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An Investigation of Dengue Deaths in Vientiane Capital and Champasack Province, Lao People's Democratic Republic, 2013

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Abstract

Introduction

Dengue is endemic in the Lao People's Democratic Republic. In 2013, dengue cases exceeded the epidemic threshold from January onwards. A high case fatality ratio (CFR) was reported from Vientiane Capital and Champasack Province. Thisstudy aimed to identify the causes of dengue deaths during the 2013 outbreak in the two provinces in order to make recommendations for improvement of case management.

Methods

Dengue data were collected from the Lao Early Warning Alert and Responsesystem. All dengue deaths admitted to seven hospitals during the dengue epidemic in 2013in Vientiane Capital and Champasack province were analyzed. Data were collected from the hospitals by reviewing the mortality forms and dengue case management forms. Descriptive statistical analyses were performed.

Results

A total of 44 171 dengue cases including 95 deaths were reported in 2013 (CFR=0.21%). The majority of deaths were reported from Champasack (n=35) and Vientiane Capital (n=26); most (74%) were aged less than 15 years. Most of the death cases were admitted to the hospital late (median of 4 days from onset) with severe bleeding(59%) or fluid overloading due to prior intravenous fluid therapy (41%). Late or incorrectdiagnosis for dengue with warning signs was not uncommon (10/61, 16%).

Conclusion

It was the largest epidemic year for dengue in 2013 with a high number offatal cases. Ongoing training for healthcare providers should be implemented to improve diagnosis, case management, and treatment outcomes. Further community-based surveys on the health-seeking behavior of dengue patients may indicate potential risk factors for severe dengue outcomes.

Introduction

Dengue fever is a severe, flu-like illness that affects infants, young children, and adults, but seldom causes death. There are four dengue virus serotypes (Den1, Den2, Den3, Den4) and all can cause dengue fever. The dengue virus belongs to the genus Flavivirus and the Flaviviridae family. 'Dengue virus is primarily transmitted by Aedes mosquitoes, particularly Aedes Aegypti.**[1]** There is no specific treatment for dengue fever.' Only symptom management, which can vary from oral rehydration therapy at home with close follow-up to hospital admission with administration of intravenous fluidsand/or blood

transfusion, is used for dengue treatment. The mortality of dengue infections is 1-5% without treatment, and less than 1% with adequate treatment.**[1]** Previous studies revealed that the reasons for death include lack of access to prompttreatment (late health-seeking behavior), late diagnosis or diagnosis errors, fluid accumulation (leading to heart failure or pulmonaire edema), respiratory distress, severe organ involvement, severe bleeding, and shock.**[4]**

Dengue virus infection is a global health threat and is currently endemic in more than 125 countries worldwide. There are estimated 50 to 100 million dengue infections worldwide every year, with half a million cases requiring hospitalization and approximately 25,000 deaths.**[2]** In the Western Pacific Region, dengue infections are most common during the rainy season (April to October) peaking in late August and September historically.**[3]** Dengue is endemic in the Lao People's Democratic Republic. Between 2006 and 2012, the annual dengue notification rate ranged between 62 and 367 cases per 100,000 population. The case fatality ratio (CFR) was 0.2% for all years except 2008 at 0.5%. In the epidemic year of 2010, 22 890 cases and 46 deaths were reported; with anestimated 367 cases per 100,000 population.**[5]**

In 2013, a large dengue epidemic occurred with cases reported from all 17 provinces and deaths occurring in eleven provinces in Lao People's Democratic Republic. The 2013 epidemic was detected in January 2013 by the National Center for Laboratory and Epidemiology (NCLE) through the national routine surveillance system, Lao Early Warning Alert and Response (LaoEWARN), which receives daily reports from central and provincial hospitals through all provincial health departments. In week 38, the CFR of Vientiane Capital and Champasack Province were 0.32% and 0.67%, respectively;the CFRs were much higher than the previous national ones and most of the denguedeaths were from these two provinces.

This study was conducted to reveal the underlying causes of the increased dengue CFRs by investigating the dengue fatal cases in Vientiane Capital and Champasack Province in 2013, to deduce specific recommendations to improve dengue case management and reduce the severity of dengue infections in Lao People's DemocraticRepublic in future.

Methods

We conducted a descriptive analysis that comprised all dengue death cases who were admitted in hospitals from Vientiane Capital and Champasack Province in the Lao People'sDemocratic Republic from August 2013 to January 2014. Five hospitals from Vientiane Capital and two from Champasack Province were included in the analysis.

Case Definitions

Dengue cases were defined according to the 2009 World Health Organization revised case definitions for dengue. A clinical dengue case was defined as a person with a fever of 2–7 days and having two of the following symptoms: nausea/vomiting, rash, aches and pains, and a tourniquet-positive test of leukopenia. A dengue case with warning signs was defined as a clinical dengue case with any warning signs including abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, restlessness, liver enlargement >2cm, and/or increase in hematocrit concurrent with rapid decrease in platelet count. A severe dengue case was defined as a dengue with warning signs case and had severe plasma leakage, leading to shock syndrome; fluid accumulation with respiratory distress; severe bleeding; or severe organ involvement.**[6]**

Data Collection and Analysis

Data were collected from the hospitals using a standard mortality form and from theIntegrated Dengue Case Management form. Data collected included demographics, clinical and treatment details, cause of death, and laboratory results of the cases.' Data on dengue laboratory confirmation and serotyping from the National Centerfor Laboratory and Epidemiology (NCLE) were collected. These included the results of the NS1 dengue rapid test (Microbix Biosystems Inc., Mississauga, Canada), Enzyme-Linked Immunosorbent Assay (Panbio® Dengue IgM Capture ELISA, Alere Inc., Waltham, Massachusetts, USA) and polymerase chain reaction test (Invitrogen, ThermoFisher Scientific, Waltham, Massachusetts, USA).

All data were analyzed descriptively using Epi Data software (Version 3.1) and MicrosoftExcel (Version 2010).

Results

In 2013, there were 44,171 cases of dengue and 95 deaths reported in the Lao People's Democratic Republic (CFR = 0.21%). Of the 95 deaths, 61 (64.2%) were residents of Vientiane Capital or Champasack province. Most deaths (74%) occurredamong people aged under 15 years. No sex differences were found among the cases (male-to-female ratio = 1:1.03). Most of the death cases (51/61, 84%) presented withsevere dengue; and the rest (10/61, 16%) presented with dengue with warning signs.

Comorbidity was present in 38% of the fatal cases, including thalassemia, cardiovascular diseases, hypertension, asthma, epistaxis, menstruation, and chronic otitis. About 75% of the cases sought health care prior to death; 56% sought health careonly once; 10% sought care again after initial treatment. Almost half (48%) of all cases visited medical personnel in the villages. About one-third (34%) had therapy before admission, mostly Intravenous (IV) fluids **(Table 1)**. The median time from symptom onset to hospital admission was 4 days in Vientiane Capital (range 1 – 5) and 3 days in Champasack Province (range 1-4). The median time from admission to death was one day in both provinces (range 0-1). The time for admission to death ranged from 0-8 days **(Table 1)**.

Table 1: Characteristics of dengue death cases, VientianeCapital and Champasack Province, 2013. (n=61)*

Characteristics	Frequency	Percentage (%)
Age (years)		
0 – 1	12	19.6
1-14	33	54.0
15-30	10	16.4

30-39	3	4.9
40+	3	4.9
Sex		
Male	31	50.8
Female	30	49.2
Comorbidity		
None	34	55.7
Thalassemia	2	3.3
Cardiovascular Disease	2	3.3
Hypertension	1	1.6
Asthma	1	1.6
Epistaxis	1	1.6
Menstruation	1	1.6
Pregnancy	1	1.6
Chronic otitis	1	1.6
Days between onset and admission		
0	1	1.6
1-2	2	3.3
3-4	40	65.6
5-6	18	29.5
Days between admission and death		
0	12	19.7
1-2	39	65.9
3-4	5	8.2
5+	3	4.9
Presented to healthcare facilities		
No	15	24.6
Yes	46	75.4
Types of healthcare facility presented (n=46)		
Medical personnel in the village	22	47.8
Pharmacy	2	4.3
Private Clinic	8	17.3
Health Center	3	6.5
District Hospital	10	21.7
Referral hospital	1	2.2
Therapy before admission(n=46)		
Intravenous Infusion	21	34.4

Acetaminophen	13	28.2
Oral Rehydration Salt	1	2.1
Number of health care visits (n=46)		
1	34	55.7
2	6	9.8
Clinical Characteristics (n=46)		
Urine output	1	1.6
Oral intake	2	3.3
CCTVR**	33	54.1

*Not all variables will add up to 61 (100%) due to missing data

**CCTVR, Color Capillary Temperature Volume Rate

The proximate cause of death was documented in all cases. Of 36 patients who died due to severe bleeding, 11 (30%) received blood products more than 24 hours after the blood transfusion request by the doctor and 11 did not receive them at all. Of 25 patients whose proximate cause of death was fluid overload, 19 (76%) had received IV fluid infusion from another Health care facility prior to admission, and six (24%) at admission. Late or incorrect diagnosis for dengue with warning signs was common among the death cases. Lack of constant monitoring of vital signs (due to the shortfall ofdoctors and nurses) was reported among 61 death cases.

Twenty-eight (46%) of death cases had specimens submitted for laboratory testing. All28 (100%) specimens tested were positive by at least one laboratory assay, including14.2% (4/28) by rapid test, 71.4% (20/28) by ELISA, and 14.2% (4/28) by PCR.

The CFR was higher in Champasack Province than in Vientiane Capital but was less than1% in both districts **(Table 2)**.

Table 2: Mortality (per 10,000 population) of dengue cases, Vientiane Capital and Champasack Province, Lao People's Democratic Republic, 2013 (n=61)

District	Total Population	No. of Cases	No. of Deaths	Morbidity Rate/10 000	Mortality Rate/10 000	CFR (%)
Vientiane Capital	871 499	8453	26	96.99	0.30	0.31
Chanthabury	78 173	812	3	103.87	0.38	0.37
Sikhottabong	126 997	951	3	74.88	0.24	0.32
Xaysetha	120 235	1287	3	107.04	0.25	0.23
Sisattanak	78 552	919	2	116.99	0.25	0.22
Nasaythong	73 206	534	2	72.94	0.27	0.37
Xaythany	213 933	2487	6	116.25	0.28	0.24
Hatxayfong	91 138	1096	4	120.26	0.44	0.36
Sangthong	32 654	102	0	31.24	0.00	0.00
PakNgeum	56 611	265	3	46.81	0.53	1.13
Champasack Province	713 233	4971	35	69.70	0.49	0.70
Pakse	91 542	940	2	102.69	0.22	0.21

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Sanasomboune	68 064	789	7	115.92	1.03	0.89
Bachieng	64 673	667	2	103.13	0.31	0.30
Paksong	86 176	135	0	15.67	0.00	0.00
Pathoumphone	59 155	426	2	72.01	0.34	0.47
Phonethong	95 766	545	8	56.91	0.84	1.47
Champasack	60 942	270	1	44.30	0.16	0.37
Sukhuma	61 609	306	3	49.67	0.49	0.98
Moonlapamok	44 504	301	1	67.63	0.22	0.33
Khong	80 802	592	9	73.27	1.11	1.52

Discussion

The CFR for dengue in Vientiane Capital and Champasack province was higher than that of the annual national average of the Lao People's Democratic Republic.**[5]** This is most likely due to the hospitals in these provinces being overwhelmed with cases. In Champasack Province, one provincial hospital and nine district hospitals managed around 5000 dengue cases, while in Vientiane Capital, seven central hospitals managed 8453 dengue cases in 2013. Champasack province had a much lower doctor-patient ratio which might explain the higher CFR, in comparison to Vientiane Capital. Shortfalls of doctors and nurses might result in incomplete constant monitoring of vitalsigns.

Late or incorrect diagnosis for dengue with warning signs was common among the fatal cases. Healthcare-seeking delays resulting in high fever development and delay of hospital admissions probably contributed to this observation. There were delays in blood transfusion for patients with severe bleeding, which resulted in patients not being stabilized for the administration of normal saline or polyglukin for treatment. The results also revealed an excess use of IV fluids prior to hospitalization in several death cases, as these dengue patients presented with symptoms of fluid overload. This indicated thattreatment guidelines from WHO **[6]** were not used in the early stages of the outbreak.

Measures from the Lao People's Democratic Republic government were implemented to control the outbreak in July 2013. These included: (i) Strengthen case management resources in hospitals to manage the high dengue case numbers and (ii) Advocacy meetings with multi-sectoral dengue task forces at all levels. (iii) Strengthen NCLE dengue surveillance by receiving daily reports for rapid response to cluster (vi) Information Education for Health campaigns to improve early healthcare-seeking behavior. Also, the government provided extra medical students to each hospital to assist with case management, reporting of dengue cases, and conducting vector control measures. Training on dengue clinical management in healthcare facilities was also provided before raining season in 2013. The cases had been reduced dramatically afterthese interventions.

There were some limitations in this study. The analysis was done by using secondary data sources. Some data were missing from the records, especially those in Champasack province. Certain analyses could not be conducted due to the large amount ofdata missing in certain variables. Also, data collection was time-consuming and we could not avoid human errors during the process.

Based on the results, we recommend better recognition and diagnosis of dengue, especially early in the dengue season; also, better treatment and monitoring of patients through ongoing staff training, including urgent requests for blood when required, closely following up evaluations, and documenting all interventions are encouraged. As fluid overload was a common factor for severe dengue outcomes, we should ensure thatpatients who have already received IVF at home or in other hospitals do not repeat the treatment when admitted. It is also useful to use standardized reporting forms at all levels for documenting the case details.

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