

## SEROEPIDEMIOLOGY OF DENGUE AND ASSESSMENT OF PUBLIC AWARENESS IN THE DOMINICAN REPUBLIC

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**Abstract:** Dengue fever (DF) is a major public health concern in the Dominican Republic. In recent years, several epidemics of DF have been reported to the Pan American Health Office (PAHO), but the extent of the epidemics has not been clearly understood yet. Therefore, we conducted a nationwide seroepidemiology of dengue (DEN) infection. At the same time, we conducted an interview survey to assess public awareness regarding the disease. The serum samples were collected at seven main cities in the Dominican Republic and screened for DEN antibody with a commercial ELISA kit. A total of 2007 serum specimens were examined. The prevalence of DEN antibody in the seven cities varied between 43.1 and 89.7%. Neutralization (N) test carried out on the ELISA-positive serum from Samana, one of the high antibody-prevalent cities, revealed that all the sera showed positive to at least two DEN serotypes. Geometric mean N titers against DEN-1, 2, 3 and 4 were 40.5, 463.7, 59.9 and 454.4 respectively. No difference in antibody prevalence was observed between males and females. It appeared that a high level of awareness regarding DF did little affect DEN prevalence. Strong, concrete public health strategies that motivate the local community to combat DF are required.

### INTRODUCTION

The Dominican Republic is located at the Greater Antilles in the Caribbean Sea, on the east border of Haiti. The land area is 48,442km<sup>2</sup> and the population about 8.7million. In recent years, service industries have exceeded agriculture as the main industry due to the growth of tourism and the development of free trade zones.

Control and prevention of infectious diseases are the major public health problems in the Dominican Republic. Dengue fever/dengue hemorrhagic fever (DF/DHF) is a public health concern that, in severe cases, causes hemorrhagic diatheses and death due to hemorrhagic shock [1,2]. Four serotypes of dengue virus (DEN-1 to DEN-4) form a single antigenic complex. The main vector is *Aedes aegypti*, which is commonly found in tropical and subtropical areas including the Dominican Republic [3]. The first laboratory-confirmed dengue epidemic (DEN-3) in the Dominican Republic was in 1963 [4]. Since then, epidemics caused by multiple serotypes of DEN virus have been reported [5]. In 1988, four cases of DHF were reported for the first time in the country [4]. During a worldwide pandemic of DF/DHF

in 1998, a total of 2,335 cases including 176 cases of confirmed DHF with 10 deaths were reported in the Dominican Republic [4]. In 1997, the Ministry of Public Health initiated the DEN Control Campaign through surveillance and eradication of *Aedes aegypti* and health education to the community. Although the campaign seemed effective in combating mosquitoes, the DEN epidemic persisted. In 2000, 3,462 cases of DF, including 58 DHF with 6 deaths were reported. During this epidemic, all four serotypes of DEN virus were isolated [4].

In view of background, we conducted serological and interview surveys of DEN infection at the seven main cities in the Dominican Republic in order to determine the extent of DEN infection in the country and to assess public awareness regarding DF/DHF. In this paper, we report the results of the survey on DEN infection among a healthy population living in the seven main cities of the Dominican Republic. To our knowledge, this was the first nationwide survey of DEN infection in the Dominican Republic.

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## MATERIALS AND METHODS

### *Interview survey and collection of serum specimens*

During the period from September 2000 to July 2001, we conducted a survey of DEN together with a health checkup for local residents of seven main cities (Santo Domingo, S.P. de Macoris, La Romana, Bani, Samana, La Vega, and Santiago) in the Dominican Republic with the collaboration of the staff of local health centers, medical students and an NPO group (Fig. 1). Before initiating the health checkup, we explained the DEN survey project to the participants and others who wished to volunteer for the project, then proceeded to the interview survey and blood collection. The teaching staff of the epidemiology section at CEMADOJA did the interview in Spanish. The questionnaire consisted of demographic information, the location of water containers (including the presence or absence of lids) in and around their residence. The knowledge on DEN was evaluated by the questions "Have you ever heard of DF?" "Do you have any idea what transmits DF?" and "What would you do to avoid DF?"

Since no ethical code had been established at this point, the teaching staff explained the survey to the participants verbally, and only those who consented were subjected to the interview and blood sampling.

The serum specimens were stored at either -20 or -80°C until use.



Figure 1. Map of the Dominican Republic. The survey sites are indicated by numbers.

### *Detection of DEN antibody*

Commercial ELISA kit (Microwell ELISA Dengue IgG, Diagnostic Automation Inc. California, U.S.A.) was used according to the manufacture's instructions. An antibody (Ab) index (titer) of 0.9 or over was considered positive.

Fifty-percent focus-reduction neutralization (N) test, using Vero cells, was carried out [6,7]. An N titer of 20 or

over was considered positive.

### *Statistics*

The  $\chi^2$  test was used to compare the Ab prevalence between different locations. It was also used to analyze the difference of Ab titer/prevalence among various settings. The unpaired-student's- t-test was used to compare the Ab titers between subjects with and without DEN-related knowledge. We used the Statistical Package for Biosciences (SPBS, Winestem Institute of Community Medicine, Toda, Saitama, Japan).

## RESULTS

### *Serum specimens*

A total of 2007 serum specimens were collected. The number of serum specimens collected at the seven cities is shown in Table 1. Females predominated in six cities, but accounted for only 42.2% in one city (Bani) (overall female proportion was 72.2%). The age distribution of the volunteers varied from 16 to 97 years with a median age between 34 and 43 years.

### *Prevalence of DEN Ab*

The prevalence of DEN Ab is presented with demographic data from each city in Table 1. The Ab prevalence varied from 43.1 to 89.7%, and southern cities seemed to have a lower prevalence than eastern and northern cities (south vs. east:  $\chi^2=46.906$ ,  $P<0.001$ ; south vs. north:  $\chi^2=33.777$ ,  $P<0.001$ ). There was no statistical difference in Ab prevalence between males and females ( $P=0.097$  by Mantel-Haenszel method).

Samana was one of the most highly prevalent areas (Ab prevalence of 86.0% by ELISA). In order to examine which Ab to DEN serotypes was predominant in this area, 50 Ab-positive sera were randomly selected and N test was performed. All the sera showed positive to at least two DEN serotypes. Geometric mean N titers against DEN-1, 2, 3 and 4 were 40.5, 463.7, 59.9 and 454.4 respectively.

### *Interview survey*

A total of 1,988 volunteers responded to the inquiry. Most of them (1,986 individuals) stated that they had cisterns inside the house. Among these, only 255 (12.8%) stated that they placed a lid on the cistern (Table 2). Commonly found utensils containing water were vases and planters. When asked about DF, a majority of the volunteers (80.6%) answered "yes", meaning that they had some DEN-related knowledge. More people living in St. Domingo, the capital, knew about DEN (94.6%) than those in other cities (Table 3). There was no statistical correlation between DEN

Table 1. Demography and DEN antibody prevalence

	Total	South				East	North	
		St Domongo	S.P.Macoris	La Romana	Bani	Samana	La Vega	Santiago
Population (x103)	4,707	2,694	262	215	223	82	391	840
No.specimens	2,007	492	274	252	258	250	250	231
Age (years)								
Median	39	41.5	34	39	36	40	43	40
Range	16-97	19-97	17-71	18-85	19-80	19-76	16-85	19-78
Gender								
Male (%)	624 (31.1)	131 (26.6)	70 (25.5)	56 (22.2)	149 (57.8)	61 (24.4)	82 (32.8)	75 (32.5)
Female (%)	1,383 (68.9)	361 (73.4)	204 (74.5)	196 (77.8)	109 (42.2)	189 (75.6)	168 (67.2)	156 (67.5)
DEN-Ab positive								
Total (%)	1,369 (68.2)	327 (66.5)	118 (43.1)	226 (89.7)	115 (44.6)	215 (86.0)	169 (67.6)	199 (86.1)
Regional subtotal (%)			786 (61.6)			215 (86.0)		368 (76.5)
Male (%)	394 (63.1)	85 (64.9)	29 (41.4)	48 (85.7)	60 (40.3)	52 (85.2)	54 (65.9)	66 (88.0)
Female (%)	975 (70.5)	242 (67.0)	89 (43.6)	178 (90.8)	55 (50.5)	163 (86.2)	115 (68.5)	133 (85.3)
DEN-Ab negative								
Total (%)	638 (31.8)	165 (33.5)	156 (56.9)	26 (10.3)	143 (55.4)	35 (14.0)	81 (32.4)	32 (13.9)
Male (%)	230 (36.9)	46 (35.1)	41 (58.6)	8 (14.3)	89 (59.7)	9 (14.8)	28 (34.1)	9 (12.0)
Female (%)	408 (29.5)	119 (33.0)	115 (56.4)	18 (9.2)	54 (49.5)	26 (13.8)	53 (31.5)	23 (14.7)
Mean Ab index (SD)	1.5 (1.1)	1.5 (1.0)	0.8 (0.6)	2.1 (0.8)	0.9 (0.9)	1.6 (0.7)	1.4 (0.8)	2.4 (1.5)

Table 2. Results of interview survey on dengue

Total	1,988
Cistern inside house?	
“yes”	1,986
with lid	255
without lid	1,731
Any utensil containing water?	
vase and planter	1,090
old tire	238
empty bottle	92
other containers	315
no answer	253
Do you know DF?	
“yes”	1,603
“no”	385

Table 3. Results of interview survey and DEN antibody prevalence

Do you know dengue?	Total	South				East	North	
		St Domingo	sp Macoris	La Romana	Bani	Samana	La Vega	Santiago
No.interviewe	1,988	479	273	250	257	249	249	231
Answered “yes”	1,602	453	221	194	207	177	193	157
(%)	(80.6)	(94.6)	(81.0)	(77.6)	(80.5)	(71.1)	(77.5)	(68.0)
Serodiagnosis negative	52.5	153	122	18	119	25	66	22
(%)	(32.8)	(33.8)	(55.2)	(9.3)	(57.5)	(14.1)	(34.2)	(14.0)
Serodiagnosis positive	1,077	300	99	176	88	152	127	135
(%)	(67.2)	(66.2)	(44.8)	(90.7)	(42.5)	(85.9)	(65.8)	(86.0)
Answered “no”	386	26	52	56	50	72	56	74
(%)	(19.4)	(5.4)	(19.0)	(22.4)	(19.5)	(28.9)	(22.5)	(32.0)
Serodiansis negative	109	8	35	8	23	10	15	10
(%)	(28.2)	(30.8)	(67.3)	(14.3)	(46.0)	(13.9)	(26.8)	(13.5)
Serodiagnosis positive	277	18	17	48	27	62	41	64
(%)	(71.8)	(69.2)	(32.7)	(85.7)	(54.0)	(86.1)	(73.2)	(86.5)
P value ( $\chi^2$ -test)	0.086	0.752	0.112	0.280	0.143	0.961	0.297	0.918

P value: The difference of Ab prevalence between “yes”and “no” was calculated.

-related knowledge and Ab prevalence. The difference in mean Ab index between those who answered "yes" and "no" was also not statistically different (1.5 vs. 1.6; P: 0.094 by unpaired- student's-t-test).

#### DISCUSSION

The Dominican Republic has experienced several DEN epidemics in recent years. However, few virological or seroepidemiological analyses have been carried out. Therefore, we conducted a nationwide serological survey of DEN infection, together with virus isolation from DEN suspected cases. Since our survey was carried out during office hours on weekdays, more female (mainly homemakers) could participate in it. The Ab-positive rate varied from 43.1 to 89.7% with an overall rate of 68.2%. Bani and S.P. de Macoris appeared to be relatively low DEN endemic areas. Bani is well known for its mango plantations and the contributions of these make the city's financial stability. The city of S.P. de Macoris, meanwhile, is the eastern center of the country and has a medical school and international baseball stadium where many foreign athletes gather. The health-administration systems of these cities should be evaluated in more detail.

The N titers to DEN-2 and DEN-4 appeared higher than DEN-1 and DEN-3, although it is not clear how many of these Abs represent prior DEN infection or cross-reactive response. It should be noted that during this period, DEN-2 was isolated from patients with unknown fever. These results were consistent with the report that multiple serotypes of DEN virus had circulated in the Dominican Republic for the past few years [4].

The government conducted community programs to promote DEN-related knowledge through televised public service announcements, posters, health education, etc. Our interview survey also showed that a considerable proportion of the volunteers (68.0-94.6%) had some knowledge of DF. Despite good public awareness, DF was still endemic in these areas. Our data showed that there was no direct association between the knowledge of DF and the prevalence of DEN antibody. In 2003, another DF/DHF epidemic occurred and 5,170 cases with 107 deaths were registered [8]. In nearby Puerto Rico, where DF is also a major health problem, a variety of programs have been conducted. These have resulted in an elevation of awareness, some behavioral changes, and a limited change in larval indices [9]. These findings indicate that more specific information about the behaviors that need to be changed should be provided along with political and financial support.

In the present study, an interview survey among adult and young adult populations was conducted to determine

the level of the public awareness regarding DF prevention together with a serological survey. A serological survey on children, who are more susceptible to DEN but who were not included in the present study, will be conducted in a subsequent study. Recently, Ab to West Nile virus (WNV) was detected from domestic birds in the Dominican Republic [10]. Although no human case has been reported, all members of the genus *Flavivirus*, including WNV and DEN, share common antigenic sites [11], and thus care should be taken in interpreting the antibody-positive results of serological tests.

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