.001) and platelet count (p = 0.001) were statistically significant in the severity of hand, foot, and mouth disease (p < 0.05). There is no relationship between age group, gender, diet, education level, number of days of onset, and initial treatment with the severity of HFMD.*

Keywords: *Hand, foot, and mouth, relationship, relevance.*

I. INTRODUCTION

Hand, foot, and mouth disease (HFMD) is an acute infectious disease caused by an intestinal virus with typical clinical manifestations: bullous rash on the hands, feet, buttocks or mouth ulcers. The disease can spread very quickly from one child to another through two fecal-oral and respiratory routes. Hand, foot, and mouth disease is mostly mild and goes away on its own within a week. However, there is still a low rate of the disease having serious complications and leading to death. According to the Ministry of Health, in the first 6 months of 2023, there were 8.995 cases of hand, foot, and mouth disease, including 03 deaths[1]. The number of cases of hand, foot, and mouth disease has tended to increase in the past month. Currently, in Vietnam, there are still few general studies on the epidemiology, clinical, and subclinical of hand, foot, and mouth disease, so we conducted this study to determine some factors related to the severity of hand, foot, and mouth disease. The severity of hand, foot, and mouth disease in children [1].

II. MATERIALS AND METHODS

2.1. Research subjects

The child was diagnosed with Hand, Foot and Mouth Disease, treated and hospitalized at Children's Hospital.

Inclusion criteria: Children were diagnosed with hand, foot and mouth and grouped based on both clinical and paraclinical criteria according to the Ministry of Health's 2012 guidelines.

Exclusion criteria: Family refuses to participate in the study. Children with HFMD have other diseases before HFMD including liver failure, kidney failure, nephrotic syndrome, birth defects, other underlying diseases, etc.

2.2. Research methods

Research design: A cross-sectional descriptive study with analysis.

Place and time of research: Can Tho Children's Hospital, 12/2022-12/2023.

Sample size: Calculate according to the formula $n=Z^2_{1-\frac{\alpha}{2}}\frac{p(1-p)}{d^2}$ if $\alpha=0.05$, then $Z_{0.975}=1.96$, d=0.05, and p = 4% (rate of severe HFMD according to Su Na Chin in 2018 [2]). We estimated the minimum sample size to be 59 samples. We actually collected 200 samples.

Sampling method: Take the entire sample.

Research content: General characteristics, clinical and paraclinical characteristics, and factors related to hand, foot and mouth disease in children from 2 months to 5 years old at Can Tho Children's Hospital.

The method of data collection: All eligible children were asked about their medical history, physical examination, and laboratory tests. Data collected on the survey form was unified.

Data processing: Data were processed using SPSS 20.0 software. The main method is descriptive analysis of frequencies and percentages; Determine the association in the form of frequency, percentage, odds ratio (OR), 95% confidence interval (CI) OR, chi-square test with significance level $\alpha= 0.05$.

III. RESULTS

3.1. General characteristics of research subjects

Table 1. General characteristics of research subjects

Characteristic		Frequency	Ratio (%)
Gender	Male	121	60.5
	Female	79	39.5
Age group	<12 months	28	14
	12 - 24 months	87	43.5
	25 - 36 months	53	26.5
	>36 months	32	16
Educational level of primary caregiver	Elementary	14	7
	Secondary school	83	41.5
	High school	101	50.5
	College, university	2	1
Occupation of primary caregiver	Housewife	57	28.5
	Farmer	39	19.5
	Workers and Employees	58	29
	Other	46	23

Regarding gender, there are 121 male (60.5%) and 79 female (39.5%). Regarding age group, the group of children 12-24 months accounts for the highest proportion with 43.5%. Regarding the educational level of the primary caregiver, no one is illiterate and the group with high school education accounts for the highest rate at 50.5%. The majority of child caregivers are housewives (28.5%) and workers and civil servants (29%).

Table 2. Prevalence of hand, foot and mouth risk factors

Characteristic		Frequency	Ratio (%)
Diet for the first 6 months	Breastfeed exclusively	110	55
	Incomplete breastfeeding	90	45
Date of onset and admission to hospital	<=72h	179	89.5
	>72h	21	10.5
Reason for hospitalization	Fever	191	95.5
	Startle	36	18
	Rash, blisters	78	39
	Vomit	15	7.5
	Mouth sores	133	66.5
	Diarrhea	9	4.5
Initial treatment	Yes	78	39
	No	122	61

Regarding diet in the first 6 months, 110 children are exclusively breastfed (55%). The majority of children were hospitalized within 72 hours of onset (89.5%). Regarding the reason for hospitalization, the most common reason is fever (84.7%), followed by mouth ulcers (66.5%), rash, and blisters (39%). Only 9/200 cases were hospitalized for diarrhea. Regarding initial treatment, the majority of children did not receive initial treatment at a rate of 61%.

3.2. Some factors related to the severity of hand, foot, and mouth disease

Table 3. Some factors related to the severity of hand, foot, and mouth disease

Related factors	Severe HFMD n (%)	Mild HFMD n (%)	OR 95% CI	p
Age group				
<12 months	2 (7.1)	26 (92.9)	0,432 (0.097 – 1.931)	0.259
>=12 months	26 (15.1)	146 (84.9)		
Gender				
Female	11 (13.9)	68 (86.1)	0.990 (0.437 – 2.242)	0.980
Male	17 (14)	104 (86)		
Diet for the first 6 months				
Incomplete breastfeeding	14 (15.6)	76 (84.4)	1.263 (0.568 – 2.810)	0.566
Breastfeed exclusively	14 (12.7)	96 (87.3)		
Educational level				
Elementary/Secondary school	11 (11.3)	86 (88.7)	0.647 (0.286 – 1.462)	0.293
High school	17 (16.5)	86 (83.5)		
Address				
Countryside	21 (14.1)	128 (85.9)	1.031 (0.410 – 2.591)	0.948
City	7 (13.7)	44 (86.3)		
Date of onset and admission to hospital				
<=72h	5 (23.8)	16 (76.2)	2.120 (0.709 – 6.339)	0.171
>72h	23 (12.8)	156 (87.2)		
Initial treatment				
No	18 (14.8)	104 (85.2)	1.177 (0.513 – 2.702)	0.701
Yes	10 (12.8)	68 (87.2)		
WBC				
>=16x1G/l	14 (34.1)	27 (65.9)	5.370 (2.302 – 12.528)	0.0001
<16x1G/l	14 (8.8)	145 (91.2)		
Platelet				
>=400x10^9/l	16 (40)	24 (60)	8.222 (3.466 – 19.505)	0.0001
<400x10^9/l	12 (7.5)	148 (92.5)		

Among the factors related to the severity of hand, foot, and mouth disease, only the number of white blood cells (p = 0.001) and platelets (p = 0.001) are statistically significantly related to the severity of hand, foot and mouth disease (p <0.05). The high white blood cell count above 16000 cells/mm^3 (34.1%) in children at risk of severe illness is 3.9 times higher than the white blood cell count lower than 16000 cells/mm^3. The increased platelet count above 400000 cells/mm3 in children at risk of severe illness is 5.3 times higher than the platelet count lower than 400000 cells/mm^3.

IV. DISCUSSION

4.1. General characteristics of research subjects

Regarding gender, there are more male children than female children (60.5% male and 39.5% female), the male/female ratio is 1.53/1. Many studies by other authors also showed similar results: In Vietnam, Chu Thi Ha's research (2022) recorded that 60.3% of male children and 39.7% of female children, the male/female ratio is 1.52/1). Regarding age

groups, the 12-24 months group accounts for the highest proportion with 43.5%, and the <12 months age group accounts for the lowest proportion with 14%. The results are similar to Vi Ngoc Linh's study (2020) with the age group hospitalized from 12-24 months accounting for the highest proportion (47.5%) and the age group <12 months accounting for 30.0% [3]. Regarding educational level, there are 101 cases with high school level accounting for 50.5%, the lowest level being intermediate, college, and university level accounting for 1%. Our research is similar to Mr. Do Quang Thanh's research (2020) with the highest proportion of the high school group accounting for 50.7% and the lowest proportion of the elementary school group accounting for 2.1% [4]. In terms of occupation, the majority of childcare workers are workers, civil servants (29%), and housewives (28.5%). Our results are different from Do Quang Thanh's research (2020), the housewife group accounts for 34.3%, higher than the group of workers and officials at 22.9% [4].

We recorded the diet in the first 6 months, the exclusively breastfed group accounted for 110 cases (55.0%) and the group who were not exclusively breastfed accounted for 90 cases (45%). In Do Quang Thanh's study, only 3.2% of children were exclusively breastfed for the first 6 months and 96.8% of children were not exclusively breastfed [4].

We recorded that the number of days of onset <=72 hours before admission accounted for 89.5%, and the number of days of onset >72 hours accounted for 10.5%. The results of our study are similar to the study of Nguyen Kim Thu (2016), the onset date <=72 hours accounted for 81.1%, higher than the time before hospitalization >72 hours accounted for 18.9% [5].

Regarding the reason for admission to the hospital, we recorded fever as the reason accounting for the highest rate (95.5%), followed by startle at 6.0%. Similarly, according to the Tang Chi Thuong study, 90.7% of children were hospitalized due to fever, and 74.5% due to startling [6]. In addition, Che Thanh Doan's research also noted that the majority of children were hospitalized due to fever (88.9%), and less common reasons such as rash (7.4%) [7]. This shows that fever and startle are the two leading reasons that family members bring children to the hospital for examination and hospitalization [8].

4.2. Some factors related to the severity of hand, foot, and mouth disease

Regarding age group factors, our study found that children in the age group >12 months with severe HFMD were 15.1% higher than the risk of severe HFMD in the age group <12 months (7.1%). However, this difference is not statistically significant (p>0.05). Some studies report a high rate of severe HFMD in any age group, which is different from our results such as Nguyen Kim Thu's study [5], the majority of hospitalizations (97.7%) from under 5 years old (60 months), of which under 3 years old (36 months) accounts for 88.4%, the hospitalized age group from 13 to 24 months accounts for the highest rate (42.6%). However, when studying the distribution of severe disease (from grade 2b and above) by age, Nguyen Kim Thu's research shows that severe disease occurs at a rate of over 20% and is almost equivalent in all age groups. We also show similar results with Thai Quang Hung's study [5] the age group with hand, foot, and mouth disease is mainly under 5 years old, especially the age group from 1 to 3 years old accounts for the highest rate (accounting for 61,000). first%). The explanation for the distribution of diseases by age has two main factors, the first is that children receive antibodies from their mothers in the early stages of life, this influence can affect the risk of disease and can also affect the disease.

affects the ability to fight disease. The second factor is the development and improvement of the child's immune system [9].

Regarding gender factors, male children have a higher risk of severe HFMD (14%) than female children (13.9%). However, this difference is not statistically significant (p>0.05). The results of Thai Quang Hung [8] showed that the ratio of hand, foot, and mouth disease in men/women, respectively by year, was 1.29; 1.53; 1.57 and 1.45 are correlative evidence with our actual observational data as well as those of other authors. Research results by Do Quang Thanh [4] also show that men account for a higher proportion than women with a sex ratio ranging from 1.44 to 1.84. Vi Ngoc Linh's results [3] showed that there were 79 male children (65.8%) and 41 female children (34.2%), the male/female ratio was 1.9/1. Some hypotheses are that boys are often more active than girls, so in the same space where there is a source of infection, boys will be more likely to be exposed to the source of infection and at a higher risk of getting sick, which means This may explain why the incidence of the disease in male children is higher in HFMD cases in general[10]. However, this hypothesis cannot explain severe cases. More research is needed to better understand the relationship between gender and severe illness[10].

Evaluating children's diets, research has shown that the rate of incomplete breastfeeding in the first 6 months in children with severe HFMD is 15.6%, higher than in children exclusively breastfed in the first 6 months. 12.7 %, however this relationship is not statistically significant (p > 0.05). This is equivalent to research by author Thai Quang Hung [4] in which children who are not exclusively breastfed in the first 6 months from birth are 7.83 times more likely to have severe HFMD (95% CI from 1, 01 to 3.46) compared to children who are exclusively breastfed and research by Do Quang Thanh [5] evaluating children's diet, the study has shown that the rate of exclusive breastfeeding in the first 6 months is very low at only 3.2%. Up to 79.6% of babies are exclusively fed formula milk in the first 6 months.

Regarding the education level of the primary caregiver, our study recorded that 16.5% of children with severe HFMD had caregivers with an educational level of high school or higher, compared to children with caregivers with higher education levels. primary/secondary school level, however this result is not statistically significant (p > 0.05). However, Thai Quang Hung's research contradicts ours, showing that the mother's education level is related to the severity of HFMD[8]. Children in the group of mothers with low education (illiterate or primary school level) have a higher risk of severe HFMD than children in the group of mothers with education from secondary school or higher (OR Mc Nemar = 3.40, CI 95 %: 1.20 - 11.79). Hand, foot and mouth disease is an infectious disease caused by a virus. Most HFMD cases are mild, so proper care of sick children is extremely important in terms of disease prevention for the community as well as minimizing complications for the children themselves.

Regarding white blood cell count, we found that pediatric patients with white blood cell counts >=16x1G/l have a 3.9 times higher risk of severe disease than children with white blood cell counts <16x1G/l (p = 0.001).). This result correlates with Nguyen Kim Thu's study [5] on the relationship between WBC count >=16x1G/l and severe disease with p < 0.05 and OR= 1.5. However, the results of Vi Ngoc Linh [3] are opposite to ours, 55% of patients had white blood cell increase > 12x1G/l, white blood cell count > 16x1G/l was lower than 45% and had no relation. to the severity of HFMD in this study. Perhaps the

increased number of WBC in HFMD is related to the inflammatory response. The sicker the patient, the greater the inflammatory response and the increased BC.

Regarding platelet count, the study results also showed that there is an association between platelet count and severe disease with OR = 8.222 and p = 0.001. We correlate with Nguyen Kim Thu's study, the relationship between platelet count and severe disease with OR = 2.2 and p < 0.05[5]. In testing the association by Do Quang Thanh [4], it was noted that increased severity of hand, foot, and mouth disease was associated with increased platelets >=400x109/l in the blood, the result was statistically significant with p < 0.05. and OR = 1.01, Perhaps like in leukocytosis, the mechanism causing thrombocytosis is due to the inflammatory response[9]. This result is statistically significant for us, which shows that children with hand, foot, and mouth disease have a strong inflammatory response that stimulates the number of neutrophils and platelets in the body to proliferate to fight back.

V. CONCLUSION

Factors such as white blood cell count (p = 0.001) and platelet count (p = 0.001) were statistically significant in the severity of hand, foot, and mouth disease (p < 0.05). There is no relationship between age group, gender, diet, education level, number of days of onset, and initial treatment with the severity of HFMD.

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