

Analysis of Dengue Fever Cases Recorded between 2005 and 2007 in Taiwan

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Abstract

This report analyzed dengue fever case data collected between 2005 and 2007. It includes cases reported to Taiwan's Center for Disease Control through its communicable disease surveillance system, as well as contactor cases and cases detected by fever screening centers at international airports and sea ports. In 2005, 17.9% of reported cases tested positive. This percentage increased to 37.8% in 2006, and again to 51.3% in 2007. A gradual year on year increase in the positive test rate of both the serum tests and the reverse transcriptase polymerase chain reaction tests shows that clinical practitioners are experienced in diagnosing dengue fever infections, and are able to identify suspected cases and collect samples for early prevention and treatment. In 2007, 77 residents from the Tainan Municipal Honorable Citizens' Home and 32 people in another residential area in Tainan were infected. This shows dengue outbreaks can occur in both crowded and less crowded residential areas. Eighty percent of imported dengue fever cases came from five countries: Vietnam, Indonesia, the Philippines, Cambodia, and

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Thailand. In 2007, China also accounted for 5% of imported dengue cases in Taiwan. People travelling frequently between Taiwan and China should be alert to the risk of dengue infection. The increasing number of positive cases detected by fever screeners at international airports and sea ports also indicates that quarantine in ports plays an important role in preventing dengue fever. The biggest challenge is to detect and stop the spread of dengue cases at this first line of defense. Data from the past three years shows that the onset of dengue outbreaks seems to be occurring earlier each year. The same trend is noticeable in neighboring countries like the Philippines. However, more study is needed to establish whether global warming could be leading to earlier and more prolonged dengue fever outbreaks in Taiwan.

Keywords: Dengue fever, Contactors, Fever screening at airports and sea port

Introduction

Dengue fever is an acute febrile disease caused by dengue viruses and is transmitted by the bite of the *Aedes aegypti* and *Aedes albopictus* mosquitoes. It is mainly found in tropical and subtropical regions like Africa, the Americas, the Middle East, South-East Asia and the Western Pacific. Between 50 million and one billion people are infected with dengue fever each year. Approximately 20,000 people die annually from this disease[1,2].

There are three forms of dengue fever. In increasing severity, they are: dengue fever; dengue hemorrhagic fever; and dengue shock syndrome. Typical symptoms of dengue fever include fever, headache, muscle and joint pains, rashes, and retro-orbital pain. Dengue hemorrhagic fever occurs when all of the above symptoms are accompanied by plasma leakage and hemorrhagic phenomena. When patients develop shock as well as leakage and hemorrhagic phenomena,

they are diagnosed as having dengue shock syndrome. Dengue virus has four serotypes: DENV-1, -2, -3 and -4. Infection with one of these serotypes provides lifetime immunity to that serotype, but very limited protection against other serotypes.

The three diagnostic methods currently being used are virus isolation, retro-transcriptase polymerase chain reaction (RT-PCR), and serum tests. With virus isolation, because the virus only lasts in a patient's serum for a short time, only serum taken within a week of the onset of symptoms (acute phase serum) can be used. RT-PCR is mainly used to detect the presence of RNA in the dengue virus. Because of its high specificity and sensitivity, RT-PCR is often used to test samples in the acute phase for early diagnosis. Serum tests are mainly used to examine samples taken between 8 and 13 days of onset (early recovery serum) and between 14 and 30 days (late recovery serum). This method uses enzyme to capture the IgM and IgG antibodies in the sera (IgM and IgG enzyme-linked immunosorbent assay (ELISA) kit).

A patient is diagnosed with dengue virus infection when any of the above methods returns a positive result. A positive result in the serum tests means that either the sample tests positive for IgG and IgM antibodies, or that the titres of IgG and IgM antibodies in the paired sera show more than four time difference, but the IgM in the control serum tests negative against Japanese encephalitis virus[3,4].

Regional and national dengue epidemics occur in Taiwan from time to time. The island-wide outbreaks in 1915, 1931, 1942, and the outbreaks in the Kaohsiung region in 1987, 1988 and 2002 were the most notorious. Other than the communicable disease reporting system, set up by the Centers for Disease Control (CDC) in Taiwan according to the Communicable Disease Prevention and

Treatment Law, the CDC have also been monitoring dengue patients regularly. They have broadened the scope of the sample size in an effort to locate the infected contactors as soon as possible. Results comparing RNA sequences show that all of Taiwan's dengue outbreaks in recent years were caused by imported viruses[5], with a potential risk of cross-infection. Thus, it is essential to stop or reduce transmission of imported viruses. The CDC's fever screening centers at international ports have been important tools to prevent the spread of imported viruses through monitoring visitors' temperatures.

This report analyzes: dengue fever cases reported to the CDC's communicable disease surveillance system between 2005 and 2007; contactors of the patients; and cases identified by fever screening centers at international airports and sea ports. The aims of this study were to evaluate the effectiveness of CDC's strategies of dengue fever testing, prevention and control, in order to improve epidemic prevention in the future.

Materials and Methods

1. Data sources

The original data were obtained from the CDC's database of communicable diseases. According to the notifiable diseases surveillance system and symptoms surveillance system, suspected samples of dengue fever, dengue hemorrhagic fever, and dengue shock syndrome cases must be submitted for testing. These samples were then divided into three groups according to their sources: reported cases; their contactors (in general surveys and broadened surveys); and cases identified by fever screening centers at international airports and sea ports.

2. Definition of positive cases

According to the CDC's standard protocol, a positive case of dengue virus means a positive result in virus isolation, RT-PCR or in serum tests, when IgG and IgM antibodies in the serum test positive, when the titers of IgG and IgM antibodies in the paired sera are four times bigger while the titers of IgM antibodies in the control serum tests negative against Japanese encephalitis virus. A positive case was marked 'positive' in the 'Final result' column of the database.

3. Data excluded

Data were excluded when the patient's sample origin, age or country where patient was infected was not specified in the relevant columns.

Results

1. Number of samples and positive rate of dengue fever virus (Table 1)

1) Results from RT-PCR

- A) In reported cases, RT-PCR identified 8.9% positive cases (70/788) in 2005, 23.5% (461/1,965) in 2006, and 35.7% (1,174/3,290) in 2007.
- B) Of the contactors, 0% (0/33) tested positive by RT-PCR in 2005, 2.9% (26/905) in 2006, and 11.1% (73/656) in 2007.
- C) Of those identified by the fever screening centers at international airports and sea ports, 1.5% (18/1,204) tested positive by RT-CPR in 2006, and 12% (73/5,926) in 2007.

2) Results from serum tests

- A) In reported cases, serum tests identified 15.5% (552/3,550) positive cases in 2005, 27.2% (2,252/8,285) in 2006, and 32.2% (3,675/11,423) in 2007.

B) In 2005, 1.1% (49/4,589) of the contactors were tested positive by serum tests. The percentage increased to 2.9% (611/21,749) in 2006, and 3.2% (914/28,434) in 2007.

C) Cases screened by fever screening centers tested 0.9% positive (22/2,461) in 2006 and 0.3% (38/11,966) in 2007.

Table 1. Number of dengue fever samples

	RT-PCR ^a		Serum tests ^b		Imported		Number	Positive rate (%)
	cases tested	Positive rate (%)	Cases tested	Positive rate (%)	Yes (%)	No (%)		
2005								
Reported	788	70(8.9)	3,550	552(15.5)	44(25.3)	130(74.7)	973	174(17.9)
Contactors	33	0(0)	4,589	49(1.1)	1(25)	4(75)	3,713	5(0.1)
From fever screening centers	NA	NA	NA	NA	NA	NA	NA	NA
Total	821	70(8.5)	8,139	601(7.4)	45(25.1)	134(74.9)	4,686	179(3.8)
2006								
Reported cases	1,965	461(23.5)	8,285	2,252(27.2)	74(8.4)	804(91.6)	2,328	878(37.8)
Contactors	905	26(2.9)	21,749	622(2.9)	3(2)	150(98)	18,668	153(0.8)
From fever screening centers	1,204	18(1.5)	2,461	22(0.9)	11(100)	0	1,220	11(0.9)
Total	4,074	505(12.4)	32,495	2896(8.9)	88(8.4)	954(91.6)	22,216	1042(4.7)
2007								
Reported cases	3,290	1,174(35.7)	11,423	3,675(32.2)	83(4.8)	1631(95.2)	3,342	1,714(51.3)
Contactors	656	73(11.1)	28,434	914(3.2)	11(3.3)	323(96.7)	22,800	334(1.5)
From fever screening centers	5,926	73(1.2)	11,966	38(0.3)	77(100)	0	5,969	77(1.3)
Total	9,872	1320(13.4)	51,823	4627(8.9)	171(8)	1954(92)	32,111	2125(6.6)

a: The denominator is the number of samples received within 7 days of the onset of symptoms. The numerator is the number of samples marked as positive in the column 'final result'. Multiple samples or different types of samples may be taken from the same patient.

b: The denominator is the number of samples of serum and cerebral spinal fluid. The numerator is the number of samples marked as positive in the column 'final result'. Multiple samples or different types of samples may be taken from the same patient.

c: Data of fever screening samples in 2005 was not available.

2. Number of local dengue fever cases by month

Figure 1 shows that the dengue epidemic in 2005 first broke out in August and reached its peak in November, when 32.3% of infections (42/130) were reported. In 2006, the outbreak started in July and peaked in October, when

29.7% (239/804) of cases were reported. In 2007, the index case was recorded even earlier (in June) and 33.7% (550/1631) of the cases were reported in November, at the height of the outbreak.

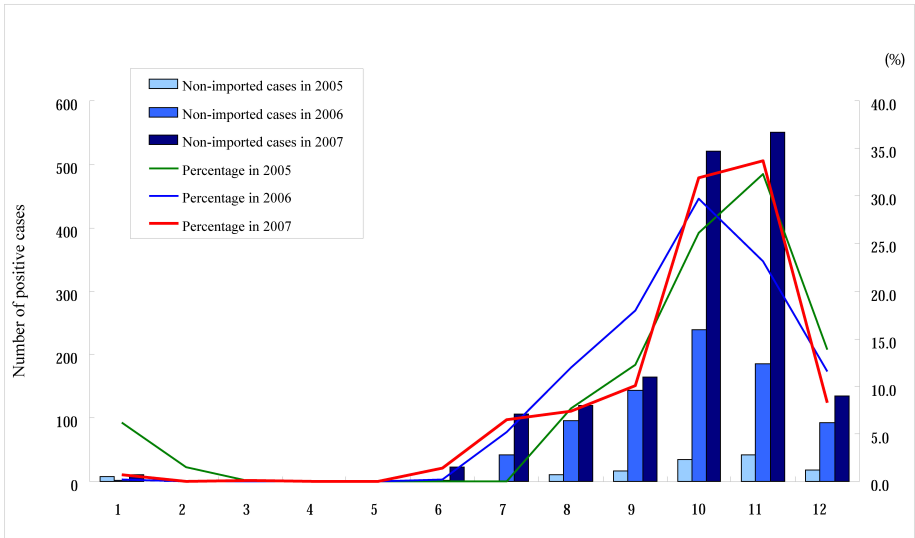


Figure 1. Number of non-imported dengue fever cases by month

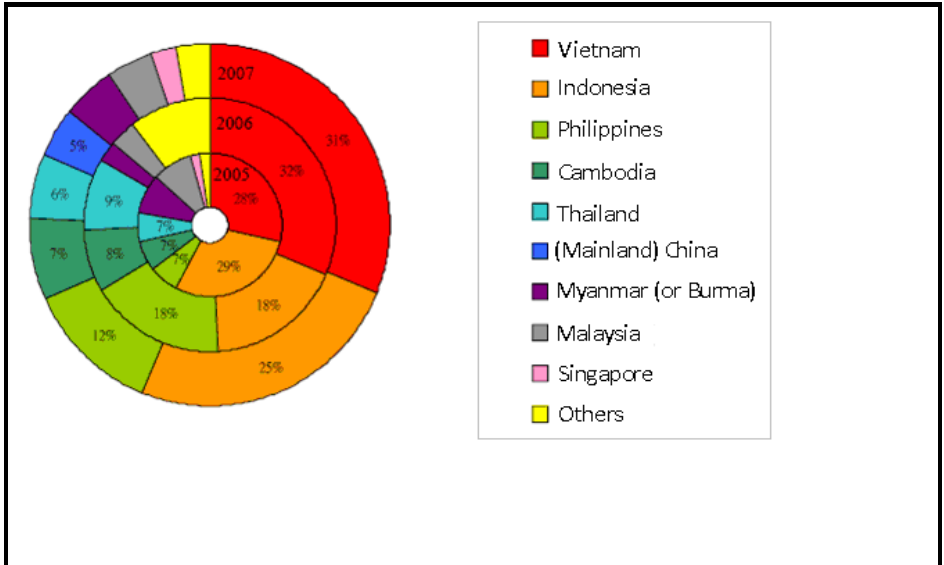


Figure 2. Source countries of imported dengue cases

These results show that not only have the epidemics spread wider, they have also started earlier. From 2005 - 2007, October/November was the peak season. In 2005, 58.5% of cases (76/130) appeared in this season. In 2006, this figure was 52.8% (425/804), and in 2007 65.6% (1070/1631). Epidemics are usually over by January or February of the following year.

3. Number of non-imported dengue fever cases by age group

All age groups are under threat from localized dengue fever. However, older age groups report the highest rate of infection. Those aged 61 -70 are most at risk, with an incidence rate of 1.95, 7.45, and 17.12 per 100,000 people in 2005, 2006 and 2007 respectively, followed by 51 - 60 year olds. However, younger groups are more likely to be infected with imported dengue virus (Table 2).

Table 2 Dengue fever cases by age group^a

Age group	2005				2006				2007			
	Imported	Incidence rate	Non imported	Incidence rate	Imported	Incidence rate	Non imported	Incidence rate	Imported	Incidence rate	Non imported	Incidence rate ^b
0-10	1	0.03	7	0.24	5	0.18	56	1.96	7	0.26	95	3.47
11~20	2	0.06	10	0.31	4	0.12	91	2.84	5	0.16	211	6.55
21~30	6	0.15	7	0.18	7	0.18	97	2.50	8	0.21	222	5.89
31~40	7	0.19	19	0.52	25	0.68	131	3.58	25	0.68	263	7.13
41~50	8	0.22	19	0.51	12	0.32	185	4.96	42	1.12	332	8.85
51~60	7	0.28	33	1.34	9	0.34	206	7.74	36	1.26	346	12.15
61~70	3	0.20	29	1.95	9	0.61	110	7.45	7	0.47	254	17.12
71~80	0	0.00	7	0.69	1	0.10	56	5.44	0	0.00	144	13.85
81~90	0	0.00	2	0.61	0	0.00	8	2.25	0	0.00	59	15.42
≥91	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	6	15.01
Total	34	0.15	133	0.58	72	0.31	940	4.11	130	0.57	1932	8.42

a: non-Taiwanese citizens were excluded

b: per 100 thousand people

4. The geographic distribution of local cases and the sources of imported cases.

1) Geographic distribution of localized dengue cases

Cases selected were those marked 'no' in the 'imported?' column of the CDC's database. In 2005, 59% of localized dengue cases (79/134) were found in Kaohsiung County and Kaohsiung City, followed by 37.3% (50/134) in Tainan County and Tainan City. In 2006, Kaohsiung County and City had 97.8% of the cases (933/954). By 2007, the affected area had moved north to Tainan County and City, which had 90.2% of cases (1,763/1,954) compared with 9.0% (176/1,954) for Kaohsiung County and City. Tainan City suffered the most.

2) The sources of imported cases

In 2005, the vast majority of imported cases came from five countries: 13 cases (30%) each from Indonesia and Vietnam, and 3 cases (7%)

each from the Philippines, Thailand, and Cambodia. Nine cases (21%) came from other countries.

In 2006, the top five source countries were Vietnam (27 cases, 31%), Indonesia and the Philippines (15 cases, 17% each), Thailand (8 cases, 9%) and Cambodia (7 cases, 8%). Fifteen people (17%) were infected in other countries.

In 2007, Vietnam again supplied the most cases (53 people, 31%), followed by Indonesia (43 people, 25%), the Philippines (21 people, 12%), Cambodia (12 people, 7%) and Thailand (10 people, 6%). 32 cases (19%) came from other countries.

The above information shows that Vietnam, Indonesia and the Philippines are the top three source countries of Taiwan's imported dengue cases.

5. Dengue sample turnaround time

In 2005, the average turnaround time (from receipt to confirmation of test results) was 7.8 days for reported cases and 6.0 days for contactors. In 2006, the turnaround time required for reported cases, contactors, and cases from fever screening centers was 6.8, 5.8 and 2.4 days respectively. These numbers were 6.4, 5.9 and 2.2 days in 2007. The turnaround time has been reduced.

Discussion

1. Reported cases of dengue fever infections

The positive rate of samples submitted was 17.9% (174 out of 493 cases) in 2005 and 37.8% (878/2,328) in 2006. This rate reached as high as 51.3% (1,714/3,342) in 2007. The positive rate in the serum and RT-PCR test

results is increasing every year. It shows that clinical practitioners have accumulated enough experience and knowledge and have been able to diagnose dengue fever accurately and immediately. In addition, the number of reported dengue cases has been decreasing each year from 97.2% (174/179) in 2005 to 84.2% (878/1042) in 2006 to 80.7% (1714/2125) in 2007. On the other hand, the percentage of positive cases among contactors increased from 2.8% (5/179) in 2005 to 14.7% (153/1042) in 2006 and 15.7% (334/2125) in 2007. This shows that local health authorities have been vigilant in dengue control to prevent further spread of the disease. Fever screening centers at airports have also been successful. Their positive rate increased from 0.9% (11/1042) in 2006 to 1.3% (77/2125) in 2007. This proves that quarantine in ports is a useful method for reducing imported dengue cases.

2. Contactors

All positive contactors identified in 2005 were infected by different people. In 2006, two positive people infected two contactors each. In 2007, two cluster outbreaks were reported. One broke out in the Tainan Municipal Honorable Citizens' Home, where 77 people were infected. The index case was recorded on 26 July and the last case on 14 September. The second cluster outbreak appeared in a residential area in Tainan, where 32 people were infected. The index case in this outbreak was reported on 10 June and the last case on 5 August. These events show that crowded senior centers or less congested residential areas are equally vulnerable to communicable disease outbreaks. This poses an enormous challenge to local health authorities in charge of mobilizing officers and managing diseases.

3. Fever screenings at international ports and imported dengue cases

During the 2003 SARS outbreak, CDC Taiwan set up fever screening centers at each international port to detect passengers with fever and stop the virus spreading by international travel. Since then, this equipment has become part of the surveillance system to detect, with great success, fever-associated diseases such as dengue fever and shigellosis[6]. Of imported dengue cases, 12.5% (11/88) in 2006 and 45.0% (77/171) in 2007 were detected at airports. Fever screenings at airports is the first line of defense. If these cases were not stopped at the airports, they could have spread the virus further and brought us an unimaginable disaster.

About 80% of imported cases came from Vietnam, Indonesia, the Philippines, Cambodia, and Thailand. Since 2007, China has also become one of the source countries, with 5% of cases (8/171). Travelling between Taiwan and China has been frequent, so our citizens should be more alert to the risk of getting infected while travelling. More effort should be spent strengthening fever screening at airports and educating citizens about avoiding mosquito bites when traveling to areas where dengue occurs.

4. Comprehensive discussion

Climate factors play a significant role in dengue outbreaks. Past studies show that air pressure, temperature, humidity, and rainfall have statistically significant effects on the density of larvae which spread dengue fever[7]. Analysis of monthly dengue cases between 2005 and 2007 showed that index cases are occurring earlier. Previously the epidemic season of dengue fever in Taiwan ran from July through to November. But the current study found that the outbreaks in 2006 and 2007 occurred in each case a month earlier than the year before. According to the Central Weather Bureau, Taiwan, the average temperature in 2007 was slightly higher than in 2006[8].

The June temperature in 2007 was already as hot as the July of previous years - a perfect temperature for mosquitoes. It's probably why the outbreaks occurred earlier. The same situation also happened in the countries where most of Taiwan's imported dengue cases came from. In the Philippines, dengue outbreaks have been appearing two months earlier every year since 2005 (June in 2005, April in 2006 and February in 2007.) Further study is required to determine whether global warming will result in earlier and longer dengue outbreaks in Taiwan.

As regards age of infection, the result of this study is similar to those of previous studies that show dengue fever in Taiwan mainly affects adults. In this, Taiwan is similar to countries like Singapore and Cuba, but quite different from Vietnam where the most affected people have been children younger than 15. This study also found that those aged 61 - 70 are most at risk, but has yet to find the reasons.

Dengue fever is a community environmental disease which easily breaks out as long as there is a suitable environment for the vector mosquitoes. In summer, when the temperature is right and when there are enough breeding grounds for mosquitoes (empty boxes, cans, polystyrene containers and tires), dengue virus will start to spread. All it needs is to find its first victim. The CDC has set up fever screening centers at airports as the first line of defense, to reduce imported cases. The CDC has also broadened the scope of screenings in potential contactors in order to stop the disease from spreading as early as possible. Still, the most effective way to prevent dengue fever is to eliminate the breeding grounds of mosquitoes and to educate citizens about the importance of creating a mosquito-free environment.

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