

EPIDEMIOLOGICAL CHARACTERISTICS OF DENGUE AMONG VIETNAMESE CHILDREN IN THE 2017 DENGUE OUTBREAK

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Abstract

Background: Dengue has spread rapidly in all regions during recent years and the epidemiological features of the disease have changed considerably despite many advances in epidemic prevention. Children and young adults have been the populations most at risk of dengue fever and severe complications.

Objectives: Evaluate epidemiological characteristics and the severity of dengue among children in the 2017 dengue outbreak.

Results: A review of 1446 paediatric cases with dengue in 2017 showed that male occupied predominantly for 56.9% of the total patients. Patients ≤ 1 year old, 2-5 years old, 6-12 years old and 13-18 years old accounted for 5.2%, 13.8%, 36.6% and 44.4% of the study sample, respectively. The major age group at the Children's Hospital 1 was from 6-12 years old (44.4%) while at the National Hospital for Tropical Diseases, it was from 13-18 years old (61.6%). Dengue outbreak happens widely across Vietnam. In the Southern region, dengue occurs all year round and peaks in the rainy season from June to October, after that, the infection decreases at the end of the year but still maintaining until the beginning of next year. In comparison, dengue transmission in the Northern region had suddenly increased since June 2017, then hit a peak in August 2017 and declined in the remaining months until the end of the year. Speciality, the infection is highly endemic in the Southwest region. It also expanded to the Southeast provinces such as Dong Nai and Binh Duong where emerging industrial zones located. The number of patients with dengue fever in Hanoi in 2017 was not only the greatest in the Northern region but also in the whole country. Comorbidities reported in children were rare with the most frequent diseases being respiratory diseases, gastroenteritis or infections. The incidence of dengue fever, dengue haemorrhagic fever and dengue shock syndrome made up 42%, 35.5% and 22.4%, respectively.

Conclusions: Our findings potentially develop a strategy for early detection, prognosis and proactive prevention of dengue in order to reduce the number of cases as well as the fatality rates.

Keywords: Children, dengue, DF, epidemiology, Vietnam.

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INTRODUCTION

Dengue has been the most popular mosquito-borne viral disease that poses major public health challenges around the world. The disease is caused by one of four serotypes of dengue viruses (DENV 1-4) which occur in urban and semi-urban areas of tropical and sub-tropical countries [1]. Each of them can be associated with severe disease depending on the sequence and time between infections. DENVs are transmitted between humans by Aedes mosquitoes, including the primary vector of Aedes aegypti and a secondary vector of Aedes albopictus. Over the past decades, the considerable increase in dengue incidence worldwide

may be due to the rapid urbanization, global human travel and urban to rural migration [2, 3].

The clinical spectrum of dengue ranges from asymptomatic infections (50-90% of infections) to classical dengue fever which is a self-limiting acute illness, to life-threatening severe disease characterized by vascular leakage, haemorrhage, and shock [2]. The probability of symptomatic dengue due to dengue virus infection is altered by the previous dengue immune status [4]. Exposure to one serotype of DENV provides lifelong immunity to only one serotype, but not lasting the protection to the other serotypes. Actually, prior

Epidemiological Characteristics Of Dengue Among Vietnamese Children In The 2017 Dengue Outbreak

infection with a different DENV serotype is the most significant risk factor to develop severe disease [5]. There is no licensed vaccines or specific anti-viral therapeutic for treatment and prevention of dengue. As several promising vaccines candidates have been in the later stages of clinical development, there is an urgent need to field test dengue vaccines, which might ultimately control the broad spread of dengue across the world [6, 7]. A complete understanding of high-risk populations of complications and poor outcomes in endemic settings is critical to implement dengue vaccines and anti-viral medicines in the future.

In Vietnam, dengue hemorrhagic fever was first explored in the 1960s in the Mekong Delta region in the South of Vietnam [8]. Dengue is considered as an endemic in the country with higher incidence in Southern region compared to Northern areas. The disease control for dengue is coordinated by the Vietnam National Dengue Control Program. The aims of the national strategy are based on the reduction in mosquito breeding sites, insecticide spraying, management, and treatment of symptomatic cases. Hence, the fatality rates of dengue have declined dramatically over the last two decades [9, 10].

The disease has spread in many localities across Vietnam. Hanoi and Ho Chi Minh City, which are two major cities, have the largest number of dengue patients. Children are more susceptible to dengue fever than adults and many serious complications in this age group are highly likely to lead to death. The onset symptoms of dengue fever in children are frequently nonspecific, overlooked or confused with other conditions [2]. Although adults often experience shock, vascular leakage is generally more severe in young children [11]. Furthermore, dengue shock syndrome has been seen primarily in the pediatric population. Several studies conducted in Asian countries figured out that a heavy burden of symptomatic dengue was among children, who are at a higher risk of severe disease [12, 13]. Earlier studies from Latin America and the Caribbean reported that the mortality rate was largest among children in the Caribbean countries [14, 15].

In Vietnam, studies on socioeconomic impact of dengue were conducted in the last few years, regarding economic burden of dengue, knowledge-attitude-practices (KAP) on dengue prevention, and willingness to pay for dengue vaccine. In 2018, two KAP studies agreed that Southern citizens had limited knowledge about dengue but moderate-to-high attitude and practice about dengue prevention [16, 17]. On the other hand, university students showed higher score on KAP than common population [18]. Other studies on a tertiary hospital in southern Vietnam resulted that cases of dengue doubled from 2013 to 2015 [19]. Hospitalization cost posed significant impact on total treatment cost of dengue per year [20]. Interestingly, despite no available marketed dengue vaccine, 89.2% Vietnamese interviewees were willing to pay for a future vaccination program, ranging from 2 to 5 millions VND [21].

As research on epidemiological characteristics among child patients have been conducted mostly in the Southern region, there is a lack of a general picture for the whole country. This study aimed not only to determine the aspects regarding clinical epidemiology but also to identify the severity of dengue among children in the 2017 outbreak.

METHODS

Study design

We performed a retrospective study at National Hospital of Tropical Diseases and Children's Hospital 1. The study collected medical records of dengue cases in children during the outbreak in 2017 which were diagnosed based on clinical signs, symptoms, and haematological tests and classified by severity grade according to the Vietnam Ministry of Health guidelines 2011. The exclusion criteria were medical records missing over 20% of details, being admitted to hospital with severe conditions or patients with HIV.

The sample size was calculated by the formula [22]

$$N = \frac{z^2_{1-\alpha/2} (1-p)}{pe^2}$$

With N as the minimum sample size is determined, $z_{1-\alpha/2}$ as the value of normal distribution at 95% confidence level (1.96), p as the proportion of dengue patients (0.1), ϵ as tolerable standard error (0.25). Taking this equation, the minimum sample size was 553. This study presumed at 20% of missing information rate, so we will collect at least 665 medical records of child patients. Therefore, a total of 1330 patients from National Hospital of Tropical Diseases and Children's Hospital 1 were recruited in the research.

We choose a sample based on the study period, clinical manifestations as well as the severity of the disease. According to the sample size, medical records were collected following the proportion of patients hospitalized monthly in the year at each hospital. It is assumed that the number of patients with severe complications has distributed randomly. The random selection of medical records in a month will ensure the randomization of the severity of illness.

Statistical analysis

Recorded data were entered to Microsoft Excel 2013 before being exported to SPSS (Statistical Package for the Social Sciences) version 22.0 for analysis. Descriptive statistics were employed to summarize socio-demographic characteristics, the regional distributions, past medical history, family history and classifications of dengue virus infections. Categorical variables were presented as frequencies and percentages whereas continuous variables were described as mean and 95% CI.

Ethical approval

The study was approved by the Ethical Committee of both National Hospital of Tropical Diseases and Children's Hospital 1. The obtained data from two hospitals were kept confidentially and only used for research purpose.

RESULTS

Sociodemographic characteristics of patients with dengue presented in Table 1. Thereby, majority of patients was male and aged between 13 to 18. Two hospitals revealed the same results regarding gender and age. Approximate half of patients were admitted from the Red River Delta, followed by from southeast and southwest region (Table 2). Table 3 and Table 4 showed the history of patients, including family history and medical history. According to Table 5, 42% of dengue cases were simply fever, 35.5% were haemorrhagic fever, and 22.4% had shock syndrome.

Table 1. Socio-demographic characteristics of patients

Characteristic	NHTD		CHI		Total	
	n	%	n	%	n	%
Gender						
Male	411	57.4	412	56.4	823	56.9

*Epidemiological Characteristics Of Dengue Among Vietnamese Children In The 2017
Dengue Outbreak*

Female	305	42.6	318	43.6	623	43.1
Age groups (years)						
≤ 1	9	1.3	66	9	75	5.2
2 - 5	61	8.5	139	19	200	13.8
6 - 12	205	28.6	324	44.4	529	36.6
13 - 18	441	61.6	201	27.6	642	44.4
Month of admission						
January	5	0.7	71	9.7	76	5.3
February	1	0.1	35	4.8	36	2.5
March	2	0.3	73	10	75	5.2
April	1	0.1	35	4.8	36	2.5
May	15	2.1	29	4	44	3
June	28	3.9	60	8.2	88	6.1
July	135	18.9	65	8.9	200	13.8
August	248	34.6	92	12.6	340	23.5
September	148	20.7	57	7.8	205	14.2
October	77	10.8	84	11.5	161	11.1
November	47	6.6	69	9.5	116	8
December	9	1.2	60	8.2	69	4.8
No. days of admission						
1 - 3	191	26.7	265	36.3	456	31.5
4 - 6	488	68.2	431	59	919	63.6
> 6	37	5.1	34	4.7	71	4.9
Mean	4.3		3.9		4.1	
Max-Min	(0-9)		(0-9)		(0-9)	
(95%CI)	(95%CI: 4.2-4.4)		(95%CI: 3.8-4.0)		(95%CI: 4.0-4.2)	

Table 2. Distribution of dengue cases according to regions

Region	Number of cases	
	n	%
Northeast	3	0.2
Red River Delta	106	48.8
Northwest	6	0.4
North Central	18	1.2
Central Highlands	5	0.3
South Central Coast	15	1.0
Southeast	517	35.7
Southwest	176	12.2
Total	1446	100.0

Table 3. Past medical history of dengue patients

Medical history	NHTD		CHI		Total	
	n	%	n	%	n	%
Neurological disorders	5	0.7	4	5.5	9	6.2
Down Syndrome, Cerebral Palsy, Intellectual Retardation	2		2		4	
Mental disorder	1		1		2	
Epilepsy	2		1		3	
Blood diseases	1	0.1	9	1.2	10	0.7
Thalasemia	1		4		5	
G6PD deficiency	0		1		1	
Hemophilia A	0		1		1	
Hemophagocytic Lymphohistiocytosis	0		2		2	
Immune Thrombocytopenic Purpura	0		1		1	
Dengue fever	2	0.28	4	0.6	6	0.41
Allergies and autoimmune diseases	8	1.1	2	0.27	10	0.69
Allergies (seafood, medicine, host factor)	5		1		6	
Henoch Scholein Purpura	1		0		1	

*Epidemiological Characteristics Of Dengue Among Vietnamese Children In The 2017
Dengue Outbreak*

Atopic Dermatitis	2	0	2
Systemic lupus erythematosus	0	1	1
Malignant disease		1 0.1	1 0.07
Kidney cancer	0	1	1
Congenital and genetics diseases	3 0.4	2 2.7	5 0.3
Quadripareisis	0	1	1
Congenital heart defect	2	1	2
Hirschsprung disease	1	0	1
Infectious disease	2 0.3	11 1.5	13 0.9
Sepsis	0	1	1
Meningitis	0	2	2
Tuberculosis	0	2	2
Measles, mumps, chicken pox, hand - foot - mouth disease	0	5	5
Pneumonia	2	1	3
Surgery	1 0.1	2 0.3	3 0.2
Intussusception	0	2	3
Spinal cord injury	1	0	1
Other diseases	33 4.6	21 2.9	54 3.7
Fatty liver disease	1	0	1
Gastroenteritis	11	3	14 1.0
Febrile seizure	3	0	2
Stroke	1	0	1
Kidney diseases	2	3	4
Hepatitis	1	1	3
Asthma	8	10	18 1.2
Other pulmonary disease	3	4	6 0.5
Diabetes	1	0	1
Hypertension	1	0	1
Peptic ulcer disease	1	0	1
No comorbidity	658 91.9	673 92.2	1331 92

Table 4. Family history of dengue patients

Epidemiological factors	NHTD		CH1		Total	
	n	%	n	%	n	%
Family history	47	6.6	2	0.3	49	0.9

Table 5. Classification of dengue virus infections

Classification	NHTD		CH1		Total	
	n	%	n	%	n	%
Dengue fever	310	43.3	298	40.8	608	42.0
Dengue haemorrhagic fever	293	40.9	221	30.3	514	35.5
Dengue shock syndrome	113	15.8	211	28.9	324	22.4
<i>Total</i>	<i>716</i>	<i>100.0</i>	<i>730</i>	<i>100.0</i>	<i>1446</i>	<i>100.0</i>

DISCUSSION

Epidemiological characteristics of dengue patients

Gender

In the present study, the majority of patients was male in both National Hospital of Tropical Diseases (57,4%), Children's Hospital 1 (56,4%) as well as the study population (56.9%). Our findings were consistent with Anders KL et al.'s study, which showed that male patients were predominant with 57% of 132,480 the pediatric dengue patients being admitted to three study hospital from 1996 to 2009, compared to female counterparts with 43% [9]. Similarly, Anker M et al.'s study across 6 Asian countries, the proportion of male cases in Laos from 2000-2006 was 57.9%, the Philippines from 1998-2000

was 57.2%, Singapore from 1999-2005 was 60.7%, Sri Lanka from 1996-2005 was 61.8% and Cambodia in 2010 was 60.1%. In Malaysia, the percentage of males among reported cases ranged from 54.4 to 61.5% yearly between 1997 and 2008 [23].

Age

Most of the patients in our study aged 6 years old or above with 90.2% in National Hospital of Tropical Diseases, 72% in Children's Hospital 1 and 81% of the study population. While 44.4% of patients in National Hospital of Tropical Diseases were from 6 to 12 years old, 61.6% of patients in Children's Hospital 1 belong to the 13-18 age group. This was in line with the epidemiological characteristics of dengue fever in the North, Central and Southeast regions in recent years with

Epidemiological Characteristics Of Dengue Among Vietnamese Children In The 2017 Dengue Outbreak

older children and adults mainly getting dengue fever. Meanwhile, a large number of young children from the Southwest region were admitted to Children's Hospital 1 to treat dengue fever [24]. Research by Nguyen et al. among 2060 pediatric patients at 7 hospitals including Children's Hospital 1, Children's Hospital 2, Tropical Diseases Hospital in Ho Chi Minh City, Dong Nai Children's Hospital, Tien Giang Center General Hospital, Long An General Hospital and Binh Duong General Hospital investigated that the median age of dengue patients was 9 (quartile range: 7-11) [25]. By a 10-year retrospective study in Nha Trang city, Duong et al. pointed out that the majority of dengue cases were in children and young adults in those aged 5–24 years. Recently, the peak incidence tended to have shifted toward younger age groups, with children younger than 5 years experiencing comparable incidence rates as older children [26].

Month of admission

Our results highlighted that the proportion of dengue cases were affected by the seasons as well as regional geography. Patients with DF were admitted to Children's Hospital 1 almost all year round due to the hot and humid weather in the South of Vietnam. According to Pasteur Institute in Ho Chi Minh City, the number of dengue patients in the southern region has increased significantly in the rainy season between May and October, then decreased but still remained stable until the beginning of next year. In comparison, the number of dengue cases in the North of Vietnam usually rises from June to September, subsequently, it goes down in the last months of the year when the temperature has declined [24].

Provinces and regions

Our findings depicted that the distribution of dengue fever was broad, consisting of most of provinces and cities across Vietnam in 2017. The outbreak mainly occurs in the Southwest region and several provinces in the Southeast such as Dong Nai, Binh Duong as well as other emerging industrial areas. Regarding Northern regions, Hanoi has the largest number of dengue cases in 2017 [24]. There have been no dengue cases in Northern border provinces. It can be explained that these provinces are in the mountainous area which often has cold weather. Another possible reason is that patients have visited local health stations instead of a healthcare center like National Hospital of Tropical Diseases. Similarly, no case was reported in some provinces in the Central region, namely Quang Tri, Da Nang, Khanh Hoa, and in the Central Highlands like Kon Tum, and in the Red River Delta such as Hai Phong because of the geographical distance from the two research sites in the current study including National Hospital of Tropical Diseases in Hanoi and Children's Hospital 1 in Ho Chi Minh City.

Date of admissions

This study found that the majority of patients hospitalized with dengue fever in the period of 4-6 days accounting for 63.6%, followed by 31.5% with 1-3 days of the length of stay and only 4.9% of the study population stayed over 6 days.

Past medical history

To our best knowledge, this study is the first research which demonstrated past medical history among patients with dengue fever in Vietnam. Although comorbidity is not as common in children as adults, individuals with different internal and surgical problems may get dengue fever [2]. An interesting feature is that the most common underlying disorders in children patients were lung disease and asthma (1.7%), gastroenteritis (1%) and infectious diseases (0.9%).

Family history

The overall rate of patients who have had family members with dengue in the entire study subjects was 0.9%.

The severity of dengue

This study illustrates that the prevalence of patients with dengue shock syndrome in of Children's Hospital 1 was 28.9%, in comparison with 15.8% in National Hospital of Tropical Diseases and 22.4% for the study sample. The difference between the prevalence in Children's Hospital 1 and in National Hospital of Tropical Diseases may be due to the higher percentage of young children patients in Children's Hospital 1. Previous studies by Anders KL et al. also emphasized that younger age groups tend to get more severe illness than older children [9].

CONCLUSIONS

Our study gave a relatively complete picture of the epidemiological aspects of dengue fever in children in the epidemic in 2017, especially about the characteristics in term of age, gender, length of stay, geographical features, comorbidity as well as the severity. The findings potentially help develop a surveillance program for early detection, prognosis and proactive prevention plan in order to reduce the incidence of dengue fever and the mortality rate. It is essential to investigate the clinical epidemiological characteristics of dengue fever among adults and identify the relationship between climate change and the increase of confirmed dengue cases. Moreover, an integrated urban and industrial development strategy with solutions of eliminating mosquito larvae should be taken into account so as to prevent the spread of dengue fever.

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CONFLICTS OF INTERESTED

The authors declare that they had no conflicts of interest.

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*Epidemiological Characteristics Of Dengue Among Vietnamese Children In The 2017
Dengue Outbreak*

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