ISSN 1021-366X

Department of Health
REPUBLIC OF CHINA

Vol. 9 No. 12/December 25, 1993

Epidemiology Bulletin

Serological Surveillance of Dengue Fever in Kaohsiung City

1. Introduction

Since the dengue fever outbreak in 1987 in the southern part of Taiwan, index cases of disease epidemics have been reported by physicians. The success of the control of epidemics is highly associated with the extent of the epidemics as understood by the health authorities. Then outbreak in Kaohsiung City in 1988 reported several hundreds of cases, eventually led to a major outbreak with 2,636 confirmed cases in the year, the number of unreported cases was estimated to be ten times more. In 1991, a minor outbreak occurred in Kaohsiung City again. When it was noted by the health authorities, there were 11 accumulated cases. With effective control, the number of confirmed cases in the year was only 113. This was an improvement over what it was in 1988. There are many reasons attributable to the effective control in 1991, early detection of the disease is an important reason not to be overlooked.

The current method in the detection of dengue fever epidemics in Taiwan Area is the clinical surveillance method, that is, for physicians to report suspected cases to health authorities. In some counties and cities the community surveillance method is also practiced, that is, health workers, during their routine home visitings for health programs, also notice and report dengue fever in the communities[1]. To early detect diseases, in addition to closer contact with physicians, other surveillance methods should also be developed to supplement the surveillance shortage caused by un-reportings due to negligence, atypical symptoms of patients or implicit infections.

The study intends, through the screening of the general public for dengue virus IgM antibody, to supplement the detection of dengue fever in high risk areas.

2. Materials and Methods

(1) Sources and treatment of serum specimens

There were three sources of sera: blood collected in the physical examinations

for military draftees in 1992 in Kaohsiung City, blood collected at health stations for general physical examination and ante-natal care, and blood of the blood center. Though most blood of the two later sources was collected from residents of Kaohsiung City, some were from residents of Kaohsiung and Pingtung counties.

Serum specimens thus collected were sent in a temperature under 10°C to the National Institute of Preventive Medicine and stored under −20°C.

(2) Testing for dengue fever IgM antibody

The ABC MAC-ELISA method reported by Chow[2] was applied. The antigens used were the ones collected from the brain of sucking mice infected with dengue virus type 1 (Hawaii strain) and Japanese encephalitis virus (JaGAr 01 strain)[3] then purified by sucrose and acetone. Findings were considered positive only when dengue virus IgM antibody was positive and Japanese encephalitis IgM antibody was negative.

(3) Disease surveillance

The resident area and working place of the IgM positive cases were visited by health workers, at least 20 families in one locality. An individual was considered to be suspected case if he or she had the first and one of the following rest symptoms:

(a) fever at 38°C and above;
(b) severe headache, ache of rear eye-ground, joint ache and muscle ache during fever;
(c) eruption over the body 3-4 days after fever;
(d) itch over the body during fever.

3. Results

(1) Screening by month

A total of 45,412 specimens (7,287 from military draftees, 8,974 from physical examinations and 29,151 from blood donations) had been screened between July 1992 and May 1993, with 16 IgM positive cases (1 of military draftees, 5 of physical examinations and 10 from blood donations). Positive cases concentrated in periods between October and November 1992 and February and March 1993. Table 1 shows findings of screenings by month.

(2) The IgM antibody positive cases

Information of the 16 IgM antibody positive cases is shown in Table 2. They are 9 from Kaohsiung City, 4 from Kaohsiung County and 3 from Pingtung County; 3 in age group 10-19 years, 6 in age group 20-29 years, 4 in age group 30-39 years, and one each aged 43, 51 and 63 years. 10 are male and 6 female.

Of them, 15 cases reported neither high fever nor uncomfortable feelings in the three month period before blood collection. The 11th case had both fever and eruption in November and December 1992.

(3) Disease surveillance of IgM antibody positive cases

IgM antibody positive cases were home visited by health workers for disease surveillance. Except the 11th case, no disease was noted (see Table 2).

The 10th and 11th cases were further investigated. The 10th case lived in Hsiaokang District and worked in Kushan District of Kaohsiung City. In Hsiaokang District, 33 more households were visited and 42 blood specimens collected; in Kushan District, 30 households were visited and 58 blood specimens collected. No suspected cases were identified and all blood showed IgM antibody negative. The 11th case was a student in a school in Sanmin District of Kaohsiung City though lived in Jenwu Township of Kaohsiung County. In March 1993, 83 households in the neighborhood were visited without any suspected cases; and 170 blood specimens collected, all negative of IgM antibody. Of the students in the same class and neighboring classes visited, 24 indicated fever in the last three months. Their blood and 31 more blood specimens of students without fever at a total of 55 were collected. Except one student with fever showed positive of IgM antibody, the rest were negative. This IgM antibody positive student lived in Chienchen District and had fever and eruption in November 1992. 24 family members and neighbors were visited without suspected cases and 54 blood specimens collected, all negative of IgM antibody.

4. Discussion

The serological surveillance method mentioned in the study is a sentinel surveillance assuming that each individual is a sentinel and by screening his/her dengue fever IgM antibody, the disease situation of the area can be detected. The method has the following advantages to make up the shortcomings of the clinical surveillance method which relies primarily on clinical symptoms:

(1) easy access to specimens, low cost, and mass screening is possible: sera have already been collected for other purposes, they are easily available in large quantity covering a large area; cost of treatment is low.

(2) disease can be detected with or without clinical symptoms: IgM antibody is related to infection and not to clinical symptoms, this method, therefore, is also effective on implicit infection or patients of atypical symptoms that are often un-detected by the clinical method.

(3) the duration of IgM antibody is adequate for disease detection: IgM antibody stays for about 2 to 3 months. The duration is adequate. If too short, the detection rate will be low; if too long, it would be difficult to tell if the case was recently infected. The screening can adequately reflect the disease situation of the area.

This method, however, has the following shortcomings. It should be used to supplement the clinical surveillance rather to replace it.

(1) with this method, disease can only be detected in the mid-period of the disease process[2], whereas the clinical method can detect the disease at its early stage; the later is more effective in timing;

(2) pathogenic agents cannot be isolated with this method for virus typing;

(3) the testing methods used should be of high specificity and sensitivity and the specimens tested should be in large quantity to be of alerting value.

The positive rate of 0.035% (16/45,412, 95% confidence interval of 0.018-0.053%) obtained by the study was low. During the period, the number of confirmed cases in Kaohsiung City, Kaohsiung County and Pingtung County as reported by physicians and from other sources was 5, of them, one was indigenous by infected case reported in November 1992 in Chienchen District of Kaohsiung City. When findings of two surveillance methods were compared, it could be concluded that the dengue fever epidemics in the three counties and city during this period was relatively stable.

Of the 16 positive cases, only one student had clinical symptoms. His blood was collected in February 1993, though the symptoms appeared in November and December 1992. Further surveillance located another positive case, a classmate of his, who had symptoms in end of November 1992. The onset time of these two cases corresponded to that of the confirmed cases in Kaohsiung City reported by physicians. 107 households in the neighborhood of these students were visited without further suspected cases; 224 blood specimens tested, all negative of IgM antibody. These facts indicate that though there was still dengue fever infections in Kaohsiung City around the end of 1992, the epidemics was relatively minor.

The specificity of the testing method applied by the study was 99.5%[2]. However, the criteria of positiveness were relatively broad, suspected positive cases could be treated as positive. In this study, the criteria were made more strict, the specificity, therefore, was higher. 15 positive cases did not develop clinical symptoms. They could be false-positive, they could also be implicit infections. From the time of blood collection, they were more likely to be implicit infections. The positive rates were higher in October and November 1992. They corresponded to the peak months of the indigenous dengue fever epidemics in the southern part of Taiwan in 1987, 1988, 1989 and 1990. Positive cases were still detected in March 1993. They could have been infected at the end of 1992, for example, the blood of the one with clinical symptoms was collected in March.

When positive rates by month of blood specimens collected from different sources were compared, no statistically significant difference (Fisher's exact test, $p > 0.05$) was noted. As the target groups were the general public, and general public tended to have similar susceptibility of dengue virus.

Specimens were not analyzed for sex, age and residence. They came from special

groups: young boys of 18-19 years for the military draftees, child-bearing age women for the ante-natal care, young persons of 20-30 years applying for various examinations for the general physical examination, and young male for blood donation. The military draftees came exclusively from Kaohsiung City, and the others from either Kaohsiung County or Pingtung County. The epidemilogical analysis of high risk groups was not feasible.

This was a pilot study to develop another surveillance method for the detection of dengue fever. With the following improvements, this method seems practicable:

1) more specimens of high risk groups, blood of patients of other diseases in hospitals, blood collected through physical examination of foreign laborers, should be included in the screening;

2) more laboratory instrument should be used to replace manual work to increase efficiency and accuracy;

3) other laboratory testing methods of higher specificity should be developed to determine whether a asymptomatic IgM antibody positive case is an implicit infection;

4) data bank should be developed to include information of cases their residences and dates of blood collection for better surveillance of the area concerned. More specimens should be collected from areas of low collection rate. If specimens come from hospitals, detection rates of various diseases can also be calculated. This will help the study of diseases and the improvement of surveillance as well.

5. Acknowledgement

Thanks are due to the Kaohsiung City Health Department and the Pingtung County Health Bureau for their assistance in the survey.

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Table 1. Screening for Dengue Fever IgM Antibody in Kaohsiung City (July 1992 — May 1993)

Blood Collected Month Year	IgM antibody to dengu							
	Specimen source							
	Military	Draftee	Physical	Exam	Blood	Donation	Total	
	No.	(+)	No.	(+)	No.	(+)	No	(+)
Jul 1992	2,760	1	441	0			3,201	1
Aug	4,527	0	1,064	0			5,591	0
Sep			1,994	0			1,994	0
Oct			1,954	3	2,077	2	4,031	5
Nov			211	0	6,345	3	6,556	3
Dec					6,583	0	6,583	0
Jan 1993					4,528	0	4,528	0
Feb			511	1	2,411	2	2,922	3
Mar			1,214	1	3,126	3	4,340	4
Apr			1,325	0	4,081	0	5,406	0
May			260	0			260	0
Total	7,287	1	8,974	5	29,151	10	45,412	16

Table 2. Information of Dengue Fever IgM Antibody Positive Cases

No	Month of Blood Collection	Residence	Age	Sex	Source	Symptom*	Disease Surveillance	
							No. Visited**	No Positive
1	Jul 92′	Chichin, Kaohsiung C.	19	M	Military	none	20	0
2	Oct	Fenshan, Kaohsiung Co.	51	F	Physical	none	70	0
3	Oct	Fenshan, Kaohsiung Co.	33	F	Physical	none	44	0
4	Oct	Sanmin, Kaohsiung C.	35	F	Physical	none	100	0
5	Oct	Kaoshu, Pingtung Co.	26	M	Donation	none	18	0
6	Oct	Kushan, Kaohsiung C.	23	M	Donation	none	20	0
7	Nov	Hsiaokang, Kaohsiung C.	23	M	Donation	none	1***	0
8	Nov	Wantan, Pingtung Co	34	M	Donation	none	20	0
9	Nov	Chienchen, Kaohsiung C	22	M	Donation	none	53	0
10	Feb 93′	Hsiankang, Kaohsiung C.	33	F	Physical	none	63	0
11	Feb	Jenwu, Kaohsiung Co.	19	M	Donation	yes	83	1
12	Feb	Chienchen, Kaohsiung Co.	63	M	Donation	none	50	0
13	Mar	Fenshan, Kaohsiung Co	27	F	Physical	none	50	0
14	Mar	Hengchun, Pingtung Co.	18	F	Donation	none	45	0
15	Mar	Sanmin, Kaohsiung C	20	M	Donation	none	50	0
16	Mar	Lingya, Kaohsiung C.	43	M	Donation	none	50	0

* suspected dengue fever symptoms within three months prior to blood collection

** including places of residence and work

*** no neighbor within 50 meter of residence

C City, Co: County