

Hand Foot Mouth Disease During the SARS-CoV-2 Pandemic: A Multicentric Study

ALPANA MOHTA,¹ SUMITI PAREEK,¹ MANOJ KUMAR SHARMA,³ ADITI AGGRWAL,¹ KAPIL VYAS,⁴ HARSHITA PANDEY,² SURESH KUMAR JAIN⁵

¹Department of Dermatology, Venereology and Leprology, Sardar Patel Medical College, Bikaner, Rajasthan.

²Department of Microbiology, Sardar Patel Medical College, Bikaner, Rajasthan.

³Department of Dermatology, Venereology and Leprology, Jhalawar Medical College, Jhalawar, Rajasthan.

⁴Department of Dermatology, Venereology and Leprology, Geetanjali Medical College, Udaipur, Rajasthan.

⁵Department of Microbiology, Government Medical College, Kota, Rajasthan.

Correspondence to:

Dr Alpana Mohta,
Department of Dermatology,
Venereology and Leprosy,
Sardar Patel Medical College,
Bikaner, Rajasthan 334 001.
dralpanamohta10@gmail.com

Received: Oct 13, 2022;

Initial review: Nov 18, 2022;

Accepted: Feb 17, 2023.

Objectives: This prospective observational study aimed to identify the current trend of the circulating viral strains responsible for hand foot mouth disease (HFMD) outbreak in four tertiary care centers in Rajasthan, amidst the coronavirus disease (COVID-19) pandemic (April-October 2022). **Methods:** Cases with suspected HFMD, presenting to our skin outpatient department were assessed clinically and serologically (IgM antibodies against coxsackie virus (CV) A6, A16 and enterovirus 71) for evidence of the disease. **Results:** We identified 718 new HFMD patients (161 adults) with peaks in May and August, 2022. Male:female ratio decreased with increasing age. Most children were asymptomatic. A total of 385/409 patients assessed serologically, were found positive, most commonly against CV-A6. **Conclusion:** Though HFMD typically affects young children, an unusually higher proportion of adults were affected during the current pandemic. There were some differences between pediatric and adult presentation of HFMD.

Keywords: Co-Infection, Picornavirus, Coxsackie virus.

Published online: Feb, 21, 2023; PII: S097475591600501

Hand, foot and mouth disease (HFMD) is a cutaneous viral infection that commonly affects children under 5 years of age. The disease is caused by enterovirus 71 (EV-71), coxsackievirus A6 (CV-A6) or coxsackievirus A16 (CV-A16). CVA6 is responsible for more severe dermatological manifestations than the other two viruses [1]. In the majority of cases, the disease is asymptomatic or has only mild symptoms, including vesiculation over hands, feet, and oral mucosa [2]. The non-pharmacological interventions implemented by the Indian Government, for prevention of coronavirus disease (COVID-19) transmission [3], has helped in reducing the incidence of not only COVID-19 but also other viral infections, including HFMD [1]. With subsidence of the pandemic, and gradual reopening of schools and other daycare centers, there have been reports of HFMD across the nation [4].

In this prospective observational study, we investigated the current trend of the circulating viral strains responsible for HFMD outbreak in four tertiary care centers in Rajasthan, amidst the COVID-19 pandemic. A secondary objective was to identify the differentiating

features between the disease in pediatric and adult population.

METHODS

This multicentric study, conducted between April and October, 2022, was initiated after obtaining approval from the institutional ethics committee from the involved centers. Cases with suspected HFMD, presenting to our dermatology and pediatrics outpatient departments were assessed for the clinical signs of the disease and were recruited after obtaining written informed consent. The diagnosis of HFMD was made in a patient having maculopapular or vesicular rash on their hands, feet, buttocks, or oral mucosa, with or without fever. Those having at least one of the following were diagnosed with severe HFMD: acute flaccid paralysis, myocarditis, encephalitis, pulmonary edema, pulmonary hemorrhage, cardiopulmonary collapse, aseptic meningitis, encephalitis, or death. Patients with underlying immunodeficiency, or concurrent presence of any other vesicular disease were excluded. Blood samples were collected for detection of IgM antibodies against Coxsackie virus A6 (CV A6), Coxsackie virus A16 (CV A16), and enterovirus 71 (E71).

Most of the samples were collected at the time of the two outbreaks in May, 2022 and August, 2022.

RESULTS

We identified 718 new HFMD patients (161 adult cases) with the first peak of cases in May, 2022 (27.6%), followed by another peak in August, 2022 (29.7%), with a slight rise again in September, 2022 (14.1%) (**Fig.1**). The clinicoepidemiological characteristics of cases are shown in **Table I**. We divided the cases into two groups according to age: Group A including cases under 18 years of age, and Group B including cases over 18 years. We observed that as the age increased, there was a linear fall in male to female ratio (**Fig. 2**).

Of the 161 adults with HFMD, 23 had a positive family history of HFMD (mainly in child members of the family). In 341 (61.2%) children and 29 (18%) adults, mild fever and constitutional symptoms appeared 24-48 hours before the onset of typical cutaneous and mouth lesions (**Table I**). Oral involvement was seen in the form of labial, palatal, buccal, and tongue lesions. The patients had varying degrees of the typical vesicular lesions on their hands, feet, elbows, or buttocks. Clinical features seen exclusively in children included upper respiratory catarrh in 10.5%, painful deglutition in 18.5%, and lethargy or irritability in 16.3% cases. For mild dehydration or high grade fever ($>39.4^{\circ}\text{C}$), 19 (3.41%) of children required hospitalization. Most admissions were done due to high grade fever. None of the hospitalized cases had any clinical signs consistent with meningitis.

Of the 409 patients whose samples were sent for, 385 cases were positive for IgM CV-A6, CV-A16 and EV-71 antibodies, most commonly detected viral antibodies were against CV-A6.

DISCUSSION

India has experienced a sudden resurgence of HFMD in the last six months, with the virus spreading to many cities

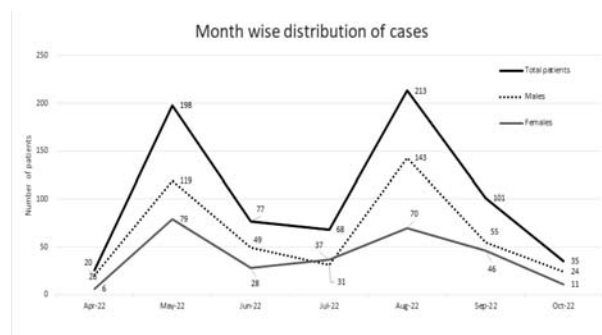


Fig. 1 Month-wise incidences of patients with hand foot mouth disease.

Table I Clinical Features of Patients With Hand Foot Mouth Disease, Rajasthan, April-October, 2022 (N= 718)

Clinical features	Age (≤ 18 y) (n=557)	Age (> 18 y) (n=161)
Involvement of buttocks	302 (54.2)	23 (14.3)
Acral	549 (98.6)	156 (96.9)
Mucosal	469 (84.2)	74 (46)
Associated symptoms		
Fever	341 (61.2)	29 (18)
Pruritus/burning sensation	202 (36.3)	128 (79.5)
Nail changes during recovery	9 (1.6)	1 (0.6)

All values are in frequency (%).

of the country [4]. Between 2009 to 2019, the epidemiological map of India [5] reported only 38 sporadic cases of HFMD from Rajasthan, depicting a significantly lower incidence of HFMD than what we observed during the pandemic outbreak. Though, HFMD is a contagious virus typically affecting young children, it rarely involves adults [6]. During the current outbreak, our study encountered a significant proportion of adult cases. This plethora of adult cases could perhaps be attributable to a viral mutation in the picornavirus family amidst the COVID-19 pandemic. Other peculiar features of our cases, which differ from the traditional clinical description of HFMD, were the involvement of buttocks in a large number of cases and presence of large bullous lesions, unlike the classical lesions of HFMD.

Though infection with EV-71, CV-A6 and CV-A16 are self-limiting, they may rarely lead to serious complications like aseptic meningoencephalitis [7,8]. We did not find any such case. We encountered 10 patients with shedding of nails or onychomadesis, as reported earlier [6].

Conventionally, HFMD cases tend to cluster between February and May [6]. We believe that since the COVID-19 outbreak took place from January to March, 2022, the upsurge of HFMD patients got delayed. COVID-19

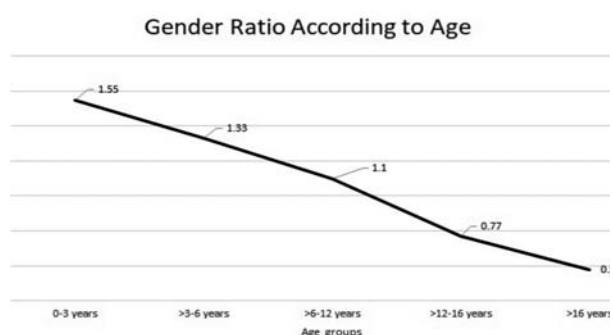


Fig. 2 Change in sex ratio of patients presenting with hand foot mouth disease with increasing age.

WHAT THIS STUDY ADDS?

- We report a sudden surge in cases of hand foot and mouth disease in both children and adults in Rajasthan, during the ongoing COVID-19 pandemic.
- Majority of cases were caused by coxsackie virus A6.

could cause genetic changes in the existing strains of these viruses. Considering the sudden resurgence of cases post-pandemic, it is advisable to perform genome sequencing on these strains to find out how it is currently different from its ancestral form.

Co-infections with SARS-CoV-2 and EV-71 are very likely to happen in the spring. Additionally, the HFMD and COVID-19 share routes of transmission including the hands-to-oral pathway and respiratory droplets. In this study, the highest frequency of HFMD was seen in cases between the ages of 0-3 years (38%). These findings are in concordance with previous reports [9]. Jiang, et al. [10] has raised concerns about children being infected with both COVID-19 and another viral infection, such as dengue virus, influenza virus and enterovirus. A report by Wu, et al. [11] also found that around half of children with COVID-19 also had another respiratory illness at the same time. Our study; however, did not assess the presence of co-infection with COVID-19.

Due to the absence of any existing literature, our study was limited by the absence of any comparison of the current outbreak from pre-pandemic outbreaks and outbreaks from other places during the same time.

In conclusion, our study highlights that there has been a sudden surge in cases of HFMD in both children and adults in Rajasthan during the ongoing COVID-19 pandemic. Surveillance programs are needed to identify the causes behind this spike and researchers, healthcare providers, and the medical community should play a vital role in enhancing public awareness, especially among mothers, to decrease or even prevent the incidence of future HFMD outbreaks.

Ethics clearance: SPMC ethics committee; No. F/SPMC/IERB/2022/2219 dated April 4, 2022.

Contributors: AM: concept and designed the study, analyzed data and drafted the manuscript; SP,MKS,AA,KV,HP,SKJ: collected the data and helped in data analysis. All authors reviewed and approved the final manuscript.

Funding: None; **Competing interests:** None stated.

REFERENCES

1. Bian L, Wang Y, Yao X, et al. Coxsackievirus A6: A new emerging pathogen causing hand, foot and mouth disease outbreaks worldwide. *Expert Rev Anti Infect Ther*. 2015; 13:1061-71.
2. Carmona RCC, Machado BC, Reis FC, et al. Hand, foot, and mouth disease outbreak by Coxsackievirus A6 during COVID-19 pandemic in 2021, São Paulo, Brazil. *J Clin Virol*. 2022;154:105245.
3. Weekly Epidemiological and Operational updates, October, 2022. Accessed Oct 23, 2022. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>
4. Farahat RA, Shaheen N, Kundu M, Shaheen A, Abdelaal A. The resurfacing of hand, foot, and mouth disease: Are we on the verge of another epidemic? *Ann Med Surg (Lond)*. 2022;81:104419.
5. Sharma A, Mahajan VK, Mehta KS, et al. Hand, foot and mouth disease: A single centre retrospective study of 403 new cases and brief review of relevant Indian literature to understand clinical, epidemiological, and virological attributes of a long lasting Indian epidemic. *Indian Dermatol Online J*. 2022;13:310-20.
6. Nelson BR, Edinur HA, Abdullah MT. Compendium of hand, foot and mouth disease data in Malaysia from years 2010-2017. *Data Brief*. 2019;24:103868.
7. Koh WM, Badaruddin H, La H, et al. Severity and burden of hand, foot and mouth disease in Asia: a modelling study. *BMJ Glob Health*. 2018;3:e000442.
8. Kimmis BD, Downing C, Tying S. Hand-foot-and-mouth disease caused by coxsackievirus A6 on the rise. *Cutis*. 2018;102:353-6.
9. Jiang FC, Yang F, Chen L, et al. Meteorological factors affect the hand, foot, and mouth disease epidemic in Qing-dao, China, 2007-2014. *Epidemiol Infect*. 2016;144:2354-62.
10. Jiang L, Wang J, Yu B, Ning C, Tan Y. Potential dual outbreak of COVID-19 and HFMD among children in Asia-Pacific countries in the HFMD-endemic area. *Biosaf Health*. 2021;3:129-30.
11. Wu Q, Xing Y, Shi L, et al. Coinfection and other clinical characteristics of COVID-19 in children. *Pediatrics*. 2020; 146:e20200961.