

Largest outbreak of hand, foot and mouth disease (HFMD) in India at an altitude of 3524 meters (11,562 ft.) in Leh, Union Territory (UT) of Ladakh, India 2016

Abstract

Introduction: There is an increasing occurrence of Hand, Foot and Mouth Disease (HFMD) in India, Asia, and Australia. The largest ever outbreak in India is discussed in this paper. The geographic location of the case control study was in Leh province which has an average altitude over 3,000 meters (11,000 feet).

Objective: This case control study, and review was done to determine if there is evidence of an increase in HFMD. There is concern that the increase of HFMD will lead to an increase in the number of attributed deaths.

Methods: District Surveillance Unit (DSU) collected the data on a daily basis upon presentation of symptoms. The unit was comprised of: an epidemiologist, a pediatrician, and a District Health Officer (DHO).

Results: There were four hundred and sixty-five confirmed cases of HFMD recorded in the study. Two hundred and sixty-one, 56%, of the cases were male. Two hundred and four, 44%, of the cases were female. The majority of cases affect children ages less than 5.

Discussion: HFMD is usually a childhood disease. Adults who contract the disease are most often caregivers. HFMD is caused by a virus, most often one of the picornaviruses belonging to serotypes EV-A or less frequently the enterovirus EV-A71. EV-A71 infections may more often result in severe complications or death.

Conclusion: Healthcare professionals and government oversight agencies must be vigilant in the detection and control of HFMD outbreaks. Appropriate protocol and incident reporting needs to be standardized.

Keywords: oral poliovirus vaccine, inactivated poliovirus vaccine, ribonucleic acid, Hand Foot Mouth Disease

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Abbreviations: DHO, district health officer; HFMD, hand foot mouth disease; RNA, ribonucleic acid; IPV, inactivated poliovirus vaccine; WBC, white blood count

Introduction

India as a country is prone to Hand-Foot-Mouth Disease (HFMD) outbreaks. This may be due to poor and inadequate hygiene, overcrowding, and limited access to healthcare. The disease affects primarily young people. There is not a commonly available vaccine nor antiviral treatment available to treat HFMD.¹ There are two vaccines approved for use in China in 2015 and early 2016.² The vaccines though recently available, are not included in National Immunization Program. HFMD is predominantly transmitted by direct contact with mucus, saliva or fecal material. Its occurrence is most prevalent during the summer and fall months. The preponderance of cases is reported in children age five and less. There is concern among medical professionals that more virulent serotypes of the virus will result in increasing numbers of severe complications. Most of the time infected individuals recover in about two weeks.

HFMD is caused by an Enterovirus. Enteroviruses are single positive-stranded ribonucleic acid (RNA) viruses called Picornaviridae. Enteroviruses are classified based on the homology within the RNA region coding for the VP1 capsid protein. Recently, new enterovirus serotypes have been characterized by molecular methods, bringing the number of known serotypes to more than 100

within 12 species,³ including polioviruses, coxsackievirus A2 (CV-A2), CV-A3, CV-A4, CV-A5, CV-A6, CV-A7, CV-A8, CV-A10, CV-A12, CV-A14, CV-A16, these were formerly designated as coxsackie group. Historically polio (poliomyelitis) was the major disease caused by an enterovirus. Some researchers believe that widespread polio vaccinations have led to an increase in the instances of HFMD. "There is no normal enteric virus flora; usually only one type of enterovirus multiplies within the intestines of an individual at any given time. Polio vaccinations have eliminated polio viruses from the gut, thereby increasing the chances of enterovirus viral and echoviral infections".⁴ Most of the world uses oral poliovirus vaccine(OPV).⁵ The United States has used the inactivated poliovirus vaccine(IPV) since 2000.⁶ It is interesting to note that there has not been a death due to HFMD in the United States since the IPV has been in use.

The chief symptoms of HFMD include one or more of the following: fever, sore throat, ulcers in the oral area, headache, loss of appetite, and skin rash. A patient with HFMD may experience only rash or mouth sores. Most complications from HFMD are mild. Severe complications occur more often with EV-A71 virus. A small proportion of HFMD patients develop neurological complications that can lead to death. The complications include but are not limited to: encephalitis, acute flaccid paralysis, myocarditis, pulmonary edema or death.⁷ Severe cases are defined as having at least two of the following symptoms: continuous high fever, weakness, vomiting, irritability, etc., abnormal White Blood count (WBC), high blood glucose level, and or poor circulation in the limbs.⁸

There has been a steadily increasing number of documented reported HFMD cases in Asia and Australia since 1997. In 1997, 34 children died in an outbreak in Sarawak, Malaysia. In 1998, an outbreak occurred in Taiwan. There were 405 reported cases with severe complications resulting in 78 deaths of children. In 2006, seven people died from an outbreak in Kuching, Sarawak. In April of 2007 there were 688 cases reported in Singapore. In May of the same year over 30 cases were reported in Maldives. In March of 2008, an outbreak occurred in Fuyang, Anhui, China. There were 25,000 reported cases and 42 deaths by May 13. Other outbreaks occurred in Singapore, more than 2,600 cases were reported by April 20th, 2008. Vietnam reported 2,300 cases and eleven deaths. 1,600 cases were reported in Mongolia during the same time period.⁸ In 2003, Calcutta, India experienced an outbreak of papulovesicular lesions on skin and in oral mucosa in children from October to November. The NCID investigated the outbreak. All 81 children recovered within one to two weeks. The Journal of Indian Pediatrics reported an outbreak of HFMD from July to August, 2013.⁷ In 2015, the National Medical Journal of India, reported an outbreak of HFMD from the hills of northern India. The report was from a tertiary teaching hospital in northern India.¹

Methods

This outbreak investigation was a case control study, it was active surveillance where data was collected from the affected zone. Data was analyzed and then recommendations were given to the affected community(-ies) so they could take preventive measures in to hopefully prevent spread of the disease. The District Surveillance Unit (DSU) collected data on daily basis. The unit was comprised of: an epidemiologist, a pediatrician, and a District Health Officer (DHO). The DSU was located in district Leh, and is part of the Integrated Disease Surveillance program (IDSP) unit Kashmir, India. The line listings of cases were entered in excel sheet format for further analysis of gender, age and location. The daily surveillance continued until the outbreak declined. The data collection began in April and continued through June of the same year. The diagnosis of HFMD was done on clinical presentation of the disease. The State Surveillance Officer (SSO) visited the affected area during the outbreak. The SSO monitored the situation and the collection of data.

Results

Data was examined on the basis of age, location, gender and dates. The age analysis is as follows: 354, 76%, of the HFMD cases occurred in children age five and under eleven children, that is 2%, were under the age of a year, had confirmed cases of the disease, and 93 cases, 20%, occurred in children less than two years of age and more than one year of age. 18%, that is, eighty-three cases occurred in children between the ages of two and three. 52 of the confirmed cases, 11%, were children were between the ages of three and four. 13%, or 60 cases occurred in children between the ages of four and five. 55, or 12% of confirmed cases of the disease were reported in children between the ages of five and six. 95% of the total HFMD cases occurred in children eight years of age and younger. 87 children, 19%, of the reported cases occurred in children between the ages of six and eight. 8%, 37 cases were children six years of age. 6%, 27 of the children were seven years of age. 23, 5% of the HFMD cases were eight years of age. It is thought that the childrens' immune systems are not fully developed, and this may be part of the reason HFMD is more prevalent. Children also are not conscious of the need for cleanliness and personal space. 21 cases, 4.5% of the reported cases occurred in children between the ages of nine and twelve. This accounts for 99%

of all reported cases of HFMD. Three adults, 1%, ages 23, 26 and 32 contracted HFMD. Refer to Figure 1.

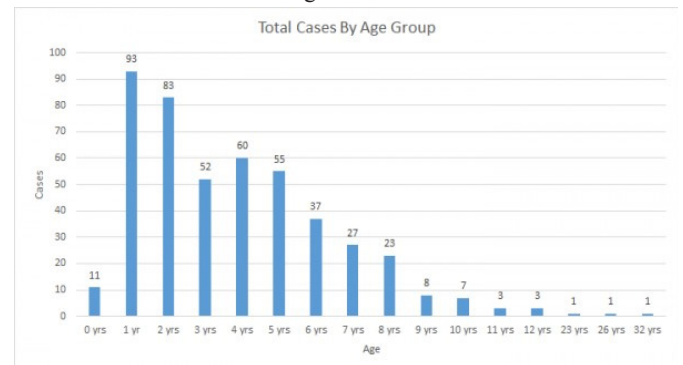


Figure 1 Cases by age.

Geographic location was evaluated and the following results recorded. 62% or 287, of the reported cases occurred in 46 locations. 47 cases (10%) occurred in one location, Choglamsar. 30% of the cases occurred in nine locations, including Choglamsar. Frequency of occurrence ranged from 47 to nine cases in the nine locations. A total of 51% of the HFMD cases occurred in 23 locations. An additional 50 (11%) cases occurred in 23 locations.

The remaining 187 (38%) cases were reported with a rate of one per location. These areas were more populous. Refer to Figure 2.



Figure 2 Cases by location.

There were 465 confirmed cases of HFMD recorded in the real-time data study. 261, 56%, of the cases were male. 204, 44%, of the cases were female. See Figure 3: Gender Distribution.

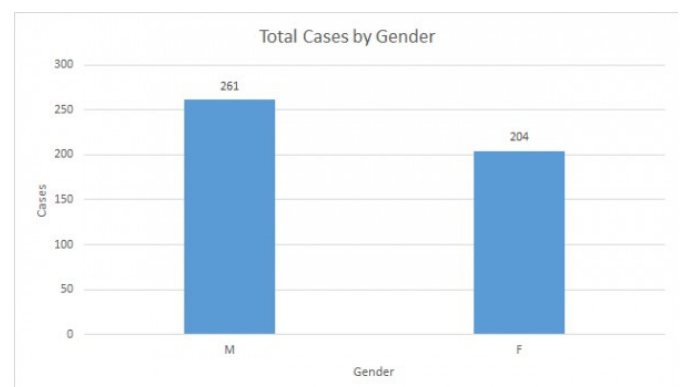


Figure 3 Cases by gender.

A comparison was also made between the male to female ratios in selected locations. The locations chosen had four or more confirmed cases of HFMD. 303 of the total 465 cases were included. 164 of the reported cases were males. That is 54% of the total. There were 139 female cases (46%). Two adult HFMD cases included in the data that is 6%.

There were a total of three adult cases in the entire study, this is .6% of the cases. 303, 67%, of the total 465 cases. In the comparison of the total sex ratio, there were 54% of males in the select group as compared to 56% in the total analysis. The select group had 46% female cases as compared to 44% of the entire study. There appears to be a consistent trend between the number of males versus female incidences of HFMD. Refer to Figure 4 & 5.

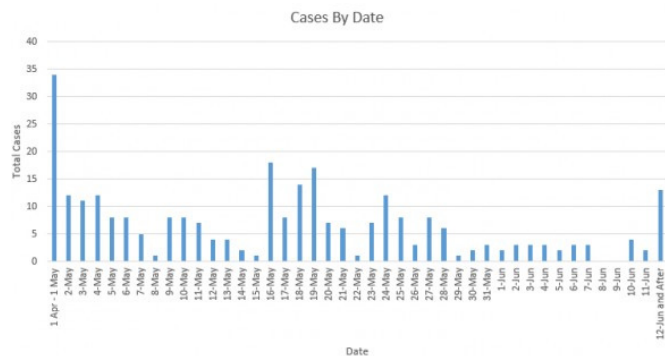


Figure 4 Cases by date.

Location	Number	# of Males	% Male	# of Females	% Female
Chogamansar	47	27	57	20	43
Thaksay	16	8	50	8	50
Chuchot	13	9	69	4	31
Sakli	12	7	58	5	42
Unreported	12	6	50	6	50
Matho	11	5	45	6	55
Stok	11	2	18	9	82
Leh	10	7	70	3	30
Igloo	9	7	78	2	22
Bango	8	4	50	4	50
Islamia Public School	8	1	12.5	7	87.5
Nimoo	8	6	75	2	25
Phyang	8	4	50	4	50
Dalhi Public School	7	5	71	2	29
Hamsa	7	6	86	1	14
Housing Colony	7	5	71	2	29
Nepal	7	6	86	1	14
Shry	7	1	14	6	86
DPS	6	1	17	5	83
Slava	6	2	33	4	67
Sharbatan	6	4	67	2	33
Spituk	6	2	33	4	67
Chernalay	5	3	60	2	40
Ladakh	5	2	40	3	60
Nery	5	4	80	1	20
Skatzangling	5	4	80	1	20
Skampai	5	4	80	1	20
Tangtse	5	1	20	4	80
Zanskar	5	4	80	1	20
Colony	4	0	0	4	100
Liker	4	3	75	1	25
Martselang	4	3	75	1	25
Moravian Mission School	4	1	25	3	75
Nubra	4	2	50	2	50
Nurla	4	1	25	3	75
Skindyang	4	2	50	2	50
Solar Colony	4	3	75	1	25
Wanta	4	2	50	2	50
TOTAL	303	164	54	139	46
Total HFMD	465	261	56	204	44

Figure 5 Ratio comparison of Male/ Female numbers in selected locations.

Photographs showing the presentation of the pathogen HFMD: (Figure 6 & 7)



Figure 6 Virus outbreaks on a child's hand.



Figure 7 Virus outbreak in a child's mouth.

Discussion

The increase in the rate of HFMD may be attributed to the limited access to healthcare and inadequate hygiene. HFMD is most often a childhood disease. Adults who contract the disease are usually caregivers. Most of the children who contract HFMD recover with few or minor problems. HFMD is caused by a virus, often of the less virulent serotypes EV-A or less frequently the enterovirus EV-A71. There is great concern that the occurrence of EV-A71 is increasing. EV-A71 infections may result in severe complications that lead to some type of disability or death. The emergence of the EV-A71 epidemic in the Asia-Pacific region has been associated with the transmission of viruses with of different genetic lines. The virus may to be undergoing rapid genetic changes. The association between the gene structure of the EV-A71 virus and the factors that ensure its survival, circulation, and evasion of immunity is still unknown. EV-A71 infection has emerged as an important global public health problem. Vaccine development, including the development of inactivated whole-virus live attenuated, sub-viral particles, and DNA vaccines, continues. There are two vaccines developed in China, both are killed(inactivated) vaccines.

Identification of serotype of virus will be necessary in order to determine if the virus is changing. Continued studies, data collection and pathogen classification is essential in the endeavor to control HFMD.

Conclusion

There continues to be an alarming increase of HFMD in India, Asia and Australia.

If HFMD is increasing in many areas across the globe including India, Asia, Australia and the United States, it is not a stretch to think that reason for such a large and widespread occurrence of HFMD may be due to the emergence of a new strain(s), across the globe. Researchers agree that there is a need to establish a standardized system of data collection and oversight. This must include an expeditious and economical method of laboratory viral serotype identification and outbreak containment.¹ In 2008 the National Institute of Communicable Diseases (India) stated that they must be more vigilant about detection and control of HFMD outbreaks. They must have a testing facility for the laboratory samples. There is a clearly stated recommendation for response, in the case of an outbreak.⁸ A general set of guidelines can be adapted from NICD report and the “Guidelines for Hand Foot and Mouth Disease HFMD”. The United States CDC has an Investigation form for HFMD, it would be of value in the development of protocol for the India NICD.

Healthcare professionals and government oversight agencies must be vigilant in the early detection and control of HFMD. Continued studies into the conditions that are precursors to the disease must be identified, so the disease can be better understood. The World Bank reports that India’s population was 1.3 billion in 2015. The population growth rate of India is at 1.58%. India is predicted to have a population of 1.53 billion people by the end of 2030. This will make India the world’s most populous country. As population and environmental pressures increase, there is a strong probability that outbreaks of HFMD and other diseases will increase. According to India online statistics, more than 50% of India’s current population is under the age of 25. 65% of the population is under the age of 35.

The future of India and the world is its children. The future of the world’s health is of paramount concern. India and most countries are striving to improve the general health of their populations. HFMD is among the many diseases that should be monitored and controlled. Advances in understanding and controlling HFMD can help find solutions to other public health issues.

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Conflicts of interest

The authors have declared that no competing interests exist.

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