

Original Research Article

CLINICAL MANIFESTATIONS SUGGESTIVE OF DEPRESSION IN PATIENTS SERVED WITH FEBRILE ILLNESS IN CAMPO GRANDE (MS) AND DOURADOS (MS), BRAZIL

Abstract

Introduction: In Brazil, a country with high temperatures, favorable to the development of the vector, the mosquito has already become a problem, not only because of Dengue, Zika and Chikungunya, which plague some Brazilian regions. **Objectives:** To identify patients assisted in Campo Grande (MS) and Dourados (MS) with febrile symptoms and their possible depressive symptoms. **Methodology:** This is a cohort study with patients who obtained a proven clinical-epidemiological and laboratory diagnosis of Dengue (ELISA; qRT-PCR and NS1), treated at the SUS network in the cities of Campo Grande (MS) and Dourados (MS). The collection period was from 2018, starting from April to September 2019. The CES-D instrument was used to perform the possible diagnosis of depression. **Results:** In the 115 participants positive for Dengue, a sample in V0 was verified with 63.5% who developed symptoms of depression. In period V14, patients positive for Dengue totaled 37.4% and these patients did not develop depression according to the sample of the instrument used and totaled 62.6%. **Discussion:** It was possible to verify in this study that depression is a mood disorder whose symptom together brings suffering and, mainly, social and occupational damage to the analyzed sample. **Conclusion:** There is a significant direct relationship between the number of patients who developed depression in the illness process of febrile illnesses.

Keywords: Dengue, immune response, depression, CES-D, hemorrhagic fever.

INTRODUCTION

Infectious and febrile diseases are transmitted by vectors and affect about 700,000 people who die each year in Brazil and worldwide ^{28, 29}, in Brazil febrile diseases such as dengue, Zika and Chikungunya are a concern for the public health system due to its increasing incidence in the last ten years ²⁹.

Dengue, Zika and Chikungunya are characterized as a febrile disease and dengue is caused by the DENV virus, which belongs to four different groups of interrelated microorganisms (serotypes) ⁰¹. These are diseases transmitted by the main vector of the genus *Aedes* ^{01, 02}.

In recent years, a large percentage of the Brazilian population is considered to be symptomatic during the period of illness with dengue ^{05,07}. And the most common manifestations found in Brazil for febrile illness are; fever (38° C), vomiting, myalgia, arthralgia and skin rash ⁰⁶⁻⁰⁸.

Dengue, Zika and Chikungunya have shown a high morbidity rate in recent years²⁹, in clinical forms and with severe signs, has led the public health system to increase cases and the development of epidemic regions characterizing the co-circulation of DENV viruses, CHIKV and ZIKV. What has most concerned Brazilian researchers⁰⁸ is that 5% of symptomatic patients with dengue, Zika or Chikungunya may develop atypical manifestations such as neuropsychiatric¹⁴ and these atypical manifestations in about a third of these patients are severe and are characterized by the need for support psychiatric^{08, 11, 14, 17}.

That is why, in recent years, depressive disorders as a response to infectious processes have been considered a priority in the Brazilian public health system, by the World Health Organization (WHO) as mentioned in the study by Dalgarrondo (2008).

Dengue fever and other hemorrhagic or non-hemorrhagic febrile diseases have been well documented in Brazil in recent years in terms of their physical consequences, however little is known about late psychological comorbidities, such as depression^{11, 13, 15}.

It is important to consider that human well-being and happiness is directly linked to good health^{08, 12}, as a poor state of health can presume incapacity in day-to-day tasks^{25, 27}.

Neuropsychiatric worsening can occur in any of these phases directly or indirectly, depending on the action of the virus^{10, 12}. And the neuropsychiatric or mental worsening of the individual is related to the infectious process with any of the four dengue virus serotypes and can cause a wide spectrum of symptoms that can range from asymptomatic infection to a serious illness with neuropsychiatric complications^{15, 16, 20}.

And in addition to neuropsychiatric and lethal complications, mental life conditions serve to measure the individual's health burden with dengue, chronic and acute diseases^{24 - 27}. In the literature, the report we have is that dengue significantly worsens the mental quality of individuals²⁴.

In short, the physical condition of people affected by dengue or other febrile illnesses greatly affects their psychological health^{20, 22, 24}. In previously published studies, it was already known that dengue infection can affect the central nervous system of the body, justifying psychiatric manifestations during the course of the disease, such as depression, anxiety and anguish^{14, 27, 28}.

Thus, this study aimed to identify patients treated in Campo Grande and Dourados in the State of Mato Grosso do Sul with dengue who had a depressed mood in the period from 2018 to 2019.

METHODS

This observational and descriptive cohort study was based on data collected from patients with a proven clinical-epidemiological and laboratory diagnosis of dengue ((ELISA/NS1/qRT-PCR) treated at the emergency health care network in the region of Campo Grande and Dourados in the State of Mato Grosso do Sul. And, data were collected from April 2018 to September 2019. The Pan American Health Organization (PAHO) and World Health Organization (WHO) inclusion criteria were considered clinical confirmation for dengue, Zika and Chikungunya²⁹. And, the selected individuals were of both sexes, aged between 18 years and 99 years⁰¹ and presented inflammatory post-organic depressive symptoms which responded to the questioning through the CES-D instrument to investigate patients with psychological alterations on D0 and D14. The confirmed cases for dengue for inclusion in the study using the CES-D instrument were 115 patients and 175 patients of Zika and Chikungunya with a positive result for febrile illness. The clinical evolution of dengue, Zika and Chikungunya was performed by clinical monitoring and application of the CES-D instrument, in the initial phase between one and six months after the initial diagnosis. In the secondary and tertiary period between 7 and 12 months, as well as between 13 and 20 months.

The characterization of mental worsening in dengue was based on the time between the onset of clinical symptoms and mental worsening according to the instrument used CES-D in the period D0 and D14²⁴. The scores used were individuals with a sum greater than or equal to 16 points on the CES-D instrument and patients who underwent at least 03 outpatient monitoring appointments²⁴. Meanwhile, scores lower than 16 points found in the CES-D instrument were not used²⁴. Microsoft Excel was used in all analyzes performed for descriptive statistics, a significance level of 5% was considered ($p = 0.05$).

RESULTS

Table 01 - Distribution of the number of Dengue cases confirmed by clinical epidemiological and laboratory diagnosis (ELISA/NS1/RT-PCR), Campo Grande (MS) and Dourados (MS), from April 2018 to September 2019 (N = 115).

VARIABLES	POSITIVE CASES OF DENGUE (V0)		POSITIVE CASES OF DENGUE (V14)	
	f%	n (115)	f%	n (115)
SEX				
Masculine	31.3	36	31.3	36
Feminine	68.7	79	68.7	79
AGE				
18 - 24 Years	13.9	16	13.9	16
25 - 34 Years	28.7	33	28.7	33
35 - 44 Years	23.5	27	23.5	27
45 - 54 Years	20.0	23	20.0	23
55 - 64 Years	11.3	13	11.3	13
65 years or older	2.6	03	2.6	03
EDUCATION				
Illiterate	0.9	01	0.9	01
Incomplete Elementary School	19.1	22	19.1	22
Complete primary education	8.7	10	8.7	10
Incomplete high school	17.4	20	17.4	20
Complete high school	40.0	46	40.0	46
Incomplete Higher Education	4.3	05	4.3	05
Complete Higher Education	8.7	10	8.7	10
Postgraduate	0.0	00	0.0	00
Master's degree	0.9	01	0.9	01
USE OF CIGARETTES				
Yes	10.4	12	10.4	12
No	89.6	103	89.6	103
USE OF ALCOHOLIC BEVERAGES				
Yes	41.9	48	41.9	48
No	58.2	67	58.2	67
USE OF ILLICIT DRUGS				
Yes	2.8	03	2.8	03
No	97.2	112	97.2	112
ARTERIAL HYPERTENSION				
Yes	17.4	20	17.4	20
No	82.6	95	82.6	95
DIABETES MELLITUS				
Yes	4.3	05	4.3	05
No	95.7	110	95.7	110

Of the 115 patients with clinical and laboratory diagnosis of dengue by (ELISA/NS1/RT-PCR), 68.7% (n=79) were female and 31.3% (n=36) were male in V0 (**Table 01**). Distributed in the age profile with greater presence in the range of 25 to 34 years old equivalent to 28.7% (n=33), followed by 35 to 44 years old equivalent to 23.5% (n=27) and 45 to 54 years old with a percentage of 20% (n=23), however, for the elderly aged 55 years or older, the epidemiological percentage was characterized by 13.9% (n=16) in the V0 period (**Table 01**).

Schooling was equivalent with a higher percentage of 40% (n=46) for complete secondary education followed by incomplete elementary education with a percentage of 19.1% (n=22) and still, with 17.4% (n=20) referring to incomplete high school in the period of V0 (**Table 01**). Regarding the presence of chronic diseases, such as Diabetes Mellitus (DM) and Systemic Arterial Hypertension (SAH), it was possible to observe that 95.7% (n= 110) do not have DM, and around 4.3% (n = 05) are carriers of DM in the period of V0. In relation to SAH, a total of 82.6% (n = 95) do not have SAH and a percentage of 17.4% (n = 20) have SAH in the V0 period (**Table 01**).

97.2% (n= 112) of the patients included in the study are not illicit drug users and 2.8% (n= 03) are illicit drug users in the V0 period. The non-use of cigarettes 89.6% (n= 103) was the most frequent result and 10.4% (n= 12) use cigarettes. Already the use of alcoholic beverages had a percentage of 58.2% (n = 67) with no use and 41.9% (n = 48) do not use alcoholic beverages in the period of treatment for dengue in the period of V0. Regarding V14, the results in the 115 patients with clinical and laboratory diagnosis evaluated for dengue by (ELISA/NS1/qRT-PCR) were; 62.4% (n=72) were female and 37.6% (n=42) were male.

And, this gender profile was distributed according to age, that is, it presented an older profile in the range of 25 to 34 years with a percentage of 28.6% (n=33) and followed by 23.4% (n= 37) in the range of 35 to 44 years. As for schooling, it was possible to observe in this sample that 40% (n=46) had completed high school and 19.3% (n=22) had incomplete elementary school and this sample was significant in the study, as it presented a $p = 0.043$. When addressing Diabetes Mellitus (DM) in the sampling, it was possible to verify that a percentage of 95.6% (n = 110) did not present a diagnosis for Diabetes Mellitus (**Table 01**).

And, hypertension is observed in V14 a significance with $p= 0.021$, that is, with a percentage in the sample of 82.6% (n= 95) that did not present hypertension in the period of dengue treatment.

A total of 97.4% (n=112) reported not using illicit drugs during the dengue treatment period. As for the use of cigarettes, it is possible to verify a slight equity, since 89.5% (n=103) do not use cigarettes and 97.4% (n=112) did not use alcohol during the treatment period.

Table 1- Distribution of the number of cases of febrile illnesses in V0 and V14 for Zika or Chikungunya (n=175) .

VARIABLES	NEGATIVE CASES FOR DENGUE WITH POSITIVE DIAGNOSIS OF ZIKA OR CHIKUNGUNYA (V0) AND (V14) (n-175)	
	n (175)	f%
SEX		
Masculine	91	52
Feminine	84	48
AGE		
18 - 24 Years	61	34.8
25 - 34 Years	54	30.8
35 - 44 Years	27	15.4
45 - 54 Years	18	10.3
55 - 64 Years	7	4.0
65 years or older	8	4.5
EDUCATION		
Illiterate	0	0
Incomplete Elementary School	49	28
Complete primary education	25	14.2
Incomplete high school	25	14.2
Complete high school	39	22.2
Incomplete Higher Education	18	10.2
Complete Higher Education	6	3.4
Postgraduate	two	1.1
Master's degree	1	0.57
USE OF CIGARETTES		
Yes	50	28.5
No	125	71.4
USE OF ALCOHOLIC BEVERAGES		
Yes	54	30.8
No	121	69.1
USE OF ILLICIT DRUGS		
Yes	0	0.0
No	175	100.0
ARTERIAL HYPERTENSION		
Yes	53	12.8
No	122	87.2
DIABETES MELLITUS		
Yes	57	32.5
No	118	67.4

Of the 175 patients with clinical and laboratory diagnosis of Zika or Chikungunya by (ELISA/NS1/RT-PCR) in V0 and V14, 91 (52%) were male and 84 (48%) were female in V0 (**Table 02**), however, there was a loss of 50 individuals at the V0 moment for negativity for febrile diseases (Zika, Dengue and Chikungunya) usually due to the casuistry of another disease such as autoimmune or bacterial.

Distributed in the age profile with greater presence in the range of 25 to 34 years old equivalent to 54 (30.8%), followed by 18 to 24 years old equivalent to 34.8% (n=61) and 35 to 44 years old with a percentage of 15.4% (n=27) (**Table 02**).

Table 2- Characterization between the CES-D components in period V0 and V14 in cases of patients with depressive signs for febrile illnesses (Dengue, Zika and Chikungunya) (N=290).

VARIABLE		POPULATION				
POSITIVE ASPECTS		V0	%	V14	%	P
12 - I've Been Happy	Few times.	13	11.4	06	5.3	0.06
	Sometimes.	14	12.2	16	13.9	
	Rarely or never.	7	6.0	01	0.8	
	Almost always or always.	81	70.4	92	80.0	
16 - I had fun	Few times.	16	13.9	16	13.9	0.011
	Sometimes.	26	22.6	29	25.3	
	Rarely or never.	19	16.6	19	16.5	
	Almost always or always.	54	46.9	51	44.3	
08 – I felt hopeful about the future.	Few times.	01	0.9	1	0.9	< 0.001
	Sometimes.	12	10.5	5	4.4	
	Rarely or never.	02	1.7	two	1.7	
	Almost always or always.	100	86.9	107	93.0	
VARIABLE		POPULATION				
POSITIVE ASPECTS		V0	%	V14	%	P
04 – I feel as good as other people.	Few times.	20	17.4	17	14.7	0.014
	Sometimes.	19	16.6	21	18.3	
	Rarely or never.	18	15.6	18	15.6	
	Almost always or always.	58	50.4	59	51.4	
NEGATIVE ASPECTS		V0	%	V14	%	
06 – I felt depressed.	Few times.	18	15.6	17	14.7	< 0.001
	Sometimes.	25	21.7	22	19.2	
	Rarely or never.	66	57.4	75	65.3	
	Almost always or always.	06	5.3	01	0.8	
18 – I felt sad.	Few times.	23	20.0	13	11.4	< 0.001
	Sometimes.	39	33.9	15	13.1	
	Rarely or never.	49	42.6	86	74.7	
	Almost always or always.	04	3.5	1	0.8	
NEGATIVE ASPECTS		V0	%	V14	%	
14 – I felt lonely.	Few times.	18	15.7	14	12.3	< 0.001
	Sometimes.	21	18.3	17	14.7	
	Rarely or never.	71	61.7	80	69.6	
	Almost always or always.	05	4.3	4	3.4	
13. I talked less than usual.	Few times.	21	18.4	14	12.2	< 0.012
	Sometimes.	24	20.8	26	22.6	
	Rarely or never.	54	46.9	72	62.6	
	Almost always or always.	16	13.9	3	2.6	
17 – I had crying spells.	Few times.	16	13.9	14	12.2	< 0.001
	Sometimes.	15	13.0	8	6.9	
	Rarely or never.	73	63.5	90	78.3	
	Almost always or always.	11	9.5	3	2.6	
10 – I felt scared.	Few times.	15	13.2	7	6.1	< 0.001
	Sometimes.	31	26.9	6	5.3	
	Rarely or never.	60	52.1	101	87.8	
	Almost always or always.	09	7.8	01	0.8	
09 – I thought my life had been a failure.	Few times.	13	11.4	18	15.6	0.001
	Sometimes.	14	12.2	15	13.1	
	Rarely or never.	84	73.0	78	67.8	
	Almost always or always.	04	3.4	4	3.5	

SOMATIC ASPECTS		V0	%	V14	%	P
03 – I feel that I could not get rid of the sadness even with the help of my family or friends.	Few times.	14	12.2	15	13.2	< 0.001
	Sometimes.	13	11.4	10	8.6	
	Rarely or never.	76	66.0	87	75.6	
	Almost always or always.	12	10.4	3	2.6	
20 – I feel discouraged.	Few times.	08	6.9	15	13.0	< 0.001
	Sometimes.	42	36.5	31	26.9	
	Rarely or never.	52	45.3	64	55.7	
	Almost always or always.	13	11.3	5	4.4	
VARIABLE		POPULATION				
SOMATIC ASPECTS		V0	%	V14	%	P
05 – I had trouble staying focused on what I was doing.	Few times.	18	15.7	11	9.5	0.792
	Sometimes.	28	24.3	21	18.3	
	Rarely or never.	59	51.3	76	66.1	
	Almost always or always.	10	8.7	7	6.1	
07 – I feel that everything I did was very costly.	Few times.	21	18.3	8	6.9	0.596
	Sometimes.	18	15.6	16	13.9	
	Rarely or never.	45	39.2	82	71.4	
	Almost always or always.	31	26.9	9	7.8	
01 – I got upset about things that normally didn't bother me.	Few times.	17	14.8	23	20.0	0.001
	Sometimes.	27	23.4	13	11.3	
	Rarely or never.	53	46.1	75	65.3	
	Almost always or always.	18	15.7	4	3.4	
SOMATIC ASPECTS		V0	%	V14	%	P
11 – My sleep was agitated.	Few times.	19	16.5	15	13.1	0.033
	Sometimes.	21	18.3	24	20.8	
	Rarely or never.	39	33.9	66	57.4	
	Almost always or always.	36	31.3	10	8.7	
02 – I didn't feel like eating; I had no appetite.	Few times.	24	20.8	17	14.7	0.009
	Sometimes.	23	20.0	20	17.4	
	Rarely or never.	33	28.7	71	61.7	
	Almost always or always.	35	30.5	7	6.2	
INTERPERSONAL PROBLEMS		V0	%	V14	%	P
19. I felt that people didn't like me.	Few times.	18	15.7	14	12.2	0.001
	Sometimes.	18	15.7	7	6.1	
	Rarely or never.	76	66.0	92	80.0	
	Almost always or always.	03	2.6	two	1.7	
15 – People were not friendly.	Few times.	19	16.5	11	9.6	0.013

Regarding the casuistry's score on the 20 scale questions in the initial phase of symptoms in patients with suspected febrile illness (Dengue/Zika/Chikungunya) (V0/V14), it

was evidenced that the most frequently achieved score was for the item “I felt hopeful about the future”, with the affirmative answer “Almost always or always” (86.9% in V0) and (93.0% in V14), referring to the subscale related to the positive aspects with $p < 0.001$, which presents significance in the analyzed result, followed by one of the items related to the subscale related to the negative aspects, “I thought that my life has been a failure”, with the affirmative answer “Rarely or never” (73% in V0) and (67.8% in V14) with $p = 0.0001$ (**Table 03**).

The score most frequently related to the somatic aspect was characterized by the item “I feel that I could not get rid of sadness even with the help of my family or friends”, with the affirmative answer “Rarely or Never” equivalent to (66% in V0) and 75.6% in V14) with significance of $p=0.001$ (**Table 03**).

Therefore, the study becomes validated in the somatic aspect of depression with the sub-item “I feel discouraged”, with p equivalent to the value 0.001 and the presence of depression is also highlighted in the sub-item “I got upset about things that I normally don’t think about”. upset”, with $p = 0.001$, as we used a cutoff value of 0.05 for the p -value, so we rejected the null hypothesis and concluded that there is a statistically significant difference between the sub-items (**Table 03**).

It is noteworthy that the presence of depression is reinforced in the negative aspect in the sub-item “I feel alone”, with p equivalent to 0.001 and “I thought that my life has been a failure”, with a significant p of 0.001 (**Table 03**).

Still in the interpersonal aspects in the sub-item “I felt that people don't like me” there is a significant difference between V0 and V14 of $p=0.001$, which reinforces the presence of worsening of the main depressive symptoms in V14, therefore, it is possible to relate to the dengue infectious process (**Table 03**).

DISCUSSION

The state of Mato Grosso do Sul, in recent decades, has been affected with great impact by the epidemics caused by Dengue, Zika and Chikungunya and the consequences in the aftermath of these febrile illnesses are related to the predominance of the viral type, in Dengue, for example, the DENV-2 and DENV-4 types and their sequelae, mainly in the cities of Campo Grande (MS) and Dourados (MS)^{01, 03}.

Following this context, Campo Grande (MS) and Dourados (MS) reported, from April 2018 to August 2019, a total of 10,762 cases of patients with Dengue or hemorrhagic fever related to sociodemographic indicators (**Table 01**)^{07, 12, 21}, such as age, sex, education and use of alcohol or illicit drugs, especially in cases of Zika and Chikungunya (**Table 02**),

whose frequency of alcohol use in the population was a total of 47.2% in accordance with published studies previously^{03, 06}.

The 115 patients included with dengue and 175 with Zika and Chikungunya, obtained serological confirmation by ELISA/NS1/qRT-PCR. When considering the general lethality rate in Mato Grosso do Sul, a constant equivalent to 1.4% is observed, considering only cases of hemorrhagic fever^{02, 04, 08}, the World Health Organization (WHO) maintains an acceptable lethality around 1.0%²⁸, that is, the cities of Campo Grande and Dourados in the state of Mato Grosso do Sul are 0.4 points higher than the index desired by the World Health Organization (WHO)²⁸.

The result of this study demonstrated that the mean prevalence was in the age range equivalent to 25 - 34 years old with a frequency equal to 28.6% (n=33 in agreement with the data found in the study by Santos et al. (2019), specifically for dengue, whose age group with the highest frequency of illness was in the range of 19 to 59 years old (**Table 01**).

In the confirmed cases of Zika and Chikungunya in this study, a higher frequency was observed in females with a total of 31 cases in the age group of 18 to 44 years and the highest risk for diagnosis of Zika and Chikungunya was found in females in the same age group and in the rainy season, similarly to the study by Rasmussen et al (2016), which increased mainly in the rainy summer season, due to the wide dissemination of the Aedes Aegypti mosquito and its great capacity as a transmitter of these febrile diseases.

In this case, Zika (ZIKV), it was possible to observe the lack of herd immunity in the population, since, given the non-exposure to the virus in a high form until the moment presented by Rasmussen et al (2016), therefore, one can say that in this study the high incidence of Zika, verified in the cities of Campo Grande (MS) and Dourados (MS) during the study period, occurred due to the lack of herd immunity (**Table 02**).

Furthermore, the distribution of cases related to sex and systemic arterial hypertension in this study are equivalent to the studies by Santos et al. (2019), making it possible to associate these results with the Brazilian sociocultural characteristics, mainly due to the fact that the female individual spends a long period of the day indoors or outside the home, and it can also be considered that the male gender presents a lower percentage in the search for the service compared to females and, probably because of this, there is a smaller amount of underreporting compared to males (**Table 01**).

This occurred in this study due to the fact that the city of Campo Grande (MS) and Dourados (MS) have a higher degree of urbanization and higher population density and these indicators are a risk factor for the occurrence of dengue, Zika and Chikungunya^{03, 06}. Most

of the population lives in urban areas, such as the cities of Campo Grande (MS) and Dourados (MS)^{04, 08, 09}, showing the vulnerability in areas with an environment conducive to the proliferation of *Aedes Aegypti*^{21, 27}.

As for education, it should be noted that in this study a correct record was made in the compulsory notification forms of Dengue cases in Mato Grosso do Sul, in which 46% had completed high school, differing from the study by Santos et al. (2019), with more than 50% of registered cases ignored or left blank at the time of notification^{20 - 27}.

Not recording sociodemographic data brings fragility to the public health system²², and it is possible to highlight when analyzing the studies in general that the participants who presented an average level of school knowledge differing from other studies that considered that the lower the educational level, the lower their knowledge about aspects related to dengue, which in turn increases the infection²³.

When addressing depression in febrile illnesses, the World Health Organization considers that traditional problems, and in cases related to infectious diseases, such as Dengue, Zika and Chikungunya and malnutrition^{13, 17}, are allocated among the main needs of the population and will certainly be replaced by diseases such as depression, as a result of the long post-febrile illness period^{24, 28}.

The World Health Organization (WHO)²⁸ considers the biomedical and social changes that justified the data shown in Table 01 and Table 02 mainly associated with the clinical signs of neuro-Dengue, Zika and Chikungunya and, generally, the development of depressive signs in the disease fever are related to immunological mechanisms activated in the excessive production of pro-inflammatory cytokines^{25 - 27}, which have the function of inducing organic depression in the viral infectious process seen in this study^{17, 18, 19}.

The process of diagnosing mental illnesses such as depression does not follow the logic and objectivity that other diagnoses have, therefore it becomes difficult and confusing, and develops according to the symptoms presented during the illness period^{24, 26, 28}.

Generally, depressive disorders will be influenced by the subjectivity of the examiner¹⁸. And the good health professional must know how to recognize, in the patient's speech, the signs of depression, as well as its symptoms, in order to then make the appropriate referral and even act preventively^{12, 16, 19}.

However, what actually happens is that depression is still underdiagnosed and undertreated in the state of Mato Grosso do Sul when related to infectious processes of febrile diseases such as Dengue, Zika and Chikungunya. And, this study is primary in the report

when evaluating the prevalence of depression in patients with Dengue when using a screening tool, in this case, CES-D used for standardized screening in structured interviews to collect information about the main signs and psychiatric manifestations of depression at the beginning of the infectious period.

The positive and somatic aspects among patients in V0 and V14 can be caused by the presence, mainly, of myalgia and arthralgia, which can be considered one of the triggers for the increase in the score of the depressive symptom^{14, 17, 18}.

These characteristics are predictors of an increase in the depressive symptoms score, mainly in V14 analyzed in this study^{19, 26}. In this study, it was reinforced that 50% of the patients developed fatigue mainly in the initial period (V0), experienced in the somatic aspects (**Table 03**) that aggravate the depressive signs and symptoms.

These manifestations occur because the infectious alterations are the result of the deposition of immunocomplexes, mainly in the acute phase in the central nervous system^{19, 23}, and thus, symptoms such as headache, convulsions with fever or delirium and insomnia accompanied by restlessness and irritability followed by other sensory depressive signs with behavioral disorders will be accentuated²⁵, however, the clinical manifestations occurred in this study in a higher percentage in the chronic period in the initial acute phase of the illness period (**Table 02**). These symptoms are usually associated with thrombocytopenia or disseminated coagulopathy, and this occurs as a consequence of immunological reactions of the viral infection in Dengue, generally associated with perivascular inflammation^{17, 26}.

These patients or participants will develop cerebral edema with vascular congestion that causes focal hemorrhages due to perivascular lymphocytic infiltrates, as they cause several foci of perivenous demyelination with formation of immune complexes during the infectious period^{21 - 26}.

In this pioneering study on the presence of depression in patients with febrile illnesses using the CES-D instrument²⁴, it was possible to verify a variety of likely contexts for the development of depression in the participant, mainly cultural, since the CES-D through solutions factorials adjusted for sociodemographic aspects is capable of identifying the presence of depression in a simple way and at no high cost^{24 -28}.

Therefore, it is important to develop therapeutic strategies used in the treatment of depression for patients with dengue, Zika and Chikungunya, this includes enabling health

professionals to identify the development of depression in the illness process, the use of antidepressants and rapid cognitive therapy, with the purpose of reducing the psychic suffering of this patient and, thus, bringing a better quality of life for this individual.

Thus, further studies should be carried out in order to assess the presence of depression in patients with Dengue with greater precision in biochemistry and histology.

CONCLUSION

Febrile illnesses in the State of Mato Grosso do Sul continue to be an important problem, due to their high incidence, mainly with the development of evolution to deaths and this high percentage of lethality (1.4%) has great repercussions on public health in the state. In this study, there was a prevalence of depressive disorder in patients followed up from 2018 to 2019. However, more longitudinal studies are needed to corroborate this hypothesis.

Consent

As per international standard or university standard, patient (s) written consent has been collected and preserved by the author(s).

Ethical Approval

The study was approved by the ethics committee of the Federal University of Mato Grosso do Sul with opinion CAEE - 71611417.9.2005.0021, included in the multicenter study called “Traditional study for identification, characterization and validation of diagnostic tests and severity markers in febrile illnesses”.

REFERENCES

1. Almeida CP, Silva RM. Analysis of the occurrence of dengue cases and their relationship with socio-environmental conditions in urban spaces: the cases of João Pessoa, Cabedelo and Bayeux, in the state of Paraíba - Brazil. *Hygeia*, 2018, 14, 26:56-79. <https://doi.org/10.14393/Hygeia142705>. Available at: <https://seer.ufu.br/index.php/hygeia/article/view/38370>
2. Andries AC, et al. Evaluation of the performances of six commercial kits designed for dengue NS1 and anti-dengue IgM, IgG and IgA detection in urine and saliva clinical specimens. *BMC Infectious Diseases*, 2016, 16, 16:1-9. DOI 10.1186/s12879-016-1551-x. Available at: <https://pubmed.ncbi.nlm.nih.gov/27184801/>

3. BachXT , et AL . Cost-of-Illness and the Health-Related Quality of Life of Patients in the Dengue Fever Outbreak in Hanoi in 2017. *Int. J. Environ. Res. Public Health*, 2018, 15:1174. Available at: <https://pubmed.ncbi.nlm.nih.gov/29874790/>
4. BRAZIL. Ministry of Health. Health Surveillance Secretariat. Epidemiological Bulletin – Monitoring of cases of dengue fever, chikungunya fever and Zika virus fever until Epidemiological Week 16. Brasília, DF: Ministry of Health, 2016. Available at: <https://www.saude.gov.br/images/pdf/2016/december/20/2016-033---Dengue-SE49-publicacao.pdf>
5. BRAZIL. Ministry of Health. Secretary of Health Surveillance. Epidemiological Bulletin n. 18 . Ministry of Health, Brasilia, DF, v. 51, no. 18, Apr. 2020a. Available at: <https://www.saude.gov.br/images/pdf/2020/May/04/Boletim-epidemiologico-SVS-18.pdf>
6. Aguiar S, Lorenz C, Virginio F, Suesdek L, Chiaravalloti NF. Potential Risks of Zika and Chikungunya Outbreaks in Brazil: a Modeling Study. *Int J Infect Dis*. 2018;(18):342-3.
7. Rajendra SJ, Pankaj KG, Rakesh A , Sunil K, Kapil K. An unusual case of dengue infection presenting with hypokalemic paralysis with hypomagnesemia, *Journal of Clinical Virology*, 2015, 69:197-199, ISSN 1386-6532, <https://doi.org/10.1016/j.jcv.2015.06.098> (<https://www.sciencedirect.com/science/article/pii/S1386653215002838>)
8. BRAZIL. Ministry of Health. Health Surveillance Secretariat . Monitoring of cases of dengue fever, chikungunya fever and acute Zika virus disease until Epidemiological Week 23 of 2018. *Epidemiological Bulletin* , v. 49 , Jun. , 2018. Available at: <https://www.saude.gov.br/images/pdf/2018/novembro/23/Publicacao-2018-57-SE44.pdf> .
9. Khetarpal N, Khanna I. Dengue Fever: Causes, Complications, and Vaccine Strategies. *J Immunol Res*. 2016; 2016:6803098. doi: 10.1155/2016/6803098. Epub 2016 Jul 20. PMID: 27525287; PMCID: PMC4971387. Available at: <https://pubmed.ncbi.nlm.nih.gov/27525287/>
10. Carneiro, MAF, et al. Environmental factors can influence dengue reported cases. *Rev. Assoc. Med. Bras*. 2017, 63, (11): 957-961. Available at: https://www.scielo.br/scielo.php?pid=S010442302017001100957&script=sci_abstract&lng=en .
11. Dalgallarrondo D P. *Psychopathology and semiology of mental disorders* . 2nd ed. Porto Alegre: Artmed. 2008.
12. , Eleomar VM , *et al*. Implications of the clinical gestational diagnosis of ZIKV infection in the manifestation of symptoms of postpartum depression: a case-control study. *BMC Psychiatry* , v. 19 , no. 199 , June, 2019. doi: <https://doi.org/10.1186/s12888-019-2157-9> .
13. Moraes EV, Toledo OR, David FL, Godoi BN, Monteiro KA, Deluqui TC, Teixeira TW, Carvalho AL, Avelino MM. Implications of the clinical gestational diagnosis of ZIKV infection in the manifestation of symptoms of postpartum depression: a case-control study. *BMC Psychiatry*. 2019 Jun 26;19(1):199. doi: 10.1186/s12888-019-2157-9. PMID: 31242891; PMCID: PMC6595702. Available at: <https://pubmed.ncbi.nlm.nih.gov/31242891/>

14. Fleck MPA. et al. Guidelines of the Brazilian Medical Association for the treatment of depression (full version). Rev Bras Psiquiatr. 2003, 25 (2): 114-122. Available at: <https://www.scielo.br/pdf/rbp/v25n2/v25n02a13.pdf>.
15. Gunathilaka N, Chandradasa M, Champika L, Siriwardana S, Wijesooriya L. Delayed anxiety and depressive morbidity among dengue patients in a multi-ethnic urban setting: first report from Sri Lanka. Int J Ment Health Syst. 2018 May 2;12:20. doi: 10.1186/s13033-018-0202-6. PMID: 29743940; PMCID: PMC5930431. Available at: <https://pubmed.ncbi.nlm.nih.gov/29743940/>
16. Gunathillaka K , Chandradasa M, Champika L, Mendis J. Association of duration of untreated psychosis and functional level, in first episode of schizophrenia attending an outpatient clinic in Sri Lanka. J . Postgrad Inst . Med. 2016, 3(E33): 1–6 , Dec. Available at: <https://jpgim.sljol.info/articles/abstract/10.4038/jpgim.8112/>.
17. Maes M. Inflammatory and oxidative and nitrosative stress cascades as new drug targets in myalgic encephalomyelitis and chronic fatigue syndrome. Mod Trends Pharmacopsychiatry. 2013; 28 :162-74. doi: 10.1159/000343982. Epub 2013 Feb 27. PMID: 25224898. Available at: <https://pubmed.ncbi.nlm.nih.gov/25224898/>
18. Malta DC, et al . Depression and health behaviors in Brazilian adults – PNS 2013. Rev. Public Health, São Paulo, 2017, 51 (supl.1): 1-8, jun. Available at: https://www.scielo.br/pdf/rsp/v51s1/pt_0034-8910-rsp-S1518-87872017051000084.pdf.
19. Araújo VEV de, et al. Increased dengue burden in Brazil and federated units, 2000 and 2015: analysis of the Global Burden of Disease Study 2015. Revista Brasileira de Epidemiologia [online]. 2017, v. 20, no. Suppl 01 [Accessed 25 February 2022], pp. 205-216. ISSN 1980-5497. Available at: <https://doi.org/10.1590/1980-5497201700050017>
20. MATO GROSSO DO SUL. Secretary of State for Health. Health Surveillance. Dengue Epidemiological Bulletin 2020 : Epidemiological Week 35. Campo Grande, MS: SES, 2019. Available at: <https://www.vs.saude.ms.gov.br/wp-content/uploads/2020/09/Boletim-Epidemiologico-Dengue-SE-35.pdf>.
21. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika Virus and Birth Defects--Reviewing the Evidence for Causality. N Engl J Med. 2016 May 19;374(20):1981-7. doi: 10.1056/NEJMsrl604338. Epub 2016 Apr 13. PMID: 27074377. Available at: <https://pubmed.ncbi.nlm.nih.gov/27074377/>
22. Santos LKF, et al. Epidemiological profile of dengue in a northeastern Brazilian state, 2011 to 2015 . Revista Eletrônica Acervo Saúde , 2019, 11 (10) , e423 : 1-10, May. Available at: https://www.researchgate.net/publication/333196330_Perfil_epidemiologico_da_dengue_em_um_estado_do_nordeste_brasileiro_2011_a_2015
23. Batistoni SST, Neri AL Cupertino APFB Validity of the Center for Epidemiological Studies depression scale among elderly Brazilians. Revista De Saúde Pública, 41 (Rev. Saúde Pública, 2007, 41(4)). <https://doi.org/10.1590/S0034-89102007000400014> . Available at: <https://www.scielo.br/j/rsp/a/dZRPJGB5R8497638MykwBGp/#>

24. Terra MR, Da Silva RS, Pereira MGN, Lima AF. Aedes Aegypti and emerging arboviroses in Brazil. *Uningá Review*, 2017, 30(3). Retrieved from <https://revista.uninga.br/uningareviews/article/view/2028>
25. Vidal ECF, et al. Characterization of Temporal Trends of Dengue Fever in Municipalities in the Brazilian Northeast Outback. *International Archives of Medicine*. 2015, 8 (113): 1-10.
26. Herbuela VRDM, de Guzman FS, Sobrepeña GD, Claudio ABF, Tomas ACV, Arriola-Delos Reyes CM, Regalado RA, Teodoro MM, Watanabe K. Depressive and Anxiety Symptoms among Pediatric In-Patients with Dengue Fever: A Case-Control Study. *Int J Environ Res Public Health*. 2019 Dec 21;17(1):99. doi: 10.3390/ijerph17010099. PMID: 31877808; PMCID: PMC6981716. Available at: <https://pubmed.ncbi.nlm.nih.gov/31877808/>
27. WORLD HEALTH ORGANIZATION. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. New Edition 2009. Available at: <http://www.who.int/tdr/publications/documents/dengue-diagnosis.pdf>
28. Salles, TS, da Encarnação Sá-Guimarães, T., de Alvarenga, ESL et al. History, epidemiology and diagnostics of dengue in the American and Brazilian contexts: a review. *vector parasites* 11 , 264 (2018). <https://doi.org/10.1186/s13071-018-2830-8> . Available at: <https://parasitesandvectors.biomedcentral.com/articles/10.1186/s13071-018-2830-8>
29. Vega FLR, Bezerra JMT, Said RF de C, Gama Neto AN da, Côtrim EC, Mendez D, et al. Emergence of chikungunya and Zika in a municipality endemic to dengue, Santa Luzia, MG, Brazil, 2015-2017. *Rev Soc Bras Med Trop* [Internet]. 2019;52(Rev. Soc. Bras. Med. Trop., 2019 52). Available from: <https://doi.org/10.1590/0037-8682-0347-2018>

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