Factors Associated with Chikungunya Relapse in Acapulco, Mexico: A Cross-Sectional Study

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Abstract

Objective: To estimate the occurrence of self-reported chikungunya relapse and identify associated factors.

Materials and Methods: A cross-sectional study in December 2015 included 1305 homes in eight urban clusters considered representative of Acapulco in southern Mexico. Administered questionnaires collated information on 5870 individuals, including sociodemographic variables, a history of chronic conditions, and the self-reporting of chikungunya. Bivariate and multivariate analyses relied on a cluster-adjusted Mantel–Haenszel procedure to identify the factors associated with chikungunya and its relapse.

Results: Some 66% (3531/5870) of the population reported suffering chikungunya and 31.1% (1098/3531) reported a relapse. Factors associated with relapse included the severity of the chikungunya case (odds ratio [OR]: 3.35; clusters adjusted 95% confidence interval [95% CIca]: 3.16–3.55); history of arthralgia (OR: 2.96; 95% CIca: 2.27–3.86); age 30 years or older (OR: 1.85; 95% CIca: 1.72–1.98); female (OR: 1.64; 95% CIca: 1.42–1.90); and higher education households (OR: 1.18; 95% CIca: 1.11–1.27).

Conclusions: The high occurrence of chikungunya and its relapse are a public health problem. The factors associated with relapse do not immediately suggest specific prevention strategies but emphasize the dire need for effective approaches to vector control.

Keywords: chikungunya, relapse, occurrence, associated factors

Introduction

CHIKUNGUNYA FEVER IS caused by an alphavirus (WHO 2017), transmitted mainly by the mosquitos *Aedes aegypti* and *Aedes Albopictus*, implicated now in various epidemics and in the transmission of the dengue and zika viruses (Her et al. 2009, Coffey et al. 2014). Given the wide distribution of these vectors in the Americas, the currently uninfected population is susceptible to chikungunya infection (PAHO/CDC 2011, Rivera-Ávila 2014). Relapse occurs generally 1 month after a symptom-free period after the initial infection (Couturier et al. 2012), due to persistence of the virus in the cells of musculoskeletal tissue; joint pain can be the same or greater than that experienced during the initial occurrence (Borgherini et al. 2008).

In 2015, 991,134 chikungunya cases were reported in the region of the Americas, with 11,468 of the 125,235 cases reported in Mexico confirmed by laboratory tests (PAHO/WHO 2015). With 1673 confirmed cases, the state of Guerrero was in second place nationally after Veracruz, with 2000 cases (SSA 2016a). After the 2015 outbreak (Rivera-Ávila 2014), the rapid spread of the epidemic in Guerrero received official recognition, presenting, according to the Directorate-General for Epidemiology of the National Monitoring System, the highest number of cases in 2016 (SSA 2015a, 2016a). No circulation of the Zika virus occurred that year (SSA 2016b) and the incidence of dengue was low (SSA 2015b).

Little is known about factors associated with relapse of chikungunya. In the first experience with chikungunya in other countries, factors reported to date include the severity

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of the case during the acute stage (initial severe pain), being >40 years of age, being female, comorbidities (a history of arthritis, arthralgia, and diabetes), and a depressed emotional state (Vijayakumar et al. 2011, Couturier et al. 2012, Kularatne et al. 2012, Gérardin et al. 2013). This study aimed to estimate the occurrence of chikungunya relapse and identify associated factors in Acapulco, as part of a bigger study.

Materials and Methods

Sample

A cross-sectional study contacted homes in eight urban clusters in Acapulco in December 2015. The purposive (nonprobabilistic) sampling sought to reflect urban average conditions in the municipality, without reference to the reported occurrence of dengue, chikungunya, and Zika. Survey sites have a high population density and residents have access to health care and education services, water supply, and basic sanitation. We included all households in each cluster.

Interviewer training

Interviewers selected had high school or higher education and received training in questionnaire administration, how to obtain informed verbal consent, and how to avoid missing data.

Pilot test

Before the application of the questionnaire, two pilot tests verified the questions were clear, pertinent, and useful for subsequent analysis. We also noted the time for administering the questionnaire, the levels and mechanisms of missing data, and logistics for fieldwork.

Data collection

Interviewers administered the questionnaire household by household, moving radially outwards from a central point. They asked about sociodemographic variables: age; gender; type of housing; gender of the informant; educational level and occupation of the head of the family; number of people living in the household; and whether the household was a beneficiary of the Prospera program that provides cash incentives for families who participate in government health, nutrition, and educational activities.

The questionnaire included variables related to chikungunya: the month in which the patient fell ill, where the patient was treated, whether the patient's condition was severe, whether the patient suffered chikungunya relapse and how many, and the number of people who had fallen ill. We also asked about comorbidities before contracting chikungunya, such as hypertension, diabetes, arthritis, and arthralgia. There is evidence that self-reported chikungunya cases are strongly related to those confirmed clinically or serologically (Staikowsky et al. 2008).

Operational definition of key variables

Chikungunya relapse. A reported recurrence of chikungunya symptoms (joint pain and inflammation) after 1 month having recovered from the disease, measured with the question: *How many relapses have you experienced of chikungunya?*

Severity of the disease. The respondent mentioned having fallen ill with chikungunya, this we determined with the question: *Were you seriously ill?*

Age. Years of age as stated by the interviewee.

History of arthralgia. Self-reported suffering joint pain before falling ill with chikungunya.

Educational level of the head of the family. Schooling declared by the respondent on being asked *Until what year did the head of the family study?*

Fieldwork. Before the interviews, we informed local authorities about the study and requested their authorization. Each interviewer received a sketch indicating their route and household coverage. After presenting themselves to each household, interviewers explain the objectives of study and request verbal consent, before administering the questionnaire.

Data capture and analysis. Trained operators entered data twice using the EpiData software (Lauritsen and Bruus 2005), with validation to minimize keystroke errors. Analysis relied on CIETmap open-source software (Andersson and Mitchell 2002) to obtain the simple frequencies for the variables. We calculated the odds ratio (OR) in bivariate and multivariate analyses adjusted by cluster through the Mantel-Haenszel procedure (Mantel and Haenszel 1959) in accordance with Lamothe (2011) to estimate cluster-adjusted 95% confidence interval (95% CI_{ca}) (Cornfield 1956).

Multivariate analysis began with a saturated model including all variables associated with the outcome in the bivariate analysis, using step-wise deletion of the least significant association until all the remaining variables were significantly associated with the outcome at the 5% level. We tested for effect modification using Woolf's χ^2 test for heterogeneity (Woolf 1955).

Results

We interviewed 1305 households in eight urban clusters in Acapulco, with women making up 72% (943/1305) of the respondents. Information referred to 5870 people, with an average age of 33.6 ($n=5870$, range: 0–90; standard deviation [SD]: 22.162). The average number of people per household was 4.5 (5870/1305) (range: 1–16; SD: 2.24). Most housing, 79% (1035/1305), was permanent with 15.3% (200/1305) semipermanent, 3.9% (51/1305) provisional, and 1.5% (19/1305) not specified.

The educational level of the head of the family showed 15.7% (205/1305) not having studied, 16.1% (210/1305) stated that they had not finished primary education, 17.2% (226/1305) described having concluded primary education, 2.6% (34/1305) stated that they had not completed secondary education, 17.6% (230/1305) had concluded secondary education, 2.1% (28/1305) had not completed high school, 13.3% (174/1305) finished high school, 13.3% (173/1305) had been educated to technical or professional level, and 1.9% (25/1305) did not know or did not answer.

Some 74% (965/1341) of households were beneficiaries of the Prospera program, 24% (313/1305) indicated an affiliation to the program, and 2% (26/1305) did not know or did not provide information in this regard.

FIG. 1. Distribution of self-reported chikungunya cases per month in the urban area of Acapulco, Mexico, 2015.

No <87% (1136/1305) of respondents reported one or more cases of chikungunya in 2015 (range: 1–13), with 66% (3531/5870) among household members covered by the questionnaire. Of these, 57.6% (2034/3531) were female and the average age was 36 years ($n=3531$, range: 0–90; SD: 22.05). Of the chikungunya cases reported, 14.2% (500/3531) were severe, with 60.9% (2149/3531) of respondents having sought public or private medical treatment, 36.9% (1303/3531) having been treated at home, and 2.2% (7/3531) did not know or did not answer. Asked about the type of medical conditions experienced before presenting chikungunya fever, 14.4% (510/

3531) reported hypertension, 10% (352/3531) reported diabetes mellitus, 8.1% (286/3531) reported arthritis, and 8.0% (284/3531) reported arthralgia. Most cases, 71.2% (2405/3377), presented between April and August, 2015 (Fig. 1).

Of cases reported in the interviews, 31.1% (1098/3531) were described as having relapsed, of whom 65.8% (722/1098) were female. The average age was 40.69 years (range: 0–90; SD: 21.27). The distribution of relapse is shown in Fig. 2. The frequency of relapse was very similar when the respondent was male or female 29.2% (229/783) and 32.6% (863/2650), respectively.

FIG. 2. Frequency of chikungunya relapse in the urban area of Acapulco, Mexico, 2015.

TABLE 1. BIVARIATE ANALYSIS OF FACTORS ASSOCIATED WITH CHIKUNGUNYA RELAPSE IN THE URBAN AREA OF ACAPULCO, GUERRERO, MEXICO 2015

Variable	Levels	Proportion	Percentage	OR	95% CIca
Age	≥ 30	727/1941	37.5	1.85	1.72–1.98
	<30	369/1506	24.5		
Gender	Female	722/1989	36.3	1.64	1.42–1.90
	Male	374/1453	25.7		
Place where treated	Public or private sector	781/2133	36.6	1.84	1.52–2.23
	At home	309/1295	23.9		
Severe case	Yes	276/491	56.2	3.35	3.16–3.55
	No	816/2944	27.7		
Number of chikungunya cases in the home	<5 cases	707/2032	34.8	1.39	1.09–1.77
	≥ 5 cases	388/1398	27.8		
History of hypertension	Yes	200/502	39.8	1.54	1.33–1.73
	No	889/2929	30.4		
History of diabetes	Yes	144/347	41.5	1.60	1.11–2.30
	No	947/3078	30.8		
History of arthritis	Yes	157/282	55.7	2.96	2.54–3.45
	No	936/3144	29.8		
History of arthralgia	Yes	156/280	55.7	2.96	2.27–3.86
	No	935/3138	29.8		
Type of housing	Permanent	885/2696	32.8	1.25	1.10–1.40
	Flimsy/provisional and semipermanent	204/724	28.2		
Gender of the respondent	Female	863/2650	32.6	1.17	1.07–1.28
	Male	229/783	29.2		
Educational level of the head of the family	≥ 5th grade primary	781/2374	32.9	1.18	1.11–1.27
	<5th grade primary/did not study	300/1025	29.3		
Occupation of the head of family	Does not work	394/1260	31.3	0.97	0.84–1.13
	Paid employment	680/2133	31.9		
Number of people living in the home	<5 people	503/1407	35.7	1.35	1.13–1.62
	≥ 5 people	595/2043	29.1		
Household is beneficiary of the <i>Prospera</i> program	No	771/2298	33.6	1.26	1.10–1.43
	Yes	315/1099	28.7		

OR, odds ratio; 95% CIca, clusters adjusted 95% confidence interval.

Table 1 shows the factors associated with chikungunya relapse in bivariate analysis. Table 2 shows the results of the multivariate analysis of factors associated with chikungunya relapse: severity of the initial episode, experiencing arthralgia before contracting chikungunya, being aged 30 years or

over, being female, and the head of the family having a high educational level.

Discussion

With a self-reported history of chikungunya of 66% in urban Acapulco, household informants reported relapse in one in every three cases. Factors associated with relapse were severity of the initial case, a history of arthralgia, age >29 years, female, and higher education households. The high occurrence of chikungunya reflects susceptibility of the Guerrero population. This study aimed to identify factors associated with chikungunya relapse in Acapulco.

A limitation in generalizing the results is purposive sample, selected in our study to reflect urban conditions with good access to health care but without reference to chikungunya, Zika, or dengue patterns. Although reported rates of chikungunya infection and recurrence were high, it is likely these rates were higher in less well to do population sectors.

We recognize the limits of self-reporting chikungunya infection and relapses; abstracted from an epidemic, people might confuse the signs and symptoms with other infections such as dengue or Zika. Given the high level of knowledge during the epidemic, and widespread familiarity with the alternatives, we consider this unlikely. The literature suggests self-reporting of chikungunya cases is probably reliable

TABLE 2. MULTIVARIATE ANALYSIS OF FACTORS ASSOCIATED WITH CHIKUNGUNYA RELAPSE IN THE URBAN AREA OF ACAPULCO, MEXICO 2015

Variables	OR	Adjusted OR	95% CIca	χ^2 het	p
Severe case of chikungunya	3.35	3.05	2.50–3.71	19.85	0.13
History of arthralgia	2.87	2.20	1.68–2.89	14.82	0.46
Age >29 years	1.84	1.66	1.41–1.94	12.47	0.64
Female	1.66	1.57	1.34–1.84	16.99	0.31
Educational level of head of the family ≥ 5th grade primary	1.18	1.39	1.17–1.65	16.55	0.34

The factors revealed by the saturated model were type of housing, beneficiary of the *Prospera* program, number of people living in the household, number of chikungunya cases per household, place of treatment, high blood pressure, and having diabetes and arthritis.

χ^2 het, Woolf's χ^2 test for heterogeneity.

(Gérardin et al. 2008), since people present acute joint pain and disability in an epidemic context (PAHO/CDC 2011, PAHO/WHO 2017). Staikowsky et al. (2008) reported that there were no significant differences between self-reported chikungunya cases and those cases confirmed clinically or serologically.

Our measured occurrence of chikungunya in this previously unaffected population was similar (63% 209/331) to that in the Comoros (Sergon et al. 2007), and higher (38.9%) than that reported by Staikowsky et al. (2008). Another study in Kenya reported 75% affected (Sergon et al. 2008). As in Mexico, these results refer to the first introduction of the virus. Authors reporting on re-emergence of chikungunya occurrences suggested rates between 22.3% and 36.9% (Balasubramaniam et al. 2011, Chattopadhyay et al. 2016).

The occurrence of chikungunya relapse in our study was similar to that reported in other new introduction of the virus, for example, by Gerardin et al. (2013), who observed that 32.1% (111/346) of chikungunya patients presented relapse. Other studies have reported higher relapse rates (48.9 and 72%) (Staikowsky et al. 2008, Couturier et al. 2012), and a lower relapse rate (21%) (Borgherini et al. 2008).

Consistent with the literature about outbreaks after the first introduction of chikungunya virus, we found the severity of the chikungunya case associated with relapse. Gerardin et al. (2013) found that the initial severity of the rheumatic symptoms caused by chikungunya increased the risk of relapse (OR 3.6; 95% CI: 1.5–8.2).

We found that a history of arthralgia associated with relapse, similar to Couturier et al. (2012), who observed that chikungunya patients with rigid or inflamed joints had a greater risk of relapse. This could be due to the immune response and osteodegenerative processes. This study also confirmed the effect of age, wherein chikungunya relapse is associated with ages >29 years. Gerardin et al. (2013) found people between 45 and 59 years of age at higher risk of chikungunya relapse (OR 2.9; 95% CI: 1.0–8.6), the risk increasing again over the age of 59 years (OR 10.4; 95% CI: 3.5–31.1). The increased risk with age might be due to comorbidities (Couturier et al., 2012). Vijayakumar et al. (2011) reported on re-emergence of chikungunya that patients >40 years had a higher risk of relapse (OR 1.26; 95% CI: 1.03–1.54).

Compatible with other studies, we found women and girls at higher risk of relapse, a result similar in a re-emergent outbreak that was found by Kularatne et al. (2012) (OR 1.53; 95% CI: 1.04–2.29). This may be related to higher activity levels of female household members (food preparation, washing and ironing of clothes, household cleaning, and child and elderly care). We also found higher educational level associated with relapse, although we could not confirm this in the published literature. We do not rule out a reporting bias, with higher educated households being more informed about chikungunya and the epidemic. If such a bias exists, it implies underreporting in lower education households.

Despite long-standing efforts to control *A. aegypti*, the high levels of chikungunya were because the population had no immunity in their first contact with the virus. The high rate of relapse affects quality of life, a problem that made worse by the fact that it frequently occurs during the productive stage of life, with implications in an individual, family, employment, and health context. The factors we found associated with chikungunya relapse are related to personal conditions, implying a more vulnerable segment of the population gets affected.

Acapulco has a predominantly subhumid warm climate with average annual temperature of 22–28°C (INEGI 2015). Our results may be relevant to populations living in similar urban areas.

Conclusions

The high occurrence and relapse of chikungunya confirm that this disease is a public health problem of note. The factors associated suggest relapse affects vulnerable population segments and we note possible under-reporting of relapse in households with lower levels of education. Our study adds to the urgent call for effective prevention and control of *A. aegypti*, something that is not happening using current pesticide-based approaches, but that is possible with community-engaged approaches (Andersson et al. 2015).

Author Disclosure Statement

No conflicting financial interests exist.

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