



# Analysis of the Epidemiologic Characteristics of Children with Hand, Foot and Mouth Disease in China

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## Abstract

**Background:** We aimed to investigate the epidemiological characteristics of hand, foot and mouth disease (HFMD) and provide recommendations for its control and prevention.

**Methods:** A descriptive epidemiological analysis was designed for HFMD in children through direct network report from 2015 to 2019.

**Results:** From 2015 to 2019, a total 27,395 HFMD cases were reported at Infection Clinic of Shanghai Children's Hospital, Shanghai, China, accounting for 79.24% of the number of reported notifiable infectious disease cases (34,573). The cases number increased since May and reached a peak from June to September, then decreased from October to December with a second small peak in some years. The proportion of cases in boys is higher than in girls (59.7% vs. 40.3%). The cases number of stay-at-home children was higher in 2016 and 2018 (60.07% and 60.95%) than in 2019 (33.47%), and that of kindergarten children and students in 2019 (51.73% and 9.75%) was significantly higher than in other years. Overall, 22606 cases were reported in <5 years group, accounting for 82.52% of the total number of cases during 2015-2019. The proportion of the cases in 5-10 and >10 years groups increased year by year from 2015 to 2019, which is statistically significant. ( $\chi^2=71.105$ ,  $P=0.00$  ;  $\chi^2=78.413$  ,  $P=0.00$ )

**Conclusion:** The epidemiological characteristics of HFMD had changed during 2015-2019. Analysis of these data can provide helpful evidence to prevention and early treatment of the HFMD, and identification severe cases and handling the outbreaks.

**Keywords:** Hand; Foot and mouth disease; Epidemiological characteristic; Children

## Introduction

Hand, foot and mouth disease (HFMD) is an acute infectious disease in children caused by enteroviruses, characterized by hand and foot rash and oral mucosal herpes or ulcers. Due to the

large number of patients and a wide range of impacts, the disease has always been a key infectious disease monitored by health administrative departments and hospitals. The pathogens that



cause HFMD are a variety of enteroviruses, mainly enterovirus 71 (Ev71) and CoxA16, in addition, other enteroviruses were also isolated during the HFMD epidemic in Asia, Europe and America, including CoxA2, CoxA4, CoxA5, CoxA6, CoxA9, CoxA10, CoxA12, CoxA24, CoxB1, CoxB2, CoxB3, CoxB4, CoxB5, CoxB6, CoxB10, CoxB16, CoxB24, Echo-4, Echo-5, Echo-6, Echo-7, Echo-9, Echo-11, Echo-27, Echo-30 (1-3).

Different pathogens alternately prevalence in different spaces, times and populations. Since the introduction of the Ev71 vaccine in 2016, the epidemiological characteristics of HFMD have also changed. Therefore, monitoring the prevalence of HFMD and understanding the epidemiological characteristics of the affected population are important for us to make better prevention strategies.

This study describes and analyzes the epidemiological characteristics of HFMD cases in a Tertiary Children's Hospital in Shanghai from 2015 to 2019.

## Methods

### Data collection

Analyze the epidemiological characteristics of the cases of HFMD that diagnosed at Infection Clinic of Shanghai Children's Hospital during 2015-2019. The diagnose of HFMD was according to *Guidance for Preventing and Controlling the HFMD (2010)* by Ministry of Public Health, P.R.C. Data were checked on Disease Surveillance Information System of China CDC. Repeated cases were deleted.

his study was performed in strict accordance with the standards of the Ethics Review Committee of Children's Hospital of Shanghai (No.2022R 131-F01).

### Statistical Analysis

SPSS 19.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Chi-squared Test was used to compare the difference of constituent ratios. 5% p value ( $P < 0.05$ ) was defined as statistically significant

## Results

From 2015 to 2019, a total 27,395 HFMD cases were reported in our hospital, accounting for 0.26% of the total number of outpatients (10,480,416) and 79.24% of the number of notifiable infectious diseases cases (34,573) reported in the hospital.

In 2016, the number of cases of HFMD accounted for 82.98% of the number of notifiable infectious diseases cases, and 0.38% of the total number of outpatients, the highest in five years, followed by the number of cases in 2018, accounting for 79.03% of infectious diseases and 0.37% of the outpatients. The number of cases of HFMD in 2015 and 2017 accounted for 0.15% of the total outpatients, which was the lowest year. Analysis of the proportion of the number of HFMD cases in the number of outpatients in five years shows significantly statistic difference. ( $\chi^2=4298$ ,  $P=0.00$ ). Profile of reported cases of hand, foot and mouth disease at Infection Clinic of Shanghai Children's Hospital during 2015-2019 was presented in Table 1.

**Table 1:** Profile of reported cases of hand, foot and mouth disease in 2015-19

Year	Outpatients	Cases of Notifiable Infectious Diseases	Cases of HFMD	Proportion of HFMD cases in the Notifiable infectious disease cases	Proportion of HFMD cases in the outpatients
2015	1975549	4166	2932	70.38	0.15
2016	2100498	9737	8080	82.98	0.38
2017	2357309	5668	3543	62.51	0.15
2018	2312789	10732	8481	79.03	0.37
2019	1734271	6353	4359	68.61	0.25
Total	10480416	34573	27395	79.24	0.26

### Time distribution

To study the time distribution of the incidence of cases, the author firstly counts the monthly number of cases, and finds that the number of cases

increased significantly since May, and reached a peak from June to September, then decreased from October to December with a second small peak in some years, as shown in Fig. 1.

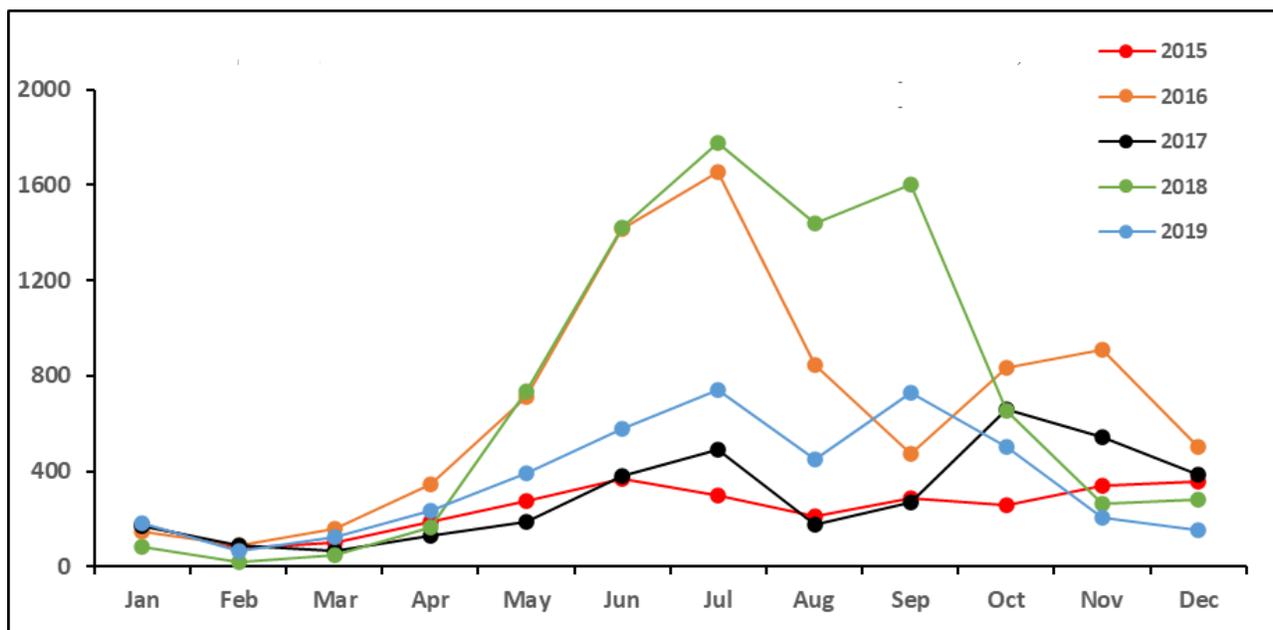


Fig. 1: Time distribution of the number of HFMD cases reported in Shanghai Children's Hospital during 2015-2019

Further statistics on the number of cases by quarter, found that the number of cases in the third quarter accounted for 41.77% of the entire year, followed by 27.48% in the second quarter and 24.94% in the fourth quarter and the least in the first quarter, accounting for 5.8%. There are significant differences in the incidence of each season in different years, Data has been shown in Table 2.

The number of cases during 2015-2017 was mostly in the fourth quarter (32.43-44.76%). In 2018 and 2019, the number of cases in the fourth quarter decreased significantly (14.08-19.71%) and the peak incidence occurred in the third quarter (44.12-56.74%).

### Gender distribution

There was no statistically significant difference in the gender composition ratio of cases in five

years ( $\chi^2=1.519$ ,  $P=0.823$ ). The proportion of cases in boys is higher than girls (59.7% vs. 40.3%).

### Occupation and household registration distribution

The majority of the HFMD cases admitted to the hospital were Shanghai household registration (93.87%), while cases of other cities household registration account for 5.53% while the cases of foreigners account for 0.59%. The proportion of cases with Shanghai household registration in 2019 (95.96%) was significantly higher than in 2015 (90.11%) ( $\chi^2=126.0$ ,  $P=0.00$ ). Combined statistics of cases of foreigners and other cities household registration also shows a significant difference in five years ( $\chi^2=47.78$ ,  $P=0.00$ ). Data has been shown in Table 3.

**Table 2:** Time distribution of onset of Hand, Foot and Mouth Disease

<i>Time period</i>	<i>2015</i>	<i>2016</i>	<i>2017</i>	<i>2018</i>	<i>2019</i>	<i>Five years total</i>	$\chi^2$	<i>p</i>
Jan	176(6.0)*	145(1.79)	172(4.85)	85(1.00)	183(4.19)	761(2.78)		
Feb	76(2.59)	88(1.09)	88(2.48)	16(0.19)	68(1.56)	336(1.23)		
Mar	99(3.37)	161(1.99)	64(1.81)	48(0.57)	124(2.84)	496(1.81)		
The 1 <sup>st</sup> quarter	351(11.97)	394(4.88)	324(9.14)	149(1.76)	375(8.60)	1593(5.80)	604.5	0.00
Apr	187(6.37)	344(4.26)	128(3.61)	165(1.95)	234(5.37)	1058(3.86)		
May	275(9.35)	714(8.84)	190(5.36)	737(8.69)	391(8.97)	2307(8.42)		
Jun	369(12.59)	1415(17.51)	377(10.64)	1424(16.79)	577(13.24)	4162(15.19)		
The 2 <sup>nd</sup> quarter	831(28.34)	2473(30.6)	695(19.62)	2326(27.4)	1202(27.99)	7527(27.48)	150.7	0.00
Jul	299(10.19)	1652(20.45)	493(13.91)	1774(20.92)	743(17.05)	4961(18.11)		
Aug	212(7.23)	843(10.43)	177(5.00)	1438(16.96)	449(10.3)	3119(11.39)		
Sep	288(9.82)	475(5.88)	268(7.56)	1600(18.87)	731(16.77)	3362(12.27)		
The 3 <sup>rd</sup> quarter	799(27.25)	2970(36.76)	938(26.47)	4812(56.74)	1923(44.12)	11442(41.77)	1469.5	0.00
Oct	259(8.83)	833(10.31)	660(18.63)	651(7.68)	503(11.54)	2906(10.61)		
Nov	338(11.53)	907(11.23)	543(15.33)	262(3.09)	203(4.66)	2253(8.22)		
Dec	354(12.07)	503(6.23)	383(10.81)	281(3.31)	153(3.51)	1674(6.11)		
The 4 <sup>th</sup> quarter	951(32.43)	2243(27.76)	1586(44.76)	1194(14.08)	859(19.71)	6833(24.94)	1464.2	0.00
Total	2932	8080	3543	8481	4359	27395		

\*Percentage of annual cases

According to occupation, the cases are divided to four groups: 1) stay-at-home children, (2) kindergarten children, 3) students and 4) other children, while the composition ratio had a significant statistical difference in five years (  $P=0.00$ . The number of cases of stay-at-home children was the

largest in 2016 and 2018 (accounting for 60.07 and 60.95% respectively) while only accounting for 33.47% in 2019. The number of cases of kindergarten children and students in 2019(51.73% and 9.75%) was significantly higher than other years (30.59% and 4.50% in 2016).

**Table 3:** Gender, Household Registration and Occupations distribution of HFMD Cases (2015-2019)

<i>Year &amp; No. of cases</i>	<i>Gender</i>		<i>Household registration</i>			<i>Occupation</i>			
	Boy	Girl	Shanghai	Other City	Foreigner	Stay-at-home Children	Kindergarten Children	Student	Other
2015 (n=2932)	1764 (60.16)	1168 (39.83)	2642 (90.11)	154 (5.25)	136 (4.64)	1576 (53.75)	1142 (38.95)	184 (6.28)	30 (1.02)
2016 (n=8080)	4833 (59.81)	3247 (40.19)	7525 (93.13)	547 (6.77)	8 (0.09)	4854 (60.07)	2472 (30.59)	364 (4.50)	390 (4.83)
2017 (n=3543)	2110 (59.55)	1433 (40.45)	3325 (93.85)	211 (5.96)	7 (0.19)	1797 (50.72)	1505 (42.47)	211 (5.96)	30 (0.85)
2018 (n=8481)	5079 (59.88)	3402 (40.11)	8041 (94.81)	428 (5.05)	12 (0.14)	5169 (60.95)	2469 (32.65)	539 (6.36)	4 (0.05)
2019 (n=4359)	2569 (58.94)	1790 (41.06)	4183 (95.26)	176 (4.04)	0	1459 (33.47)	2255 (51.73)	425 (9.75)	220 (5.04)
(n=27395)	16335 (59.7)	11040 (40.29)	25716 (93.87)	1516 (5.53)	163 (0.59)	14855 (54.23)	10143 (37.02)	1723 (6.28)	674 (2.46)

### Age distribution

Table 4 shows the age distribution. The onset age of HFMD in the hospital ranges from 0-16 years. Statistical comparisons were made in groups of 0-5 years, 5-10 years, and > 10 years. Overall, 22,606 cases were reported in the 0-5 yr group, accounting for 82.52% of the total number of

reported cases. There was a significant difference in the proportion of the cases in the 0-5 yr group from 2015 to 2019. The year with the highest proportion was 2015 and then it decreased year by year to only 77.24% in 2019. The proportion of the cases in 5-10 and >10 years groups significantly increased year by year from 2015 to 2019.

**Table 4:** Age distribution of reported cases of HFMD (proportion %)

Age (yr)	2015	2016	2017	2018	2019	Five years total	$\chi$	P
0-1	274(9.35)	596(7.38)	318(8.98)	751(8.86)	282(6.47)	2221(8.11)		
-2	820(27.97)	2186(27.05)	890(25.12)	2439(28.76)	945(21.68)	7280(26.57)		
-3	522(17.80)	1492(18.47)	588(16.60)	1458(17.19)	732(16.79)	4792(17.49)		
-4	630(21.49)	1484(18.37)	678(19.14)	1404(16.55)	837(19.20)	5033(18.37)		
-5	280(9.55)	1033(12.78)	446(12.59)	950(11.20)	571(13.10)	3280(11.97)		
0-5 group	2526(86.15)	6791(84.05)	2920(82.42)	7002(82.56)	3367(77.24)	22606(82.52)	124.08	0.00
-6	160(5.46)	518(6.41)	251(7.08)	548(6.46)	363(8.33)	1840(6.72)		
-7	64(2.18)	289(3.58)	133(3.75)	383(4.52)	234(5.37)	1103(4.03)		
-8	58(1.98)	132(1.63)	79(2.23)	165(1.95)	115(2.64)	549(2.00)		
-9	52(1.77)	126(1.56)	44(1.24)	105(1.24)	60(1.38)	387(1.41)		
-10	14(0.48)	96(1.19)	33(0.96)	83(0.98)	43(0.99)	269(0.98)		
5-10 group	348(11.87)	1161(14.37)	540(15.24)	1284(15.14)	815(18.69)	4148(15.14)	71.105	0.00
-11	22(0.75)	43(0.53)	26(0.73)	65(0.77)	57(1.31)	213(0.78)		
-12	12(0.41)	40(0.50)	24(0.68)	41(0.48)	34(0.78)	151(0.55)		
-13	6(0.20)	20(0.25)	11(0.31)	60(0.71)	48(1.10)	145(0.53)		
-14	12(0.41)	12(0.15)	15(0.42)	21(0.25)	19(0.44)	79(0.29)		
-15	4(0.14)	9(0.11)	4(0.11)	5(0.06)	7(0.16)	29(0.11)		
-16	2(0.07)	4(0.05)	3(0.08)	3(0.04)	12(0.28)	24(0.09)		
>10 group	58(1.98)	128(1.58)	83(2.34)	195(2.30)	177(4.06)	641(2.34)	78.413	0.00

### Discussion

HFMD is a common infectious rash disease in children. The incidence rate has always been the first among reported cases of infectious diseases. The affected population is mainly children. The symptoms include herpes-like rashes on the hands & feet and damage to the oral mucosa. Since the outbreak of HFMD in 2008, 2009-2015

is the peak period of research on HFMD. After 2015, the HFMD epidemic has entered a stable control stage and related literature reports have decreased. In 2016, the Ev71 inactivated monovalent vaccine developed in China was approved for marketing and application. After several years of vaccination, the epidemiological characteristics of HFMD have also changed. Dynamic monitoring of this common infectious disease in children

is necessary to understand the epidemic trend of the disease and provide supports for developing the prevention and control strategies to the infectious diseases.

This study conducted a retrospective statistical analysis of the epidemiological data of HFMD cases in Shanghai Children's Hospital from 2015 to 2019. A total of 27,395 cases were reported in 5 years, accounting for 0.26% of the total number of outpatients and 79.24% of the number of notifiable infectious diseases cases. HFMD has consistently ranked first among infectious disease cases in five years. Comparing this data with the relevant data from 2012 to 2014, the number of reported HFMD cases in the past 5 years has not shown an upward trend, but a fluctuating downward trend (4).

The analysis of the gender of the cases showed that the proportion of cases in boys (59.7%) was higher than that in girls (40.29%) in five years, which is consistent with the previous studies (4,5). A significant difference in the proportion of the cases in the 0-5 yr group was observed in this study, supporting the conclusion that the proportion of the cases in the 0-5 years group decreased year by year. Precious studies have counted the proportion of the cases in 0-5 years as well, with the results that it accounted for 82.48% during 2012-2014, 75.84% during 2015-2016, and 89.10% in 2012-2016 (6,7), which is consistent with this study. Different to the previous study, the number of cases showed a downward trend in the 0-5 years group, while an upward trend in the 5-10 and >10 years group (6). The data of this study more meticulously reflects the epidemiological changes of HFMD in the past five years.

In this study, we also analyzed the proportion of cases according to the occupation that was divided into stay-at-home children, kindergarten children, student, and other children. Surprisingly, the proportion of stay-at-home children's cases suddenly decreased in 2019, whereas the number of cases of kindergarten children and students in 2019 was significantly increased. Moreover, the HFMD cases of stay-at-home children and kindergartens children accounted for 61.42% and

33.67% respectively during 2015-2018, which is generally consistent with this study (8,9). Therefore, it can be concluded that the HFMD cases in different populations show different epidemiological characteristics in different years, which puts higher requirements on the prevention and control strategies of infectious diseases. The experience should be treated with caution.

The prevalence of HFMD is seasonal. This study shows that the number of cases increased significantly since May each year, and reached a peak from June to September, then decreased from October to December with a second small peak in some years. April to July was the peak season of the disease, which is slightly different from this study, possibly because the data were collected during 2008- 2014 (10,11). The seasonally epidemic peaks of HFMD in the early years are different from those in 2015-2019. Analyzing the cumulative number of cases by quarter, the study found that the number of cases in the third quarter was the largest, followed by the second quarter and the fourth quarter, and the least in the first quarter. Comparing the number of cases in each quarter in five years, there were significant differences in the incidence of each season in different years, which shows that the epidemic season of the disease is constantly changing in different years. The number of cases in 2015-2017 was the largest in the fourth quarter, while in 2018 and 2019, the number of cases in the fourth quarter of decreased significantly, and showed a significant peak in the third quarter. Podin et al reviewed the 7-year history of HFMD and proposed that the disease presents a periodic epidemically peak every two years (12).

Since this study involves 5 years, the analysis of data suggests the seasonal peaks of the epidemic alternate every year, the further continuously monitoring the data of HFMD cases is expected to obtain more accurate conclusions.

## Conclusion

The epidemiological characteristics of HFMD from 2015 to 2019 are as follows: Boys are infected more than girls are; mainly young children

are infected, but the number of cases over 5 years old tends to increase; The cases of stay-at-home children and kindergarten children account for the majority and the cases of kindergarten children tend to increase. The seasonal peaks of infections alternate every year. Continuously monitoring of HFMD is helpful to development of prevention and control policies and treatment of the disease.

## Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

## Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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