RESEARCH PAPER

Hand, Foot and Mouth Disease in the Andaman Islands, India

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Objectives: To investigate an outbreak of Hand, foot and mouth disease (HFMD) in Andaman Islands during 2013. **Methods:** Epidemiological, clinical data and samples were collected from HFMD patients who attended selected hospitals. Data were analyzed and samples were processed for detection of Enterovirus and further confirmed by sequencing. Serotype-specific molecular typing was also done to identify the etiological agent. **Results:** Of the 246 suspected patients, most were affected in August 2013 (92/246, 37.4%). Fever (71.2%) associated with typical HFMD rashes (100%) were the most common presenting symptoms and rashes were mostly distributed on hands (100%), legs (92%), mouth (77%), and buttocks (52.8%). All cases were reported as mild and recovered completely without any complications. Enterovirus was detected in 63 cases (50.4%). **Conclusion:** HFMD was mild, mostly reported in children <60 months of age, and in boys. Coxsackie virus A16 was found to be the only etiological agent for this specific outbreak.

Keywords: *Epidemiology, Coxsackievirus-A16, Rash.*

Hand, foot and mouth disease (HFMD) is characterized by rashes or vesicular lesions mainly on the hands, feet and mouth. It usually affects children, and is most commonly caused by Enterovirus-A (EV-A) species, including Coxsackievirus-A16 (CV-A16) and Enterovirus-71 (EV-71) [1]. Usually, HFMD caused due to CV-A16 is less severe disease as compared to that caused by EV-71 [2]. However, severe complications, including deaths have been reported rarely [3].

In India, outbreaks of HFMD have been reported from various places, including Kerala, Odisha**,** Himachal Pradesh and Uttarakhand [4-7]. Furthermore, there has been no published report on epidemiological and clinical features of HFMD in the Andaman and Nicobar (A&N) Islands, a remote group of islands in the Bay of Bengal. In 2013, cases of HFMD were reported from various hospitals in Port Blair. The present study aimed to explore the epidemiology, clinical characteristics and causative agents of HFMD in these patients.

Methods

It was a hospital-based, observational study on patients who were clinically diagnosed with HFMD at pediatric outpatient department in three selected hospitals (GB Pant Hospital, INHS Dhanvantri Hospital, and Chirayu Child Care Hospital) of Port Blair, the A&N Islands. The study was approved by the Institutional Ethical Committee, Regional Medical Research Centre (RMRC), Port Blair and the Directorate of Health Services (DHS) of the A&N Islands, India. Children presenting to these hospitals between August, 2013 and January, 2014 were included in the study. Additionally, a retrospective investigation was also done for the period from 29th May, 2013 to 30th July, 2013 to investigate and understand the epidemiology of the outbreak. The patients and their parents/guardians were interviewed using the standard virology case proforma available at RMRC that elicited epidemiological and clinical information about each case. With their consent, at least one of the possible samples *viz*. the external lesions swab, throat swab, nasal swab and stool were collected from patients for laboratory investigations. Patients were followed up till complete recovery of illness. The patient was considered as positive for laboratory tests if any of the specimens showed positivity.

Reverse-transcription nested PCR was performed to screen for the presence of enterovirus targeting 5'non-coding region (5'-NCR) [8,9]. Positive specimens were randomly selected for cDNA sequencing. Molecular evolutionary genetic analysis was done using MEGA 6 software [10]. Phylogenetic tree was constructed using the neighbor-joining method with bootstrap testing of 1000 replicates to estimate the stability of the

WHAT THIS STUDY ADDS?

- Hand-Foot-Mouth Disease outbreak due to Coxsackie virus A-16 with mild clinical course occurred in Andaman and Nicobar Islands in 2013.

phylogenetic tree. The evolutionary distances were computed using the Kimura 2-parameter method (K2P) as a method of nucleotide substitution. The closely related genetic distance of the study isolates was inferred by comparison with reference sequences, based on pair-wise genetic distance. Furthermore, all the positive enterovirus specimens were subjected for molecular typing specific to enterovirus serotypes *viz*. CV-A16, EV-71 and CV-A6 targeting partial *VP1* gene [11-13].

RESULTS

Out of 246 clinically diagnosed HFMD cases in the hospitals, 125 consented to participate in the study. Maximum (99.2%) cases were reported from South Andaman district. The peak of the outbreak was reached in the period from July to September, 2013 (203/246, 82.5%) with its highest peak in the month of August 2013 (*n*=92).

All 125 patients had characteristic rashes, including maculopapular rash (72%), papular rash (38, 30.4%), petechial rash (9,7.2%), erythematous rash (23, 18.4%), vesicular and pustular rash (40, 32%), or oral ulcer (97, 77.6%). Rashes were distributed most commonly on hands (125, 100%; predominantly on palms, dorsa of hand and elbows), followed by legs (115, 92%;), mouth (97, 77.6%), buttocks (66, 52.8%), trunk (25, 20%), and face and neck (16, 12.8%). Most oral lesions were observed in the palate (60, 61.9%), followed by buccal mucosa (48, 49.5%), lips (42, 43.3%), tongue (33, 34%) and gingiva (25, 25.8%).

Other clinical features recorded were fever (89, 71.2%), chills and rigor (4, 3.2%), cough (43, 34.4%), cold (20, 16%), coryza (16, 12.8%), sore throat (25, 20%), headache (4, 3.2%), abdominal pain (9, 7.2%), vomiting (6, 4.8%), diarrhea (4, 3.2%), malaise (87, 69.6%), anorexia (88, 70.4%), and pruritus (9, 7.2%). All cases were reported as mild; no severe complications/death were reported during the study period. The rashes completely resolved within a period of 2 to 3 weeks of onset in all patients.

Sixty-three (50.4%) children were detected to be positive for enterovirus infection. All enterovirus positive specimens subjected for molecular typing confirmed that CV-A16 was responsible for the specific outbreak in these islands during the study period. Phylogenetic analysis (***Web Fig.* 1**) showed that the study isolates of Andaman were closely grouped with reference sequences of mainland India (KT275250 and KT275251, K2P=0.008%), followed by Malaysia (JQ746672 and JQ746678, K2P=0.018%).

DISCUSSION

In this report, we documented an outbreak of HFMD with its epidemiological and clinical features in Andaman and Nicobar islands. All cases were mild, and Coxsackievirus-A16 was the causative agent.

The study represents the patients reported to the referral hospitals at South Andaman district only. The actual number of cases during the outbreak is likely to be much higher as many patients with mild disease may not have reported to the hospitals.

Like many other studies where HFMD outbreaks were seen mostly in summer and fall [1], the peak of the outbreak in Andaman Islands was also seen in the month of August with the similar seasonal pattern. In the present report, with respect to the involvement of oral mucosa, the number of lesions were more on the palate region unlike an earlier report [6] from Shimla, India, where buccal mucosa was the most common site (82.9%) followed by palate. Most of the signs and symptoms in our series were almost similar to most other reported studies from India [4,6]. However, a report from Southern India documented HFMD with severe complications such as aseptic meningitis and acute encephalitis syndrome in 12.3% of the total cases [14]. The causative agent CV-A16 of the present outbreak was also commonly reported from other parts of the country [15]. The probable reason of emergence of this disease in Andaman islands could be the influx of tourists from mainland India to these Islands.

Being one of the new illnesses, HFMD is also a threat to public health of Andaman population, especially to the children. Surveillance and public health awareness would help to keep the infection localized to prevent future outbreaks.

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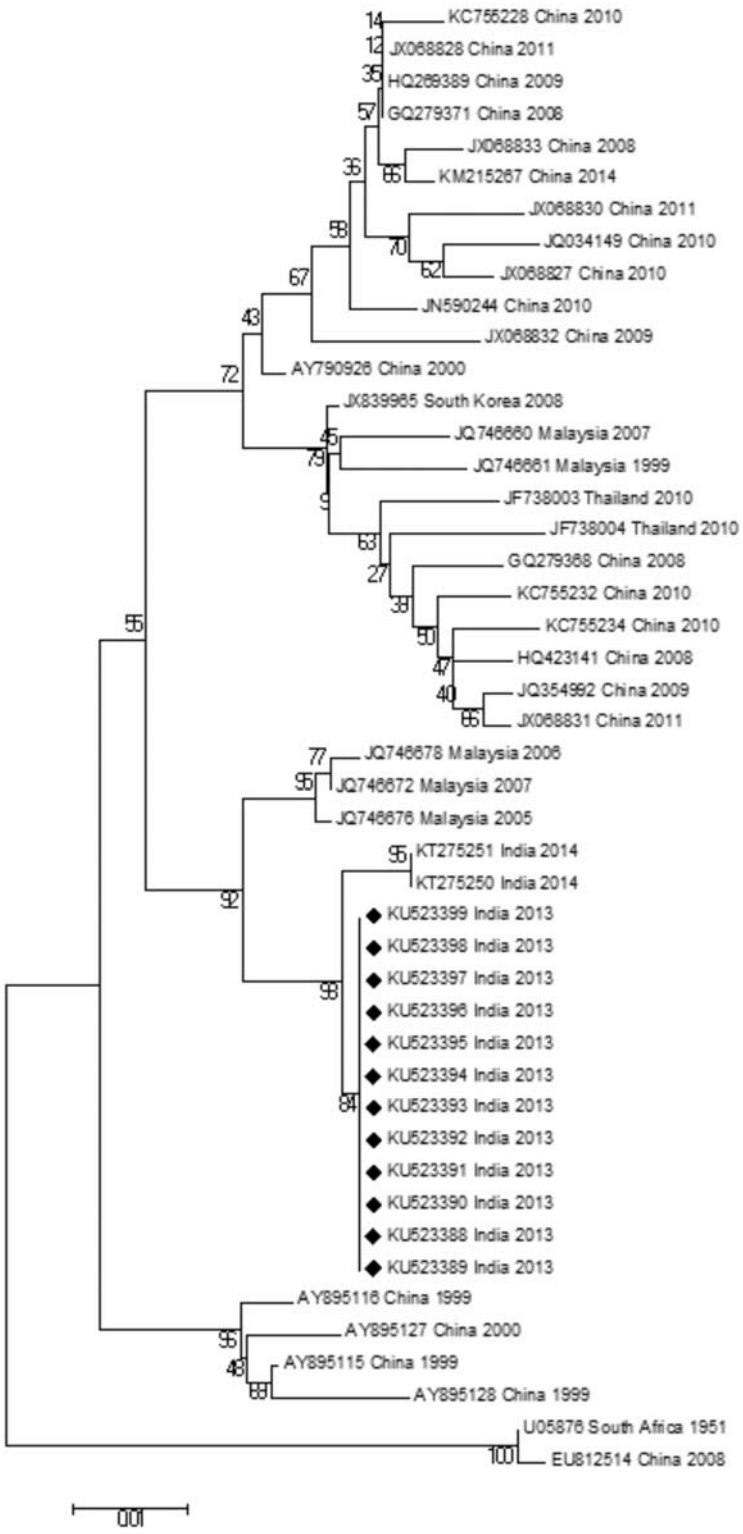

***WEB FIG.* 1** *Phylogenetic trees of partial 5'-NCR (396 nt) sequences of CV-A16 showing the genetic relatedness between isolates of Andaman (GenBank accession numbers of partial 5'NCR: KU523388 – KU523399) and intra-serotype reference sequences. Neighbor-Joining tree was constructed using MEGA 6 software with the bootstrap testing of 1000 replicates. The evolutionary distances of the nucleotides were computed using the Kimura 2-parameter (K2P) model as a method for nucleotide substitution.*