

## AN INVESTIGATION AND MANAGEMENT OF OUTBREAK OF HAND FOOT AND MOUTH DISEASE IN SOUTHERN INDIA

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### Abstract

**Introduction:** Hand foot and mouth disease (HFMD) is a viral illness that mainly affects young children is mostly caused by Coxsackie A16 or Enterovirus 71. In India, HFMD outbreaks are uncommon. The authors report an outbreak of HFMD in Wellington, Dist Conoor (Tamilnadu) India recently.

**Methods:** Based on clinical parameters a case definition was adopted. Cases were recorded on structured case investigation forms. Laboratory diagnosis was done by using Enterovirus PCR in 5' non coding region and nucleotide sequencing of VP1.

**Results:** 101 children with the clinical diagnosis of HFMD reported to the hospital within 17 days. The age ranged from 10 months to 11 yrs and 5 months. HFMD started with fever and common cold/ nasal discharge. Mouth sores were present in 69 (68.3%) children, multiple vesiculopapular rash with erythematous base were observed over hands and feet in 88 (87.1%) and 83 (82.17%) cases respectively. Of the 34 various types of samples collected, 18 were found to be positive for Coxsackie A16.

**Conclusion:** An epidemic of HFMD swept through Dist Conoor due to Coxsackie A16 which was controlled by adopting simple yet effective measures. Early diagnosis and awareness about this highly contagious disease can help prevent and contain an epidemic.

**Key words:** Hand foot and mouth disease (HFMD), Coxsackie virus A16, Enterovirus 71.

### Introduction

Wellington is a hill station in Conoor district of Tamil Nadu. The cohort population consists are 1459 children {445 (less than 5 year), 600 (between 5- 12 yrs) and 414 (more than 12 years)} in Wellington.

Recently, cases characterized by typical rash on hand, foot and mouth occurred amongst children. Nine cases in three days prompted an immediate and rapid investigation of the outbreak. In view of the typical rash and its location a probable diagnosis of Hand, Foot

and Mouth disease (HFMD) was made. The town was experiencing early winter conditions during this time. No outbreaks of HFMD have been recorded in Wellington in the past. Recently an epidemic of HFMD was recorded in Thane and parts of Mumbai. A Central Govt sponsored Enteroviral Research Institute team had isolated Coxsackie A6 in their sample <sup>[1]</sup>.

HFMD is caused by members of genus Enterovirus of the family Picornaviridae. Outbreaks of HFMD have been mainly caused by Coxsackie virus A16 (CAV16) or Enterovirus 71 <sup>[2,3,4,5,6]</sup>. This disease is highly contagious and spreads from person to person by direct contact, with secretions from the nose or mouth or from stool. Outbreaks of HFMD occur more frequently in summer and early winter <sup>[7, 8, 9, 10, 11, and 12]</sup>. Here we report another outbreak of hand foot and mouth disease caused by Coxsackie virus A16 in 101 children in Wellington, Tamil Nadu.

### **Methods: Investigation of the outbreak**

#### **Verification of the diagnosis**

#### **Case Definition**

The following case definition was adopted: ‘Presence of characteristic macular / papular / vesicular rash on limbs or buttocks with or without oral ulcers, fever, coryza, malaise or irritability <sup>[3,6,12, and 13]</sup>. Diagnosis of all cases was confirmed by the same pediatrician before being line-listed.

#### **Lab Confirmation**

Throat swabs, lesion swabs and voided stool samples were collected by virologists from Enteroviral Research Institute, Mumbai and Dept of microbiology of this hospital for identification of viral etiology of the disease. The samples were collected in viral transport medium and were transported in temperature controlled environment.

DNA was extracted using – QIAamp DNA Mini Kit from QIAGEN Diagnostics. Sequencing was carried out using ABI PRISM 3100 Genetic Analyzer which is a

multi-color fluorescence-based DNA analysis system using technology of capillary electrophoresis with 16 capillaries operating in parallel confirming Coxsackie A16 in 18 of 34 samples collected.

#### **Confirmation of outbreak**

No previous record of any outbreak of HFMD in Wellington was available. There was an apparent clustering of cases in time and place from one particular residential complex in Wellington. Hence, existence of an outbreak with potential to become an epidemic was confirmed.

#### **Population at risk**

Entire Wellington town was deemed to be at risk. As all cases were in the pediatric age group, entire pediatric population of the area was taken as the denominator. As per last census done in Jan 2010, there were 1459 children {445 (less than 5 year), 600 (5- 12 yrs) and 414 (more than 12 years)} staying in Wellington cantonment.

#### **Case finding**

##### **(a) Active surveillance for new cases**

General practitioners, school authorities and local hospitals were informed about the increased incidence of HFMD disease in the pediatric population of the town and survey was carried out in the areas reporting high incidence of cases. Later door to door campaign was launched. Self-reporting was encouraged by informing the population about the disease. All suspected cases were referred to our hospital for confirmation of diagnosis. Based on the cases reporting for treatment, an epidemiological case sheet was prepared for line listing of cases.

##### **(b) Search for more Cases**

School teachers were educated on early signs of the disease and proved a valuable resource for early diagnosis. Local authorities were also requested to encourage reporting of cases. House to house survey was carried out to educate the families and detect new or unreported cases.

## Results

### Time distribution of cases

A total of 101 children with the clinical diagnosis of HFMD reported to this hospital. The first case which reported had a history of travel to Kerala, endemic for HFMD [13]. The initial case had taken part in a carnival organized eight days prior in Wellington. Subsequently, most of the cases had attended birthday party of the elder sibling of the initial case. Among the 101 children 99 (98.01%) had mild HFMD. Only two cases (1.98%) were recorded as complicated HFMD. One case had aseptic meningitis and other was diagnosed as Viral Pneumonia.

The initial rise in the number of cases coincided with the 3 to 7 days incubation period of HFMD. Subsequent rise in number of cases is consistent with the pattern of a propagated epidemic (fig 1).

### Place distribution of cases

94 out 101 cases from of the cohort reported from various localities of the Wellington town.

### Person distribution of cases

**(a) Age:** The age range of the cases was from 10 months to 11 yrs and 5 months. 82% cases occurred in children 1 to 6 years of age (fig 2). No cases of HFMD were reported in adolescent or adult population.

**(b) Sex:** Out of 101 cases, 51 were female and 50 were male children (Male: female ratio- 1:1.02). There was no sex predilection for infection with respect to gender recorded in this study.

**(c) Clinical Features of Cases:** The disease started with prodromal symptoms like fever, coryza, cough, malaise, along with irritability. Common cold/ nasal discharge was observed in 54 (53.46%) cases with the mean duration of 7.09 days $\pm$  2.03. In 23 cases (22.77%) HFMD started with fever (mean duration of fever 2.65 days, SD 0.77). Cough was observed in 16 (15.84%) cases (mean duration 5.31 days, SD 1.92), Loss of appetite and irritability was observed in 30

(29.70%) and 37 (36.63%) respectively. The frequency of occurrence of various clinical symptoms and signs are presented in table 1.

**Characteristic of rash:** All HFMD patients had rash. Mouth sore were present in 69 (68.3%) children, whereas multiple vesiculopapular rash with erythematous base were observed over hand, foot, knee, buttock, groin and arms in 88 (87.1%), 83 (82.17%), 22 (21.7%), 23 (22.7%), 8 (7.9%) and 4 (3.96%) respectively. When lesions resolved, nail shredding or nail matrix arrest were observed in 11 cases (10.8%) and this was observed 23.7 ( $\pm$ 4.3) days after the crust formation of rash (Fig 3).

### (e) Secondary attack rates

Amongst 174 susceptible school children from one particular school (Primary section), 41 fell ill after the initial case. Thus the secondary attack rate (SAR) of HFMD in school contacts was 23.56%. Amongst the household contacts, 136 children were at risk among 84 families (children below 12 yrs) and 101 developed the disease. The SAR amongst household contact was 74.26%. This shows that HFMD is a highly infectious disease

### (f) Treatment

Except the two complicated cases all the other cases were treated symptomatically with paracetamol (acetaminophen), lactocalamine, and local anesthetic mouth paint. The first complication was of 11 month male child who developed bronchopneumonia with features of myocarditis. This child was treated with intravenous human Immunoglobulin (@ 400mg/kg/day for 5 days). The second complicated case was of a 3 year old girl who develops aseptic meningitis (CSF finding consistent with diagnosis), treated with supportive care only and did not face any complication so far (recovered without neurological deficit). No death was reported during the epidemic and/ or thereafter.

### Control measures

The source of infection was probably a case / carrier of infection in the Carnival organized on 23 Jan 2010 at Wellington. The few children who contracted the infection possibly spread it to other children due to close contact in their common school, playground, school bus and social interactions and confined places (eg. Birthday parties, Cinema halls, Clubs, etc). Given the high infectivity of the infection, the disease spread to all localities of Wellington station till the number of susceptible population decreased significantly and strict control measures were implemented (Figure 4).

The following control measures were instituted :

- (a) Schools in Wellington were advised to close for indefinite period till abatement of the epidemic.
- (b) All the classrooms, toilets, playground fixtures, school buses, etc were wiped / sprayed / fumigated with antiseptics containing phenolic compounds.
- (c) Parents, school teachers, local administrators and children were educated on modes of transmission, signs and symptoms and preventive measures of HFMD and were encouraged to report early any suspected case. Health advisory on the subject was issued to all concerned.
- (d) Personal hygiene measures like covering nose and mouth while coughing / sneezing, proper hand washing technique, avoiding touching nose / mouth / conjunctiva with fingers, etc were emphasized. Demonstrations for hygienic hand washing were given to all parents, teachers for implementation/ education of children.
- (e) Home Quarantine of affected children was followed.
- (f) House-to-house visits to increase case detection and suitable quarantine action

to prevent further spread of infection to susceptible contacts were advised.

- (g) Local health authorities were advised to implement preventive / control measures as above.

### Discussion

Hand Foot and mouth disease (HFMD) is a common acute viral exanthema that primarily affects infants and young children. The disease derives its name from the characteristic papular or vesicular lesions involving primarily the skin of the hand and feet and the buccal mucosa <sup>[2,3,4,5,6]</sup>. It usually starts with fever, irritability, and poor appetite. Within 2–3 days, painful sores develop in the mouth. A skin rash may develop shortly after appearance of the mouth sores, usually restricted to the hands and soles of the feet and occasionally on the buttocks, knees, or other areas. In most instances, this is a mild self-limiting illness, usually lasting for a total of 7–10 days <sup>[7,8,9,10,11]</sup>.

Hand-foot-and-mouth disease is caused by viruses of members of in the genus Enterovirus of Picornaviridae family. Outbreaks of HFMD have been mainly caused by Coxsackie virus A16 or Enterovirus 71. Some outbreaks have been associated with Coxsackie virus A10 and sporadic cases involving other enteroviruses like Coxsackie A4-7, 9, 10, B 1-3 and 5 serotype have been reported <sup>[12-12]</sup>.

The diagnosis of HFMD in India is not as easy as described, due to unawareness of this entity among clinicians and due to similarity with other common skin infections (e.g. mosquito bite, papular urticaria, Chicken pox etc.), rarity of the cases and spontaneous resolution of lesion without any specific treatment <sup>[14,15,16]</sup>. Generally the cases resolve spontaneously but complications do occur <sup>[17]</sup>. Confirmed laboratory diagnosis can be obtained by isolation of the virus in the cell cultures or by molecular methods such as real time

reverse transcriptase - polymerase chain reaction (RT-PCR) amplification of the viral <sup>[18]</sup>. In our study coxsackie A 16 was identified in stool, vesicular fluid, serum and throat swab samples collected during acute phase of the disease by virus isolation, PCR and sequencing.

In India, first reported outbreak was in Calicut, Kerala in 2003 due to Enterovirus 71 <sup>[13]</sup>. Since then many case reports and epidemics have been reported from different part of India including West Bengal <sup>[14]</sup>, Jorhat (Assam) <sup>[15]</sup>, Nagpur <sup>[16]</sup> and Mumbai (Maharashtra) due to Coxsackie A6 <sup>[13]</sup>. No laboratory diagnosis was attempted in the outbreaks reported from West Bengal and Jorhat, Assam failed due to unavailability of facilities <sup>[14,15]</sup>. Only one case out of four cases reported from Nagpur [16]. Coxsackie A16 has been isolated but till date no epidemic is reported caused by Coxsackie A16 from India except in our study

These published and unpublished reports suggest, India is no more a rare country to not have this highly contagious disease as previously thought. Although most of the cases of HFMD resolved without any significant complications, this is especially true in coxsackie A16, but HFMD can be fatal if caused by Enterovirus 71 <sup>[6,7]</sup>. Enterovirus 71 can lead to myocarditis, aseptic meningitis, encephalitis, pulmonary oedema and sometimes associated with acute flaccid paralysis. Clinically it is difficult to differentiate HFMD caused by Coxsackie virus to Enterovirus 71 hence identification of aetiological agent is necessary <sup>[6,7,17,19,20]</sup>.

### Conclusion

An epidemic of Hand Foot and Mouth Disease swept through Wellington area during recently affecting 6.92% of the total child population. The disease was due to Coxsackie virus A16. It resolved without many complications. The epidemic was controlled by simple measures that

prevented close contact with patients and personal hygiene such as closing of schools for the duration of incubation period, and repeated health education lectures, demonstrations to encourage healthy hygienic practices.

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Nil

### Conflict of interests

All authors have none to declare.

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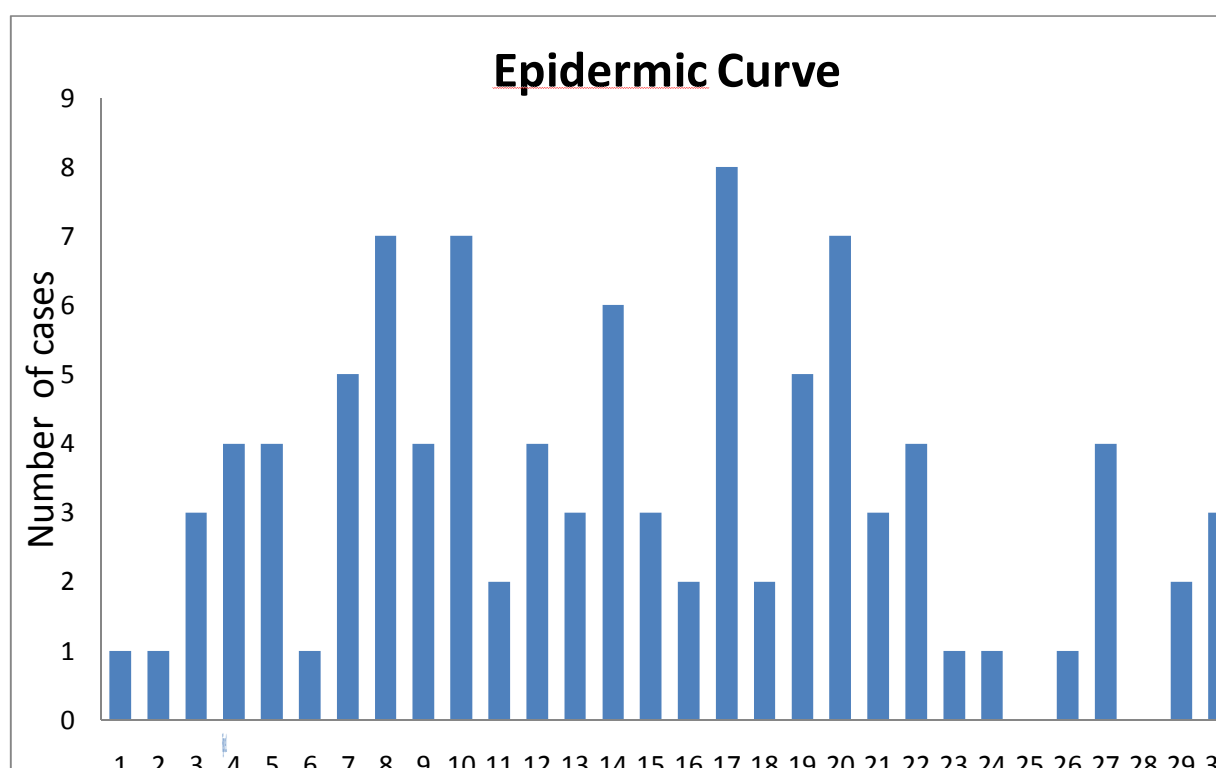


Fig 1. No of cases each day

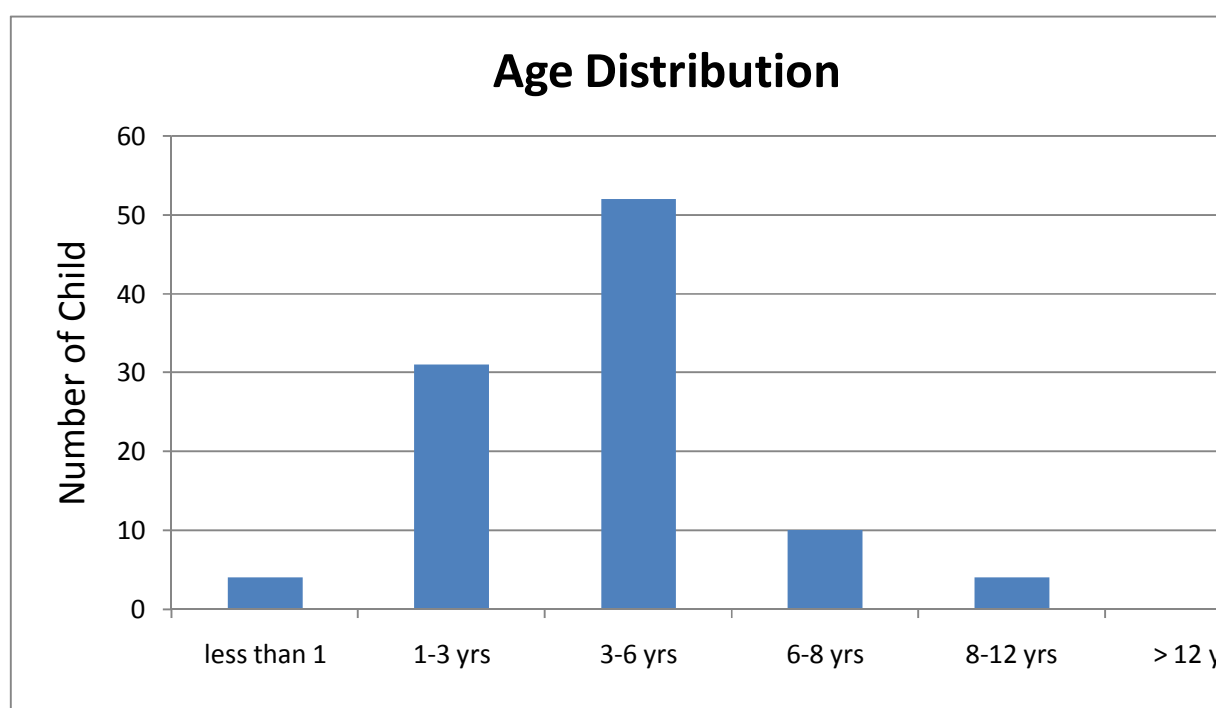


Fig 2. Age profile of cases



Fig 3. maculopapular rashes in hand (a), mouth (b), foot (c) and knee (d)

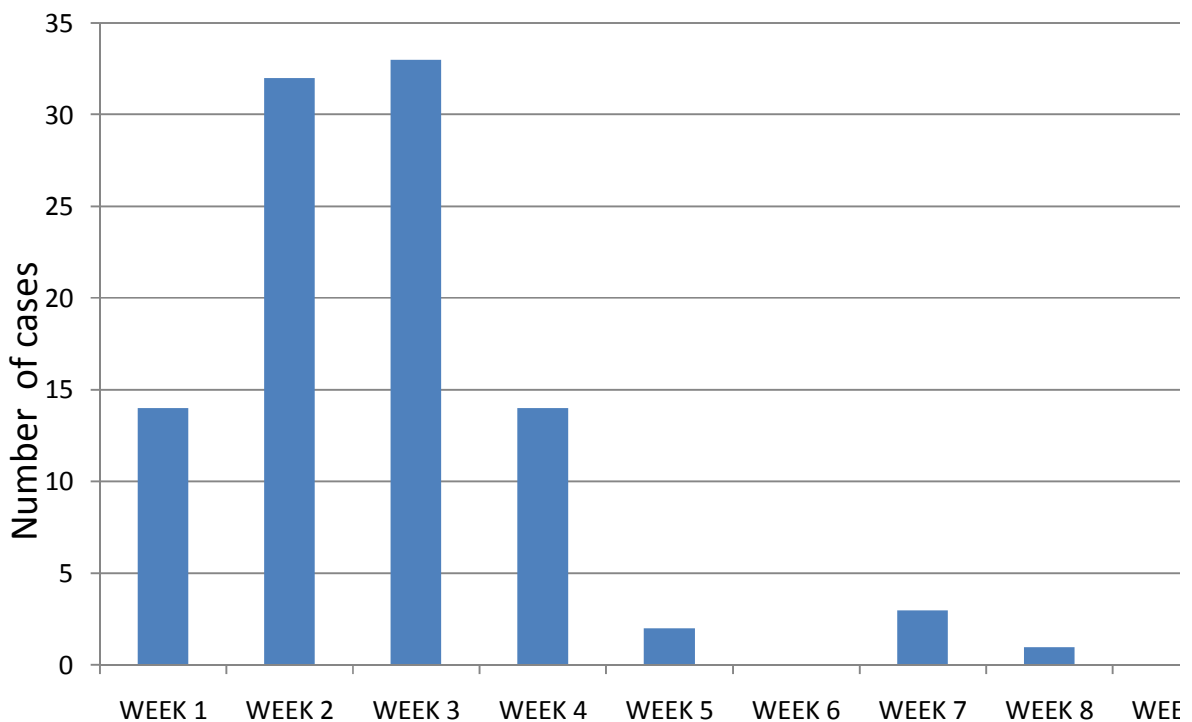


Fig 4. Effect of control measures over weekly incidence



**Table 1: Symptoms / Signs**

Symptoms and signs	Number of cases	Duration of Symptoms/ Sign (Mean and Standard Deviation)
Fever	23	2.65 Days (SD - 0.77)
Common cold/ Nasal discharge	54	7.09 Days (SD – 2.03)
Cough	16	5.31 Days (SD – 1.92)
Decreased intake	30	5.3 Days (SD – 2.12)
High grade Fever	04	3.25 Days (SD-1.5)
Irritability	37	4.72 Days (SD- 1.37)
Malaise	20	4.3 Days (SD- 1.49)
Vomiting	02	
Diarrhoea	02	
Pain abdomen	03	
Tachycardia	01	
Tachypnea	01	
None	26	