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Review on epidemiology and clinical characteristics of hand, foot and mouth disease in Sarawak

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Abstract

A major outbreak of HFMD virus reported in Sarawak, Malaysia involving 29 fatal cases. This study explore, epidemiology and clinical characteristics of HFMD in Sarawak which aims to study the trend of HFMD outbreak in Sarawak as well to create awareness among the community on the severity of HFMD. A search strategy was employed to obtain relates study. Only two studies fit the inclusion criteria that focused on the HFMD outbreak in Sarawak where the recruited patients were children <6 years old. Those studies explain clinical symptoms and duration of HFMD were due to rapid onset and progression of the brain-stem encephalitis. Apart from that, abnormal coagulation profile and gastrointestinal profile may contribute to the disease progression.

Keywords: HFMD, Sarawak, Malaysia, virus

Introduction

Hand, foot and mouth disease (HFMD) is an infection caused by enteroviruses, particularly Coxsackievirus A16 (CA16) and Enterovirus 71 (EV71). Humans are the only reservoir for these enteroviruses, and incidences commonly occur among paediatrics (1). The typical clinical manifestations of HFMD are fever, rashes, blisters and ulcers on hands, feet and mouth. Generally, HFMD is contagious and life-threatening in children especially for those associated with EV71 infection due to involvement of neurological complication and cardiopulmonary failure (2). Since early 1970s, many HFMD outbreaks have been reported globally with the involvement of both typical symptoms and severe central nervous system (CNS) diseases or pulmonary edema (3). In 1997, a major outbreak of HFMD virus reported in Sarawak, Malaysia with 2628 cases reported involving 29 fatal cases (4). According to Ministry of Health Malaysia, HFMD peaks every three years with EV-A71 epidemics occurring in 1997, 2000, 2003 and 2006 (5). In 2016, HFMD cases occurred nationwide where there were 1108 cases reported in Sarawak (6). This review covers 2 major parts, epidemiology and clinical characteristics of HFMD in Sarawak which aims to study the trend of HFMD outbreak in Sarawak as well to create awareness among the community on the severity of HFMD.

Methods

Search Strategy and Study Selection

We performed electronic searches via different search engines such as Google Scholar and PubMed by using combination of related search terms like “Hand Foot Mouth Disease”, “Sarawak”, “Epidemiology”, “Outbreak of HFMD in Sarawak” and “Clinical Characteristics”.

The articles included in this review were:

- (1) the published articles conducted from 1997 to 2017
- (2) the studies with epidemiologic information about incidence and prevalence of HFMD in Sarawak, Malaysia
- (3) the studies with clinical characteristics of HFMD in Sarawak, Malaysia

The articles that did not fulfil all of these three criteria excluded from this review.

Results

Search Results

There were two studies that fulfil the inclusion criteria. These two studies focused on the HFMD outbreak in Sarawak during 1997, 2000 and 2003 where the recruited patients were children <6 years old. One of the studies entirely conducted at Sibu Hospital whereas another study included the patients who died from HFMD in whole Sarawak

Epidemiology

A conducted which focused on HFMD outbreak in 1997 (4). During this outbreak, there were approximately 2600 cases reported in Sarawak with around 33% admitted to hospital, 1.5% involved neurological complications and about 1% of fatal cases. The median age of children in fatal cases was 1.5 years (mean: 1.7 years, range: 0.5-5.9 years) (4). In another study conducted during 2000 and 2003 HFMD outbreaks in Sibu, 725 children recruited. 74.5% had mild HFMD; 11.5% had severe HFMD with no CNS complication; and 14% had HFMD with CNS involvement. There are three (0.4%) out of 725 children were died throughout the study (7).

Clinical Characteristics

In study conducted by Chan et al., the significant clinical presentations among case patients before admission were fever, mouth ulcer, extremity rashes, vomiting and cough. Fever is the most prominent symptoms where 100% and 69% of the case patients had history of fever before and upon hospital admission respectively. The other physical presentation on admission included cyanosis, tachycardia, tachypnea, pulmonary crepitation and poor peripheral perfusion. During hospitalization, the illness rapidly deteriorated to neurological features (e.g.: seizure and flaccid limb weakness) and/or cardiopulmonary diseases (pulmonary oedema or left ventricular dysfunction), leading to cardiac arrest despite supportive therapy (4).

Table 1: Symptoms of case patients before hospitalization

Symptoms	No. of patients, n (%)
Fever	29 (100)
Mouth ulcer	19 (66)
Extremity rash	18 (62)
Vomiting	17 (59)
Cough or cold	10 (35)
Seizure	8 (28)
Diarrhoea	6 (21)
Limb weakness/ paralysis	5 (17)

Table 2. Physical findings of case patients upon hospitalisation

Findings	No. of patients, n (%)
Temperature $\geq 37^{\circ}\text{C}$	20 (69)
Cyanosis	19 (66)
Crackles on lung examination	18 (62)
Heart rate ≥ 180 beats/min	12 (41)
Respiratory rate ≥ 40 breaths/min	13 (45)
Capillary refill time $> 2\text{s}$	12 (41)

In another study carried out in Sibul, case patients infected with EV-71 viruses compared between those with CNS disease and those without CNS disease regardless of the severity of HFMD. The history of presenting illness before admission including fever, vomiting, cold limbs, breathlessness, reduced urine output and neurological manifestations favoured in patient with CNS disease. During examination, patient with CNS disease more likely to appear toxic-look, dehydrated, febrile and lethargic. On the other hand, mouth ulcers were less likely in patient with CNS disease. Three out of 273 children suffered from HFMD complicated by acute flaccid paralysis (7).

Discussion

Human Enterovirus (HEV-71) infection was one of the main public health concerns in developing countries all around the world since 1997. HEV-71 caused large outbreaks of hand-foot-and-mouth disease with central nervous system complication (CNS). Children at young age were prone to have severe fever, vomiting and hyperglycaemia when they were

infected with HEV-71 infection. Apart from that, symptoms such as tachycardia, breathlessness and the absence of mouth ulcers appeared when CNS infection involved (7).

According to Table 3, patients with CNS disease were more likely to have symptoms like fever, dehydration, unconsciousness, or neck stiffness instead of mouth ulcers which more prone towards non-CNS HFMD patient (7). CNS pathology has been considered to contribute for the disease progress. However, these findings were not adequate to suggest the rapid progression of cardiopulmonary disease in patient with CNS disease who presenting with seizure, lethargy, or paralysis symptoms will end with death (4).

The clinical symptoms and duration of HFMD were due to rapid onset and progression of the brain-stem encephalitis. Apart from that, abnormal coagulation profile and gastrointestinal profile may contribute to the disease progression (4).

There are several challenges and limitation in this study. There was limited articles on epidemiology of HFMD in Sarawak and only outdated version was available. In addition, the sample study was narrow which focus only in Sibu area. Hence, the result was not representative of the whole Sarawak. Due to time and budget constrain, we could not obtain all the data from each hospital in Sarawak on the incidence and prevalence of HFMD in Sarawak. As a result, we could not gather enough data for us to see the trend for number of death regarding HFMD in Sarawak.

With enough time and budget in future, hopefully we will be able to gather more data from main hospitals in Sarawak to study trend of the of HFMD outbreak in Sarawak.

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Table 3. Clinical presentation for 277 patients who had human enterovirus (HEV)-71 isolated.

Characteristic	Patients with non-CNS			Patients with CNS disease			OR (95% CI)	P value
	Mild HFMD	Severe Non- CNS HFMD	Total	HFMD with CNS complication s	AS M	Total		
No. (%) of patients	187 (68)	34 (12)	221(80)	52(19)	4(1)	56(20)	--	--
Age, median months (range)	32 (6-112)	24 (5-97)	31 (5-112)	23 (5-87)	25.5 (6-58)	23 (5-87)	--	.003
Fever before admission	141	29	170	51	4	55	16.5 (2.37-329.65)	.0003
Mouth ulcers	175	31	206	46	0	46	0.33 (0.13-0.96)	.0098
Rash	184	34	218	52	2	54	0.37 (0.04-4.57)	.2663
Vomiting	19	12	31	22	1	23	4.27 (2.11-11.11)	<.0001

							8.65)	
Cough or cold	48	12	60	19	1	20	1.49	.1364
							(0.76-	
							2.90)	
Seizure	0(0)	1(2.9)	1(0.5)	3(5.8)	2(50	5(8.9)	21.57	.0015
					.0)		(2.31-	
							1024.5	
							2)	
Diarrhoea	3	2	5	3	1	4	3.32	.0851
							(0.63-	
							15.95)	
Cold limbs	1	0	1	4	0	4	16.92	.0065
							(1.61-	
							837.01)	
Admission	37	37.7	37.1	38	38.9	38	--	<.000
temperature,	(36.4-	(36.5-	(36.4-	(36.5-39.5)	(37.	(36.5		1
median	38.20)	39)	39)		1-	-39.9)		
0C								
(range)					39.9			
					)			
Pulse of >150	2	0	2	7	2	9	20.97	<.000
beats/min							(4.09-	1
							202.37)	
Respiratory	0	0	0	4	0	4	--	.0015
abnormalities								

HEV-71 genogroup								
Genogroup	120	22	142	24	2	26	260.48	.0223
B4							(0.26-	
							0.91)	
Genogroup	24	6	30	10	1	11	1.56	.3515
B5							(0.68-	
							3.53)	
Genogroup	43	6	49	18	1	19	1.8	.0985
C1							(0.91-	
							3.57)	

NOTE: Data are no. (%) of patients, unless otherwise indicated. ASM; aseptic meningitis, HFMD; hand-foot-and-mouth disease. Repeating the analysis for 254 children (using only the first child from each family cluster) did not significantly alter any of the associations.

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