

Long-term Chikungunya Sequelae in Curaçao: Burden, Determinants, and a Novel Classification Tool

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Background. Beyond the acute illness phase, chikungunya constitutes a public health problem given its chronic disease phase, which may include long-term arthralgia, arthritis, fatigue, and depression. Currently, there is no consensus on how to define chikungunya chronicity.

Methods. A comprehensive cross-sectional survey was performed in Curaçao in June and July 2015 to evaluate 304 adult laboratory-confirmed chikungunya patients 3–16 months after diagnosis. We developed a novel tool, the Curaçao Long-Term Chikungunya Sequelae (CLTCS) score, to classify chronic chikungunya disease and estimate its burden regarding disease duration, clinical presentation, and impact on quality of life.

Results. Disease persistence was estimated to be 79% one month after symptom onset and 64% after 400 days. Chikungunya persistence was characterized by higher proportions of arthralgia, weakness, myalgia, and age 41–60 years. Individuals were classified as “highly affected,” “mildly affected,” and “recovered.” “Highly affected” disease status was associated with clinical complaints (arthralgia, weakness, loss of vitality, and being diabetic) and major decreases in quality-of-life scores.

Conclusions. In the Caribbean, a high proportion of chikungunya patients remains chronically affected. We propose the CLTCS as a suitable score to easily and rapidly classify the severity of chikungunya chronic disease and to assess the need for symptom-alleviating treatment.

Keywords. Chikungunya; chronic sequelae; Curaçao Long-term Chikungunya Sequelae score; CLTCS; quality of life.

Chikungunya is a viral vector-borne disease transmitted by the day-biting mosquitoes *Aedes aegypti* and *Aedes albopictus* [1]. The disease has become a global health problem of increasing importance given its recent rapid spread and the extent and impact of chronic disease. To date, the literature lacks consensus on how to define chronic chikungunya disease.

The first locally acquired chikungunya cases in the Caribbean island of Saint Martin in December 2013 indicated the introduction of chikungunya virus (CHIKV) in the Americas, which resulted in >1 million confirmed or suspected cases throughout the continent [2–4].

In Curaçao, the epidemic of chikungunya became evident in June–July 2014. The explosive behavior of this epidemic

resulted in 835 reported laboratory-confirmed cases and thousands of clinical cases by October 2014 [4]. These accumulated to an estimated 50 000–75 000 by the end of the outbreak in January 2015 (I. G., unpublished data).

Chikungunya disease typically manifests itself with an abrupt onset of high fever, headache, in a certain percentage with rash, and almost invariably musculoskeletal pain with predominantly incapacitating arthralgia. Treatment of the disease is purely symptomatic, focusing on pain relief through the use of nonsteroidal anti-inflammatory drugs [1]. Although the acute phase of chikungunya could be considered as relatively short (7–10 days), the disease commonly evolves into a subacute (<3 months) or chronic (>3 months) phase. The latter has been characterized by long-lasting relapsing or lingering rheumatic musculoskeletal pain, arthralgia, fatigue, and depression [5–8]. Notwithstanding the wide range of symptoms that chikungunya can cause, research mainly focuses on musculoskeletal manifestations when investigating persistence of chikungunya, thereby neglecting other disease manifestations [9]. Studies estimate that up to 60% of chikungunya patients remain symptomatic 12–36 months after infection [8, 10–12]. After 5 years, up to 12% of the infected population might still report chikungunya-related symptoms [13–15].

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It seems likely that the chronic phase of chikungunya can cause a significant decrease in quality of life (QoL), becoming an important and underestimated public health problem [10, 16]. However, to date, research on QoL related to chikungunya chronicity remains scarce and especially lacks a thorough description combined with musculoskeletal, psychological, and neurological manifestations.

The aim of this study was (1) to estimate the burden of the first chikungunya outbreak in Curaçao in terms of symptoms and duration of chronic disease, and the impact on QoL 3–16 months after diagnosis; (2) to develop a practical tool to classify chronic chikungunya disease; and (3) to identify factors associated with mild and highly chronically affected individuals.

METHODS

Study Design and Population

Following the chikungunya epidemic of 2014–2015 in Curaçao, a cross-sectional survey of adult subjects with a confirmed chikungunya infection diagnosed during the epidemic was performed between June and July 2015. Chikungunya infection was confirmed based on diagnosis of a general practitioner including a laboratorial assessment outcome of either a positive immunoglobulin M (IgM) or immunoglobulin G (IgG) (as this was the first documented chikungunya epidemic in Curaçao), positive reverse-transcription polymerase chain reaction (RT-PCR), or positive indirect fluorescent antibody (IFA). Enzyme-linked immunosorbent assay (ELISA; IBL, Germany) was performed by the Analytical Diagnostic Centre in Curaçao according to the manufacturer's protocol. Assessment by RT-PCR or IFA concerned samples transferred to the National Institute for Public Health and the Environment of The Netherlands. Twenty general practitioners working in 14 different practices representative of the population of Curaçao, both geographically and socioeconomically, provided patient data. The selected subjects were either contacted by phone or visited at their residence for inclusion. Those consenting to participate were interviewed at home.

Study Site

Curaçao is an island in the southern Caribbean Sea with a surface of 444 km² and approximately 150 000 inhabitants. The population of Curaçao is mainly concentrated in the capital, Willemstad [17]. Curaçao has a semiarid climate with a rainy season from September to January and a dry season from February to August [18].

Data Collection

Study participants were interviewed using a questionnaire containing precoded and open questions on sociodemographic characteristics (Table 1). Experienced local interviewers working for the Central Bureau of Statistics of Curaçao and speaking

Papiamentu, Dutch, English, and Spanish performed the interviews. The questionnaire was prepared in Dutch, piloted, corrected, and translated into Papiamentu, Spanish, and English.

Subjects were asked to provide the date of onset of the acute chikungunya episode and the duration of symptoms and complaints. They were asked if they (still) suffered from the precoded symptoms at the time of interview to which they could answer “yes,” “somewhat,” or “no” (Supplementary Tables 1 and 2). Finally, participants were asked to fill in a RAND 36-item Short-Form Health Survey (SF-36) questionnaire to assess their current quality of life (QoL) [19, 20]. The SF-36 was used because this tool provides a short but comprehensive assessment of QoL, including physical and emotional dimensions of health, and was previously applied to the population of Curaçao [21].

Severity of Chronic Chikungunya Disease—Development of a Novel Classifying System

To classify chronicity of chikungunya disease, subjects were asked whether they still perceived complaints of chikungunya at the time of interview. Thenceforth, 4 standard statements were assessed with a 5-point scoring scale (Table 2). The Cronbach α test, which assesses the reliability, or internal consistency, of the 4-statement scale, yielded a high score (0.891). Subsequently, a severity score was obtained by summing-up the scores of the 4 questions. This score was categorized into recovered (score = 4), mildly affected (score = 5–12), and highly affected (score = 13–20) (Supplementary Table 3). Hereinafter, we refer to this score as the Curaçao Long-Term Chikungunya Sequelae (CLTCS) score.

Data Analysis

Data were entered into a database using SPSS Data Entry Station (SPSS Inc 1996–2003, version 4.0.0). Data were checked for consistency and analysed anonymously. Based on their neighborhood, participants were allocated to geozones [17]. The distribution of the study population was analyzed and presented in a map using ArcGIS (ArcGIS Desktop: Release 10.3, Environmental Systems Research Institute, Redlands, California). The χ^2 or Fisher exact test was used to test associations between categorical variables. Continuous variables were converted into ordered categorical variables when suitable. For normally distributed quantitative data, means were compared using Student *t* test or analysis of variance; for skewed distributions, the Mann–Whitney *U* or Kruskal–Wallis test was used. A survival curve was created using the Kaplan–Meier estimator. A multivariate binary logistic regression was performed to describe characteristics of chronic chikungunya disease. General characteristics and symptoms (“no” vs “somewhat” plus “yes”) with a *P* value $\leq .2$ in the univariate analysis were included in a multivariate model to test their influence on disease status. Variables with highest *P* values were eliminated

Table 1. Socioeconomic Characteristics of the Study Population, Stratified by Chronic Disease Status Applying the Curaçao Long-Term Chikungunya Sequelae Score

Characteristic	Total (N = 304)		Recovered (n = 110)		Mildly Affected (n = 105)		Highly Affected (n = 89)		P Value ^a
Age									
18–40 y	66	(21.7)	36	(32.7)	17	(14.6)	13	(14.6)	
41–60 y	158	(52.0)	44	(40.0)	63	(57.3)	51	(57.3)	
>60 y	80	(26.3)	30	(27.3)	25	(23.8)	25	(28.1)	.005
Sex									
Female	225	(74.0)	76	(69.1)	75	(71.4)	74	(83.1)	
Male	79	(26.0)	34	(30.9)	30	(28.6)	16	(16.9)	.061
Education									
Illiterate/primary school	70	(23.0)	25	(22.7)	24	(22.9)	21	(23.6)	
Secondary school	110	(36.2)	36	(32.7)	35	(33.3)	39	(43.8)	
Intermediate vocational education	80	(26.3)	33	(30.0)	32	(30.5)	15	(16.9)	
University (of applied sciences)	44	(14.5)	16	(14.5)	14	(13.3)	14	(15.7)	.367
Occupation^b									
Unemployed/student/housewife/voluntary	58	(19.1)	19	(17.4)	18	(17.1)	21	(23.6)	
Paid job (domestic or manual)	129	(42.6)	42	(38.5)	50	(47.6)	37	(41.6)	
Paid job (not domestic or manual)	61	(20.1)	28	(25.7)	20	(19.0)	13	(14.6)	
Retired	55	(18.2)	20	(18.3)	17	(16.2)	18	(20.2)	.435
Income^c, ANG^d									
0–999	30	(10.1)	7	(6.5)	16	(15.4)	7	(8.0)	
1000–2499	121	(40.6)	40	(37.4)	41	(39.4)	40	(46.0)	
2500–4999	110	(36.9)	43	(40.2)	36	(34.6)	31	(35.6)	
>5000	37	(12.4)	17	(15.9)	11	(10.6)	9	(10.3)	.265
Underlying chronic disease									
Absence of underlying disease	152	(50.0)	61	(55.5)	60	(57.1)	31	(34.8)	.003
Joint disease	42	(13.8)	8	(7.3)	14	(13.3)	20	(22.5)	.008
Cardiovascular disease ^e	73	(24.0)	20	(18.2)	26	(24.8)	27	(30.3)	.133
Neurologic disease	11	(3.6)	4	(3.6)	4	(3.8)	3	(3.4)	1.000*
Diabetes mellitus	39	(12.8)	10	(9.1)	8	(7.6)	21	(23.6)	.001
Other diseases ^f	30	(9.9)	13	(11.8)	6	(5.7)	11	(12.4)	.209

Data are presented as No. (%) unless otherwise indicated. Values in bold are significant at the 5% level.

Abbreviations: ANG, Antillean guilder.

^aP value corresponds to the comparison of the proportions between the groups recovered, mildly affected, and highly affected.

^bTotal recovered group, n = 109.

^cTotal recovered group, n = 107; total mildly affected group, n = 104; total highly affected group, n = 87.

^d1 ANG = 0.56 US dollars.

^eCardiovascular disease group includes hypercholesterolemia and hypertension.

^fOther diseases includes chronic lung diseases, thyroid diseases, autoimmune diseases, gastrointestinal complaints, unspecified pain, allergies, and other.

*Fisher exact test.

backwards, until all variables in the model showed significance. Significance was determined at the 5% level. Data were analyzed using SPSS software (SPSS Inc, version 22.0, Chicago, Illinois).

Ethical Committee Approval

The study was approved by the Medical Ethical Board of the Saint Elisabeth Hospital in Curaçao (reference number

Table 2. Curaçao Long-Term Chikungunya Sequelae Score Assessment Form

Please check the box according to how much you agree or not with the following statements:	Do Not Agree at All					Fully Agree
	1	2	3	4	5	
1. I am fully functional again after having had chikungunya	<input type="checkbox"/>					
2. I don't have chikungunya complaints any more	<input type="checkbox"/>					
3. I still feel the effects of chikungunya disease every day	<input type="checkbox"/>					
4. The chikungunya effects seem to return again and again in my case	<input type="checkbox"/>					

Using the CLTCS (Curaçao Long-Term Chikungunya Sequelae) score to assess chronic chikungunya disease, perform the following steps: (1) Ask the patient to fill in the form; all answers are required. (2) Recode the scores of questions 1 and 2 as follows: 5 = 1; 4 = 2; 3 = 3; 2 = 4; 1 = 5. (3) After recoding, sum the scores of questions 1, 2, 3, and 4 to obtain the CLTCS score. (4) Classify chikungunya chronic disease status: recovered (no complaints) = 4; mildly affected = 5–12; highly affected = 13–20.

2015-002). All the participants who entered this study signed a written informed consent.

RESULTS

Description of the Study Population

A total of 411 participants with a recent acute chikungunya infection were contacted and invited to join the study, of whom 339 consented and participated (response rate, 82.5%). The reasons for noncontacting and nonresponse are summarized in Supplementary Table 4. Of the 337 participants, 304 had a laboratory-confirmed CHIKV infection and were included in this study. Date of onset of acute chikungunya disease ranged from April 2014 to March 2015, that is, 92–460 days before the interview. The sociodemographic characteristics and comorbidity of the study population are summarized in Table 1. The participants' age range was 18–94 years (median, 51 years; Q1, Q3 = 41, 61 years). Most participants were female (n = 225 [74.0%]), and 40.8% (n = 124) had an educational level of intermediate vocational education or university. The majority had a paid job (n = 190 [62.7%]) and approximately half of the participants had an income up to 2500 ANG (Antillean guilder; 1 ANG = 0.56 US dollars). Forty-seven of all 65 (72.3%) geozones [17] of Curaçao were represented in this study. Figure 1 shows the proportion of participants per 1000 inhabitants per geozone.

Chikungunya Chronic Disease Status

To characterize chikungunya chronic disease status, the CLTCS score was developed (see Methods). This score was stratified in 3 categories: “recovered,” “mildly affected,” and “highly affected.” The classification showed consistency with the “yes or no” question regarding chronic disease persistence (Supplementary

Table 3). Therefore, the population of this study is further described using the new classification system (ie, the CLTCS score).

Duration of Chikungunya Disease

At the time of interview, 36.2% (n = 110) were defined as fully recovered from chikungunya, while the remaining 63.8% (n = 194) were defined as still being mildly affected (n = 105 [34.5%]) or highly affected (n = 89 [29.3%]) by chronic chikungunya disease. The “recovered” study population (n = 107) estimated their disease duration between 1 and 240 days (median, 30 days; Q1, Q3 = 14, 90 days) (Figure 2). The “mildly affected” population (n = 105) reported an ongoing disease duration of 273 days on average, ranging from 94 to 426 days (standard deviation [SD], 69.4 days). Finally, the “highly affected” population (n = 89) reported having complaints for 267 days on average, ranging from 101 to 422 days (SD, 55.8 days). Of the 304 individuals, 62 (20.6%) reported to be fully recovered from chikungunya within 1 month (Figure 2). Figure 2 shows the probability to remain affected with chronic chikungunya disease over time. The model estimates that in 79.4% (95% confidence interval [CI], 74.9%–83.9%) of patients, long-term sequelae persist after a month, and in 64.0% (95% CI, 58.5%–69.5%) after 400 days.

Symptoms of Chronic Chikungunya Disease

Symptoms present at the time of interview were assessed. Subjects that answered “somewhat” or “yes” were recorded as symptomatic. These were stratified by chronic disease status and compared (Figure 3). All symptoms showed a significant association with disease status (Supplementary Table 5). The total data on the (severity of) symptoms are shown in Supplementary Tables 1 and 2. The most frequently reported symptoms within

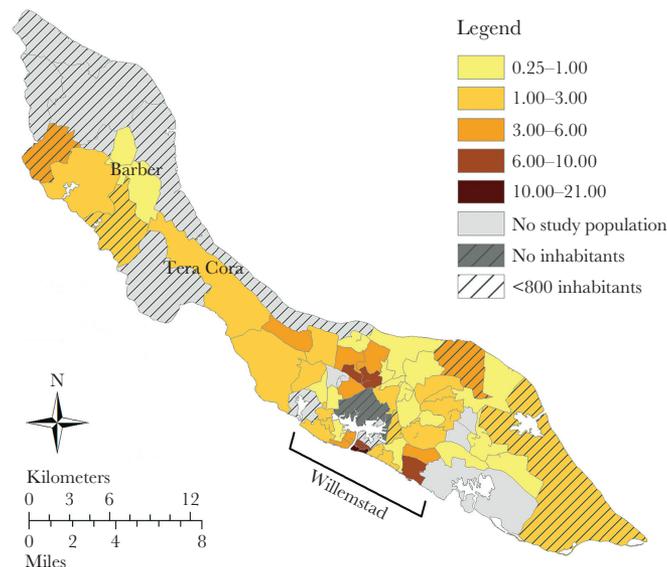


Figure 1. Distribution of the study population among geozones of Curaçao (cases per 1000 inhabitants). Willemstad (capital) covers the indicated area from the south to the north of Curaçao.

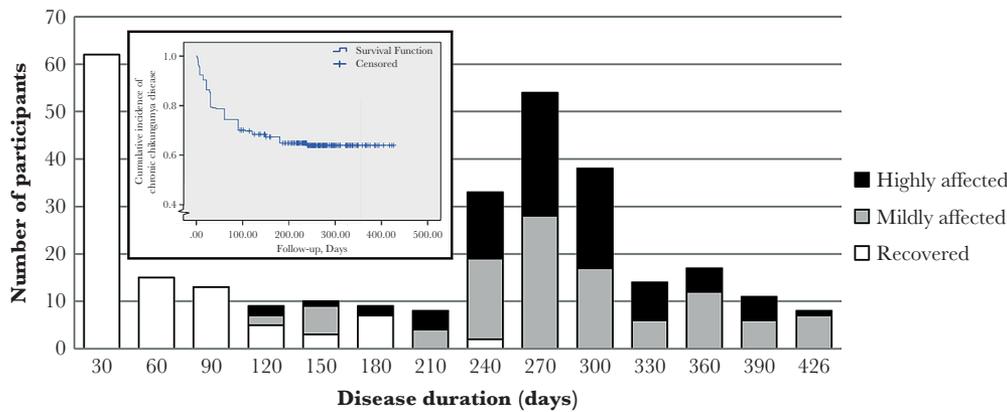


Figure 2. Distribution of disease status duration and cumulative incidence of disease persistence. The horizontal axis shows the maximum duration of disease (days) of the specific category; the number of subjects is expressed in the vertical axis. The recovered population is shown in white; the still mildly/highly affected population is shown in gray/black. The disease duration of the mildly/highly affected population is the time between disease onset and interview (ranging from 92 to 460 days), meaning that chronic disease was ongoing and may last longer than presented here. The Kaplan–Meier curve presents the cumulative incidence of disease persistence by follow-up time.

the mildly and highly affected population were arthralgia and weakness in the upper or lower extremities, myalgia, and tiredness. Other symptoms significantly associated with mildly or highly affected subjects were arthralgia and weakness in the back/neck, insomnia, somberness, loss of vitality, numbness, paresthesia (tingling), nausea, vomiting, abdominal pain, and hair loss.

Determinants of Chronic Chikungunya Disease Status

To characterize the different chronic chikungunya disease statuses, the “recovered” population vs the “affected” population (mildly plus highly affected groups) and the mildly vs highly affected groups were compared in univariate analyses (Supplementary Tables 1, 2, 6, and 7) and a binary multiple logistic regression. Supplementary Tables 8 and 9 show the general characteristics and symptoms independently associated with chronic chikungunya disease status. Individuals with chronic chikungunya disease were more likely to have arthralgia in upper (odds ratio [OR], 4.9; $P = .002$) and/or lower extremities

(OR, 12.3; $P < .001$), weakness in upper extremities (OR, 14.9; $P = .001$), myalgia (OR, 3.1; $P = .030$), and an age of 41–60 years ($P = .007$) compared with recovered subjects. Within the non-recovered subjects, the highly affected individuals were distinguished from the mildly affected by presenting more frequently arthralgia in upper (OR, 7.0; $P < .001$) and/or lower extremities (OR, 3.3; $P = .015$), weakness in lower extremities (OR, 4.2; $P = .005$), and loss of vitality (OR, 3.5; $P = .004$); and having a history of diabetes (OR, 3.7; $P = .013$). Being mildly affected was mainly associated with reporting weakness in the back or neck (OR, 6.67; $P = .001$) compared with the highly affected.

Quality of Life of a Population With Chronic Chikungunya Symptoms

Figure 4 shows the influence of chronic chikungunya disease on the QoL measured with the SF-36 questionnaire. SF-36 scores range from 0–100 and higher scores reflect better health outcomes. The recovered population showed the highest scores on all QoL dimensions, followed by the mildly affected and the highly affected population, respectively ($P \leq .001$,

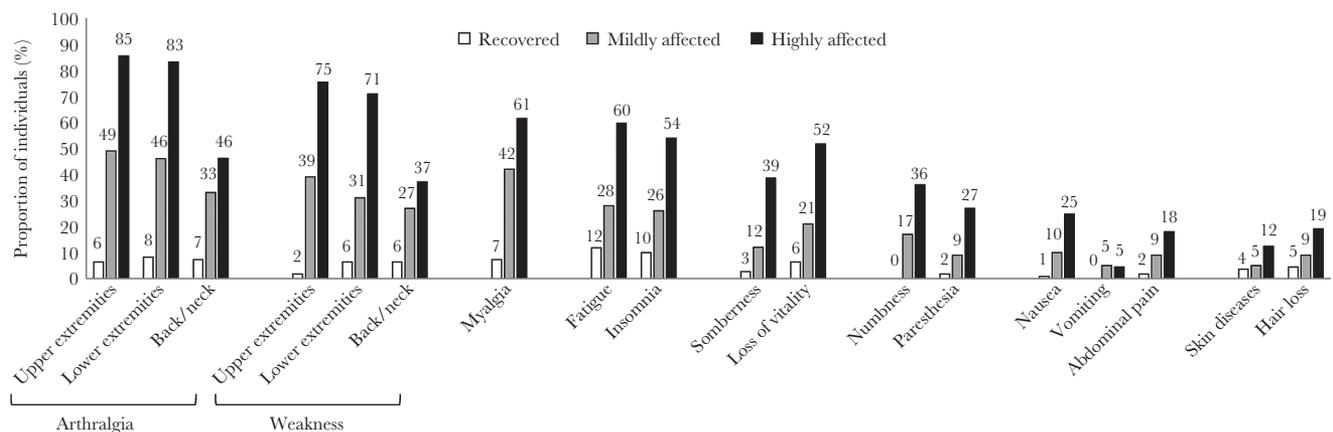


Figure 3. Symptoms of chronic chikungunya stratified by chronic disease status (Curaçao Long-Term Chikungunya Sequelae score).

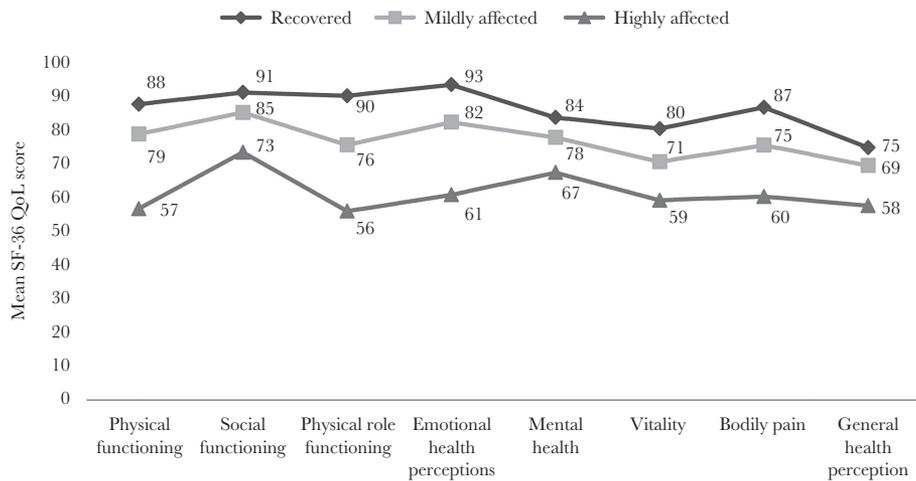


Figure 4. Mean scores of the RAND 36-Item Short-Form quality-of-life (QoL) survey (SF-36) by chronic disease status. Physical role function = (daily life) role limitations due to physical health.

Kruskal–Wallis test). Supplementary Table 10 provides the total data on SF-36 QoL score of this population.

DISCUSSION

A cross-sectional study including 304 individuals with a laboratory-confirmed recent CHIKV infection was conducted to assess the duration, symptomatology, and impact on the QoL of chronic chikungunya disease in Curaçao. This study provides comprehensive insights into the different degrees, clinical extent, and associated factors of chronic chikungunya disease. Furthermore, it introduces the CLTCS score, an easy and fast instrument for health workers to characterize the severity grades of chronic chikungunya in their patients.

The CLTCS score was developed and applied to characterize chronic chikungunya disease. Compared to other published arthritis assessment instruments (eg, the Health Assessment Questionnaire (HAQ) [22], Arthritis Impact Measurement Scales (AIMS) [23], and Rheumatoid Arthritis Severity Scale (RASS) [24]), the CLTCS score is swifter to use (than, eg, the HAQ and AIMS) and captures the broad clinical presentation of chikungunya (unlike the RASS and HAQ). Most studies describe chronic chikungunya disease based on rheumatic manifestations, classifying individuals binary as “(clinically) recovered” vs “not recovered” with self-reported recovery of chikungunya disease [25, 26] or presence of (self-perceived) persistent/relapsing rheumatic manifestations [8, 10, 27, 28] as criterion. The CLTCS score differs from most of these approaches by comprehensively assessing the patient and not solely focusing on the presence of rheumatic disease (mainly arthralgia). We believe that this score enables the healthcare worker to estimate the severity of chikungunya symptoms quickly but accurately. As a consequence, using the CLTCS score, 64% of our study population was defined as chronically affected, compared to the 51% who referred being affected when using simpler classification

methods (“recovered” vs “affected”) (Supplementary Table 3). The results of the present study imply that previous classifications might underestimate disease persistence.

Previous studies, as recently reviewed by van Aalst and colleagues [9], have shown that in 18%–60% of individuals, chronic chikungunya persisted for a period of 12–36 months [8, 10–12], whereas in 2%–12% of the subjects, chronic disease may last for up to 5 years or longer [13–15]. Our study showed a relatively high proportion of disease persistence among the population, on the basis of our classification method of chronic chikungunya. In our study population, 20.6% were defined as fully recovered within 1 month. Consistent with another study [27], the Kaplan–Meier estimate showed a 64% chance of disease persistence for >400 days. Disease persistence remained at the same proportions between 90 and 400 days. Likewise, the contribution of the highly affected to the total study population demonstrated a constant level. This implies that those who may suffer from severe disease for a longer period might be already identified 3 months after disease onset using the CLTCS score.

A wide range of chronic symptoms was associated with the different disease statuses (Supplementary Table 5). All symptoms except for “vomiting” showed a higher proportion and severity in the highly affected group (Supplementary Table 2 and 5). The affected individuals reported most frequently musculoskeletal symptoms, corresponding with other studies [8, 10, 12, 25–28], but a considerable proportion referred concomitant tiredness, sleeplessness, and neuropsychological symptoms [12, 16, 26, 29]. The importance of the scarcely described neurologic chronic manifestations associated with chikungunya virus [30–32] was demonstrated in this study.

This study is the first to assess the SF-36 QoL questionnaire combined with a wide range of symptoms. The symptoms associated with chronic disease statuses are likely to explain the differences in QoL. The QoL scores of the recovered group

were comparable with or higher than those of a normal population, in contrast to the decrease in scores in all domains of the mildly affected population, and a major decrease in QoL in the highly affected group. The QoL scores of our “recovered” group of individuals were also comparable to those of “healthy normal” individuals as observed in a previous study in Curaçao (Supplementary Table 10) [21]. This consistency between a chikungunya-“recovered” population and a “healthy normal” population was shown before [25], indicating that subjects in a “recovered” group might serve as a control group when assessing chronic chikungunya sequelae. The latter is in particular relevant for areas with high attack rates during chikungunya outbreaks as in Curaçao, where 33%–50% of the population was infected in the first chikungunya epidemic. A chikungunya-negative “healthy normal” control group is hard to recruit in such situations. That notwithstanding, lack of inclusion of this “healthy normal” group is still considered a limitation of this study.

SF-36-measured QoL scores were highly associated with chronic disease statuses. This is consistent with other studies using the SF-36 QoL questionnaire [10, 25, 29], while a study using the shorter SF-12 QoL questionnaire found a moderate impact on physical status but no impact on mental status [16]. Generally, a difference of 5–10 points in the domains of the SF-36 is considered to be a minimally clinically important difference (MCID) [33–36]. The major drop in QoL scores from the highly affected population exceeds the 10-point border on all domains when compared with the QoL scores of the recovered (score difference, 16–34) and the mildly affected population (score difference, 10–22). This finding is alarming and stresses the importance of identifying and treating these “highly affected” patients early and appropriately. However, the decrease in QoL of the “mildly affected” individuals is considerably less and implies that, although an MCID on QoL can still be achieved on some of the QoL domains, no intensive monitoring is needed for this group. Consequently, efficient psychological and physical care for chronic chikungunya patients should focus on the highly affected group.

This study investigated the characteristics that differentiate the severity of chronic chikungunya disease status. The main characteristics associated with a (highly) affected disease status were higher proportions of arthralgia and weakness in the extremities. Other studies show higher proportions of rheumatic manifestations in older participants [12, 25, 37], which is in line with the data from our study. However, participants older than 60 years had a higher chance to be defined as recovered of chronic chikungunya than those between 41 and 60 years old, implying that rheumatic manifestations in individuals older than 60 years may have been less often attributed to a previous chikungunya infection. For example, arthrosis/arthrititis (degenerative/inflammatory joint disease) may be responsible for chronic joint complaints of those stating to be recovered of

chikungunya while remaining with joint pain. Hence, classification methods of chronic chikungunya sequelae in future studies should not solely hinge on articular manifestations, or explicitly control for articular/rheumatic comorbidities. The described characteristics associated with disease status contribute to the understanding of which conditions and symptoms make patients perceive their chronic chikungunya disease as severe. Accordingly, physicians should be aware that chronic chikungunya patients presenting with the above-mentioned characteristics, as well as loss of vitality and having diabetes, have a higher risk of being highly affected.

The recruitment procedure of this study via general practitioners resulted in a study population of patients who are known by their physicians for their CHIKV infection, which might have implications for the generalizability of the study. Twenty-six percent of the study population was male, compared to 45.7% in the total population of Curaçao [17]. Results on QoL and symptoms might differ if assessed in more gender-balanced studies, as females tend to assess their QoL lower than males [38]. The higher percentage of females in this study might be explained by the findings that they visit a doctor more often [39]. Nonetheless, selection bias was limited given the high response rate of this study (82.5%). Further limitations of this study that should be taken into account are as follows: Coinfections (eg, dengue) were not excluded, the assessment of onset of chikungunya disease (at time of interview) might have led to recall bias, time between disease onset and time of interview differed, and the different interviewers performing the interviews may have induced investigator bias. The strengths of this study were its comprehensive nature and the availability of extensive qualitative data, which gave the researchers a wider context to interpret the results. Patients were visited and surveyed at home, providing a safe and confident environment. Moreover, the study population is representative of the neighborhoods, nationalities, and socioeconomic classes of the whole island.

In conclusion, this study characterized chikungunya chronic disease into “recovered,” “mildly affected,” and “highly affected” categories. The symptoms and major impact on QoL associated with this classification emphasize the need to prioritize the highly affected group in chronic chikungunya care. This group can easily be identified using the CLTCS score.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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