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Association between Chikungunya infection and depressive symptoms among healthcare workers

Associação entre infecção pelo vírus Chikungunya e sintomas depressivos entre trabalhadores e trabalhadoras da saúde

Abstract

Objective: to analyze the association between previous Chikungunya infection and depressive symptoms among healthcare workers. **Methods:** a cross-sectional study with a probabilistic sample of healthcare workers in primary and medium-complexity care settings in a municipality in the state of Bahia, Brazil. We used the rapid test DPP-ZDC-IgM/IgG to identify recent (IgM) or previous (IgG) Chikungunya virus infection, and the Patient Health Questionnaire-PHQ-9 to assess depressive symptoms. We applied regression with robust variance to estimate prevalence ratios and 95% confidence intervals. **Results:** 392 workers participated, 83.2% female. The frequency of Chikungunya virus infection was 8.9%. The prevalence of depressive symptoms was 22.7%. In the adjusted analysis, Chikungunya infection was positively associated with depressive symptoms (PR=2.00; 95%CI: 1.29; 3.07). Stratified analyses indicated a stronger association among males (PR=7.57; 95%CI: 1.15; 50.06) compared with females (PR=1.68; 95%CI: 1.03; 2.74). **Discussion:** the findings support the hypothesis of a positive association between Chikungunya and depressive symptoms. Physiopathological mechanisms resulting from viral action, as well as emotional, behavioral, and psychosocial factors associated with the disease, may explain the findings. We reiterate the importance of providing mental health care to healthcare workers.

Keywords: Chikungunya fever; mental health; depression; occupational health; health personnel; cross-sectional studies.

Resumo

Objetivo: analisar a associação entre infecção prévia por Chikungunya e sintomas depressivos em trabalhadores da saúde. **Métodos:** estudo transversal com amostra probabilística de trabalhadores atuantes na atenção primária e na média complexidade de um município do estado da Bahia, Brasil. Utilizou-se o teste rápido DPP-ZDC-IgM/IgG para identificar infecção recente (IgM) ou prévia (IgG) pelo vírus Chikungunya. O Patient Health Questionnaire-PHQ-9 foi usado para avaliar sintomas depressivos. Regressão de Poisson com variância robusta foi usada para estimar razões de prevalência e intervalos de confiança 95%. **Resultados:** participaram da pesquisa 392 trabalhadores, sendo 83,2% do sexo feminino. A frequência de infecção pelo vírus Chikungunya foi de 8,9%. A prevalência de sintomas depressivos foi de 22,7%. Na análise ajustada, a infecção por Chikungunya associou-se positivamente aos sintomas depressivos (RP=2,00; IC95%:1,29;3,07). As análises estratificadas apontaram associação de maior magnitude no sexo masculino (RP=7,57;1,15;50,06), em comparação ao feminino (RP=1,68;1,03;2,74). **Conclusão:** os achados corroboram a hipótese de associação positiva entre Chikungunya e sintomas depressivos. Mecanismos fisiopatológicos decorrentes de ação viral, bem como fatores emocionais, comportamentais e psicossociais associados à doença podem explicar os achados. Reitera-se a importância do cuidado em saúde mental para os trabalhadores da saúde.

Palavras-chave: febre de Chikungunya; saúde mental; depressão; saúde do trabalhador; pessoal de saúde; estudos transversais.

Introduction

Arboviruses (viral infections transmitted by arthropods) have become an important public health problem due to their magnitude and morbidity burden, with significant social and economic impacts^{1,2}, particularly in low- and middle-income countries. Infected mosquitoes of the genus *Aedes* transmit the Chikungunya virus (CHIKV). In Brazil, the main vector is the *Aedes aegypti*, widely distributed throughout the national territory. CHIKV was first identified in 2014, in the municipalities of Feira de Santana (Bahia) and Oiapoque (Amapá). Since then, it has spread rapidly across the country, causing major outbreaks and epidemics^{3,4} and is currently present in all regions across the country.

The disease caused by CHIKV is mostly self-limiting, characterized by fever, skin rashes, as well as myalgia and polyarthralgia—both of which can persist for up to five years⁵. Long-term clinical manifestations have been well documented in the literature^{6,7,8}. However, the repercussions of Chikungunya virus infection on mental health are still little known, despite being a disease that presents a considerable risk of impact on quality of life⁸. Diseases that cause musculoskeletal disorders, such as Chikungunya, are often associated with reduced working capacity, often requiring sick leave, rehabilitation, and, in more serious cases, retirement due to disability⁹.

Studies have described that, on average, after two years of infection, 43% to 75% of those affected by the CHIKV virus report prolonged or late onset symptoms attributable to Chikungunya⁶. Moreover, regarding mental health, individuals with a previous diagnosis of the disease seem to have memory problems¹⁰, mood disorders^{10,11}, sleep disorders^{10,12}, generalized anxiety disorder¹³, common mental disorders¹², and symptoms of depression^{6,13} due to the infection. Depression can be mediated by psychoimmune mechanisms, common in acute and chronic inflammatory processes that can lead to organic depression. Evidence has pointed to the general role of inflammatory processes in the organic causes of depression^{13,14}. On the other hand, depression can also be related to occupational and psychosocial stressors, especially in individuals with post-Chikungunya sequelae who experience difficulties in meeting work demands and requirements, as well as various limitations in social life due to loss of autonomy or restrictions in performing daily activities⁸, especially those with chronic pain.

Despite being an important cause of functional disability and absenteeism¹⁵, few studies have assessed the prevalence of CHIKV infection in working populations—including healthcare professionals—or focused on its potential impact on physical and mental health. In Brazil, the healthcare teams of the Unified Health System (SUS), especially those in primary care, are responsible for arbovirus preventive actions, monitoring sanitary conditions, and implementing the necessary control measures in territories and communities, which can offer an increased risk of infection¹⁶.

In the Brazilian health sector, especially in the Unified Health System (SUS), weaknesses can be seen in occupational health surveillance systems—in general, monitoring devices for workplace infections are lacking, as well as systems for identifying occupational risks and diagnosing their consequences. Thus, analyzing both the risk of infections and their potential relationship with other types of repercussions on health are relevant aspects for revealing the occupational risks that exist in health work, as well as for adopting preventive and health protection measures. In this perspective, this article focuses on a theme that is still little explored in Chikungunya studies. Considering the scarcity of studies on the frequency of the disease and its association with negative mental health outcomes, particularly in working populations, this study aims to analyze the association between previous Chikungunya infection and depressive symptoms in healthcare workers.

Methods

Study design and context

This is a cross-sectional epidemiological study conducted from June 2019 to January 2020 on a randomly selected representative sample of healthcare professionals from primary healthcare and secondary services in the municipality of Santo Antônio de Jesus in the Recôncavo da Bahia, Brazil. This study is part of the multicenter project “*Vigilância e Monitoramento de Doenças Infecciosas entre trabalhadores e trabalhadoras do setor saúde*” (Surveillance and Monitoring of Infectious Diseases among Healthcare Workers).

Participants

The inclusion criteria were: (1) Primary or Secondary Care healthcare workers which included specialized units, such as Psychosocial Care Centers, Occupational Health Reference Centers, Municipal Polyclinics, Testing and Counseling Centers, Mobile

Emergency Care Service, and Regulation Service; (2) at least 18 years of age; and (3) working for more than six months in municipal public healthcare services. Healthcare professionals on suspension, on vacation, or on leave were excluded.

Sample selection was defined by the following procedures: 1. Enumeration of the study population by means of a nominal list of all healthcare professionals of the Municipal Health Department; 2. Definition of the parameters for the sample calculation; 3. Stratification of the population by level of care provided and occupational groups—the percentage distribution of the population according to these two strata of the sample was estimated; and 4. Selection, by list of random numbers, of the workers, according to the sample size defined by the established stratification levels.

Sample size

The sample size calculation was originally performed to estimate the prevalence of different health outcomes rather than specifically to analyze the association investigated in this study. A target population of 622 healthcare professionals was considered, with an expected prevalence of the main outcomes of up to 42%, a 95% confidence level, and an acceptable error of 3%. Thus, a sample size of 391 individuals was calculated, which, added to 20% due to possible losses, resulted in a final sample of 469 professionals.

To avoid losses and ensure that the sample size for the considered strata was reached, an extra list (backup) was also defined by random procedure for the eventual replacement of healthcare workers who were not found or who refused. The extra list was limited to 20% of the original. Thus, in the event of loss or refusal of the selected healthcare worker, the interviewer, after three attempts, was instructed to replace them with another person from the same level of care, from the same occupation, and of the same sex as the previously selected.

Based on the objectives of this study, the required sample size was estimated to analyze the intended association, considering the 20% prevalence of depression symptoms among the unexposed, a ratio of 1:8 between unexposed and exposed, a predicted measure of association ≥ 1.8 , and 95% confidence interval, the study had an 80% power to detect as statistically significant the association of interest.

Data Collection

Data collection was performed via individual interviews, with the application of a structured

questionnaire based on the literature, which included questions regarding sociodemographic, occupational, and health data. The interviews were conducted at the workplace (in the health unit where the individual worked) and by trained interviewers. After the interview, the workers who agreed to take part in the second stage of the study had their blood taken for rapid testing for the following infectious diseases: Dengue, Zika, Chikungunya, HIV, hepatitis B and C, and syphilis.

Variables

The exposure variable was Chikungunya virus infection, previous (presence of IgG antibodies) or recent (presence of IgM antibodies), evaluated by rapid testing. The outcome variable was measured by the detection of depressive symptoms using the Patient Health Questionnaire (PHQ-9).

The analysis also included the following covariates: sex (male, female), age in years (21-34; 35-44; 45-54; 55 or more), schooling level (up to secondary education; technical education; higher education; graduate) self-declared race/skin color (Black; Mixed-race; White), occupation (community health agents; endemics disease control agents; administrative services; technician professionals; graduate professionals; support service professionals), and post-Chikungunya pain sequelae (CHIKV positive without pain; CHIKV positive with pain).

Measurement

The rapid serological test DPP ZDC IgM/IgG (Biomanguinhos – Fiocruz) was used to evaluate recent (presence of IgM antibodies) or previous (IgG) Chikungunya virus infection. The test sensitivity for IgM antibodies is 100% (95%CI: 91.2-100.65%) and 100% for IgG (95%CI: 91.4-100%). The specificity for IgM antibodies is 99.4% (95%CI: 97.9-99.9%) and 100% for IgG (95%CI: 96.5-100%), using enzyme-linked immunosorbent assays as reference. This information is described in the package leaflet of the DPP ZDC IgM/IgG test (Biomanguinhos – Fiocruz). Technical and standardization procedures were defined before the collection of the tests. Trained nurses performed the rapid tests, the results of which were recorded in a specific form. The results and their interpretation were made available to the professionals individually and privately. In cases of positive tests, the necessary referrals for treatment and follow-up were made to specialized referral services within the municipal healthcare network, after previous negotiation with the service coordinators.

The Patient Health Questionnaire (PHQ-9) was used to measure depressive symptoms. The PHQ-9 is an instrument composed of nine questions, based on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the International Classification of Diseases (ICD). Moreover, it has been widely used in investigations of suspected symptoms of major depression¹⁷⁻¹⁹. The PHQ-9 screens for symptoms of depressed mood, anhedonia, sleep disturbances, tiredness or fatigue, difficulty concentrating, changes in weight or appetite, feelings of restlessness or sluggishness, suicidal ideation, or self-aggression. The frequency of symptoms refers to the period of the last two weeks and is assessed using a Likert-type scale, ranging from 0 to 3, corresponding respectively to the answers “not at all,” “less than a week,” “a week or more,” and “nearly every day.”

The PHQ-9 scores were calculated from the sum of the scores of the questions, and the test was considered positive for depressive symptoms when the total score was equal to or greater than 9. The cut-off point adopted was based on a study by Santos et al. (2013)²⁰ that validated the PHQ-9 in an adult population in Brazil. This cut-off point was established due to being the one that maximized both sensitivity and specificity (sensitivity of 77.5% and specificity of 86.7%)²⁰.

The occupations were grouped into six categories, considering the proximity of work characteristics and occupational risk factors: community health agent, endemics disease control agent, administrative services (e.g. coordinators, managers, receptionists, typists), technician professionals (nursing technician, dental technician, radiology technician, laboratory technician), graduate professionals (e.g. nurses, doctors, dentists, psychologists, social workers), and support services professionals (e.g. general services staff, drivers, security guards, janitors).

For descriptive purposes, the sequelae of post-Chikungunya pain were evaluated by the following questions: 1. Did you have sequelae after having Chikungunya? (yes, no) and 2. If yes, did you experienced joint pain after three months of being cured of the disease (yes, no). Based on the answers and the results of the rapid test, two categories were defined: CHIKV_{positive} painless and CHIKV_{positive} with pain.

Data analysis

The database was built using the statistical package Social Package for the Social Sciences – SPSS,

version 13. The analyses were conducted using STATA, version 16. The descriptive analysis was based on absolute and relative frequencies, according to the independent variables of interest. Pearson's chi-square test was used to analyze the association between categorical variables. To assess the associations of interest, Poisson regression with robust variance was employed to estimate crude and adjusted prevalence ratios and 95% confidence intervals, adjusting for possible confounding factors (multivariable models). For the multivariable analysis, variables with a p-value ≤ 0.25 in the crude analysis were selected, and those with statistical significance at the 5% level were kept in the model. The multiple regression models were constructed based on the literature, after an exploratory analysis of the data. Finally, the analyses were stratified by sex (male; female).

Ethical considerations

This study complied with all the bioethical recommendations contained in Resolution 466/2012 and 510/2016 of the Brazilian National Health Council, ensuring anonymity, confidentiality, and the possibility of interrupting the interview at any time. All participants signed an informed consent form. This study was approved by the Ethics Committee on Research with Human Beings of the State University of Feira de Santana, under protocol CAAE 90204318.2.0000.0053.

The results of laboratory tests were delivered to each participant. The results of the study were presented to the professionals in workshops and seminars. Short courses on infectious diseases in the health sector were also offered online during the pandemic.

Results

Among the 453 individuals selected to participate in the survey, 424 agreed to perform the test and 392 provided complete information for the variables of interest in this study, making up the sample, which represents an overall response rate of 86.5%. Approximately 83% were female (**Table 1**). Most (62.7%) were up to 44 years of age; 23.7% were aged 21 to 34 years; and 39.0% were aged 35 to 44 years. Thus, this is a relatively young population. Black or mixed-race was reported by 81.6%. Around a third (32.6%) had secondary education, whereas 46.9% had higher education or graduate degree. Slightly more than a quarter of the participants (26.4%) worked as community health agents; 22.8% worked

in administration; and 17.1% worked in graduate-degree jobs.

The global frequency of Chikungunya infection was 8.9% (**Figure 1**), with 4.7% recent infection

(IgM antibodies) and 5.2% previous infection (IgG antibodies). Chronic pain secondary to previous Chikungunya was reported by 2.5% of professionals (**Table 1**).

Table 1 Sociodemographic characteristics, prevalence and factors associated with depressive symptoms among healthcare workers, Bahia, Brazil, 2019 (n=392)

Variables	Population		Depressive symptoms			
	n	%	n	%	PR (95%CI)	p-value****
Sex						
Male	66	16.8	8	12.1	1.00	
Female	326	83.2	81	24.9	2.05 (1.04;4.03)	0.038
Age (years)						
21-34	93	23.7	30	32.2	1.00	
35-44	153	39.0	29	18.9	0.59 (0.38;0.91)	0.016
45-54	98	25.0	22	24.5	0.76 (0.48;1.20)	0.220
55 or more	48	12.3	6	12.5	0.39 (0.17;0.87)	0.021
Schooling level						
Graduate	68	17.3	8	11.8	1.00	
Higher education	116	29.6	32	27.6	2.34 (1.15;4.79)	0.020
Technical Education	83	21.2	17	20.5	1.74 (0.80;3.79)	0.162
Secondary Education	125	31.9	32	25.6	2.18 (1.06;4.46)	0.034
Ethnicity/skin color						
Black	132	34.7	24	19.7	1.00	
Mixed-race	188	49.5	44	25.5	1.29 (0.85;1.98)	0.229
White	60	15.8	13	21.7	1.10 (0.61;1.99)	0.753
Occupation*						
Graduate professionals	66	17.1	8	12.1	1.00	
Technician professionals	57	14.8	11	19.3	1.59 (0.69;3.69)	0.278
Administrative services	80	20.8	20	25.0	2.06 (0.97;4.38)	0.060
CHA**	102	26.5	21	21.6	1.70 (0.80;3.61)	0.169
ECA***	50	13.0	21	43.7	3.46 (1.67;7.17)	0.001
Support Service professionals	30	7.8	8	26.7	2.20 (0.91;5.31)	0.079
Post-CHIKV sequelae						
CHIKV+ painless	25	6.4	12	48.0	1.00	
CHIKV+ with pain	10	2.5	3	30.0	0.62 (0.21;1.78)	0.378

*n= 385

**CHA: Community Healthcare Agent

***ECA: Endemic Disease Control Agent;

****Pearson's chi-square test.

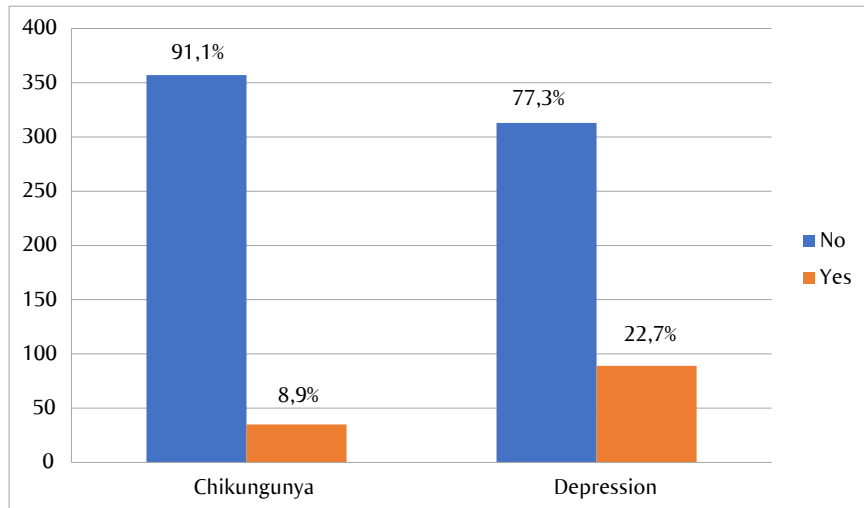


Figure 1 Frequency of Chikungunya infection and prevalence of depression in healthcare workers, Bahia, Brazil, 2019 (n=392)

The prevalence of depressive symptoms was 22.7% (**Figure 1**). The variables sex, age, schooling level, and occupation were associated with depressive symptoms (**Table 1**). Women had twice the prevalence of depression symptoms compared to men (PR=2.05; 95%CI: 1.04;4.03). For women from 35 to 44 years-old (PR:0.59; 95%CI: 0.38; 0.91) and being older than 55 years (PR=0.39; 95%CI 0.17;0.87) were factors negatively associated with the outcome when compared to the group aged 21 to 34 years. Endemic disease control agents had a 3.46

(95%CI 1.67;7.17) higher prevalence of depressive symptoms when compared to professionals with higher education.

Previous Chikungunya infection was associated with a twofold higher prevalence of depressive symptoms in the crude bivariate analysis (**Table 2**). After adjusting for age and schooling level, the association remained positive, and the effect measure was not substantially affected (PR= 2.00; 95%CI: 1.29;3.07).

Table 2 Association between Chikungunya infection and depressive symptoms in healthcare workers, Bahia, Brazil, 2019

Variables (n)	Total		Depressive symptoms			Model 1*			Model 2**		
	n	n	%	PR ¹	95%CI ²	p-value ³	PR ¹	95%CI ²	p-value ³		
Global Chikungunya Infection (392)											
No	357	74	20.7	1.00			1.00				
Yes	35	15	42.9	2.07	1.34;3.19	0.001	2.00	1.29;3.07	0.002		
Chikungunya infection in women (326)											
No	296	69	23.3	1.00			1.00				
Yes	30	12	40.0	1.72	1.06;2.79	<0.001	1.68	1.03;2.74	0.036		
Chikungunya infection in men (66)											
No	61	5	8.2	1.00			1.00				
Yes	5	3	60.0	7.32	2.40;22.25	<0.001	7.57	1.15;50.06	0.036		

*Model 1: gross; ** Model 2: Adjusted for age and schooling level; ¹PR: prevalence ratio; ²CI: Confidence Interval; ³Pearson's chi-square test.

Analyses stratified by sex showed a positive association between Chikungunya infection and depressive symptoms in both sexes, but with a stronger association in males (PR=7.57; 95%CI: 1.15; 50.06) compared to females (PR=1.68; 95%CI: 1.03; 2.74), after adjusting for age and schooling level (Table 2).

Discussion

The prevalence of depressive symptoms evidenced in this study was similar to that found in previous studies with healthcare workers. In comparison, a study of primary health care professionals, which also used the PHQ-9 to screen for depressive symptoms, found a prevalence of 18%²¹, whereas another study of community health agents found a prevalence of 20.5%¹⁷. Despite the methodological differences (sampling and recruitment of participants) with this study, the prevalence of depressive symptoms in a Brazilian national survey with household interviews using the PHQ-9 was estimated at 4.1% (95%CI: 3.8 to 4.4%)²², suggesting that healthcare professionals may be at higher risk for mental health problems than the general population.

The sample of this study is mostly composed of women, reflecting the feminization of medicine in Brazil^{18,21}. The prevalence of depressive symptoms was significantly higher among women, which is supported by the specialized literature²³. Social gender differences may be key to this relationship since women generally work a double shift, which involves, in addition to working, domestic overload and caring for children—these activities, in turn, represent a smaller share of free time for rest and leisure activities. This overload can generate physical exhaustion and mental illness²⁴.

The prevalence of depressive symptoms was higher in the younger age groups and lower in workers over 55 years of age. Prevalence rates fluctuated in the intermediate age groups, decreasing with younger age and rising again in the following age group. However, the negative association between age and depressive symptoms was statistically significant only for the comparison of the youngest with the oldest age groups and from 35 to 44 years. More experienced workers may have developed, over time, more effective coping strategies for occupational stressors or even be in less demanding jobs—everyday experience can favor the acquisition of devices that help to avoid more demanding situations, as well as providing less stressful management of professional and personal resources. In work contexts, older adults

learn to differentiate between controllable and uncontrollable stressors, which is an important developmental task that contributes to the mental health of older adults²⁵.

Regarding the 35 to 44 age group (the second group considered), we highlight the significant reduction in the prevalence of depressive symptoms when compared to younger people. Additionally, the habitual performance of the occupation, similar to older people, can contribute to better management of work demands and greater control over expectations. Thus, in this case too, strategies may have been created, even if temporarily, for better accommodation and efficiency in the responses to daily confrontations, favoring the protection of mental health.

Regarding the occupation, the high prevalence of depressive symptoms among the endemic disease control agents (ECA) is noteworthy, over 40% (three times higher than the graduate professionals group), whereas other occupational groups, such as administrative and support services (SAS) professionals, also presented high prevalence of the outcome, although the difference was not statistically significant in comparison with the reference group (graduate professionals), which may have occurred due to lack of statistical power (small number in the reference group).

ECAs perform activities related to fieldwork for endemic disease control, which involves entomological research, chemical and biological control measures for vector diseases, as well as registering households. These professionals often face precarious working conditions, exposure to different chemicals, little training to perform their tasks, invisibility, low pay, and low social appreciation, as well as not having a specific place to work—most of their activities are conducted outside. The fact that ECAs do not perform actions with immediately observable material benefits for the populations they assist may be a factor that devalues their work and hinders a more effective external collaboration in their activities. As their work often depends on access to households and the cooperation of the population, the challenges can trigger feelings of humiliation, along with lack of recognition and support. These feelings may be contributing factors to the high prevalence of depressive symptoms observed.

The work of community health agents, for example, is specifically characterized by the development of activities aimed at integrating the community and the healthcare service on a defined territorial basis. The work is conducted by identifying and registering families, making visits

to systematically collect information on living conditions and health, based on direct contact with people where they live. These agents experience the same social context as the communities, as they generally live in the area where they work²⁶ and often find it difficult to establish barriers or boundaries between work and private life, which is a potential stress factor with an impact on mental health. High prevalence was also found among administrative and support service professionals. Some of these professionals conduct activities that involve initial contact for scheduling procedures, consultations, exams, distribution of medicines and materials, which are tasks that can generate conflicts and tension between professionals, users, and companions.

These differences refer to the social determination of the health-disease process, given that occupational groups with lower incomes and worse socioeconomic conditions have a higher frequency of mental health problems^{19,21}. Moreover, the characteristics of the work and support mechanisms of the different groups can also determine different forms of mental suffering.

Regarding the main association of interest, previous infection with Chikungunya virus was strongly and positively associated with depressive symptoms, corroborating the hypothesis that guided the main analysis of this study. Stratified analyses revealed that although the positive association was present for both sexes, its magnitude was much greater for men. This finding suggests that other biological and/or social factors related to sex (and gender) may interact with the viral infection and interfere with the frequency of depressive symptoms.

Men and women have different ways of dealing with the experiences of illness. Women generally seek care and strategies to mitigate the deleterious and chronic effects of the infection, such as emotional and social support, rehabilitation, integrative practices, and specialized care. On the other hand, men find it more difficult to seek help and health services, as well as to report persistent symptoms when their health needs are not met²⁷. In this way, women can be more engaged in improving their quality of life, and this can have an impact on their mental health. A study that aimed to understand the emotional impacts of Chikungunya found that young men usually relied on their physical strength, so coping with the disease was especially difficult since they were unable to rely on their own bodies. The situation of not being able to perform simple daily activities was identified by men as the most frustrating experience, even greater than the pain itself⁸.

These findings are initial and strengthen the investigated hypothesis, but need to be confirmed

by study designs that assess the temporality of the relationship between the events satisfactorily. These results, if confirmed, open new perspectives for thinking about preventive strategies for CHIKV infection and depressive symptoms. They can also guide possibilities for the clinical management of complications and sequelae regarding the need for emotional support and social support at work. The results also point to the need to incorporate a perspective that considers sex and/or gender differences in this process.

Depressive and anxiety disorders are recognized as priority public health problems worldwide by the World Health Organization (WHO)²⁸. Recognizing psychosocial and health factors that may affect the patterns of occurrence of these morbidities in populations has the potential to broaden the range of actions to protect mental health and enhance the ways of tackling these problems. The analysis of these disorders, as done in this study, helps to make them visible since the tendency to neglect the symptoms of mental illness in the course of a viral disease still prevails¹³, especially in epidemic situations, in which healthcare services tend to be overloaded and mobilized to respond to the infectious disease.

The results of this study were consistent with previous investigations^{10,29}, considering that the prevalence of depressive symptoms was 42.9% among those seropositive for CHIKV, whereas it was 20.7% among those seronegative. In a retrospective cohort of individuals who were infected with CHIKV³⁰ during the 2005 and 2006 outbreaks on Reunion Island (overseas territory of France), significant differences in the occurrence of depressive symptoms were also found between people who were seropositive and seronegative for CHIKV, 13% and 5%, respectively, which corresponded to a relative risk of 2.5 (95%CI: 1.4;4.1). In the population-based study conducted by Gérardin and collaborators—on that same island—CHIKV+ (14.7%), CHIKV₋ (8.7%), and a crude prevalence ratio of 1.8 (95%CI: 1.2;2.7)¹⁰ were found.

As already highlighted, although the pathophysiology of CHIKV infection is still poorly understood, a spectrum of the disease that is still neglected includes organic depression with post-infectious fatigue, called CHIKV depression³⁰. Results of the scarce studies have observed an association between polyarthritides and depression at all stages of Chikungunya virus infection^{5,6}, suggesting that this could be a possible way of determining depressive symptoms.

Regarding other arboviruses, few studies have evaluated the association between dengue or Zika

and mental health. Among them, two investigations on psychiatric morbidity among individuals with dengue fever found symptoms of anxiety and depression^{31,32}. Although the exact mechanism of these manifestations is unknown, increased levels of pro-inflammatory cytokines (especially interleukins) in infectious and systemic diseases and chronic conditions have been associated with depressive symptoms¹⁴. Therefore, inflammation is a biological event that can increase the risk of depressive episodes in the same way as classic psychosocial factors³³. Furthermore, arbovirus infections are believed to function as a psychosocial stressor and/or that some mechanism of viral action may be responsible for neurochemical alterations mediated by inflammatory processes, characteristic of infectious diseases that produce psychiatric symptoms¹³. This situation can be affected differently according to the person's biological sex or gender.

Studies on quality of life also point in the same direction, showing a strong impact on the psychological domains of individuals affected by chronic CHIKV³⁴. A study investigating the prevalence of depressive symptoms in individuals with and without arthralgia found that depression was significantly higher in the group with arthralgia when compared to the group without arthralgia ($p < 0.001$), three years after the acute infection⁶. Yassen et al. compared the prevalence of depressive symptoms in people with arthralgia and people with arthritis. The prevalence of depression was significantly higher in the group with arthritis 54% (21/39) compared to the group with arthralgia 33% (11/33), respectively ($p = 0.002$)⁵.

Regarding psychosocial factors, CHIKV is a morbidity with great potential for chronicity. Its clinical and rheumatological repercussions substantially affect quality of life^{29, 35, 36}, and it can be considered a high psychosocial risk event, with possible mental health impairment. Its clinical manifestations produce a situation of physical, social, emotional, and financial stress, which affects overall functionality. A qualitative study with in-depth interviews and focused group discussions showed that patients with CHIKV reported impaired mobility and greater dependence for normal activities of daily living. Feelings of bad mood, anger, frustration, exclusion, and hopelessness have been experienced, as well as a change in identity and insecurity about the future⁸. From this perspective, mental health surveillance has been highlighted as a priority issue in healthcare workplaces³⁷ since depression can be disabling, generate a high burden of disease, and increase the risk of serious conditions such as suicidal ideation and suicide.

The results presented in this study should be interpreted considering some limitations. Since this is a cross-sectional study, the analysis of the time sequence between events is hindered, and an unknown proportion of workers could have had depressive symptoms before the Chikungunya infection. However, there seems to be no biological plausibility for a possible reverse causality in the positive association found between CHIKV and depressive symptoms since CHIKV is a vector-borne disease and is related to environmental factors. Nevertheless, there may have been a considerable time difference between previous infection and depressive symptoms in some of the cases, which would imply the need to evaluate other factors involved in the association. Another limitation is that, due to the low prevalence of exposure and limited number of participants, there may be a lack of statistical power to analyze some associations. As strengths of the study, the fact that the interviewer was unaware of the true serological status of the participants helps to avoid information bias, such as potential bias towards the exacerbation of symptoms. Moreover, the study is not susceptible to selection bias from the participation of critically ill patients, for example, as is observed in several other studies that use samples of patients from outpatient clinics or referral hospitals for treatment.

Conclusions

This study identified an association between Chikungunya and depressive symptoms, reinforcing this hypothesis. However, we recommend further studies that can identify the temporal relationship between these two events (longitudinal studies) or that assess other determining factors, as well as possible confounding factors, effect modification, and mediation. Our findings alert us to the relevance of monitoring registered CHIKV cases, as well as the need for mental health surveillance to identify and treat the symptoms of both conditions early on. To mitigate the impacts of CHIKV infection, it is recommended that mental health surveillance actions consider the recurrent epidemic outbreaks of arbovirus in their planning. Furthermore, continuous education of healthcare teams to identify workers at higher risk of mental health issues associated with Chikungunya can be a valuable tool for caring for this population, especially in occupations with greater social vulnerability.

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Authors' contribution

Helioterio MC, Feijó FR, Werneck GL, Souza FO, and Araújo TM, participated in all stages of the manuscript, from its conception, writing, analysis, data interpretation, and conclusion. Pinho PS contributed to the design and writing and critical review of the manuscript. All authors have approved the final version of the manuscript and take responsibility for all aspects of the manuscript, guaranteeing that those relating to the accuracy or integrity of any part of the manuscript have been properly investigated and resolved.

Data availability

The authors state that the data set supporting this study is not publicly available since it comes from individual interviews and contains information that allows people or workplaces to be identified, even with anonymization.

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