

Research Article

Economic burden of hand, foot, and mouth disease in Vietnam; An evidence for priority setting and efficiency management

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ABSTRACT

Hand, foot, and mouth disease (HFMD) is an acute infection in children caused by enteroviruses. Typical cases of HFMD are mild, but increasingly severe complications involving the central nervous system have been observed. With consideration for this issue, this incidence-based study estimated the total costs (converted to 2017 international dollar rates, Int\$) incurred from pediatric HFMD incidence and treatment in Vietnam. To this end, 306 cases of HFMD in children were analyzed. Most of the patients were 1 to 3 years old (274 cases, 92.9%), and 234 of the cases (79.3%) were inpatients. No fatality case was found during the study period. The total cost of illness per episode was Int\$467, which included direct medical (Int\$228) and direct non-medical (Int\$239) expenditures. The total cost was more than a half of the average monthly wage of Vietnamese individuals. HFMD remains one of the most economically burdensome communicable diseases in Vietnam. Effective solutions to the financial burdens of HFMD should therefore be implemented.

1. INTRODUCTION

Hand, foot, and mouth disease (HFMD) is an acute enterovirus-induced infection¹ that most frequently afflicts children. Typical cases of HFMD are mild, accompanied with an acute onset of fever; rashes (described typically as maculopapular or papulovesicular rashes) on palms, soles, buttocks, and knees; and vesicle lesions on buccal membranes. However, increasingly severe complications involving the central nervous system have been observed². This is a matter of concern given that HFMD is a common endemic illness all over the world, with more than 50% of children less than 5 years old potentially vulnerable to enterovirus 71 (EV71) and coxsackievirus A16 infection^{3,4}. Until now, no official vaccine or treatment for HFMD has been developed.

Many HFMD outbreaks have been reported globally, especially in the Asia-Pacific region^{5,6}, but very limited data have been obtained with respect to the epidemiological characteristics of the disease in the Vietnamese context and other regions. Following a study which was conducted at a Vietnamese central pediatric hospital where 764 children were diagnosed as having HFMD⁷. The majority of these cases were aged up to 5 years, and the diagnosis of all the patients was verified through laboratory confirmation. Among the patients, 51 (29%) developed severe neurological complications, and three in the group with EV71 infection died.

In 2007, 2008, and 2009, the total proportions of HFMD cases and lethal conditions due to HFMD in Vietnam were 5,719 cases with 23 deaths, 10,958 cases with 25 deaths, and 10,632 cases with 23 deaths, respectively⁸. Since 2011, the country's Ministry of Health has considered HFMD a severe infectious disease with outbreak potential (class B communicable disease) and has required hospitals to frequently submit official reports regarding the illness. All HFMD data are treated as a component of Vietnam's national communicable disease surveillance system. Until 2015, however, no costing study on HFMD in the country was carried out. Because the official vaccine for the disease is expected to be available in the near future, a cost-of-illness study will be valuable in evaluations of the worth of vaccines and in decision making regarding whether to include selected vaccines in the Expanded Program of Immunization for Vietnam.

Accordingly, this research estimated the total costs incurred from pediatric HFMD incidence and treatment in Vietnam. Our objective was to provide reliable data on HFMD costs to enable the government to manage the disease on setting priority of health problems and conducting studies to explore cost-effective interventions.

2. MATERIALS AND METHODS

2.1. Study design

This research was an incidence-based cost-of-illness study oriented toward the perspective of society. The study population comprised pediatric patients (up to 15 years old) of the Hospital for Tropical Diseases in Ho Chi Minh City. The inclusion criterion was a primary diagnosis of HFMD that falls under the B08.4 code of the International Classification of Diseases, 10th Revision (ICD-10). The exclusion criteria were (1) incomplete treatment (patient withdrawn from treatment or referred to other hospitals), (2) referral from other hospitals, and (3) the refusal of caregivers to participate in the study or unavailability (contacted via telephone) for a second interview after discharge. Based on time limitation of the study, data collection was conducted in two months. All cases from October to November 2015 were included in the study, so there was no need to calculate sample size.

2.2. Data collection

Prospective data were collected through questionnaire-guided interviews with caregivers. The sessions were divided into two stages. The first involved face-to-face interviews conducted on the date at which outpatients visited the hospital and the date at which inpatients were discharged. The second set of interviews was carried out via telephone at day seven after a visit or discharge.

2.3. Cost calculations

The costs of illness, from a societal perspective, is composed of direct medical costs, direct non-medical costs and indirect costs. Direct medical costs (DMCs) were defined as costs of the hospital costs including the costs of physician visits, laboratory tests, hospital admission, medical equipment, drugs, and other health facilities. A bottom-up method was applied in calculating the total charges based billing system, then, the ratio of cost to charge (RCC) was employed to adjust the charge data into economic costs. The reference ratio was employed, following a previous hospital cost analysis in Vietnam⁹. DMCs also include patients' family payment for other treatments outside the study hospital.

Direct non-medical cost (DnMC) components were the expenses that the patients' families paid for food, transportation, accommodation, personal facilities, and informal care. Expenditures related to informal care referred to the costs of time lost by caregivers, adjusted on the basis of the reference cost per day, which was calculated as the gross national income (GNI) per capita divided by 365 days. Time loss costs covered only those incurred by caregivers during official work. Such expenses were excluded if caregiving was provided by a housewife, house husband, or an unemployed individual.

Indirect costs were composed of morbidity and mortality costs. As stipulated in the work law of Vietnam, individuals have 42 years of tendering official and legal work, with service beginning at age 18 and ending at age 60¹⁰. Productivity loss was counted in the period of 42 working years. This study also applied a constant 5% GNI growth rate, which was the average percentage increase in GNI of Vietnam for the last 5 years. The discount rate for succeeding years of this estimation was 3%.

All original costs were adjusted to the 2017 values indicated in the consumer price index (CPI) of Vietnam for the healthcare industry; the rate applied in this regard was 1.83 (CPI 2015 = 100, CPI 2017 = 183)¹¹. Finally, these values were converted into 2017 international dollars using the purchasing power parity (PPP) conversion factor¹², leaving us with a conversion rate of Int\$1 = VND7,736.

3. RESULTS

3.1. Participant characteristics

This study involved 306 patients, of whom 295 (96.4%) fulfilled the criterion for eligibility. Eleven cases (3.6%) were excluded because clinical characteristics did not correspond with the chosen ICD-10 code. Among the enrolled HFMD cases, those aged 1 to 3 years constituted the majority, accounting for 92.9% (274 patients) of the sample. Children aged 4 to 5 years old and older made up 5.1% (15 cases) and 2.0% (6 cases), respectively. The mean age of the patients was 2 years. Of the sample, 234 cases (79.3%) were inpatients, and 61 cases (21.7%) were outpatients. In terms of sample composition, the male-to-female ratio was 1.4:1.

The HFMD diagnosis of the patients fell under four levels of severity: Grade 1 pertains to uncomplicated cases. Grade 2, which means that the effects of the disease extend to the central nervous system, is divided into Grades 2a and 2b. Patients with Grades 2a and 2b HFMD receive phenobarbital to suppress myoclonus. Grade 3 indicates nervous system dysregulation, and Grade 4 involves cardiopulmonary failure.

Out of the patients selected, 207 (71.2%) received prior medical treatment via drug stores (50 cases, 16.9%), private clinics (94 cases, 31.9%), and other hospitals (63 cases, 21.4%). Only 11.5% of the patients were administered treatment with the benefit of medical insurance, whereas the expenses of most of the cases (176 patients, 59.7%) were settled out of pocket by their parents/guardians. The use of insurance during treatment at the study hospital was higher than the usage of the prior treatment, with 38% (112 cases). The average length of stay of the inpatients was five days, which compelled the caregivers to take a leave from official work for four days. The mean period of time spanning the occurrence of the first symptom to full recovery was twelve days. All the aforementioned data were much lower for the outpatients, who also grappled with a full disease episode length of only seven days (Table 1).

Table 1. Characteristics of the patients.

Characteristics	Number	Percent	Characteristics	Number	Percent
Patient age (years)			Insurance (used for prior treatment)		
1 – 3	274	92.9	Out-of-pocket payment	176	59.7
4 – 5	15	5.1	Compulsory insurance	34	11.5
> 5	6	2.0	Voluntary insurance	-	-
Mean (SD): 2(1), Median: 1, Range: 1-10			Private insurance	-	-
Patient gender			N/A (no prior treatment)	85	28.8
Male	174	59.0	Insurance (used for treatment at the study hospital)		
Female	121	41.0	Out-of-pocket payment	183	62.0
Type of patient			Compulsory insurance	112	38.0
IPD	234	79.3	Voluntary insurance	-	-
OPD	61	20.7	Private insurance	-	-
Severity grade			Length of stay		
1	68	23.1	Mean(SD): 5(4), Median: 2, Range: 1-15		
2	226	76.6	Number of working day loss of caregivers		
3	1	0.3	OPD Mean(SD):1(1), Median: 3, Range: 0-5		
4	-	-	IPD Mean(SD): 4(4), Median: 3, Range: 0-16		
Prior treatment			Length of episode		
Private clinic	94	31.9	OPD Mean(SD): 7(7), Median: 2, Range: 3-12		
Hospital	63	21.4	IPD Mean(SD): 12(11), Median: 5, Range: 4-36		
Drug store	50	16.9			
Other	3	1.0			
No	85	28.8			

3.2. Direct medical costs

Data on treatment were divided into

three periods: those collected before, during, and after treatment at the study hospital. Significant differences in treatment costs or DMCs

among the periods were found (Table 2). Almost 70% of the parents had sought prior treatment at nearby private clinics or drug stores. This initial treatment cost them an estimated average of Int\$23. The majority of the DMCs were incurred during treatment at the study hospital, amounting to Int\$200 on average, which was ten times higher than the expenses paid prior to the treatment at the study hospital. After discharge, only some of the patients needed additional medical treatment, for which they paid Int\$5 as the mean cost. The total DMC for the treatment of one HFMD episode was Int\$228.

The total DMC was calculated mainly on the basis of the DMCs incurred during treatment. Of these costs, the greater proportion was accounted for by the routine service cost of hospitalization (hotel cost), which amounted to Int\$169 per episode (73.1%). The other six groups (OPD service, drugs and fluid, lab tests, diagnostic imaging, medical supplies, surgery/procedure) accounted for 36.9% of expenses, out of which 11.2% were OPD routine service costs, and 9.1% were expenses incurred from drug and fluid administration. Check-up costs were recorded only for the outpatients. For the inpatients, the payment for a hospitalization day included the costs of physician visits.

3.3. Direct non-medical costs and indirect costs

The total DnMC was estimated at Int\$239 for a full episode of HFMD. Out of this amount, the largest expense was Int\$112, which was devoted to food during treatment, but home-prepared meals were not included in the estimation. Transportation costs were estimated at Int\$59, and the income loss borne by the parents or caregivers as they spent time taking care of the HFMD patients until recovery was Int\$68. These individuals did not spend money on accommodations and hiring third-party care providers. The food expenses and income loss accounted for almost 3/4 of the total DnMC. On the basis of the aforementioned figures, the costs of transportation, food, and income loss can be regarded as significant burdens of HFMD.

The patients were children under the working age, and no deaths occurred during the study period. Therefore, no indirect costs were incurred. The total economic burden arising from HFMD comprised all the associated costs of HFMD treatment and direct non-medical costs. Such total was estimated at Int\$467 per episode.

Table 2. Cost of HFMD.

Cost (2017 Int \$)	Mean (%)	Median	SD
Total DMC	228	128	271
DMC–before treatment	23	5	38
DMC–after treatment	5	0	29
DMC–during treatment	200	100	269
Hotel cost	169 (73.1)	91	218
OPD service cost	6 (11.2)	0	12
Drugs and fluid	5 (9.1)	0	11
Lab tests	8 (5.0)	5	13
Diagnostic imaging	2 (0.8)	0	6
Medical supplies	2 (0.5)	0	6
Surgery/procedure	8 (0.3)	0	135
Total DnMC	239	222	180
DnMC – before treatment	6 (7.6)	2	14
DnMC – after treatment	4 (1.0)	0	40
DnMC – during treatment	229 (91.4)	217	174
Meal	112 (37.3)	106	103
Informal care	68 (36.0)	47	58
Transportation	59 (26.7)	35	79
Hiring	0 (0.0)	0	0
Accommodation	0 (0.0)	0	0
Indirect cost	0	0	0
Total cost of illness	467	404	368

4. DISCUSSION AND CONCLUSIONS

Using an incidence-based approach, this research evaluated the costs of an HFMD

episode from disease onset to complete recovery for all new cases admitted over a two-month period at the Hospital for Tropical Diseases in Ho Chi Minh City. We captured all healthcare-

related costs. Actual resource consumption for patient questionnaires, was analyzed. This study also applied the reference RCC⁹ for Vietnam hospitals in the calculations.

In this research, costs were recalled by the participants from memory as they were interviewed and retrieved from electronic medical records. The estimations revealed that the average cost per episode was Int\$467, which was more than 50% of the 2017 mean monthly wage of Vietnamese individuals (Int\$840)¹³. This cost burden was nearly three times the basic monthly salary levels (Int\$168)¹⁴ of cadres, civil servants, public employees, and armed forces personnel. The costs of HFMD treatment in China¹⁵⁻¹⁷ and Taiwan¹⁸ are considerably much higher than those in Vietnam. In this study, the estimated total cost of mild HFMD cases (outpatients) was about US\$34 (US\$1 = VND 22.370)¹⁹, whereas those in China and Taiwan were US\$1860¹⁵ and US\$215¹⁷ (adjusted to 2017 values). This significant difference may be attributed to the higher medical service costs and standards of living in China and Taiwan.

In Vietnam, communicable diseases that affect children other than HFMD impose tremendous burdens on society. A useful approach, therefore, is to compare to these illnesses. Rotavirus infection, for instance, is a major reason for hospitalization and clinic visits among children under 5 years of age, with the disease considerably affecting the use of healthcare resources and the costs incurred from treatment. A study that probed into total costs in societal perspective indicated that rotavirus infection resulted in a cost of US\$174.66 (2014 value)²⁰. Converting this cost into VND on the basis of the exchange rate used in that work, adjustments grounded in the CPI, and PPP conversion into 2017 international dollar would yield a rotavirus diarrhea-related expenditure of Int\$891-almost double the HFMD cost (Int\$467).

Several limitations of the study should be considered to grasp the entire picture of the phenomenon of interest. First, our estimation was based on a sample taken from only one tertiary hospital in Ho Chi Minh City, thus presenting difficulties in generalizing the estimations to the entire country. Second, EV71 and related enteroviruses are associated with various clinical symptoms, including respiratory problems, febrile rashes, neurological complications, and gastrointestinal illnesses. Because HFMD is only one of the diseases caused by enteroviruses,

HFMD, as indicated in medical records and actual illness-driven burdens determined through an analysis of the cost-effectiveness of vaccination must be higher than the values derived in this work. Third, the definition of informal care costs adopted in this research could cause an underestimation of HFMD expenditures as we did not consider the opportunity costs of caregivers such as housewives, house husbands, and other individuals engaged in unofficial work. Finally, no Grade 4 cases or death due to HFMD were observed during the study period. We recommend that future cost-of-illness studies on HFMD adopt a longer time horizon spanning an entire year to capture all situations.

In conclusion, HFMD remains one of the most alarming diseases that escalate to annual outbreaks in Vietnam. EV71-associated diseases, particularly HFMD, have caused serious problems for patients and their parents as well as Vietnam's healthcare system and society. The development of a vaccine, which is considered the most effective preventive measure against disease, is currently ongoing.

On the basis of societal perspectives, this research comprehensively examined all opportunity costs arising from HFMD. This is the first research in Vietnam to inquire into the financial burdens of HFMD on the basis of data from medical records and interviews with caregivers of nearly 300 children. This work is also the first to provide evidence-based nationally representative data on the economic losses stemming from HFMD. The results derived in this study can serve as guidance in health problem priority setting and essential data for further economic evaluations of HFMD prevention and control interventions, such as vaccine programs, in the near future. Overall, the findings illustrated that the necessary and effective solutions to the considerable hardships imposed by HFMD on society are incidence management and severity control.

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Conflict of interest

The authors declare no conflicts of interest arising in this research.

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None to declare.

Ethical considerations

This study was approved by the Ethics Review Committee of the Hospital for Tropical Diseases in Ho Chi Minh City (approval number: 08/HĐĐĐ).

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