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Dermatology

SPATIAL AND TEMPORAL DISTRIBUTION OF HAND, FOOT AND MOUTH DISEASE REPORTED IN ROUTINE SURVEILLANCE SYSTEM IN KERALA, INDIA

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ABSTRACT Hand, foot and mouth disease (HFMD) is classically described as a viral exanthem caused by Coxsackie A16 (CVA-16)virus and entero-virus 71 (EV 71). However more viral agents and mutations are being reported to be associated with HFMD making its epidemiology and clinical picture more complex. One of the major attributes of HFMD is the seasonality and cyclical trends of the outbreaks. The State of Kerala incorporated HFMD in the routine surveillance system in 2012. The aim of the current analysis is to study the trends and seasonality of this emerging disease using the secondary data available at the official website of Directorate of Health Services, Government of Kerala. A total of 1,150 cases of HFMD were reported from the State during 2012-2017 period with no fatality. The incidence of HFMD during the last six years in the State is 34.4 per million population with Idukki, being the highest endemic district with 354.9 per million population. HFMD in the State peaks in September-October, but other communicable diseases peak around June – July, the monsoon months of the State.

KEYWORDS : Hand, foot and mouth disease, Seasonal trends, Temiporo-spatial distribution

Introduction

Hand, foot and mouth disease (HFMD) is classically described as a viral exanthem caused by Coxsackie A16 (CVA-16)virus and entero-virus 71 (EV 71). However more viral agents and mutations are being reported to be associated with HFMD making its epidemiology and clinical picture more complex. HFMD has emerged as a pandemic affecting China, Eastern Asia, Southern Asia, and even Europe and America[1-3]. In Indian setting it is an infection of preschool or early school going children with skin eruptions starting as small erythematous maculo-papular lesions that rapidly enlarge and progress to vesicular eruptions with a prominent erythematous halo. The distribution of lesions is very characteristic involving the gluteal region, hands, feet, the oral mucosa and sometimes the knee. The vesicles often mimick vesicles of chicken pox and initial maculo-papular lesions simulate lesions of mosquito bites[4]. Even though HFMD mainly affect infants and children, the attack rate of this infection is very high in endemic areas and more than 50% adults show the presence of neutralising antibody[5].

Among the viruses responsible for HFMD, EV 71 was found to be more virulent and was responsible for 80-90% of fatal cases. Most of HFMD caused by other enteroviruses were found to be mild in clinical course[6,7]. However there are many instances of Coxsackie viruses causing fatal outbreaks of HFMD. Brainstem encephalitis caused by neurotropism of the causative enterovirus is thought to be the main reason for fatality in HFMD[8].

One of the major attributes of HFMD is the seasonality and cyclical trends of the outbreaks. There are many spatial and environmental factors attributed to the high incidence of the infection. Comparatively high incidence of the disease is observed in China during April to July and October to December in an year[9]. There was a 2-3 year cyclical pattern of EV-A71 epidemics in Malaysia which is mainly due to the decline of population immunity accompanying the accumulation of susceptible children between epidemics[10].There are reports which attribute climatic changes like El-Nino effect and Southern Oscillation Index (SOI) to HFMD outbreaks in China[11].

The first outbreak of HFMD was reported in Kerala, India during 2003. The available report showed that the peak of the outbreak is during October- February and the causative organsm is EV-71[12]. The State of Kerala incorporated HFMD in the routine surveillance system in 2012. The aim of the current analysis is to study the trends and seasonality of this emerging disease using the data available at the official website of Directorate of Health Services, Government of Kerala[13].

Materials and Methods

The current report is a secondary data analysis of HFMD cases reported through the routine surveillance (Integrated Disease Surveillance Project-IDSP) of Kerala State of India. Data was extracted using a structured proforma from the data published in the official website of Directorate of Health Services, Government of Kerala[13].IDSP is the official surveillance system in India, mainly for communicable diseases. The State can fix its own priority and can include the priority diseases in the system of Surveillance. HFMD is the new addition to the IDSP surveillance system of Kerala, started in 2012. Year wise data of HFMD from 2012 to 2017 were extracted separately from the website. For comparison in seasonality and spatial distribution, three other diseases were randomly selected (lot method)from the list of diseases under surveillance and the data of year 2017 of these diseases were extracted and used. The diseases included were undifferentiated fevers, Acute Diarrhoeal Diseases (ADD), and Dengue Fever. The data of major communicable diseases available at the website is limited, which included only the monthly reported cases from all the 14 districts of the State.

The extracted data was entered into Micosoft excel software and analysed. Monthly and district wise proportions were calculated to assess the temporal and spatial trends in disease reporting. Rates were calculated using the population of the districts as denominator. The populations of the districts as per 2011 census were used as denominator. Win Pepi softare[14]was used to assess the significance in seasonal fluctuations. Freedman's test for deviation from uniform incidence was used to test for significance in seasonality and the peak date was calculated based on Edward's test function of Win Pepi[14].

Results

A total of 1,150 cases of HFMD were reported from the State during 2012-2017 period with no fatality. The year 2014 witnessed the lowest rate (n=43) and the year 2017, the highest (n=345). Month wise ditribution of the cases for the six years is given in Table 1. Out of the total 1150 HFMD cases, 928 (80.7%) was found to be reported during the second half of the year. The cumulative number (%) of cases reported during the three months of September, October and November was 566 (49.2%) with the peak incidence being between the second week of September and the first week of November (Table 1). The significant Freedman's test indicated that there is seasonal fluctuation and clustering of cases. Figure 1 is the diagrammatic representation of the monthwise fluctuation in reporting of HFMD over the years.

Table 2 shows the comparison of HFMD with other three randomly selected communicable diseases under IDSP network of the State of Kerala for the year 2017. Significant seasonal fluctuation and clustering do exist for all the communicable diseases under study as indicated by the p value (<0.01) of Freedman's test. However the mode of the curve (Figure 2) is unique for HFMD which peaks in September-October, but other communicable diseases peak around June – July, the monsoon months of the State. The first four months of the year, from January to April witnessed low incidence of all the communicable diseases under study ie.20.86% of undifferentiated fevers, 27.5% of ADD, 11.3% of Dengue fever and 13.05% of HFMD (Table 2). Around half (46.84%) of undifferentiated fevers, one-third (35.55%) of Acute Diarrhoeal Diseases and two-third (63.60%) Dengue fever were reported during the three month period of June to August whereas, the proportion of HFMD during the period is only 26.95%. Majority (53.33%) of HFMD cases of the year 2017 were reported in the three month period of September to November. The proportion of undifferentiated fevers, ADD and Dengue fever reported during these months is 19.18%, 21.01% and 11.10% respectively, indicating that these months are low endemic for communicable diseases other than HFMD. The peaks of the curves are depicted in Figure 2.

Table 3 shows the spatial distribution of reported HFMD cases over the years. The district Idukki showed high rates over the years except 2012 (the year of the start of the surveillance). As per the report, the incidence of HFMD during the last six years in the State is 34.4 per million population with Idukki, being the highest endemic district with 354.9 per million population. Two districts, Ernakulum and Kannur are the silent districts. Figure 3 shows the spatial map of the State of Kerala and district wise categorization of the incidence per million population.

Discussion

The overall incidence of HFMD in the State of Kerala appear to be low (34.4 per milloin population in six years) even though very high rates were reported in some districts. The incidence of HFMD in China is as high as 114.8 per 100,000 person years and have a death toll of 0.5 per 1000 affected cases[9]. However it should be viewed in the context of gross under reporting in the current setting. The chance of under reporting is very high because the disease has been included in the IDSP reporting system very recently and the health workers who report the diseases may not have adequate experience in detecting HFMD. IDSP reporting system has its own weaknesses as it grossly reports cases from government hospitals and health centes. Cases from private hospitals and those from systems other than modern medicine could be missed[15].

The major finding of the study is the temporo-spatial clustering of cases. Majority of HFMD cases were reported during September to November in the hilly terrains of the state. Temporo-spatial clustering has also been documented in China[9,11]. High incidence of the disease is observed in China during April to July and October to December in an year[9]. The peak incidence as per the current study coincides with the second peak of China. In India, it is already reported that outbreaks of HFMD is more frequent in the hilly terrains [16,17].

Idukki, the district having unusually high incidence of HFMD is the district with highest elevation, highest rainfall, high humidity and high wind velocity compared to other parts of the State. HFMD was found to be associated with increase in temparature and humidity[9,11,18-20]. There are ample number of papers which analyse the relationship of HFMD and climatic conditions. A positive association was found between temperature and HFMD and a hockey-stick relationship was found between relative humidity and HFMD. This indicates that the risk increased with increasing humidity after a small inverse relation in extremely low humidity, with markedly increasing risks above 80% of relative humidity[18-20]. Moderate rainfall and stronger wind and solar radiation were also found to be associated with more admissions[21]. The association with temperature was found to be non-linear,wherein incidence of HFMD found to be increased with increase in temperature for a few days, but decreased with sustained high temperature situations[22].

From the current data it is evident that there is more number of reported cases of HFMD recently and the previous year 2017 witnessed the highest number of cases. There are chances of complications and fatality as the disease emerges. So it is very important to look in to the preventive strategies. There are reports recoumented that children exclusively breastfed for the first six months of life are relatively protected from HFMD and its complication[23,24]. Promoting breast feeding may be an important strategy that could be adopted as a health promotion strategy and as a mode to get the child protected from many diseases including HFMD. Vaccination is the technique that could be adopted once more evidence is generated on the endemicity of the disease and potential complications. A formalin-inactivated EV-A71 vaccine has completed clinical trial in several Asian countries. However, this vaccine cannot protect against other major emerging etiologies of HFMD such as CV-A16, CV-A6 and CV-A10. Therefore, the development of a globally representative multivalent HFMD vaccine could be the best strategy[25]. Bivalent vaccines have been found to elicit strong neutralizing antibody responses against both viruses in animal models but did not protect against Coxsackie viruses[26]. As more and more viral agents are reported as having causal role in the epidemic of HFMD, the vaccination efforts should be based on the local data[27]. So it is very important to generate more data on the epidemiology, clinical spectrum and virological aspects of HFMD from India and from the State of Kerala.

Strengths and Limitations

There is no other documentation on HFMD from India based on the routine official surveillance data. It could give some initial clues to the epidemiology of the disease. The paper speaks about more than 1000 individuals over a period of six years. However the data has got limitations. The secondary data published in the website gives no details of the individual patients, their socio-demographic details, clinical features and diagnostic mechanisms. The study is based on administrative data based on reporting by field health workers.

Table 1 Distribution of HFMD Over the Years (2012-2017) and Seasonal Fluctuation in Reported Cases

Month	2012	2013	2014	2015	2016	2017	Total
January	0	6	3	5	0	22	45
February	1	11	0	1	6	10	29
March	0	3	2	1	1	11	18
April	2	18	0	0	4	2	26
May	0	29	0	2	9	7	47
June	2	8	0	17	13	17	57
July	1	10	3	33	17	39	103
August	5	16	5	33	18	37	114
September	6	19	1	27	26	84	163
October	11	76	11	23	20	44	185
November	51	34	11	21	45	56	218
December	36	26	7	13	47	16	145
Total	115	256	43	176	215	345	1150
Peak incidence (Edward's test)	November 3rd	October 13th	November 1st	September 12th	October 1st	September 29th	October 6th
Significance (Freedman's test)	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

Table 2 Seasonality of HFMD compared to Other Selected Communicable Diseases Reported through IDSP

	HFMD	HFMD (%)	Fevers	Fever (%)	ADD	ADD (%)	Dengue	Dengue (%)
January	22	6.38	193044	5.67	32250	6.99	435	2.2
February	10	2.90	172594	5.07	30991	6.72	302	1.5
March	11	3.19	185336	5.44	33518	7.26	463	2.3
April	2	0.58	159377	4.68	30121	6.53	1066	5.3
May	7	2.03	240963	7.08	41010	8.89	2477	12.4
June	17	4.93	502371	14.76	61018	13.22	4145	20.7
July	39	11.30	695517	20.43	64523	13.98	5251	26.3
August	37	10.72	396720	11.65	40068	8.68	3320	16.6
September	84	24.35	216984	6.37	31386	6.80	1163	5.8

October	44	12.75	214361	6.30	31915	6.92	637	3.2
November	56	16.23	221661	6.51	33625	7.29	426	2.1
December	16	4.64	205217	6.03	31002	6.72	309	1.5
Total	345	100	3404145	100	461427	100	19994	100
Peak incidence (Edward's test)	September 29th		July 21st		July 1st		July 6th	
Significance (Freedman's test)	<0.01		<0.01		<0.01		<0.01	

Table 3 District wise distribution of reported HFMD cases during 2012-2017

District	2012	2013	2014	2015	2016	2017	HFMD (Total)	HFMD per million population
Thiruvananthapuram	2	6	9	9	6	12	44	13.3
Kollam	0	0	0	0	0	3	3	1.1
Pathanamthitta	0	1	0	0	0	0	1	0.8
Idukki	0	122	28	73	91	79	393	354.9
Kottayam	38	6	0	2	3	8	57	28.8
Alappuzha	0	1	0	0	12	4	17	8.0
Ernakulam	0	0	0	0	0	0	0	0.0
Thrissur	0	1	0	0	0	1	2	0.6
Palakkad	0	20	3	90	26	20	159	56.6
Malappuram	37	11	0	0	0	0	48	11.7
Kozhikode	37	78	3	2	58	201	379	122.7
Wayanad	1	10	0	0	19	16	46	56.3
Kannur	0	0	0	0	0	0	0	0.0
Kasaragode	0	0	0	0	0	1	1	0.8
Total	115	256	43	176	215	345	1150	34.4

Figure 1: Monthwise Fluctuation in Reporting of HFMD Over the Years (2012-2017)

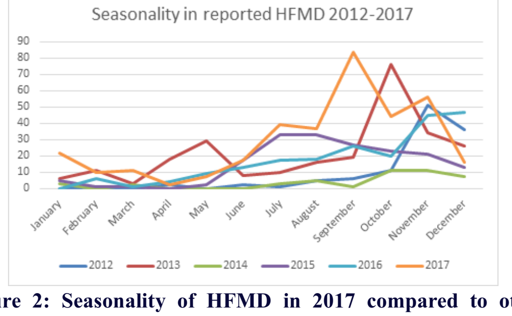


Figure 2: Seasonality of HFMD in 2017 compared to other communicable diseases

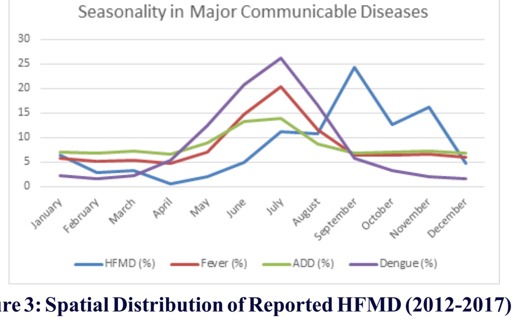
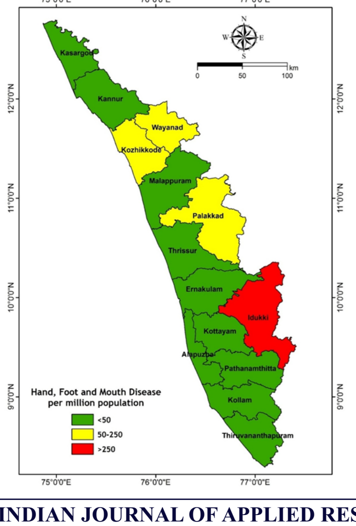


Figure 3: Spatial Distribution of Reported HFMD (2012-2017)



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