

VARIABLES IMPACTING DENGUE SURVEILLANCE IN KEY WEST FLORIDA

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Abstract

Background: Dengue fever is the most common mosquito borne viral disease in the world. Its symptoms can be fairly nonspecific and most commonly include fever, rash, headache, and eye pain. Passive surveillance is currently the most prevalent method used to detect dengue cases in the United States. Identification of positive cases can be limited by the public's awareness of the disease's symptoms, barriers to healthcare seeking behavior, and by physician approval of laboratory testing.

Objective: This study sought to evaluate barriers to dengue reporting, as well as the patient-level factors that may limit the efficacy of passive surveillance of dengue in Key West, Florida.

Methods: Cross-sectional surveys were administered across Key West, FL. Subjects were asked if they had a recent fever, additional dengue symptoms, and whether they sought medical care for these symptoms. Also the hypothetical question was posed: would you seek medical care for a fever greater than 102 F? Responses were stratified according to patient characteristics and demographics.

Results: In Key West, patient-level factors that influenced the decision to seek medical care for a high fever were: having a specific doctor call when sick ($p < 0.006$), health insurance status ($p < 0.037$), and ethnicity ($p < 0.005$). Additionally, barriers to dengue reporting were identified. The most impactful were the decision to seek medical care for symptoms consistent with dengue fever, and the doctor's decision to administer confirmatory dengue laboratory tests. Only one person with a recent fever plus one additional classic dengue symptom received laboratory testing, and this was done outside of the United States. There were four individuals who met the current WHO clinical case definition for dengue, yet none were offered laboratory testing or were diagnosed with the disease.

Conclusion: This study shows that both patients and doctors in Key West, Florida underestimate the potential for dengue when there are symptoms consistent with the disease. As such, it is certainly possible that there have been unreported cases in the country.

Table of Contents

Introduction	1
Research Methods & Materials	3
Results	5
Discussion.....	12
Future Directions	15
Conclusions	15
References	16

List of Figures and Tables

Table 1..... 5
Table 2..... 7
Figure 1 9
Figure 2 10
Figure 3 11

Introduction

Dengue fever is a viral disease transmitted by mosquitos that infects over 100 million people annually. Symptoms of the illness range from fever and muscle stiffness, to life threatening hemorrhagic shock. With over 2.5 billion individuals in the world at risk for infection, it is more common than malaria, and quite possibly the most important mosquito-borne virus from both medical and public health perspectives (11).

There is no specific therapy for dengue fever, so prevention is the most effective form of control. The mosquito *Aedes aegypti* is one of the primary viral vectors, and management strategies often target this species. Environmental control using insecticides has been found to be ineffective in Brazil and other countries (8). Present infestation reduction approaches have instead focused on lowering mosquito breeding and growth in residential areas. Health education efforts, community-based programs, and insecticide control strategies that focus on productive larval containers, have been shown to be worthwhile interventions in reducing disease transmission (1- 3, 5-6). The most productive larval containers vary by country and urban structure, but in general include water jars, plastic pots, ant traps, and outdoor water tanks made of plastic, metal, or cement (1-3).

Dengue fever has been heavily studied in much of South America and southeastern Asia where the disease has been endemic for many years. It has recently been observed in Florida and, as of 2010, 90 cases were reported in Key West (31). This study differs from others in that it concerns a dengue boundary area of North America, instead of endemic locations that have consistently high rates and awareness of the disease.

There is a need to study dengue emergence in the United States because the disease vectors *Ae. aegypti* and *Ae. albopictus* have high-density population distributions along many southern states including Texas, South Carolina, Georgia, New Orleans, and Florida (27). Key West is an ideal location for dengue research because it is one of two places in the United States that has experienced an identified outbreak in the last 50 years. Key West also has a great deal of human traffic from dengue endemic countries like Mexico, Cuba, and Puerto Rico. Local cases of the disease are shown to increase when significant portions of the population are

involved in travel to and from endemic areas (28). It is extremely important to identify the emergence of the disease in these southern states so that control efforts may be put into place, and future outbreaks prevented in the United States.

Historically, the emergence of diseases like dengue into new geographic areas is identified through passive surveillance systems; i.e. when a physician identifies and reports a case of the virus to a health department. In order for this to happen several steps must occur, outlined in Figure 3. At each step, positive cases may be missed. If a patient does not think the symptoms necessitate a visit to his primary care physician or health clinic, then the case will never be reported; same if the doctor does not recognize the disease or order a diagnostic test. Numerous factors such as insurance status, perception of severity of illness, and awareness of the physician to order a dengue laboratory test can affect reporting of dengue cases (26).

This will be the first study concerning dengue that attempts to evaluate limitations to passive surveillance, at the levels of both the patient and physician, in Key West, FL. Understanding the likelihood of our current system's ability to detect dengue emergence is a critical aspect in preparedness and planning for outbreaks. Recognition of these impediments can facilitate reduction of dengue transmission in this area and prevent a future epidemic from occurring.

Research Methods & Materials

Preparation: IRB approval was obtained for the project that encompassed this research, and an amendment was submitted that included the specific questions that were asked in this section. The project as a whole was well funded. To encourage participation in the research, the Florida Keys Mosquito Control team advertised ahead of time that there would be surveys conducted in the area during the months of June and July. The University of Arizona College of Public Health and the Department of Entomology provided equipment, funding, and training. There were collaborations with several departments in Florida and Arizona to enhance the research. These included the National Center of Atmospheric Research in Boulder, CO, Florida Keys Mosquito Control, Florida Health Department, Key West Health Department

Study design: A cross-sectional survey of 400 households in Key West was administered. Parcel data of the area was randomly selected from Key West county records to generate an initial list of randomly selected households.

Study Population: Current household heads, or their spouses, were surveyed using door-to-door recruitment, with systematic replacement of non-responding households. If a resident did not answer the door, then households to the right, left, across the street, across and to the left were attempted, in order.

Survey Questions: This work was part of a larger household survey on the knowledge, attitudes and practices surrounding dengue. Specific questions were obtained concerning recent clinical symptoms consistent with the disease, patients' healthcare seeking behaviors, access to medical care, familiarity with dengue, and demographics of the community participants.

Data Analysis: Univariable analyses were conducted on all survey variables to include a description of frequencies and odds ratios for categorical variables. Comparisons between responses were conducted using chi-square (categorical/bivariate variables) or t-tests

(continuous variables). Logistic regressions were conducted to determine the relative odds of seeking medical care by patient demographics and other factors of interest.

Results

Table 1: Decision to seek medical care for a high fever according to patient demographics

Patient Demographics	Would seek medical care for fever > 102	Would not seek medical care for fever > 102	Chi square P-value	Seek Care Odds Ratio
	N (%)	N (%)		(95% CI)
Sex			0.67	
Male	151 (46.6)	32 (43.8)		1.12 (0.67, 1.87)
Female	173 (53.4)	41 (56.2)		Ref.
Age			0.28	
1-25 years	40 (12.7)	8 (11.1)		1.17 (0.48, 2.81)
26-50 years	103 (32.7)	24 (33.3)		Ref.
51-75 years	137 (43.5)	37 (51.4)		0.86 (0.49, 1.53)
76-100 years	35 (11.1)	3 (4.2)		2.72 (0.77, 9.58)
Ethnicity			0.005	
White	196 (61.8)	45 (61.6)		Ref.
African American	30 (9.5)	4 (5.5)		1.34 (0.65, 2.73)
Hispanic/Latino	77 (24.3)	13 (17.8)		1.78 (0.60, 5.29)
Other	14 (4.4)	11 (15.1)		0.28 (0.12, 0.67)
Primary Language			0.39	
English	290 (91.2)	63 (88.7)		Ref.
Spanish	20 (6.3)	4 (5.6)		1.09 (0.36, 3.29)
Other	8 (2.5)	4 (5.6)		0.50 (0.20, 1.26)
Income			0.21	
<\$35,000	39 (12.0)	15 (20.3)		Ref.
\$35-49,999	27 (8.3)	4 (5.4)		2.60 (0.78, 8.68)
\$50-74,999	44 (13.5)	8 (10.8)		2.12 (0.81, 5.53)
\$75-99,000	27 (8.3)	10 (13.5)		1.04 (0.41, 2.66)
\$100,000+	58 (17.8)	14 (18.9)		1.59 (0.69, 3.67)
Declined	131 (40.2)	23 (31.1)		2.19 (1.04, 4.60)
Education Level			0.13	
Graduate/professional Degree	51 (16.1)	12 (16.4)		Ref.
Bachelor's or Associates	98 (31.0)	28 (38.4)		0.82 (0.39, 1.75)
Some College/high school graduate	138 (43.7)	32 (43.8)		1.02 (0.49, 2.12)
Some education, no high school degree	29 (9.2)	1 (1.4)		6.35 (0.78, 51.5)
Area of Key West			0.20	
Old Town	127 (39.0)	26 (35.1)		Ref.
Mid Town	52 (16.0)	9 (12.2)		1.18 (0.52, 2.70)
New Town	96 (29.5)	31 (41.9)		0.63 (0.35, 1.14)
Stock Island	51 (15.6)	8 (10.8)		1.31 (0.55, 3.07)

To determine healthcare seeking behavior, we asked Key West residents if they would seek medical care for a fever greater than 102F. This was a symptom consistent with dengue, but one that was also non-specific and familiar enough to patients that they could make an educated response. We then stratified answers according to patient demographics. Of these, only ethnicity had a statistically significant impact ($p < 0.005$). Hispanics/Latinos were most likely to seek care for a high fever (OR 1.78), followed by African Americans (OR 1.34) and then Caucasians.

Income level did not affect the decision to seek care in a significant way, but it did show some interesting trends. Poorer residents earning less than \$35,000/year were, as expected, the least likely to seek care and used as a reference for the other income groups. Middle-income residents earning \$35,000-49,999/year were the most likely to seek care (OR 2.60), while residents in higher income brackets like \$100,000+ annually were less likely (OR 1.59). Those declining to answer the question also showed an increased affinity for seeking medical care (OR 2.19). The data suggests that in Key West, middle-income residents are more likely than the poor or wealthy to seek an outside opinion when presented with a febrile illness.

Table 2: Decision to seek medical care for a high fever based on access to health care and patient perception of disease

Patient factor of interest	Would seek medical care for fever >102 N (%)	Would not seek medical care for fever >102 N (%)	Chi square P-value	Seek Care Odds Ratio (95% CI)
Has a specific doctor to call when sick	211 (65.1)	35 (48.0)	0.006	2.03 (1.21, 3.39)
Health Insurance status			0.037	
Public	85 (26.7)	13 (18.1)		Ref.
Private	142 (44.7)	30 (41.7)		0.72 (0.36, 1.46)
Both	32 (10.0)	5 (6.9)		0.98 (0.32, 2.97)
None	59 (18.6)	24 (33.3)		0.38 (0.18, 0.80)
Years spent in Key West			0.49	
<1 year	19 (6.1)	5 (6.9)		0.70 (0.23, 2.11)
1-5 years	56 (17.9)	10 (13.9)		1.02 (0.44, 2.39)
5+ years	145 (46.3)	40 (55.6)		0.66 (0.36, 1.24)
Lifelong resident	93 (29.7)	17 (23.6)		Ref.
Dengue Knowledge				
No knowledge prior to interview	168 (51.5)	42 (56.8)	0.42	0.81 (0.49, 1.35)
Has heard of Dengue	85 (53.1)	16 (50.0)	0.75	1.13 (0.53, 2.42)
Has known someone personally with Dengue	73 (29.4)	21 (37.5)	0.24	0.70 (0.38, 1.27)
Can name at least 3 Symptoms of Dengue	39 (15.5)	6 (10.5)	0.33	1.56 (0.63, 3.89)
How serious a problem is Dengue for the Florida Keys on a scale of 1-5			0.21	
1. Not at all serious	43 (17.8)	9 (16.7)		Ref.
2. Slightly serious	57 (23.6)	18 (33.3)		0.66 (0.27, 1.62)
3. Somewhat serious	60 (24.8)	17 (31.5)		0.74 (0.30, 1.81)
4. Very serious	42 (17.4)	5 (9.3)		1.76 (0.54, 5.68)
5. Extremely serious	40 (16.5)	5 (9.3)		1.67 (0.52, 5.42)
Patient perception of likelihood they/someone in their family will get Dengue in lifetime			0.26	
Very likely: >80% chance	14 (5.9)	4 (7.3)		1.08 (0.33, 3.51)
Somewhat likely: 51-80% chance	11 (4.6)	1 (1.8)		3.39 (0.42, 27.3)
Equally likely/unlikely: 50% chance	40 (16.7)	6 (10.9)		2.06 (0.80, 5.28)
Somewhat unlikely: 10-49% chance	67 (28.0)	11 (20.0)		1.88 (0.89, 3.97)
Very unlikely: <10% chance	107 (44.8)	33 (60.0)		Ref.

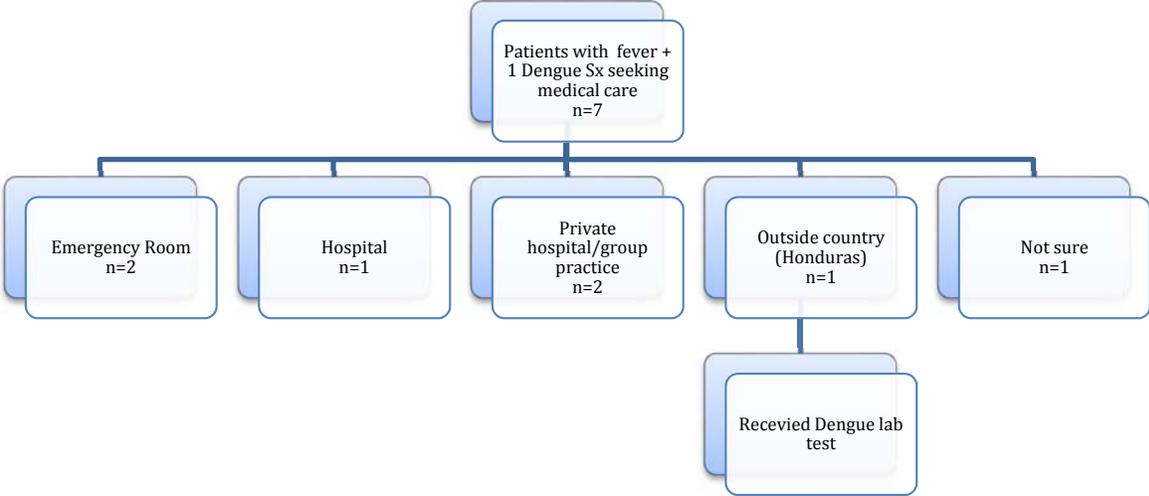
The decision to seek medical care for a high fever was also analyzed according to a variety of other patient factors. The two statistically significant variables were health insurance status ($p < 0.037$) and having a specific doctor to call when sick ($p < 0.006$). The type of health insurance was not particularly influential; rather it was the lack thereof that made an impact. People with no health insurance were less likely than the rest of the population to seek medical care for a fever (OR 0.38). On the other end of the spectrum, 246 of the 400 survey participants had not only health insurance, but also specific doctor to call when sick. These people were twice as likely as the normal population to seek care for a high fever (OR 2.03), probably because of the easy access to a physician. Interestingly, years spent in Key West, dengue knowledge, and the perception of its seriousness/prevalence did not influence the decision to seek medical care.

Figure 1: Distribution of persons receiving medical care and laboratory testing for symptoms consistent with Dengue Fever. Additional Dengue symptoms included: eye pain, headache, body ache, bleeding, and rash.



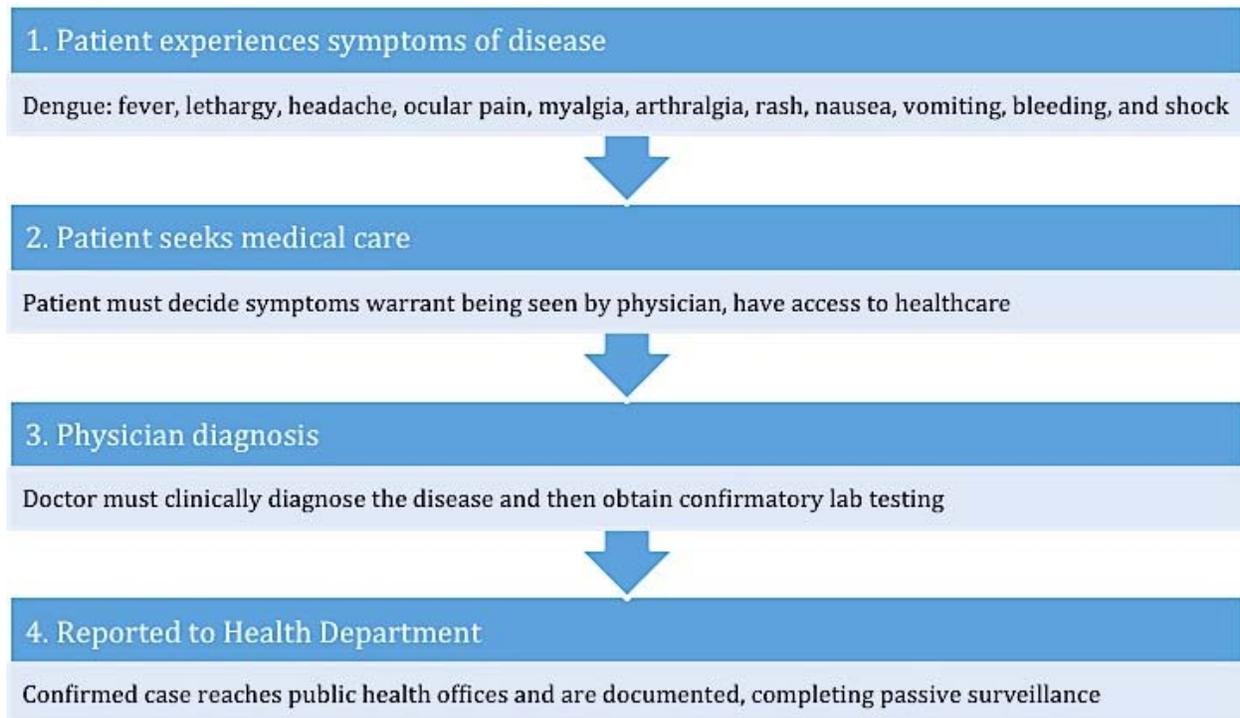
A view of the current system's efficacy in diagnosing cases and reporting the disease is outlined. Of the 16 people in our sample who had both a high fever and an additional dengue symptom, only seven (43.8%) participants sought medical care for their symptoms, and of these seven only one (14.3%) received confirmatory laboratory testing. Four patients in the sample met the current case definition for dengue without warning signs, yet none were diagnosed with the disease.

Figure 2: Healthcare providers used by Key West locals experiencing symptoms consistent with Dengue Fever.



Note that the only person to receive laboratory testing was in Honduras during the workup.

Figure 3: Steps in passive surveillance



Discussion

The aim of this study was to determine barriers that prevent dengue cases from being reported through passive surveillance systems. Passive surveillance occurs through routine reporting of diseases; this is limited by physicians' ability to correctly diagnose the disease and notify the health department. Furthermore, reporting of cases only occurs after they have been confirmed by laboratory testing. In our study, none of the patients who presented for symptoms consistent with dengue received this kind of testing in the United States. This is concerning considering that in 2009-2010, 90 people were found to have laboratory-positive dengue infections in Key West (31). Now, just a few years later, potential cases are not being confirmed by physicians. It is likely that there are dengue cases going unreported because they have not been established with the appropriate serologic tests.

In 2009, the WHO dengue case definition was modified because the 1997 definition was limited in terms of its applicability. The current WHO classification for dengue and its severity is divided into: dengue without warning signs, dengue with warning signs, and severe dengue. The case definition of dengue without warning signs includes fever and two of the following: nausea, vomiting, rash, aches and pains, leukopenia, or a positive tourniquet test (29). Other symptoms that used to be part of the diagnosis include: ocular pain, headache, epistaxis and other hemorrhagic manifestations. As such, we asked patients who had a recent fever if they had experienced any of these symptoms as well. Four patients in the sample met the current case definition for dengue without warning signs, yet none were clinically diagnosed with the disease. This suggests that dengue fever is not high on local physicians' differential diagnosis for these symptoms, which is certainly a barrier to passive surveillance. In 2010, 5.4% of Key West residents were found to be positive for a particular dengue serotype through active surveillance, and public health interventions were aimed at both the community and local physicians (31). It appears that health department visits to clinicians has not been entirely effective in promoting dengue awareness.

Patients can also be responsible for breakdowns in passive surveillance. If a patient has symptoms consistent with dengue, then they need to decide to seek medical care so a doctor may diagnose it. Patient demographics can affect the decision to seek medical care. In this

study, only ethnicity, health insurance status, and having a specific doctor to call when sick caused a significant difference in patient response. It is curious to see that Hispanics/Latinos were the most likely to seek medical care for a high fever, considering that more than ¼ of Hispanic adults in the US lack a consistent healthcare provider (32). This statistic is tightly linked with socioeconomic and health insurance status, however, and not an intrinsic indifference to health maintenance. Since the question of seeking care was hypothetical, it may be that Latino responders did not have to take financial constraints into consideration. The geographical background of these people may also have played a role. Dengue has a higher prevalence in the Latin/Caribbean countries that many of these people hail from. One could be tempted to postulate that a heightened familiarity with the disease was involved, but prior dengue knowledge was not found to be a significant factor in the decision.

It was not as surprising that people without health insurance were less likely to seek medical care than the general population. A lack of health insurance is intimately associated with other socioeconomic variables including lower income, less education, and fewer transportation abilities, all of which negatively influence access to health care services (33). It makes intuitive sense that, if someone cannot pay for medical services, they will be less likely to seek those services for a high fever or rash. Unfortunately for these people, they are also at higher risk for dengue transmission. Areas with high population density have increased potential for clustered infections, whereas an increase in per capita income of a residential area is associated with decreased dengue risk (34). People living in lower income residential areas may be more likely to keep their windows open rather than using air conditioning units, another risk factor for encountering the mosquito vectors. Poorer housing construction and yard maintenance can increase the number of productive larval containers, also increasing mosquito activity in the area.

To maximize generalizability of this data, the original population based sampling scheme used randomly selected parcel data from Key West county records. There was a strong sample size of 400 participants, and surveys were taken across the entire island, covering a variety of socioeconomic areas. There were still some limitations to this study, however. An element of participation bias was almost certainly involved. The surveys were administered during working

hours, so the people at home who were willing to talk to the surveyors may have been a different population than people who worked all day or were unwilling to answer the door. Because of this, it is not possible to extrapolate this data beyond those who were surveyed and make sweeping generalizations of all Key West. There was also the potential for differential misclassification and recall bias in this study. Residents with recent fevers were asked to remember what other symptoms they had at the time, and how physicians worked them up (i.e. laboratory testing). This was hopefully minimized by asking only for symptoms within the last 2 months, but responses could certainly have been inaccurate nevertheless.

Future Directions

This project elucidated health care seeking behaviors in a population of Key West. Surveys with the same question sets are being distributed in Arizona and Mexico, two other dengue boundary areas. Resident responses from these different locations will be compared to see if there are region-specific patient demographics that influence the decision to seek care for dengue symptoms.

The lack of laboratory testing for dengue specific symptoms suggests that physicians could benefit from more education on dengue symptoms. Further surveys and interventions may be administered to doctors, to understand their barriers in ordering the testing required to report a case to the health department.

Conclusions

This project sought to determine what patient-level factors influenced the decision to seek medical care for symptoms consistent with dengue. The only patient characteristics to show statistical significance were ethnicity, health insurance status, and having a specific doctor to call when sick.

Hispanic/Latino populations were the most likely to seek medical care for a fever greater than 102F, followed by African American and then Caucasian populations. Having a specific doctor to call when sick made it twice as likely that a person would seek medical care for a high fever as compared to others. Finally, the lack of health insurance made a resident less likely to seek medical care when sick with a fever.

Two major barriers to passive surveillance were identified. These were the decision to seek medical care for symptoms consistent with dengue fever, and the doctor's decision to administer confirmatory dengue laboratory tests. Not a single person surveyed said they received a laboratory test in the United States when presenting with a high fever and another dengue symptom. Dengue cases in the United States are likely being missed since passive surveillance relies on this testing.

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